भारतीय रासायनिक जीवविज्ञान संस्थान
INDIAN INSTITUTE OF CHEMICAL BIOLOGY

आई आई सी बी
IICB
वार्षिक प्रतिवेदन
Annual Report
2007-2008

भारतीय रासायनिक जीवविज्ञान संस्थान
Indian Institute of Chemical Biology

(सी. एस. आई. आर. का एक प्रतिष्ठान)
(A Unit of Council of Scientific & Industrial Research)

4, राजा एस. सी. मल्लिक रोड, यादवपुर, कोलकाता - 700 032, भारत
4, Raja S. C. Mullick Road, Kolkata - 700 032, India

आई आई सी बी में, सी एस आई आर के महानिर्देशक के रूप में, प्रोफ. एस के ब्रह्मचारी द्वारा प्रथम अभिभाषण

संरक्षक की ओर से

प्रत्येक वर्ष संस्थान सम्पूर्ण विश्व के बन्धु- हितैषी एवं वैज्ञानिक समुदाय की जानकारी के लिए अपने अनुसंधान कार्य का संक्षिप्त विवरण विशेष रूप से, प्रकाशित कार्य एवं पेटेन्ट पर आधारित वार्षिक कार्यक्रम का प्रकाशन करता है। एक बार फिर अप्रैल 2007 से मार्च 2008 की अवधि का वार्षिक प्रतिवेदन प्रस्तुत करते हुए मुझे हर्ष हो रहा है। वैज्ञानिक सहयोग के अतिरिक्त इस रिपोर्ट (प्रतिवेदन)में अंतः संरचना, बाहरी रोकड़ (वाह्य वित्तीय सहयोग) बौद्धिक संपदा तथा वैज्ञानिक व्यवस्था एवं प्रशासन संबधी विभिन्न दृष्टिकोण की आलोचनात्मक सूचना सम्मिलित है।

अनुसंधान संस्थाओं की प्रगति अनिवार्यतः आर एण्ड डी -एवं आईआईसीबी की गतिविधियों पर आधारित है जो इसके आरंभिक वर्षों से उत्तम विज्ञान के माध्यम से निरंतर विकास के क्रम में है। हमने भारतीय देशज पौधों एवं प्राकृतिक संसाधनों के माध्यम से औषध विकसित करने की प्रक्रिया पर भरपूर ध्यान केन्द्रित किया है। रसायन विभाग ने बायोऐक्टिव अणुओं के माध्यम से औषधीय पौधों की प्रतिलिशमेनिया, प्रतिबैक्टिरियल, प्रतिफंगल कैन्सररोधी, प्रतिवायरल सक्रियता को प्रस्तुत कर एक बड़ी सफलता हासिल की है। प्रोसटेलीन, प्रोस्टेट रोग के उपचार के लिए बाजार में लंच किया गया है जिसका तकनीकी विकास इस विभाग के वैज्ञानिकों द्वारा किया गया है। आणविक एवं मानव जेनेटिक्स (मानव आनुवंशिकी) विभाग ने एक तकनीक विकसित किया है, जिससे प्रोटीन कोडिंग आरएनए की रचना एवं पद्धति से माइटोकान्ड्रियल दुष्क्रिया को ठीक किया जा सके। यह विभाग मस्तिष्क एवं गर्दन कैंसर (एचएनएससीसी), हीमोफिलिया, ग्लूकोमा एवं विल्सन रोग आदि का आणविक आधार पर व्याख्या करने में कार्यरत है एवं विब्रियो कालेरी जीनों के अन्य पहलू एवं रोगजनन में उसकी भूमिका के संदर्भ में अध्ययनरत है।

संक्रामक रोग एव प्रतिरक्षा विभाग लीशमेनिया एवं हैजा के कुछ वर्गीकृत क्षेत्र के अनुसंधान में कार्यरत हैं। यह विभाग प्रति लीशमेनिया एवं कैंसर रोधी क्रियाकलाप से युक्त लीशमेनिया एवं सूत्रबद्ध औषध के विरूद्ध एंटीजेन एवं डीएनए वैक्सीन (टीका) का विकास करने में सफलता अर्जित कर लिया है। ए.एल.एल के निदान हेतु दी गई हैं। इसकी तकनीक उद्योग जगत को हस्तांतरित कर दिया गया है। कोश जैव वैज्ञानिक एवं शरीर वैज्ञानिक पैथोफीजियोलाजी रूप में (व्याधि शरीर विज्ञान) एवं कुछ मेटाबोलिक एवं डीजेनेरेटीय रोगों के क्रिया प्रणाली को समझने में कार्यरत है। इस विभाग के वैज्ञानिकों ने मनुष्य में एच आई भी के संक्रमण से बचने के लिए माइक्रोबाईसाइड के साथ एक गर्भनिरोधक का विकास किया है। औषध विकास, निदान सूचक एवं जैवतकनीकी विभाग ने वानस्पतिक पौधों एवं विष से एक नए उत्पाद को विकसित करने में अनुसंधानरत हैं जिसका वाणिज्यिक एवं औद्योगिक महत्व के साथ चिकित्सीय प्रभावी भूमिका अनिवार्यता के साथ ट्यूबरक्लोसिस लीशमेनिया, हैजा, कैंसर, डायबीटिज आदि रोगों में सिद्ध हो सके।

ग्यारहवीं पंच वर्षीय योजना में आईआईसीबी ने 3 विभिन्न क्षेत्रों में अपना नेटवर्क प्रस्तावित किया है। (I) जीवविज्ञान एवं जैवतकनीकी (II) फार्मास्यूटिकल स्वास्थ्य रक्षा एवं औषधि (III) परिस्थिति विज्ञान एवं पर्यावरण। 15 परियोजनाएँ आईआईसीबी को प्रदान की गयी हैं। जिसके अंतर्गत 4 नोडल नेटवर्क परियोजनाएं तथा 11 पार्टनर नेटवर्क परियोजानाएं हैं। पार्टनर नेटर्वक परियोजानाओं के अन्तर्गत दसवीं प्लान में दो विस्तारित परियोजनाएं हैं। सभी परियोजनाएं मुख्यता जीवविज्ञान एवं जैव तकनीक क्षेत्र की हैं जबकि नोडल नेटर्वक परियोजना फार्मास्यूटिकल, स्वास्थ्य रक्षा एवं औषध विभाग से सम्बद्ध है।

संस्थान के अनुसंधान के विकास में उच्चकोटि के प्रकाशन की निरंतर वृद्धि एवं उच्चतम प्रभावी पत्रिका के प्रकाशन की निरंतरता एक महत्वपूर्ण उपलब्धि है। मुझे इस बात की प्रसन्नता हो रही है कि आईआईसीबी का औसत प्रभावी प्रकाशन इस वर्ष 3.1 से भी अधिक है।

रिपोर्ट अवधि के दौरान आई.आई.सी.बी. ने संश्लेषण, निदान, वैक्सीन, जड़ी-बूटी से पायी गई जैवसक्रीय मिश्रण जैसे 13 राष्ट्रीय एवं अन्तराष्ट्रीय पेटेन्ट को दर्ज किया है जिसके माध्यम से कालाजार, प्रोस्टेट कैंसर, ब्लड कैंसर, डायबीटिज, और अन्य रोगों से मानव को निजात दिलाने में सहायक होंगे। इस अवधि के दौरान कुल 7 पेटेन्ट स्वीकृत किए गए है जिसमे से 6 पेटेन्ट को विदेश द्वारा स्वीकृति मिली है।

आई.आई.सी.बी ने हमेशा होनहार वैज्ञानिकों को जैविक एवं रासायनिक क्षेत्र में काम करने के लिए प्रोत्साहित किया है। संस्थान इस वर्ष सम्पूर्ण भारतवर्ष से होनहार युवा शोध कर्ताओं एवं अनुसंधान सहायकों को आकृष्ट करने में सफल रहा है जिससे जीव विज्ञान एवं रसायन विज्ञान के विभिन्न क्षेत्रों एवं अन्य संबंधित क्षेत्र में पर्याप्त प्रशिक्षित मानवीय संसाधन उत्पन्न किया जा सके जिससे अनुसंधान की सही दिशा में विकास हो सके। वर्ष 2007- 08 के दौरान 200 अनुसंधानकर्ता एवं अनुसंधान सहायकों ने संस्थान में मूलभूत एवं व्यावहारिक अनुसंधान के क्षेत्र में कार्य करते हुए श्रेष्ठता हासिल की है। एक बड़ी सख्था में देश-विदेश के सुप्रसिद्ध वैज्ञानिकों ने आकर आईआईसीबी में अनुसंधानरत अनुसंधानकर्ताओं के बीच अपना व्याख्यान प्रस्तुत किया है एवं विभिन्न चर्चा-परिचर्चाओं में भाग लिया है। भारत के विभिन्न विश्वविद्यालयों एवं संस्थानों से लगभग 105 विद्यार्थियों ने यहाँ ग्रीष्म प्रशिक्षण एवं अन्य प्रशिक्षण हासिल किया है। एक बड़ी संख्या में वैज्ञानिकों प्रतिवेशी विश्वविद्यालयों एवं संस्थानों में अध्यापन तथा प्रशिक्षण कार्यक्रम में भागीदारी बनी रही । विभिन्न वैज्ञानिक संगोष्ठयों के अतिरिक्त संस्थान में 'संस्थान स्थापना दिवस' एवं 'सीएसआईआर स्थापना दिवस' को मनाया गया।

मैं संस्थान के सभी वैज्ञानिक तकनीकी एवं प्रशासनिक कर्मचारियों को आई.आई.सी.बी की ख्याति तथा विकास के अनुरक्षण हेतु उनकी लम्बी निष्ठावान क्रिया कलाप एवं सहयोगिता के लिए अपना हार्दिक आभार प्रकट करना चाहता हूँ । मुझे विश्वास है कि मेरे सहयोगियों की निष्ठा संस्थान को आने वाले दिनों में नई ऊँचाई पर ले जाएगी।

प्रो० सिद्धार्थ राय
आई.आई.सी.बी.कोलकाता

उपलब्धियों की एक झलक

सम्मान

- प्रों सिद्धार्थ राय को डी बी टी, भारत सरकार द्वारा "टाटा इननोभेंसन एर्वाड" से पुरस्कृत किया गया है।
- डॉ. हेमन्त कुमार मजुमदार को नेशनल एकाडमी ऑफ साइन्स, इलाहाबाद वर्ष 2008-2010 के लिए "कोलकाता चेप्टर के अध्यक्ष" के रूप में नामांकित किया गया हैं।
- डॉ. पिजुस कुमार दास ने भारतीय प्रतिरक्षाविज्ञान समाज के "वरिष्ठ वैज्ञानिक व्याख्यान पुरस्कार" प्राप्त किया।
- डॉ. जे. आर. वेदाशिरोमणी को भारतीय औषधविज्ञान के "कर्नल आर.एन.चोपड़ा व्याख्यान पुरस्कार" से पुरस्कृत किया गया था।
- डॉ. स्नेहासिकता स्वर्णकार ने डी बी टी, भारत सरकार द्वारा "कैरियर विकास के लिए राष्ट्रीय जैवविज्ञान पुरस्कार" प्राप्त किया।
- डॉ. शिव शंकर राय ने सी एस आई आर के "रमण अनुसंधान मैत्रीभाव" प्राप्त किया।

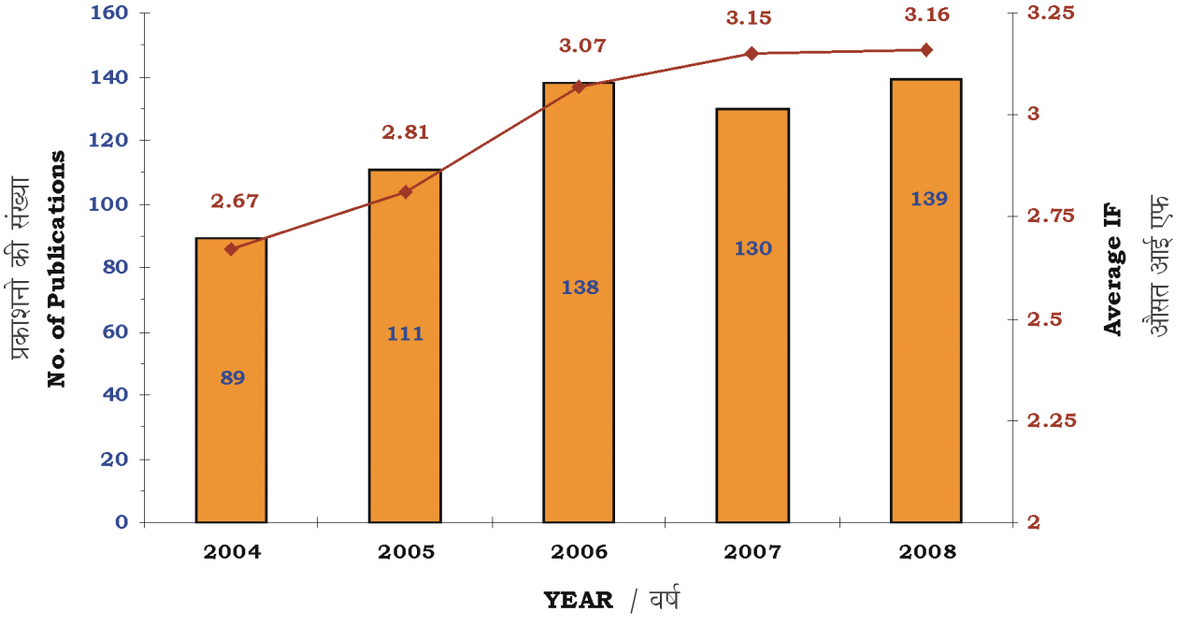
उपलब्धियों की एक झलक

प्रकाशन

संस्थान के अनुसंधान की प्रगति के लिए उच्चकोटि का प्रकाशन एक श्रेष्ठसूचक चिह्न हैं। वार्षिक प्रकाशन तथा पिछले पांच वर्ष तक का औसत प्रभावी कारक (आईएफ) निम्नलिखित हैं।

आईआईसीबी प्रकाशन

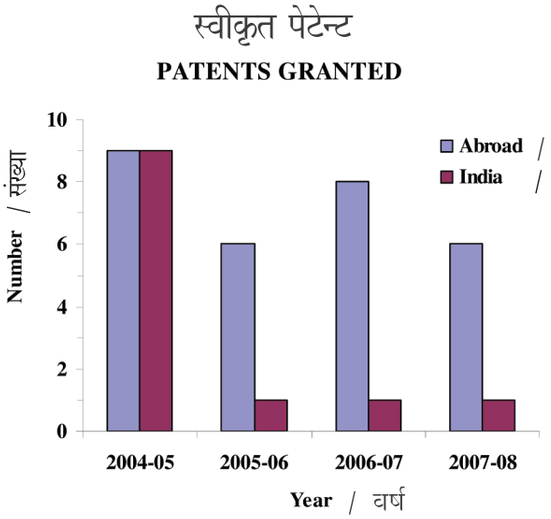
IICB PUBLICATION

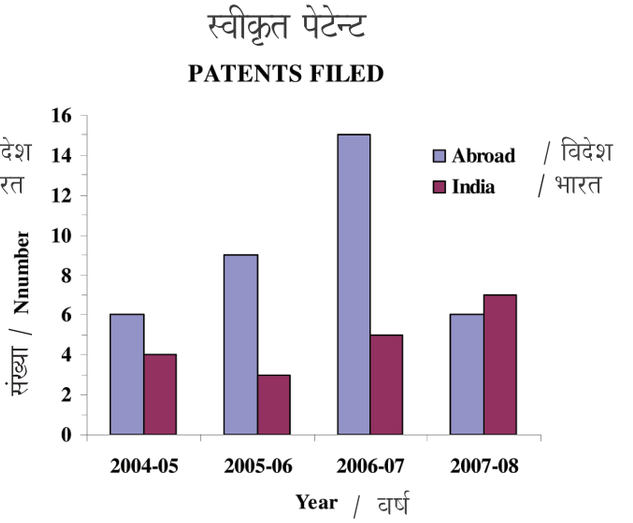


2007-08 के लिए प्रकाशनों की विस्तृत सूची अन्दर अलग दिया गया हैं।

उपलब्धियों की एक झलक / पेटेन्ट्स

संस्थान में प्रत्येक वर्ष स्थायी रूप से कई पेटेन्ट का पंजीकरण एवं स्वीकृति।





वर्ष 2007-08 में पंजीकृत एवं स्वीकृत पेटेन्ट की सूची संस्थान के प्रकाशन एवं सूचना विभाग के रिपोर्ट में दर्ज है।

उपलब्धियों की एक झलक

उद्योग -संस्थान का गठजोड़।

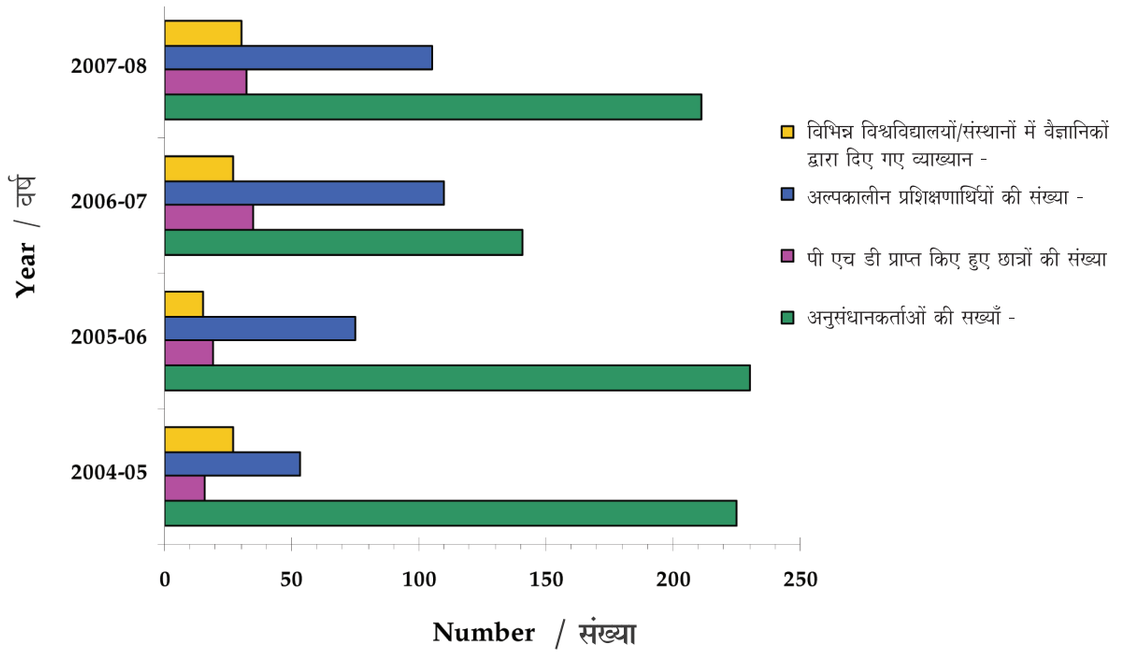
संस्थान, उद्योग के साथ निरंतर एकीकरण बनाए रखा हैं एवं सफलतापूर्वक ज्ञान को धन में परिवर्तित कर रहा हैं। इस वर्ष आईआईसीबी के वैज्ञानिकों ने उद्योग के साथ पारस्परिक संबंध को बनाए रखने में एवं पर्याप्त मानवीय एवं वित्तीय संसाधन जुटाने में अपने को सक्षम बनाए रखा। गेट (GATT) - भारत व्यवस्था के साथ सम्पूर्ण विकास के लिए हमारे सहयोगी इस प्रकार हैं -

- मेरियल एस ए एस, लिन, फ्रांस।
- एनर्जीओजेन फार्मास्यूटिकलस, ओस्ट्रेलिया।
- क्वायर बोर्ड कोची।
- एलबर्ट डेविस लिमिटेड, कोलकाता।
- चटर्जी मनेजमेन्ट सर्वीसेस प्राइवेट लिमिटेड, कोलकाता।
- पीरामल लाइफ सर्वीसेस लिमिटेड, मुंबई।
- दे मेडिकल स्टोर्स (मैनुफैक्चरिंग) लिमिटेड, कोलकाता।
- डीएनडीआई, फ्रांस।
- ईस्ट इंडिया फार्मास्यूटिकल्स वर्क्स लिमिटेड, कोलकाता।
- केमबायोटेक रिसर्च इन्टरनेशनल प्राइवेट लिमिटेड, कोलकाता।
- क्वालप्रो डायग्नोस्टिक्स, गोवा।
- शान्ता बायोटेकनिक्स लिमिटेड, हैदराबाद।
- जेफर बायोमेडिकल्स, गोवा।
- बायोटेक कानसोरटीयम (आई) लिमिटेड, नई दिल्ली।

उपलब्धियों की एक झलक

मानव संसाधन विकास

हर वर्ष कई अनुसंधानकर्ता डॉक्टरेट एवं पोस्टडॉक्टेरेट स्तर पर अपना अनुसंधान जारी रखते हैं। देश के विभिन्न विश्वविद्यालयों से अनेक विद्यार्थी यहाँ हर वर्ष अल्पकालीन प्रशिक्षण प्राप्त करते हैं। चालू वर्ष का आँकड़ा इस प्रकार है।



मुख्य विवरण

2 अप्रैल, 2007- आई आई सी बी स्थापना दिवस का समारोह का आयोजन । भारतीय सांख्यिकी संस्थान कोलकाता के निदेशक प्रो.एस.के.पाल मुख्य अतिथि के रूप में विराजमान थे। एल. आई. सी. आर / डब्ल्यू. इ. एइच. आई आस्ट्रेलिया के प्रो. आर.जे.सिम्पसन ने जे.सी. राय मेमोरियल व्याख्यान प्रस्तुत किया। आईआईसीबी के वैज्ञानिक डॉ. उदय बंदोपाध्याय द्वारा 'मलेरिया एक बुद्धिजीवी परजीवी' लोकप्रिय व्याख्यान प्रस्तुत किया गया।

16 मई 2007 - आई. आई. सी. बी परिसर में केवी वाई पी कार्यक्रम आयोजित किया गया। भारत वर्ष के विभिन्न क्षेत्रों से लगभग **46** छात्रों ने इस कार्यक्रम में हिस्सा लिया । आईआईसीबी के निदेशक प्रो. सिद्धार्थ राय ने 'जीन एवं उसके विकास' विषय पर एक लोकप्रिय व्याख्यान दिया। डॉ.एच के मजुमदार वैज्ञानिक, निदेशक ग्रेड ने 'डीएनए टोपोएसोरोमेरासेस छुपा हुआ खजाना' पर अपना व्याख्यान प्रस्तुत किया ।

15 अगस्त 2007 - स्वाधीनता दिवस समारोह का आयोजन किया गया।

14 सितंबर 2007 - हिंदी दिवस समारोह का आयोजन किया गया। मुख्य अतिथि के रूप में हिंदी शिक्षण योजना, भारत सरकार, कोलकाता पूर्व के उपनिदेशक श्री.एस.एल.एस पुर्ती उपस्थित थे।

26 सितंबर 2007 - सीएसआईआर स्थापना दिवस समारोह मनाया गया। आईआईसीबी के निदेशक प्रो.सिद्धार्थ राय ने स्वागत भाषण दिया। बोस इंस्टीट्यूट कोलकाता के पूर्व निदेशक प्रो.बी.बी.विश्वास ने उद्घाटन भाषण दिया। एन.सी.सी. एन पूणे के निदेशक डॉ.जी.सी.मिश्रा ने डांसिंग द इम्युनोलोजिकल टू स्टेप साइनेप्स- आरचेस्टेटस द म्यूजिक - द एंटीजेन आफ द कास्टीनुलेशन, पर अपना व्याख्यान प्रस्तुत किया।

5 नवम्बर 2007 - राष्ट्रीय फार्मास्यूटिकल शिक्षण एवं अनुसंधान संस्थान (एन आई पी .आइ.आर) कोलकाता का उद्घाटन समारोह का आयोजन किया गया।

28 एवं 29 दिसंबर 2007- सी एस आईआर का कार्यक्रम- विज्ञान में युवा नेतृत्व (सीपीवाईएलएस-2007) का आयोजन। पश्चिम बंगाल प्रौद्योगिकी विश्वविद्यालय के उप कुलपति प्रो.अशोक रंजन ठाकुर मुख्य अतिथि के रूप में विराजमान थे। आईआईसीबी के वैज्ञानिक डॉ.एच.के.मजुमदार, निदेशक ग्रेड वैज्ञानिक ने स्वागत भाषण दिया एवं डॉ. कुणाल राय ने लोकप्रिय व्याख्यान प्रस्तुत किया।

28 फरवरी 2008 - राष्ट्रीय विज्ञान दिवस समारोह। प्रो. जान गैस्टेगर, एरलान्जेन विश्वविद्यालय, न्यूरेमवर्ग,जर्मनी द्वारा 'केमीइन्फॉमोटिक्स इन ड्रग डिजाइन', विषय पर वैज्ञानिक व्याख्यान प्रस्तुत किया गया।

CONTENTS

From Director's Desk

Every year the Institute publishes its Annual Report to disseminate a brief account of our research activities particularly based on published works and patents to our friends, well wishers and scientific communities across the globe. It's my pleasure once again to present the Annual Report of this Institute for the period from April 2007 to March 2008. Apart from the scientific contributions, this report also includes critical information about our infrastructure, extramural funding, intellectual property and other various aspects of scientific management and administration.

The progress of a research institution essentially depends on its R&D activities and IICB, like preceding years, continued its growth through quality science. We have offered substantial attention in developing drug from our indigenous and natural resources like native Indian plants. The chemistry division has been able to achieve major success by isolating bioactive molecules having potential antileishmanial, antibacterial, antifungal, anticancer and antiviral activities from medicinal plants. Prostalyn, a drug for the treatment of prostate diseases has been launched in market by industry, the technology of which is developed by the scientists of this division. The molecular and human genetics division has developed a technology regarding compositions and methods for delivery of Protein-coding RNAs to correct mitochondrial dysfunction. This division is also engaged to interpret molecular basis of head and neck cancer (HNSCC), Haemophilia, Glaucoma, Wilson disease etc and studying various aspects of Vibrio cholerae genes and their role in pathogenesis. The infectious disease and immunology division is involved in research on assorted fields of Leishmaniasis and Cholera. This division has been able to develop antigen and DNA Vaccines against Leishmaniasis and formulated drugs having anti-leishmaniasis and anti cancer activities. A technology regarding diagnosis of ALL has been transferred to industry. The cell biologists and physiologists are engaged in understanding physiology, pathophysiology and mechanism of certain metabolic and degenerative diseases. The scientists of this division have developed a contraceptive with microbicide for preventing HIV transmission in human. The drug development, diagnostics & biotechnology division is involved in research to promote development of new products, processes and technologies of commercial and industrial importance from plants and venoms whereas the structural biology & bio-informatics division is accomplishing research on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases like tuberculosis, leishmaniasis, cholera, cancer, diabetes etc.

In Eleventh Five Year Plan, IICB proposed network projects in 3 different sectors e.g. (i) Biology & Biotechnology, (ii) Pharmaceuticals, Healthcare & Drugs and (iii) Ecology & Environment. 15 projects have been granted to IICB of which 4 are Nodal Network Projects and 11 are Partner Network Projects. In Partner Network Projects there are two extension Projects of Tenth Plan. All the projects are mainly from Biology & Biotechnology sector except one nodal network project which is from Pharmaceuticals, Healthcare & Drugs sector.

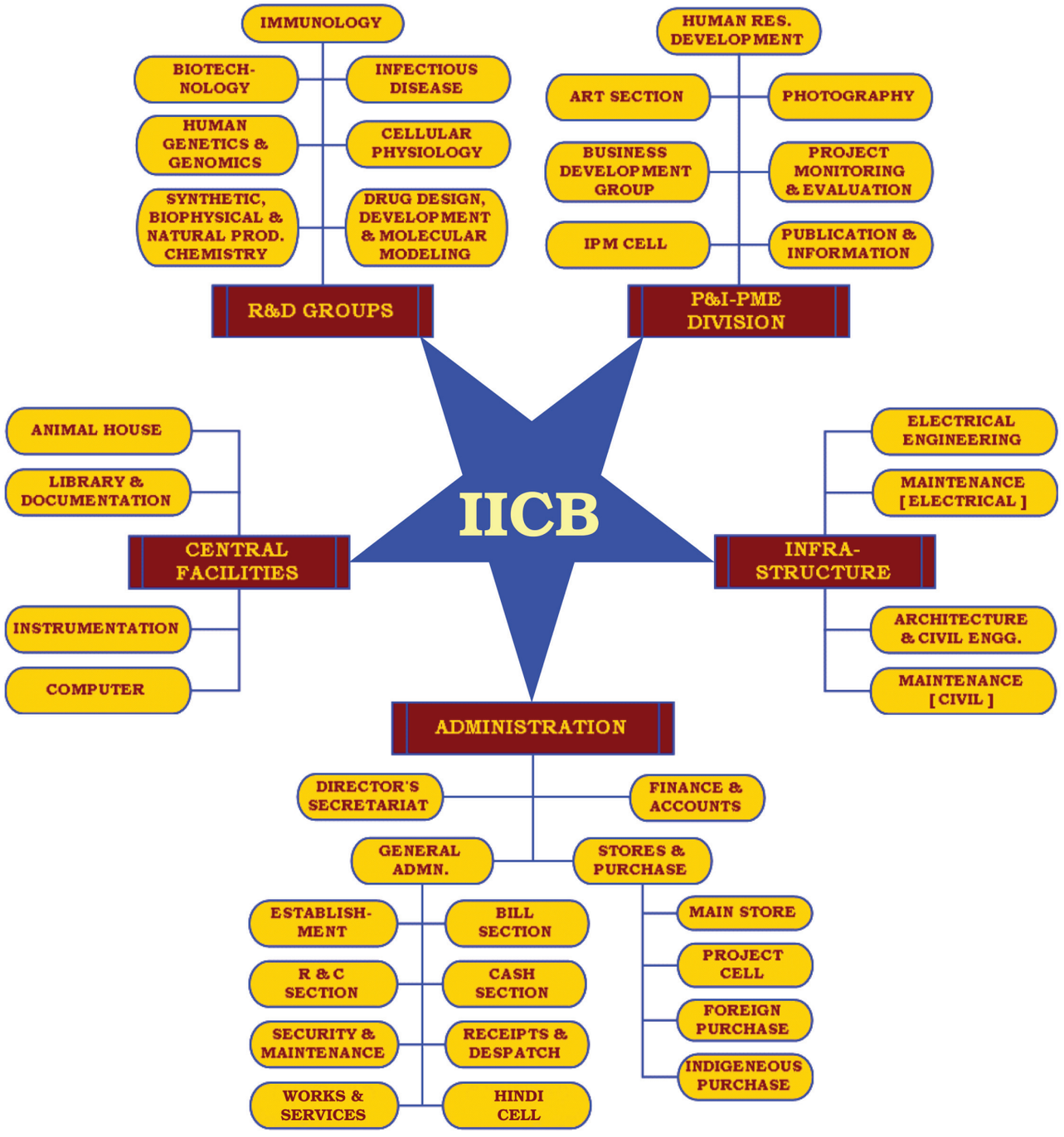
A steady number of quality publications in high to very high impact journals are the hallmark of the Institute's progress in research and the average impact factor of publications is increasing continuously. I am proud in finding that the average impact factor of publications of IICB is more than 3.1 this year.

During the reporting period IICB has filed thirteen national and international patents related to synthesis, diagnosis, vaccination, extraction of bioactive compounds from herbal resources to combat against kala azar, prostate cancer, blood cancer, diabetes and other common human diseases. Total seven patents have been granted in this period and out of them six patents are granted in abroad.

IICB has always remained as a choice for budding scientists with aspiration to work in biological and chemical fields. This year the institute has attracted a large number of bright, young research fellows and research associates from all over the country to generate adequate and trained human resource in the different fields of Biology and Chemistry and related areas for meeting the requirement of cutting edge research. During 2007-08 around 200 fellows and research associates worked in this Institute with strong motivation of work in basic and applied fields of research and generated excellence. A large number of distinguished scientists both from India and abroad visited, delivered lectures and hold discussions with the research groups in IICB. About 105 students from different Universities and Institutes of India received summer training and other training programmes. A large number of Scientists were involved in teaching and training programmes of neighbouring universities and institutes. Despite of organizing different scientific symposia the institute also observed Institute Foundation day and CSIR Foundation day.

I extend my cordial gratitude to all the scientific, technical and administrative staff of our Institute for their year long sincere activity and cooperation in sustaining growth and maintaining the reputation of IICB. I also believe that the dedication offered by my colleagues will raise the Institute to a new height in coming days.

Prof. Siddhartha Roy
IICB, Kolkata


IICB
R&D GROUPS
IMMUNOLOGY
BIOTECH-NOLOGY
INFECTIOUS DISEASE
HUMAN GENETICS & GENOMICS
CELLULAR PHYSIOLOGY
SYNTHETIC, BIOPHYSICAL & NATURAL PROD. CHEMISTRY
DRUG DESIGN, DEVELOPMENT & MOLECULAR MODELING
P&I-PME DIVISION
HUMAN RES. DEVELOPMENT
ART SECTION
PHOTOGRAPHY
BUSINESS DEVELOPMENT GROUP
PROJECT MONITORING & EVALUATION
IPM CELL
PUBLICATION & INFORMATION
CENTRAL FACILITIES
ANIMAL HOUSE
LIBRARY & DOCUMENTATION
INSTRUMENTATION
COMPUTER
INFRA-STRUCTURE
ELECTRICAL ENGINEERING
MAINTENANCE [ELECTRICAL]
ARCHITECTURE & CIVIL ENGG.
MAINTENANCE [CIVIL]
ADMINISTRATION
DIRECTOR'S SECRETARIAT
FINANCE & ACCOUNTS
GENERAL ADMN.
STORES & PURCHASE
ESTABLISH-MENT
BILL SECTION
R & C SECTION
CASH SECTION
SECURITY & MAINTENANCE
RECEIPTS & DESPATCH
WORKS & SERVICES
HINDI CELL
MAIN STORE
PROJECT CELL
FOREIGN PURCHASE
INDIGENEOUS PURCHASE

Performance at a Glance

THE LAURELS

★ Prof. Siddhartha Roy has been awarded "Tata Innovation Award" by DBT, Govt. of India.

★ Dr. Hemanta K. Majumder has been nominated as "Chairman of Kolkata Chapter" of The National Academy of Sciences, Allahabad for the year 2008 – 2010.

★ Dr. Pijush K. Das received "Senior Scientist Oration Award" of Indian Immunology Society.

★ Dr. J.R. Vedasiromoni was awarded "Col. R.N. Chopra Oration Award" of Indian Pharmacological Society.

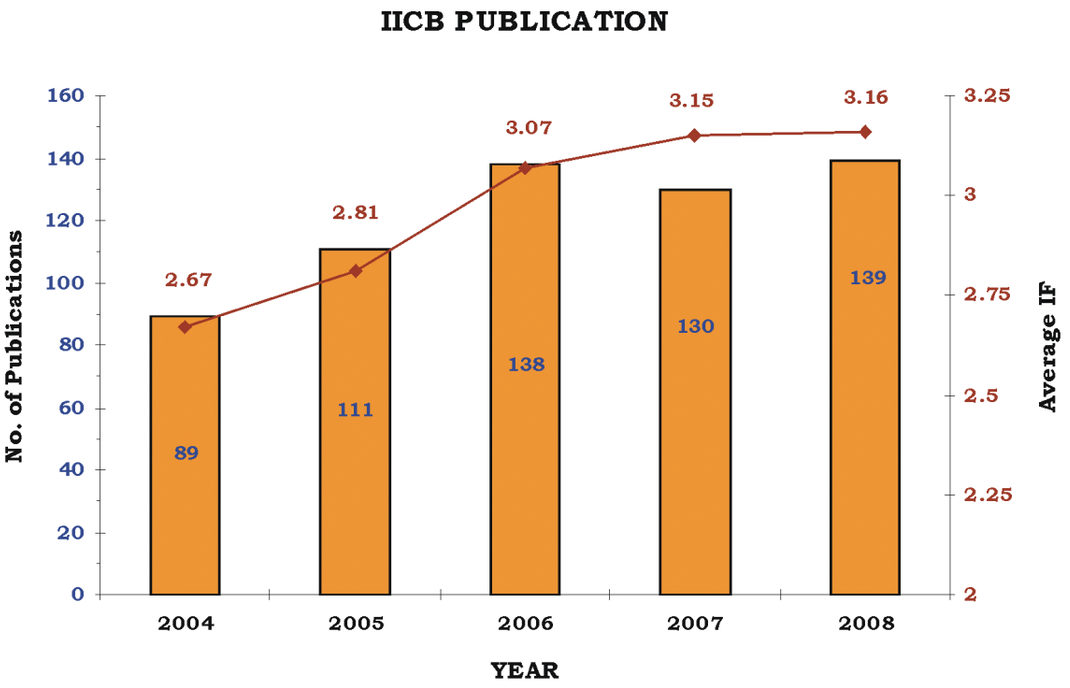
★ Dr. Snehashikta Swarnakar received "National Bioscience Award for Career Development" by DBT, Govt. of India.

★ Dr. Sib Sankar Roy received "Raman Research Fellowship" of CSIR

Performance at a Glance

PUBLICATIONS

A steady number of quality publications are the hallmark of the Institute's progress in research. Year-wise publications* and average impact factor (IF) for the last five years are given below:

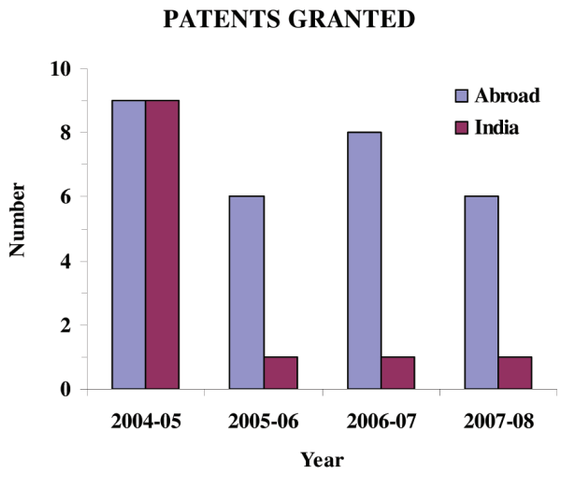


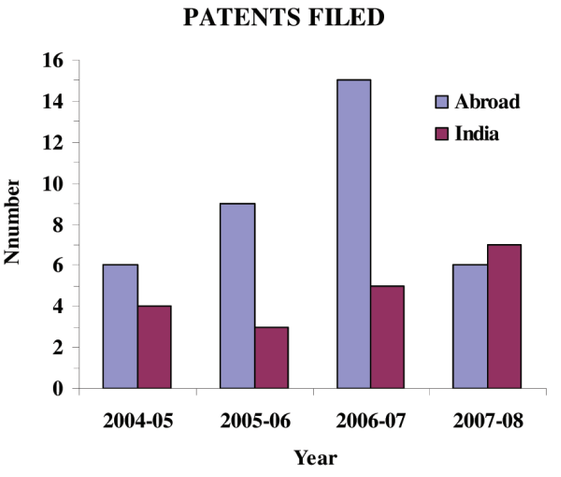
*Detailed list of publications for 2007-08 is given inside separately.

Performance at a Glance

PATENTS

A steady number of patents* are filed every year from the Institute and are granted.





*List of patents filed and granted in 2007-08 are given inside in reports of P&I-PME Division.

Performance at a Glance

INSTITUTE – INDUSTRY TIE UP

The Institute is continuously building synergy with the industries and successfully converting knowledge into wealth. This year, IICB scientists have managed to sustain the same level of interaction with the industry and earn a considerable amount of resources both human and financial.

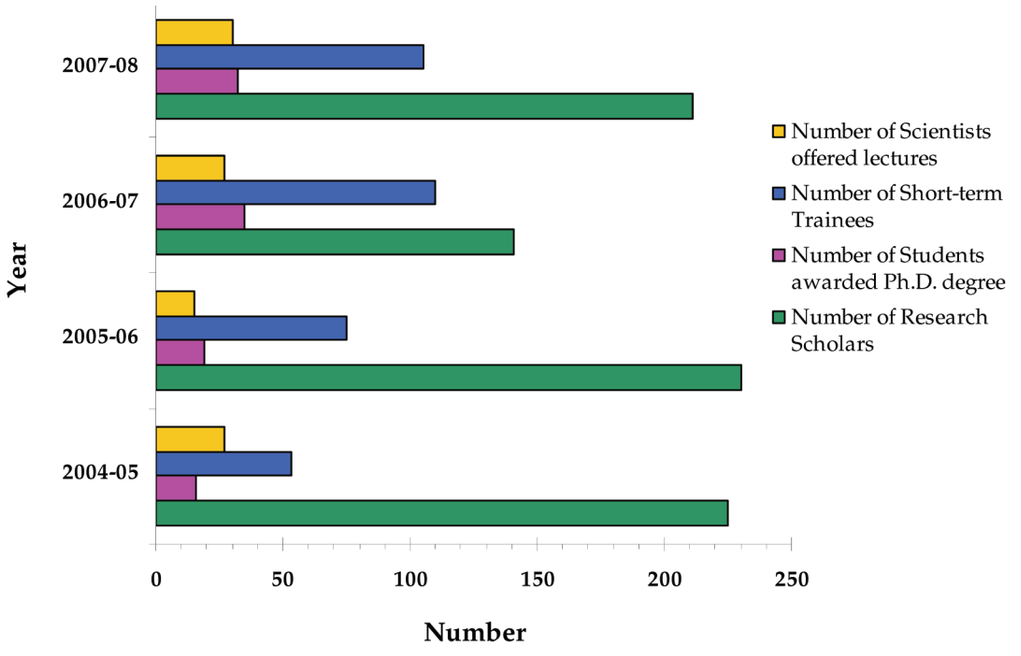
Our partners for the overall growth towards a GATI-India regime are as follows:

- ⇨ Merial SAS Lyn, France
- ⇨ Angiogen Pharmaceuticals, Australia
- ⇨ Coir Board, Kochi
- ⇨ Albert David Ltd., Kolkata
- ⇨ Chatterjee Management Services Pvt. Ltd., Kolkata
- ⇨ Piramal Life Sciences Ltd., Mumbai
- ⇨ Dey's Medical Stores (Mfg.) Ltd., Kolkata
- ⇨ DNDi, France
- ⇨ East India Pharmaceutical Works Ltd., Kolkata
- ⇨ Chembiotech Research Intl. Pvt. Ltd., Kolkata
- ⇨ Qualpro Diagnostics, Goa
- ⇨ Santha Biotechnics Ltd., Hyderabad
- ⇨ Zephyr Biomedical, Goa
- ⇨ Biotech Consortium (I) Ltd., New Delhi

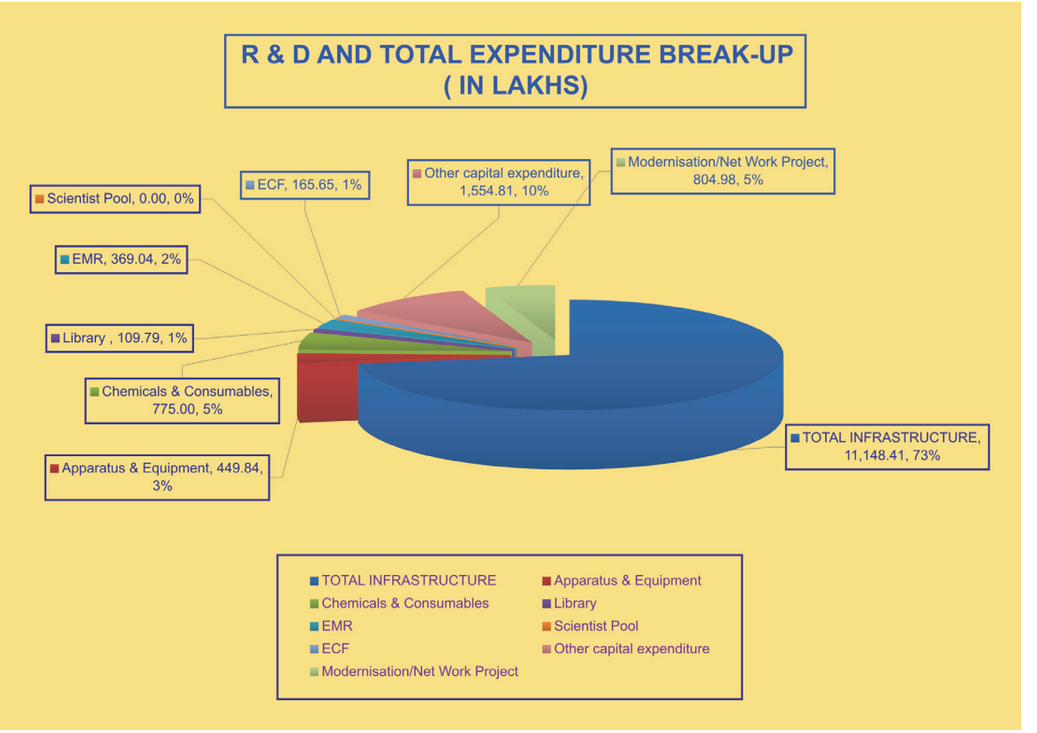
Performance at a Glance

HUMAN RESOURCE DEVELOPMENT

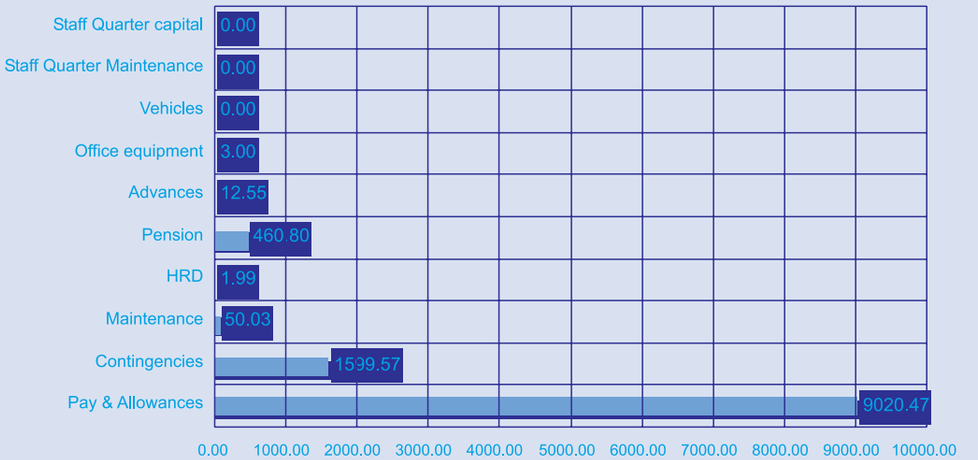
A number of research scholars carry out research at Doctoral and Post-doctoral levels each year. Several students from various universities of the country get short-term training in every year. Data for the last four years are presented graphically.



Performance at a Glance

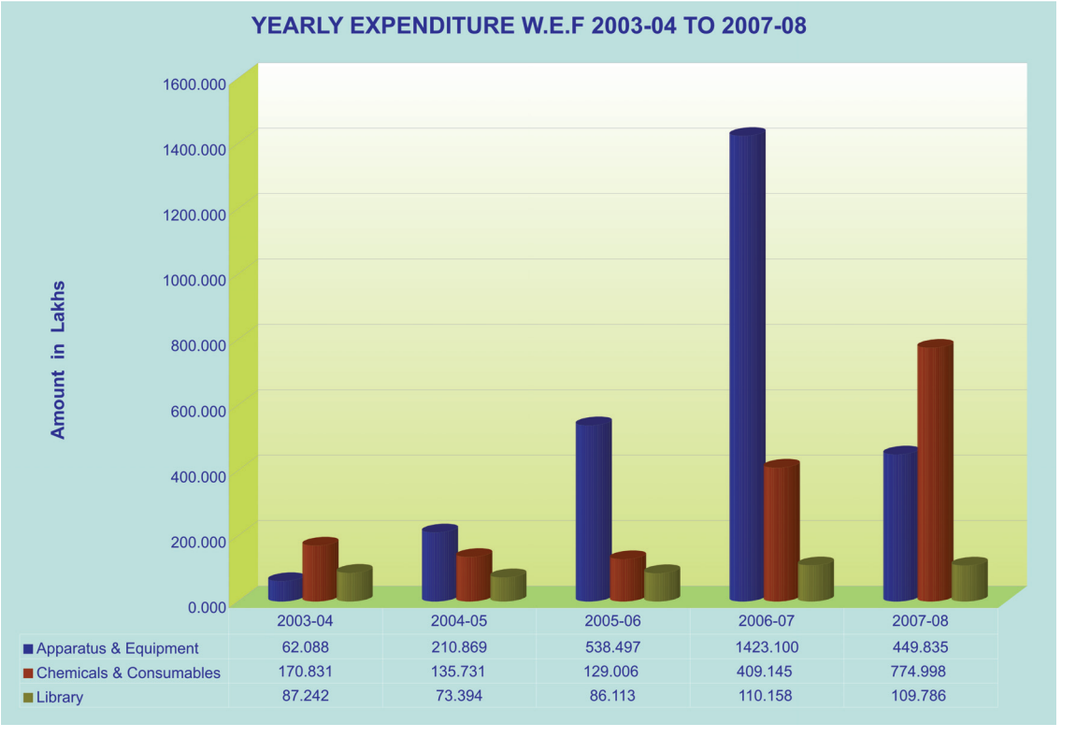


SOURCE: IICB

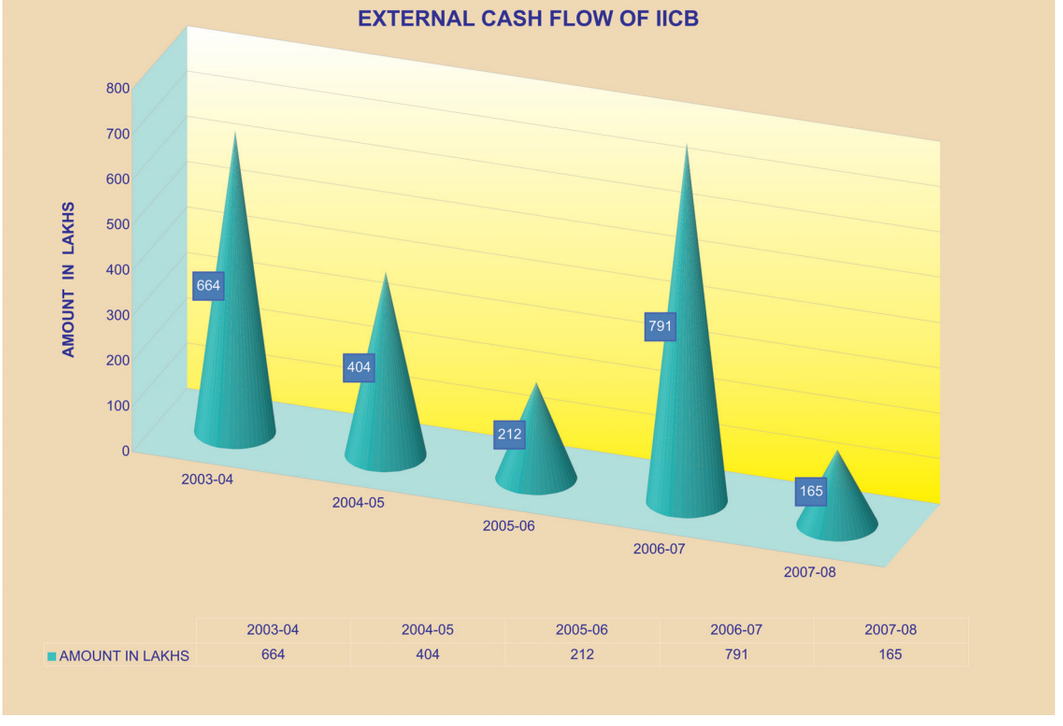


	Pay & Allowances	Contingencies	Maintenance	HRD	Pension	Advances	Office equipment	Vehicles	Staff Quarter Mainten	Staff Quarter capital
AMOUNT IN LAKHS	9020.47	1599.57	50.03	1.99	460.80	12.55	3.00	0.00	0.00	0.00

Performance at a Glance

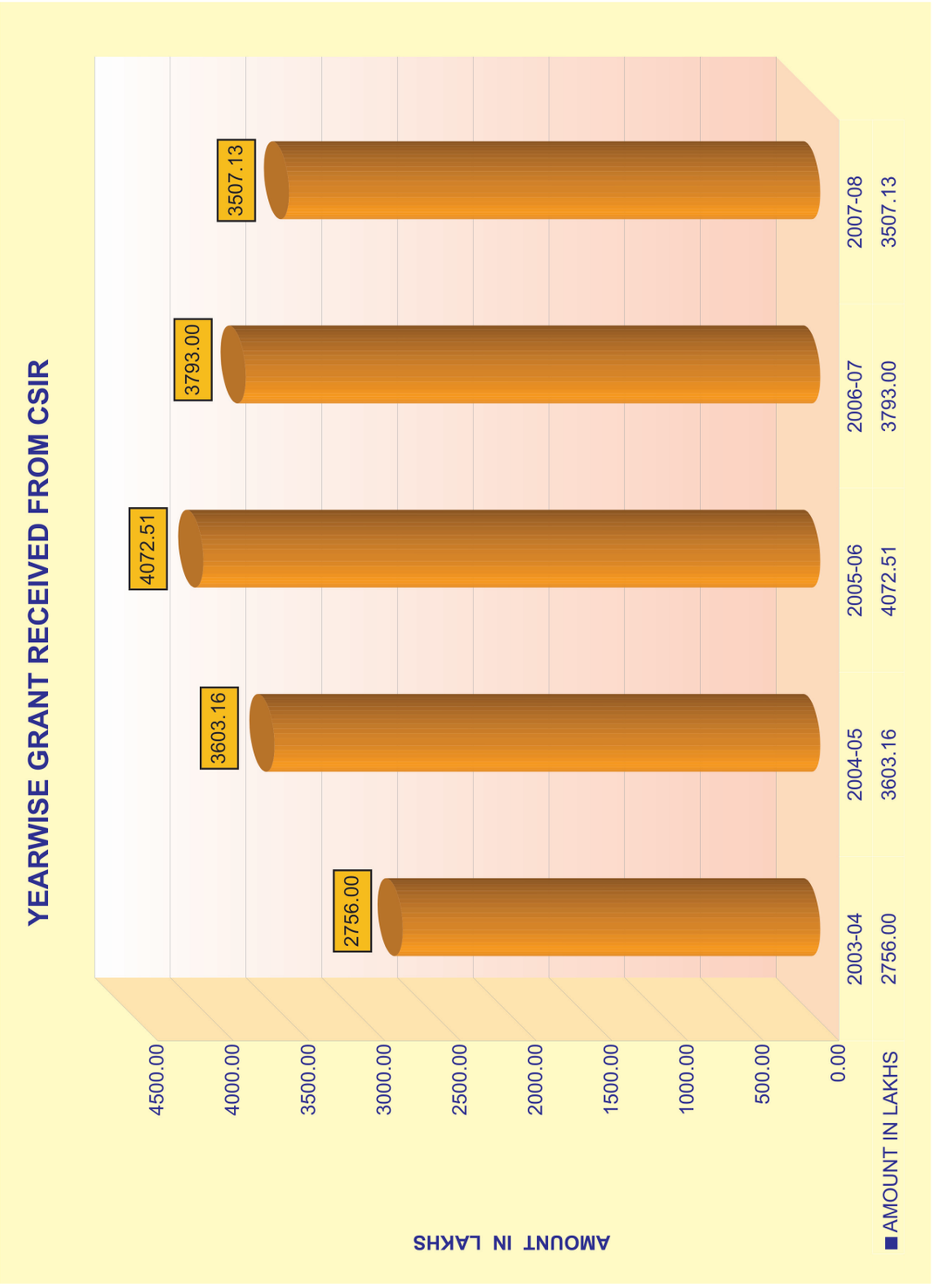


	2003-04	2004-05	2005-06	2006-07	2007-08
Apparatus & Equipment	62.088	210.869	538.497	1423.100	449.835
Chemicals & Consumables	170.831	135.731	129.006	409.145	774.998
Library	87.242	73.394	86.113	110.158	109.786



	2003-04	2004-05	2005-06	2006-07	2007-08
AMOUNT IN LAKHS	664	404	212	791	165

Performance at a Glance



Infectious Diseases and immunology

Dr. Hemanta K. Majumder, Dr. Pijush K. Das, Dr. (Mrs.) Chitra Mandal, Dr. Syamal Roy, Dr. Santu Bandopadhyay, Dr. (Mrs.) Nahid Ali, Dr. (Mrs.) Rukhsana Chaudhury, Dr. Rupak K. Bhadra, Mrs. Neeta V. M. Khalkho, Dr. (Mrs.) Debjani Mandal, Dr. (Mrs.) Tripte De, Dr. Uday Bandopadhyay, Dr. (Mrs.) Malini Sen

Research activity of infectious diseases and immunology group involves various fields of biological sciences with special interest to *Leishmania* and *Cholera*.

Dr. H. K. Majumder

Molecular architecture of type IB DNA topoisomerase of Leishmania

Topoisomerases are ubiquitious enzymes that resolve the torsional strain in DNA built up during vital cellular processes such as replication, transcription, recombination etc. The unusual bi-subunit topoisomerase IB of *Leishmania* is a paradigm shift in the evolution of type IB topoisomerases.

Kinetoplastid topoisomerase IB is an unusual bisubunit enzyme where reconstitution of the large (LdTOPIL or L) and small (LdTOPIS or S) subunits shows functional activity. It is yet to be deciphered whether one subunit or both navigate the heterodimer to its cellular DNA targets. Tethering a specific DNA-binding protein to topoisomerase I alters its site specificity. The chimeric constructs UMSBP–LdTOPIL/S or U–L/S (fusion of UMSBP to the Nterminus of L and reconstituted with S) and LdTOPIL/UMSBP–LdTOPIS or L/U–S (fusion of UMSBP to the N-terminus of S and reconstituted with L) exhibit relaxation activity. Only U–L/S shows altered site specificity and enhanced DNA-binding affinity for the universal minicircle sequence (UMS) containing substrate. This proves that L alone serves as the 'molecular steer' for this heterodimer. Reconstituted U–L/S also induces cleavage close to UMS and causes minicircle linearization. The differential properties of the reconstituted chimeras U–L/S and L/U–S reveal the structural and functional asymmetry between the heterodimer. Therefore this study helps in a better understanding of the mechanistic details underlying topoisomerization by this bi-subunit enzyme.

Topoisomerases of Leishmania with reference to development of therapeutics

The enormous development of molecular and cellular biology in recent times have provided opportunity for discovering newer molecular targets for drug designing, which form a rational basis for the development of improved anti parasitic therapy. This laboratory has been involved in developing DNA topoisomerase targeted anti leishmanial agents.

ATP-binding cassette (ABC) transporters constitute the biggest family of membrane proteins involved in drug resistance and other biological activities. Resistance of leishmanial parasites to therapeutic drugs continues to escalate in developing countries and in many instances it is due to overexpressed ABC efflux pumps. Progressively adapted camptothecin (CPT)-resistant parasites show overexpression of a novel ABC transporter, which was classified as ABCG6. Transfection and overexpression of LdABCG6 in wild type parasites, shows its localization primarily in the plasma membrane and flagellar pocket region. Overexpressed LdABCG6 confers substantial CPT resistance to the parasites by rapid drug efflux. Various inhibitors have been tested for their ability to revert the CPT-resistant phenotype to specifically understand the inhibition of LdABCG6 transporter. Transport

experiments using everted membrane vesicles were carried out to gain an insight into the kinetics of drug transport. This study provides further knowledge of specific membrane traffic ATPase and its involvement in the chemoresistance of *Leishmania*.

Programmed cell death in Leishmania

Programmed cell death (PCD) involves genetically controlled mechanisms that eliminate unnecessary cells and regulate growth and development of an organism. In *Leishmania*, PCD helps in altruistic growth control and organizes them into clonal populations. It maximizes their biological fitness and facilitates their adaptation to the digenic life cycle

(i) In the post-genomic perspective, the quest of programmed cell death (PCD) mechanisms in kinetoplastid parasites lies in the identification and characterization of cell death executer proteins. Here, we show that baicalein (BLN), a potent topoisomerase IB inhibitor, generates an oxidative stress in the parasites leading to altered physiological and morphological parameters, which are characteristic of PCD. For the first time we elucidate that, caspase-independent activation of a novel effector molecule, endonucleaseG (LdEndoG), mediates BLN-induced cell death. Functional characterization of LdEndoG identifies Flap endonuclease-1 (LdFEN-1) and LdTatD-like nuclease as other effector molecules. BLN treatment translocates LdEndoG from mitochondria to nucleus, where it forms separate complexes with LdFEN-1 and LdTatD to constitute a DNA degradesome' unique to these parasites. Conditional antisense knockdown of LdEndoG provides protection against PCD. This knowledge paves the path toward a better understanding of the PCD pathway in simpler systems, which could be exploited in antileishmanial chemotherapy.

(ii) Mitochondria are the principal site for the generation of cellular ATP by oxidative phosphorylation. F0F1-ATP synthase, a complex V of the electron transport chain, is an important constituent of mitochondria-dependent signaling pathways involved in apoptosis. In the present study, we have shown for the first time that 3,3'-diindolylmethane (DIM), a DNA topoisomerase I poison, inhibits mitochondrial F0F1-ATP synthase of *L. donovani* and induces programmed cell death (PCD), which is a novel insight into the mechanism in protozoan parasites. DIM-induced inhibition of F0F1-ATP synthase activity causes depletion of mitochondrial ATP levels and significant stimulation of mitochondrial reactive oxygen species (ROS) production, followed by depolarization of mitochondrial membrane potential ($\Delta\psi m$). Because $\Delta\psi m$ is the driving force for mitochondrial ATP synthesis, loss of ($\Delta\psi m$) results in depletion of cellular ATP level. The loss of $\Delta\psi m$ causes the cellular ROS generation and in turn leads to the oxidative DNA lesions followed by DNA fragmentation. In contrast, loss of $\Delta\psi m$ leads to release of cytochrome *c* into the cytosol and subsequently activates the caspase-like proteases, which lead to oligonucleosomal DNA cleavage. We have also shown that mitochondrial DNA-depleted cells are insensitive to DIM to induce PCD. Therefore, mitochondria are necessary for cytotoxicity of DIM in kinetoplastid parasites. Taken together, our study indicates for the first time that DIM-induced mitochondrial dysfunction by inhibition of F0F1-ATP synthase activity leads to PCD in *Leishmania* spp. parasites, which could be exploited to develop newer potential therapeutic targets.

(iii) Curcumin, a polyphenol compound, has been recognized as a promising anti-cancer drug. The purpose of the present study was to investigate the cytotoxicity of curcumin to *L. donovani*, the causative agent for visceral leishmaniasis. Flow cytometric analysis revealed that curcumin induced cell cycle arrest at G2/M phase. Incubation of Leishmania promastigotes with curcumin caused exposure of phosphatidylserine to the outer leaflet of plasma membrane. This event is preceded by curcumin induced formation of reactive oxygen species (ROS) and elevation of cytosolic calcium through the release of calcium ions from intracellular stores as well as by influx of extracellular calcium. Elevation of cytosolic calcium is responsible for depolarization of mitochondrial membrane potential (DWm), release of cytochrome c

into the cytosol and concomitant nuclear alterations that included deoxynucleotidyltransferase-mediated dUTP end labeling (TUNEL) and DNA fragmentation. Taken together, these data indicate that curcumin has promising antileishmanial activity that is mediated by programmed cell death and, accordingly, merits further investigation as a therapeutic option for the treatment of leishmaniasis.

Dr. Pijush K. Das

The work in my laboratory is centered on studying macrophage biology using visceral leishmaniasis as a model disease of macrophage. It may be broadly divided into two aspects: direct therapeutic approaches in general for macrophage-associated diseases and indirect therapeutic approaches based on unique cellular or metabolic events. In our indirect therapeutic approaches we are working on comprehensive understanding of cyclic nucleotide signaling in the establishment of *Leishmania* infection in macrophages. Even though the human parasite *L. donovani* encounters tremendous oxidative burst during macrophage invasion, a set of parasites survive and proliferate intracellularly leading to transformation from promastigote to amastigote form and disease manifestation. The striking shift of temperature (from 22^{o}C in the insect gut to 37^{o}C in the mammalian host) and pH (7.2 in the insect gut to 5.5 in the parasitophorous vacuole of macrophages) are the key environmental triggers for differentiation as these cause an arrest in the G1 stage of cell cycle and initiate transformation. Using established *in vitro* culture and differentiation system our study demonstrates that differentiation-triggering environment induces resistance to oxidative damage and consequently enhances the infectivity. Differentiation condition caused a 3-4-fold elevation of cAMP level as well as cAMP dependent protein kinase activity. Similar to stress exposure positive modulation of intracellular cAMP resulted in blockage of cell cycle progression and induction of resistance against oxidative damage. Resistance against prooxidants by either stress or cAMP may be associated with up regulation of the expression of three major antioxidant genes, peroxidoxin 1, trypanothione reductase and superoxide dismutase A. Positive modulation of intracellular cAMP response enables cells to resist cytotoxic effect of prooxidants. On the contrary, down regulation of intracellular cAMP by over expressing cAMP phosphodiesterase A resulted in decrease of resistance against oxidative damage and reduced infectivity towards activated macrophages. The study for the first time reveals the importance of cAMP response in the life cycle and infectivity of *Leishmania* parasite. In our direct therapeutic approaches, we were successful in generating a natural peptide with strong immunomodulatory activity, which has the potential in general for all macrophage-associated diseases. Peptide derived from cystatin, a natural cysteine protease inhibitor, has strong antileishmanial activity with curative effect on experimental visceral leishmaniasis associated with upregulation of nitric oxide and favourable T cell response. The transductional mechanisms underlying these cellular responses have been investigated in the murine macrophage cell line RAW 264.7 and in the BALB/c mouse model of visceral leishmaniasis using specific inhibitors and dominant-negative constructs of various interacting kinases and transcription factors.

Future plans include (i) detailed molecular characterization of a comprehensive cyclic nucleotide signaling in the infectivity of parasites, (ii) studies on dysfunction of macrophage signal transduction mechanisms due to *Leishmania* infection. (iii) in vivo effects of immunomodulators of natural origin regarding organ specificity, pharmacokinetics as well as various upstream signaling pathways for NF-κB activation leading to up-regulation of iNOS and Th1 cytokines.

Dr. (Mrs.) Chitra Mandal

Impact of glycosylation of bio-moleculs in health and disease

The expanding field of glycobiology deals with the investigation of carbohydrate molecules and the role they play in biological systems. Carbohydrates specially sialic acids and its derivatives are emerging as important determinants of the immune response which is reflected in its regulation of a multitude of cellular and molecular

interactions. The main attention of this laboratory is focused on the understanding of the importance of glycosylation in leukemia and visceral leishmaniasis. The identification of modified carbohydrate structures and its utility as potential disease specific biomarkers for monitoring the disease status for the following projects has been taken up.

Status of disease specific sugar molecules in Indian Visceral Leishmaniasis (VL) and their clinical applications

We have earlier conclusively established that an enhanced presence of 9-*O*-acetylated sialoglycoconjugate *(9-O*-AcSG) and developed a user friendly, simple blood based assay for the diagnosis of VL by detecting disease specific antigen and transferred this technology to Zyphyr Biomedical, Goa. These *9-O*-AcSG triggers the alternate complement pathway in Indian VL. Antibodies directed against these glycotope are important source of classical complement activator even under normal physiological conditions suggesting their role in conferring host protection against parasite infection.

Future plan:

- Immunomodulatory role of these *9-O*-AcSGs
- Biological significance of differentially expressed sialoglycans
- Proteomic of a few affinity purified sialoglycans from VL patients and parasites
- Investigation of differential glycosylation pattern on different clinical isolates

Identification of high level of sialate-O-acetyltransferase in lymphoblasts: responsible for O-acetylation of sialic acids and its correlation with disease status in childhood Acute Lymphoblastic leukaemia (ALL)

Earlier studies have established an enhanced presence of 9-*O*-acetylated sialoglycoproteins (Neu5,9Ac2-GPs) on lymphoblasts of ALL. Three distinct leukaemia-specific molecular determinants along with the enhanced presence of anti-Neu5,9Ac2-GP$_{ALL}$ antibody has been characterized and explored to develop assay for diagnosis and monitoring of these children. Additionally, newly identified circulatory immune-complexed Neu5,9Ac2-GP$_{ALL}$ has also been explored for disease management. The role of Neu5,9Ac2-GPs$_{ALL}$ in the survival of lymphoblasts has been observed.

Now we have identified an enzyme, sialate-*O*-acetyltransferase (sialate-*O*AT), in lymphoblasts from bone marrow (BM) and peripheral blood (PB) of twenty-five B- and T-ALL patients. The mean sialate-*O*AT activity in lymphoblasts, at disease presentation, increased 24.34 fold as compared to normal healthy donors. V_{max} of the enzymatic reaction was 14.27 fold higher than normal. The average utilization of AcCoA by endogenous acceptors present in microsomes of lymphoblasts increased 22.4 fold as compared to normal donors. Transfer of acetyl group only to sialic acid was established by various approaches. Additionally, we have developed an ELISA, a 6.58 fold increase in lectin-binding in patients as compared to normal donors conclusively demonstrated this selective transfer. A positive correlation was observed between sialate-*O*AT activity and the Neu5,9Ac2-GPs^{+} cells found in patients. Sialate-*O*AT increased at presentation of disease, decreased with clinical remission and sharply increased in patients that relapsed. Therefore, this ELISA could serve as an alternative method for detection of sialate-OAT helpful for monitoring and early prediction of relapse in childhood ALL.

We have also observed enhanced levels of glycolipid, 9-*O*-acetylated GD3 (9-*O*-AcGD3), in the lymphoblasts of patients in comparison to the normal cells. Localization of GD3 and 9-*O*-AcGD3 on mitochondria of patient's lymphoblasts has been demonstrated. While GD3 induced apoptosis in lymphoblasts, in contrast, 9-*O*-AcGD3 failed to induce such apoptosis. GD3 caused mitochondria-dependent apoptotic pathway, however, under identical conditions, 9-*O*-AcGD3 failed to induce similar effects. Interestingly, 9-*O*-AcGD3 protected the lymphoblasts from GD3 induced apoptosis. Although both GD3 and 9-*O*-acetyl GD3 localize to mitochondria, these two structurally related molecules may play different roles in ALL-disease biology. Taken together, our results

suggest that *O*-acetylation of GD3, like that of *O*-acetylated sialoglycoproteins, might be a general strategy adopted by leukaemic blasts towards survival in ALL.

Future plan:

- Identification and characterization of other enzymes responsible for enhanced sialylation specifically induced on lymphoblasts
- Proteomic of a few affinity purified sialoglycans from lymphoblasts of these children
- Search for new anti-leukemic compound
- Factors responsible for mobilization of hematopoietic stem cells in ALL

Studies on hematopoietic stem cell and its potential application in leukemia

The main objectives of the proposed project are to identify and characterize normal population stem cells from bone marrow (BM) as well as peripheral blood (PB) from children with leukemia for their potential application. Accordingly, different derivatives of sialic acids on stem cells were evaluated at presentation of the disease. A distinct pattern of differential sialylation between BM and PB stem cells has emerged out. The putative role of these sialic acid derivatives in mobilization and maturation has been explored.
Further characterization of this normal stem cell population is ongoing.

Investigation of human C-reactive protein in acute phase responses

C-reactive protein (CRP) is a clinically important acute phase protein whose level increases upto 1000 folds in acute inflammatory conditions. We have demonstrated, for the first time, that human CRP is glycosylated and existence of disease-specific molecular variants. Although, phosphorylcholine (PC) is a classical ligand for CRP, we have reported a *Staphylococcus aureus* cell-surface Protein A as a new ligand establishing an extended definition of CRP.

Future plan: Binding of these CRPs to microbes and parasites and their biological implication are in progress.

Dr. Syamal Roy

Immunobiology of leishmaniasis: An approach to understand the cause of immune suppression

The disease visceral leishmaniasis is characterized by the defective cell mediated immunity – the cause of which is still largely unknown. Previously we showed that *Leishmania donovani* infected macrophage showed increase in membrane fluidity coupled with defective antigen presenting ability, which could be corrected by the liposomal delivery of cholesterol rich liposomes. The increase in membrane fluidity when corrected by liposomal delivery of choleserol, such infected macrophages are perfectly capable of presenting antigen. On the basis of our previous *in vitro* results, we endeavoured to learn the host-protective ability of cholesterol-rich liposomes in experimental infection in hamsters. Our study very clearly showed that liposomal delivery of cholesterol in infected hamsters offered significant level of protection. The effect was cholesterol specific because liposomes made up of cholesterol analogue (4-cholest-3-one) failed to offer any protection. Our studies also showed that cholesterol-liposome treatment favour the expansion of T-cells that produce host-protective cytokines. Thus, this may be yet another way for therapeutic intervention of the dreaded disease. Further studies are underway to understand the mechanism of protection.

An approach to understand the role of host cell ABC transporters in antimony resistance

The first line of treatment of visceral leishmaniasis is antimonials. However, in the recent years development of antinomy resistance in sizable member of kala-azar patients is of major concern. We tried to investigate how host cells participate in the process of antinomy resistance. Here we show that ABC transporters (MRP-1 and Pgp) expressed in macrophages when infected with antimony resistant leishmania parasites *in vitro*. These transports favour efflux of antimony from the host cells. Inhibition of ABC transporters with variety of pharmacological inhibitors (verapanil, probenecid and lovastatin allowed the accumulation of antimony, which was associated with the intracellular antimony accumulation and resulting in parasite killing. Exactly similar results were observed *in vivo* in experimental infection. This result provided us with a newer, affordable strategy to treat antimony resistant kala-azar patients.

Dr. Santu Bandopadhyay

Broad-spectrum anti-cancer activity of the Piper betel leaf extract

Piper betel leaves possess a number of medicinal activities. Here we report that the methanolic extract of *Piper betel* leaves (Me-PB) induces apoptosis and necrosis of several cancer cell lines *in vitro* and destroys several human tumor xenografts *in vivo*. In contrast, this extract has no appreciable effects on the viability of normal human peripheral blood mononuclear cells (hPBMC). We demonstrate that the initial signal for Me-PB-induced apoptosis and necrosis is derived from reactive oxygen species (ROS). Exposure of MIA PaCa2 cells to growth-suppressive concentrations of Me-PB resulted in early generation of H_2O_2 followed by induction of nitric oxide (NO) which was accompanied by disruption of mitochondrial membrane potential, cytosolic release of cytochrome c, activation of caspase 3 and apoptosis. All these effects were significantly blocked by pretreatment with NO scavenger C-PTIO. Involvement of eNOS-mediated NO in Me-PB-induced apoptosis was confirmed by nitric oxide synthase (NOS)-specific pharmacological inhibitors and siRNAs. Me-PB-induced NO generation and apoptosis was attenuated by pretreatment with NAC or Peg-Cat but not with Peg-SOD. We also demonstrate that JNK phosphorylation is increased in MIA PaCa2 cells after treatment with Me-PB and pretreatment with JNK inhibitor SP600125 reverses Me-PB-induced apoptosis. Collectively, Me-PB treatment resulted in H_2O_2-dependent activation of eNOS leading to cancer cell death via JNK pathway.

Dr. (Mrs.) Nahid Ali

Gp63 in association with cationic liposomes induce strong durable immunity and long term protection against visceral leishmaniasis

The difficulty in making successful vaccines against leishmaniasis is partly due to lack of an appropriate adjuvant. Non-coding plasmid DNA (pDNA) bearing immunostimulatory sequences is a potent activator of innate immunity and can thus act as an adjuvant with vaccine antigen. Evaluation of the vaccine efficacy of pDNA and soluble leishmanial antigens (SLA) to protect against *L. donovani* infection revealed strong immunomodulatory activity of pDNA potentiating Th1 immune responses leading to enhanced protection with SLA. Adding cationic liposomes to the antigen with pDNA, either complexed or entrapped within, increased the potentiating effect of pDNA. Comparison of the two vaccine formulations demonstrated an impressive increase in the protective efficacy when both the antigen and pDNA were within the vesicle.

Cationic liposomes by virtue of their positive charge interact strongly with nucleic acids, leishmanial membrane proteins as well as surface molecules on APCs which are largely negatively charged, making these vesicles superior adjuvants compared to anionic and neutral liposomes. Cationic liposomes formulated with distearoyl phosphatidylcholine (DSPC), a saturated phospholipid with a high transition temperature, render the vesicles

more stable and enhance the cationic lipid-mediated endosomal membrane destabilization. Thus these vesicles can deliver antigens not only to the cytosol for eliciting a $CD8^+$ T-cell response but can also have the advantage of persistent antigen presentation enabling durable immunity through protein-based vaccination. Gp63 corresponds to the infective stage and virulence of visceralizing species of *Leishmania*, *e.g. L. donovani.* Gp63 could thus be the key antigen for vaccination against visceral leishmaniasis. However, no vaccine study of any form of *L. donovani* gp63 has been carried out for this disease. Our recent studies show that gp63 purified from *L. donovani* (Fig. 1) formulated in cationic DSPC liposomes is highly immunogenic and could prevent infection in virulent challenges using *L. donovani* parasites, not only after a short vaccination protocol but also 12 weeks after immunization (Fig. 2). The protective immune response by gp63 contained within liposomes was dependent on the dose of the antigen, with the optimum dose eliciting maximum immunogenicity and protection. Further, the use of liposomal gp63 induced sustained immunity through specific $CD4^+$ and $CD8^+$ T cells that controlled chronic infection.

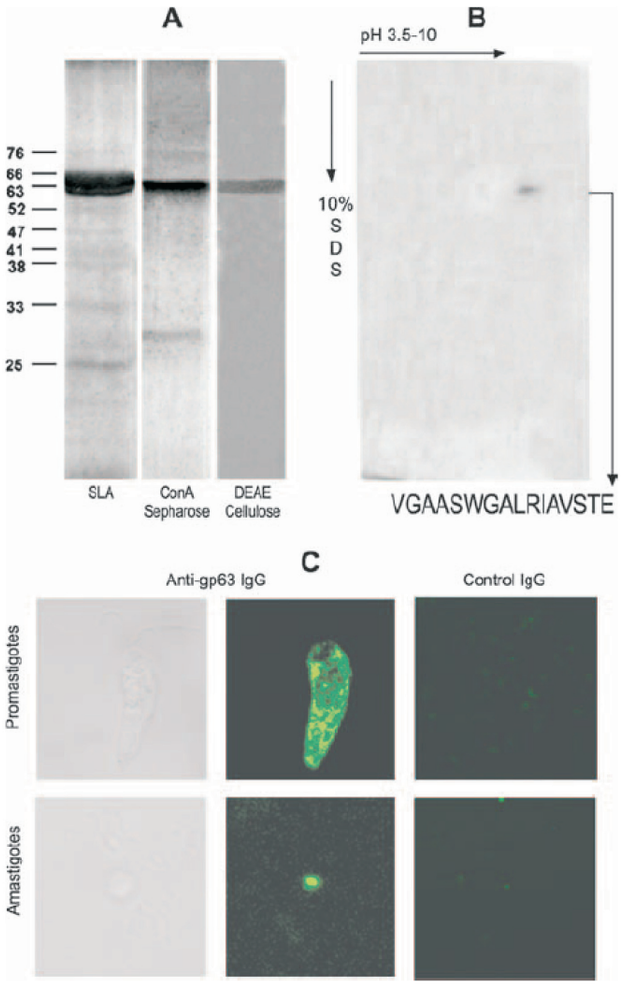


Fig. 1. Purification and characterization of *L. donovani* gp63. SLAg (SLA) from *L. donovani* promastigotes was subjected to affinity chromatography on ConA-Sepharose resin equilibrated with 5 mM Tris HCl (pH 7.6)–0.1% octyl-β-D-glucopyranoside, and the bound proteins were eluted in the same buffer with 0 to 500 mM linear methyl-α-D-mannopyranoside gradient. A pool of enriched ConASepharose fractions was further loaded onto a DEAE-cellulose column equilibrated with 5 mM Tris-HCl (pH 8.5)–0.2% Zwittergent 3.12. The elution of gp63 was performed with a linear gradient of 0 to 500 mM NaCl. (A) Silver-stained 10% SDS-PAGE gels showing (from left to the right) SLAg (6 μg),

proteins eluted from ConA Sepharose resin (6 μg), and purified gp63 (4 μg) through use of a DEAE-cellulose column. The numbers at the left represent apparent molecular masses in kilodaltons. (B) Two-dimensional PAGE of purified gp63 (4 μg) stained with ammoniacal silver nitrate solution. The arrow at the right side of the panel indicates the amino acid sequence of native gp63 at the NH2 terminus. (C) *L. donovani* promastigotes and amastigotes were fixed in formaldehyde followed by staining with 20 μg/ml rabbit anti-gp63 FITC-IgG and studied by both phase-contrast and confocal microscopy. Cells treated with identical concentrations of normal rabbit-FITC IgG served as controls. The photographs are representative of the results of one of three similar studies.

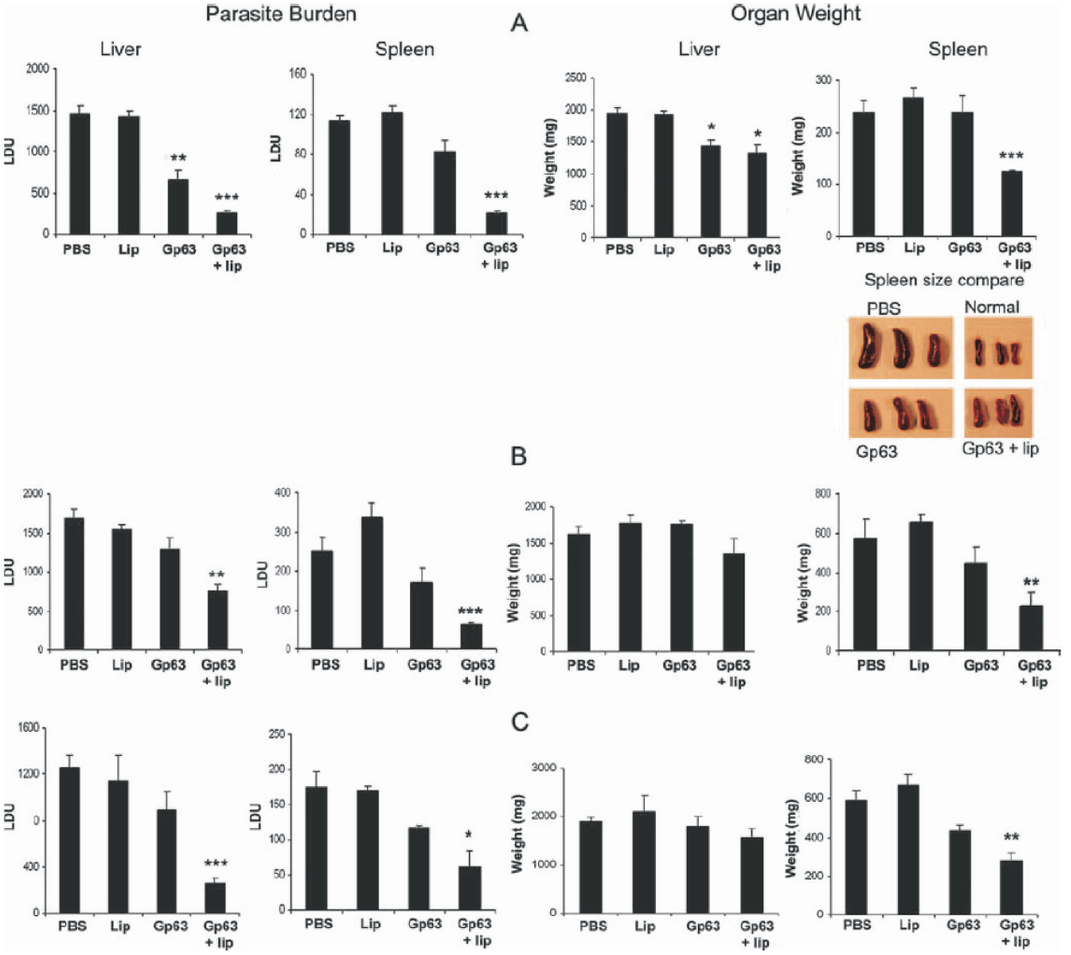


Fig. 2. Evaluation of protectionagainst visceral leishmaniasis in BALB/c mice. Animals were immunized i.p. and were twice given booster injections at 2-week intervals with PBS, with empty liposomes (Lip), and with free gp63 or gp63 entrapped in cationic liposomes (lip). (A) Parasite burden and organ weights in the liver and spleen of mice challenged 10 days after the last immunization were determined at 3 months. Data are representative of the results of two independent experiments. (B) Splenocytes (2 x 10^7) of mice after 10 days of vaccination were transferred to naïve mice, and 7 days postvaccination the animals were challenged. The parasite load and organ weights were examined in the liver and spleen after 3 months. Photographs of the spleens of infected controls and vaccinated animals are shown at upper right. (C) In a separate experiment, mice were immunized with PBS, empty liposomes, or gp63 alone or in association with liposome and were challenged 12 weeks after vaccination. At the end of 3 months of infection, liver and spleen parasite loads and corresponding organ weights were determined. Data represent Leishman-Donovan units (LDU) standard errors of the means and organ weights ± standard errors of the means determined for individual mice (n = 3 or 4). Significant (*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$) differences in the results were obtained using vaccinated versus control mice, as determined by Student's t test.

Mechanism of stearylamine-bearing cationic liposomes to kill Leishmania parasites and oral therapy with conventional antihypertensive drugs and serotonin reuptake inhibitor against L. donovani infection

Lipid-associated formulations of antileishmanial agents have proved to be more effective therapies with reduced toxicities. Previous studies from our group and others revealed that liposomes bearing phosphatidylcholine and stearylamine (SA) themselves kill Leishmania and other protozoan parasites in vitro and in vivo, without causing any adverse effect on host. Here, we offer detailed insights into the mechanism of action of these liposomes. Mechanism study was carried out using fluorometric, confocal and electron microscopic methods. Herein, we provide evidence for induction of membrane disruption by specific interaction with surface phosphatidylserine (PS) of *Leishmania* promastigotes (Fig. 3) and amastigotes, phospholipids normally not found on mammalian cell surface, with SA-containing liposomes. Cell surface PS on different forms of Leishmania facilitated liposome-induced parasite killing (Fig. 4). The target selectivity of the liposomes was further proved through inhibition of antileishmanial activity with annexinV, and strong affinity with anionic PS rather than phosphatidic acid-containing liposomes for leishmanicidal activity. SA-bearing liposomes specifically kill *Leishmania*, but are non-toxic to murine peritoneal macrophages and human erythrocytes.

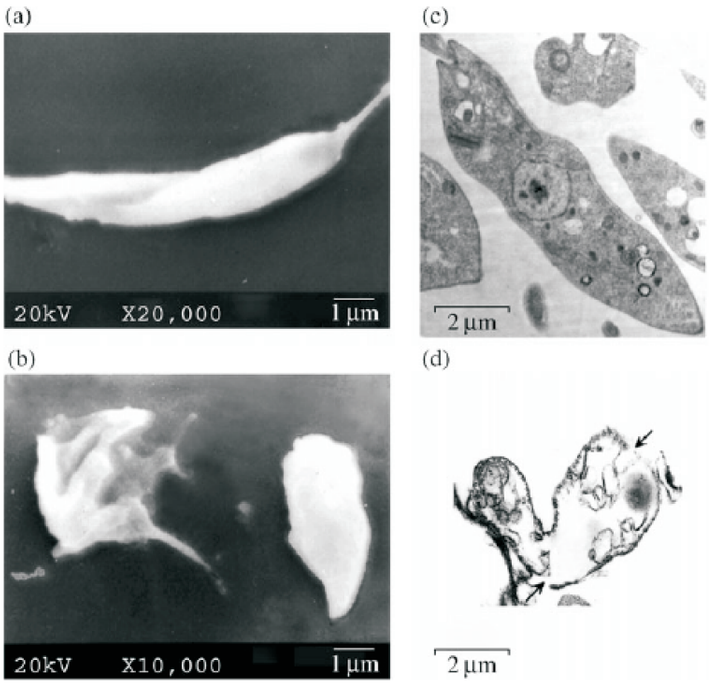


Fig. 3. Scanning and transmission electron microscopy of promastigotes treated with PC–SA liposomes. Promastigotes were incubated for 1 h under standard conditions with medium alone (a and c) or 213 mM (b and d) of PC–SA liposomes. Two representative scanning electron micrographs of untreated (a) and treated (b) cells revealed severe distortion and rupture of the cell membrane. Two representative transmission electron micrographs of untreated (c) and treated (d) cells revealed membrane disruption, extensive vacuolization and membrane breakage (arrow) as well as depletion of electron-dense cytoplasmic material. Scale bars: 1 µm (a and b), 2 µm (c and d). Pictures are representative of three similar studies. Contrast and brightness modification was performed in Adobe Photoshop 6.0.

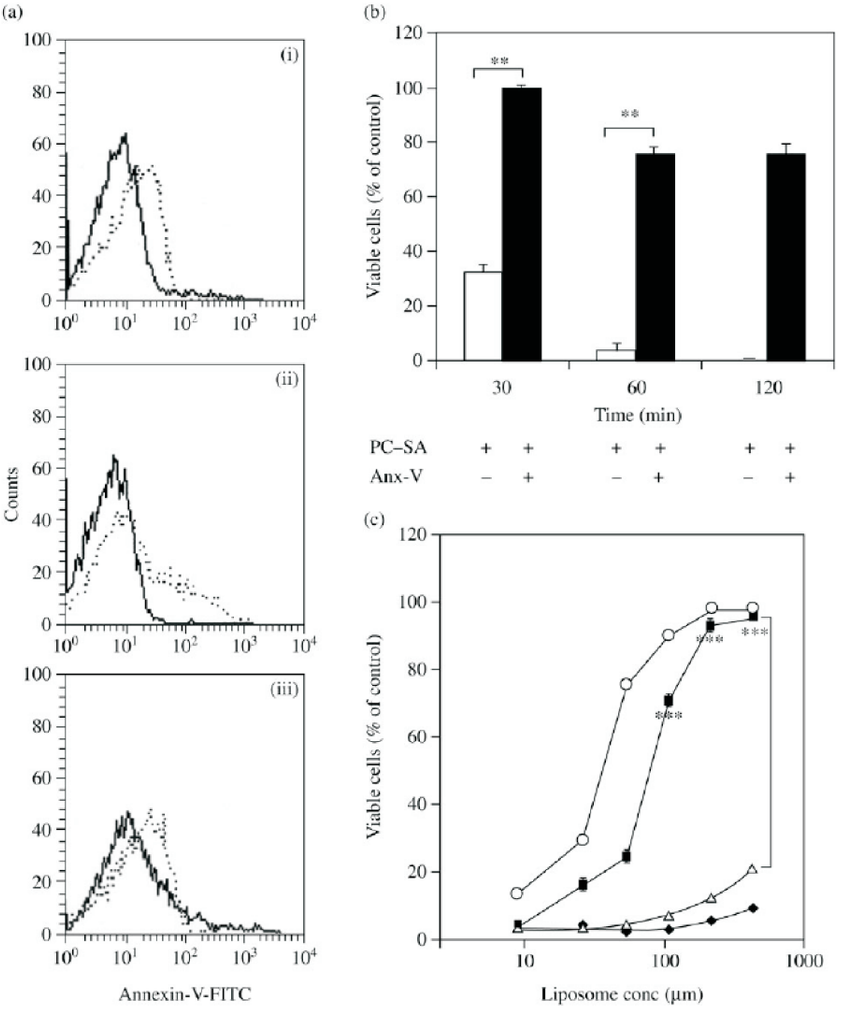


Fig. 4. (a) PS is differentially exposed by different forms of Leishmania. Cells were incubated with fluorescein-labelled annexinV (broken line) or in buffer alone as control (continuous line) and analysed by flow cytometry. (i) AG83 promastigotes, Δ mean fluorescence intensity (MFI) = 6.92; (ii) freshly isolated AG83 intracellular amastigotes, ΔMFI = 36.56, and (iii) normal murine peritoneal macrophages, ΔMFI = 2.9. Analysis of PS exposure was conducted after monitoring the viability of an aliquot of the parasites by PI incorporation under fluorescence microscope. (b) Blocking of leishmanicidal activity of PC–SA liposomes by annexinV. AG83 promastigotes were incubated with (black bars) or without (white bars) annexinV (1 μg/2 x 10^6) at 26°C for 30 min in binding buffer. PC–SA liposomes were added subsequently and viability of the parasites was determined by MTT assay after 30, 60 and 120 min. (c) Inhibition of leishmanicidal activity of PC–SA liposomes by PC–PS liposomes. PC–SA liposomes (213 μM) were incubated for 30 min with different concentrations of PC–Chol, 7:2 (filled diamonds), PC–PA, 7:2 (open triangles), PC–PS, 7:2 (filled squares) and 1:1 (open circles), liposomes prior to incubation with promastigotes. Data points represent the mean of triplicate samples ± SEM from a single experiment, representative of three different experiments. Significant difference: $^{**}P < 0.001$, $^{***}P < 0.0001$.

The main line of defense against visceral leishamaniasis is chemotherapy. The launching of miltefosin, the only oral therapy, related to toxicities, low therapeutic window, etc. pose limitations on its use, emphasizing the need for safer, effective and cheaper chemotherapeutic agents for treating leishmaniasis, preferentially by oral route. Amlodipine and lacidipine, conventional antihypertensive drugs, inhibited *L. donovani* infection in vitro (Fig. 5) and in BALB/c mice when administered orally (Fig. 6). These 1,4-dihydropyridine derivatives functioned through dose-dependent inhibition of oxygen consumption, triggering caspase 3-like activation-mediated programmed cell death of the parasites.

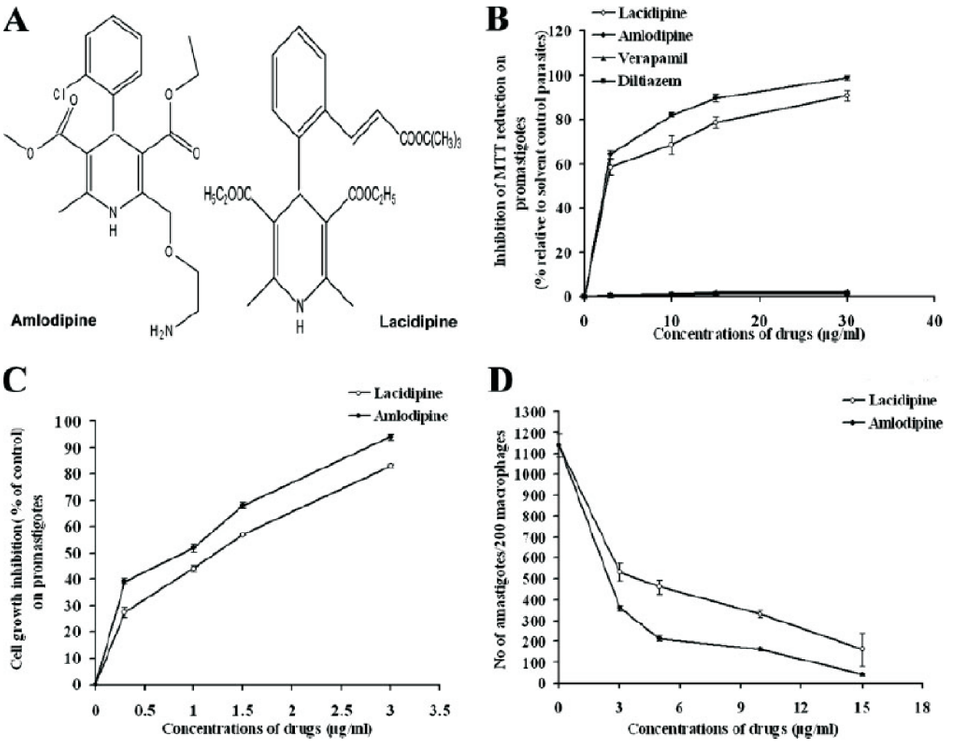


Fig. 5. Effects of amlodipine and lacidipine on the killing and growth of *L. donovani* AG83 promastigotes and intracellular amastigotes in vitro. (A) Molecular structures of amlodipine and lacidipine. (B) Promastigotes of strain AG83 were cultured in M199 medium supplemented with 10% fetal calf serum. Aliquots of a stationary-phase AG83 culture were incubated with graded concentrations (3, 10, 15, and 30 µg/ml) of amlodipine, lacidipine, verapamil, and diltiazem (Sun Pharmaceuticals Ltd., India) for 2 h at 22°C. Parasite viability was estimated by MTT assay and expressed as the cell number relative to those for solvent control (0.2% dimethyl sulfoxide [DMSO]) cultures. (C) Effects of amlodipine and lacidipine on the long-term growth of viable *L. donovani* promastigotes at doses of 0.3, 1, 1.5, and 3 µg/ml. Parasite growth inhibition after 3 days of continuous drug treatment was evaluated by MTT assay, and results are represented as percent growth inhibition with respect to solvent controls (0.2% DMSO). (D) Effects of the two drugs at various doses (3, 5, 10, and 15 µg/ml) on the survival of *L. donovani* amastigotes internalized in murine peritoneal macrophages at 48 h posttreatment. Amastigotes were counted by Giemsa staining and are represented in the figure as numbers of amastigotes per 200 macrophages with respect to solvent controls (0.2% DMSO). The results are expressed as means standard errors for triplicate values from one experiment that is representative of two performed.

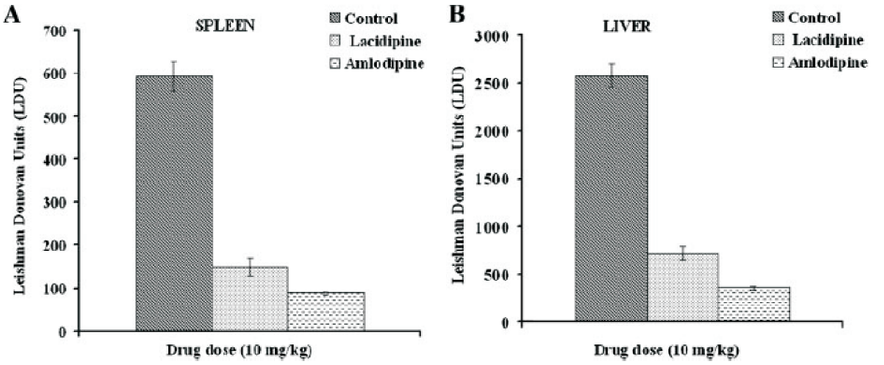


Fig. 6. Evaluation of leishmanicidal activity of amlodipine and lacidipine in established infection model of VL in BALB/c mice. Mice infected for 8 weeks were treated orally with a dose of 10 mg/kg of body weight of amlodipine and lacidipine in PBS weekly for 1 month. Control infected animals received only PBS. Mice were sacrificed at 30 days posttreatment. Levels of parasite burden in spleens (A) and livers (B) are expressed as Leishman Donovan units. Values represent the means ± standard errors for four animals per group.

We extended our studies to oral therapy with sertraline, a selective serotonin reuptake inhibitor, also reported to have antimicrobial activity. Sertraline also demonstrated antileishmanial activity *in vitro*, as well as *in vivo*, eliminating significant levels of parasitic load through oral therapy (Fig. 7). A sertraline-induced fall in cytoplasmic ATP and oxygen consumption rate in promastigotes suggests the involvement of an apoptosis mode of cell death in the treated parasites.

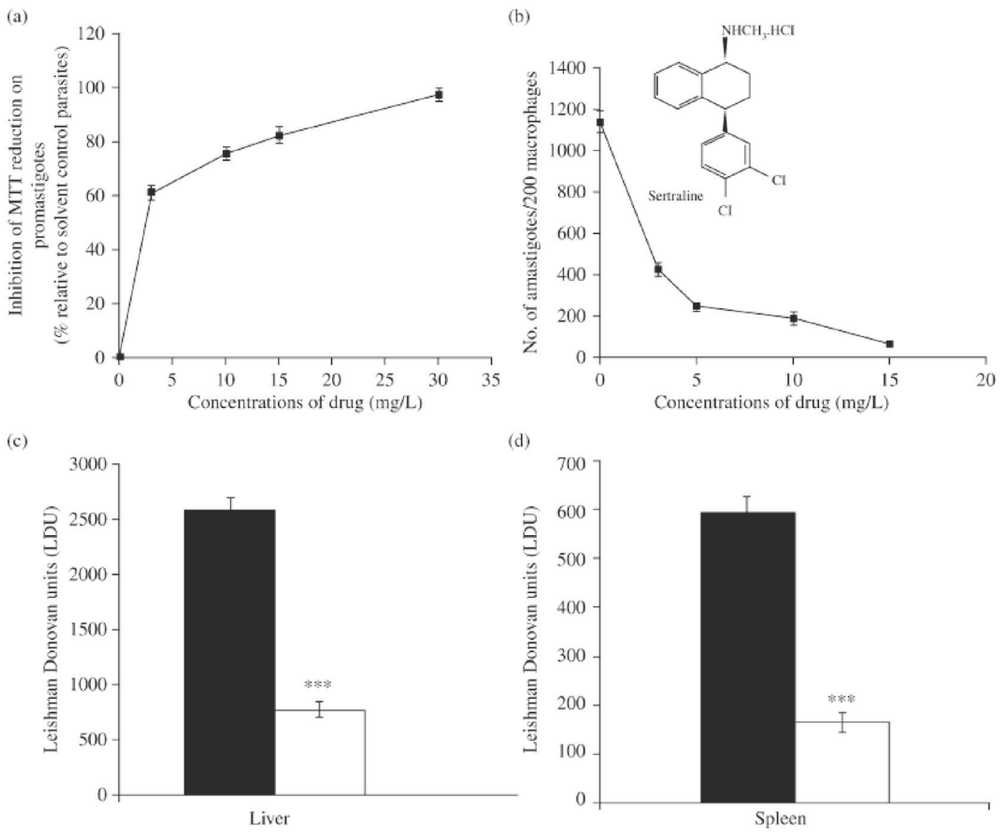


Fig. 7. Antileishmanial activity of sertraline against *L. donovani* AG83 promastigotes and intracellular amastigotes in vitro, and in vivo against established VL infection in BALB/c mice. Promastigotes of AG83 strain (a) were cultured in M199 medium with graded doses (3, 10, 15 and 30 mg/L) of sertraline for 2 h at 228C. Parasite viability was estimated by the MTT assay and expressed as the cell number relative to those for solvent control (0.2% DMSO) cultures. Effect of the drug at various doses (3, 5, 10 and 15 mg/L) on the survival of L. donovani amastigotes (b) internalized in murine peritoneal macrophages 48 h post-treatment. Amastigotes were counted by Giemsa staining and are represented in the figure as the number of amastigotes per 200 macrophages with respect to solvent controls (0.2% DMSO). The results are expressed as the means±SE of triplicate values from one experiment representative of two performed. (a) and (b) Sertraline-treated parasites are represented by filled squares. The molecular structure of sertraline has been incorporated as an inset in (b). Eight-week infected mice were treated orally with a dose of 10 mg/kg of body weight of sertraline in PBS (0.02 M), twice weekly for 1 month. Control untreated group received only PBS (0.02 M). Mice were sacrificed 4 weeks post-treatment. Levels of parasite burden in liver (c) and spleen (d) were counted and expressed as LDUs. Values represent the means ± SE. Untreated control group, black bars; drug treated, white bars. ***$P < 0.0001$ when compared with untreated controls.

IL-10 and TGF-β-mediated susceptibility in Kala-azar and post-Kala-azar dermal leishmaniasis: the significance of Amphotericin B in the control of L. donovani infection in India

Kala-azar is known to be associated with a mixed Th1 and Th2 response, and effective host defense requires the induction of IFN-γ and IL-12. We observed a differential decline of IL-10 and TGF-β in response to sodium antimony gluconate (SAG) and Amphotericin-B (AmB) treatment in Indian kala-azar patients, and an importance of IL-10 and TGF-β in development and progression of post kala-azar dermal leishmaniasis (PKDL). Cure through SAG and AmB corresponded with elevation in IFN-γ and IL-12 production, and down regulation of IL-10 and TGF-β. Retention and maintenance of residual IL-10 and TGF-β in some SAG treated individuals, and the elevation of IL-10 and TGF-β in PKDL, a sequel to kala-azar, probably reflects the role of these cytokines in reactivation of the disease in the form of PKDL. Treatment with AmB, on the other hand, resulted in negligible TGF-β levels and absolute elimination of IL-10 reflecting its better therapeutic efficacy, as well as its probable role in the recent decline in PKDL occurrences in India. Elucidation of immune responses in PKDL patients revealed a spectral pattern of disease progression where disease severity could be correlated inversely with lymphoproliferation, and directly with TGF-β, IL-10 and antibody production. In addition, enhancement of $CD4^+CD25^+$ T cells in active kala-azar, their decline at cure, and reactivation in PKDL suggest their probable immunosuppressive role in these disease forms (Fig. 8).

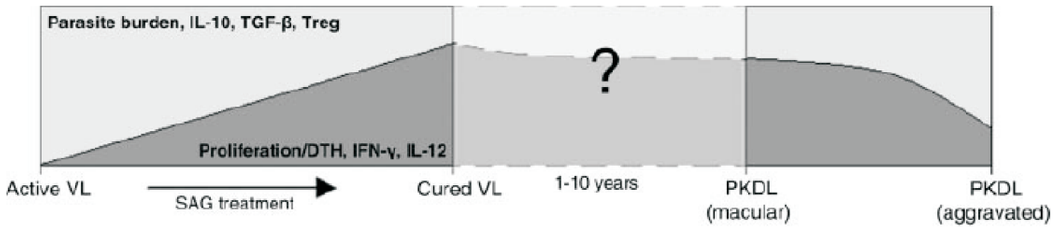


Fig. 8. A schematic model of dynamic relationship in the clinical and immunological spectrum of Indian VL and PKDL in terms of parasite burden, lymphoproliferation/DTH, and *Leishmania*-specific in vitro cytokine production. *Upper panel* of the figure (shaded light gray) represents responses related to susceptibility in terms of parasite burden, IL-10, and TGF-β production and the percentage of Treg cells, whereas the *lower panel* (shaded dark gray) indicates responses related to protection in terms of lymphoproliferation/DTH, IFN-γ, and IL-12 production. The change in area of the shaded panels represents the extent of modulation of the above responses. The model is indicative of the hypothesis that the residual IL-10 and TGF-β after SAG treatment are somehow responsible for the reactivation of PKDL. The intermediate immunomodulatory sequences during 1–10 years after a successful cure from VL with antimony is not yet clear (hazily shaded, and the probable transition is represented by discontinuous lines). The differences in immune status among PKDL patients with different grades of lesions indicate that the up-regulation of IL-10 and TGF-β production is responsible for the disease aggravation and the resulting clinical and immunological spectrum among PKDL patients.

Dr. (Mrs.) Rukhsana Chowdhury

Mechanism of modulation of virulence regulatory processes by environmental conditions.

In the course of infection, the enteric bacterium *Vibrio cholerae*, encounter a variety of physical, biochemical, nutritional, and other parameters that constitute the microenvironment of the various niches of the human gut, and these may impose a temporal control on the expression of virulence factors of the bacterium at different stages of the pathogenesis cycle. We have earlier reported that bile, invariably encountered by enteric bacteria in the course of infection of their human hosts, induces pleiotropic responses that affect production of virulence factors, motility, and other phenotypes in *V. cholerae*. We have also shown that the active components in bile are the unsaturated fatty acids, arachidonic, linoleic and oleic acid. Unsaturated fatty acids completely repress expression of the major virulence genes of *V. cholerae* including *ctxAB* encoding cholera toxin. The entire pathway from sensing and responding to fatty acids to the integration of the fatty acid signal transduction system to the transcriptional repression of the *ctxAB* genes is being investigated. A mutation has been constructed in the *fadD* gene that is involved in converting fatty acids to fatty acyl-CoA and simultaneous uptake into the cytosol. The *fadD* mutant exhibited decreased expression of virulence factors and increased motility.

Competitive exclusion of classical biotype by El Tor biotype of V. cholerae.

The El Tor biotype of *V. cholerae* emerged in 1961 and within a few years almost totally displaced the then existing classical biotype as the causative agent of pandemic cholera. The nature of the fitness gain acquired by the El Tor biotype is being investigated. A laboratory model for the competitive exclusion of El Tor biotype strains by the classical biotype has been developed.

Host-pathogen interaction

The adherence of V. cholerae to the intestinal epithelial cell line INT407 has been examined. Optimum adherence was obtained when INT407 was incubated with *V. cholerae* at MOI 50 for 30 minutes. Further increase in MOI or incubation time had no significant effect on adherence. Although many studies have described the effects of a variety of environmental parameters on the expression of the ToxR-ToxT virulence regulon of *V. cholerae*, the effect of contact with host cells on the expression of the regulon has not been investigated. As this is of primary importance in host-pathogen interaction leading to disease, expression of the ToxR-ToxT regulon was examined in *V. cholerae* following adherence to INT407 cells. The results obtained indicated that the virulence regulatory gene *toxT* as well as the virulence genes encoding cholera toxin and the colonization factor TCP were strongly induced in cell associated bacteria. The induction was not due to host cell components secreted from INT-407 but requires direct contact of the bacteria with the host cells.

Dr. Rupak K. Bhadra

Vibrio cholerae and *Shigella spp.* are two major human pathogens causing frequent diarrhoeal outbreaks in developing countries including India. So far no safe and effective immunoprophylactic measures against these pathogens are available for public heath. The situation is further complicated by frequent emergence of new pathogenic clones with multiple drug resistance. In this regard recent spread of the hybrid *V. cholerae* El Tor strains carrying classical type CTX phages in Africa and Indian Subcontinent is noteworthy. However, recent progress in bacterial genomics and proteomics has dramatically altered the study of bacterial pathogenesis and designing of experiments for complete understanding the virulence mechanism, growth, survival and persistence of the pathogens in various environmental niches. As a result new genes and regulatory circuits of the above pathogens are identified. It is also necessary to understand the role played by various mobile genetic elements in the evolution of new pathogenic clones. Different physico-chemical stress signals including nutrition

deprivation received by these pathogens in environmental reservoirs as well as under in vivo situations are quite dissimilar and probably play critical roles in adaptation through genetic mutation and help a pathogen to evolve further. In this context, the following studies were undertaken.

Genetic mapping of integration of classical CTX prophage in the genome of hybrid V. cholerae O1 biotype El Tor

The cholera toxin (CT) is a critical virulence-determining factor of epidemic *Vibrio cholerae* strains. The *ctxAB* operon coding for CT is carried by a filamentous phage, called CTXϕ. The classical biotype of *V. cholerae* O1 is the sixth pandemic strain, which was replaced completely by the current seventh pandemic El Tor biotype strains. One of the important differences between the two biotypes is that slight but specific differences in *ctxB* gene sequences; classical and El Tor strains carry *ctxB*class and *ctxB*ElTor alleles, respectively. Recently, an unusual strain of *Vibrio cholerae* O1 biotype El Tor carrying multiple tandem copies of classical CTX prophage caused a massive cholera epidemic in Mozambique in 2004. Thus, the evolution of the hybrid El Tor strain is a mystery. Furthermore, the location of the classical CTX prophage in the genome of the Mozambique strain was unknown. To determine this, pulsed field gel electrophoresis (PFGE) of the whole genome along with Southern hybridization experiments indicated that the classical CTX prophage present in the Mozambique strain is located in the small chromosome and the large chromosome does not carry any prophage. To determine the CTX prophage integration site in the small chromosome of Mozambique strain, the 5'and 3' junctions of the prophage and small chromosome were cloned and sequenced. Sequence analysis revealed that the CTX prophage was integrated in the conserved *dif* site of the replication terminus region of the strain. Interesting, while using an O1 El Tor isolate VC44 as a control, which carries tandem copies of CTX prophage in its small chromosome like the Mozambique strain, it was unexpectedly detected that the strain VC44 also carries *ctxB*class allele. Since the strain VC44 was isolated in Kolkata, India just prior to O139 Bengal outbreak in 1992, it seems that the hybrid El Tor strains were prevalent in India much before the emergence of Mozambique strain and supports the view that the latter strain has most probably originated from a VC44-like strain. Further genetic and molecular studies are underway to elucidate the evolution of hybrid *V. cholerae* O1 El Tor strains.

Molecular basis of survival of V. cholerae under nutritional stress

During the study period we have constructed several *relA* and *spoT* deletion mutants of *V. cholerae*. Our mutational analysis suggested that the *spoT* gene is essential in *V. cholerae* under *relA*$^+$ genetic background. Interestingly, the *V. cholerae* Δ*relA* Δ*spoT* strains still accumulated (p)ppGpp molecules under glucose or fatty acid starved condition, which raises the probability that there could be an alternative source of (p)ppGpp production in *V. cholerae* besides RelA and SpoT. Unlike *E. coli relA spoT* mutant [ppGpp$^{(0)}$ strain], the *V. cholerae relA spoT* mutants showed certain unusual phenotypes, which are (a) resistance towards 3-amino-1,2,4-triazole (AT); (b) growth in nutrient poor M9 minimal medium; (c) ability to stringently regulate cellular rRNA accumulation under glucose starvation and (d) initial growth defect in nutrient rich medium. Since these phenotypes of Δ*relA* Δ*spoT* mutants could be reverted back to Δ*relA* phenotypes by providing SpoT in trans, it appears that the *spoT* gene function is crucial in *V. cholerae*. Currently studies are also going on to identify the genetic source of (p)ppGpp in Δ*relA* Δ*spoT* strains of *V. cholerae*. We have also dissected the SpoT function in *V. cholerae* and our preliminary results suggest that the ACT domain of the protein is critical for its hydrolase function. Stringent response in bacteria is also regulated by a factor, called DksA (product of the gene *dksA*). We have generated *dksA* mutant of *V. cholerae* and characterization of the mutant phenotypes are in progress. Preliminary studies indicate that DksA may be involved in regulation of motility of *V. cholerae* apart from its normal function related to stringent response. Role of stringent response genes *relA*, *spoT* and *dksA* will be further explored for their involvement, if any, in quorum sensing, biofilm formation, long-term starvation survival and relation with stationary phase sigma factor gene (*rpoS*) expression. We are also working on the

essential GTP binding protein *cgtA* and previously we showed that like *spoT* the *cgtA* gene is also essential in *V. cholerae*. We have deleted the chromosomal cgtA gene of *V. cholerae* by providing CgtA in trans through an inducible promoter. Further studies are going on to understand the role C-terminal domain of the CgtA protein. Apart from these studies we are also trying to understand the role(s) of nutritional/metabolic differences between biotypes, classical and El Tor, in the evolution of epidemic clones of *V. cholerae.*

Comparative analysis of the genomes of Shigella dysenteriae type 2 and type7 strains

We have already constructed I-*Ceu*I maps of *Shigella dysenteriae* strains belonging to serotypes 2 and 7. Comparison of these maps with the whole genome sequenced strains *S. dysenteriae* type 1 and *S. flexneri* type 2a revealed that the type 7 strain is very close to that of the type 1 strain, while the genome of type 2 strain is very similar to that of *S. flexneri* type 2a strain. Further studies are going on certain virulence loci to understand molecular differences among these strains of *Shigella dysenteriae.*

Mrs. Neeta V. M. Khalkho

Cloning, expression, purification, activity and biochemical activity of UMSBP-2 from L. donovani and its comparison with UMSBP-1

Stage specific and species specific UMSBP 1 and UMSBP 2 expression studies revealed interesting facts. Fold of expression of UMSBP 1 in *L. tropica* and *L. tarentolae* was higher and *L. major* was lower when compared to that of *L. donovani.* Interestingly, fold of expression of UMSBP 2 was exactly opposite. Fold of expression of UMSBP 2 with respect to UMSBP 1 in promastigotes was always lower irrespective of different species by different degrees. Fold of expression UMSBP2 with respect to UMSBP1 in Amastigotes was also found to be less. We are first to report UMSBP1 and UMSBP2 from *L. donovani*. These studies will help us in better understanding of the biochemical nature of these proteins.

Dr. (Mrs.) Tripti De

Protective efficacy of galactose terminal glycoconjugates of Leishmania donovani promastigotes

A 29-kDa protein was purified from the avirulent *L. donovani* by affinity chromatography on a pea-nut agglutinin-Sepharose column. Prophylactic immunization with this protein resulted in ~ 98% clearance of splenic and hepatic parasite load of *L. donovani* infected BALB/c mice. The N- terminal region of the protein was sequenced. Blast search revealed ~ 90% homology with a hypothetical protein in chromosome 13 of the *L. major* database. Primers were designed and by PCR a single amplification product was documented. Work is in progress to generate the recombinant protein.

Developmentaly regulated galactosyltransferase, galactose terminal glycoconjugates and attenuation of L. donovani promastigotes

In *Leishmania* glycosylation disorders have been co-related to virulence phenotypes. Modifications of surface glycoconjugates with the expression of terminal galactose residues were seen to be associated with virulence attenuation of *L. donovani*. To study the relationship between galactosylation and virulence attenuation, avirulent clonal populations were generated. Removal of terminal galactose resulted in conversion of the avirulent clones to highly infective parasites, indicating a direct correlation between the terminal galactosylation and virulence attenuation. The rapid clearance of ^{14}[C] labeled attenuated parasites from circulation, with concomitant appearance of labeled parasites in the liver indicated that the terminal galactose of the attenuated parasites was recognized by the hepatic receptors.

Dr. Uday Bandopadhyay

Antiplasmodial Activity of [(Aryl)arylsulfanylmethyl]pyridine

A series of [(aryl)arylsufanylmethyl]pyridines (AASMP) have been synthesized. These compounds inhibited hemozoin formation, formed complexes (K_D = 12-20 μM) with free heme (ferriprotoporphyrin IX) at a pH close to the pH of the parasite food vacuole and exhibited antimalarial activity *in vitro*. The inhibition of hemozoin formation may develop oxidative stress in *P. falciparum* due to the accumulation of free heme. Interestingly, AASMP developed oxidative stress in the parasite as evident from the decreased level of GSH, increased formation of lipid peroxide, H_2O_2, and hydroxyl radical ($^{\bullet}OH$) in *P. falciparum*. AASMP also caused mitochondrial dysfunction by decreasing mitochondrial potential ($\Delta\psi m$) in malaria parasite as measured by both flow cytometry and fluorescence microscopy. Furthermore, the generation of $^{\bullet}OH$ may be mainly responsible for the antimalarial effect of AASMP as $^{\bullet}OH$ scavengers such as mannitol as well as spin traps, α-phenyl-n-tertbutylnitrone (PBN) significantly protected *P. falciparum* from AASMP-mediated growth inhibition. Cytotoxicity testing of the active compounds showed selective activity against malaria parasite with selectivity indices greater than 100. AASMP also exhibited profound antimalarial activity *in vivo* against chloroquine resistant *P. yoelii* (MDR). Thus, AASMP represents a novel class of antimalarial. Our work focused on the evaluation of the antimalarial activity of these compounds including the mechanistic details on the effect of heme interaction, hemozoin formation and *in vitro* and *in vivo* antimalarial effect.

Bilirubin inhibits Plasmodium falciparum growth through the generation of reactive oxygen species

Free heme is very toxic because it generates highly reactive hydroxyl radicals ($^{\bullet}OH$) to cause oxidative damage. Detoxification of free heme by heme oxygenase (HO) system is a very common phenomenon by which it catabolizes free heme to form bilirubin as an end product. Interestingly, malaria parasite, *Plasmodium falciparum* lacks HO system, but it forms hemozoin mainly to detoxify free heme. Here, we report that bilirubin significantly induces oxidative stress in the parasite as evident from the increased formation of lipid peroxide, decrease in glutathione (GSH) content and increased formation of H_2O_2 and $^{\bullet}OH$. Bilirubin can effectively inhibit hemozoin formation also. Furthermore, results indicate that bilirubin inhibits parasite growth and induces caspase – like protease activity, up-regulates the expression of apoptosis related protein (Gene ID PFI0450c) and reduces the mitochondrial membrane potential ($\Delta\psi m$). $^{\bullet}OH$ scavengers such as mannitol as well as spin trap, α-phenyl-n-tertbutylnitrone (PBN) or 2, $2^{/}$, 6, $6^{/}$- tetramethyl-1-piperidine-N-oxide (TEMPO) effectively protect parasite from bilirubin-induced oxidative stress and growth inhibition. These findings suggest that bilirubin through the development of oxidative stress induces *P. falciparum* cell death and malaria parasite lacks HO system probably to protect itself from bilirubin–induced cell death as a second line of defense

Melatonin inhibits free radical-mediated mitochondrial-dependent hepatocyte apoptosis and liver damage induced during malarial infection

We showed earlier that malarial infection significantly induces liver apoptosis mediated by oxidative stress mechanisms [Faseb. J. **20:** 1224-1226, 2006]. Thus, a non-toxic antioxidant-antiapoptotic molecule may be beneficial for hepatoprotection. Melatonin remarkably prevents hepatocyte apoptosis in mice induced during malaria as indicated by caspase 3 and TUNEL assays as well as transmission electron microscopy (TEM) of the liver tissue. The mitochondrial apoptotic pathway, which plays a critical role in liver cell death during malarial infection, was almost completely suppressed by melatonin since it corrects both the overexpression of bax and downregulation of bcl-2 as revealed by semiquantitative RT-PCR. Fluorometric studies using JC-1 documented that melatonin also restores mitochondrial transmembrane potential ($\Delta\psi m$) in malaria-infected mice liver. The antiapoptotic effect of melatonin is associated with its antioxidant role because melatonin protects liver from oxidative stress induced during malaria by scavenging the hydroxyl radicals, preventing

the depletion of GSH, inhibiting lipid peroxidation and protein carbonyl formation. The effective antioxidant dose of melatonin to protect liver from oxidative stress during malaria is 20 times lower than that of known antioxidants, vitamin C and vitamin E. Apoptosis of hepatocytes during malarial infection is well correlated with dysfunction of the liver while melatonin offers hepatoprotective effects as indicated by different liver function tests. Thus, melatonin may well be effective in combating oxidative stress-induced apoptosis and liver damage during malaria infection.

Dr. (Mrs.) Malini Sen

Evaluating the role of Wnt signaling in rheumatoid arthritis and other inflammatory disorders

Evaluating the role of WISP3 (Wnt induced secreted protein 3) in the regulation of oxidative stress and fibrosis.

Dr. (Mrs.) Mita Chatterjee Debnath

Drug incorporated PLGA nanoparticle formulation, characterization, technetium -99m labeling and biodistribution studies

Nanoparticles are solid colloidal particles ranging in size from 1 to 1000 nm, consisting of various macromolecules in which drugs can be adsorbed, entrapped or covalently attached. They serve as novel drug delivery system. Although there are a number of different polymers that have been investigated for formulating biodegradable nanoparticles, of these poly L-lactic acid (PLA), and its copolymers with glycolic acid (PLGA) have been extensively used in last decade for controlled drug delivery systems.

Chloramphenicol (CHL) is an antibacterial drug, extremely lipid soluble and easily cross the BBB. Because of its excellent CSF penetration, chloramphenicol remains the first choice treatment for staphyloccal brain abscess. Chloramphenicol is also recommended by WHO as the first line treatment of meningitis in low-income countries and is much cheaper than ceftriaxone. However most serious side effect of chloramphenicol treatment is bone marrow suppression and aplastic anaemia. Moreover, it requires several hours to cross the BBB. To minimize the toxicity of the antibiotic and to improve its bioavailability chloramphenicol (CHL) incorporated PLGA nanoparticles were prepared by emulsification solvent evaporation technique either by using polyvinyl alcohol (PVA) as emulsion stabilizer or polysorbate80 (PS-80) as surfactant and characterised by transmission electron microscopy (Fig. 9), zeta-potential measurements. The nanoparticles were radiolabeled with technetium-99m by stannous reduction method. Labeling conditions were optimised to achieve high labeling efficiency, invitro and invivo (serum) stability. The labeled complexes also showed very low transchelation as determined by DTPA challenge test (Fig. 10). Biodistribution studies of ^{99m}Tc-labeled complexes were performed after intravenous administration in mice. The concentration of ^{99m}Tc-labeled CHL-loaded PS-80 coated PLGA-NPs was relatively higher (almost 9 times) in brain than that of free drug both in 1hr and 24hr post injection and at 4hr post injection it was 5 times higher than that of free drug. However the brain uptake of CHL-loaded PLGA-NPs (containing PVA as emulsion stabilizer) in the above time periods was only 2 to 2.5 times higher than that of the free CHL. Although overall brain uptake of technetium labeled CHL-loaded nanoparticles was not very high, the significantly higher concentration of CHL-loaded PS-80 coated PLGA- NPS reaching the brain at 1hr and 24hr post injection compared to that of CHL-loaded PLGA-NPs suggesting the greater brain transport of the former. The bone marrow uptake of ^{99m}Tc-labeled CHL-loaded PLGA nanoparticles was much less than that of radiolabeled free CHL at all time points studied. At 1hr post injection period the concentration of ^{99m}Tc-labeled free drug in the bone marrow was 2 to 2.5 times higher than that of the drug loaded NPs. Where as at 24hr the injected counts of ^{99m}Tc-CHL in the bone marrow was 6 and 9.6 fold higher than that of the CHL-loaded PLGA-NPs and CHL-loaded PS-80 coated PLGA-NPs respectively. The concentration of

CHL-loaded PLGA nanoparticle coated with PS-80 exhibited relatively high brain uptake with comparatively low accumulation in bone marrow to that of free drug and CHL loaded PLGA NPs (PVA, used as emulsion stabilizer) at 24hr post injection time period. This indicates the usefulness of above delivery system for prolonged use of the antibiotic.

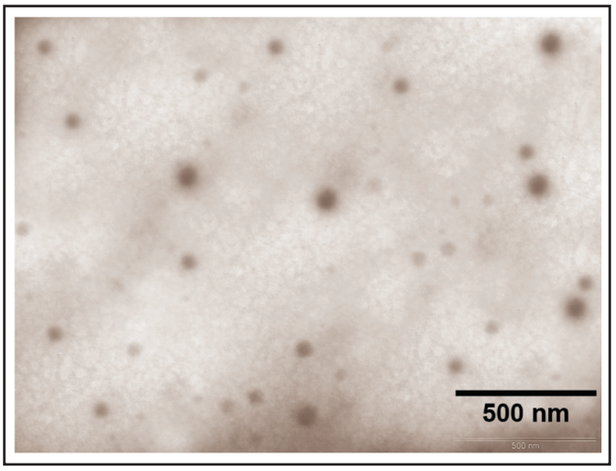


Fig. 9a

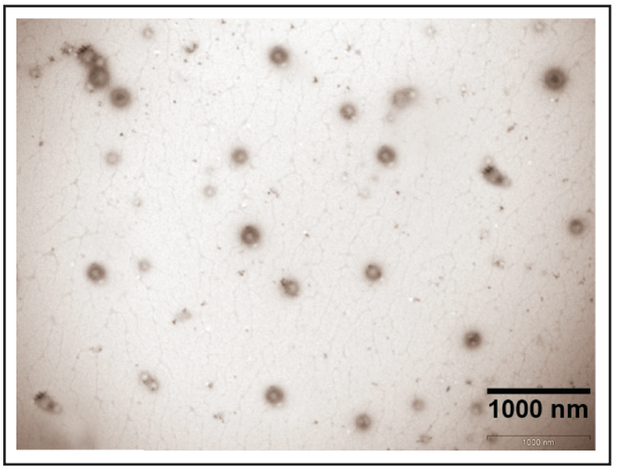


Fig. 9b

Fig. 9. Transmission electron micrograph of chloramphenicol loaded PLGA nanoparticles. (a) PVA used as emulsifier and (b) PS-80 used as surfactant.

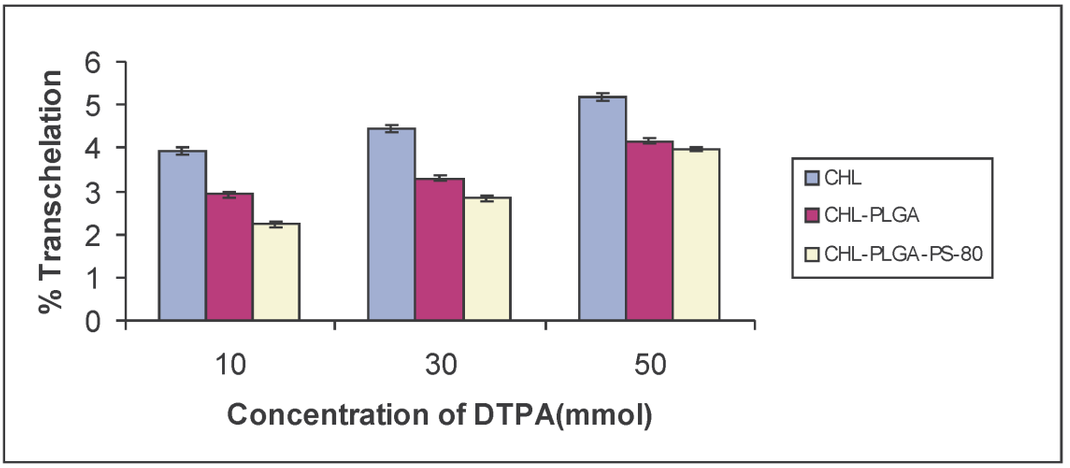


Fig. 10. Effect of DTPA on transchelation of ^{99m}Tc-labeled complexes of chloramphenicol (CHL), CHL-loaded PLGA NPs and CHL-loaded PS-80 coated PLGA NPs.

Dr. (Mrs.) Mridula Misra

Synthesis of a new peptide radiopharmaceutical for brain imaging

A new peptide Phe-Phe-Cys-Acm was synthesized by solid phase peptide synthesis (SPPS) using Fmoc chemistry. Radiolabelling of peptide was performed by addition of 0.5 ml of sterile 0.9% saline solution to the freeze dried product followed by addition of 0.5 ml sodium Pertechnetate (99mTcO4-, 1GBq in sterile 0.9% saline solution, (generated from kits supplied by BRIT, Mumbai) in nitrogen-purged water. Complexation efficiency and radiochemical purity of the corresponding complexes will be analyzed by TLC (Table 1), column chromatography and HPLC (Figs. 11 and 12).

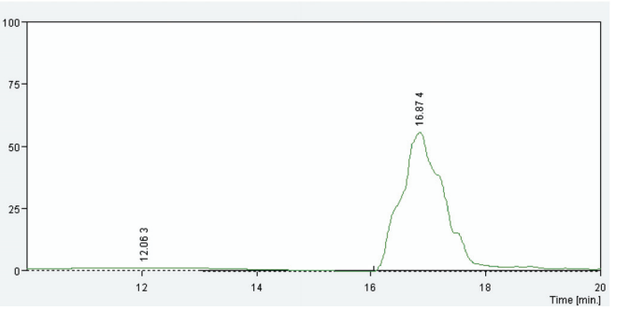


Fig. 11. HPLC of Phe-Phe-Cys-Acm (at 280nm)

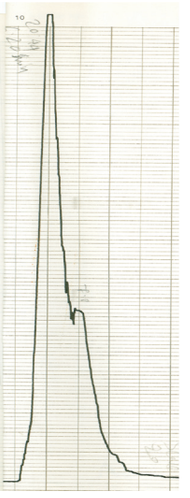


Fig. 12. HPLC of ^{99m}Tc Phe-Phe-Cys-Acm.

Table 1. Thin layer chromatography of $^{99m}TcO4^-$ and ^{99m}Tc Phe-Phe-Cys-Acm in different solvents.

Compound	Solvent System			
	Rf values			
	Methanol	Acetone	Acetonitrile	Acetonitrile: water(1:1)
$^{99m}TcO4^-$	0.1-0.75	1	0.35-0.45	
Pep Acm	0.5	0.5	0.5	0.5

Bio-distribution studies were performed in rats (200-300 g in body wieght). About 100-500 µCi chelate complexes will be injected intravenously. The organs of interest will be excised, weighed and counted at different time intervals in a well type gamma counter (Table 2).

Table 2. Biodistribution studies of ^{99m}Tc Phe-Phe-Cys-Acm in Sprauge-Dawley rat at different time points.

Organ	2min	5min	15min
Heart	0.33 ± 0.03	**0.168±0.02**	**0.089±0.035**
Blood	0.5385± 0.068	**0.3709±0.077**	**0.1125±0.067**
Liver	4.5208± 0.196	**3.86±0.201**	**2.89±0.115**
Lungs	0.654± 0.05	**0.558±0.03**	**0.465±0.04**
Spleen	4.5888± 0.13	**4.01±0.114**	**2.29±0.12**
Kidney	**13.38± 6.48**	**8.68±7.75**	**3.45±3.45**
Intestine	**0.98± 0.0087**	**0.578±0.0056**	**0.109±0.0036**
Stomach	3.91± 0.75	**2.65±0.57**	**1.76±0.58**
Bladder	35.97± 3.44	**28.97±1.45**	**18.44±0.94**
Brain	0.71± 0.006	**0.52±0.008**	**0.46±0.011**

Plasma clearance study of all radiopharmaceuticals was calculated from multiple samples after a single injection by using established method (Fig. 13).

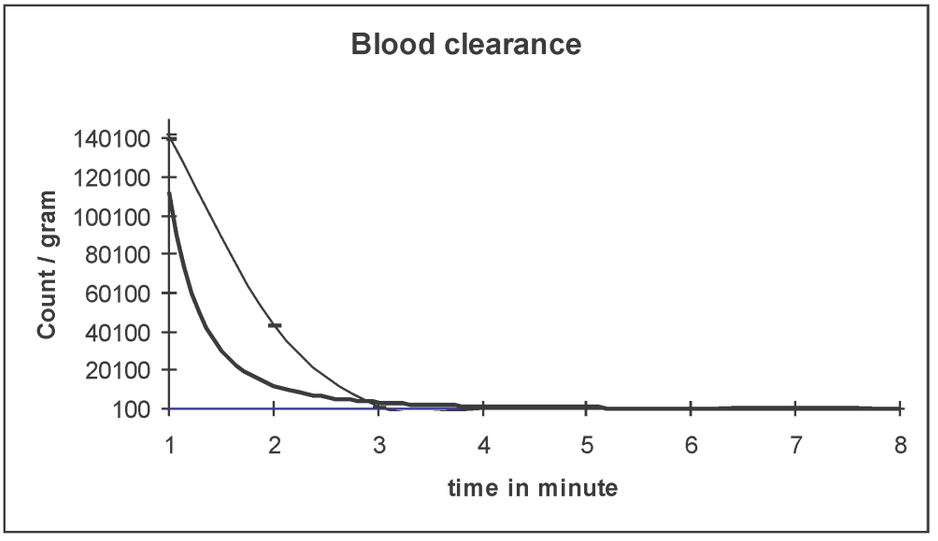


Fig. 13. Blood clearance study of ^{99m}Tc Phe-Phe-Cys-Acm in rat.

Protein binding of the radiopharmaceuticals was determined in the controls and labeled peptide treated animals by Amicon ultrafiltration unit.
% Protein Bound = (1- cpm in ultrafiltrate/cpm in plasma) x 100
% unbound = 89.87%

Imaging studies in animals

Imaging study was performed in rabbits (2.5 to 3.0 kg body weght), with peptide radiopharmaceuticals. The animals were anaesthetized (urethane) and placed under gamma camera and the radiopharmaceutical was injected through the femoral vein. Pictures were taken at regular intervals up to 1 hour with exposure of 200 to 400 K of counts.

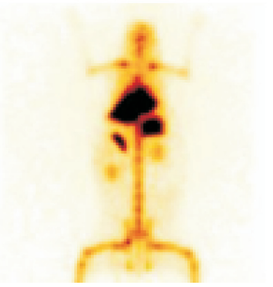


Fig. 14. Image of rabbit under gamma camera of ^{99m}Tc Phe-Phe-Cys-Acm at 2 minute PI.

Effect of plant extract on the labeling of blood elements with technetium-99m and on the morphology of red blood cells

In nuclear medicine, red blood cells (RBC) labeled with technetium-99m (^{99m}Tc) have several clinical applications. As *Bacopa monniera* (BM) is extensively used in medicine, we evaluated its influence on the labeling of RBC (BC) and plasma proteins (P) using ^{99m}Tc. The %ATI significantly decreased on BC from 95.53±0.45 to 35.41 ± 0.44, on IF-P from 80.20±1.16 to 7.40±0.69 and on IF-BC from 73.31±1.76 to 21.26± 1.40. The morphology study of RBC revealed important morphological alterations due to treatment with BM extracts (Figs. 15 and 16). We suggest that the BM extract effect could be explained by an inhibition of the stannous and pertechnetate ions or oxidation of the stannous ion or by damages induced in the plasma membrane.

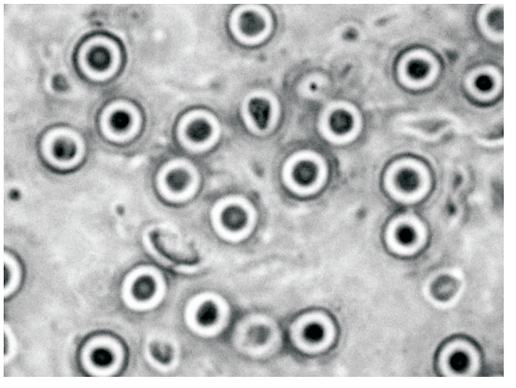


Fig. 15. Photomicrography of blood smears prepared with samples of whole blood used to label RBC with 99mTc (blood samples were previously treated BM extract 200 mg/ml). After fixing and staining the morphology of the red blood cells was evaluated under an optical microscope (X1000).

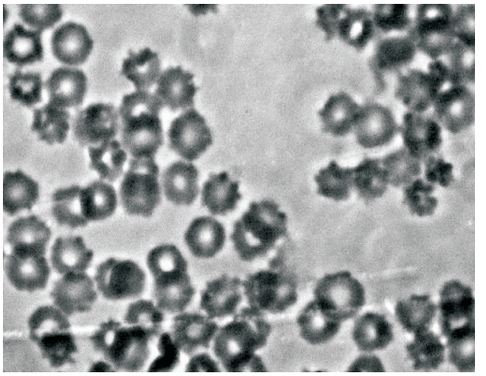


Fig. 16. Photomicrography of blood smears prepared with samples of whole blood used to label RBC with 99mTc (control). After fixing and staining the morphology of the red blood cells were evaluated under an optical microscope (X1000).

Technical Staff

Mr. Rabindra Nath Mandi, Mrs. Arti Khetrapal, Mr. Asish Mallick, Mr. Kshudiram Naskar, Mr. Anirban Manna, Dr. Kalidas Paul, Mr. Pratap C. Koyal, Mr. T. K. Chakraborty

Pool Officers, RAs, Research Fellows etc.

Dr. Neeta Datta, Dr. Saswati Laha, Mr. Agenyo Ganguly, Mr. Amit Roy, Mr. Somdeb Bose Dasgupta, Mrs. Rakhee Das, Mrs. Bijoylaxmi Banerjee, Mr. Souvik Sengupta, Dr. Tapasi Das, Dr. Anindita Bhattacharya, Mr. Arijit Bhattacharya, Mr. Susanta Kar, Ms. Arunima Biswas, Ms. Gunjan Sharma, Mr. Writoban BasuBall, Mr. Supriya Srivastava, Mr. Suschandra Chowdhury, Ms. Angana Ghosal, Mr. Chandan Mandal, Ms. Susmita Mandal, Mr. Sajal Samanta, Mr. Biswajit Khatua, Dr. Rajatava Basu,Dr. Suniti Bhaumik, Ms. Jayati Basu, Ms Subha Sen, Mr Rajan Guha, Mr. Ranjan Dhar, Ms. June Ghosh, Dr. Labanya Mandal, Dr. Srabanti Rakshit, Mrs. Jayashree Bagchi Chakraborty, Mr. Kausik Paul, Mr. Nabendu Biswas, Ms. Sudipta Bhowmick, Ms. Smriti Mondal, Mr. Partha Palit, Mr. Saumyabrata Mazumdar, Ms. Amrita Das, Mr. Mithun Maji, Dr. Tanusree Das, Mr. Amit De, Ms. Epshita Chatterjee, Mr. Amit K. Baidya, Ms. Subhra Pradhan, Mr. Raghawan, Mr. Debarshi Sengupta, Mr. Bhabatosh Das, Ms. Sangita Shah, Mr. Ritesh Ranjan Pal, Mr. Kalpataru Halder, Mr. Stayabrata Bag, Mr. Joubert Banjop Kharlyngdoh, Mr. Siddhartha Kumar Bhaumik, Mr. Manoj Kumar Singh, Mr. Subir Karmakar, Mr. Chinmoy Pal, Mr. Manish Goyal, Mr. Sumanta Dey, Mr. Samik Bindu, Mr**.** Kamal Krishna Halder, Ms. Sarmistha Majumder,Mr. R Srinivas Rao, Mr. Debdut Naskar, Mr. Supratim Mandal, Mr. George Maiti, , Dr. (Mrs.) Kakai De, Ms. Susmita Chandra

Names of Project Assistants

Mrs. Rita Maity, Mr. Saptrashi Roy, Mr. Kaushik Bhattacharya, Ms. Sayantani Sarkar, Dr. Monidipa Ghosh Ray, Mr. Avik Acharya Chowdhury, Mr. Jaydeep Chowdhuri, Mr. Surjendu Bikash Debnath, Ms. Roma Sinha, Mr. Pradyot Bhattacharya, Ms. Manjarika De, Ms. Srijani Ray, Mr. Sourav Chackraborty, Mr. Athar Alam.

Summer Trainees

Ms. Paulomi Biswas, Ms. Rajani Gupta, Ms. Saheli Chakraborty, Ms. Saswati Ghosh, Mr. Abhishek Kumar, Mr. Saurav Rawal, Ms. Moumita Sarkar, Ms. Ranita Datta, Ms. Roshni Roychoudhury, Mr. Alimpon Mukherjee

Administrative Staff

Mr. Dipak Guin, Mrs. Moumita Majumdar, Mr. Asim Roy

Lab Assistant

Mr. Narendra Pradhan, Mr. Biswajit Mandal, Mrs Seema Halder, Sib Prasad Sharma


BIACORE
IICB-LB-31

Cell Biology & Physiology

Drs. K. P. Mohanakumar, Sumantra Das, Syed N. Kabir, Smritinath Chakraborty, Tuli Biswas, Chhanda Mitra, Arun Bandyopadhyay, Tushar Chakraborty, Sandhya R. Dungdung, Sib Sankar Roy, Padma Das, Mrinal Kanti Ghosh

CELL BIOLOGY

Dr. Tuli Biswas and group

Iron deprivation as an approach in the development of antileishmanial therapeutics

Leishmania sp. requires iron (Fe) for their growth and survival. While residing within phagosomes, pathogens gain access to adequate Fe for their growth from endogenous macrophage sources. To assess the efficacy of metal chelation on the proliferation of the parasites, we tested the antileishmanial function of Quercetin (Qr) [3, 3', 4', 5, 7-pentahydroxyflavone], 5-hydroxy 3, 6, 7, 3', 4' pentamethoxyflavone and deferoxamine (DFO) under an *in vivo* treatment schedule. Among the compounds studied, the antiproliferative activity of Qr was significantly more effective than the other two (Fig. 1).

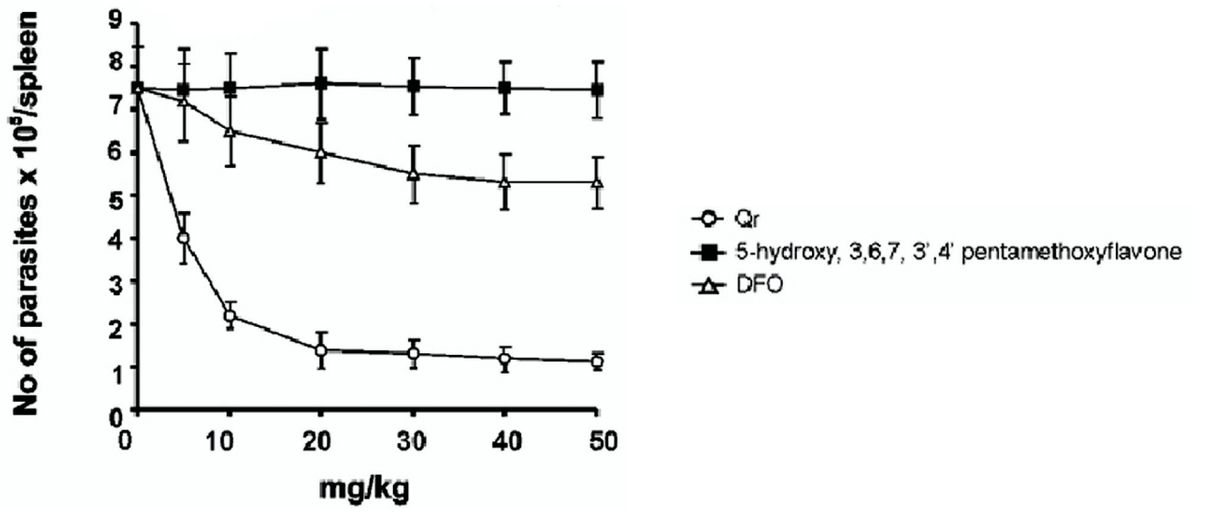


Fig. 1. Effect of metal chelation on the proliferation of parasites: Splenic parasite load in infected hamsters subjected to in vivo treatment with different drugs. Results are mean ± SEM.

Since lipophilicity of a compound is a crucial factor in determining its permeability across the cell membrane, greater effectiveness of Qr may be partly due to its lipophilicity, allowing the flavonoid to permeate the cell membrane and reach to the Fe pools more readily than the less lipid soluble chelator, DFO. Interaction with metal ions can result in the formation of chelates and the reduction of metal ion, both depending on the flavonoid structure. Fe^{3+} reducing capacity of the flavonoids has been assigned to the simultaneous presence of catechol groups in 3', 4' positions in the B ring and 3-hydroxy group in the C ring (Fig. 2).

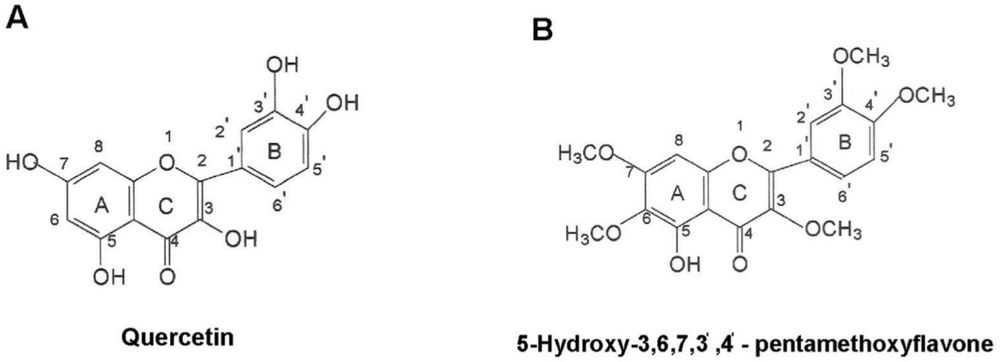


Fig. 2. Structures of flavonoids. (A) Qr (B) 5-hydroxy 3, 6, 7, 3', 4' pentamethoxyflavone.

Qr satisfies these structural features, which is reflected from the 25 nm bathochromic shift in the band I spectrum in the presence of Fe^{3+}. 5-hydroxy 3, 6, 7, 3', 4' pentamethoxyflavone lacks these structural advantages essential for the metal chelating ability, thus exhibiting no spectral shift under similar experimental conditions. Methylation prevented 5-hydroxy 3, 6, 7, 3', 4' pentamethoxyflavone to bind with Fe^{3+} and induce antileishmanial activity (Fig. 3). Results indicate on the importance of Fe-binding domain in the flavonoids for their antileishmanial function, implicating Fe as a target in the development of antileishmanial therapeutics.

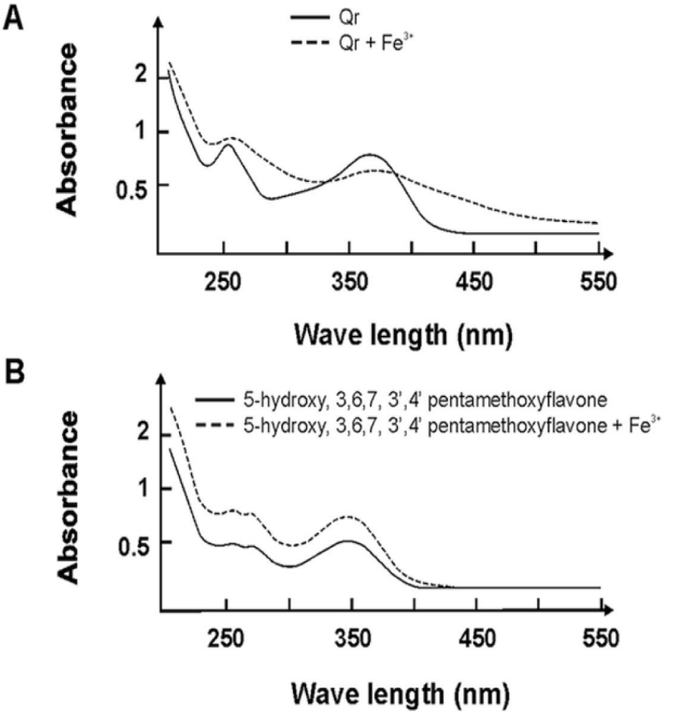


Fig. 3. Evaluation of iron chelation capacity of (A) Qr and (B) 5-hydroxy 3, 6, 7, 3', 4' pentamethoxyflavone. Spectral shifts in band I (300-550 nm) and band II (240-285 nm) of the flavonoids were determined in absence (continuous line) or in presence (broken line) of equimolar concentration of Fe^{3+}.

Studies on the mechanism of hemolysis in chronic arsenic toxicity

Arsenic contamination through drinking water is a major health problem of global concern. In West Bengal, more than 6 million people show symptoms of arsenic toxicity and a large number of people are suspected to be sub-clinically affected. Exposure to arsenic is known to result in anemia with an implication towards hemolytic mechanism. A collaborative study with Dr. A. K. Giri of Human Genetics and Genomic group has been undertaken with an objective to study the effect of chronic arsenic exposure on erythrocyte structure and function which may contribute to the understanding of the pathogenesis of vascular diseases in arsenic-exposed individuals.

We have observed profound changes in the ultrastructure of erythrocytes resulting from arsenic toxicity. Decreased cellular deformability is likely to account for the increased red cell destruction in the exposed population. lipid bilayer constituting the membrane has been entrusted with the responsibility for preserving cellular deformability. Normally phospholipids (PLP) are asymmetrically distributed across the lipid bilayer of the erythrocyte membrane with the lipids of the outer monolayer being closely packed than the lipids of the inner membrane leaflet. The fluorescent dye MC540 was used as a probe to monitor the molecular packing of PLP in the outer leaflet of the red cell membrane. Fig. 4 depicts substantial intercalation of the dye into the disordered outer layer of the exposed red cell membrane confirming the disruption of lipid packing in these cells. Results indicate the role of arsenic in the disruption of cell membrane integrity, which promotes a hemolytic response leading to the development of anemia.

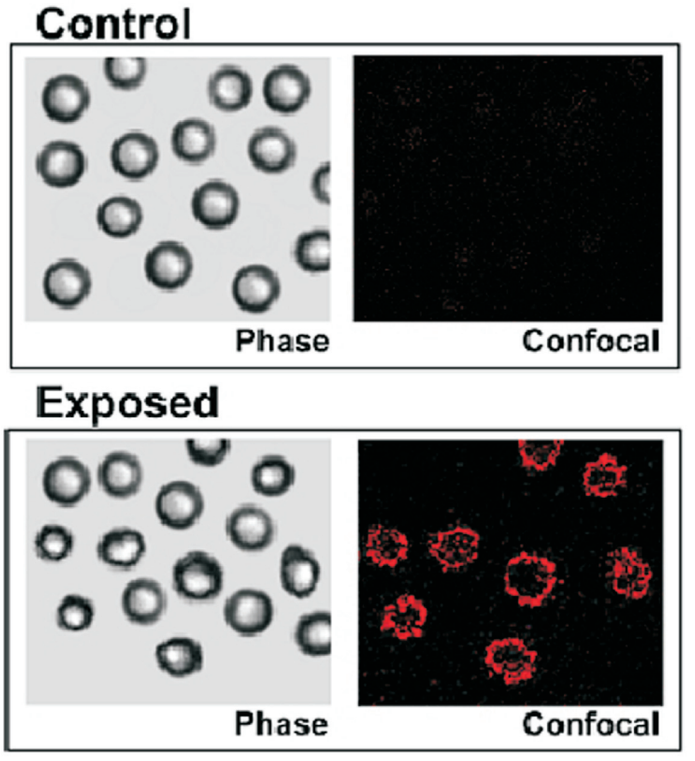


Fig. 4. Alteration of erythrocyte membrane lipid asymmetry due to arsenic exposure. Phase contrast (left panel) and confocal (right panel) images of erythrocytes from the exposed population. The confocal image shows fluorescence due to the binding of MC540 to the exposed erythrocyte membrane.

MOLECULAR ENDOCRINOLOGY

Dr. Arun Bandyopadhyay and group

Understanding molecular mechanism of dysfunction of hypertrophied

The myocardial remodeling and fibrosis contributes significantly to cardiac dysfunction by altering cardiac contractility and ventricular pump function in diseased hearts. We have also developed a hypertrophy model in rat by administering dexamethasone, a synthetic analogue of glucocorticoid, for a period of 2-3 weeks. In this model, we have examined the signaling mechanism leading to cardiac remodeling, contractile abnormality and dysfunction. We have monitored various parameters of the hemodynamics by recording PV-loops of the hypertrophied heart. Moreover, we have also studied remodeling, collagen metabolism, fibrosis, hypoxia and oxidative stress in the same model. Dexamethasone caused time dependent increase in the heart weight to body weight ratio (P<0.001, n=20) and an increased deposition of collagens in the extracellular matrix of the left ventricle which were inhibited by both mifepristone and losartan (Table 1, Fig. 5). The mRNA levels of angiotensinogen and angiotensin II type 1 receptor were increased by dexamethasone which was not blocked by mifepristone or losartan. The rate of oxygen consumption was decreased in association with increased expression of hypoxia inducible factor in dexamethasone treated rat heart suggesting the dysfunction of mitochondrial respiration in hypertrophied heart (Fig. 6). Lipid peroxidation in left ventricular tissue was significantly (P<0.01, n=3) increased by dexamethasone. The activity of superoxide dismutase was significantly (P<0.01, n= 3) increased whereas the catalase activity was reduced in dexamethasone treated rat ventricular tissue. Dexamethasone treatment resulted higher level of heat shock protein 70 in left ventricular tissues and increased lactate level in the serum. The systolic blood pressure was increased whereas the heart beat, ejection fraction and cardiac output (n=6) were decreased in dexamethasone treated rat (Table 2). All these changes were reversed by mifepristone and losartan. The excess of glucocorticoid causes pathophysiolgical changes of the myocardium which might lead to slower heart beat, reduced cardiac output and dysfunction in angiotensin II dependent manner. Therefore, angiotensin II appears to play a crucial role in glucocorticoid-induced cardiac malfunction.

Table 1. Dexamethasone-induced cardiac hypertrophy is inhibited by mifepristone and losartan.

Treatment	Control	DEX	DEX + MIF	DEX + LOS
HW (mg)	583 ± 3.1	723 ± 9.7*	588 ± 2.45	592 ± 2.88
BW (g)	205 ± 1.5	185 ± 1.6	200 ± 1.44	197 ± 1.3
HW/BW (mg/g)	2.84 ± 0.02	3.90±0.04*	2.94 ±0.02	3.0 ± 0.03

* P< 0.001 vs control, n=20

Table 2. Hemodynamic parameters of heart function

Experiment	Control	DEX	DEX + MIF	DEX + LOS
Heart beat	333.86 ± 14.79	275.93 ± 5.41*	370.87 ± 4.86	370.73 ± 7.47
Pmax	108.35 ± 4.6	147.93 ± 1.54*	86.45 ± 3.3	110.99 ± 5.68
Pmin	20.08 ± 0.91	14.11 ± 0.51	14.02 ± 2.28	21.76 ± 0.14
EF	25.46 ± 1.38	14.83 ± 0.91*	28.75 ± 2.06	28.03 ± 3.96
CO	24053 ± 740	7997 ± 121*	22936 ± 2105	23011 ± 121
dP/dt max	5402 ± 665	4274 ± 34*	6441 ± 185	5102 ± 283
dP/dt min	5115 ± 529	3555 ± 195*	4193 ± 80	5680 ± 897

* P< 0.01 vs control, n=6

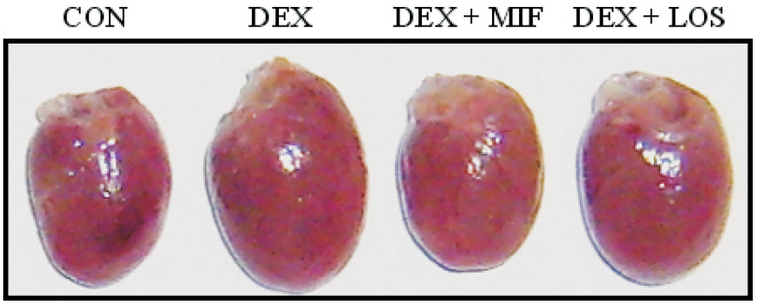


Fig. 5. Representative image showing enlarged ventricular portion after 15 days of treatment with either with vehicle (CON), dexamethasone (DEX) or dexamethasone with mifepristone (DEX + MIF) or losartan (DEX + LOS) for 2 weeks.

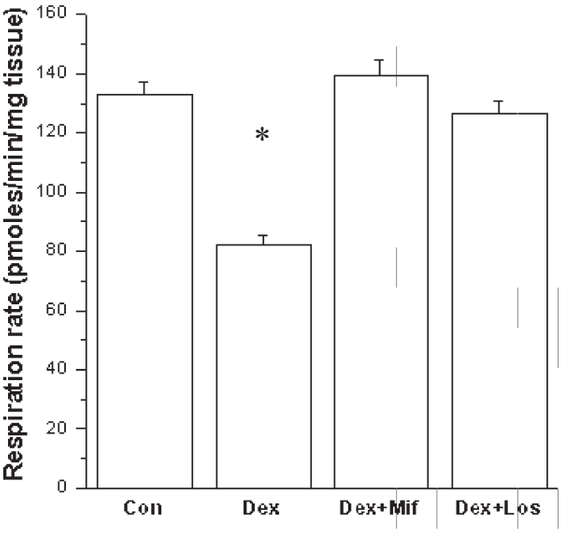


Fig. 6. Oxygen consumption in hypertrophied left ventricle. Rate of respiration was measured using ventricular tissues of rat treated either with vehicle or dexamethasone (DEX) or dexamethasone with mifepristone (DEX + MIF) or dexamethasone with losartan (DEX + LOS) for 15 days. Ventricular tissue was minced to very small pieces and the rate of oxygen upake was measured as described in Methods and Methods. Each bar represents mean ± SEM of 3 separate observations. * Significantly different at P <0.01 vs control.

Dr. Sib Sankar Roy and group

Pitx2 Homeodomain Transcription Factor: Transcriptional regulation of target genes in ovarian tissue for development and maintenance

Our group has shown the expression of Pitx2 gene, a bicoid related homeodomain transcription factor in rat ovary and testis and also in human subjects (Ghosh et al. Cell Physiol Biochem, 20: 887-898, 2007). We were interested to look into other functions that it plays in mammalian gonads. Besides maintaining ovarian structural integrity, Pitx2 is essential for cellular proliferation and it is a transcriptional regulator of crucial cell cycle controlling genes, like, cyclin D1, -D2 and c-myc in gonadal tissue. A cluster of gene that is probable target of Pitx2 has been identified by ChIP-chip method. We have identified the cofactors that are associated with Pitx2 in ovary and regulate different target gene expression in association with Pitx2. Looking into its target genes and associated functions, it was presumed that Pitx2 could be inevitable for ovarian development, too. These information will be very much useful for understanding the pathophysiology of ovarian tissue and for further therapeutic application.

The role of different homeodomain transcription factors in embryonic development is well documented. Pitx2, a member of this family plays important role during development of multiple organs like heart, brain, pituitary, and left-right asymmetry determination but till now its expression and function in gonad is poorly known. Our previous study suggests the involvement of different Pitx isoforms in ovarian function in adult rat. The present study shows the temporal and spatial expression pattern and localization of Pitx2 throughout the embryonic development (like ED-14.5, -16.5, -18.5 and -20.5) as well as in neonatal and adult gonads of both sexes. This expression has been shown by RT-PCR, Real-time PCR, immunohistochemical and immunofluorescence techniques. At the same time a Pitx2 interacting cascades of different co-factors like Pit-1, Lhx3, GCMa was observed to interact physically and co-localize with Pitx2 in the same tissue in stage dependent manner, which was detected by Co-IP and co-immunofluoresence microscopy. Pitx2 could act as a down stream effector of Wnt/TGF-β signalling pathway in tissue dependent manner. Our preliminary study shows that Wnt signalling pathway play an important role in gonadal development and the significant up and down regulation as well as overlapping and non-overlapping pattern of Wnt signalling components like Lef-1, TCF-1, TCF-4, Axin2 was observed in stage dependent manner. All these information support that Pitx2-controlled regulatory network play important role during gonadal development. Further and detail study is necessary to explore complete Pitx2 networking during gonadal development (Fig. 7).

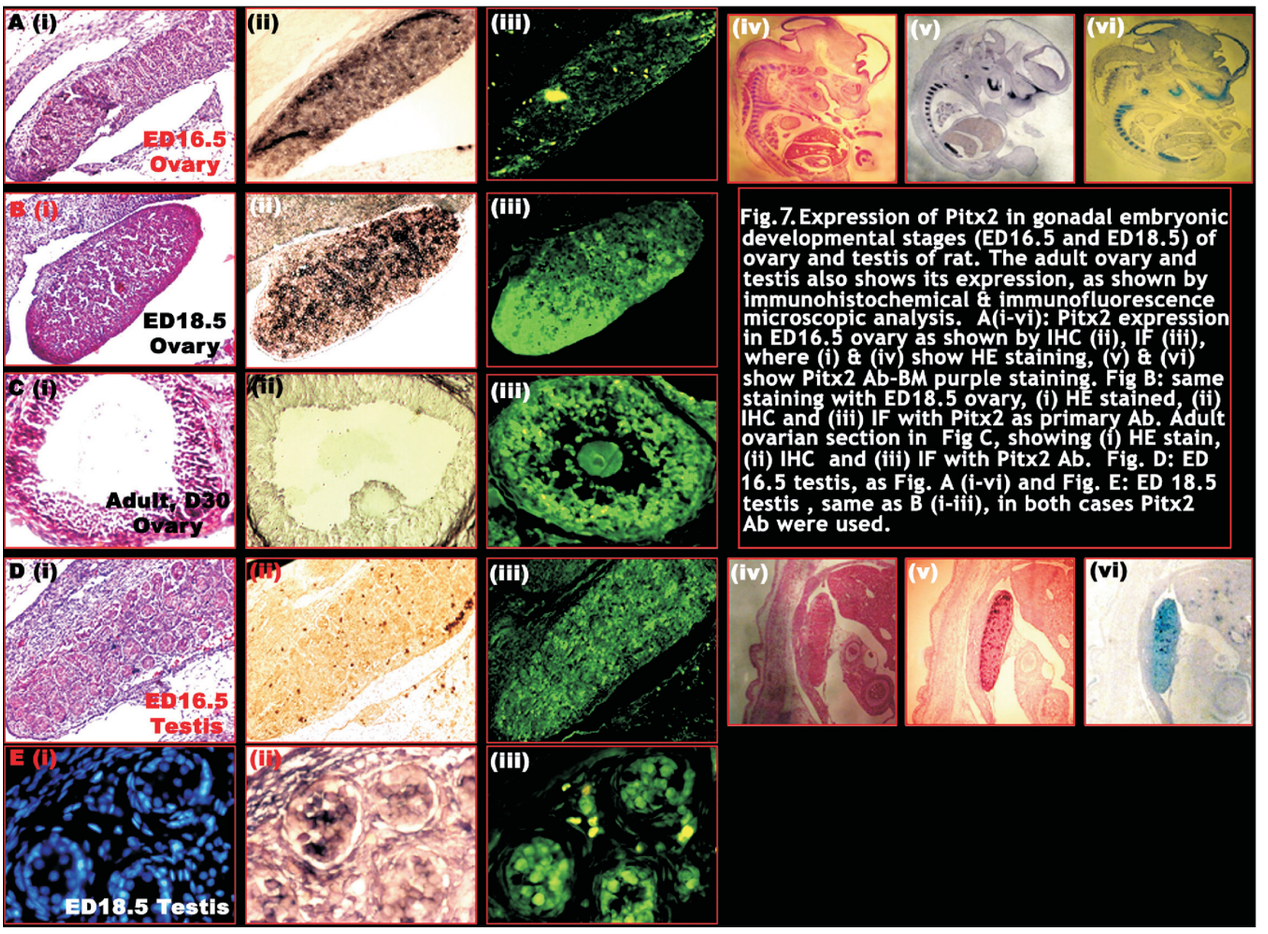


Fig. 7. Expression of Pitx2 in gonadal embryonic developmental stages (ED16.5 and ED18.5) of ovary and testis of rat. The adult ovary and testis also shows its expression, as shown by immunohistochemical & immunofluorescence microscopic analysis. A(i-vi): Pitx2 expression in ED16.5 ovary as shown by IHC (ii), IF (iii), where (i) & (iv) show HE staining, (v) & (vi) show Pitx2 Ab-BM purple staining. Fig B: same staining with ED18.5 ovary, (i) HE stained, (ii) IHC and (iii) IF with Pitx2 as primary Ab. Adult ovarian section in Fig C, showing (i) HE stain, (ii) IHC and (iii) IF with Pitx2 Ab. Fig. D: ED 16.5 testis, as Fig. A (i-vi) and Fig. E: ED 18.5 testis , same as B (i-iii), in both cases Pitx2 Ab were used.

Hypothyroidism associated ovarian disorders: a molecular and biochemical study

Our group had earlier shown the role of lysyl hydroxylase and matrix metalloproteases in collagen metabolism in ovarian tissue in normal and hypothyroid condition. The results indicate that in hypothyroid condition collagen biosynthesis in ovary seems to be disturbed with concomitant enhancement in collagen degradation resulting in disintegration of overall ovarian structure. To unravel the regulation of Plod2 gene expression in ovary, we identified and deciphered the function of Pitx2 in ovary and showed that it binds to Plod2 promoter by chromatin immunoprecipitation technique (ChIP) and that it is an upstream activator of Plod2 gene by siRNA mediated gene knock down study. Ets-related factor mediated transcriptional regulation of different identified MMPs in ovarian tissue is being studied. Hence, to understand the genetic, molecular and biochemical basis of hypothyroidism-associated reproductive disorders, our group has identified and characterized several significant genes. We are also trying to find out the role of other related genes in these disorders.

Role of mitochondrial dysfunction and insulin resistance in type 2 Diabetes and evaluation of anti-diabetic principles

In this project we want to investigate the molecular mechanism of insulin resistance. Insulin resistance or loss of insulin signal is a complicated process; it involves the action of many genes. The detail mechanism of insulin resistance and diabetes type 2 is not known yet. The role of mitochondria and mitochondrial proteins is very much important in causing diabetes type 2. We have shown the expression profiles of mitochondrial genes that are involved in diabetes type 2. In this regard the role of PGC1α and uncoupling proteins (UCP-2 and -3) is also shown. The extent of mitochondrial membrane viscosity and membrane potential in diabetic animal model is being studied. A number of herbal components are also being screened for their antidiabetic activity by using sensitive biochemical and molecular biological techniques. Their mode of action is being investigated in different type 2 diabetic rat and mice models.

NEUROSCIENCE

Dr. K. P. Mohanakumar and group

Neurodegeneration and Neuroprotection

Pathophysiology of neurodegenerative disorders such as Parkinson's disease (PD) and Huntington's disease (HD) and neuroprotective measures were investigated. During the period under report, it has been demonstrated that mitochondrial complex-I dysfunction is present in the 3-nitropropionic acid (3-NP) model of HD. We have also shown that long-term L-DOPA treatment of the mainstay PD drug L-DOPA, increase the dopamine levels at the cost of serotonin metabolism in discrete regions of the rat brain. This imbalance of neurotransmitter metabolism may be the cause of overt cognitive, motor and psychological functional aberrations seen in parkinsonian patients following prolonged L-DOPA treatment. In another study, we have shown that controlled release of dopamine in the striatum from a biodegradable hydrogel leads to functional recovery in a hemiparkinsonism rat model of PD. In another study we have demonstrated that muscarinic cholinergic receptor antagonist, atropine increases serotonin, but not dopamine levels in discrete brain regions of mice.

Mitochondrial dysfunction in huntington's disease

Mitochondrial complex-I dysfunction has been observed in patients of Huntington's disease (HD). We assessed whether such a defect is present in the 3-nitropropionic acid (3-NP) model of HD. Rats treated with 3-NP (10-20 mg/kg i.p., for four days) exhibited weight loss, gait abnormalities and striatal lesions with increased

glial fibrillary acidic protein immunostaining on 5th and 9th days, while increase in striatal dopamine and loss of tyrosine hydroxylase immunoreactivity were observed on 5th day following treatment. We report for the first time a dose-dependent reduction in complex-I activity in the cerebral cortex when analyzed spectrophotometrically and by blue native-polyacrylamide gel electrophoresis following 3-NP treatment. The citrate synthase normalised activities of mitochondrial complex-I, -II, -(I+III) and -IV were decreased in the cortex of 3-NP treated rats. In addition, succinate driven state 3 respiration was also significantly inhibited *in vivo* and *in vitro* in the isolated mitochondria. These findings taken together with the observation of a significant decrease *in vivo* but not *in vitro* of state 3 respiration with NAD^+-linked substrates, implicate complex-I dysfunction in addition to irreversible inhibition of complex-II and succinate dehydrogenase activity as a contributing factor in 3-NP-induced cortico-striatal lesion (Fig. 8-10).

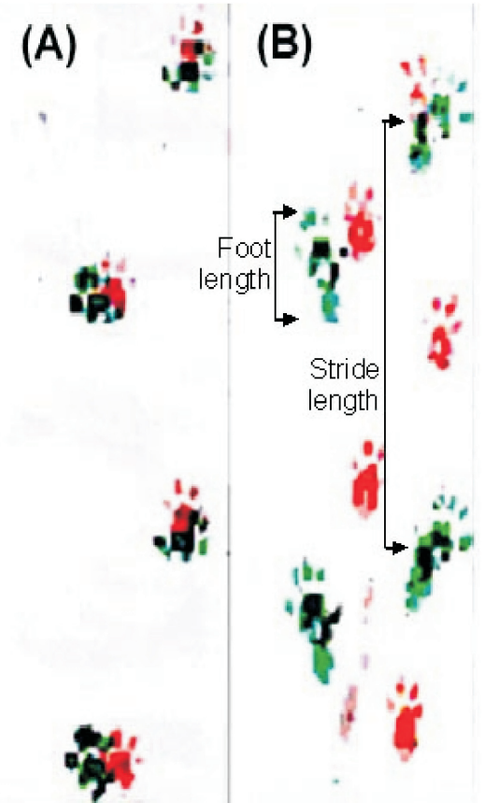


Fig. 8. 3-NP-induced changes in behavior were measured in rats administered saline or 3-NP (10 or 20 mg/kg, i.p, once daily for 4 days). Representative footprint pattern obtained from **(A)** a control animal and **(B)** a 3-NP (20 mg/kg) treated animal on day 5. The set of points, between which stride length and footprint length are measured, have been marked out.

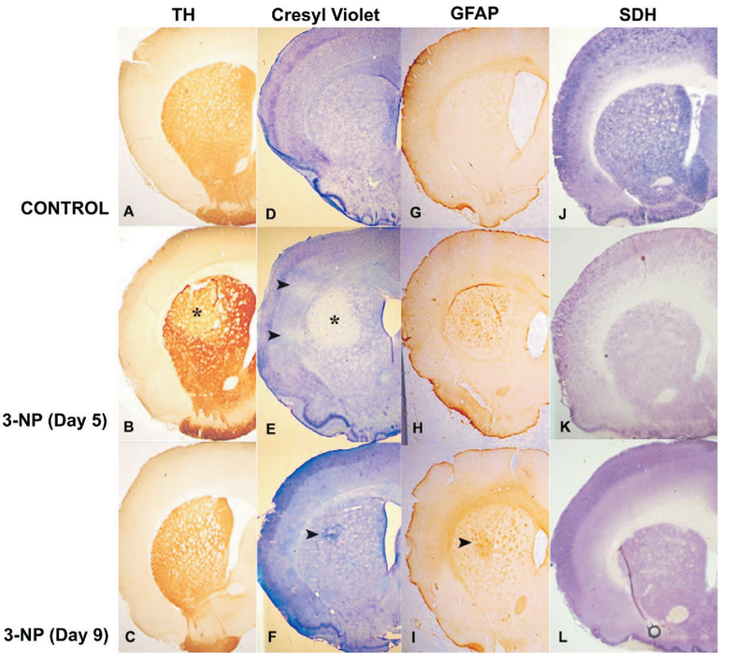


Fig. 9. Brain sections from sham control **(A, D, G, J)** or 3-NP (20 mg/kg) treated rats were processed on the 5th day **(B, E, H, K)** or 9th day **(C, F, I, L)** for tyrosine hydroxylase immuno-reactivity **(A, B, C)**, cresyl violet staining **(D, E, F)**, glial fibrillary acidic protein immunoreactivity **(G, H, I)** and succinate dehydrogenase activity **(J, K, L)**. Representative sections from n = 4-5 animals are shown at a magnification of 2.5X. Stars indicate the striatal lesions, the arrowheads in **E** indicate the cortical lesion and those in **F** and **I** point out the reactive gliosis in the striatal lesion.

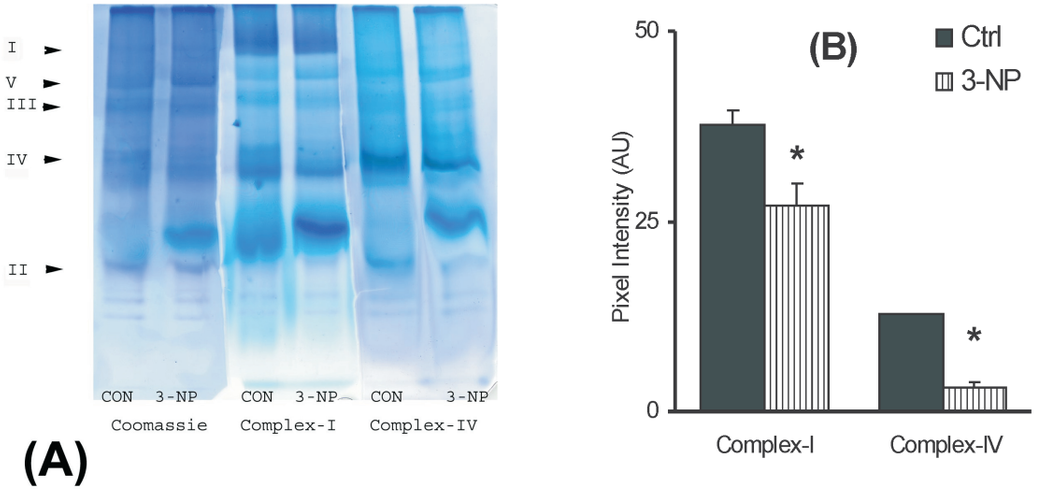


Fig. 10. Saline (CON) and 3-NP treated (20 mg/kg) rats were sacrificed and the mitochondria from cerebral cortex were prepared for BN-PAGE. **(A)** Representative BN-PAGE, showing protein staining (lanes 1,2), activity staining for complex-I (lanes 3,4) and complex-IV (lanes 5,6). The positions based on activities of the various mitochondrial complexes are indicated on the left. **(B)** Intensity of complex-I and -IV is plotted as arbitrary units. The activity bands of complex-I (6A, Lane 3, 4) were divided by the intensity of the protein bands of complex-I (6A, Lane 1, 2). Similarly, the activity bands of complex-IV (6A, Lane 5, 6) were divided by their protein bands (6A, Lane 1, 2). The experiment was done in triplicate using samples prepared from 3 animals in each experiment.

Long-term L-DOPA treatment increase the dopamine levels at the cost of serotonin metabolism

The treatment of choice for Parkinson's disease is 3,4-dihydroxyphenylalanine (L-DOPA) with peripheral decarboxylase inhibitor, but long-term therapy leads to motor and psychiatric complications. In the present study we investigated 5-hydroxytryptamine (5-HT) and dopamine (DA) concentrations in serotonergic and dopaminergic nuclei following chronic administration of L-DOPA. Rats were administered L-DOPA (250 mg/kg) and carbidopa (25 mg/kg) daily for 59 and 60 days, and sacrificed on the 60th day, respectively at 24 h and 30 min after the last injections. L-DOPA, norepinephrine (NE), 5-HT, 5-hydroxyindoleacetic acid (5-HIAA), DA, homovanillic acid (HVA) and 3,4-dihydroxyphenylacetic acid (DOPAC) were measured in striatum, nucleus raphe dorsalis (NRD), nucleus accumbens (NAc), substantia nigra, cerebellum and cortex employing HPLC-electrochemical procedure. The present results suggest that long-term L-DOPA treatment results in significant loss of 5-HT in serotonergic and dopaminergic regions of the brain. Furthermore, while L-DOPA metabolism *per se* was uninfluenced, dopamine metabolism was severely impaired in all the regions. The imbalance of serotonin and dopamine metabolism may be the cause of overt cognitive, motor and psychological functional aberrations seen in parkinsonian patients following prolonged L-DOPA treatment (Fig. 11-13).

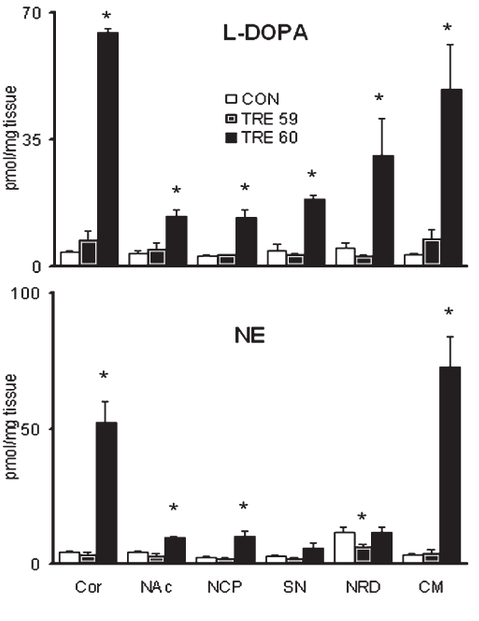


Fig. 11. L-DOPA accumulation is different in various brain regions. L-DOPA concentrations in different brain regions were found to be comparable to the control value 24 h after chronic administration of L-DOPA. However, the dopamine precursor levels detected in various brain regions were found to be significantly different following 30 min of its administration, as for eg, while cerebellum and cortex showed 16- and 17-fold increase, NRD, NCP, SN and NAc depicted respectively 6-, 5-, 4.5- and 4-fold increase in L-DOPA concentration (upper panel). Levels of NE was found be increased in NAc, NCP, cortex and cerebellum (lower panel).

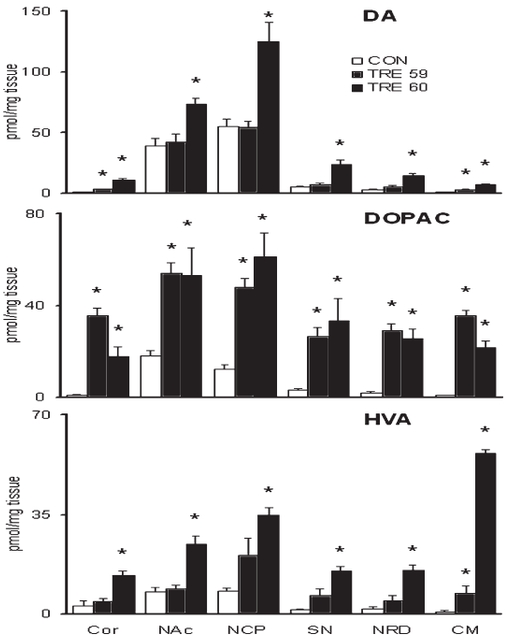


Fig. 12. Effects of long-term administration of L-DOPA on DA metabolism. In animals administered with L-DOPA for 60 days and analyzed half an hour after the last dose, a significant increase of DA in NCP, SN, NAc, NRD, cortex and cerebellum was observed (upper panel). Whereas, in animals administered L-DOPA for 59 days and analyzed on the 60th day, a significant increase of DA was available only in the cortex and cerebellum. DOPAC was significantly increased in all the regions studied following 30 min or 24 h after prolonged L-DOPA administration (middle panel). However, HVA was found to be increased in all the brain areas only after 30 min of L-DOPA, but not in animals sacrificed after 24 h (lower panel).

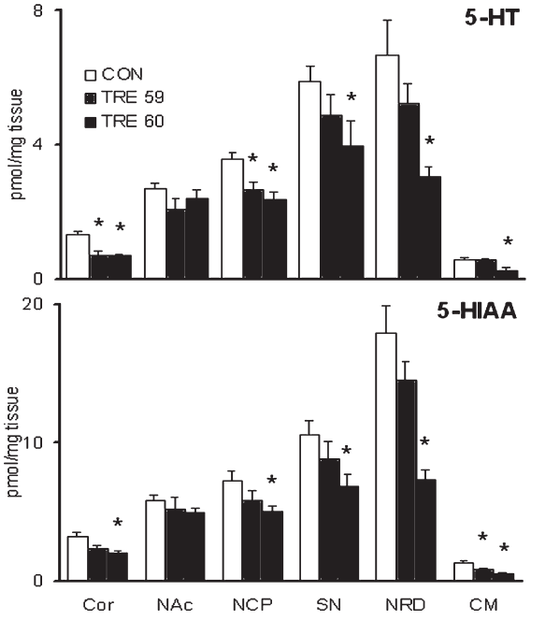


Fig. 13. Effects of long-term administration of L-DOPA on 5-HT metabolism. A significant decrease in 5-HT (upper panel) and 5-HIAA (lower panel) levels in all the brain regions, except NAc was seen in the animals analyzed after 60 days of L-DOPA treatment (sacrificed after half an hour of last L-DOPA dose). In animals treated with L-DOPA for 59 days a decrease in 5-HT level was found only in the cortex and NCP after 24 h.

Unilateral implantation of dopamine loaded biodegradable hydrogel in the striatum attenuates motor abnormalities in the 6-hydroxydopamine model of hemi-parkinsonism

Currently available therapies for PD are symptomatic. In the present investigation, we studied the effects of controlled release of dopamine (DA) in the striatum from the polymer matrices on functional recovery in a rat model of hemiparkinsonism, created by unilateral intranigral infusion of the well-known dopaminergic neurotoxin, 6-hydroxydopamine (6-OHDA). Intranigral administration of 6-OHDA (8 g in l) caused significant DA depletion (>80%) in the striatum, ipsilateral to the side of infusion on the 18th day. These animals displayed amphetamine-induced ipsilateral and apomorphine-induced contralateral rotational behavior, when examined on the 14th and 16th days respectively. Implantation of a controlled release delivery system (a hydrogel obtained by mixing dextran dialdehyde cross-linked with gelatin) containing DA in the denervated striatum on the 1st day significantly abolished the amphetamine and apomorphine-induced stereotypic rotational behaviour in these animals. The hydrogel embedded with dopamine implanted on the 18th day post-6-OHDA infusion significantly attenuated apomorphine-induced contralateral circling behaviour in these rats. The recovery was visible for about 17 days thereafter, the syndrome fully reappeared. The present results indicate that DA released from the polymer matrix alleviates experimental parkinsonism in 6-OHDA-lesioned rats, suggesting that controlled intrastriatal release of DA or any DA-ergic drugs from a polymer matrix may provide an alternative method for the treatment of Parkinson's disease. This approach may be useful in substantially reducing the oral dose of drugs that develop tolerance, and with severe systemic effects (Fig. 14-18).

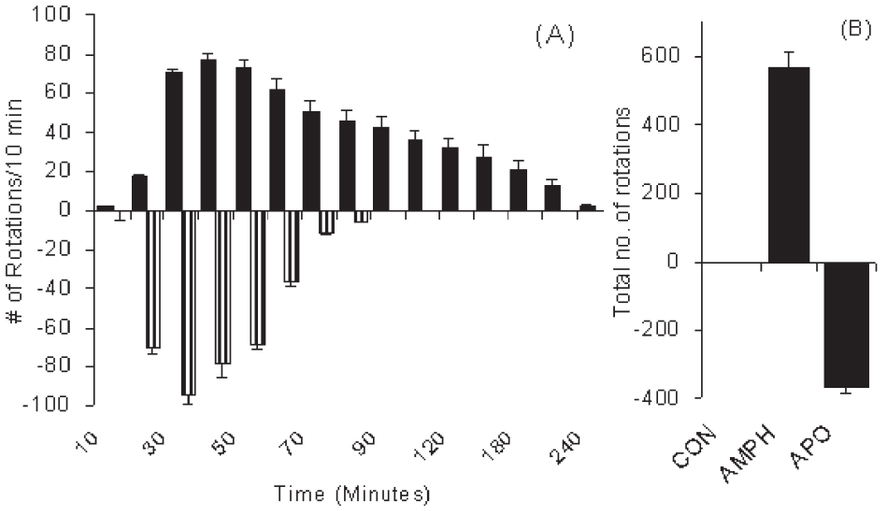


Fig. 14. Effects of 6-OHDA on amphetamine- and apomorphine induced rotations. Adult male Sprague-Dawley rats were intranigrally infused with 6-OHDA (8 µg in 1 l), or vehicle. (A) On the 14th day the animals were injected with amphetamine (5 mg/kg; i.p.). Amphetamine-induced ipsilateral rotations are depicted as positive values, merely to indicate the rotations to be ipsilateral to the side of infusion. Similarly apomorphine treatment (1 mg/kg, s.c.) on the 16th day produced contralateral rotations and are given in negative values. In (B) is provided the total number of rotations obtained for the duration of the study.

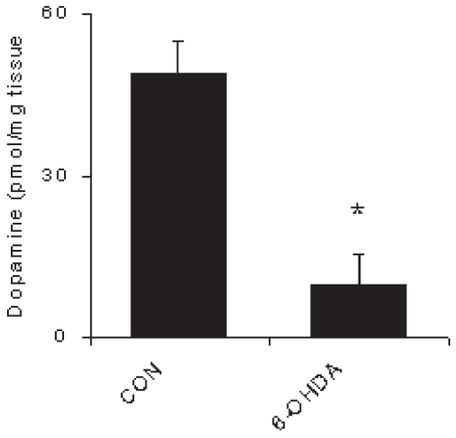


Fig. 15. Effects of intranigral infusion of 6-OHDA on striatal dopamine levels. 6-OHDA-induced changes in striatal dopamine and TH immunoreactivity in SN and NCP. Adult male Sprague-Dawley rats were intranigrally infused with 6-OHDA (8 µg in 1 µl) in the right side. The left side received the vehicle in 1 µl. On the 18th day animals were sacrificed and the left and right striata (NCP) were dissected out and assayed for dopamine levels employing an HPLC coupled with an electrochemical detector.

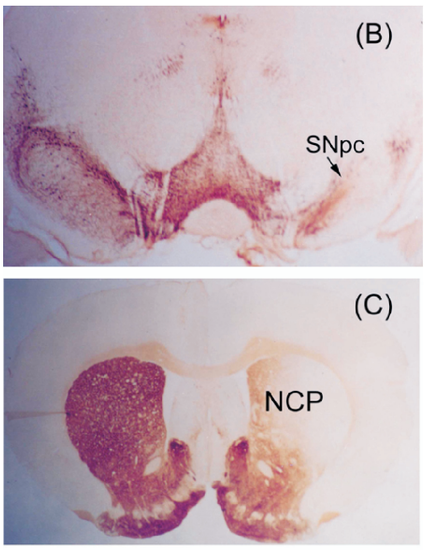


Fig. 16. Effect of 6-OHDA on tyrosine hydroxylase immunoreactivity in SN and NCP.
Coronal sections passing through the (A) substantia nigra pars compacta (SNpc), and (B) nucleus caudatus putamen (NCP) were processed for tyrosine hydroxylase (TH) immunohiistochemistry on the 18th day following 6-OHDA infusion. Note the loss of TH positive cells in the SNpc region on the side of where 6-OHDA has been infused. The striatum ipsilateral to the side of infusion also shows significant reduction in TH immunoreactivity. Magnification: SN - 16X; NCP - 12X.

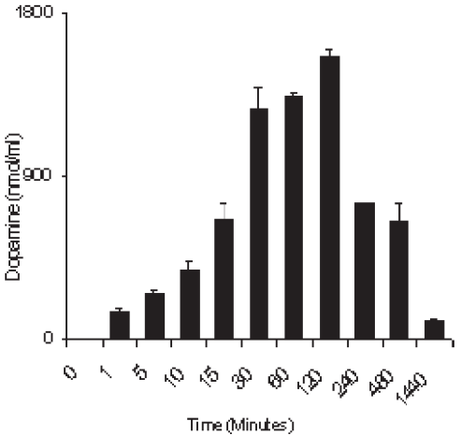


Fig. 17. In vitro DA release study from the hydrogel. DA release from the polymer matrices. Dopamine (50µg in 1µl) was embedded into polymer matrices (10 µl). In vitro release of the dopamine from the hydrogel into the incubation medium of 1 ml artificial cerebrospinal fluid was monitored at different time intervals (1 min - 24 h) employing a sensitive HPLC-electrochemical procedure. Every point of analysis (0, 1, 5, 10, 15, 30, 60, 120, 240, 480 and 1440 min) the bath fluid was replaced by fresh sample. Results are expressed as nmol/ml and are Mean ± SEM.

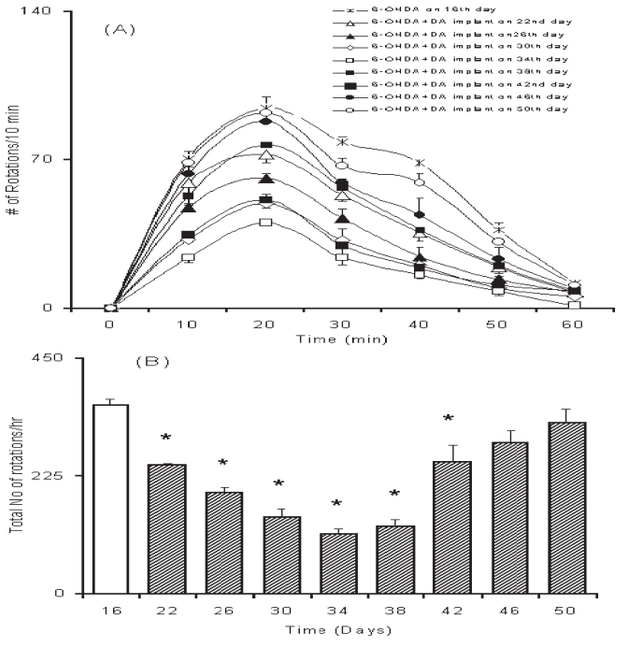


Fig. 18. Effects of implantation of DA loaded polymer on the day of 6-OHDA infusion on apomorphine-induced rotation. Effect of dopamine (DA) loaded polymer implants on apomorphine-induced rotational behavior in 6-OHDA-lesioned animals. Adult male Sprague-Dawley rats were intranigrally infused with 6-OHDA (8 µg in 1 µl). DA loaded polymers or polymer alone were implanted in denervated striatum on the 18th day. Animals were injected with apomorphine (1 mg/kg; s.c.) on every four days (i.e., on the 22, 26, 30, 34, 38, 42, 46 and 50th day) following the DA loaded hydrogel implantation, and the apomorphine-induced rotations were recorded for 60 min. (A). Rotations recorded, for every 10 min duration, for a period of 60 min. Each curve representing one of the day's analysis. The 16th day's data (top of the curve) serves as the control. The lowest count was obtained for the 34th day. (B). Total number of rotations over a period of 60 min on each day of the experiment.

Atropine, a muscarinic cholinergic receptor antagonist increases serotonin, but not dopamine levels in discrete brain regions of mice

We investigated the effects of atropine, a muscarinic acetylcholine receptor antagonist, on the level of serotonin in discrete brain regions, the nucleus raphe dorsalis (NRD), nucleus caudatus putamen, cerebral cortex and the cerebellum. Biogenic amines were assayed employing HPLC electrochemistry in these regions 30 min following different doses of atropine (5, 10, 25 mg/kg; i.p., Fig. 19), and at various time points (15, 30, 60, 120 min, Fig. 20) after 25 mg/kg of the drug. The cholinergic receptor antagonist caused a dose-dependent alteration in the level of serotonin in NRD, but the increase was not dose-dependent for other regions studied. The metabolite of serotonin, 5-hydroxyindoleacetic acid was unaffected. Atropine did not affect the levels of dopamine or its metabolites dihydroxyphenyl acetic acid and homovanillic acid. The present study suggests significant effect of this antimuscarinic agent on the synthesis of serotonin in the central serotoninergic pathways, which may have clinical relevance (Fig. 19 and 20).

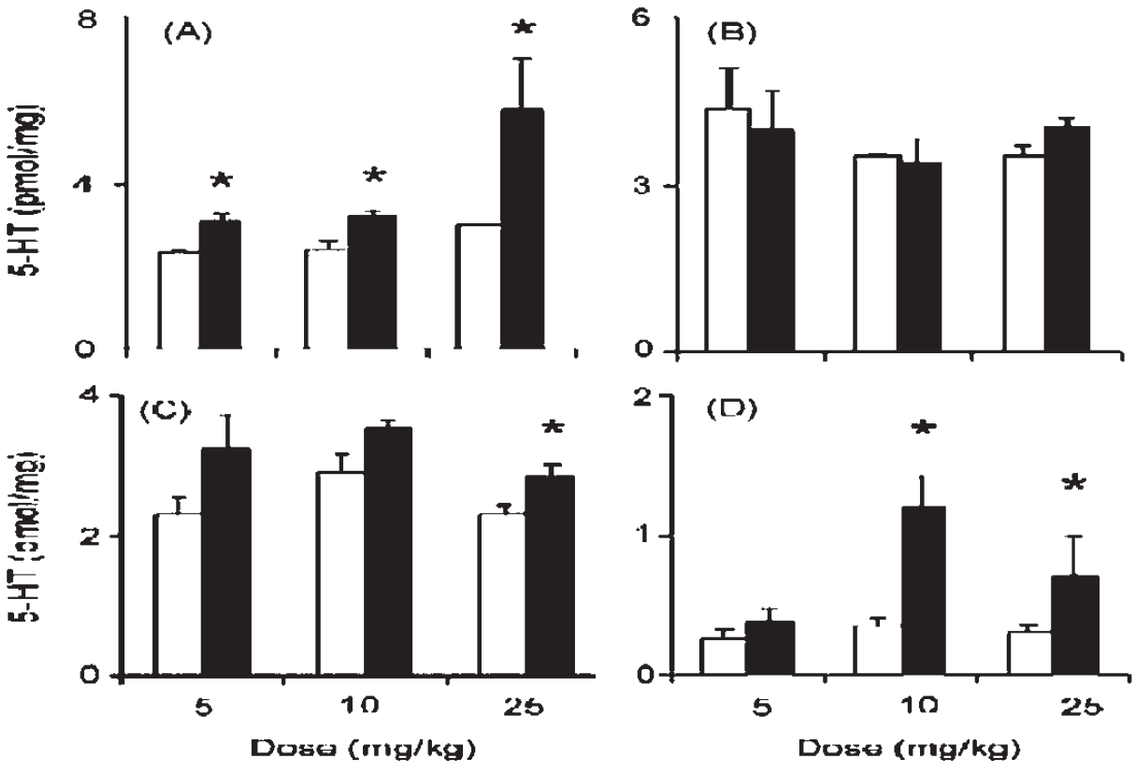


Fig. 19. Serotonin levels in discrete brain regions of mice following different doses of atropine. Atropine (5, 10 and 25 mg/kg) was adminstered in adult male Balb/c mice and the animals were sacrificed after 30 min. 5-HT content in (A) nucleus raphe dorsalis (NRD), (B) nucleus caudate putamen (NCP), (C) cortex and (D)cerebellum were measured employing HPLC-electrochemistry. Blank bars indicate control values while filled bars denote values for the treated samples. Results are expressed as pmol/mg fresh tissue and presented as mean $\pm$ S.E.M.. n=6, *p $\leq$ 0.05 in comparison to the respective control.

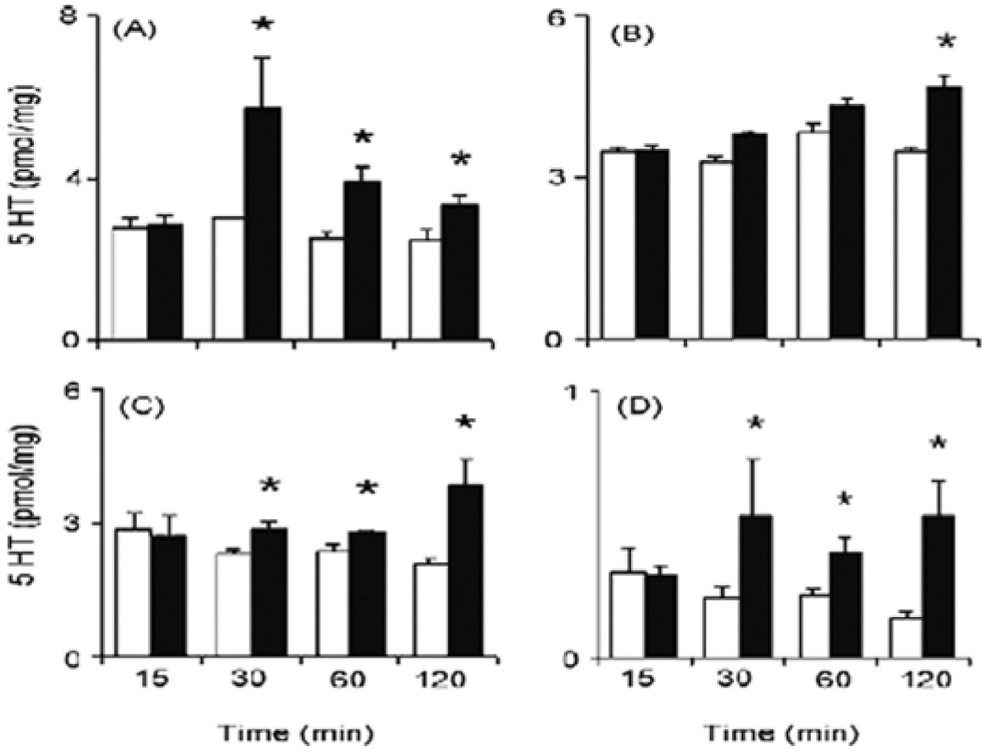


Fig. 20. Time-dependent effect of atropine on serotonin levels in discrete brain regions of mice. Atropine (25 mg/kg, i.p.) was adminstered in adult male Balb/c mice and were sacrificed after 15, 30, 60 and 120 min. Serotonin (5-HT) contents in (A) nucleus raphe dorsalis (NRD), (B) nucleus caudate putamen (NCP), (C) cortex and (D)cerebellum were analyzed employing HPLC-electrochemistry. Blank and filled bars respectively indicate control and treated sample values. The values are expressed as pmol/mg fresh tissue and presented as mean ± S.E.M.. n=6, *p ≤ 0.05 in comparison to the respective control.

Dr. Sumantra Das and group

Structure, function and altered function of astroglial cells

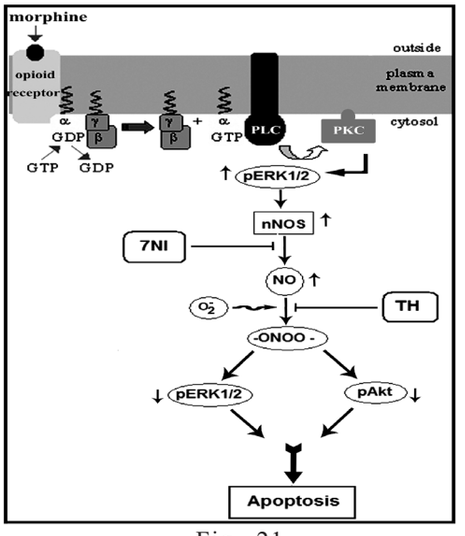


Fig. 21

Unlike other brain cells, astrocytes possess the unique ability to resist morphine-induced cell death. Investigations suggest that thyroid hormones (TH) protect astrocytes by inducing glutathione (GSH) synthesis in the cells. It was observed that the nitric oxide homeostasis, in cultured astroglial cells exposed to morphine, is markedly altered in presence and absence of TH. Under TH-deficiency, intracellular nitric oxide produced by morphine-induced activation of nNOS, is converted to peroxinitrite (-ONOO $^-$) by oxygen free radicals and readily nitrates endogenous proteins leading to cell death. However, when cells are grown under normal levels of TH, GSH levels in the cells are increased which scavenges endogenous oxygen free radicals so that the NO produced is unable to form peroxinitrite and is released outside the cells. The signaling pathway involved has been studied in detail (Fig. 21).

We had earlier observed a unique role of omega-3 polyunsaturated fatty acid, docosahexaenoic acid (DHA, 22:6n-3) in facilitating some of the vital functions of astrocytes in the developing brain. Since fatty acids are important constituent of the cell membrane, the effects of the fatty acids of various levels of unsaturation, namely, stearic acid, linoleic acid, arachidonic acid and DHA, on the sodium potassium ATPase of cultured rat cortical astrocytes was studied. Linoleic acid or DHA supplementation to astrocyte cultures significantly increases the enzyme activity as compared to the cultures grown in the absence of any fatty acids, maximum increase being observed during linoleic acid treatment of the cells (Fig. 22). The sensitivity of the pump to varying Na^+ ion concentration during various fatty acid supplementation conditions was also investigated. Alterations in the Na^+ dependence of Na^+K^+ATPase activity was attributed to variations in the expression of the various isoenzymes during these treatment conditions which was supported by immunocytochemical studies of the treated cultures as well as by the mRNA levels of the various isoforms of the enzyme (Fig. 22).

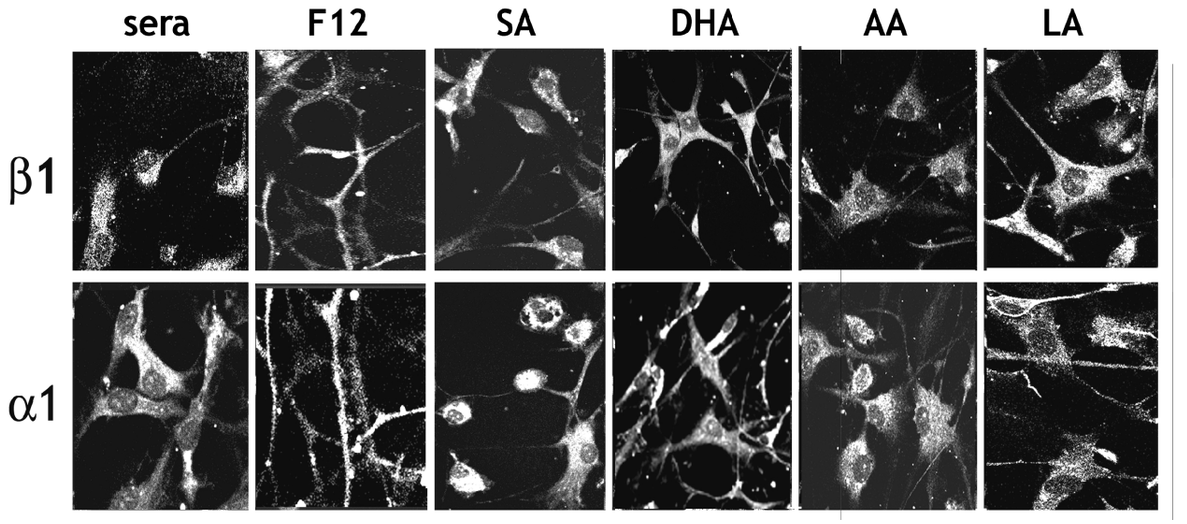


Fig. 22. Morphology of astrocytes supplemented with different fatty acids immunostained with α1 and β1 antibodies. Astrocytes were cultured in DMEM (with sera), F12 medium (devoid of sera), stearic acid (SA), docosahexanoic acid (DHA), arachidonic acid (AA) and linoleic acid (LA) respectively and immunostained with α1 and β1 antibodies and observed with a confocal microscope. Magnification, x 1000.

Newer approaches for the treatment and understanding of narcotic addiction

Based on established 3D pharmacophore, a series of quinoline derivatives were synthesized by the Syntheic, Biophysical and Natural Product Chemistry group and their binding activities to opioid receptors and pharmacotherapeutic ability in controlling the naloxone precipited withdrawal in morphine dependent mice were investigated. The compounds showed varying degree of activities at the κ and μ opioid receptors with negligible interactions at the δ receptor. One such compound successfully inhibited two most prominent quantitative features of naloxone precipitated withdrawal symptoms; stereotyped jumping and body weight loss. In conclusion, quinoline derivatives could offer potential tool for treatment of narcotic addictions.

Another collaborative project with a psychiatric clinic, Baulmon, Kolkata has been undertaken to carry out genetic epidemiological studies on opioid addiction by investigating the possible association of specific SNPs of certain candidate genes like nNOS, CREB, κ- opioid receptor etc. in addiction using PCR based RFLP as well as DNA sequencing analysis.

Proteomic approaches to identify target molecules involved in relapse in narcotic addicts are underway. Recent reports that morphine induces neuronal changes that persist for a long time following cessation of exposure suggest functional implications in the development of relapse in abused individuals. The cytoskeleton being an important constituent in the maintenance of cellular morphology, studies are being carried out with the aim to explore changes in protein pattern profile of several cytoskeletal associated proteins in discrete regions of the brain upon withdrawal of morphine in chronic morphine treated rats. A few protein spots after 2D-gel electrophoresis were found to be regulated in morphine tolerant and dependent animals much after abstinence of morphine in the animal (Fig. 23). The spots were identified with the help of MALDI-TOF –TOF using tryptic digestion .Of the six spots analyzed, four showed good protein score (greater than 100%), both in the case of MS and MS/MS and matched with published sequence in the literature. The functional significance of these proteins in the development of relapse are being understood.

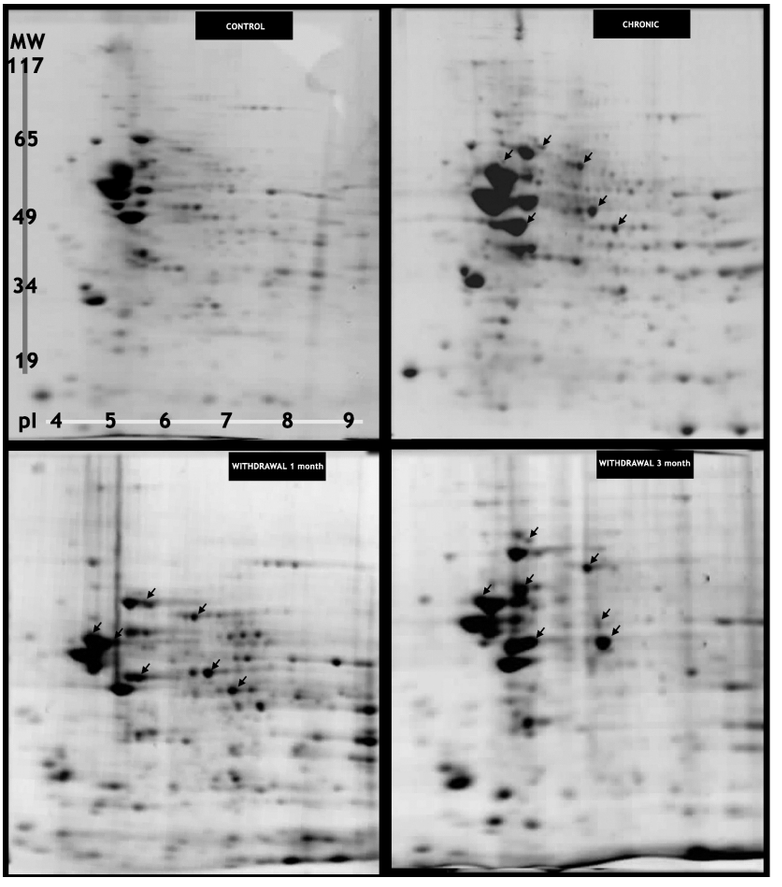
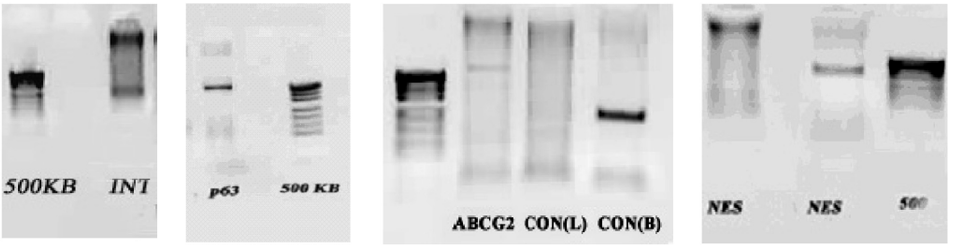


Fig. 23. Respresentative photo-micrograph of the cypro ruby staining pattern of total protein of rat cortex under various treatment conditions subjected to 2D gel electrophoresis. Control (upper left panel) represents cortex of rat treated chronically with vehicle while chronic upper right panel represents cortex of rats marked chronically with morphine for 7 days. Lower panels demonstrate stained pattern of cortical proteins of chronic morphine treated rats after abstinence of the drug for 1 month (left) and 3 months (right) respectively. Spots marked with arrow are either appearance of new spots or increased expression of existing spots with reference to control.

Limbal stem cell culture

A collaborative project with Regional Institute of Ophthalmology, Kolkata has been initiated with the purpose of reconstructing damaged cornea in ocular surface disorders by transplantation of corneal epithelium from cultured limbal stem cells (Fig. 24).



Integrin β1 **δNp63** **ABCG2** **Connexion** **Nestin**

Fig. 24. RT-PCR analysis for the presence of limbal cell specific mRNA. Presence of five different mRNAs were analysed. ABCG2 , δNp63 and Integrinβ1 are positive markers for limbal cells. Nestin and Connexion are negative markers for limbal cell (L) but positive markers for human blood cell (B).

REPRODUCTIVE BIOLOGY

Dr. Sandhya R. Dungdung and group

Biochemical basis of the regulation of sperm motility

A special characteristic of spermatozoa is that they possess forward progression, which is essential for their fertility potential. A forward motility stimulating factor (FMSF) has been purified to apparent homogeneity from goat blood serum and some of its physical, biochemical and physiological characteristics have been established using the homologous sperm system. Goat FMSF has been purified from goat blood serum using several purification steps such as boiling of serum, ammonium sulphate precipitation, CM-Cellulose cation exchanger column chromatography, Sephacryl S-200 gel filtration column chromatography and non-denaturing polyacrylamide gel electrophoresis (PAGE). It is a heat-stable 66 kDa protein. Its purity and molecular weight was confirmed by SDS-PAGE (Fig. 25), Sephacryl S-200 gel filtration and high performance liquid chromatography (HPLC). Addition of FMSF, enhanced markedly sperm forward motility. The numbers of forward motile cells increased markedly with the increase in the concentration of FMSF. A proportional increase in FMSF activity was observed up to approx. 4 units of purified FMSF (0.6 M : 40 g/ml). The factor showed maximal activity at concentration as low as 0.9 M when it induced forward motility in nearly 60-70% of the total number of cells (Fig. 26). FMSF is a Mg^{2+} -dependent monomeric protein. Mg^{2+} at 0.8 mM level caused maximal activation of FMSF activity. Antibody has been raised against the forward motility stimulating protein. Immunological characterization is in progress.

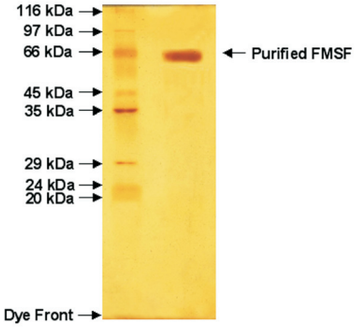


Fig. 25: Determination and of molecular weight and purity of goat blood serum FMSF by SDS-PAGE using 10% polyacrylamide gel.

Goat sperm plasma membrane contains a protein that apparantly functions in the agglutination of goat maturing spermatozoa. Triton extract of the mature goat cauda sperm plasma membrane showed high efficacy to agglutinate rabbit erythrocytes as well as caput sperm cells. The sugar binding protein is a calcium dependent lectin. Agglutination was strongly inhibited by D-galactose (50 mM). Purification and characterization of sperm membrane bound lectin is under progress.

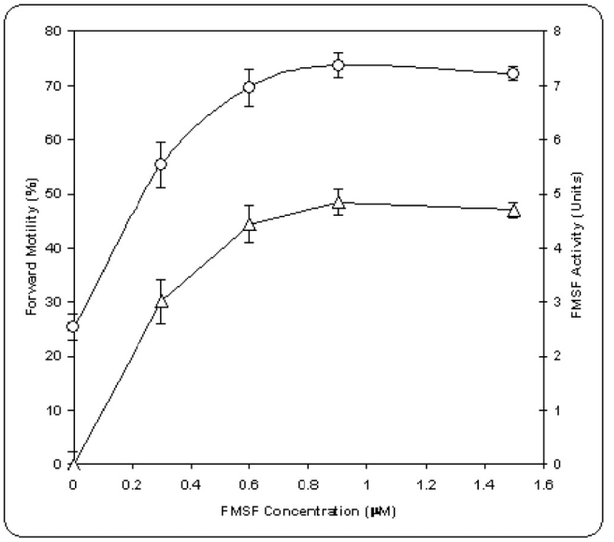


Fig. 26: Effect of goat serum FMSF at different concentrations on sperm motility under the standard microscopic assay conditions. (+o-o-+): Forward motility, (+Δ-Δ-+): Activity units. The values indicate the mean ± SEM of four experiments.

Dr. Syed N. Kabir and group

Physiological and pathophysiological aspects of female reproduction: Animal model for premature ovarian failure

We have been working on development of animal model for premature ovarian failure (POF), a highly heterogeneous entity for which the etiological bases or pathophysiologic mechanisms are largely unknown. We have demonstrated earlier that embryonic galactosyltransferase (GalTase) plays important roles in the process of germ cell migration, and attenuation of embryonic GalTase activity restricts oogonial migration leading to development of ovary with deficient follicular reserve. This intervention led to a sequel of ovarian dysfunction including delayed onset of puberty, increased rate of follicular atresia, and poor ovarian response to exogenous gonadotropins that characterizes the basic tenets of POF. As compared to sham-operated control rats (transplantation of a wedge of fat), transplantation of ovary from control immature rats under the ovarian bursa of the follicle-deficient ovary advanced the onset of puberty; improved the follicular response to gonadotropins; and the increased rate of granulosa cell apoptosis and follicular atresia that were prevalent in the follicle-deficient parental ovary were significantly attenuated. Using mathematical model it has been demonstrated that follicular reserve declines at an exponential rate that gradually changes throughout life leading to accelerated rate of atresia during the years preceding menopause. We postulate that perhaps certain quantum of follicular reserve is mandatory to provide an ovarian milieu that favours follicle survival; and as the milieu wanes below the threshold level either due to expenditure of follicles during the course of reproductive years, or following an insult (mechanical, chemical or radiation), the rate of atresia increases (Fig. 27).

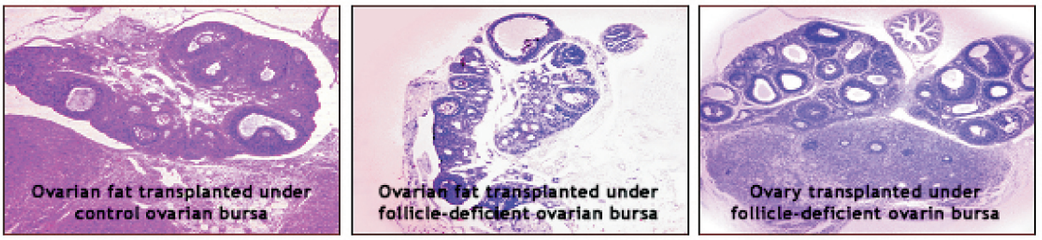


Fig. 27. Stimulation of follicular growth in follicle-deficient ovaries following transplantation of immature rat ovaries with normal follicular quantum.

Spermicidal and anti-HIV effects of Acaciaside-Benriched fraction of the seeds of Acacia auriculiformis

The population explosion coupled with steer rise in the incidence of HIV infection through heterosexual contacts has regenerated our interest to develop topical microbicides with discerning spermicidal property that would prevent unwanted pregnancies and curb the rising HIV epidemic. We have demonstrated earlier that an isolate of the extracts of *A. auriculiformis* seeds comprising of a mixture of Ac-A and Ac-B possesses spermicidal activity. Subsequent studies have shown that Ac-A and Ac-B individually possesses spermicidal property; however, Ac-A is shown to be a mutagen. Ac-B is spermicidal at significantly lower concentrations, and is also demonstrated to attenuate HIV-1 transmission in vitro, but the major limitation is its poor yield through extraction; and synthetic preparation of Ac-B is also not possible. During the extraction and isolation of the acaciasides, a crude fraction was obtained with high yield that is mostly comprised of (>38% by weight) Acaciaside-B with no trace of Ac-A (henceforth referred to as Ac-B-enriched (Ac-B-en) fraction. We took interest to investigate the spermicidal potential and anti-HIV property of Ac-B-*en* fraction and explore if it can substitute pure Ac-B without compromising the efficacy.

Ac-B-*en*, like Ac-B exerts dose-dependent sperm-immobilizing effects. The minimum concentration of Ac-B-*en* that induces 100% immobilization of sperm (MEC) in 20 sec was found to be 120 µg/ml as against 550 µg/ml for nonoxynol-9 60 µg/ml for Ac-B. As evaluated by viability of human spermatozoa using dual fluorescent live/dead staining with SYBR 14 and propidium iodide, Ac-B-*en* was shown to have spermicidal but not spermatostatic effects. The EC50 dose of Ac-B-*en* was calculated to be 26.5 µg/ml. The spermicidal effects involve increased membrane lipid peroxidation leading to loss of sperm plasma membrane integrity (Fig. 28).

From the safety point of view, Ac-B-en offers no detrimental effects on Lacobacillus growth cultured in vitro. Ames test demonstrates it to be non-mutagenic. As evaluated in TZM-bl cells infected with HIV-1 NL4-3 virus, Ac-B-en was shown to have potent anti-HIV property (IC 50=0.42 mcg/ml), as against its CC50 (cytotoxicity) of 8.6 mcg/ml (safety index ~20) (Investigation was done in collaboration with Dr. D. Mitra, NCCS, Pune).

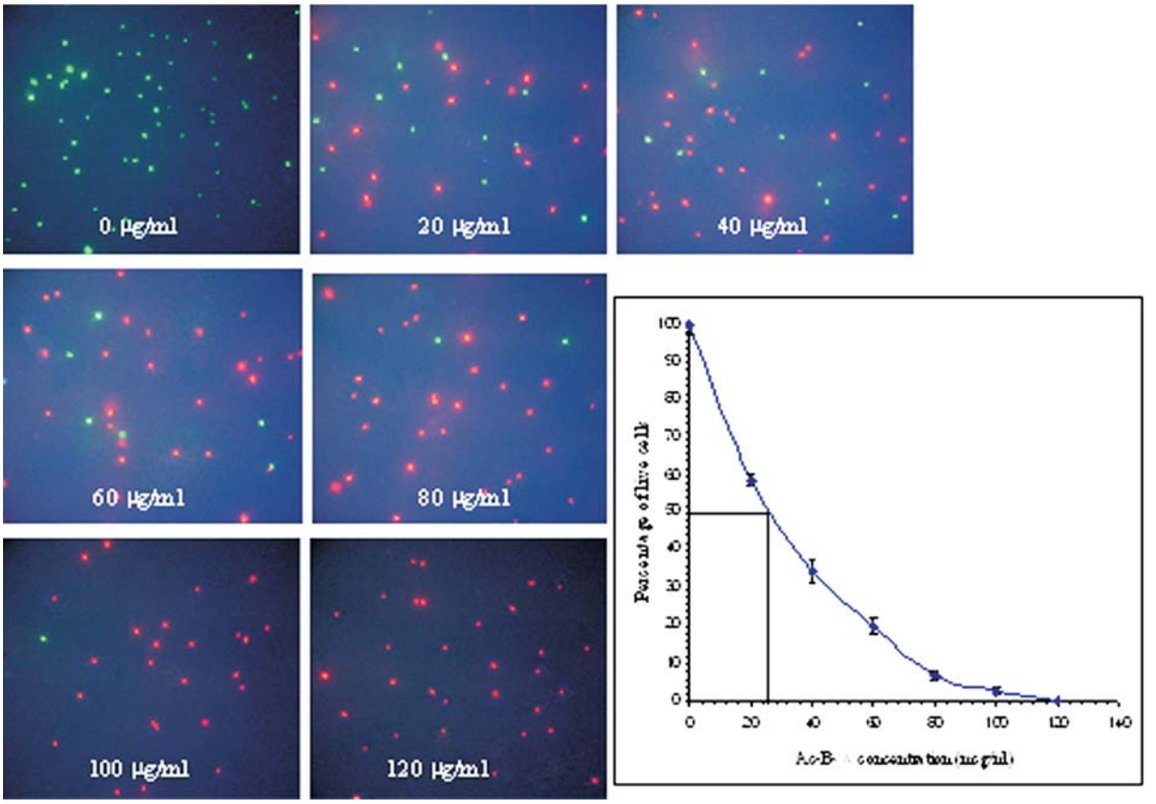


Fig. 28. Overlaid fluorescence images of human spermatozoa stained with SYBR14 and propidium iodide to differentiate live (green) and dead (red). The picture exhibits dose-dependent spermicidal effects of Ac-B-en, while the graph represents the same data to show the EC50.

Dr. S N Chakraborty and group

Search for fertility regulating agents from natural resources or of synthetic origin

Fertility regulating potentials of the saponin isolated from the roots of *Sesbania sesban* Meril were investigated using pregnant female rats and spermicidal effect on rat sperms. Aqueous solution of the compound was given by gavage at different doses to sperm positive female rats during early pregnancy in two different stages. Sent percent abortifacient activity was observed when administered from day 5 to day 10 of gestation at the dose level 100 mg kg^{-1} day, but insignificant anti-implantation effect was obtained when treated from day 1 to day 5 of gestation. Measurement of serum oestrogen and progesterone by radioimmunoassays from blood collected by cardiac puncture on necropsy on day 12 revealed significant increase in oestrogen and decline in progesterone levels in comparison to control. But bioassay using immature female rats revealed no oestrogenic potential of the compound. Total plasma cholesterol level (TPC) was measured both in pregnant, as well as in animal fed with cholesterol diet. The saponin indeed reduced TPC both in pregnancy and in the animals fed with high cholesterol diet. Progesterone level rises rapidly during pregnancy, whereas oestrogen level increases to some extent. Most probably the foetal-placental unit suffered cholesterol deficiency (because of lower TPC) rate limited synthesis of the progesterone that disturbs the delicate balance of progesterone oestrogen ratio. The down stream events, in sustenance of pregnancy that are controlled by progesterone, were adversely affected leading to foetal loss. However, the compound could not influence the corpus luteal function and was unable to affect implantation significantly.

Semen samples were collected from the healthy volunteer and concentration of donor sperm was determined using Mackler chamber after liquefaction. Washed in BWW medium maintained at 37^{O} C and the motile sperm were collected using swim up method. These sperms were utilised for spermicidal activity assessed initially by spot assay method. Viability assay conducted by eosin dye. The spermatozoa incubated with the compound in different concentration at 37^{O} C and percentage motility was calculated after 30 minutes using a microscope, the stage and surrounding environment of which maintained at 37^{O} C.

A dose dependent decline in motility (%) and viability (%) was observed with the saponin tested presently. 25 µg/ml found to be 100% effective dose

Potential male contraceptive efficacy of quinolines

A collaborative works with Dr. N B Mondal of Steroid and Terpenoid Chemistry group was carried out to develop a male contraceptive fertility regulating potential of the synthetic compound 2 (2´´chloroacetamidobenzyl) -3-(3´indolyl) quinoline in male rats. Functional fertility epididymal sperm count, spermatogenesis were quantitated. Reproductive hormones and related biochemical parameters were measured. Functional fertility reduced significantly and so the sperm counts and testicular cells. Testosterone level declined but increase in FSH level occurred. Fertility gradually regained after 4 weeks of withdrawal of the agent. The compound can be explored further as male contraceptive following rigours toxicological investigation.

Biocompatibility studies of polymer composities as replacement of skin graft, bone etc.

Wound healing is a complex process and is promoted by dressings that maintain a moist environment but allow excess fluid to escape without permitting wound dessication. Chitosan is biodegradable, biocompatible, non-toxic and antithrombogenic, thus allowing it to be a good biomaterial for wound management, space filling implants etc.

This collaborative study with Dr. S Pal, Bio-Science and Engineering Department, Jadavpur University, aims at the development of advanced biomaterial having desirable mechanical as well as biological properties for wound management. This includes the development of chitosan-PVA blended membrane and chitosan-HA composite membrane, characterization and comparison of results, along with invivo assessment of the membranes for their effectiveness as wound healing material. Chitosan (Ch) was dissolved in lactic acid, blended with poly-vinyl-alcohol (PVA)/hydroxyapetite (HA) to prepare Ch-PVA and Ch-HA membrane respectively by conventional solvent casting method with Lactic acid as a solvent.

The membranes were characterized for their strength, swelling properties and effect of sol viscosity on membrane strength and absorption. Also analysis was done for hemo-compatability using human blood and for their effectiveness as wound healing material using albino rats and human clinical trials with ethical clearance. Ch-PVA 1:2 membranes had ultimate strength, swelling of 26.84 + 4.3 M Pa and an elongation break of about 145 + 41%. Swelling of Ch-HA membrane has shown consistency with Ch-PVA 2:1 membrane had 405.6 + 69.6 absorption while Ch-PVA 1:1 membrane had 431.36 + 42.2 % after 60 minutes. Increased sol viscosity led to higher strength and improved absorption. These membranes did not elicit adverse reactions and were biodegradable over the course of application. Ch-HA membrane promoted better healing by effective adherence to the wound site, with faster and orderly reorganization of wounded area into healthy skin in rats. Clinical trial on paraplegic patients with bedsores, elicited good wound healing. In conclusion, all the analysis that was done yielded favorable results for the Ch-HA membrane as a wound healing dressing. Mechanical strength, physicochemical characteristics and fluid handling capacity of the dressing are important for effective healing of exuding wounds like ulcers, pressure sores or burns. The observed desired features in the membrane make it a significant and effective wound dressing.

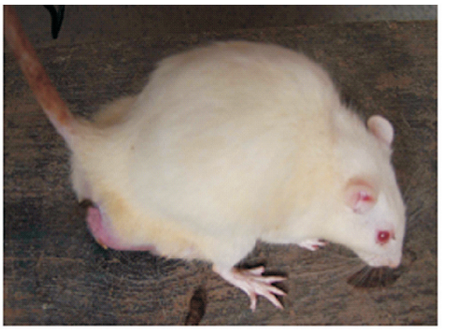
In continuation of earlier works on biocompatibility studies *in vivo* tests of bio-glass coated polymer- ceramic composite plates and hip-prosthesis were conducted for soft tissue attachment into rat muscle and/or bone replacement implanted surgically in rabbit's hip-joint and kept for a period for 6 months movements were observed. At the end the rats were sacrificed and coated strips with muscle were taken out, observed under dissecting microscope or SEM. Attachment and regeneration of muscle on coated surface of composite strip and movement of rabbits were perfectly normal.

Search for regulating agent/s of breast, ovarian or other steroid hormone target organs tumors/cancers or of metabolic disorders

Increasing numbers of evidences indicate that the sex hormone estrogen no longer solely acts as an endocrine agent; instead it has some general metabolic roles that are not directly involved in the reproductive process. These include action on vascular function, lipid, carbohydrate metabolism, as well as bone mineralization and epiphyseal closure in both sexes. Ever going references also suggests that altered metabolism of estrogen accelerates incidences of induction of cancers of the breast [50%], cervices, gonads or other steroid hormone target organs by different pathway. Recent study also highlighted that in post menopausal women specifically those who used HRT [hormone replacement therapy], of the breast carcinomas [75%] are dependent on estrogen for their induction and growth. In post menopausal women the ovaries cease to produce estrogen, instead it is produced in a number of extra-gonadal sites and acts locally at these site as a paracrine or even intracrine factor. These sites include the mesenchymal cells of adipose tissue, osteoblast, condrocytes of bone, the vascular endothelium and aortic smooth muscle cells and numerous sites in the brain. Biosynthesis of estrogen (E2) within these places is catalyzed by a microsomal enzyme Aromatase (cytochrome P450 superfamily). Androgens [C19 steroid precursors] serve as substrate for the synthesis. Physiologically estrogen action is mediated via specific receptor, ER α & ER β. With advancing of age in women (late reproductive years) the androgenic precursor started to decline markedly. These are the fundamental reasons why women are at increased risk for bone mineral loss, fracture and decline of cognitive function. Aromatase expression in these various sites is regulated by different cohorts of transcription factor. Thus in principle pharmaceutical agents which deprive signals of estrogen action, inhibitor of estrogen synthesis, aromatage or estrogen receptors actions could be useful in breast, cervical, uterine cancer treatment/prevention.

Murine models of estrogen dependent tumors were developed using estrogen [DES] in combination with a mitogen [*N*- methyl-N-nitrosourea], were given by gavage with suspension of PH-DIM [60mg/kg/day] in water with gum acacia at 2 days in a week for 4 or 8 weeks.. Animals were sacrificed for scoring and measurement of tumors at 30 weeks of age. The tumors sizes were measured using slide calipers. Some tumors were fixed for histological examination. Tumor tissue volume measurement indicated that PH DIM reduces tumor size significantly depending on period of treatment (Fig. 29).

A. Tumor inducd with DES and N- methyl -N-nitrosourea (Untreated control).



B. Treated with PH-DIM (60mg/kg/day) for 4 weeks.

C. Treated with PH-DIM (60mg/kg/day) for 8 weeks

A. Tumor tissue of untreated control animal.
B. Tumor tissue of animals treated with PH-DIM for 4 weeks
C. Tumor tissue of animals treated with PH-DIM 8 weeks.

Fig. 29.

Dr. Padma Das and group

Studies on the estrogenic effects of plant extract

Various parts of *Sesbania grandiflora*, have been used in the Indian system of medicine, In the present investigation, the estrogenic property of the crude methanolic flower extract (CFE) of *the* plant was tested in ovary–intact and ovariectomized (OVX) rats. The study was carried out by histological observations of ovarian follicles in an ovary-intact model and by histological observations of the endometrial epitheliaum in both OVX and ovary-intact rats. The CFE was suspended in distilled water and administered to the rats in a dose of 1g//kg body weight/day. CFE administration was continuing through three consecutive estrus cycles (for ovary-intact model) from onset of proestrus or 12 days in OVX model. As evident from the histological architecture, in the control ovaries, healthy follicles could be characterized by the presence of oocytes surrounded by granulosa cells and theca cells. Multiple layers of granulosa cells covered by the theca interna and the theca externa were prominent in the normal ovarian structure and the administration of CFE in normal rats resulted in overall increase in follicle number. The endometrial glands are observed poorly developed in OVX rat. The oral

administration of CFE to OVX rats restores the proliferation of the endometrial luminal epithelium. The study was compared to estradiol-17β treated rats which was used as reference drug. In OVX rats, the effect of CFE on uterine epithelium was corroborative with effect of E_2. In the present investigation, the exact chemical structure and /or nature of the active compound(s) is yet to be determined. The effects exerted by the crude extract on the ovary and on the uterus may be due to either a single compound or multiple compounds present in the flowers extract of *Sesbania grandiflora.*

Studies on the anti-cancer activity of Sesbania grandiflora

This is part of net work project (IAP 0001). Bioassay guided separation was also carried out to identify the fraction possessing the anti-cancer activity. In the present study we evaluated the anti cancer activity of *Sesbania grandiflora* in human leukemic cell line K562 and U937. Experiments are in progress and results are yet to be obtained.

GENE REGULATION & METAGENOMICS

Dr Tushar Chakraborty and group

Towards accelerated bioleaching of Copper by indigenous microbial communities associated with subsurface Chalcopyrites from Indian copper mines

Chalcopyrites are one of the abundant and widespread copper iron sulfide mineral found in most copper mines, which are low-grade in terms of copper and highly refractory to conventional Bioleaching. Combing recent tools from microbial molecular genetics and microbial ecology, I have attempted Bioleaching of Chalcopyrites collected from three different copper mines in India. The ability of native isolates of Acidithiobacillus ferrooxidans and leptospirrilum ferrooxidans isolated from the mine waters and mine sediments were first tested for Bioleaching of Chalcopyrites. Bioleaching of Chalcopyrites by these dominant-leaching microbes was very poor when compared to mixed oxides or chalcocytes. However, native Microbial Communities associated with Chalcopyrites ores were found to be more efficient. Hence, a methodology for isolation and amplification of such community was developed. By a differential growth strategy, where rapid growing commensally associated microorganisms were reduced and removed – so that the critical slow growing players for Bioleaching and their essential support organisms can be stabilized within the selected microcosm. A comparative study of the Chalcopyrites from multiple sites revealed identity of the possible critical players. Several thermophilic bacteria and archaea were identified in this community by 16s rRNA phylogeny. The Dynamics of the population flux during progress of Bioleaching were studied by time – series experiments. Encouraging results were obtained in laboratory scale study. We explain these phenomena of accelerated Bioleaching of copper by the indigenous microbial community as a mutualism between minerals and associated microbes. The interesting flux or dynamics of the microbial population during Bioleaching of Chalcopyrites can be modeled as metabiosis, which is perhaps central to natural biogeotechnology

Association study of Glutathione –S –Transferase (GST) polymorphism in Arsenic exposer, tolerance and toxicity

Human exposure to arsenic is becoming common on a global scale mostly due to consumption of arsenic contaminated subsoil water. Several Districts of West Bengal in India is affected by such arsenic toxicity. We are investigating molecular changes associated with arsenic exposure among this population. The clinical feature and Gst polymorphism in 80 study subjects were investigated Most of these arsenic affected patients have developed skin manifestations. Pigmentation and keratosis was the most common feature of arsenicosis.We found, Glutathione –S –Transferase (GST) polymorphism has a unique correlation with arsenic induced

methylation changes in these subjects. Persons having GSTM1 or GST T1 null genotype were identified among them., People chronically exposed to arsenic with GSTM1 & GSTT1 null genotype were frequently associated with DNA hypermethylation (in p53 promoter region and genome wide) in comparison to GSTM1 & GSTT1 wild type population. The arsenic induced clinical symptom score were also low in GST M1T1 wild type population of the same arsenic exposure group. So humans with null genotype of GST M1 and T1 have been considered to be a high risk group of people who retain arsenic in their body due to incomplete metabolism of arsenic.

The polymorphic deletion of GST M1 and GST T1 gene was genotyped using the multiplex PCR approach. An 861 base pair (bp) fragment amplified from â globin gene serves as an internal control. Negative and positive controls were included in each elongation series. The presence of one or both GSTM1 allele identified by a 230 bp fragment and its complete deletion was (null genotype) analysed by electrophoresis on 1.5 % agarose gel. The absence of amplifiable 230 bp fragment indicates GSTM1 null genotype. Similarly absence of 112 bp fragment is an indicative of GSTT1 null genotype (Fig. 30).

We found clinical symptom score of arsenic toxicity to be high in GST M1T1 null genotype, when compared to wild type population. The level of total urinary arsenic was also found to be significantly higher in them. Comparison was made in GSTM1 or GSTT1 null polymorphic subjects with GSTM1T1 wild type subjects of same arsenic exposure group while drawing such conclusion. This may be one of the possible mechanism underlying arsenic tolerance in endemic region.

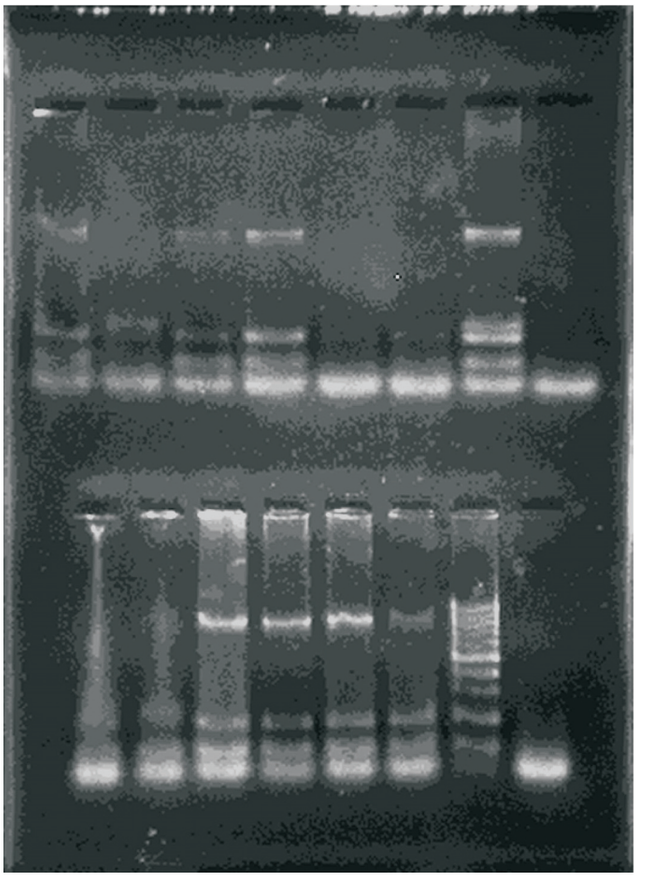


Fig. 30. Representative gel picture of GSTM1T1 polymorphism

Isolation of Microbial Consortia which can biodegrade peptide nanomaterials

Nanomaterials are often refractory to biodegradation , and poses challenge to the environmental safety concerns. We have screened and selected microbial consortia from soil that can degrade and consume peptide nanomaterials which are refractory to biodegradation by normal proteases of broad specificity (proteinase K). The consortia showed differential ability towards peptide nanomaterials of different composition – which suggested high degree of specificity in this process.

Names of Technical staff

Dr. Herambananda Ray, Dr. Shampa Sarkar, Mr. Swapan Kumar Mandal, Mr. P. C. Deuri

Names of RAs, Pool Officers, SRFs and JRFs

Dr. Anindita Joardar, Dr. Kakali De, Dr. Sarmistha Chanda, Dr. Sonali Ghosh, Ms. Ambili Appukuttan, Mr. Anupom Borah, Ms. Asmita Dasgupta, Mr. Debabrata Biswas, Ms. Debanjali Mitra, Mr. Deepak Kumar, Mr. Goutam Chandra, Ms. Ishani Deb, Mr. Kaustav Dutta Chowdhury, Mr. Mausam Ghosh, Ms. Merina Varghese, Mr. Mritunjay Pandey, Ms. Poornima Chandran, Ms. Priyanka De, Ms. Reena Haobam, Ms. Shrabanti Kumar, Mr. Shyam Sundar Nandi, Ms. Sreerupa Ghose Roy, Ms. Sreetama Sen, Ms. Sudipa Saha Roy, Mr. Sudipta Saha, Ms. Sumita Mishra, Mr. Tathagata Sengupta, Ms. Debasmita Tripathy, Mr. Dijendra Nath Roy, Ms. Jayashri Roy, Mr. Joy Chakroborty, Mr. Kunal Basu, Ms. Moitri Basu, Mr. Samir Mandal, Mr. Sudarshan Bhattacharya, Mr. Sujoy Das, Mr. Vivek Chander

Names of Project Assistants and Trainees

Dr. Gargi Sen, Mr. Dipak Kar, Mr. Saptatshi Dutta, Mr. Rohan Mitra, Ms. Tanima Banerjee, Mr. Amit Vij, Ms. Megha Rohatgi, Mr. Niladri Shekhar Panda, Ms. Nilanjana Das, Mr. Oyadeyi Ayodele Stephen


ConfoCor 3

Molecular & Human Genetics

Dr. Samit Adhya, Dr. Keya Chaudhury, Dr. Kunal Ray, Dr. Ashok Kumar Giri, Dr. Susanta Roychaudhury, Dr. Samir Kumar Dutta and Dr. Suvendra Nath Bhattacharya

Brief Preamble:

The broad aims of the division are to understand the molecular genetic basis of diseases common in Indian populations, to study gene expression and function in pathogenic microorganisms, and to develop transgenic plants with improved characteristics.

The specific objectives are; (a) to decipher the molecular basis of the genomic instabilities in head and neck cancer (HNSCC) and to identify the putative tumor suppressor genes involved in the development of this cancer; (b) to identify susceptibility alleles in *Helicobacter pylori* associated gastroduodenal diseases: to study the molecular pathogenesis of oral submucous fibrosis; (c) to understand the molecular genetics of haemophilia, glaucoma, Wilson disease, and oculo-cutaneous albinism; (d) to assess the health effects, genetic damage and genetic variants in populations exposed to arsenic through drinking water in West Bengal; (e) to test the antimutagenic and anicarcinogenic effects of black tea polyphenols theaflavins and thearubigins; (f) to identify differentially expressed *V. cholerae* genes following infection to host and their role in pathogenesis, and to study the response of human intestinal epithelial cells to *V. cholerae* infection; (g) to study the molecular basis of the import of nuclear-encoded tRNAs into the mitochondria of the kinetoplastid protozoon *Leishmania* using a combination of biochemical and reverse genetic approaches and (h) to identify, isolate and modify genes from non-host plants involved in self-defence mechanisms against pests, and to transfer them as bio-pesticides to host plants.

Dr. S. Adhya and Group

Necessary and sufficient factors for import of tRNA into the kinetoplast-mitochondrion

The mechanism of active transport of tRNAs across membranes is largely unknown. Factors mediating mitochondrial tRNA import in the kinetoplastid protozoon *Leishmania tropica* are organized at the inner membrane into a multiprotein RNA Import Complex (RIC). The first total characterization of this complex in terms of the identities and functionalities of its subunits is presented. The complex contains three mitochondrion- and eight nucleus-encoded subunits; six of the latter are necessary and sufficient for import. Antisense-mediated knockdown of essential subunits resulted in depletion of mitochondrial tRNAs and inhibition of organellar translation. Functional complexes were reconstituted with recombinant subunits expressed in *E. coli*. Several essential RIC subunits are identical to specific subunits of respiratory complexes. These findings shed new light on the evolution of tRNA import, and provide the foundation for detailed structural and mechanistic studies.

Proton-guided movements of tRNA within the Leishmania mitochondrial RNA Import Complex

The RNA Import Complex (RIC) from the mitochondrion of the kinetoplastid protozoon *Leishmania tropica* contains two subunits that directly bind to import signals on two distinct subsets of tRNA and interact with each other allosterically. What happens to the tRNA subsequent to its loading on the complex is unknown. A third subunit - RIC9 - has intrinsic affinity for both types of tRNA and is essential for import in vivo. Here we show that antibody against RIC9 inhibited the import of both types of tRNA into mitoplasts in vitro,

but failed to inhibit the binding of these tRNAs to their respective receptors, indicating that RIC9 acts in a subsequent step. Using photoaffinity crosslinking-immunoprecipitation to detect translocation intermediates, it was observed that tRNA was transferred from its cognate receptor to RIC9, followed by translocation across the membrane and release as free tRNA in the inner compartment. Transfer required elevated temperatures and ATP, but ATP was substituted by acid pH. These tRNA movements were sensitive to uncouplers and inhibitors, suggesting distinct roles of the electrical and chemical components of the protonmotive force generated by vectorial proton translocation accompanying ATP hydrolysis. The results have implications for the mechanism of tRNA import.

Targeted mRNA degradation by complex-mediated delivery of antisense RNAs to intracellular human mitochondria

Mitochondrial dysfunction underlies a large number of acute or progressive diseases, as well as aging. However, proposed therapies for mitochondrial mutations suffer from poor transformation of mitochondria with exogenous DNA, or lack of functionality of the transferred nucleic acid within the organelle. We show that a transfer RNA import complex (RIC) from the parasitic protozoon *Leishmania tropica* rapidly and efficiently delivered signal-tagged antisense (STAS) RNA or DNA to mitochondria of cultured human cells. STAS induced specific degradation of the targeted mitochondrial mRNA, with downstream effects on respiration. These results reveal the existence of a novel small RNA-mediated mRNA degradation pathway in mammalian mitochondria, and suggest that RIC-mediated delivery could be used to target therapeutic RNAs to the organelle within intact cells.

Dr. Keya Chowdhury and group

Molecular analysis of human diseases

***Host-Vibrio cholerae interaction*:**

Vibro cholerae, the etiological agent of cholera, colonizes the small intestine, produces an enterotoxin and causes acute inflammatory response at intestinal epithelial surface; the signals for such induction are still unknown. We determined the mRNA expression of proinflammatory and anti-inflammatory cytokines in Int407 cells following infection with *V. cholerae* or its mutants by semiquantitaive and quantitative real-time RT-PCR. *V. cholerae* induces the coordinated expression and up-regulation of IL-1(α and β), TNF-α, IL-6, IL-8, GM-CSF, MCP-1 and ENA-78 with chemoattractant and proinflammatory properties of various cytokine families and down-regulation of TGF-β in Int407 cells. These proinflammatory cytokines also showed increased expression in T84 cells, except for IL-6, whereas a striking dissimilarity in cytokine expression was observed in Caco-2 cells. *V. cholerae* culture supernatant harbors strong inducer(s) of IL-6 and MCP-1 and moderate inducer(s) of IL-1α and GM-CSF. Cholera toxin- or lipopolysaccharide-induced cytokine expression is facilitated by activation of nuclear factor-kB (p65 and p50) and cAMP response element binding protein (CREB) in Int407 cells. Studies with ctxA mutants of *V. cholerae* revealed that the mutant activates the p65 subunit of NF-κB and CREB protein, and as such the activation is mediated by cholera toxin-independent factors as well. Apart from the above factors, significant reduction in IL-1α, GM-CSF and MCP-1 mRNA expression was observed upon infection with the less motile and less adherent strain O395YN. This association is supported by the absence of nuclear translocation of NF-κB (p50 subunit) upon infection with O395YN in contrast to wild-type. Moreover, TPCK treatment prior to *V. cholerae* infection indicated that proinflammatory cytokine gene expression in Int407 cells is NF-κB mediated. Thus, *V. cholerae* induces proinflammatory cytokine response in Int407 cells, is mediated by NF-κB and is modulated, in part, by adherence or motility of this organism.

Moreover, our studies with an engineered aflagellate *V.cholerae flaA* mutant (O395FLAN) and with crude flagellar protein indicated that flagellin of *V.cholerae* could induce IL-1β expression by recognizing TLR5 that activate NF-κB and MAP kinase in Int407. We have identified a set of genes, which are induced by the virulence regulator ToxR and presumed to be involved in virulence of *V. cholerae*. We hope to mutate these genes and look into the host response.

Identification of genomic islands

Many of the available methods for detecting Genomic Islands (GIs) in prokaryotic genomes use markers such as transposons, proximal tRNAs, flanking repeats etc., or they use other supervised techniques requiring training datasets. Most of these methods, however, either do not use any formal statistical test of significance or use statistical tests for which the critical values and the P-values are not adequately justified. We have proposed a method, which is unsupervised in nature and uses Monte-Carlo statistical tests based on randomly selected segments of a chromosome. Such tests are supported by precise statistical distribution theory, and consequently, the resulting P-values are quite reliable for making the decision.

Our algorithm (named Design-Island, an acronym for Detection of Statistically Significant Genomic Island) runs in two phases. Some putative GIs are identified in the first phase, and those are refined into smaller segments containing horizontally acquired genes in the refinement phase. This method is applied to *Salmonella typhi* CT18 genome leading to the discovery of several new pathogenicity, antibiotic resistance and metabolic islands that were missed by earlier methods. Many of these islands contain mobile genetic elements like phage-mediated genes, transposons, integrase and IS elements confirming their horizontal acquirement. The performance of our method is better than many other well-known methods in terms of their sensitivity and accuracy, and in terms of specificity, it is comparable to other methods. With GI software we have identified a region of *V. cholerae*, which was un-annotated in the complete genome sequence of *V. cholerae*. This region, found to be horizontally transferred, harbored two new ORFs. With our Repeat-searching algorithm, we detected cadherin repeat domains in these ORFs. These were experimentally characterized to code for new toxin that appeared to be RTX-like.

Radiation Biology

The methotrexate-resistant cell strain M5, derived from Chinese hamster lung fibroblast cell line V79, provides a good model to study differential gene expression in response to stress. Genes coding for human homologues of myosin phosphatase, filamin-like protein, phosphate transporter 1 and hnRNP E2 were upregulated in M5 as determined by RAP-PCR. The Gene Expression Array (GEArray) analysis showed increased expression of caspase-6 and Hsp90 in M5 cells compared to that observed in V79 cells. Genomic amplification of SSBP2 as well as its transcriptional upregulation was also detected in M5 cells. Following γ-irradiation, expressions of SSBP2, Hsp90 and hnRNP E2 increased steadily in V79 cells. However, expression of hnRNP K and hnRNP A2 genes decreased at first and then increased, while hnRNP C1 gene expression remained unaffected up to the time studied. Thus, SSBP2, Hsp90 and hnRNP E2 are involved in the radiation response of V79 cells.

We have also investigated the changes in ultrastructural features of dermal collagen fibrils of mice following exposure to different cumulative chronic low-dose X-irradiation through digital image analysis-based statistical modeling. Pubertal mice were X-irradiated and dorsal skin biopsies were collected and processed for transmission electron microscopic (TEM) analysis. TEM features of collagen fibrils showed alteration in the cross-sectional area, population density and in the axial periodic pattern of light and dark bands. The mathematical analysis of histogram data from TEM images revealed some adaptive behavior in collagen structures of the X-irradiated group. This finding indicated that exposure to chronic low-dose X-radiation induced an altered steady state with adaptive variation in dermal collagen fibrils in irradiated mice.

Reduction of sodium arsenite induced toxicity by aqueous garlic extract. Arsenic has emerged rapidly as a major pollutant of drinking water in several districts of West Bengal, India, Bangladesh, Taiwan and several other countries. Despite arsenic being a health hazard and a well-documented human carcinogen, a potentially effective remedy with high restorative property against arsenic-induced toxic effects still eludes us. In the present study, therapeutic efficacy of aqueous garlic extract (AGE) was analyzed in terms of reducing arsenic burden, as well as recovery in the altered biochemical variables particularly suggestive of oxidative stress, *in vitro* and *in vivo*. AGE (2mg/ml) co-administered with 10μM sodium arsenite (NaAsO2). Attenuated NaAsO2 induced cytotoxicity, reduced intracellular reactive oxygen species (ROS) level and decreased mRNA expression of stress response genes in human malignant melanoma A375 cells. Moreover, AGE application in NaAsO2-intoxicated Sprague-Dawley rats resulted in a marked inhibition of tissue lipid peroxide generation; enhanced level of total tissue sulfhydryl groups and glutathione; and also increased the activities of anti-oxidant enzymes, superoxide dismutase and catalase to near normal. An increase in blood ROS level and myeloperoxidase activity in arsenic-intoxicated rats was effectively prevented by AGE co-administration. AGE was also able to counter arsenic mediated incongruity in blood hematological variables and glucose level. The restorative property of AGE was attributed to its arsenic antioxidant activity, chelating efficacy, and/or oxidizing capability of trivalent arsenic to its less toxic pentavalent form. Taken together, evidence indicates that AGE can be a potential protective regimen for arsenic mediated toxicity.

Pathophysiology of Oral Submucous Fibrosis (OSF):Oral submucous fibrosis (OSF) is a precancerous condition of the oral cavity & oropharynx, a significant number of which transform into oral squamous cell carcinoma (OSCC). Presently, diagnosis of OSF is assumed mainly through qualitative histopathological evaluation, and at the level of diagnostic molecular biology, the genetic marker is still elusive. This study evaluates histopathological changes in the epithelium and subepithelial connective tissue of OSF through quantitative digital image analysis in respect to specific candidate features. The analysis revealed that there are subtle quantitative differences in the histological images of OSF compared to normal oral mucosa (NOM). The thickness of the epithelium and cell population in its different zones, radius of curvature of rete-ridges and connective tissue papillae decreased but length of rete-ridges and connective tissue papillae, fibrocity and the number of cellular components (predominantly inflammatory cells) in the subepithelial connective tissue increased in OSF. This study establishes a distinct quantitative difference between NOM and OSF in respect to their histological features. This study was done in collaboration with Dept of Electronics, IIT-Kharagpur.

Dr. Kunal Ray and group

Molecular Genetic Studies on Human Diseases

A few genetic diseases that are common in India have been targeted which include eye disorders (primary open angle glaucoma, POAG & oculocutaneous albinism, OCA), neurological disorders (Wilson disease & Parkinson's disease), and bleeding disorder (Haemophilia). A brief overview of the studies is provided below. The intent of the study is to understand the molecular basis of these diseases.

Eye Disorders: The human eye is a complex organ, comprising a number of different tissue types that are derived from all three embryological layers. It is not surprising, therefore, that the eye is one of the commonest sites of genetic disease. The importance of this group of disorders is also reflected in the simple fact that genetic eye diseases comprise the commonest causes of blindness in children and adults. We are involved in molecular genetic studies on (a) glaucoma, which affects 67 million people worldwide and about 1.5 million people are blind due to glaucoma; and (b) Oculo-cutaneous albinism (OCA), a group of autosomal recessive disorders characterized by deficient synthesis of melanin pigment, associated with common developmental abnormalities of the eye. It is one of the major causes of childhood blindness in India.

To identify and evaluate variant alleles in myocillin (*MYOC*) as a candidate gene in patients with primary open-angle glaucoma (POAG) and age-matched control subjects in an Indian population, 315 patients and 100 unrelated control subjects from the same ethnic background were enrolled in the study. Thus, we observed 2.2% *MYOC* mutations in our patient cohort which include one novel mutation (Gly399Asp), 6 reported mutations (Gln48His, Thr256Met, Thr353Ile, Gln368Stop, Pro370Leu and Ala427Thr), and 6 single nucleotide polymorphisms. Four single nucleotide polymorphisms genotyped in control subjects were highly heterozygous and displayed a similar pattern of linkage disequilibrium among all linguistic groups of India. (Bhattacharjee et al, *Archives of Ophthalmology*, 125: 823-829, 2007). Studying the genetics of POAG is helpful for preclinical identification and for better disease management.

We also investigated the molecular basis of primary open-angle glaucoma (POAG) using Opticin (*OPTC*) as a candidate gene on the basis of its expression in the trabecular meshwork cells involved in the disease pathogenesis. Two hundred POAG patients and 100 controls were enrolled in this study. We detected two missense (p.Glu66Gly & p.Ile89Thr) and one silent change (p.Phe162Phe; c.602 C>T) that was present in 3 different patients but in none of the 100 controls screened. The mutant (c.602T) mRNA was predicted to have remarkably different secondary structure compared to the wild-type transcript by *in silico* approaches. Subsequent wet-lab experiments showed lower expression of the gene both at the mRNA and protein levels. Our study suggests *OPTC* as a candidate gene for POAG. Further, it highlights the importance of investigating the 'silent' variations for functional implication that might not be apparent from only *in silico* analysis (Acharya et al, *BMC Molecular Biology*, 8: 21, 2007). These studies have been done in collaboration with Regional Institute of Ophthalmology, Medical College, Kolkata; and Dristi Pradip, Kolkata.

Our OCA patient pool consists of 50 unrelated OCA pedigrees covering 17 ethnic groups of eastern and southern India. In the patient cohort, 20 cases (from 19 affected families), lacking any mutation in the *tyrosinase* gene (*TYR*), were screened further for nucleotide variants in *SLC45A2*. Four novel mutations (c.126G>A [Met42Ile], c.190G>A [Gly64Ser], c.904A>T [Thr302Ser] and c.1042C>T [Arg348Cys]), one reported mutation (c.469G>A [Asp157Asn]) and two SNPs (E272K and L374F) that have been reported to be associated with human ethnicities were identified. Our study reveals that 10% of the total OCA cases from eastern and southern Indian ethnic groups carry mutations in *SLC45A2* (Sengupta et al, *Molecular Vision*, 13:1406-1411, 2007). Direct detection of the mutations prevalent in specific ethnic groups could be used for carrier detection and genetic counseling.

Neurological Disorders: Among neurological disorders our group works on Wilson's disease (WD), Parkinson's disease (PD) and dystonia. The focus of the study is to identify the molecular basis of the disease among Indians. The studies are conducted in collaboration with Bangur Institute of Neurology for clinical areas of the study. While our group is focused primarily on Wilson disease, studies on PD and dystonia are done with Prof. Jharna Ray (SN Pradhan Centre of Neurosciences, Calcutta University) who is the principal investigator for the latter two diseases.

Wilson's disease is an inborn error of copper metabolism due to mutation in the copper-transporting gene *ATP7B* and characterized by excessive copper deposition predominantly in the liver and brain. The frequency of the disease is about 1 in 5000 to 1 in 30000 live births and based on this estimate the carrier frequency is approximately 1 in 90. WD can be thwarted if detected at a presymptomatic stage, but occasional recombination during carrier detection with dinucleotide repeat markers flanking the WD locus may lead to faulty diagnosis. We examined the use of intragenic single-nucleotide polymorphism (SNP) markers to avoid this limitation. We prepared genomic DNA from the peripheral blood of Indian WD patients. By use of PCR, we amplified the exons and flanking regions of the WD gene and then performed sequencing to identify the nucleotide variants. Also, genotypes of selected SNPs in 1871 normal individuals, representing different ethnic groups of India, were determined by use of the Sequenom mass array system. In the patient

cohort, we identified one mutation accounting for 11% (19 of 174) of WD chromosomes in addition to 4 prevalent mutations characterized previously. Among 24 innocuous allelic variants identified, we selected 3 SNPs found to have high heterozygosity (>0.40) for the detection of mutant WD chromosomes. On analyzing these SNPs in 28 test individuals, who were sibs to 17 unrelated WD patients, we obtained unequivocal genotyping in 25 cases (approximately 89%). The remaining 3 cases were genotyped by dinucleotide repeat marker (D13S133). Sets of SNP markers are highly heterozygous across most world populations and could be used in combination with analysis of prevalent mutations as a comprehensive strategy for determining presymptomatic and carrier sibs of WD patients.

Parkinson's disease (PD), the second most common neurodegenerative disorder, affects at least 1% of the population over the age of 50. However, very little information is available regarding the molecular basis of PD among Indians. Since the largest number of mutations has been detected in the Parkin gene among all known PD loci, we aim to use Parkin as the candidate gene to assess its role in PD-related pathogenesis in Indian patients. A total of 138 PD patients and 141 controls were recruited for the study from eastern India. In addition to disease causing mutations, published previously, we examined SNPs for association with the disease. Our data clearly indicates that homozygous Ser167 and Val380 are significantly associated with the disease suggesting that the Parkin polymorphisms are risk factors for PD, and their frequency is greatly influenced by ethnic origin. This study also provides an opportunity to correlate genetic variation with epidemiological data in Indian population.

Bleeding disorder: Currently our lab is engaged in molecular genetic studies on Haemophilia. This X-linked disease is caused independently by defects in Factor VIII and Factor IX genes resulting in Haemophilia A and Haemophilia B, respectively. Usually females carry and males are affected with the disease. At present the most practical approach to contain haemophilia relates to strategies for carrier detection and prenatal diagnosis.

We examined variations of single nucleotide polymorphism (SNP) in Factor VIII gene in the Indian population and established the utility of a combination of SNP and microsatellite markers for the successful identification of carriers in the affected families. Our studies on the Indian population and the available data on International HAPMAP population groups suggest that microsatellite markers, and not SNPs, should preferably be used for carrier detection of hemophilia A. Among these multi-allelic markers, the intron 9 CT-repeat showing higher heterozygosity should be tested across different population groups for wide application for carrier detection.

Genomic Variation in Indian Population in the disease associated genes: The study has been undertaken in 10th Five Year Program under the mission mode project on 'Predictive medicine using repeat and single nucleotide polymorphisms'. This program is designed to identify the single nucleotide polymorphisms (SNPs) in genes in different population groups of India. Sequence variation in human genes is largely confined to SNPs and is valuable in tests of association with complex disease, markers for monogenenic disorders, susceptibility to infectious diseases and pharmacogenetics traits. This network program has been undertaken by six CSIR laboratories including IICB. From Dr. Ray's group genotyping has been completed for selected SNPs in the genes that are related to ocular, neurological and bleeding disorders in about 1500 genomic DNA collected from normal individuals across different population groups of India. Some of the findings have been published as mentioned above and analyses on other genes are currently underway.

Dr. Susanta Roychoudhury and group

Molecular Genetics of Head and Neck Cancer

Complex Interplay between human papilloma virus infection and p53 gene alterations in head and neck squamous cell carcinoma

We investigated the complex interplay between human papilloma virus (HPV) infection and p53 gene alteration in head and neck squamous cell carcinoma (HNSCC) and leukoplakia samples from eastern India. DNA isolated from 92 head and neck squamous cell carcinoma (HNSCC) and 28 leukoplakia samples were subjected to HPV detection, loss of heterozygosity (LOH) analysis of the chromosome 17p region harbouring *p53,* genotyping at the p53 codon 72 locus and sequencing of the entire *p53* gene to identify somatic mutations. Codon 72 heterozygotes carrying the p53 mutation were further cloned and re-sequenced to identify the allele harbouring the mutation. HPV positivity in the HNSCC samples was 69%; 21% of the HNSCC were found to harbour p53 mutations in the coding region of the gene. The absence of the p53 mutation in HPV positive tumours was statistically significant compared to the HPV negative tumours ($p = 0.01$), but the same did not hold true for p53 LOH ($p = 1.0$). Among the germline p53 codon 72 heterozygotes, the Pro allele was preferentially lost ($p = 0.02$) while the Arg allele was mutated in the majority of cases. The risk of HPV mediated tumourigenesis increased with the increase in number of Arg alleles at the codon 72 locus. It has been proposed that genetic and epigenetic alteration of p53 follow distinct pathways during the development of HNSCC from normal epithelium via dysplasia. The p53 mutation and HPV mediated p53 inactivation possibly constitute two independent pathways of tumourigenesis.

Dr. Ashok K. Giri and group

Antimutagenic and anticancer effects of black tea polyphenols in multiple test systems:

This study investigated the induction of apoptosis in human skin cancer cells after treatment of Theaflavins (TF) and thearubigins (TR). In our system, Bax translocation to mitochondria persuaded depolarization of mitochondrial membrane potential, cytochrome *c* release in cytosol and induced activation of caspase-9, caspase-3 and PARP (poly (ADP-ribose) polymerase) cleavage. Our intricate investigations on apoptosis also explained that TF and TR augmented Bax/Bcl2 ratio, upregulated the expression of p53 as well as p21 and inhibited phosphorylation of the cell survival protein Akt. Furthermore, TF and TR elicited intracellular ROS (reactive oxygen species) generation in A375 cells. These observations raise speculations that TF as well as TR might exert chemopreventive effect through cell cycle arrest and induction of apoptogenic signals via mitochondrial death cascade in human skin cancer cells.

Assessment of genetic damage and genetic variants in the arsenic exposed individuals:

Although a large number of individuals are exposed to arsenic through drinking water but only 15-20% individuals showed arsenic induced skin lesions. This indicates that genetic variants play an important role in arsenic induced toxicity and carcinogenicity. Potential of allelic variants of various genes of arsenic toxicity pathway (PNP, As3MT, GSTO1 and GSTO2) and others (p53 and ERCC2) have been examined for association with the phenotypic alteration. Among the four candidate genes, PNP, As3MT, GSTO1 and GSTO2, we found that distribution of three exonic polymorphisms of PNP was associated with arsenicism. Genotype having the minor alleles were significantly overrepresented in the skin lesions group (DeChaudhuri et al., 2008). The results of p53 polymorphism showed that arsenic induced keratosis has a significant association with the R/R and S/S alleles. We wanted to see the chromosomal aberrations (CA) in the both R/R genotype group and compare with the other genotype i.e. R/P and P/P. A significant increase in the CA in the risk genotype (R/R) was observed (DeChaudhuri et al., 2008a).

ERCC2 codon 751 polymorphism (A→C; Lys→Gln) is implicated in several types of cancer. We wanted to find out any possible association of ERCC2 codon 751 polymorphism with arsenic specific premalignant Hyperkeratosis. In the ERCC2 polymorphism the AA genotype was significantly over represented in the arsenic induced Hyperkeratosis exhibiting group, indicating that it is strongly associated with the development of arsenic specific precancerous Hyperkeratosis. Alkaline comet assay and Challenge assay were carried out in whole blood and chromosomal aberrations study in lymphocytes to find out the DNA damage and DNA repair capacity in both hyperkeratotic and without skin lesion individuals. Challenge assay showed that upon induction of DNA damage the repair capacity in the exposed individuals with premalignant hyperkeratosis is significantly less than that of individuals without skin lesion, although the basal level of DNA damage was similar in both. Thus the deficiency in DNA repair capacities in the hyperkeratotic individuals emerges as a prime contender for arsenic carcinogenicity.

To find out the effect of chronic arsenic exposure on the haematological studies and immunological systems of the arsenic exposed population we studied mechanism of cell death in erythrocytes and its effect on T cell proliferation and cytokine secretion in the lymphocytes of arsenic exposed individuals. Our results showed that arsenic toxicity intervened into red cell membrane integrity leading to destabilization and haemoglobin release (Biswas et al., 2008). The T cell proliferation and cytokine secretion were significantly reduced in the arsenic exposed individuals compared to the unexposed individuals (Biswas et al., 2008). We also found that arsenic induced mitochondria mediated apoptosis in the lymphocytes of exposed individuals which follows the mitochondria mediated pathway (Banerjee et al., 2008).

Dr. Samir Dutta and Group

Plant Protease inhibitor as a potential bio-pesticide:

Winged bean (*Psophocarpus tetragonolobus*) is a leguminous plant and is a very rich source of protease inhibitors. Artificial feeding trials with two homogeneous protease inhibitors from winged bean seeds, one inhibiting both trypsin and chymotrypsin (WbTI-1B) and the other inhibiting only trypsin (WbTI-2), were found to be detrimental to this polyphagous pest larva. Soon after, the genes for both WbTI-1B and WbTI-2 have been cloned in our lab and sequenced. The GenBank Accession numbers are AY997024 and DQ363437 respectively. The recombinant proteins expressed in *E. coli* were equally effective against *Hellicoverpa* like the seed proteins. Thus, the genes might be useful as an arsenal against the polyphagous pest *Hellicoverpa*. (Artificial feeding trial has been done in collaboration with NCL, Pune).

Interestingly, the chymotrypsin/ trypsin inhibitor (WbTI-1B) has been mutated to produce two different mutants, one of which inhibits trypsin only whereas the other inhibits chymotrypsin only. Computer aided molecular modelling gave an idea about the changes in the reactive site loop (RSL) structure of these two mutants.

Technical staff and others:

Bhaskar Basu , Tapas Chaudhury, Rajat Banerjee (on E.O.L.) , Mahua Bhattacharya, Tanay Ray

Project Assistants

Qudsia Zarrin, Arun Roy

Pool Officers, RAs, Research Fellows

Saikat Mukherjee, Gunjan Dhar, Biraj Mahato, Sandip Koley, Sukanta Jash, Deblina Banerjee, Atreyee Saha, Suddhasil Mookherjee, Mainak Sengupta, Maitreyee Mondal and Subhodip Chakraborty, Dr. Antara Banerjee, Mr. Shiladitya Sengupta, Ms. Chaitali Mishra, Ms. Taraswi Banerjee, Ms. Dipanjana Dutta De, Ms. Swati Bajaj, Mr. Somsubhra Nath, Mr. Pinaki Mondal and Ms. Sumana Bhattacharya, Saheli Sengupta, Shiladitya Mitra, Satarupa Dey, Manikarna Dinda, Deepak Verma, Sunandini Basu, Priyadarsan Chatterjee, Qudsia Zamin, Arun Roy, Deblina Banerjee, Pritha Ghosh, Mayukh Banerjee, Nilanjana Banerjee, Udayan Bhattacharya, Manjari Kundu, Dr. Susri Roychoudhury, Dr Tapasi Das, Raghunath Chatterjee, Arunava Bandyopadhaya, Sumit Ranjan Das, Pratim Chaudhuri, Rajdeep Chowdhury.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Drs. Tarun Kumar Dhar, Mina Mukherjee, Rajan Vedasiromoni, Anil Ghosh, Smita Mitra (upto Dec 2007), Aparna Gomes, Nirmalendu Das, Pratap K. Das, Suman Khowala, Sharmila Chattopadhyay, Snehasikta Swarnakar

This group is involved in studies on bioactive compounds for improving health and quality of life, as also for promoting future economic growth through innovation in biotechnology. The major field of activity includes – therapeutic principles from plants and venoms; engineered plant genes for improved production of pharmaceuticals/nutraceuticals; mechanism of gastric ulceration; immunodiagnostic strategies; liposomal drug delivary; mushroom sporulation; trehalose metabolism and microbial glycosidase enzymes.

Dr. J.Rajan Vedasiromoni, Dr. (Mrs.) Smita Mitra, Dr. (Mrs.) Aparna Gomes and group

Development of drugs from plant materials, animal products and synthetic agents

Anti-inflammatory and antineoplastic studies were carried out with some commonly available plant materials like leaf extracts of *Sweitenia Mahagoni*, *Lichi Chinensis* and *Wattakaka volubilis* and the seed extract of *Sweitenia Mahagoni*.

The anti-inflammatory activity of leaf extract of *Wattakaka volubilis* was evaluated using acute, sub-chronic and chronic models of inflammation in rodents. The antipyretic and analgesic activities were evaluated in mouse models. In acute toxicity study, it was found that the extract was non-toxic up to 1g/kg, i.p. The extract (50, 100 and 200 mg/kg, i.p.) was found to possess anti-inflammatory, analgesic and antipyretic activities in a dose-dependent manner and the effect was comparable with that produced by the standard drug, ibuprofen. The extract significantly inhibited the arachidonic acid induced paw oedema in rats, indicating that the extract inhibited both the cyclooxygenase and lipooxygenase pathways of arachidonic acid metabolism. The extract also significantly enhanced macrophage count in mice in a dose- and time-dependent manner.It is possible that the saponins present in the extract may be responsible for these activities.

Litchi chinensis leaf extract (LCLE) was found to possess apoptotic activity in three human leukemic cell lines-U937, K562 and HL-60. LCLE inhibited cell growth and metabolic activity of the leukemic cells and showed characteristic features of apoptosis. Flow cytometric analysis showed appreciable number of cells in early and late apoptotic stages. While U937 and K562 cell populations were arrested in the G2-M phase, the HL-60 cell population was arrested in the G1 phase of cell cycle. LCLE induced apoptosis is mediated through mitochondrial intrinsic pathway involving the release of cytochrome c into the cytosol and activation of caspase-9 and caspase-3.

Pharmacological studies were carried out with the methanolic extract of dried seeds of *Swietenia mahagoni* (SMSE) on experimental rodents. The extract was found to possess potent anti-inflammatory and analgesic activities. Acute toxicity studies revealed that the extract, up to a dose of 1.2g/kg intraperitoneally, was nontoxic. The results of the experiment on arachidonic acid induced paw oedema in rat revealed that the extract produced anti-inflammatory activity through dual inhibition of the cyclooxygenase and lipooxygenase pathways of arachidonic acid metabolism. SMSE also enhanced peritoneal cell exudates along with macrophage significantly. The triterpenoids present in SMSE may be responsible for these activities.

NK-31, a heat stable cytotoxic-cardiotoxic protein has been identified from the venom of the Indian monocellate cobra (*Naja kaouthia*). The protein was purified to homogeneity by ion-exchange chromatography

and HPLC. Molecular weight of NK-31 was found to be 6757D and N-terminal first 20 amino acid sequence was LKCNKLVPLFYKTCPAGKNL. NK-31 significantly inhibited proliferation of human leukemic U937 and K562 cells in a dose and time dependent manner, as judged by trypan blue exclusion method and MTT assay. IC50 of NK-31 on U937 and K562 cells were 3.5 μg/ml & 1.1 μg/ml respectively. Morphometry and cell sorting studies showed an induction of apoptosis in NK-31 treated leukemic cells. NK-31 induced apoptosis was caspase 3 & 9 dependent. The cell-cycle machinery of NK-31 treated leukemic cells were arrested in sub-G1 stage. IC50 dose of NK-31 showed low cytotoxic effect on normal human leukocytes as compared with imatinib mesylate. NK-31 (30 μg/ml) produced 100% irreversible blockade of isolated guinea-pig auricle within 4±1.11 min, which was Ca^{2+} dependent. NK-31 also showed positive PLA2 activity. Cytotoxic, cardiotoxic and PLA2 activities were however abolished after trypsin treatment. Further structural-functional studies of NK-31 are warranted. The results are shown in the Figure 1

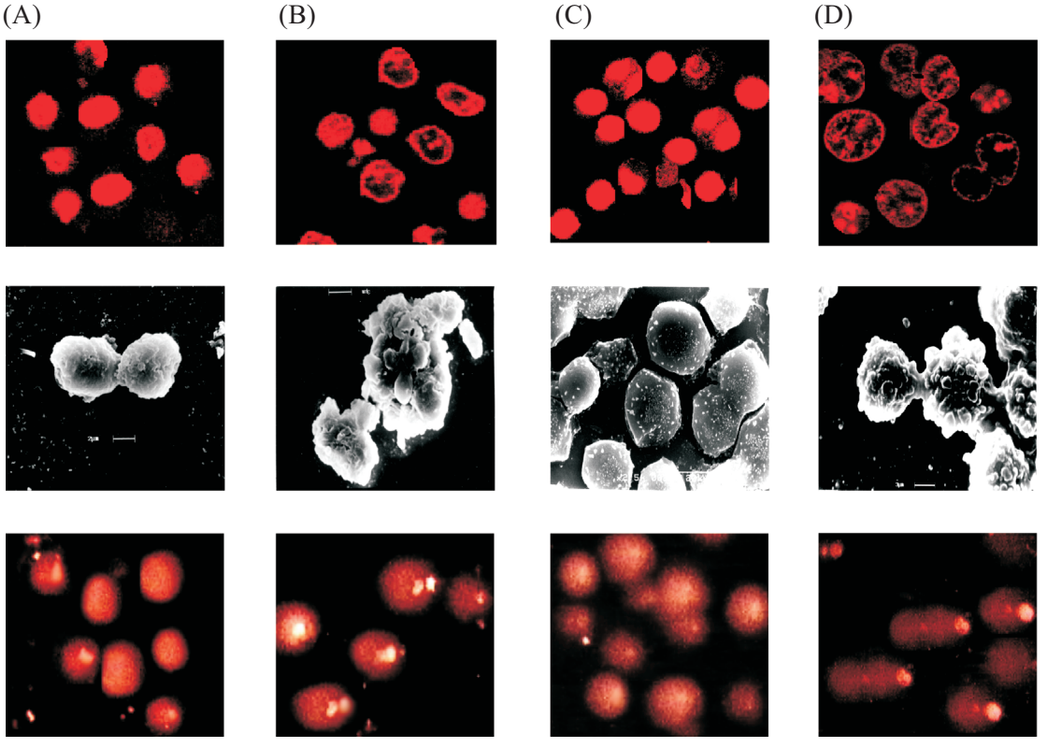


Fig. 1. Confocal microscopy, scanning electron microscopy and single cell gel electrophoresis pattern (comet assay). Morphological changes and comet assay of control and NK-31 treated U937/K562 cells.

Upper panel - Confocal micrography of control U937 cells **(A)**, treated U937 cells **(B)**, control K562 **(C)**, and treated K562 cells **(D)** using PI. The control cells showed intact nucleus and the NK-31 treated cells showed apoptotic bodies in both cells indicated by (→). Magnification (1000X).

Middle panel - Scanning Electron micrography of control U937 cells **(A)**, treated U937 cells **(B)**, control K562 **(C)**, and treated K562 cells **(D)**. The control cells showed intact plasma membrane while treated cells showed presence of deep ridges and furrows as indicated by (→). Magnification (3000X).

Lower panel - Single cell gel electrophoresis pattern (comet assay) of control U937 cells **(A)**, treated U937 cells **(B)**, control K562 **(C)**, and treated K562 cells **(D)**. (→) indicates tail formation due to DNA breakage. Magnification (100X).

The group is also engaged in bioevaluation of some herbal preparations of M/S Dey's Medicals Pvt.Ltd., as part of the collaboration between them and IICB and carries out pharmacokinetic studies of molecules identified in the Institute.

Dr. Pratap K. Das and group

Screening of Indian biodiversity and Indian Systems of medicine for anti gastric ulcer principle(s)

The development of appropriate strategy and protocol(s) for effective screening of Indian biodiversity and Indian Systems of Medicine with a view to examining their efficacy against peptic ulcer diseases has been the main frame of this research endeavour. The central objective is to dovetail traditional knowledge base and information systems with the help of currently understood biological targets to generate newer leads, and transfer such know-how to national and multinational pharmaceutical companies for commercial exploitation.

During the period under consideration, we have screened about 2200 samples of plant, bacterial and fungal origin, and a few single molecules of natural product origin in gastric antisecretory and anti H. pylori models. We could primarily fish out about 22 plant samples, one microbial extract, and 8 single molecules as active (12 as anti H. pylori and 19 as antisecretory), with no traditional preparations being screened during this period. We have also been reexamining them with repeat collection and repeat extraction to validate the primary findings, and to take the sample(s) to next stage of investigation through bioassay-guided fractionation approach. Meanwhile, previously screened samples along with a few from (10 plant samples and 2 microbial samples) were revalidated during the period under consideration; however, none among these could be considered worthy of further development through Drug Discovery exercises.

Towards developing new-biology based models, we wanted to investigate the effects of different putative agents on the shuttle functioning of the K^+ flux through the gastric mucosa in regulating gastric acid secretion. We have developed an ion chromatographic method for the detection and quantification of ppm level K^+ in gastric fluids in the presence of high Na^+. Employing C2 250 silica gel column with carboxy groups as stationary phase, an otherwise difficult quantification of ppm-level K^+ in the presence of high ppm-level Na^+ was achieved by incorporating 18-crown-6 ether in the mobile phase. Optimized analytical conditions were established in terms of relative standard deviation (%) of retention time, peak area and calibration equations, and also by peak asymmetry factor. The net efflux of K^+ into the gastric lumen under in vitro conditions of acid secretion by the physiological secretagogue histamine was investigated in Ussing chamber model. The characteristic decline of K^+ efflux in presence of H_2 receptor blocker cimetidine, and the rise of the same in presence of H^+,K^+-ATPase inhibitor omeprazole (suicide inhibitor type) and SCH 28080 (K^+ competitive type) were conspicuously discernible (Fig. 2), thereby validating the usefulness of ion chromatography based K^+ quantification method under biological experimental conditions.

Screening of plant extracts against the ulcer causing bacterium indicated that *Tephrosia purpurea*, a traditionally well-used plant in the management of different types of wounds, has the potential to be an effective anti H. pylori agent. The methanolic extract showed promising activity against standard strains and also clinical isolates, including metronidazole-resistant strains. Fractionation of the extract revealed n-hexane and chloroform fractions, and not the n-butanol and aqueous fractions, with marked activity. Neither the extract nor the fractions showed anti bacterial activity against common aerobic bacteria indicating specific anti H. pylori activity of the material. The extract and the two less polar fractions showed effective bactericidal activity in acidic condition similar to stomach environment, as evidenced through kill-kinetics experiments as a function of acidic pH (Fig. 3), exhibited consistent bacteriostatic activity during successive exposure of bacteria to sub-inhibitory concentrations, and demonstrated synergism, complete or partial, even with antibiotic-resistant strains. The work has been carried out in collaboration with Dr. UV Mallavadhani of IMMT (CSIR).

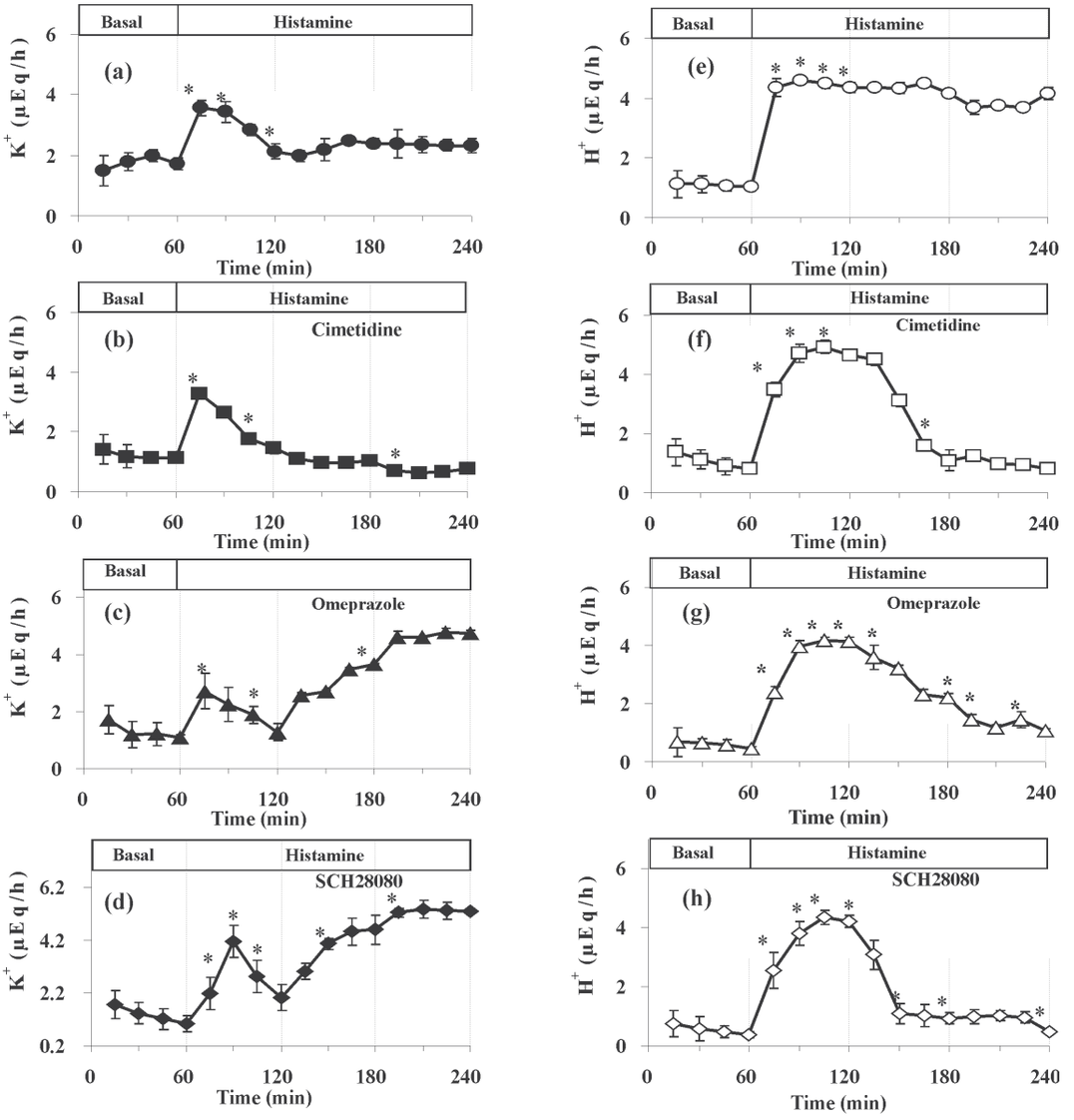


Fig. 2. Rate and extent of K^+ and H^+ efflux under influence of cimetidine, omeprazole and SCH28080 in histamine stimulated frog gastric mucosa. Panels **a-d** describe net K^+ efflux data and panels e-h H^+ transport data for control (a and d), cimetidine (**b** and **f**), omeprazole (**c** and **g**) and SCH28080 (**d** and **h**) respectively. For each compound, the experimental results were plotted using same symbols for K^+ (closed) and H^+ values (open). Cimetidine was given at a single dose of 1 mM at 120 min from the nutrient side with a change after 1 hour. Both omeprazole and SCH28080 were given from the nutrient side at a graded dose of 0.01 and 0.02 mM at 120 and 180 min respectively. Data for control, cimetidine, omeprazole and SCH28080 are mean ± SEM (n = 3-4). An asterisk (*) indicates a statistically significant difference (at least $p < 0.05$) from the prior steady-state values.

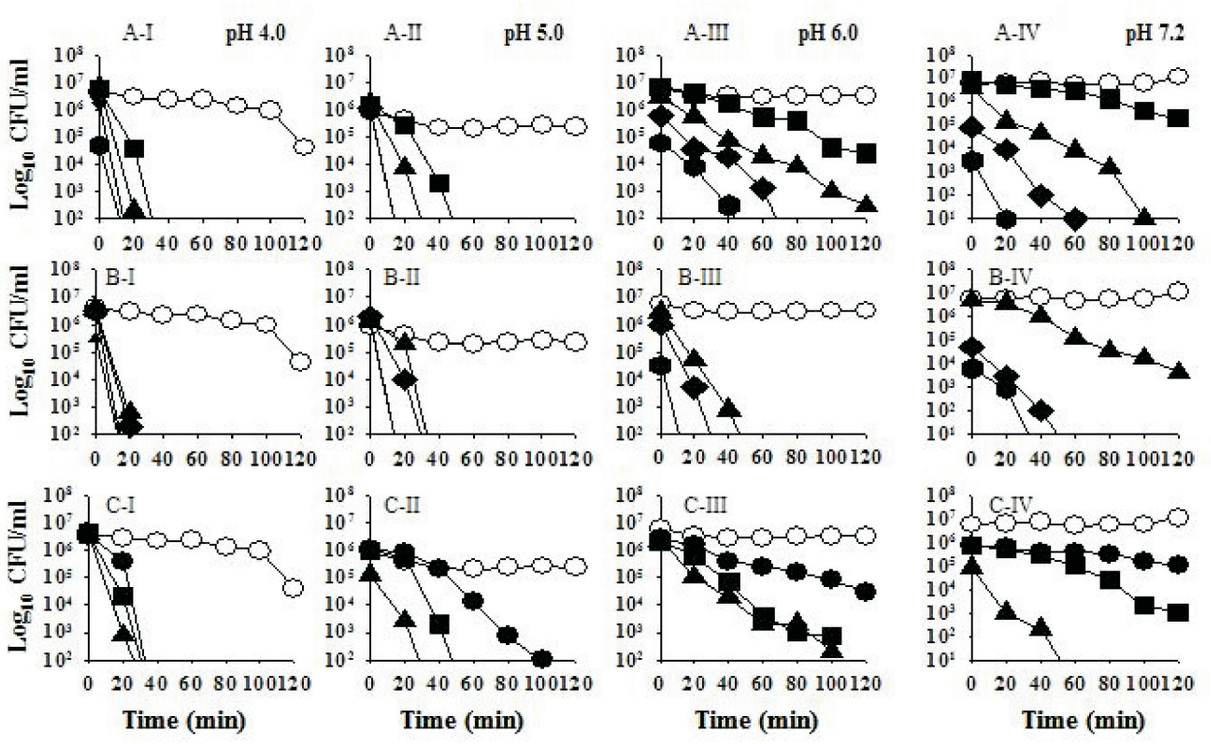


Fig. 3. **Time kill kinetics of *H. pylori* ATCC 43504 strain by the methanolic extract and its two active fractions (n-hexane and chloroform) as a function of pH ranging 4.0-7.2.** The short term kill-kinetics by the methanolic extract (panels **A-I** – **A-IV**), n-hexane fraction (panels **B-I** – **B-IV**) and chloroform fraction (panels **C-I** – **C-IV**) were assessed at 37C under microaerophilic condition with shaking at 150 rpm. Aliquots (100 µl) were taken at indicated time intervals and the rate of killing was assessed with respect to control in terms of viable count. The symbols are: -○- control; -●- 2xMIC; -■- 4xMIC; -▲- 8xMIC; -◆-12xMIC and -⬢- 16xMIC.

In another effort, a steroid-based anti gastric ulcer compound, 3-acetoxy-17-acetamido-16-formyl-androst-5,17-diene has been developed in collaboration with Dr. RC Boruah of NEIST (CSIR). The compound exhibited in vitro inhibition of gastric H^+,K^+-ATPase activity, dose-dependent inhibition of histamine-stimulated acid secretion in gastric parietal cell (Fig. 4), and potent anti ulcer effect against indomethacin-induced ulcer in vivo. The invention has been submitted for Indian patent.

The overall impact of such programme will have its bearing on the development of better, safer and cheaper anti-ulcer medicines from alternate sources. Future studies will be initiated towards development of a few more new-biology based models, like gastric cancer cell culture, so as to be able to be globally competitive in such drug development programme of revisiting Indian biodiversity.

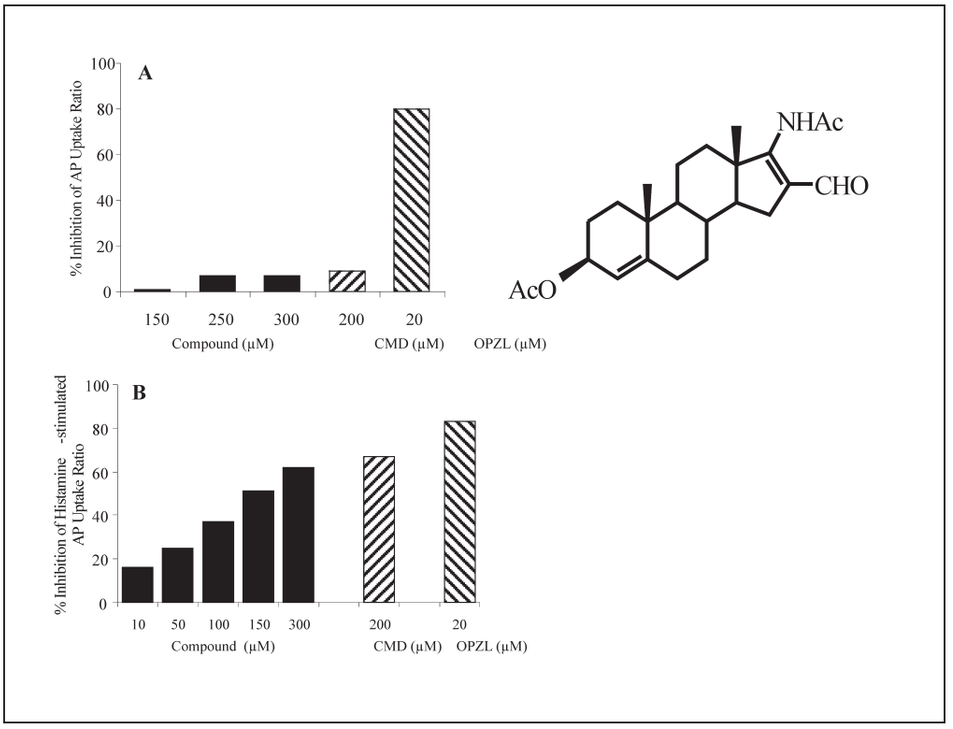


Fig. 4: **Effect of the compound on basal (A) and histamine-stimulated (B) acid secretion in gastric parietal cell**. Dose-dependent inhibition of aminopyrine uptake ratio was measured after treatment of parietal cell suspension (5x10^6 cells) with the compound for 1 h at indicated concentrations. Histamine (0.1 mM)-stimulated aminopyrine uptake ratio was considered as 100%. CMD: cimetidine; OPZL: omeprazole.

Under Drugs & Pharmaceuticals Programme of DST, a research programme is under progress with Funds from DST and an Industry, M/s Dey's Medical. In this inter-institutional programme entitled 'Chemical Standardization & Biological Evaluation with a View to Increase Efficacy of Herbal Medicines' wherein two products of the company are being scientifically examined for their efficacy. The purpose of such R&D tie up of DST-Industry-IICB has been to find out the modern scientific basis of these traditional medicines that would permit them to compete in national and international market under the changed global scenario of Drugs and Pharmaceuticals sector in the era of patent, and IPR.

Dr. Snehasikta Swarnakar and group

Role of matrix metalloproteinases in remodeling of extracelular matrix of gastric tissues during inflammation: Mechanism of action of melatonin

The main objective of present research is to elucidate the therapeutic potential of pineal hormone melatonin (N-acetyl-5-methoxytryptamine) on regression of gastric ulceration and endometriosis. Matrix metalloproteinases (MMPs) are Zn dependent endopeptidases that selectively degrade the components of extracellular matrix (ECM) such as collagen IV, gelatin, elastin and fibronectin, and play an important role in ECM homeostasis. Both gastric ulceration and endometriosis are associated with selective breakdown of ECM and basement membrane proteins by MMPs. Herein, we are interested to focus on the activities of MMPs and their regulation during disease progression and healing of gastric ulcer as well as endometriosis.

The enzymatic activities of MMPs can also be regulated by their endogenous inhibitors like tissue inhibitors of MMPs (TIMPs) hence we are interested to decipher their regulation on MMPs during gastric ulceration and endometriosis. However, literature is scanty regarding the regulation of MMPs and TIMPs in both types of diseases and the mechanistic aspects are yet to be elucidated during the healing process. Melatonin represents a primary secretory product of the pineal gland and is well known for its effects on seasonal reproduction, circadian rhythmicity, and sleep. Additionally, melatonin has also been shown to have a variety of other functions, e.g. influence of immune function as well as antiproliferative and antioxidative actions, age-related oxidative damage in the central nervous system, Alzheimer's disease, Parkinson's disease etc. With reactive oxygen species (ROS) becoming an increasingly tempting target for disease intervention, novel biomolecules with potent antioxidant potential is the main theme of our work.

Gastric ulcers were generated in Balb/C mice by oral administration of either indomethacin (80 mg/kg b.w.) or 50% ethanol (8 ml/kg b.w.). Herein, we have investigated the protective effect of melatonin against both types of gastric ulceration. Melatonin (120 mg/kg b.w. in 10% alcohol) was injected intraperitoneally prior to indomethacin or ethanol treatment. The control mice were received vehicle (8 ml of 10% ethanol/kg b.w.) orally. After 4hr, mice were sacrificed and the stomachs were processed for histological analysis. Histological examination of ulcerated tissues revealed that both indomethacin and ethanol caused severe damage in gastric epithelium along with disrupted gastric pits and glands (Fig. 5B & C) as compared with control (Fig. 5A). The gastric damage was completely abolished in melatonin pretreated (D & E) samples where intact gastric epithelium along with continuous gastric pits and glands were seen.

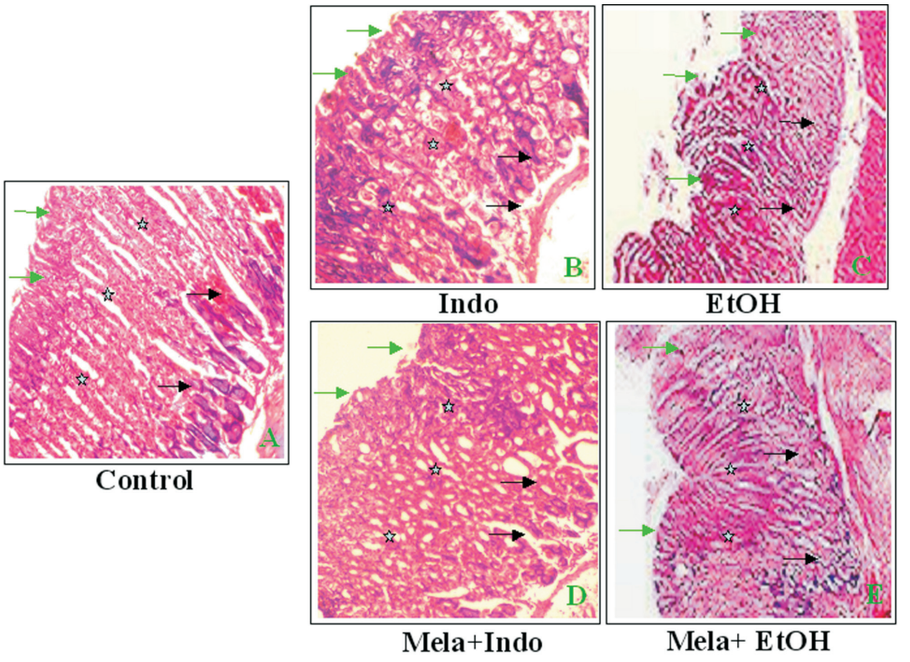


Fig. 5. Histological analysis of mouse gastric tissues after indomethacin and ethanol-induced ulceration and protection by melatonin: Gastric ulcers were induced by indomethacin or ethanol in mice. Histological sections were stained with H&E and photographs were taken at Histological appearances of gastric epithelium, pits and glands in (**A**) control, (**B**) indomethacin-treated, (**C**) ethanol-treated, (**D**) melatonin-pretreated indomethacin-treated, and (**E**) melatonin-pretreated ethanol-treated tissues at 25X magnification. Gastric mucosal epithelium (green arrow), gastric pits (black asterisk), and gastric glands (black arrow)

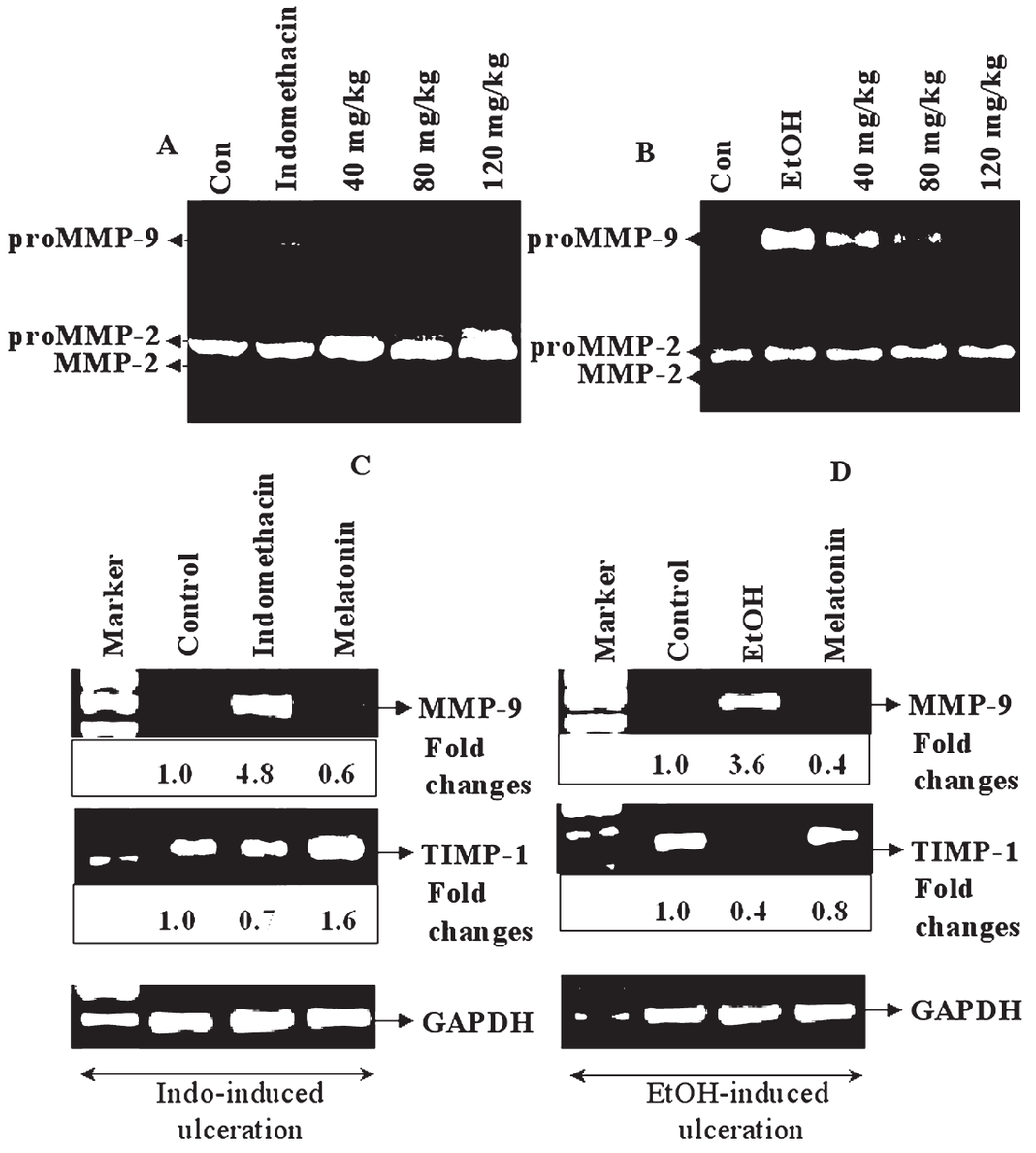


Fig. 6. Effect of melatonin on secreted MMP-9 and -2 activities and MMP-9 gene expressions during prevention of indomethacin and ethanol induced gastric ulcer:

Different doses of melatonin (40, 80 and 120 mg/kg bw) were administered intraperitonially to different groups of mice prior to indomethacin and ethanol treatment. After 4 hr animals were sacrificed and gelatin zymography was conducted using partially purified PBS extracts of gastric tissues from melatonin-pretreated indomethacin-induced groups (**A**) and melatonin-pretreated ethanol-treated groups (**B**). Total RNA was extracted from control, indomethacin or ethanol-treated and melatonin-pretreated groups. RT-PCR analysis was conducted for the detection of MMP-9, TIMP-1 and GAPDH mRNA expressions in indomethacin (**C**) and ethanol (**D**) treated groups respectively. The fold changes are mentioned below the respective figures.

We have further tested about melatonin`s action on activity and gene expression of MMPs during prevention of gastric ulceration. The gelatin zymogram in Fig. 6A and C shows that varying doses of melatonin significantly downregulated both MMP-9 and -2 activities while healing. Herein, melatonin prevented gastric ulceration through downregulation (~80%) of secreted proMMP-9 activity and upregulation of both pro and active MMP-2 activities (Fig. 6B & D). The RT-PCR analysis in Fig. 7A & B show that the expression of MMP-9 mRNA was enhanced ~5 and 3.5 folds in indomethacin-induced and ethanol-induced ulceration respectively while TIMP-1 decreased ~0.5 folds in both the cases. Herein, melatonin significantly suppressed MMP-9 transcription and induced TIMP-1 transcription during prevention of gastric ulceration.

The other interest is to study the regulation of MMP-9 and -3 by melatonin during protection against endometriosis. Three categories of endometriotic samples e.g., severe endometriosis, moderate endometriosis and mild endometriosis were collected from consented patients. Eutopic endometrium from normal women was used as control. Peritoneal endometriosis was induced in mice (Paul et al JPR 2008). Post-endometriosis mice were administered with melatonin (48 mg/kg b.w.) as well as vehicle intraperitoneally, once daily for the following 10 and 20 days from the 15th day of post endometriosis induction. Endometriotic lesions in melatonin-treated and vehicle-treated mice was monitored after sacrificing them on the 10th and 20th day.

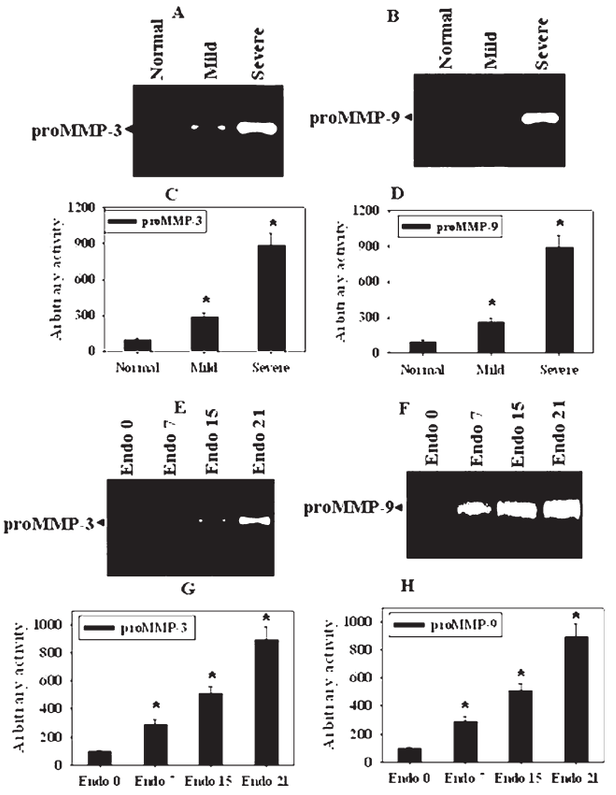


Fig. 7 : Severity-dependent increase in proMMP-3 and-9 activities in endometriotic tissues of mice. Casein zymography and gelatin zymography were performed to monitor the activity of proMMP-3 (**A**) and pro-MMP-9 (**B**) in human endometriosis tissues. Histographic representation of proMMP-3 (**C**) and pro-MMP-9 (**D**) activities. Tissues of mouse endometriosis were monitored for pro-MMP-3 (**E**) and pro-MMP-9 (**F**) activities. Histographic representation of proMMP-3 (**G**) and pro-MMP-9 (**H**) activities in mice. Values represented were measured by Lab Image software. Values are ±S.E.M. of the above zymograms and three other representative zymograms from independent experiments. Sample number n = 12. *P < 0.001 versus the appropriate control using ANOVA followed by Student–Newman–Keuls test.

To test whether peritoneal endometriosis in mice is associated with MMP-3 activity we performed casein zymography from endometriotic tissues. It was seen that from 7th day onwards activity of proMMP-3 gradually increased from ~4-fold and attained ~9-fold increment on the 21st day of post endometriosis induction as compared to control (Fig. 7E). Similarly, proMMP-9 activity was elevated by ~10-fold on 21st day (Fig 7F). Moreover, upregulation of proMMP-9 and -3 activities were seen in human endometriosis. To monitor the therapeutic effects of melatonin in regression of endometriosis, we started melatonin administration from day 15 onwards.

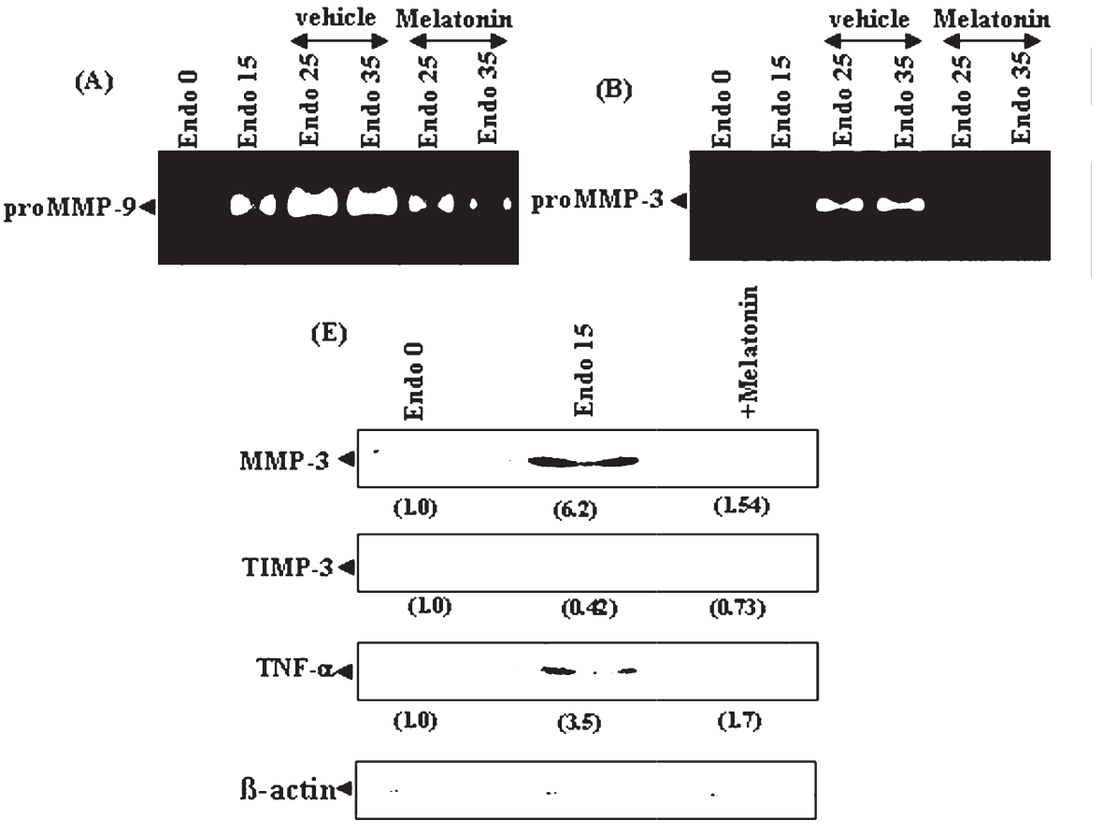


Fig. 8. Therapeutic effect of melatonin in regressing peritoneal endometriosis in mice. Animals were administered intraperitoneally with melatonin (48 mg/kg b.w.) 15th day of postendometriosis for another extra 10 and 20 days. The animals were sacrificed on day 10 and 20 post-melatonin or vehicle treatment. Gelatin zymography was performed to detect the activity of proMMP-9 (**A**) and-3 (**B**). Melatonin-pretreated endometriotic tissues from mice were subjected to Western blot and probed with polyclonal anti-MMP-3, anti-TIMP-3, anti-TNF-α and monoclonal anti-β actin antibody. (**C**) Western blot of-actin was performed to confirm equal protein loading in the above blots. Representative Western blot with their corresponding fold changes as measured by Lab Image software from the above blots and three other representative blots from independent experiments in each case. Values are ±S.E.M. of the above zymograms and blots. Sample number n =12. ****P*** <0.001 versus the appropriate control using ANOVA followed by Student–Newman–Keuls test.

We observed that endometriosis was halted in a time-dependent manner on a therapeutic regimen of melatonin administration lasting for the next 20 days. Administration of melatonin progressively decreased both the proMMP-3 and-9 activity by ~ 40% and ~ 80% on the 25th and 35th day of post-endometriosis as compared to vehicle-treated ones (Fig 8A & B). To elucidate the possible mechanism by which melatonin attenuated proMMP-3 activity we tested for the expression levels of MMP-3, TIMP-3and TNF-á by Western blot analysis in tissue extracts. Our results clearly provide evidence that melatonin pretreatment blocked the expression of proMMP-3 compared to 15th day post-endometriosis mice. Moreover, melatonin was equally potent in attenuating the increased expressions of TNF-á thereby reducing inflammation (Fig 8C). It also stimulated the expression of TIMP-3 by approximately twofold as compared to non-treated ones.

Dr. T. K. Dhar and group

Development of antibody-based analysis techniques

Development of a novel ELISA for aflatoxin B1 with increased specificity: Enzyme-linked immunosorbent assays (ELISA) is widely used for the detection and quantification of many low molecular weight analytes (haptens) in food, agriculture, and environmental samples. At present the most favored approach is competitive ELISA both in the antibody-immobilized and antigen-immobilized formats. However, it is well recognized that antibodies used in these assays are not absolutely specific and do exhibit cross reactivity to other molecules. During the last few years, we have focused on aflatoxin B_1 (AFB_1) and developed several novel immunoassays using polyclonal antibodies raised against AFB_1-*O*- carboxymethyloxime- BSA conjugates as immunogen. The cross-reactivity of the antibodies previously assessed towards AFB_2, AFG_1 and AFG_2 compared to AFB_1 were approximately 14.5, 16.5 and to 2.4 % respectively. Minimizing the undesirable cross reactivity to different aflatoxin is important for improving the assay specificity.

In the present study, we describe a novel competitive immunoassay using AFB_1-protein conjugate and the same anti-AFB_1 antibody for detection of AFB_1 with high specificity. Our approach involves competitive immunochemical reaction between AFB_1 and AFB_1-protein conjugate followed detection of antibody bound protein conjugate by means of biotinylated anti-AFB_1- antibody and avidin-HRP conjugate. The concentration of protein conjugate, coating antibody and biotinylated detection antibody were optimized. The cross-reactivity towards AFB_2, AFG_1 and AFG_2 compared to AFB_1 was studied. The results showed high selectivity for AFB_1 and the cross-reactivity obtained for AFB_2, AFG_1 and AFG_2 was 10, 7, 0.001% respectively. This study provides a simple approach to solve the cross-reactivity problem for small molecule immunoassay. Application of the method for the determination of AFB_1 in food sample is in progress.

***Filtration-based staining of proteins on membranes*:** The determination of protein concentration is very important in modern biological experiments including general biochemistry, proteomics and routine clinical laboratories. Recently, several solid-phase assays have been developed using membranes such as nitrocellulose or PVDF for the quantification of proteins in the nanogram to microgram range. Several dyes like Coomassie blue, Ponceau S and Indian ink have been successfully used for staining with a detection sensitivity of approximately 50 ng protein. However, in all these techniques the staining and destaining steps of these techniques (performed by incubation with shaking) are both laborious and time consuming. We have developed a filtration-based staining method for sensitive estimation of proteins in a batch of samples. The method is based on focused absorption of an applied protein standard (or sample) and dye solution on nitrocellulose membrane through an aqueous network of capillary channels formed between the membrane and a wetted filter paper. The method does not require any equipment for creating vacuum. The scanned images of the membrane strips obtained after the assays by filtration and conventional pouring-incubation methods and the comparative dose-response curves obtained by densitometry are shown in Fig 9. The results show that

in spite of the fast staining and destaining steps in the filtration method, spot intensities were slightly higher compared to the pouring method.

The filtration-based protein estimation method promises to be particularly useful in situations where a large number of samples are to be assayed. Compared with the conventional pouring methods, the new approach reduces the consumption of staining solution and lowers the staining and the destaining time (from 1.5 h to about 10 min), without compromising the sensitivity.

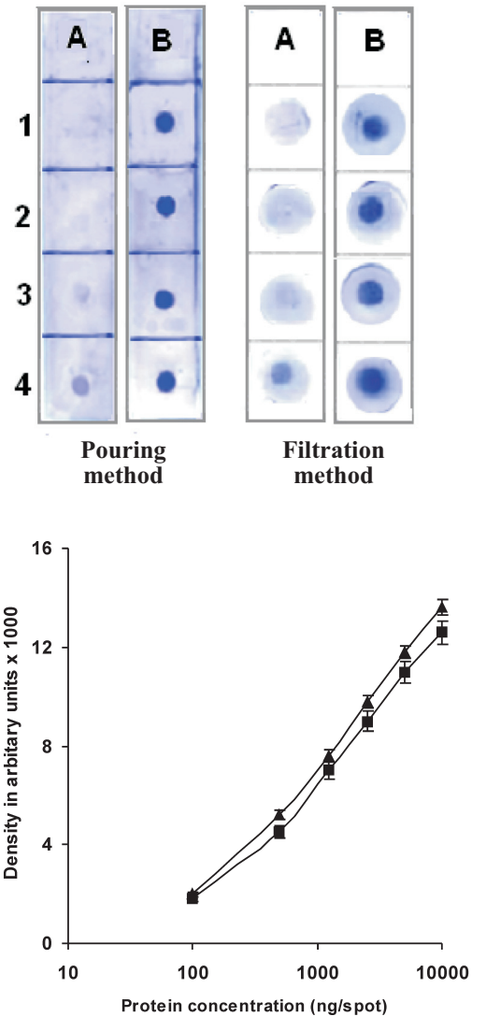


Fig. 9. Comparison of scanned images of strips after protein assays and dose-response curves obtained by densitometry for filtration (▲) and conventional pouring methods (■). Nitrocellulose membrane strips (**A & B**) were spotted with 5 µl of two-fold diluted BSA containing: 1A, control (without BSA); 2A, 50 ng; 3A, 100 ng; 4A, 500 ng; 1B, 1250 ng; 2B, 2500 ng; 3B, 5000 ng; 4B, 10000 ng. Strips were stained with Coomassie blue and analyzed by densitometry after destaining. Each point of the curve represents the mean and standard deviation of four measurements in duplicate.

Dr. Nirmalendu Das and group

Flavonoidal Nanoparticle in combating age related cerebral oxidative injury

Reactive oxygen species e.g. $O_2^{\cdot -}$, H_2O_2 and $^{\cdot}OH$ generated by the induction of oxidative stress exert a potential threat on the activity of endogenous antioxidant enzymes and substantially influence the aging process and age-dependant neuropathology. Chemical antioxidant is almost ineffective in protecting neuronal cells from oxidative damage as Blood Brain Barrier exists in between blood and brain interstitial fluid that restricts undegradable influx from the circulation into cerebral region. Quercetin (QC), a flavonoidal antioxidant is known as a potent antioxidant for its polyphenolic configuration. Formulation of QC in polylactide nanocapsule has been done and the efficacy of this vesicular flavonoid has been tested against cerebral ischemia induced oxidative damage in young and old rat brains. Antioxidant potential of QC loaded in nanocapsule (QC 7.2 mmol/kg b.wt., size 50 nm) was investigated by an in vivo model of cerebral ischemia and reperfusion on Sprague Dawley young (2 months, b.wt. 160–180 g) and aged (20 months, b.wt. 415–440 g) rats.

Diene level, the index of lipid peroxidation (Table 2) and GSSG/GSH ratio were found to be higher in normal aged, compared to normal young rat brain. Endogenous antioxidants activities were lower in aged rat brain compared to young. Further reduction of these antioxidants were observed in aged rat brain by the induction of cerebral ischemia - reperfusion. Nanocapsule encapsulated QC treatment resulted a significant protection to endogenous antioxidant enzymes against ischemia induced oxidative damage in neuronal cells of young and old rats (Table1 &3).

Table 1. Effect of Quercetin(QC) in free and nanocapsule-encapsulated form on the changes in GSH-Px, G6PDH,GR and GST activities in young and aged rat brain by the induction of cerebral ischemia and reperfusion.

Experimental condition	**GSH-Px µmol NADPH oxidation/min/mg protein**		**G6PDH nmoleNADP reduced /min/mgprotein**		**GR..pmole of NADPH oxidation/min/mg protein**	
	Young	Aged	Young	Aged	Young	Aged
Normal	9.11 ±0.78	6.27 ±0.52	12.76 ±1.12	8.83 ±0.86	36.41 ±1.39	24.81 ±2.16
Cerebral ischemia reperfused (A)	4.72 ±0.31	2.89 ±0.48	7.62 ±0.96	5.26 ±0.72	21.26 ±2.11	14.56 ±1.67
(A) + Free QC treated	4.96 ±0.82	3.11 ±0.73	8.17 ±0.76	5.76 ±0.59	26.72 ±1.99	17.36 ±2.72
(A) + Empty nanocapsule treated	4.82 ±0.72	2.78 ±0.51	7.86 ±0.49	5.31 ±0.91	20.91 ±1.71	15.11 ±2.11
(A) + Nanocapsulated QC treated	9.05±0.07	6.10 ±0.09	12.50 ±0.20	8.45 ±0.30	35.58 ±0.07	24.37 ±0.06

Results are expressed as mean±SD. Cerebral ischemia –reperfused groups were compared with normal and the values were significantly different $p<0.01$. Experimental groups (QC entrapped in nanocapsule) were also compared with ischemia-reperfused groups and all those cases $p<0.05$.

Table 2. Effect of Quercetin in free, and nanocapsulated vesicular forms on the age related formation of conjugated diene in rat brain tissue by the induction of cerebral ischemia and reperfusion:

Experimental condition	Lipohydroperoxide content µmol/mg protein	
	Young	aged
Normal	1.87±0.13	3.45±0.58
Cerebral ischemia reperfused(A)	4.37±0.66	7.92±0.93
(A) + free Quercetin(QC) treated	4.07±0.52	7.63±1.01
(A) + empty nanocapsulated treated	4.13±0.87	7.87±0.83
(A) + nanocapsulated QC treated	1.83±0.08	3.40±0.02

Rats were made ischemia and reperfusion was done as described in methods section. Prior to cerebral ischemia 1.32µmol of Quercetin /kg b.wt in free, and nanoparticle encapsulated forms was orally fed into rats of experimental groups. Results are expressed as mean±S.D. Cerebral ischemia –reperfused groups were compared with normal and the values were significantly different $P<0.01$. Experimental groups (QC entrapped in nanoparticles) were also compared with ischemia-reperfused groups and all those cases $P<0.05$.

Table 3. Effect of Quercetin in free, and in nanocapsulated vesicular vesicular forms on the age related formation of antioxidant enzymes in rat brain tissue by the induction of cerebral ischemia and reperfusion:

Experimental conditions	Superoxide Dismutase (U/mg protein)		Catalase (U/mg protein)	
	Young	aged	young	aged
Normal	6.01 ±0.24	4.47±0.34	0.235±0.02	0.145±0.03
Cerebral ischemia reperfused (A)	3.11 ±0.38	2.06±0.29	0.140±0.03	0.089±0.01
(A) + Free Quercetin (QC) treated	3.08 ±0.47	2.01±0.35	0.138±0.02	0.081±0.02
(A) + Empty Nanoparticule treated	3.17 ±0.25	2.13 ±0.42	0.142±0.03	0.087±0.03
(A) + Nanoparticulated QC treated	5.98 ±0.02	4.39 ±0.09	0.226±0.02	0.139±0.03

Results are expressed as mean±SD. Cerebral ischemia –reperfused groups were compared with normal and the values were significantly different $p<0.01$. Experimental groups (QC entrapped in nanocapsule) were also compared with ischemia-reperfused groups and all those cases $p<0.05$.

Dr. Mina Mukherjee and group

Biochemical understanding of sporulation for the development of sporeless strains of oyster mushroom (Pleurotus spp).

Production of Lactobionic acid from Lactose by Cellobiose dehydrogenase from Termitomyces clypeatus (CDHtc). CDHtc produced in the culture filtrate of *T. clypeatus* was purified and characterized (Fig. 10). Lactose was found to be a very good substrate of the enzyme. CDHtc efficiently produce lactobionic acid from lactose. Almost complete conversion of 150µM lactose by 1 U CDHtc was observed in 5 h (half-reaction time ca 1.5 h). In addition of other applications lactobionic acid is used mainly as an ingredient in solutions stabilizing organs before transplantation.

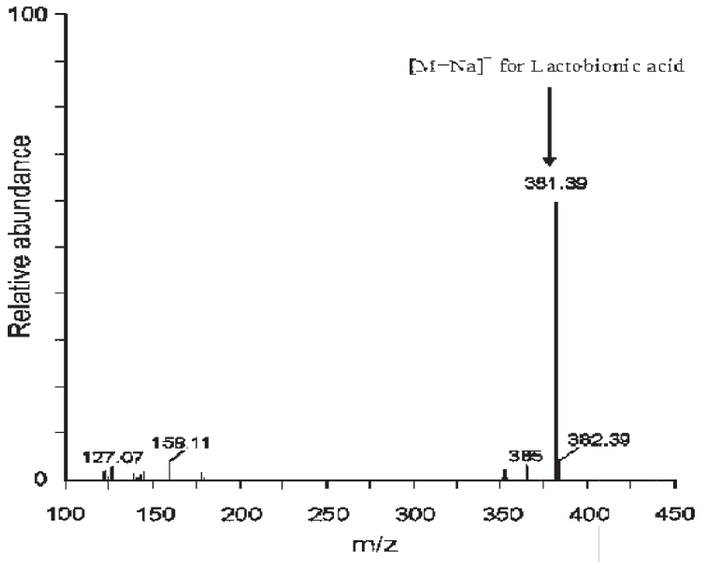


Fig. 10. Mass spectrometric analysis of the reaction products after incubation of lactose with purified CDHtc.

Development of a new method to determine total antioxidant concentration of human plasma: In conventional method total antioxidant concentration of plasma is determined by metmyoglobin -hydrogen peroxide method. Laccase is an enzyme that uses molecular oxygen for oxidation of the substrates. A method has been developed in this laboratory by which metmyoglobin and hydrogen peroxide can be replaced by laccase and the method gives more accurate information about the total antioxidant concentration in plasma.

Dr. Anil K. Ghosh and group

Characterization of trehalose-6-phosphate synthase from Saccharomyces cerevisiae.

Purified trehalose-6-phosphate synthase (TPS) of *Saccharomyces cerevisiae* was effective over a wide range of substrates, although differing with regard to their relative activity. Polyanions heparin, chondroitin sulfate were seen to stimulate TPS activity, particularly when a pyrimidine glucose nucleotide like UDPG was used, rather than a purine glucose nucleotide like GDPG. A high Vm and a low Km value of UDPG show its greatest affinity with TPS than GDPG or TDPG.

Effect of heparin was also extended to the purification of TPS activity, as it helped to retain both stability and activity of the final purified enzyme. Metal co-factors, specifically MnCl2 acted as stimulators, while enzyme inhibitors had very little effect on TPS activity. Metal chelators like CDTA, EGTA stimulated enzyme activity by chelation of metal inhibitors. The purified enzyme was also inhibited by high phosphate concentration, possibly due to separation of associated subunits at high ionic strength. Temperature and pH optima of the purified enzyme were determined to be 40°C and pH 8.5 respectively. Enzyme activity was stable at 0-40ºC and at alkaline pH.

Purification of neutral trehalase from Candida utilis. A *Candida utilis* strain, deficient in any acid trehalase activity, was shown to contain only neutral trehalase activity. This strain could utilize extracellular trehalose as sole carbon source. The neutral trehalase activity from the *C. utilis* strain was purified to electrophoretic homogeneity. Gel filtration chromatography and analytical ultracentrifugation data have proved that the functional form of the enzyme was a protein of molecular weight 168 kDa, while the molecular weight of the single protein band in SDS-PAGE was estimated to be 56 kDa. So, it was hypothesized that the functional protein was a tri-mer of a 56 kDa polypeptide. The N-terminal amino acid sequence of the 56 kDa polypeptide and the physico-chemical characterization proved that the purified enzyme is distinct from other trehalase enzymes reported from yeast. While most of the physico-chemical characters, including pH optimum, were similar to those of neutral trehalase from *S. cerevisiae,* few resembled the characters of acid trehalase activity.

Chemical Standardization and Biological Evaluation with a view to Increase Efficacy of Herbal Medicines: Bioefficacy and Analytical Evaluation (Antimicrobial activity) Itone Eye Drops (CLP 214)

Itone is a poly herbal eye drop consisting of 21 herbs and 2 preservatives. Earlier we have shown that Itone consists of some essential oils; among them three oils namely eugenol, carvacrol and camphene were identified as a biomarker. In an attempt to find the microbicidal activity of Itone, antimicrobial assay was performed by measuring the growth of two types of microorganisms, yeast and bacteria, in the presence and absence of the test materials and the MIC of Itone on them was found.

This year the study was carried out further by investigating the effect of the individual ingredients on the above mentioned microorganisms. Some of the ingredients showed MIC values as low as 1% whereas few did not have any effect at all. An attempt was made to understand the role of preservatives in Itone. Agar cup well diffusion assay method was used to study the antibacterial effect of Itone with preservatives and Itone without preservatives samples. It was found that Itone batch No.2284, 2294, 2295 (without preservatives) did not produce any zone of inhibition whereas Batch No.2296 and 2299 produced a zone of inhibition. When batch no.2284 (without preservatives) was subjected to GC-MS it was found that no peaks of essential oils was obtained whereas when GC-MS of Itone batch No.2284 with preservatives was done, peaks of Camphor and Menthol were obtained. Thus, it was concluded that the preservatives may help in trapping the essential oils in Itone.

Standardization and Identification of ingredients present in TRASINA.

Trasina, a polyherbal medicine, has five herbal ingredients and is currently marketed to provide adaptogenic strength to patients suffering from stress related conditions. Earlier, we have standardized the product by measuring the total sugar and total sterol present there, by delimiting the batch to batch variations and also two bio-markers, namely S-Adenosyl-L-Methionine (AdoMet) and oleanolic acid were identified.

This year, we have measured the total glucose and total trehalose(anti-stress chemical compound) content of four new batches of the product namely TR330, TR332, TR333 and TR334. The analysis was made in triplicates. The amount of trehalose varied from 0.019–0.046 mg/100 mg of Trasina, and the amount of glucose varied from 0.543- 0.916 mg/100mg of Trasina.

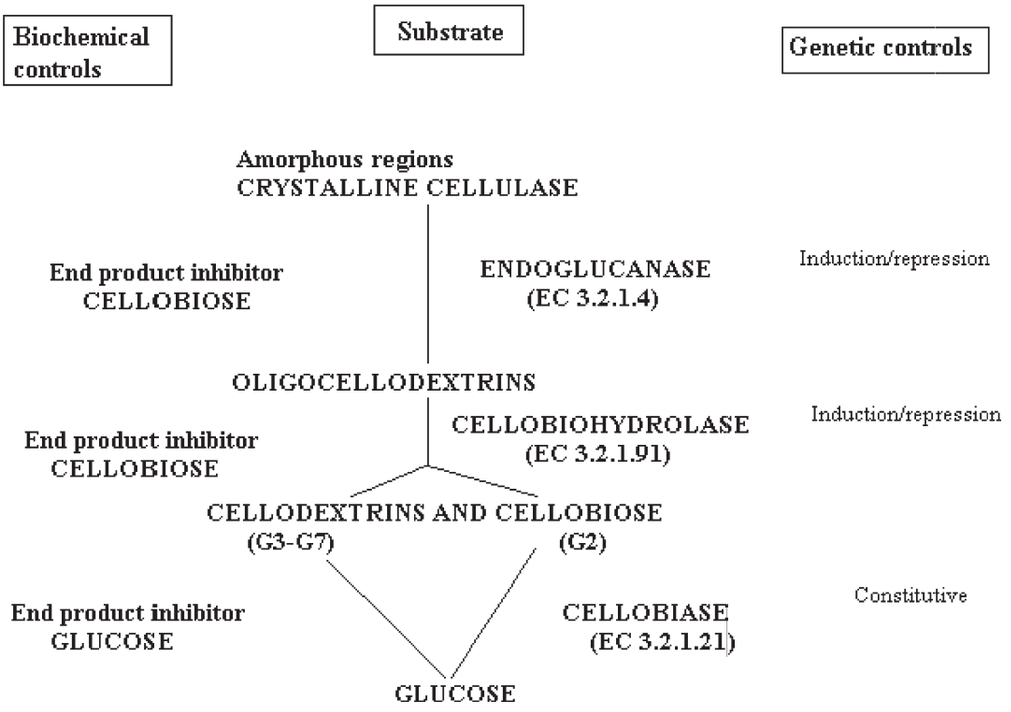
Dr. Suman Khowala and group

Molecular mechanisms regulating production and secretion of carbohydrases in the fungus Termitomyces clypeatus.

Objectives of the project are to understand the regulatory mechanisms of production and secretion of cellobiase from filamentous fungus *Termitomyces clypeatus* influenced by intracellular processing and translocation of the enzymes by post-translational modification in presence of glycosylation inhibitors. Another approach is to understand the significance of hetero-aggregation of sucrase with cellobiase in the secretory pathway affecting activity, stability and conformation of the enzymes.

Regulatory effects of glycosylation inhibitors on activity and secretion of cellobiase in T. clypeatus. *T. clypeatus*, a filamentous fungus is being studied for production and characterization of a number of carbohydrases. Majority of extracellular proteins, in fungi, is glycosylated. Glycosylation of a variety of proteins from fungi and yeast is known to play a vital role on the activity, stability and secretion of proteins. However, mechanism of the biochemical pathways involved in glycosylation is little known in filamentous fungi. Earlier we reported that post-translational modification by glycosylation had significant regulation on production, activity & secretion of the cellobiase enzyme and proteins in the fungus, where in presence of glycosylation inhibitor 2-deoxy glucose cellobiase activity increased by approximately 10-30 times and protein synthesis was also high. Total protein secretion also increased to ~95%. During the study of regulated protein secretion for production of extracellular cellobiase in the fungus, cellobiase produced in presence of glycosylation inhibitor 2-Deoxy-D-Glucose was purified and characterized for its physico-chemical properties. The enzyme produced under restricted glycosylation was much more active than that of the control enzyme, and also had higher susceptibility towards temperature and digestion to endo-glycosidases.

Feasibility of cellulose hydrolysis by the cellulase complex of the fungus. The enzyme cellobiase is the key enzyme of cellulose hydrolysis (Scheme 1). In fact cellulose hydrolysis requires synergistic actions of several cellulase components in a heterogeneous reaction system, which includes endocellulase (endoglucanase), exoglucanase (cellobiohydrolase) and cellobiase. Ordinary cellulose resists hydrolytic cleavage due to its crystalline structure that restricts its biodegradation in the solid residues by cellulolytic enzymes. Other factor is accumulation of cellobiose, which remains unutilized, as all the high cellulase producer organisms are low producer of cellobiase. The scheme below indicates the biochemical and genetic controls associated with the cellulose saccharification process. Hydrolysis of cellulose to oligocellodextrins and further to cellobiose is very much dependent on availability of efficient cellobiase activity for conversion of accumulated cellobiose into glucose. The enzyme is commercially important for its use in paper, detergent and textile industry. The capacity of *T. clypeatus* for high-level protein secretion can also be exploited as a potential host for producing high value recombinant therapeutic protein.



Scheme 1. Conversion of cellulose into glucose: Biochemical and genetic controls of the enzymatic saccharification

Apart from high cellobiase activity the fungus *T. clypeatus* also produced endo-cellulase and filter paper enzyme activity in the culture filtrate. Efficacy of the cellulolytic enzyme complex produced by the fungus *T. clypeatus* was tested through saccharification of CM-cellulose (2%, w/v), and results were compared with those observed with cellulolytic enzymes available from market (Table 4). It was found that crude cellobiase preparation alone in much lower concentration could release more than 28% of reducing sugar in 1h, similar to the mixture of cellulolytic enzymes in higher concentration in addition to the cellobiase from *T. clypeatus*. Liberation of glucose was higher at 3.69% with cellobiase of the fungus in comparison to 3.2% obtained from the mixture of cellulase and cellobiohydrolase along with the cellobiase in the digest. It was concluded that crude cellobiase from *T. clypeatus* was more efficient for saccharification of CM cellulose, without external supplementation of endo or exo-glucanase.

Table 4. Saccharification of Carboxymethyl cellulose by crude cellobiase of *T. clypeatus*

Saccharification	Enzyme	1hr	2hr	4hr
Glucose (%)	E E+CL+CBH	3.69 3.2	3.9 3.5	4.1 3.9
Reducing sugar (%)	E E+CL+CBH	28.26 27.9	28.9 27	33.67 27.9

E: cellobiase enzyme (10u/ml) from culture medium of *T. clypeatus,* CL: Commercial cellulase (60u/ml); CBH: commercial cellobiohydrolase (6u/ml)

Co-aggregation of cellobiase and sucrase in the fungus T. clypeatus. Earlier it was demonstrated that cellobiase and sucrase are co-aggregated in the intra and extracellular fractions of the fungus. Biophysical and biochemical characterization of the co-aggregates showed that the sucrase-cellobiase co-aggregates are folded differently in intracellular & extracellular fractions. The extracellular form (with regards to cellobiase activity) has better stability in presence of these agents (full activity retention with 10% Triton X, 70% with 0.4% SDS, 75% with 2 mM Urea, 76.5% with 0.5 mM Gd-HCl) unlike the intracellular form (90% with Triton X, 70% with SDS, 22% with Urea, & 46% with Gd-HCl). All the above studies point towards novel aggregation patterns of these secreted glycohydrolases delineation of which will help us better understand the protein-protein aggregation phenomenon.

Dr. Sharmila Chattopadhyay and group

Medicinal plants and metabolic engineering

The main objective of this study is the judicial manipulation of plant biosynthetic pathway/s for the improvement of important traits such as disease and/or stress resistance as well as to improve the nutritional qualities of the target plants or to obtain desired metabolites. Here, the model system of Nicotiana tabacum (tobacco) is used for basic studies, and Mentha spp., Podophyllum sp., Phyllanthus amarus etc. are the target plants. 'Plant Disease resistance: mechanism and signaling networks' - is another ongoing project of my laboratory.

To unravel the dynamic complexity of plant metabolic networks, plant metabolic engineering holds a great promise, which has been explored further in plants of economic importance like Podophyllum sp., Phyllanthus amarus, Mentha spp. Molecular cloning of pinoresinol lariciresinol reductase (PLR), one essential enzyme of podophyllotoxin and other therapeutic lignan's biosynthetic pathway, has been reported from Podophyllum hexandrum, Phyllanthus amarus etc. Further, transgenic tobacco lines (T1) overexpressing PLR, have been developed which confers tolerance to various extremities and also enhances value added production of pharmaceutically important secondary metabolites (Fig. 11A). y-ECS and/or GS overexpressing lines have been developed with model and target plant (pudina) for value added production of GSH, the cell's master antioxidant. Transgenic P. amarus has been developed which are ready to transfer to soil (Fig. 11B). Transgenesis of P. amarus was confirmed by RT-PCR at the expression level and by Southern blot analysis to confirm the chromosomal integration of the gene of interest (Fig. 11C, D).

Natural antioxidants are in great demand around the world as neutraceuticals as well as dietary supplements. Stevia rebaudiana, commonly known as sugar leaf, has been reported here as a strikingly potential source of herbal antioxidant (Table 5). The ethyl acetate fraction, rich in flavonoids, showed a potentially significant activity against DNA strand scission by •OH generated in Fenton's reaction on pBluescript II SK (–) DNA which showed better efficacy than that of quercetin (Fig.11E). Densitometric analysis confirms the data (Fig. 11F). This bioactive fraction also noted with inhibition capacity of lipid peroxidation induced with 25 mM FeSO4 on rat liver homogenate as a lipid source. Hence, this popularly known front-line herb may be explored further as a neutraceutical or dietary supplements.

Table 5. Comparative study of IC_{50}

Assay	**IC_{50} (μg/ml)**		
	CAE	EAE	Quercetin
DPPH Scavenging Activity	47.66 ± 1.04	9.26 ± 0.04	3.35 ± 0.07
$ABTS^{+}$ Scavenging Activity	28.6 ± 0.64	3.04 ± 0.22	1.3 ± 0.06
$^{\bullet}OH$ Scavenging Activity	33.9 ± 9.58	3.08 ± 0.19	7.45 ± 0.43

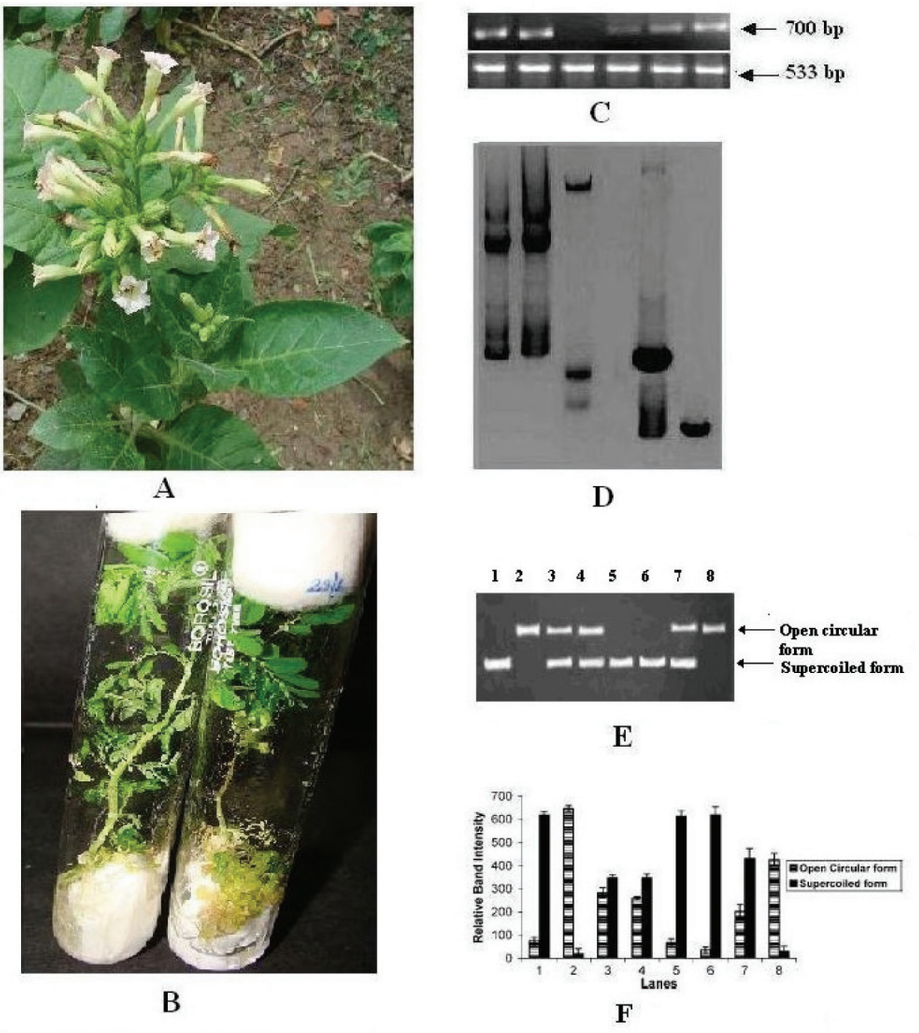


Fig. 11. Transgenic *Nicotiana tabacum* (A) and *Phyllanthus amarus* (B).

Transgenesis of *P. amarus:* RT-PCR anlysis (C) and Southern Blot analysis (D).

(E). Electrophoretic pattern of pBluescript II SK (–) DNA breaks by •OH generated from the Fenton reaction and prevented by CAE and EAE. Lane 1: untreated control DNA (250 ng), lane 2: $FeSO_4$ (0.5 mM) + H_2O_2 (25 mM) + DNA (250 ng), lane 3: only H_2O_2 (25 mM) + DNA (250 ng), lane 4: only $FeSO_4$ (0.5 mM) + DNA (250 ng), lanes 5–8: $FeSO_4$ (0.5 mM) + H_2O_2 (25 mM) + DNA (250 ng) in the presence of EAE (1 µg), CAE (10 µg), Quercetin (1 mM), and Stevioside (100 µg), respectively (n=3); **(F)** Densitometric analysis of open circular and supercoiled DNA damage induced by •OH generated from the Fenton reaction in the presence or absence of CAE and EAE (mean ± SD, n = 3)

Technical Officers

Dr. (Mrs.) Shila E. Besra, Dr. Ramdhan Majhi, Dr. Ardhendu K. Mandal, Mrs. Dipika Roy, Mr. M. L. Jana.

Research Associates

Dr. (Mrs.) Mrinalini Bhattacharya, Dr. (Mrs) Anamika V. Sharma –RA/CSIR Dr. (Miss) Neela Sen Gupta, Dr (Mrs) Archita Saha, Dr Sibani Sarkar,

Research Fellows

Ms. Debjani Saha, Mr. Debopam Acharya, Mr. Arghya Basu, Mrs.Papiya Ghosh, Miss.Anindita Debnath, Ms. Chinniah Annalakshmi, Mr. Sudip K. Kar, Mr. Parag Kundu, Mr. Krishnendu Ganguly, Mr. Sumit Paul, Deba Prasad Jana, Mr. Laishram Pradeep Singh, Mr. Sanjib Dey, Mr. Amartya Mishra, Mr. Dhananjoy Soren, Ms. Sharmishtha Mazumder, Ms. Tanima Saha, Ms Sudeshna Chowdhury, Ms Shakuntala Ghorai, Mr Samudra Prosad Banik, Ms. Anindita Banerjee, Ms. Srijani Ghanta, Ms. Amrita Chakraborty, Ms. Debannita Dutta**,** Mr. Dipto Bhattacharya, Mr.Shubho Dasgupta, Ms Swagata Pal, Avijit Poddar, Ms Aparajita Ghosh , Mr. Deepak Verma, Miss Tanaya Das, Ms. Poulami Karmakar.

Project Assistants

Miss. Soma Roy, Miss. Sumana Mallick, Mr. Shamik Bhattacharya, Ms Sarupa Ghosh, Ms Debasree Ghosh, Miss Anwesha Majumdar, Ms. Shilpi Bose, Ms Soumya Mukherjee, Ms Baishali Guha, Ms Arpita Maity, Mr Rajib Mazumdar.

Summer Trainees

Ms. Prianka Jain, Ms Arpita Samanta, Mr B Nandi, Ms Sahana Ghosh Mr Somesubhra Thakur Chaudhuri, Mr. Upal Das Ghosh, Miss Suhana Chattopadhyay, Mr. Deep Chatterjee, Ms. Minakhshee, Ms. Krittika Sasmal, Ms. Urmi Chakraborty, Ms. Saborni Maity, Ms. Archana Kumari, Mr.Vijetashree Prasad.

Administrative Staff

Mrs. Moumita Majumdar

Lab Attendant

Mr Ashit Mitra, Mr. Narendra Pradhan, Mr. Biswajit Mandal


FOUNDATION DAY CELEBRATION
POST-GOLDEN JUBILEE
APRIL 2nd, 2007

Chemistry

V. S. Giri (Head), S. B. Mandal, Ajoy K. Banerjee, P. K. Bhattacharya(Late), B. C. Pal, A. K. Sen (Sr.), A. K. Sen (Jr.), S. Mukhopadhyay, P. Chattopadhyay, S. Bandopadhyay, G. Suresh Kumar, N. B. Mondal, B. Das, P. Jaisankar, R. Mukhopadhyay, Ashis K. Banerjee, R. C. Yadav, Chinmay Chowdhury, Arindam Banerjee and S. Garai

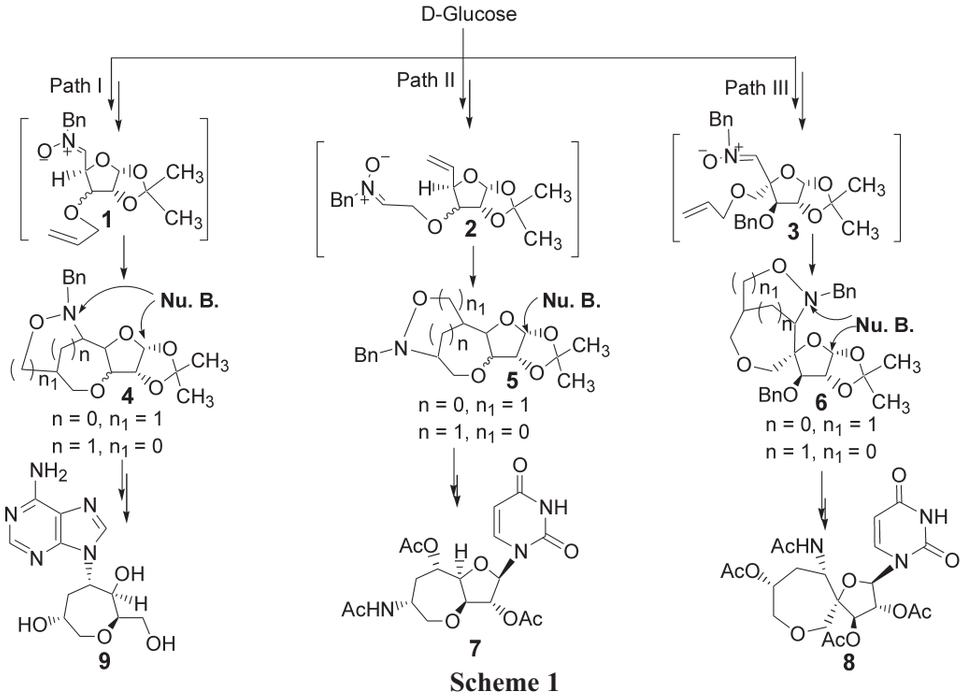
The major areas in which work has been carried out by investigators of the division in the recent past includes synthesis of chiral heterocycles, synthesis of novel nucleosides, synthesis of benz-annulated medium size rings, synthetic studies on heterocyclic chemistry, novel synthetic routes (enantioselective) to natural products, synthetic studies in homogeneous and organised media, synthesis of anti-leishmanial compounds, studies in bacterial cell surface antigens, plant polysaccharides and neoglycoproteins, chemical investigation of medicinal plants for bioactive substances and nucleic acid polymorphism. Additional recruitment of manpower in the division has given a new fillip to the division particularly in the area of nanochemistry. The division has also been engaged in some important collaborative industrial projects and has been successful in establishing a link with few established pharmaceutical industries .The chemistry group has taken advantage of the multidisciplinary character of the Institute and has been working in tandem with other groups in the Institute.

Dr. S. B. Mandal and group

Synthetic approaches to structurally novel chiral nucleosides and analogues from D-glucose

The principal objective of the subproject is to develop synthetic routes to structurally unique nucleosides and analogues through judicious manipulation of D-glucose derived precursors.

Synthesis of Oxepane Ring Containing Monocyclic, Conformationally Restricted Bicyclic and Spirocyclic Nucleosides from D-Glucose: A Cycloaddition Approach: Carbohydrate-derived substrates having (i) C-5 nitrone and C-3-O-allyl (type **1**), (ii) C-4 vinyl and a C-3-O-tethered nitrone (type **2**), and (iii) C-5 nitrone and C-4-allyloxymethyl (type **3**) upon intramolecular nitrone cycloaddition reactions with BnNHOH generated tetracyclic isoxazolidino-oxepane/-pyran ring systems **4-6 (Scheme 1)**. Deprotection of the 1,2 acetonides of these derivatives followed by

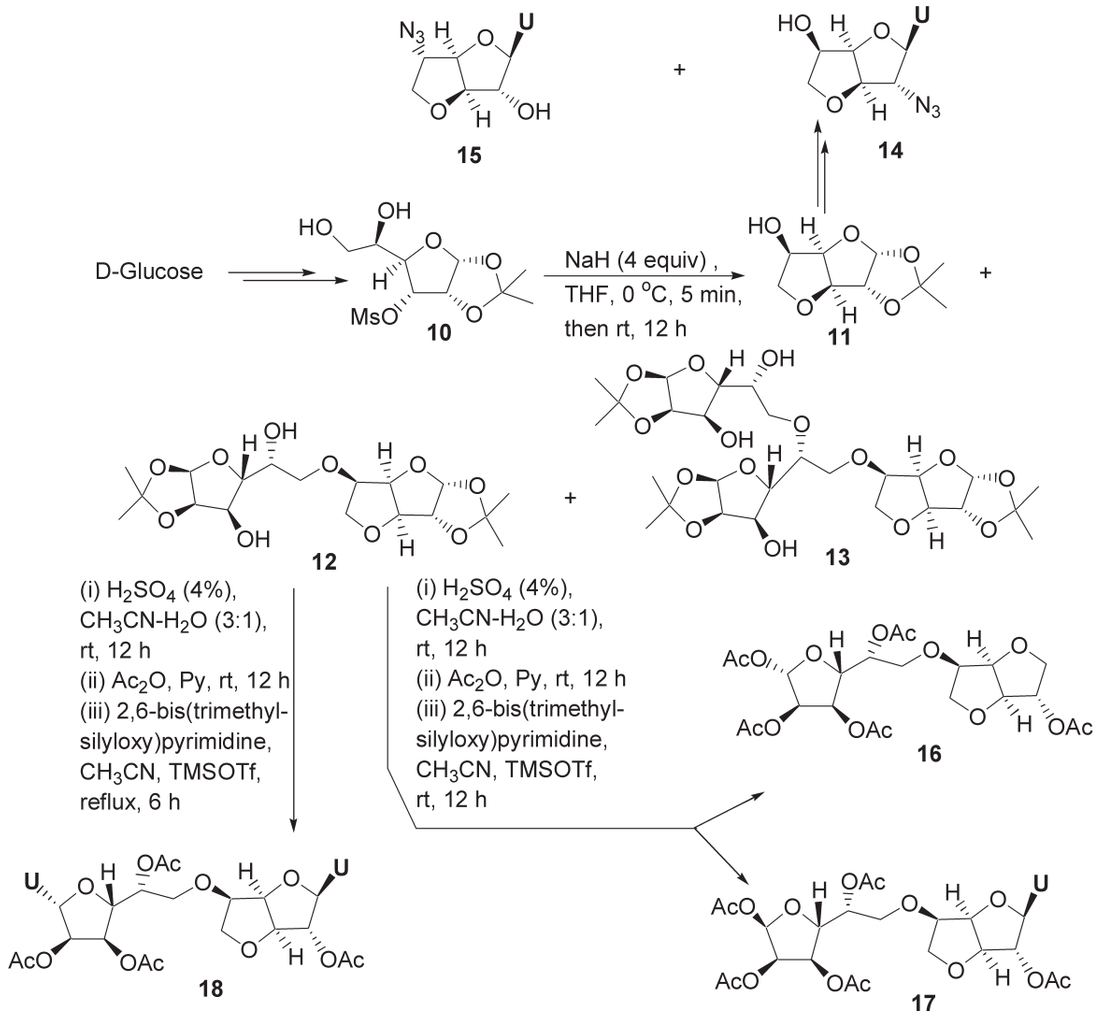


Scheme 1

introduction of uracil base via Vorbrüggen reaction condition and cleavage of the isooxazolidine rings as well as of benzyl groups by transfer hydrogenolysis and acetylation yielded oxepane ring containing bicyclic and spirocyclic nucleosides **7** and **8**. The corresponding oxepane based nucleoside analogue **9** was prepared by cleavage of isoxazolidine and furanose rings, coupling of the generated amino functionalities with 5-amino-4,6-dichloropyrimidine, cyclization to purine rings and finally aminolysis.

First example of 5/6-O-linked pseudosaccharides: synthesis of bicyclic nucleosides containing azido or extended carbohydrate moiety: Treatment of the D-glucose-derived substrate **10** with sodium hydride in tetrahydrofuran provided the 3,6-anhydro monosaccharide **11**, along with the 5,6-ether linked pseudodisaccharide **12** and pseudotrisaccharide **13**. However, reaction of 10 with sodium ethoxide in ethanol afforded **11** as the sole product, elaborated to the bicyclic azidonucleosides **14** and **15**.

Acetylated bicyclic nucleosides **16-18** with extended carbohydrate residues have been synthesized from **12** **(Scheme 2)**.



Scheme 2

Further study of this subproject will involve synthesis of new classes of bio-active nucleosides by the application of appropriate reactions on carbohydrate skeletons.

Dr. Arindam Banerjee and group

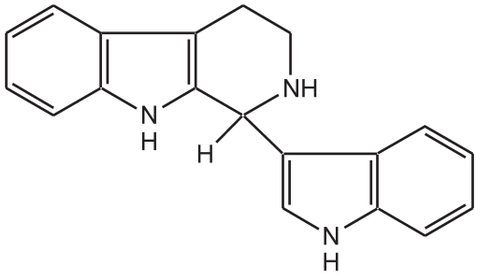
Self-assembling peptide and pesudopeptide based nanomaterials

Self-assembling pseudo-peptide based nanofibers have been used as templates for fabrication of dipeptide capped Au and Ag nanoparticles on nanofibers. Short synthetic peptides self-assemble to form various nanostructures including nanotubes, nanovesicles and others. A pH sensitive nanostructural transformation from nanotubes to nanovesicles have been observed (Refer to our 2006-07 publications) for a self-assembling synthetic water-soluble tripeptide Tyr-Aib-Ala. This peptide forms hollow nanotubular structures in acidic pH (pH 4.3-5.5), while at pH 6.5 both nanotubes and nanovesicles coexist and with an increase in pH of the solution, only nanovesicles have been formed exclusively. These nanovesicles are stable within pH range 7.0-9.2. A further increase in pH leads to the rupture of these vesicles. The pH sensitive nanovesicle formation has been used for entrapment and slow release of a physiologal dye, Congo red. Formation of dipeptide nanotubes with N-terminally located ω-amino acid residues, which are stable proteolitically, thermally, and a wide range of pH, has been observed. A series of pentapeptide-based organogels have been discovered and the role of adjacently located phenylalanine residue in gel formation has been convincingly established. A water-soluble tripeptide Aβ (9-11) self-assembles to form nanofibrilar structures and these nanofibrils exhibit amyloid-like behavior and neurotoxicity towards neuro2A cell line. The entire research work is based on new nanomaterials from self-assembling molecules of biological origin (peptides and amino acid derivatives) which opens up a new avenue of soft nanobiomaterials to use these in biological system and for aligning metal/semiconductor nanoparticles in well-defined 1D or 2D arrays.

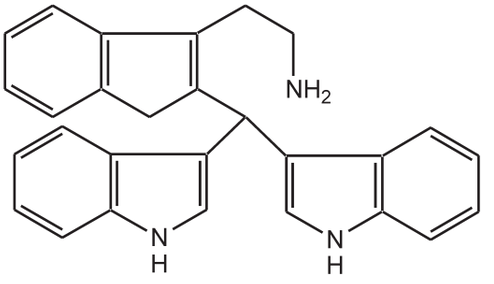
Dr. Venkatachalam Sesha Giri, Dr.Parasuraman Jaisankar and group

Synthetic Studies in Heterocyclic Chemistry

In the course of synthesizing the intermediates for preparing the indole alkloid Bengacarboline, we found (with the help of Dr. Rajan Vedasironmani's Gr. of our Institute) that a few of them (**x**) and (**y**) could inhibit cell growth in human leukemic cell lines, U937 and K562. One of them is a DIM derivative and the other one a tetrahydro-β-carboline. For comparison, cytosine arabinoside was used.

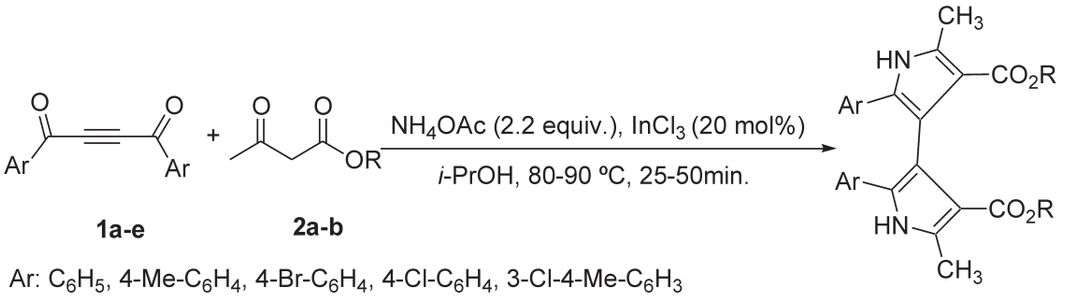


x



y

Lewis Acid-Catalysed Multicomponent Synthesis of Chiral 3,3'-Bipyrrol: 3,3'- Bipyrroles **3a-j** could be synthesized using a double Michel addition reaction involving diaroyl

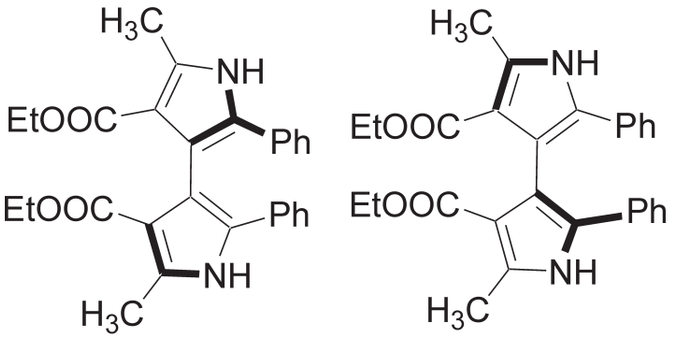


1a-e **2a-b**

Ar: C_6H_5, 4-Me-C_6H_4, 4-Br-C_6H_4, 4-Cl-C_6H_4, 3-Cl-4-Me-C_6H_3
R: OEt, OMe

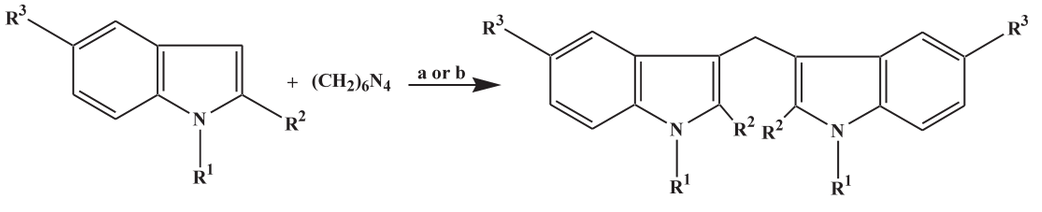
3a-j (±)

acetylene **1a-e** and the appropriate β-keto carbonyls **2a-b** using ammonium acetate as nitrogen source. The axial chirality of bipyrrole was anticipated from the x-ray crystal structure and DFT calculation and confirmed by separating the racemate into their enantiomers on a chiral column and subsequent CD-spectra of the enantiomers. The absolute configuration of the enantiomers of bipyrrole **3a** was achieved by theoretical CD-spectra calculation using ZINDO method.



(*R*)-(+)-**3a** (*S*)-(-)-**3a**

Eco-friendly synthesis and study of new plant growth promoters: 3,3'-Diindolylmethane and its derivatives: 3, 3'-Diindolylmethane (DIM) derivatives **3a-k**, prepared in one-pot from indoles **1a-k** and hexamethylenetetramine (**2**) using ionic liquid [Bmim]BF4 as eco-friendly recyclable solvent as well as catalyst, showed good plant growth promoting activity on *Oryza Sativa*. Among the DIM derivatives synthesized 3c shows potent auxin like growth promoting activity.



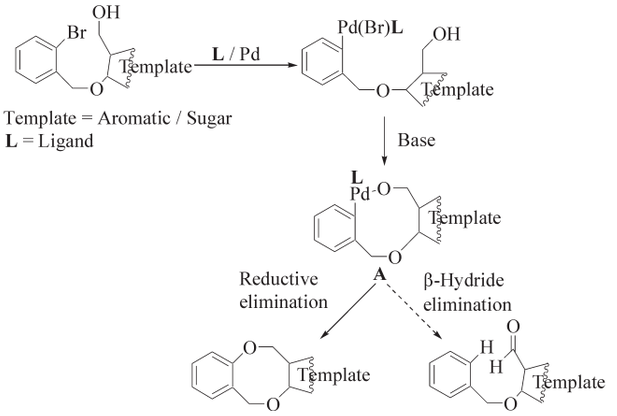
1a-k **2** **3a-k**

Reagent and conditions: (a). (i) [Bmim]BF4, 60 °C, 5-20 h; (ii) H2O, 80 °C, 30 min. (b). (i) [Bmim]BF4 20 mol%), i-PrOH, 28 °C, 7-27 h; (ii) H2O, 80 °C, 30 min

Dr. Partha Chattopadhyay and group

Synthesis of annulated medium ring heterocycles

The broad objective of this subproject is to develop synthetic methodology for medium ring ethers or analogues possessing diverse biological properties. In continuation of our previous studies on the synthesis of bezofused medium ring heterocycles (present in drugs or many biologically active product), radical cyclization has been accomplished on various sugar-derived intermediates. Pd catalyzed intramolecular arylamination of sugar derivatives has been accomplished by using biaryl phosphine ligands. Application of this reaction methodology on variety of D-glucose derived substrates led to the synthesis of highly functionalized cis-fused chiral benzoxocine derivatives and tricyclic nucleosides possessing oxazocine ring. The analogous process for the addition of alcohol to produce aromatic ethers has also been successfully established. This aryl etherification methodology constitute a convenient route for the synthesis of eight-membered oxygen heterocycles employing bulky binaphthalylphosphane or bis(diphenylphosphanyl)ferrocine ligands. An application of this reaction on a sugar derivative led to the synthesis of chiral benzodioxocine.



In an another project on green chemistry, aldoximes react with αβ-unsaturated carbonyl and sulphonyl compounds in organized aqueous media (nanoreactor system) using dodecylbenzenesulphonic acid (DBSA) as surfactant to generate N-alkylated nitrones, which undergo intermolecular cycloaddition in the same pot with maleimides to give the desired cycloadduct in absence of any organic solvent and catalyst. Divinyl sulphone was successfully used for both *N*-alkylation and intramolecular cycloaddition, affording only one cycloadduct. This is a new example of green chemistry and provides a new aspect of reactions in water.

Dr. Asish Kumar Sen (Jr.) and group

Studies on bacterial cell surface antigens

Structural studies on bacterial cell surface antigens: The objectives of this project are to isolate and elucidate the structures of the bacterial cell surface antigenic lipopolysaccharides (LPS) or polysaccharides (OPS), and capsular polysaccharides (CPS) from various pathogenic strains that are responsible for gastrointestinal diseases. The lipopolysaccharide from a clinical isolate of Vibrio parahaemolyticus O3:K6 has been isolated and purified. The LPS on mild acid hydrolysis produced the O-antigenic polysaccharide (OPS). This O-antigen contained a novel sugar 5,7-diacetamido-8-amino-3,5,7,8,9-pentadeoxy-D-glycero-D-galacto-non-2-ulosonic acid (Fig 1.). The structure of this sugar was established by 2-D NMR and ESI-MS studies. The OPS was found to be a decasscharide having molecular weight of 1977 (MALDI-TOF). Apart from glucose, galactose, L-glycero-D-

mannoheptose and the triamino sugar, the OPS contained two phosphate groups and ethanolamine group. The locations of these have been established by NMR (COSY, TOCSY, HSQC and HMBC) experiments. The structure of seven residues of the OPS from the non-reducing end has been established and further work is in progress to establish the total structure of the OPS.

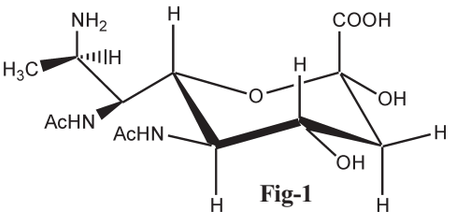


Fig-1

Synthesis of Oligosaccharides: From crystallographic studies the carbohydrate molecule that binds with banana lectin has been found (Prof. Vijayan et. al.) to be a branched mannopentose as shown in Fig. 2. The two branches of the forked shaped oligosaccharide take a definite spatial orientation and attach to the two binding sites of the lectin. We have undertaken the chemical synthesis of this pentasaccharide for further biological studies. The oligosaccharide is being synthesized by appropriate strategy using suitably protected sugar molecules.

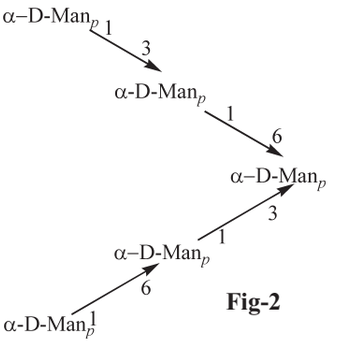


Fig-2

Studies on medicinal plant polysaccharides: The constituent polysaccharides from Aegle marmelos (Bael) have been isolated using sequential extraction protocol. An acidic polysaccharide, isolated by hot water, showed significant anti-Leishmanial and anti-diarrhoeal, and moderate anti-microbicidal activity. Combination therapy using sub-optimal dose of this compound with SAG showed clearance of >95% parasite burden in rat liver and spleen. The acidic polysaccharide has been characterized and further immunological studies are in progress.

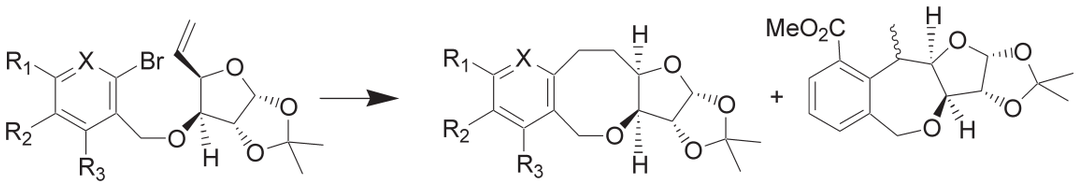
Characterization and structural modification of coir fiber for enhanced longevity: The objective of this project is to chemically characterize the constituents of coir fibre from different varieties coir found in southern coastal area of India and also to modify the coir fiber by chemical or enzyme procedure to protect them from degradation by light (UV). During this period, various types of hemicelluloses have been isolated from four different varieties of coir and were characterized. Different types of derivatives of coir fibre have been prepared by using chemical methods and their light fastness and physical parameters were evaluated at CCRI, Alleppy, Kerala. The project has been sponsored by Coir Board, Kochi from November 2006

Dr. Asish Kr. Banerjee and group

Novel synthetic routes for natural products–enantioselective approaches and radical cyclization strategies

The synthesis of conformationally flexible medium sized ring ethers, constituting the unique structural core of a large number of linearly condensed cyclic polyether marine neurotoxins has received considerable attention. Although, there are numerous methods for the generation of 7-, 8-, and 9- membered chiral ring ethers, elaboration of the ring poses considerable problem in organic synthesis. Recent developments in establishing generalized synthetic methodologies for seven to nine membered chiral ring ethers are mainly based upon intramolecular cyclisation processes, namely (i) ring closing metathesis (ii) palladium-induced reaction (iii) radical cyclisation.

Our investigation is mainly based on study of substitution effects during the synthesis of 7- and 8- membered chiral benzo- fused cyclic ethers by TBTH mediated intramolecular radical cyclisation and Pd(0) catalysed intramolecular Heck reaction, which was further extended to pyridine fused cyclic ethers also.



R_1 or R_2 or R_3 = H / OMe/ CO_2Me; X = C-Me or C-CO_2Me or N

A study on the feasibility of synthesizing chiral functionalised pyrido- fused oxocine and benzoxepine from the annulated sugar derivatives has also been carried out.

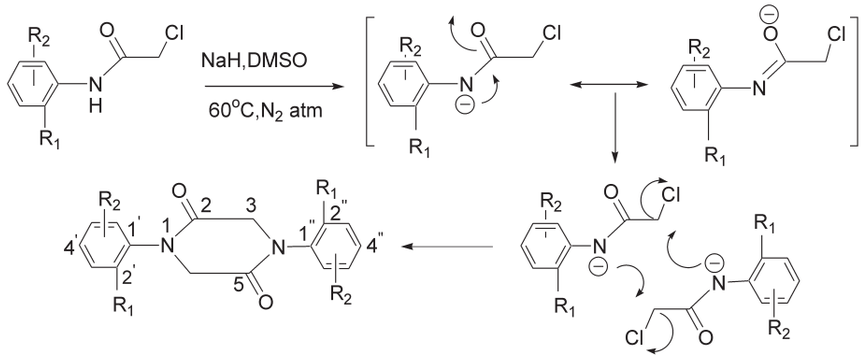
We propose to study the stereoselective model synthesis of some natural products as well the palladium catalysed intramolecular cyclisation for the construction of newer sugar based heterocyclic systems.

Dr. N. B. Mondal, Dr. Sukdeb Banerjee and group

Synthesis of structurally unique bioactive heterocycles

A series of 1,4-diphenyl-2,5-dioxopiperazine derivatives (**1-12**) were synthesized in one pot sequence. All the compounds except 1, 4 and 8 are reported for the first time. The compounds demonstrated appreciable cytotoxic activity against Leishmania donovani on both forms of the parasite, and the results suggested that di-ketopiperazine derivatives 4, 11 and 12 could be exploited as antileishmanial agents.

The purpose of this study was to investigate the fertility regulating potential of 2-(2"-chloroacetamidobenzyl)-3-(3'-indolyl) quinoline in male rats. Proven rats were treated with the compound by oral gavages for one to eight consecutive weeks. Functional fertility, testicular, epididymal and seminal vesicular weight, epididymal sperm count and spermatogenesis was quantitated. Reproductive hormones and some biochemical parameters were measured. Functional fertility reduced significantly as revealed by fall of fertility and pregnancy rate. Reproductive organs' weight reduced significantly. Reduction of sperm count and number of different types of testicular cells were observed. The treatment of the compound resulted decline of testosterone and increase of FSH hormone levels. The compound effectively reduced testicular protein, glycogen and epididymal

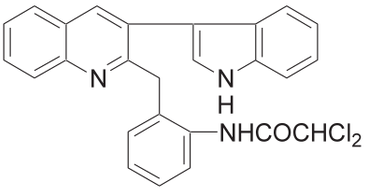


1. $R_1 = R_2 = H$
2. R_1 = OMe, R_2 = 5-Cl
3. $R_1 = H$, R_2 = 4-Me
4. R_1 = Cl, $R_2 = H$
5. R_1 = Cl, R_2 = 3-Cl

6. R_1 = Cl, R_2 = 4-Cl
7. R_1 = Cl, R_2 = 5-Cl
8. $R_1 = H$, R_2 = 4-OMe
9. $R_1 = H$, R_2 =3-$COCH_3$
10. R_1 = Cl, R_2 =4,6-Cl
11. $R_1 = H$, R_2 =3-Cl

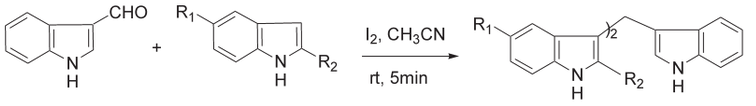
12

Glyceryl phosphorylcholine (GPC). Increase of testicular alkaline phosphatase and cholesterol were also observed. Fertility and other effects regained gradually after cessation of treatment. The results revealed from the study indicate that the compound has reversible anti-fertility activity and can be exploited as male contraceptive agent.

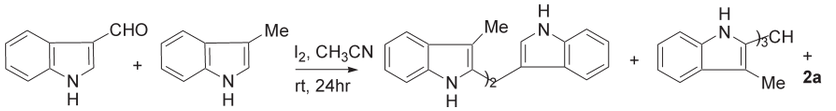


2-(2''-chloroacetamidobenzyl)-3-(3'-indolyl) quinoline

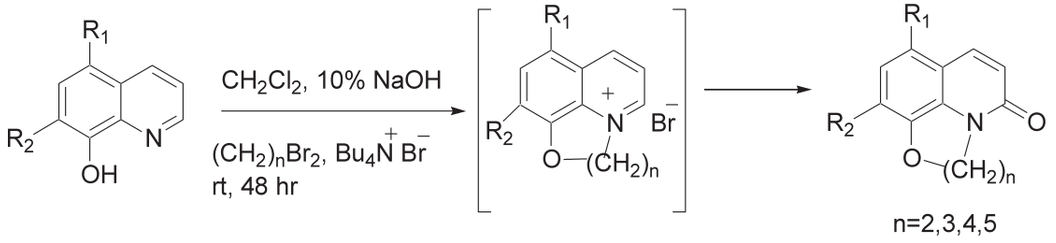
Lewis acid catalyzed synthesis of triindolylmethanes from indole-3-carboxaldehyde and several other indole derivatives is described. A systematic study was carried out to evaluate the catalytic activity of seven Lewis acids and molecular iodine. Iodine appeared to be the most efficient in affording symmetrical and unsymmetrical tri-indolylmethanes in high yield.



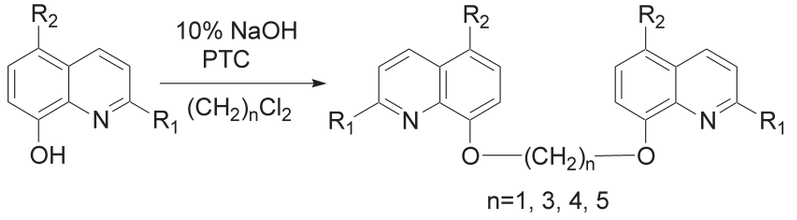
a; $R_1 = R_2 = H$
b; R_1 = Br, $R_2 = H$
c; R_1 =H, R_2 = Me



The aim and objective of this subproject is to develop/synthesis newer heterocyclic molecules of expanded ring system based on quinoline derivatives under phase transfer catalytic condition and the work are in progress



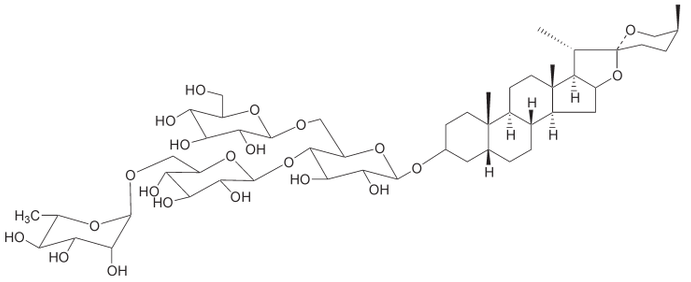
Bis-quinolines are known to possess activity against various mosquito borne diseases. Quinoline as the core moiety synthesis of some newer bis-quinoline derivatives under PTC condition has been achieved. Evaluation of the newer bis-quinolines to identify the molecules as antileishmanial and antibacterial agents are in progress.



Dr. S. Bandopadhya, Dr. N. B. Mandal and group

Chemical investigation of medicinal plants for bioactive substances

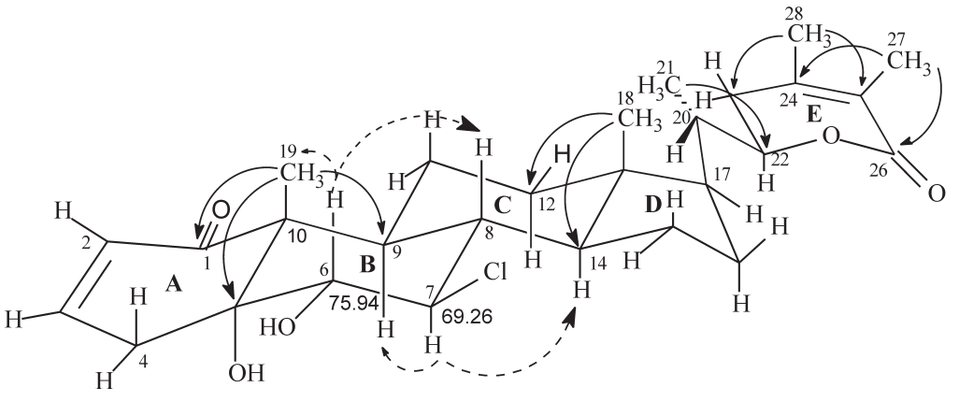
Leishmaniasis remains a major health problem of the tropical and subtropical world. The visceral form causes the most fatalities if left untreated. Dramatic increases in the rates of infection and drug resistance and the non-availability of safe vaccines have highlighted the need for identification of novel and inexpensive anti-leishmanial agents. This study reports that racemoside A, a water-soluble steroidal saponin purified from the fruits of *Asparagus racemosus*, is a potent anti-leishmanial molecule effective against antimonial-sensitive (strain AG83) and -unresponsive (strain GE1F8R) Leishmania donovani promastigotes, with IC_{50} values of 1.15 and 1.31 [mu]g/ml, respectively. Incubation of promastigotes with racemoside A caused morphological alterations including cell shrinkage, an aflagellated ovoid shape and chromatin condensation. This compound exerts its leishmanicidal effect through the induction of programmed cell death mediated by the loss of plasma membrane integrity as detected by binding of annexin V and propidium iodide, loss of mitochondrial membrane potential culminating in cell-cycle arrest at the sub-G0/G1 phase, and DNA nicking shown by deoxynucleotidyltransferase-mediated dUTP end labelling (TUNEL). Racemoside A also showed significant activity against intracellular amastigotes of AG83 and GE1F8R at a 7-8-fold lower dose, with IC_{50} values of 0.17 and 0.16 [mu]g/ml, respectively, and was non-toxic to murine peritoneal macrophages up to a concentration of 10 [mu]g/ml. Hence, racemoside A is a potent anti-leishmanial agent that merits further pharmacological investigation.



Dr. S. Mukhopadhyay and group

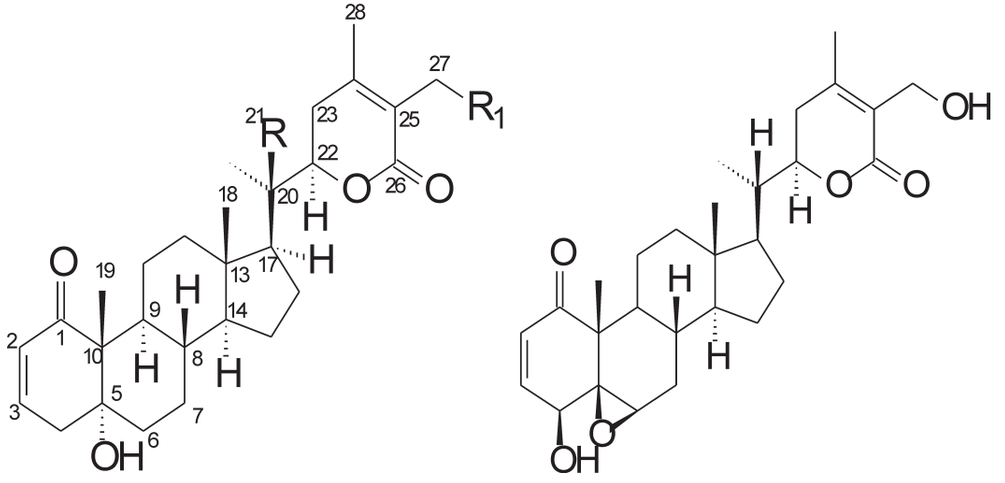
Chemistry of naturally occurring DNA topoisomerase inhibitors

Search for new topoisomerase inhibitiors from indigenous plants has been taken as the prime objective of this project. Reverse-phase preparative HPLC analysis of the n-butanol fraction of the methanolic extract of *Withania somnifera* Dunal (leaves) afforded a novel chlorinated withanolide, namely withanolide Z (**1**), along with four withanolides, withanolide B (**2**), withanolide A (**3**), 27-hydroxywithanolide B (**4**) and withaferin A (**5**). Their structures were elucidated by IR, MS, CD and a combination of 1D and 2D NMR spectral analyses.



Withanolide Z (7-chloro-5, 6-dihydroxy-1-oxo-22*R*-witha-2, 24-dienolide . **(1)**

We have performed the plasmid relaxation assay with withanolides **1-5**, keeping the well-established DNA topoisomerase I inhibitor campothecin (CPT) as a positive control. This showed that withanolide Z (**1**) exerts inhibitory activity against *L.donovani* topoisomerase I. So this compound might be exploited for therapeutic development against leishmaniasis



1 R=R_1=H, 6α-OH, 7β-Cl , **3** R=OH, R_1=H, 6α,7α-epoxy

2 R=R_1=H, 6α,7α-epoxy , **4** R=H, R_1=OH, 6α,7α-epoxy

Dr. Chinmay Chowdhury and group

Bioactive substances from Plant materials

In continuation of our search for potent bioactive phytochemicals, activity guided fractions of various plant extracts led to selection of *Semecarpus anacardium* for further intensive studies. So far, we have isolated a flavone glycoside (Kaempferol-3-O-sophoroside) from n-butanol part of leaf-extracts of *Semecarpus anacardium*. The structure was established unambiguously using 1D-NMR as well as HMBC, HMQC, COSY, TOCSY etc. Interestingly, that molecule has shown strong anti-viral activities. Besides, isolations of other molecules from different fractions are also currently underway. In conjunction with the above studies, we reasoned that chemical transformations of plant derived natural products of therapeutic importance could enhance their activities as well as water solubility. In view of this, we started a program about structural modifications of andrographolide, an important labdane diterpenoidal constituent of *Andrographis paniculata*. We have designed some important analogues through functional group modifications of C-14 hydroxy of andrographolide. In this context, we have successfully achieved several structurally fascinating molecules whose anticancer activities against various cancer cell lines are being carried out. Parallel to this, isolations, structure elucidations and screening of activities of various saponins from other medicinal plants are also in progress.

Dr. B. C. Pal and group

Development of herbal medicine

In continuation of the research work on Type II anti-diabetic molecules from different sources, we have identified two plants having the required property. Now we are trying to isolate molecule (s) from these sources. Further research work on the bioactive medicinal plants are in progress.

Drs. G. Suresh Kumar, R. C. Yadav and group

Nucleic acid polymorphic structures and their interaction with plant alkaloids.

Nucleic acid binding natural alkaloids: *New insight into the cooperativity and thermodynamic aspects of binding of berberine*: In continuation of the work on natural alkaloids binding to nucleic acid structures, the binding heterogeneity, and energetics of the interaction of the protoberberine alkaloid berberine (**Fig. 1a**) have been studied with various natural and synthetic DNAs. At low ratios of bound alkaloid to base pair, the binding exhibited cooperativity to natural DNAs with almost equal proportions of AT and GC sequences. In contrast, the binding was non-cooperative to DNAs with predominantly high AT or GC sequences. Cooperative binding was observed with poly(dA).poly(dT) and poly(dG).poly(dC) while non-cooperative binding was seen with poly(dA-dT).poly(dA-dT) and poly(dG-dC).poly(dG-dC). Both cooperative and non-cooperative bindings were remarkably dependent on the salt concentration of the media. Plots of ln Ka versus $[Na^{+}]$ for poly(dA).poly(dT) and poly(dA-dT).poly(dA-dT) showed the release of 0.56 and 0.75 sodium ions respectively per bound alkaloid. Isothermal titration calorimetry (ITC) results revealed the binding to be exothermic and favoured by both enthalpy and entropy changes in all DNAs except the two AT polymers and AT rich DNA (**Fig. 2a**), where the same was predominantly entropy driven. Heat capacity values ($\blacktriangle Cp^{o}$) of berberine binding to poly(dA).poly(dT), poly(dA-dT).poly(dA-dT), Clostridium perfringens and calf thymus DNA were –98, –140, –120 and –110 cal/mol K respectively. This study presents new insights into the binding dependent base pair heterogeneity in DNA conformation and the first complete thermodynamic profile of berberine binding to DNAs.

Comparative study of the energetics of DNA binding of berberine, palmatine and coralyne: The interaction of two natural cytotoxic protoberberine plant alkaloids berberine (**Fig. 1a**), palmatine (**Fig. 1b**) and a synthetic derivative, coralyne (**Fig. 1c**) with mammalian herring testis DNA was studied using a combination of isothermal titration calorimetry, differential scanning calorimetry and optical melting experiments in order to characterize the energetics of their binding. The binding constants of these alkaloids to DNA under identical conditions were evaluated form the UV melting data and the enthalpy of binding was elucidated from isothermal titration studies (**Fig. 2a-c**). Under identical conditions, the binding constants of berberine, palmatine and coralyne to DNA were found to be $1.15x10^4$/M and $2.84x10^4$/M and $3.5x10^6$ M^{-1} at 20^oC in buffer of 20mM [Na^+]. Parsing of the free energy change of the interaction observed into polyelectrolytic and non-polyelectrolytic components suggested that although these alkaloids are charged, the major contributor of about 75% of the binding free energy arises from the non-polyelectrolytic forces. The binding in case of palmatine and coralyne was predominantly enthalpy driven with favoring smaller entropy terms while that of berberine was favoured by both negative enthalpy and positive entropy changes. Temperature dependence of the binding enthalpies determined from ITC studies in the range 20-40^oC was used to calculate the binding induced change in heat capacity ($\blacktriangle Cp^o$) values as –117, -135 and –157 cal/mol/K respectively for berberine, palmatine and coralyne. Taken together, the results suggest that the DNA binding of the planar synthetic coralyne is stronger and thermodynamically more favored compared to the buckled natural berberine and palmatine.

CHEMISTRY

Interaction of alkaloids berberine and palmatine with tRNA and comparison to ethidium: In the recent years we have initiated studies on the interaction of small alkaloid molecules to RNA structures in pursuit of natural molecules that can substitute aminoglycosides as therapeutic agents. The interaction of the protoberberine alkaloids berberine and palmatine (**Fig. 1 a and 1b**) with $tRNA^{phe}$ was studied using various biophysical techniques and molecular modeling and the data were compared with the binding of the classical DNA intercalator, ethidium (**Fig. 1d**). Circular dichroic studies revealed that the tRNA conformation was moderately perturbed on binding of the alkaloids. The cooperative binding of both the alkaloids and ethidium to tRNA was revealed from absorbance and fluorescence studies. Fluorescence quenching studies revealed that while berberine and palmatine are partially intercalated, ethidium is fully intercalated on the tRNA molecule. The binding of the alkaloids as well as ethidium stabilized the tRNA melting, and the binding constant evaluated from melting data was in agreement with fluorescence spectral data. Differential scanning calorimetry revealed that the tRNA melted showing three close transitions that were affected on binding. Molecular docking calculations performed revealed the preferred regions of binding of these small molecules on the tRNA (**Fig. 3**). Taken together, the results suggest that the binding of the alkaloids berberine and palmatine on the tRNA structure appears to be mostly by partial intercalation while ethidium more or less fully intercalates to the tRNA. These results further advance our knowledge on the molecular aspects on the interaction of these alkaloids to tRNA.

Modulation of nucleic acid structural transition by alkaloid complexation: Induction of self structure in poly(A) by alkaloids and small molecules: Self-structure induction in single stranded poly(A) has been one typical example of the various ways that could be used to modulate nucleic acid structural aspects through binding of small molecules. For the first time, the interaction of a series of small molecules and poly(A) has been investigated to understand the nature of the structural features in these DNA binding small molecules that could be responsible for the formation of self-structure if any in single stranded poly(A) molecules. Classical intercalators like coralyne (**Fig. 1c**), ethidium (**Fig. 1d**), quinacrine (**Fig. 1e**), and proflavine (**Fig. 1f**), partial intercalators like berberine (**Fig. 1a**) and palmatine (**Fig. 1b**) and classical minor groove binders like hoechst 33258 (**Fig 1g**), and 4,6-diamidino-2-phenylindole (DAPI) (**Fig. 1h**) have been chosen for this study. The binding of each of these molecules to poly(A) has been characterized by absorption, spectral titration, jobs plot and isothermal titration calorimetry. Self-structure formation was monitored from circular dichroic melting, optical melting and differential scanning calorimetry. The results revealed for the first time that while all the intercalators studied induced self-structure, partial intercalators did not induce the same in poly(A). Of the two classical DNA minor groove binding molecules investigated, hoechst was effective

in inducing self-structure while DAPI was ineffective. Self-structure induction in poly(A) was observed to be directly linked to the cooperative binding of the molecules to poly(A) in that all the molecules that bound cooperatively induced self-structure in poly(A). Structural and thermodynamic aspects of the interaction of small molecules leading to self-structure formation in single stranded poly(A) molecules were deduced from these studies.

Structural, conformational and energetic profiles of intercalative binding of small molecule alkaloids binding to double stranded poly(A): Recognition of double-stranded ribonucleic acid is a critical event in many biological pathways like trafficking, editing and maturation of mRNA, interferon antiviral response and RNA interference. In the context of probing double-stranded RNA binding small molecules, the interaction of the antitumor protoberberine alkaloid coralyne (**Fig. 1c**) with double stranded poly(A) has been studied by various biophysical techniques. Typical hypochromic and bathochromic shift in absorption spectrum and appreciable quenching of the intrinsic fluorescence of coralyne indicated the strong affinity of coralyne to poly(A). The corresponding intrinsic binding constant evaluated from Scatchard analysis was in the order of 10^5 M^{-1}. The strong binding was further characterized by significant polarization of the alkaloid fluorescence and stabilization of poly(A) helix against thermal strand separation. The binding process was manifested by remarkable perturbation of the intrinsic circular dichroic spectrum of poly(A) with concomitant generation of optical activity in the bound alkaloid molecules that are otherwise achiral. Job's plot analysis showed the binding stoichiometry of the interaction process to be two base pairs per alkaloid molecule. The energetics of the strong interaction was studied by isothermal titration and differential scanning calorimetric techniques that suggested the binding to be exothermic and favoured by both negative enthalpy and positive entropy changes. All these results together with the Stern-Volmer quenching experiment in fluorescence revealed the molecular details of the intercalation of coralyne into duplex poly(A) leading its potential use as an agent in gene regulation in eukaryotic cells.

Future programme of this sub project is to further focus on the study of RNA binding small molecules with particular emphasis on specificity and energetics of interaction of natural and synthetic alkaloids.

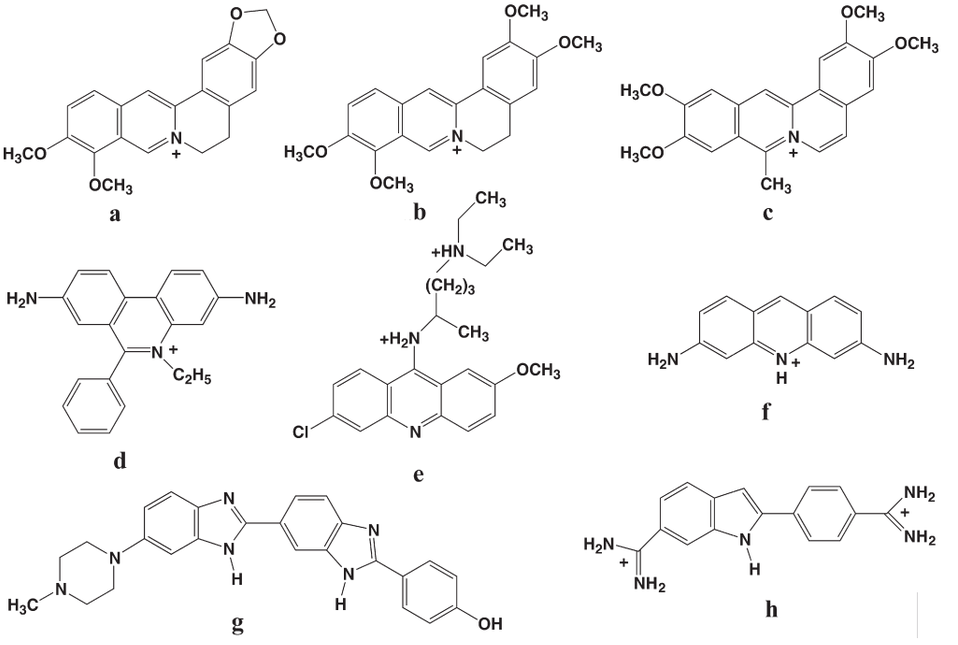


Fig. 1. Chemical structures of (**a**) berberine (**b**) palmatine (**c**) coralyne (**d**) ethidium (**e**) quinacrine (**f**) proflavine (**g**) hoechst and (**h**) DAPI.

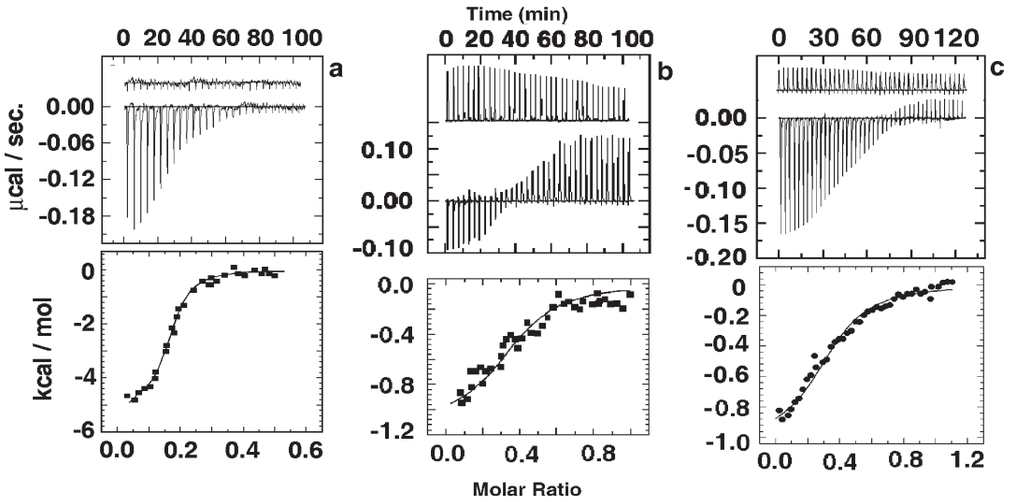


Fig. 2. Isothermal titration calorimetric titration of (a) coralyne (b) palmatine and (c) berberine with DNA at 20^{O}C.

CHEMISTRY

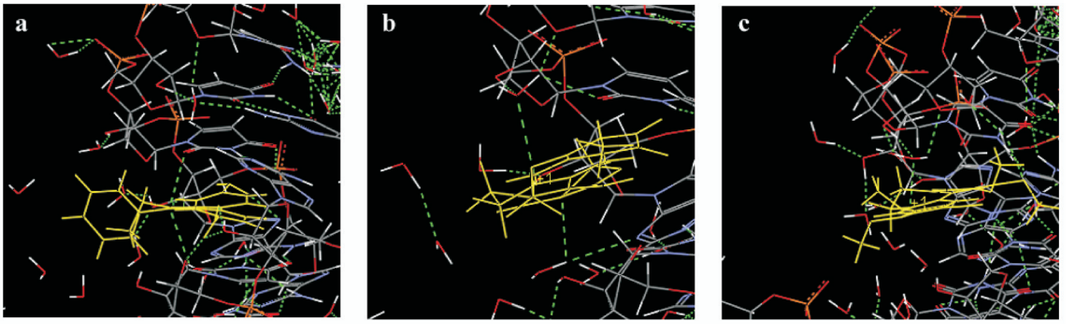


Fig. 3. Docked pose of (a) ethidium, (b) berberine and (c) palmatine on tRNA. In each case the drug is shown in yellow colour.

Technical Staff

Kalyan K. Sarkar, Asit Kumar Das, Subodh K. Roy, Sankar K. Maitra, Tapas K. Sarkar, Diptendu Bhattacharya, Gautam Gupta, Sandip Chowdhury, Sekhar Ghosh, Sarit K. Sarkhel, Rajendra Mahato, E. Padmanaban and Nimai C. Pradhan.

RAs and Research Fellows

Rangana Sinha, Mumu Chakraborty, Roshmi Roy, Abhijit Hazra, Amrita Chatterjee, Ankur Ray, Anupam Adhikari, Arpita Neogi, Ashim Roy, Biswajit Gopal Roy, Churala Pal, Debkumar Nandi, Gora Das, Goutam Biswas, Ishita Sanyal, Joy Krishna Maiti, Kakali Bhadra, Koushik Mazumder, Maidul Hossain, Mainak Banerjee, Md. Maidul Islam, Moumita Gupta, Nilendu Panda, Prabal Giri, Priyankar Paira, Ram Prasad Ghosh, Sandip K.Hota,Sarbendu Maiti, Seema Dutta, Scientist (WOS-A, DST), Shrabanti Kumar, Sumit Dey, Swapan Pramanick, Tanmoy Biswas, Tirtha Pada Majhi, Subhrangshu Mukherjee, Prithwish Jana, Shinjini Bhattacharjee, Sohini Datta, Arpita Neogi, Nirmal Das Adhikari, Krishnendu Bikash Sahu, Anup Kumar Sasmal, Raj Kumar Manna, Jewel Hossain, Sutanaka Roy, Suman Samanta, Madhumita Mondal, Tulika Mukhopadhya, Subhendu Naskar, Abhijit Ghorai, Goutam Pauli, Samit Guha, Jishu Naskar, Bimalendu Adhikari, Jayanta Nanda, Sudipta Ray, Kaushik Brahma, Rajarshi Roy Choudhury, Swarbhanu Sarkar, Sudipta Ray.

Project Assistants

Prasun K. Pradhan, Sankar K. Dutta, Sudipta Saha, Sanjit K. Mahato, J. Vinayagam, Dipanjan Majumder, Sebanti Roy Chowdhury, Sohini Sarkar, Susan Mukherjee, Pinaki Halder, Soumyanil Bhawmik, Sruti Vishwakarma, Mahua Bhattacharya, Jay Shankar Jadav, Bimalendu Das , Sanjukta Mukherjee , Sourav Sarkar

Summer Trainees

Sohani Das Sharma, Anindya Roy, Sreya Gupta, Moulisha Biswas, Himal Kanti Ganguly
Gurpreet Kaur Arora , Priyanka Acharya, Sujit De, Arindam Maity, Rupankar Paira, Argha Chakraborty, Shraboni Ghoshal, Piyali Deb Burman, Arjun Sengupta

Administrative Staff

Mr.Sankar Prasad Dutta, Sr.Stenographer

OPERATION AND MAINTENANCE OF SOPHISTICATED INSTRUMENTS

600 MHz NMR Bruker spectrometer

Dr. Ranjan Mukhopadhyay and Mr. E. Padmanaban

The highly sophisticated 600 MHz Bruker NMR spectrometer has been maintained and analyses of about 1550 samples were done during the year for both internal and external research workers. Apart from routine 1D experiments like PMR, PMR (HOD suppression), CMR, DEPT 135, DEPT 90, NOE difference and 2H-NMR various 2D and 3D experiments are being done regularly. 2D experiments include COSY, DQF-COSY, NOESY, NOESY-WG, TOCSY, TOCSY-WG, ROESY, HSQC, HMQC, HMBC, ADEQUATE and HSQCNOESY-15N.The 3D experiments mostly done are HNCOWG (13C/15N) and NOESYHSQC-15N.

300 MHz NMR Bruker spectrometer

Dr. V. S. Giri , Dr. Ranjan Mukhopadhyy and Dr. Tapas Sarkar

The 300 MHz Bruker DPX model NMR instrument has been extensively used during the year. About 3335 samples have been analyzed which includes both internal and external samples. 1D experiments mostly done are PMR, CMR (with DEPT 135 and DEPT 90), proton decoupling, NOE difference and variable temperature analyses. The 2D analyses routinely done includes COSY, NOESY, HMBC, HMQC, HSQC and COLOC experiments

Jasco 4200 FT/IR and Jasco 410 FT/ IR spectrophotometer

Dr. V. S. Giri and Dr. P. Jaisankar

The JASCO FT/IR 410 and 4200 spectrophotometers have been routinely maintained and extensively used to analyse both internal and external samples. About 800 samples have been analyzed during the year. The instruments have given support to the newly introduced NIPER course also.

LC-MS-MS-Q-TOF Micromass instrument

Dr Asish K. Banerjee, Mr. Kalyan Kumar Sarkar and Mr. Diptendu Bhattacharya

One LC-MS-MS (Q-TOF Micor) instrument was installed in the middle of 2003. Since then it has been in use for routine mass spectral analysis of both internal and external samples. Small molecules as well as bio-macromolecules like proteins, carbohydrates etc. are being analyzed. Facilities include determination of their molecular weight, MS-MS experiments etc.

Perkin-Elmer 2400 CHNS/O analyzer Series II System

Dr Asish K. Banerjee and Shri Sandip Chowdhury

The analyzer has been installed recently and routine analysis of samples are being undertaken.

Jeol AX500 GC-mass Spectrometer

Shri Ajoy Banerjee (with operational support by Shri Sandip Chowdhury)

The Jeol AX500 Mass spectrometer is being routinely maintained by us and it is functioning in different mode of analysis inspite of its constraints due to prolong use .
Both internal and external researchers are utilising the facility.

Gas liquid chromatograph

Dr. Asish K Sen (Jr.)

Two Gas Liquid Chromatography instruments (Agilent 6890 plus and Hewlett-Packard 5890, fitted with FID detectors) has been maintained and samples are analyzed throughout the year to cater to both in-house and external research workers including industries. During the year, ~180 samples within the institute and ~40 outside samples have been analyzed.

Shimadzu GC-mass spectrometer (GP5050 A)

Dr. Asish K Sen (Jr.) and Mr.A.K.Das

GLC-MS (Shimadzu, Japan) facility offered to IICB scientists and research fellows, and outsiders as well. During the year, ~191 samples within the institute and ~53 outside samples have been analyzed.

DIONEX ICS 3000 Ion Chromatography System

Dr. Asish K Sen (Jr.) and Mr.A.K.Das

The ion chromatography system is used for analytical detection and estimation of sugars (sialic acids, amino sugars, oligosaccharides etc.), amino acids and peptides in nanogram level.This facility is offered to IICB scientists and research fellows. This has been installed very recently and samples are getting analysed routinely.

VP-ITC Model Isothermal Titration Calorimeter and VP-DSC Model Differential Scanning Calorimeter

Dr. G. Suresh Kumar

An ultra sensitive Isothermal Titration Calorimetry Unit Model VP-ITC and Differential Scanning Calorimeter model VP-DSC (both from Microcal, LLC USA) for studying the thermodynamics of biomolecular interactions is providing service to researchers from several divisions of our institute.

Jasco J715 Spectropolarimeter

Dr. G. Suresh Kumar

The Circular Dichroism unit along with the Biologic stopped flow accessory is providing services to both internal and external workers. Solution conformation of peptides/proteins and nucleic acids are being routinely done.

Single crystal X-ray spectrometer

Dr. Partha Chattopadhyay

Single crystal X-ray spectrometer, Brukar model Kappa Apex-2 has been maintained and samples analyzed to serve institute research workers.


FOUNDATION DAY CELEBRATION
(POST-GOLDEN JUBILEE)
APRIL 2nd, 2007
INDIAN INSTITUTE OF CHEMICAL BIOLOGY, KOLKATA-32
PROF. SANKAR K. PAL
PROF. RICHARD J. SIMPSON
DR. T. K. DHAR

Structural Biology & Bioinformatics Division

Prof. Siddhartha Roy, Dr. M.C.Bagchi (Head), Dr. Chitra Dutta, Dr. Debasish Bhattacharyya, Dr. Nanda Ghoshal, Dr. Soumen Datta, Dr. Krishnananda Chattopadhyay, Dr. Subrata Adak

Structural characteristics and conformational specificity to a large extent determine the mode of interaction between/or among all the biological macromolecules, leading to expression of their regulated functions. This institute has a long tradition of carrying out research on protein chemistry, molecular modeling of proteins, protein nucleic acid interactions, nucleic acid-drug interactions, and drug-protein interactions. Clearly, such structure-function studies require multi-pronged approach from different angles involving several areas of biological, chemical and physical sciences. Recently, we have undertaken an effort to bring all these disciplines under a common roof, resulting in the formation of the "Structural Biology & Bio-informatics" division. The charter of this division is to carry out research in areas that focus on structural characterization of potentially prospective biological macromolecules and other small molecules of therapeutic interest against various diseases, e.g. tuberculosis, leishmaniasis, cholera, cancer, diabetes and for other anti-inflamatory, anticonvulsant and immunomodulatory activities. Fundamental studies on protein functions, protein-protein and protein-nucleic acid interactions applying modern sophisticated technologies like nuclear magnetic resonance (NMR), X-ray crystallography, analytical ultracentrifuge, fluorescence correlation spectroscopy, diode array stopped-flow spectrophotometry, mass-spectrometry, quantitative structure activity relationship (QSAR) and 3D-QSAR are also being pursued. Softwares are being developed for genome / proteome analysis, prediction, modification and analysis of macromolecular structures and for elucidating their interactions with bio-active molecules.

Prof. Siddhartha Roy & group

A Chimeric Glutamyl:Glutaminyl-tRNA Synthetase.

Aminoacyl-tRNA synthetases (aaRS) are multi-domain proteins that have evolved by domain acquisition. The anti-codon binding domain was added to the more ancient catalytic domain during aaRS evolution. Unlike in eukaryotes, the anti-codon binding domains of GluRS and GlnRS in bacteria are structurally distinct. This originates from the unique evolutionary history of GlnRS. Starting from the catalytic domain, eukaryotic GluRS evolved by acquiring the archaea/eukaryote-specific anti-codon binding domain after branching away from the eubacteria family. Subsequently, eukaryotic GlnRS evolved from GluRS by gene duplication and horizontally transferred to some bacteria. In order to study the properties of the putative ancestral GluRS in eukaryotes, formed immediately after acquiring the anti-codon binding domain, we have designed and constructed a chimeric protein cGluGlnRS, consisting of the catalytic domain (*Ec*N-GluRS) and the anti-codon binding domain of *E. coli* GlnRS (*Ec*GlnRS). In contrast to the isolated *Ec*N-GluRS, cGluGlnRS showed detectable activity of glutamylation of *E. coli* $tRNA^{glu}$ and was capable of complementing an *E. coli* ts-GluRS strain at non-permissive temperatures (Figure 1). Both cGluGlnRS and *Ec*N-GluRS were found to bind *E. coli* $tRNA^{glu}$ with native *Ec*GluRS-like affinity, suggesting that the anticodon-binding domain in cGluGlnRS enhances k_{cat} for glutamylation. This was further confirmed from similar experiments with a chimera between *Ec*N-GluRS and the substrate-binding domain of *Ec*DnaK. We have shown that an extended loop, present in the anticodon-binding domains of GlnRSs, is absent in archaeal GluRS, suggesting that the loop was a later addition, generating additional anti-codon discrimination capability in GlnRS as it evolved from GluRS in eukaryotes (Figure 2).

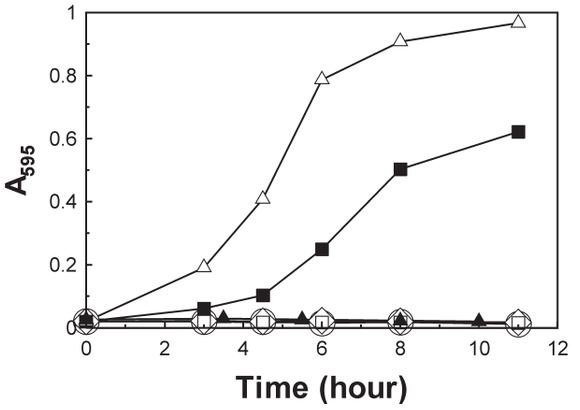
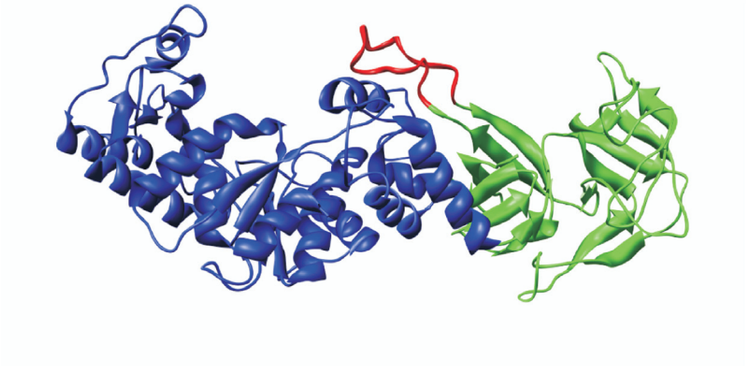


Figure 1: In vivo complementation of a ts-GluRS mutant strain. JP1449 (DE3), at 42C was transformed with different plasmids harboring genes for different proteins and growth curves were determined at non permissive 42^{O}C. The symbols represent plasmids bearing genes of: Native EcGluRS (open triangle), cGluGlnRS (solid square), pET28a (open circles), H16AGluGlnRS (open diamonds), EcN-GluRS (open square), GluRS-DnaK chimera (solid triangle). Plasmids encoding gene for EcGluRS, cGluGlnRS, H16AcGluGlnRS, EcN-GluRS, pET28A and GluRS-DnaK chimera were transformed in JP1449 (DE3) at 32°C. Small cultures were grown at 32°C from colonies obtained from the transformed plates. Overnight cultures were diluted into fresh media in such a manner as to keep the initial optical density same. Then all of them were allowed to grow at 42 °C and their growth was monitored at different time intervals.



```
Q_ECOLI   AHALPVEIRLYDRLFSVPNPGAADDFLSVINPESLVIKQGFAEPS 507
E_YEAST   KDVVPVDLVDFDHLITKDRLEEDESFEDFLTPQTEFHTDAIADLN 660
E_METJA   KDSVKVKVLMPD----------------------GEIKEGFAEKD 518
E_METM5   KDSVPVTVIDEN----------------------AEKIEGFAEKD 520
E_METTH   ESALEAEVIMPD----------------------ASRVRGVIEAD 519
E_METKA   DQAVRCEVVRPD----------------------GSVESGYAEIN 536
E_PYRFU   GKECEVIIPEGE-E--------------------LIIRKGLLEKN 538
E_SULSO   NEKVPVMVEKAERDE-------------------IKMINGYAEKI 540
E_THEVO   N-SREFQVLKPD----------------------GSIDKGLIEPA 538
E_HALMA   DGPALRLRTMDG-----------------------DVSGVAEPG 541
E_ECOLI   KVGMPLRVAVTG----------------------AGQSPALDVT 444
```

Figure 2. a) Crystal structure of E. coli GlnRS (1NYL) with the extended anti-codon binding domain loop (residues 474-495) colored red. b) Multiple sequence alignment of Saccharomyces cerevisiae GluRS (E_YEAST; P46655) and representative archaeal GluRS sequences: Methanococcus jannaschii (E_METJA; Q58772), Methanococcus maripaludis (E_METM5; A4FXG8), Methanobacterium thermoautotrophicum (E_METTH; O26157), Methanopyrus kandleri (E_METKA; Q8TXB7), Pyrococcus furiosus (E_PYRFU; Q8U064), Sulfolobus solfataricus (E_SULSO; P95968), Thermoplasma volcanium (E_THEVO; Q979Q0), Halobacterium marismortui (E_HALMA; Q5V5N9), Escherichia coli (E_ECOLI; P04805), in the region of the E. coli GlnRS (Q_ECOLI; P00962) loop (474-495).

Synthesis and NMR structure determination of Hepatitis C virus IRES RNA bound peptide complex derived from human La protein

Human La protein was originally identified in the sera from patients with systemic lupus erythematosus (SLE) and Sjögren syndrome. Based on the structure determinations three major domains La-motif (7-92), RRM1 (110-194) and RRM2 (229-327), may be identified. La protein has been shown to bind several viral and cellular IRES elements and influences their function. It has been demonstrated that La protein plays an important role in mediating HCV IRES mediated translation. It interacts at GCAC motif near initiator AUG of HCV IRES, which might trigger some conformation alterations that facilitates formation of functional initiation complex and stimulate internal initiation of translation. The central RRM (112-184) has been shown to possess a classical RRM-type fold containing four stranded beta sheet backed by two alpha helices. Previously a 24-mer peptide (LaR2C) from La central RRM was shown to bind to an RNA from HCV IRES (18-383). Further characterization of interaction motif was performed by NMR spectroscopy. In this case, since the RNA is relatively large (18-383 nt of HCV IRES), obtaining the full structure of the RNA-peptide complex (1:1) would be extremely difficult. Thus, NMR spectrum of LaR2C was studied, which was relatively simple, in the absence and presence of sub-stoichiometric amount of RNA. It was assumed that under fast exchange condition, the chemical shifts of peptide protons in the absence of RNA will be average of free and bound species (intensity of RNA protons will be insignificant due to sub-stoichiometric presence and broader line-width). Thus, comparison of peptide chemical shifts in the presence of RNA with that of the free peptide is expected to shed light on the residues that may be involved in recognition.

'Total Correlation Spectroscopy' (TOCSY) provides connectivity between all adjacent protons (three-bond connectivity) within an amino acid unit and hence a fingerprint for the type of amino acid. TOCSY spectrum in presence and absence of RNA identified several important residues involved in peptide-RNA interaction. Interestingly, the residues of the peptide responsible for RNA recognition were found to map to a seven residue turn in the context of RRM (112-184) NMR structure. This seven residue peptide was chemically synthesized (LaR2C-N7). The HCV IRES RNA bound structure of LaR2C-N7 structure was determined by NMR spectroscopy. Under bound conditions, the peptide gave several new NOEs and change of value of J for several amide protons in addition to significant line broadening. This indicates that conformational parameters derived from this experiment indeed reflect the bound form. The sequence KETD forms a â-turn as distance between Cá atoms of K and D is less than 7Å (Figure 3). However, the Ramachandran angles do not fall within any defined turn category. The KETD sequence in the RRM (112-184) structure is also a â-turn but the conformational parameters do not fall strictly into any well-defined category. Although, the structures in free and bound contexts are similar, there are noticeable differences in Ramachandran angles. Thus, there could be significant remodeling of the structure upon binding of La to the RNA.

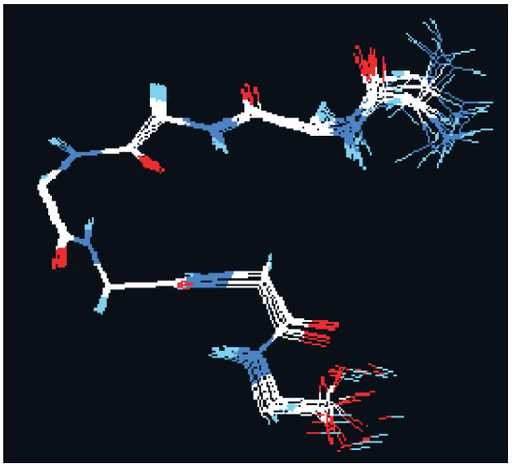


Figure 3: Superimposition of best 16 structures (backbone) of LaR2C-N7 under RNA bound conditions simulated using DYANA (Version 1.5. Peter Guentert & Kurt Wuthrich, Zurich, Switzerland).

Dr. M. C. Bagchi & group

Mathematical Modeling in Drug Design using Structural Descriptors

The major objective of the present project is to study some important topological and other structural parameters of known active compounds as well as many active analogs of the same using various linear statistical methods and non-linear counter propagation neural networks for developing quantitative structure activity relationships of anti-tubercular and anti-cancer compounds.

Application of constitutional descriptors for merging of quinoxaline data sets using linear statistical methods

An attempt has been made for unifying two different quinoxaline data sets with a wide range of substituents in 2, 3, 7 and 8 positions having excellent anti-tubercular activities with a view to developing robust and reliable structure-activity relationships. The merging has been done for these two sets of quinoxaline 1,4-di-N-oxides derivatives comprising 29 and 18 compounds respectively on the basis of constitutional descriptors, which denotes the structural characterization of the molecules. Principal component analysis was performed to see the distribution of the compounds from two data sets for the constitutional descriptors. As observed, for the entire set of constitutional descriptors, the first two PCs explain 99.5% of variances in the descriptors data matrices. To show the pattern of distribution of the molecules in the factors spaces, the first two scores are plotted against each other. Figure 1 represents the distribution of compounds in the score plots for the constitutional descriptors. It is seen that the two sets of compounds are distributed in the same region of the score1 – score2 plot without any particular demarcation. Thus, it can be concluded that the classification ability of the PCA-based method confirms that the molecules are similar in nature and can be considered as a single data set which is useful for model development. Outlier detection was performed from the standpoint of residual analysis of the PLS models. The superiority of the constitutional descriptors over other calculated molecular descriptors has been established from the standpoint of leave-one-out (LOO) cross-validation technique associated with partial least squares (PLS) analysis. Internal validation through the leave-many-out methodology was also performed with good results, assuring the stability of the models. The results obtained from linear PLS analysis lead to a statistically significant and robust QSAR modeling

Figure 4: *Plots of the first two scores obtained from the application of PCA on the constitutional descriptors.*

Application of artificial neural network in QSAR of phenolic compounds

Phenol and its congeners are found to induce casepase-mediated apoptosis activity and cytotoxicity on murine leukemia cell line (L1210), human promylolytic cell line (HL-60), human breast cancer cell line (MCF-7), parenteral human acute lymphoblastic cells (CCRF-CEM) and multidrug-resistant subline of CCRF-resistant to

vinblastine (CEM/VLB) cells. Apoptosis, scavenging of radicals, antioxidant and pro oxidant characteristics are primarily responsible for the anti tumour activities of phenolic compounds. In our efforts to study the structure-activity relationships of phenols and its derivatives, a number of predictive models have been developed from the standpoint of theoretical structural parameters and ridge regression methodology. The QSARs show that the calculated molecular descriptors can provide good quality predictive models for the phenolic compounds. QSAR models based on simple data sets and using linear statistical methods have the limited utility in finding multi-dimensional rational patterns in more complex sets of data. In this situation, non-linear algorithms such as artificial neural networks (ANN) are used. An attempt has been made to carry out a comparative study of the relative effectiveness of ridge regression vis-à-vis counter propagation neural network (CPNN), in the QSAR of phenolic compounds. The CP ANN models were tested on recall ability and with the leave-one-out test that led to an interesting and promising result in terms of quality of both r-model and r-cross validation. The electron-releasing phenols and electron-attracting phenols were merged and used to build self-organising maps (SOM). Such a map shows how the compounds are distributed within the clusters. Cluster structures within the map (figure 5) may focus the electronic properties of compounds. From the activity layer of the CPNN model (figure 6), one can recognize that the low active, medium active or highly active phenols are clustered into different closed areas in the map. If the model is used to predict the activity for a new (hypothetical) compound, this compound would be situated somewhere in the map. Its position in the map and the neighboring phenols would determine the activity of new compound.

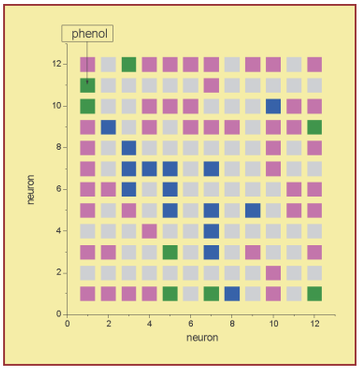


Figure 5 : SOM of merged set. (gray indicates empty neurons, magenta indicates electron releasing compounds, blue indicates electron-attracting compounds and green are neurons occupied by both.

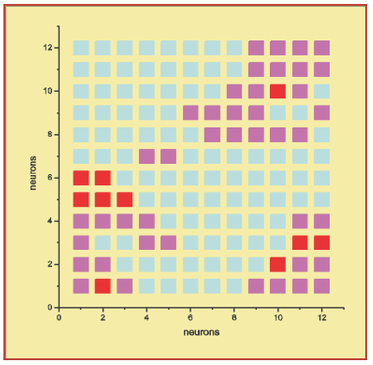


Figure 6 : Activity layer for CP ANN model. (Green indicates low active compounds, magenta indicates moderately active compounds, and red indicates highly active compounds.

Dr. Chitra Dutta and group

Genomic signatures of adaptaion in different prochlorococcus strains:

The work is an effort to analyze the nucleotide and amino acid usage patterns in all closely related strains of the marine cyanobacterial species Prochlorococcus marinus, whose genomes have been fully sequenced. These strains have been isolated from different depths of the ocean, ranging from the turbulent sea surface to the shadowy depths almost beyond the reach of the sun. Although occupying the same hierarchy in the taxonomy table, these strains have been found to adapt to these diverse conditions, which makes the study of their genomes both an interesting and intriguing task.

Statistical analysis show a clear segregation in patterns of codon and amino acid usage between the strains adapted to different depths. Especially low light adapted strains (isolated from greater oceanic depths) exhibit a strong asymmetry in usage of codons on their leading and lagging strands of replication. This asymmetry

being absent in their high light adapted cousins, which also happens to have smaller genome sizes, suggests an extensive reshuffling of genomic segments and gene loss in course of evolution. The 16S rRNA phylogeny also suggests that the extent of these differences in genomic arrangements and composition between Prochlorococcus strains is in some way correlated to their evolutionary distances from the last common ancestor. Gene rearrangement plots between strains representative of different light adaptations were drawn during the analysis which clearly shows the extent of this reshuffling.

GeneSyn: A software tool for analyzing the gene repertoire in different organisms:

Genomes are known to undergo several types of large-scale evolutionary events. Gene duplication can result in the existence of paralogous genes, whereas gene loss may remove a copy and obscure the assumption of orthology. Reordering of genetic elements occurs by mechanisms such as repeated inversion or translocation. Horizontal transfer introduces new genetic elements into bacterial genomes. Although numerous alignment calculation and visualization tools have been developed to date, the analysis of complex genomic changes, such as large insertions, deletions, inversions, translocations and duplications, still presents certain difficulties. We try to develop a genome comparison system for accounting all of these evolutionary phenomena to provide a complete picture of genetic differences among organisms (Figure 7). The software tool for orthologous gene order comparison of multiple organisms may be applied with the following aims:

1. To find out the crucial events like acquisition or loss of genes those are related to pathogenicity and antibiotic resistance, symbiosis and adaptation to new environments.
2. To detect the large chromosomal changes such as insertions, deletions, substitutions, recombinations, and duplications of chromosomal segments within two or more organisms.
3. To find out the new genetic elements in any organism, acquired by the process of horizontal gene transfer.
4. To find out the conserved sites in genomes with potential regulatory roles.

The large-scale comparisons unveil commonalities and differences between the genomes that may shed light on their evolutionary relationships, or may be characteristic of pathogenicity.

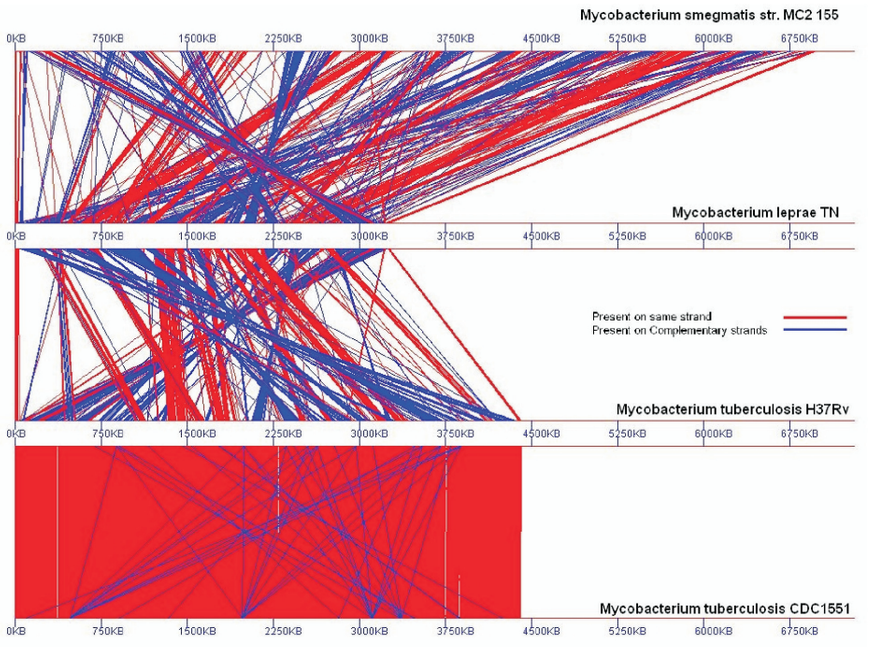


Figure 7 : *Gene synteny between different species of Mycobacteria Genes occuring in the same strand (+ or -) in both species of reference are plotted in red color, while the genes occurring in the + strand on one species and in the – strand of the other are plotted in blue.*

SPAST : A software tool for large-scale quantitative analysis of trends in nucleotide/amino acid substitution between pairs of orthologs :

Patterns in amino acid substitutions between orthologous proteins are, in general, asymmetrical in nature. Genome-scale comparative analyses of the asymmetry or bias in such substitution patterns may be beneficial for understanding the molecular basis of adaptation and evolution and for engineering novel proteins with desired characteristics. To this end, a PC-based integrated software tool SPAST (Substitution Pattern Analysis Software Tool) has been developed on the basis of a novel algorithm that allows a large-scale quantitative assessment of the bias in substitution patterns individually for all possible pairs of nucleotides/amino acids in groups of homologous genes/proteins. At the amino acid level, SPAST can compute the frequencies of substitution between each pair of residues as well as between different groups like polar to non-polar, charged to uncharged or hydrophobic to hydrophilic residues and evaluate the statistical significance of the bias, if any, in the trends of substitutions in the forward and reverse directions. At the nucleotide level, SPAST determines the direction and degree of bias in replacements between specific groups of nucleotides like Purine to Pyrimidine, Strong to Weak and Keto to Amino as well as between each pair of nucleotides.

The software may be employed to study intra- or inter-genomic variations in substitution patterns between orthologs/paralogs in different organisms. Application of SPAST in 12,024 human-mouse orthologous pairs revealed highly asymmetric and oppositely polarized trends in nucleotide and amino acid substitution in high and low GC-groups of orthologs. Pairwise comparison of 105 protein sequences from the hyperthermophilic archaeon *Nanoarchaeum equitans* and their mesophilic homologs using SPAST showed a strong bias towards replacement of uncharged polar residues of mesophilic proteins by Lys/Arg and Tyr in their *N. equitans* orthologs. On contrary, use of SPAST in sets of orthologs from halophilic and non-halophilic microorganisms revealed significant increase in negatively charged residues, Val and Thr and decrease in positively charged, large hydrophobic and Cys residues in halophiles. SPAST is particularly helpful in identification of bias in substitution between organisms marked with distinct genome composition, ecological niches or life-styles. Such patterns, when properly interpreted, may give deep insights into the molecular basis adaptation and evolution and thus, may assist in engineering novel proteins with desired characteristics.

Dr. Debasish Bhattacharyya and group

Functional regulation and assembly of multimeric enzymes, kinetic stability of proteins, characterization of venom toxins, biochemical analysis of the drug 'Placentrex' and metabolic engineering of phytoceucicals (podophyllotoxin).

Functional regulation of epimerase: The NAD bound dimeric enzyme, UDP-galactose 4-epimerase reversibly converts UDP-galactose to UDP-glucose. Regulation of activity of this enzyme from *Klyuveromyces fragilis* is being studied. Earlier it has been established that binding of substoichiometric amount of 5'-UMP, a competitive inhibitor, can completely inactivate the enzyme and its activity is restored only when the inhibitor is replaced by the substrate. Later it has been conclusively proved that the enzyme has distinct high and low affinity sites for substrate and inhibitor. Under controlled conditions of 'reductive inhibition', one of the catalytic sites could be inactivated. Currently conditions have been established under which the low substrate affinity site could be inactivated leaving the high affinity site intact. This is independent evidence that the two catalytic sites of the enzyme are not identical. Our present effort is to understand whether 5'-UMP could be recruited by the enzyme during its refolding *in vitro* and the incorporated ligand could regulate the activity of the enzyme as it does *in vivo*. Preliminary observations suggest that even if 5'-UMP is incorporated, probably it is not able to induce regulation in epimerase.

Kinetic stability of proteins is an evolutionary developed mechanism by which functional proteins are stabilized against denaturation. In this case a high energy of activation separates the functional state from the inactive state as a result the rate of unfolding becomes extremely slow. We are investigating whether bromelain – a cysteine protease from pineapple fruit and stem is stabilized by this mechanism. While the general of features of proteins stabilized

by kinetic considerations, e.g., -sheet rich structure, resistance to proteolysis and SDS binding and high E_{act} of inactivation and unfolding are maintained in bromelain. At this background, its mechanism of interaction with SDS has been elaborated using CD spectroscopy, intrinsic fluorescence emission, extrinsic fluorescence probe pyrene and isothermal calorimetric (ITC) investigations including inhibition of hydrolyzing activity. Results exhibit a number of synchronous transitions when plotted against the total SDS concentration. SDS at submicellar level caused conformation change of bromelain leading to a stable entity. ITC results confirm that the structural modifications are the result of alterations of solvent hydrophobicity and not the consequence of binding of SDS monomers. Melting temperature and G for unfolding of the SDS induced conformers were decreased at most by 4 C and 0.5 kcal/mol respectively, compared to native bromelain. Below 5 mM SDS caused large decrease in V_{max} without effecting K_m for hydrolysis of the substrate Z-Arg-Arg-NHMec. Analysis of kinetic data imply that SDS acts as a partial non-competitive inhibitor since, even at 100 mM of the detergent, residual activity of bromelain was retained by 3 %. Inhibition studies show an IC_{50} of 0.55 mM and a high K_i of 0.145 mM. These results collectively demonstrate that bromelain is resistant to SDS binding.

In continuation to characterizing venom components of Russell's viper, two isoenzymes of L-amino acid oxidase (LAAO) has been examined in terms of their kinetic properties. Phenylalanine being one of its good substrate, N-acetyltyrosine, N-acetyltryptophan amide and o-aminobenzoic acid act as its inhibitor. Effect of these individual inhibitors and cross-competition analysis among themselves indicated that there are 2-3 binding sites in the two enzymes. It is a flavo-enzyme. Since x-ray crystallographic structure of one venom LAAO is known and venom LAAOs are highly conserved in nature, based on the derived structure and mechanism of reaction, synthesis of 'suicidal substrate' will be attempted. Apart from LAAO, 5'-nucleotidase from the same venom source is being studied.

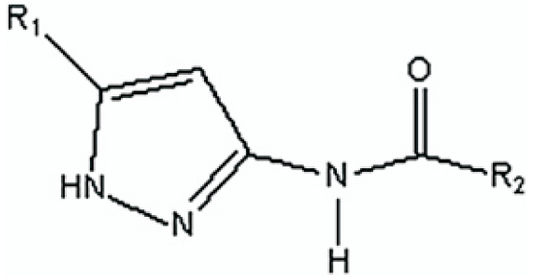
Characterization of the drug 'Placentrex', - an aqueous extract of human placenta used as efficient wound healer, is being continued. At present we are mostly concentrating on FN-peptide (fibronectin type III like peptide of 7.2 kDa) that is believed to play a key role in wound healing. It has been shown using different analytical techniques that NADPH, an important cosubstrate of enzymes, remains covalently bound to the peptide. However, the binding does not affect oxidation-reduction potency of the nucleotide, as the nicotinamide moiety of NADPH remains unaffected. The metabolic engineering network program has just initiated. We, the team members, have collected the plant materials from high altitude Himalayan range in collaboration with IHBT, Palampur**.**

Dr. Nanda Ghoshal and group

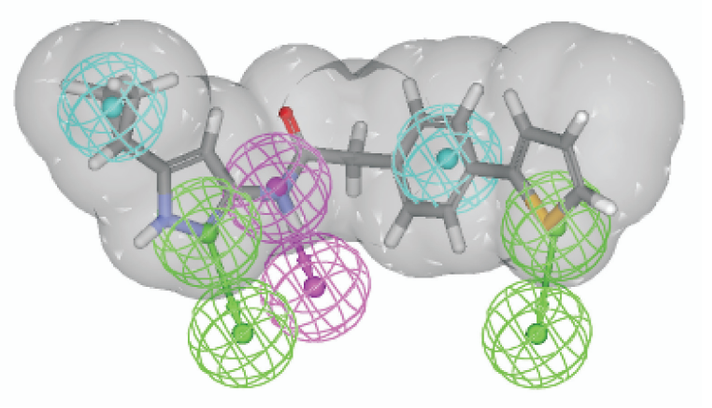
In-silico studies for rational drug design and Receptor Modelling

A. An efficient tool for identifying inhibitors based on 3D-QSAR and docking using feature-shape pharmacophore of biologically active conformation: A case study with CDK2/CyclinA

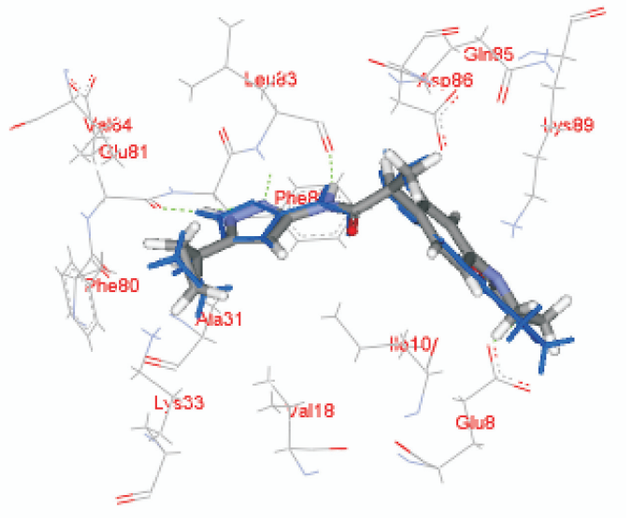
A fast and efficient method has been evolved for identifying novel inhibitors when the biologically active conformation of an inhibitor is known. The present study was carried out with CDK2/CyclinA inhibitors. The co-crystal structure of the most active ligand with CDK2/CyclinA was converted into a feature-shape query. This query served three purposes (i) alignment of molecules to generate 3D-QSAR model, (ii) rigid docking to the active site using GOLD, (iii) extracting hits from databases. A statistically valid 3D-QSAR ($r^2 = 0.867$, $q^2 = 0.887$) with good external set prediction ($r^2_{pred} = 0.890$) was obtained. The docked poses were analysed based on their interaction with hinge region (Glu81-Leu83) of CDK2. A reasonably good consensus score was generated using 11 scoring functions. The developed model was then successfully used to identify potential leads for CDK2/CyclinA inhibitors.



General structure of 3-aminopyrazoles, used in the study



A highly active compound aligned to BLP. The chemical features coloured light blue, green and violet represent HYD, HBA and HBD, respectively. The shape query is symbolized in light gray encapsulating the entire molecule.

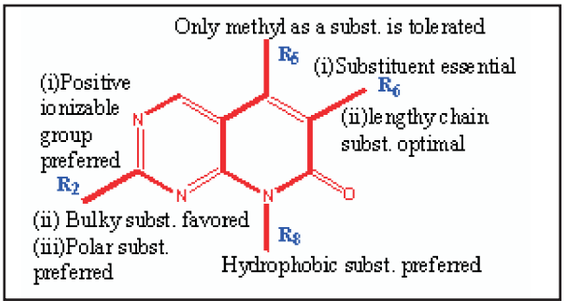


Validation of our rigid docking approach: The bioactive (blue) and the rigid docked (CPK) conformation the most active ligand (RMSD = 1.02 Å).

B. Dissecting the activity profile of pyrido[2,3-d]pyrimidin-7-ones as CDK4 inhibitors

CDK4 is a bonafide target for cancer. In the absence of an experimentally determined 3D structure of CDK4, QSARs have been explored to rationalize binding affinity in terms of physicochemical and structural parameters. The dataset consisted of 129 derivatives of pyrido[2,3-d]pyrimidin-7-ones, obtained from literature.. All the descriptors selected for the study have a physiochemical interpretation, which can guide a medicinal chemist to design prospective inhibitors, thus making these QSARs practically useful.

Two QSAR models, a linear model using stepwise multiple linear regressions (SMLR) and a non-linear model, with aid of splines, using Genetic Function Approximation (GFA) have been generated. Relevant parameters (r^2=0.607(SMLR) & 0.675(GFA)) and LOO cross-validation (q^2 = 0.527 & 0.624 respectively) as well as an external test set validation (r^2_{pred} = 0.627 & 0.700 respectively) judged the statistical significance and predictive ability of the models. The results gathered from these studies resulted in a better understanding of the specific nature of protein-ligand interactions that are crucial for CDK4 inhibition.

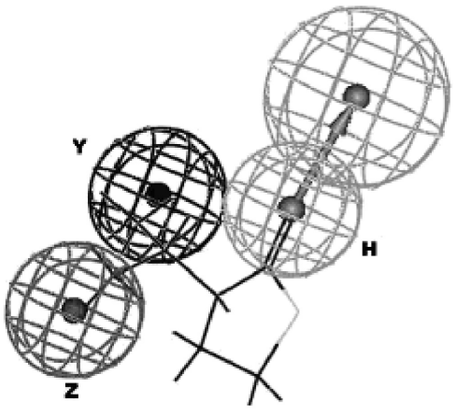


Results gathered from QSAR studies

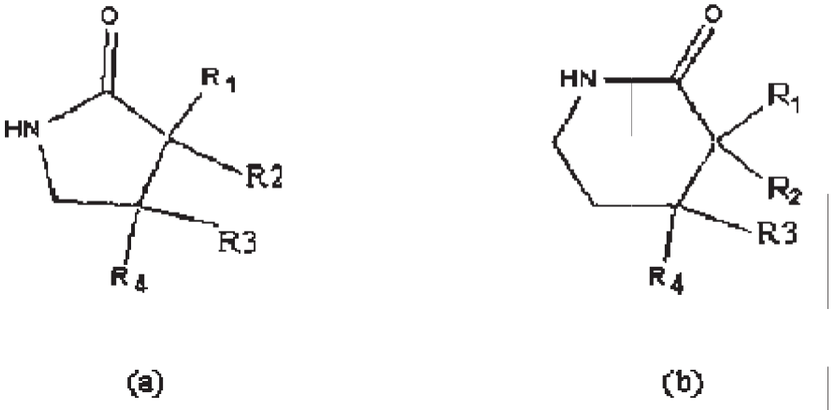
In our continued effort to understand CDK inhibition [Mascarenhas, N.M.; Ghoshal, N.; *Eur. J. Med. Chem.* doi:10.1016/j.ejmech.2007.10.016, *2007*], study has been carried out for understanding the difference between the modes of inhibition of two very similar ligands and bring to light with the aid of molecular dynamics the differences in protein-ligand interactions responsible for selectivity towards CDK4 against CDK2.

C. A Novel Approach for the Identification of Selective Anticonvulsants Based on Differential Molecular Properties for TBPS Displacement and Anticonvulsant Activity: An Integrated QSAR Modeling

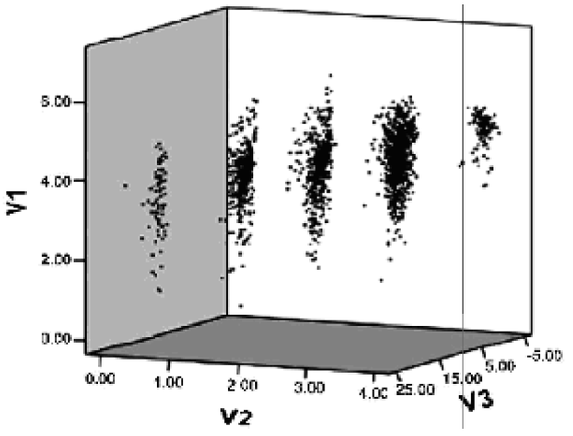
In order to gain insight into the structural and molecular requirements influencing the anticonvulsant activity against Pentylenetetrazole (PTZ) induced seizures and [^{35}S] tert-butyl-bicyclophosphorothionate (TBPS) displacement property (a measure of binding to $GABA_A$ receptor), QSAR studies have been performed on a series of congeneric anticonvulsant agents proposed to act by binding to the lactone site of the $GABA_A$ receptor. The aim of this work was to identify and analyze the various functionalities, which determine the TBPS displacement property and anticonvulsant activity by correlating with various molecular descriptors. Statistical techniques like Principal Component Analysis (PCA), Partial Least Squares (PLS), Multiple Linear Regression (MLR) and Genetic Function Approximation (GFA) were applied to identify the structural and physicochemical requirements for TBPS displacement property and anticonvulsant activity. The generated equations were statistically validated using leave-one-out cross validation technique and randomization. The best models were also validated by prediction of activity of compounds, not used for the development of QSAR models. The results from reasonably good QSAR models (statistically validated) clearly indicated that TBPS displacement property and the anticonvulsant activity are defined by different molecular parameters. Based on this finding, a novel approach is proposed, using integrated QSAR modeling, for identification of potential and selective anticonvulsant agents.



Mapping of the best compound (compound 8) to the hypothesis.
H, hydrogen bond acceptor lipid; Z, hydrophobic;Y, hydrophobic aliphatic.



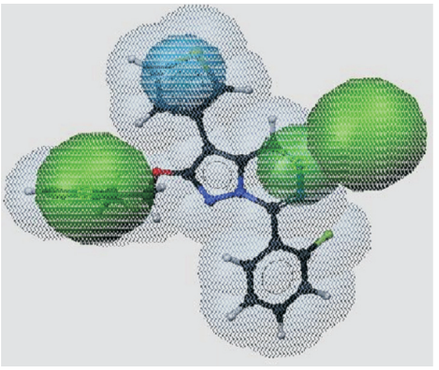
Analogue Library Generation and Screening (from pyrrolidone and piperidinone cores R groups represent substitution points).



Graph shows the screening of hits by prediction of TBPS displacement property, anticonvulsant activity and BBB virtual library. V1-anticonvulsant activity in ln[ED50], V2-BBB levels, V3-TBPS displacement values in ln[1/IC50].

D. A Fast In-silico Protocol for Identification of Anti Epileptic Drug Leads

A ligand based virtual screening procedure in tandem with Molecular Modeling and Neural Network was implemented to mine chemical databases for the identification of selective ligands for $GABA_A$ alpha 2 and 3 subtypes. A target specific Pharamacophore was developed using non congeneric molecules known to exhibit functional selectivity. The robustness of the Pharmacophore was assessed statistically. The pharmacophore was queried against databases. Those hits, which were not distributed among the known reference compounds, were regarded as outliers because a ligand based design capitalize on the fact that ligands similar to an active ligand are more likely to be active than random ligands. This strategy might be foreseen as powerful tool for identification of anti epileptic drug leads and, particularly, for projects where receptor based design is not feasible.

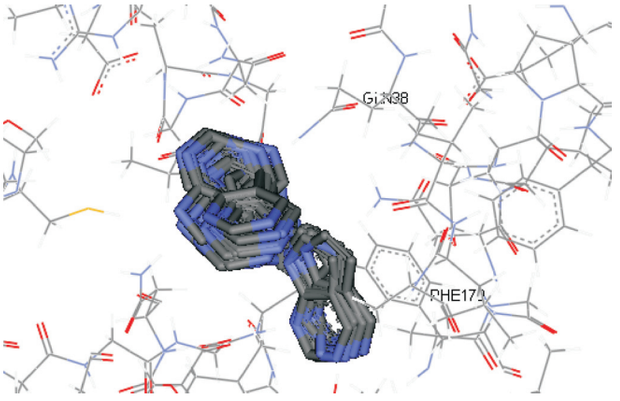


The shape features merged to the pharmacophore

E. Studies on Adenosine Kinase Inhibitors as anti-convulsant agents

Adenosine kinase (AK) is a key enzyme in the regulation of extracellular adenosine and intracellular adenylate levels. Inhibitors of adenosine kinase elevate adenosine to levels that activate nearby adenosine receptors and produce a wide variety of therapeutically beneficial activities. Adenosine Kinase (AK) converts adenosine to adenosine monophosphate in an ATP dependent manner. Recently, studies have been performed on analogues of tubercidin as potent adenosine kinase inhibitors possessing anti-convulsant activity. So far, several highly potent AK inhibitors were identified but none of them suitable for further development.

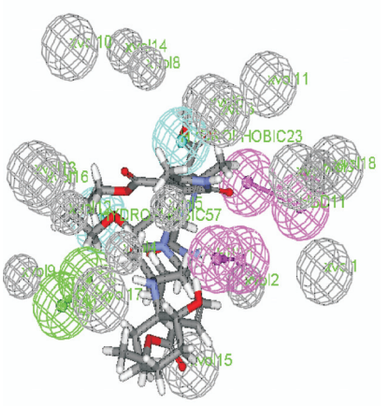
This study combines the pharmacophore analysis and docking to derive binding mode of tubercidin analogues. The docking studies prove the existence of diverse binding modes of analogues as presumed by a workgroup based on the SAR of these molecules. The hydrophobic interaction is likely to be a fundamental determinant of the difference in their binding modes. These docking based pharmacophores could be used for virtual screening of potential inhibitors.



Allignment of core moiety of nonaryl and aryl analogues within the active site

F. A comprehensive Structure Based Virtual Screening Protocol using BACE as a test system

An efficient structure based virtual screening strategy has been developed that could address the caveats of current docking protocols without compromising on computational time and accuracy. BACE1 an extensively studied protein involved in etiopathogenesis and progression of Alzheimer's disease (AD) was used as the test system.



Pharmacophore Based Pose filtering
(Intra Ligand Pose Ranking)

G. Contribution in BlockII units for Mtb database

Contributed by giving inputs for the data base structure for unit 2.5 (second line drugs – structure activity) and unit 2.6 (drug failures) for Mtb database.

H. Human Recourse Development:

- Supervised one students from School of Life Sciences, Bharathidasan University, Tamilnadu, India for his project work (M.Sc. thesis) on some aspects of *In-silico* drug design using PC and SGI machine based software.
- Supervised two summer trainees from Birla Institute of Technology, Mesra, for giving exposure on various aspects of in-silico drug designing.
- Supervising one student from Trident Academy of Creative Technology, Utkal University, India, for her project work (M.Sc. thesis) jointly with Dr. A.K. Giri, Molecular and Human Genetics Division, on some aspects of Bioinformatics.
- Supervising student from DOEACC Centre, Kolkata, for his project work in Bioinformatics, as part of his academic curriculum.
- Supervising two students from West Bengal University of Technology, for their project work, as part of M. Tech. Curriculum, on some aspects of *In-silico* drug designing.

Future Plan:

1. Studies on $GABA_A$ Receptor Modulators.
2. Targeting Clycline Dependent Kinases for clinical benefit in the pathogenesis of various types of cancer.
3. Receptor-ligand interaction studies in *Mycobacterium tuberculosis* for designing potential drugs.
4. Studies on inhibition of BACE1 an extensively studied protein involved in etiopathogenesis and progression of Alzheimer's disease (AD).

   Human Resource Development.

Dr. Saumen Datta & group

Structural investigations of macromolecules and their complexes by X-ray diffraction methods.

Structural investigation of proteins related to Type-III secretion system from Pseudomonas aeruginosa

Pseudomonas aeruginosa is a gram – negative, aerobic, rod shaped bacterium with unipolar motility. It is an opportunistic pathogen of immunocompromised individuals, typically infecting the pulmonary tract, urinary tract, burns, and wounds and also causes other blood infections. *P. aeruginosa* for its pathogenic activity uses a type III secretion system to inject toxic effector/virulent proteins into the cytoplasm of the eukarotic host cells.

From genomic analysis four effector (virulent) proteins so far have been identified in *P. aeruginosa*: exoS, exoT, exoU and exoY. We are in the process of cloning and expressing the above mentioned virulent proteins in recombinant manner to do the crystallization studies of these proteins. The diagram below (Figure 1) shows the PCR products of the virulent proteins from the genomic DNA of *P. areuginosa* strain 2192 (ATCC 39324). Complete genome sequence of *pseudomonas aeruginosa* is mainly available for three strains mainly PA01, PA7 and PA14. *P.areuginosa* 2192 (ATCC 39324) is an incomplete sequenced strain seemed to be derived from PA01 strain. We were able to get the PCR products of the genes correspond to the proteins ExoS, ExoT, and ExoY (as shown in Figure 8). Since our strain 2192 is derivative of PA01 in which ExoU is absent so we could not obtain the PCR product of the respective gene.

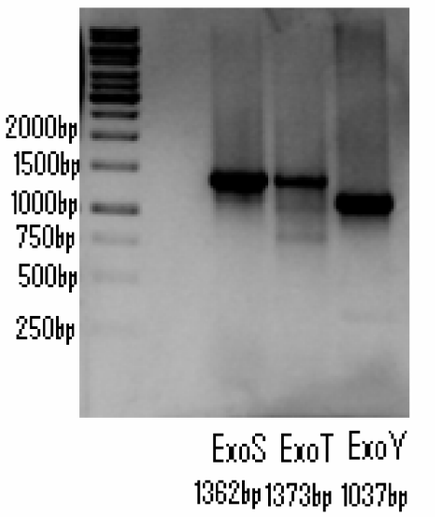


Figure 8: Lane 1 shows the DNA ladder as marked by the corresponding base pairs (bp) at the left side. Lane 2 is blank. Lane 3, 4 and 5 show the PCR products from *P.areuginosa* 2192 (ATCC 39324) genomic DNA for the virulent proteins ExoS, ExoT and ExoY respectively and are indicated under each lane. The size of the respective genes marked in bp is also given below the respective lanes.

After PCR amplification all the three proteins were cloned into vectors as mentioned below. The relevant progresses and future works are also mentioned. All the three proteins are showing induced overexpression as observed by SDS-PAGE analysis (Figure 9).

Exos: It is cloned in pET 28a+ with NdeI and BamHI (N-terminal His Tag). Expression has been studied in BL-21(DE3) pLyS with 0.5um IPTG at 37^{0}C and the protein was found to be localized in the Supernatant.

ExoT: It has been cloned in pET 28a+ with NdeI and BamHI (N-terminal His Tag). Expression has been studied in BL-21(DE3) pLyS with 0.5um IPTG at 37^{0}C and the protein was found to be localized in the Supernatant.

ExoY: It has been cloned in pET 28a+ with EcoRI and HindIII (N-Terminal HisTag). Expression has been studied in BL-21(DE3) pLyS with 0.5um IPTG at 37^{0}C and the protein was found to be localized in the Supernatant and cell debris. During dialysis after purification from the Supernatant the protein seems to aggregate so different composition of dialysis buffer needs to standardize to stop the aggregation of the protein.

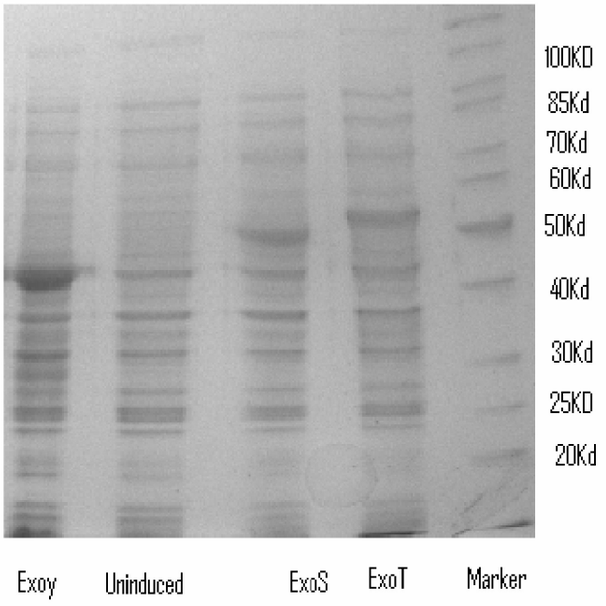


Figure 9 : A SDS-PAGE analysis of three virulent proteins, ExoS, ExoT and ExoY, from P. aeruginosa. Proteins are over expressed in BL-21(DE3) pLyS E. coli cells. The 2nd lane from left and the right most lanes show the uninduced cells and molecular weight markers respectively. These lanes are being used as reference. The other three lanes from left 1st, 3rd and 4th shows the BL-21(DE3) pLyS E. coli cells over expressed with proteins ExoY, ExoS and ExoT respectively.

There are few proteins, in P. aeruginosa, help in translocating the effector/virulent proteins are called translocator. Some of the translocator proteins are in the process of getting cloned. Detais are given below. Figure 10 shows the PCR amplified products of the respective genes mentioned below.

1) ***PopD***: This 888bp gene has been amplified by PCR and cloned in pET Duet-1 with EcoRI and XhoI (N-terminal His Tag).

2) ***PcrH:*** This 504 bp gene has been amplified by PCR and cloned in pET Duet-1 with Hind III and XhoI(N-terminal His Tag).

3) ***PopB:*** This 1173 bp gene has been amplified by PCR and cloned in pET Duet-1 with EcoRI and XhoI (N-terminal His Tag)

4) ***Pcrv:*** This 885bp gene has been amplified and cloned in pET Duet-1 with Hind III and XhoI(N-terminal His Tag).

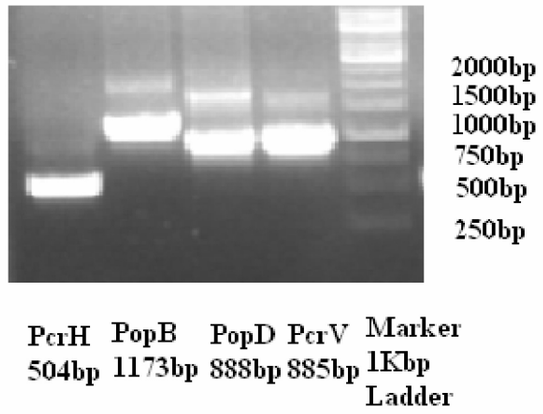


Figure 10: 1% Agarose Gel containing PopB, PopD, PcrH and PcrV PCR amplified gene products with 1Kbp ladder. The right most lane contains 1 KBp DNA ladder used as molecular weight marker. The other lanes shows the PCR amplified products of the respective genes as mentioned at the bottom of each lanes. The size of the genes in bp is alos mentioned with the name.

B) Characterization of Type-III secretion system proteins from Y. pestis.

The genus *Yersinia* includes 11 species and three of these, *Yersinia pestis*, *Yersinia pseudotuberculosis* and *Yersinia enterocolitica* are human pathogens. *Y. pestis* is of worldwide concern, being responsible for highly virulent disease bubonic plague, while other two primarily cause gastroenteritis in mammals. The pathogenicity of yersinia spp. can partly be attitributed to the presence of an extrachromosomal 70 kb virulence plasmid. Yops, Yersinia outer proteins, are a group of proteins of diverse functions that are encoded on the 70 kDa virulence plasmid and delivered to the target cells by virulence plasmid encoded type III secretion system (T3SS).

YopD, from *Yersinia enterocolitica* , has ben cloned and was overexpressed successfully. However, after breaking the cells, the major part of the overexpressed protein is found to be in the inclusion bodies. So, further research work involving tedious purification procedure of this proteins from the inclusion bodies is underway. Experimental work on some other relevant proteins is also underway.

Dr. Krishnananda Chattopadhyay and group

Protein Folding and Fluorescence Correlation Spectroscopy

We are studying protein folding using a large number of biophysical and biochemical techniques with particular emphasis to Fluorescence correlation spectroscopy (FCS). FCS is an important technique in biochemical studies to study diffusion as well as conformational transitions on time scales of sec and longer. It involves measuring fluorescence fluctuations under conditions of thermodynamic equilibrium in a small observation volume. These fluctuations may result either from a change in the number of fluorophores in the observation volume due to diffusion or a change in fluorescence properties of the molecule as a consequence of a chemical reaction or a conformational fluctuation. We have recently reported the first application of FCS to protein folding and measured sec conformational dynamics of intestinal fatty acid binding protein (IFABP) in its native and unfolded states.

We have recently setup a new laboratory at IICB to carry out FCS experiments to understand the mechanistics and dynamics of protein folding problems. The Confocor III setup from Carl Zeiss has been successfully installed and has been fully operational. The following is a picture of a typical correlation function observed (Figure 11) in our setup using tetramethyl rhodamine at pH 7.4. The data was fit (the red line shows the fit) to a model of a single diffusing species with the diffusion time of 33 msec. A number of proteins have also been labeled with different dyes and their correlation functions have been observed successfully with the new system. We have established a new laboratory for the regular experiments like molecular biology, expression and purification of proteins, labeling proteins with synthetic conjugates and other biophysical characterizations.

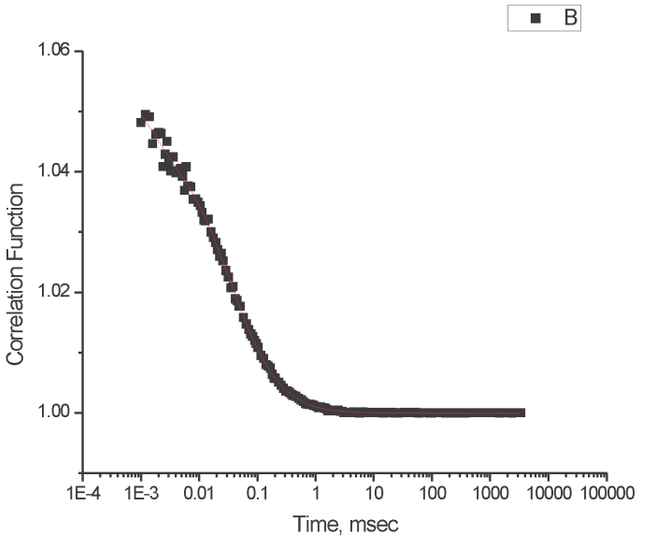


Figure 11 : Correlation function observed

Dr. Subrata Adak and group

Biochemistry of a novel plant like ascorbate peroxidase from Leishmania major.

Leishmaniasis continues to be a major health problem globally. The situation is becoming alarming due to the lack of an effective vaccine or cost-effective drug. Most available drugs are costly, require long treatment regimes and are becoming more and more ineffective necessitating the discovery of new drugs. Thus, there is an urgent need to understand the fundamental biology and biochemical processes of the parasite to identify new targets for the development of novel drugs and vaccines. One aspect of the parasite oxidative defence system, which could be very useful, in this regard is hydrogen peroxide (H_2O_2) metabolism but so far remained poorly understood. Heme peroxidases and catalase play a major role in H_2O_2-detoxification in most aerobic organisms. A little is known about the way the protozoan parasites detoxify H_2O_2 or how they evade the macrophage responses during parasitic infections in the mammalian hosts. In a wide variety of species, ranging from bacteria to higher mammals, the mechanisms of H_2O_2-detoxification are grossly distributed into variations of two mechanisms: mediated either by the heme proteins and/or by non-heme protein. But until our recent discovery of *Leishmania major* ascorbate peroxidase (LmAPX), no heme containing enzymatic defense against toxic–H_2O_2 were known for the *Leishmania species*. Our preliminary results indicate that the LmAPX has several features that are clearly unique with respect to other APXs e.g. (a) The LmAPX is the functional hybrid between cytochrome c peroxidase (CCP) and ascorbate peroxidase. (b) The specific activity of ascorbate and guaiacol oxidation by LmAPX is lower compared to the plant APX and most interestingly (c) in spite of being capable of oxidizing ascorbate, the crucial ascorbate binding residue, corresponding to that of plant APXs, is

absent in this enzyme suggesting different binding mechanism. Despite these very little is known about the biochemical features of this parasitic enzyme that includes the active site residues controlling heme activation, ligand binding, substrate specificity and electron transfer pathways. Detail investigation is also required to understand the precise intra-cellular localization, its physiological function and regulation of LmAPX within the cell.

Technical Staff

Mr. Jishu Mandal; Dr. Subhagata Ghosh, Mr. Samir Roy, Dr. (Mrs.) Aparna Laskar, Mr. Prosenjit Gangopadhyay

Pool Officers, RAs, Research Fellows

Dr. Shampa Mallick, Dr. Rina Shaha, Rajesh Saha, Amlanjyoti Dhar, Paromita Raha, Subrata Debnath, Asitkumar Manna, Neeladri Shaker Roy, Avishek Majumder, Prasenjit Chakraborty, Gitashri Naiya, Israr Ahmed, Piya Ghosh, Anirban Dutta, Munmun Sarkar, Aranyak Goswami, Somnath Mondal, Reema Bhattacharya, Debashree De, Nupur Sengupta, Debratna Saha, Srinjana Ghosh, Sangita Datta, Jyotirmoy Mitra, Ms. Savita Bhutoria, Nahren Manuel, R.Vijayan, Supratim Dey, Anindya Roy Chowdhury, Urmisha Das, Sunny Sharma, Ranendu Ghosh, Shubhasis Haldar, Nidhi Joshi, Subhankar Dolai, Rajesh Yadav, Swati Pal, Moumita Bose, Supratim Mukherjee, Arpita Konar, Payel Ghosh, Sisir Nandi.

Summer Trainees

M. Prabu, Rishika Sengupta, Shreya Ray Chaudhuri, Deblina Patra, Ballari Das, Sangita Saha, Soumen Chakraborty, Sudeshna Mukherjee

Upgradation of major infrastructural facilities

Prof. Siddhartha Roy

DNA synthesizer for synthesis of oligo.

Fluorescence Life time measurement system

Dr. Debasish Bhattacharyya

Both sedimentation velocity and sedimentation equilibrium modes of analytical ultracentrifuge, a 'proteomics' facility, are now under operation.

MDLC (Multidimensional Liquid Chromatography) is now operational.

Network Projects
In Eleventh Five Year Plan (2007-12)

The exercise to formulate Eleventh Five Year Plan (EFYP) of IICB for CSIR had begun on 1st week of June, 2006. During the Tenth Five Year Plan, IICB was involved in 14 network projects – one as the nodal lab and thirteen as a participating laboratory. We have successfully completed the projects and earned valuable experience during the Tenth Plan through these network projects.

In Eleventh Five Year Plan, IICB initially proposed 24 network projects in 3 different sectors, *e.g.* (i) Biology & Biotechnology, (ii) Pharmaceuticals, Healthcare & Drugs and (iii) Ecology & Environment. After a lot of discussion, deliberation and presentation in different forum of HQ, CSIR finally **15** projects have been cleared of which four **(4)** are **Nodal Network Projects** and eleven (**11**) are **Partner Network Projects**. In Partner Network Projects, there are two **(2) extension Projects of Tenth Plan** namely **In-silico Biology** and **Bioactive**.

All the projects are mainly from **Biology & Biotechnology sector** except one (**1**) nodal network project **(Asthma)** which is from **Pharmaceuticals, Healthcare & Drugs sector**. The projects mentioned hereunder are sanctioned by CSIR and the financial clearances are already received by IICB except in two cases namely **Plasma Proteomics** and **Pathway Engineering**.

No.	Project Title & Short Name	Proj. Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
1.	Evaluation and correction of mitochondrial dysfunction in disease **(Mitochondria)**	**SIP-007**	Supra-institutional	IICB	Dr. Samit Adhya
2.	Engineering peptides and proteins for new generation therapies **(Protein Engineering)**	**NWP-005**	Nodal Network	IICB	Dr. Anil K Ghosh
3.	Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease **(Asthma)**	**NWP-033**	Nodal Network	IICB	Dr. Arun Bandyopadhyay
4.	New insights in cancer biology : Identification of novel targets and development of target based molecular medicine **(Cancer)**	**IAP-001**	Nodal Inter-agency	IICB	Dr. Susanta Roychoudhury
5.	Plasma Proteomics in health, environment and disease (**Plasma Proteomics**)	**NWP-004**	Partner – Network	CCMB	Dr. Rukhsana Chowdhury
6.	Nanomateials and nano-devices for application in health and disease **(Nanomaterials)**	**NWP-035**	Partner – Network	CCMB	Dr. Arindam Banerjee
7.	Pathway engineering and system biology approach towards homologous and heterologous expression of high-value phytoceuticals **(Pathway Engineering)**	**NWP-008**	Partner – Network	CIMAP	Dr. Debasish Bhattacharya
8.	Biological and chemical transformation of plant compounds for production of value added products of therapeutic/aroma value **(Aroma Value)**	**NWP-009**	Partner – Network	CIMAP	Dr. Sibabrata Mukhopadhyay

No.	Project Title & Short Name	Proj. Code	Type of Project	Nodal Lab.	Nodal Scientist of IICB
9.	Identification and validation of drug targets for selected pathogens of national importance (**Drug Target**)	**NWP-038**	Partner – Network	CDRI	Dr. Pijush K Das
10.	*Diabetes mellitus* – New drug discovery R&D, molecular mechanisms and genetic and epidemiological factors **(Diabetes)**	**NWP-032**	Partner – Network	CDRI	Dr. Sibsankar Roy
11.	Zero Emmision Research Initiative **(Zero Emission)**	**NWP-044**	Partner – Network	CLRI	Dr. Suman Khowala
12.	Exploitation of India's rich microbial diversity **(Metagenomics)**	**NWP-006**	Partner – Network	IMT	Dr. Tushar Chakraborty
13.	Comparative genomics and biology of non-coding RNA in human genome **(Micro-RNA)**	**NWP-036**	Partner – Network	IGIB	Dr. G Suresh Kumar
14.	Drug Target Development using In-silico Biology (**In-silico Biology**)	**CMM-017**	Partner – Network	IGIB	Dr. Chitra Dutta
15.	Discovery, Development and Commercialization of New Bioactives and Traditional Preparations **(Bioactive)**	**COR-023**	Partner – Network	CSIR-HQ	Dr. Pratap K Das / Dr. HK Majumder

NODAL PROJECTS

1. **Title:** Evaluation and Correction of Mitochondrial Dysfunction in Disease

Project: Supra-institutional [SIP-007]

Objectives: To develop strategies to correct the effects of disease-causing mitochondrial tRNA mutations (*e.g.,* the tRNALys mutation in Myclonic Epilepsy with Ragged Red Fibers) using a tRNA import complex in patient-derived cybrid models, to develop methods for RNA delivery to mitochondria, and to study the pathways of the intracellular uptake and targeting of such complexes to mitochondria.

Significant achievements made during the first year (2007-2008):

- The project was initiated in September 2007 on receipt of sanctioned funds from CSIR. During the 6-month period Sep 2007 – Mar 2008, the major collective activity of the SIP has been the *purchase of instruments and consumables*. To start off, funds for capital and consumable purchases were allocated and transferred to the accounts of individual scientists in the computerized purchase system of the Institute. Then indents were submitted, and are in various stages of processing. These indents include those for all the major items of equipment as well as a large number of small equipment and consumable items. For purchase of the major high-value equipment, viz. small animal in vivo imaging system, a Technical Committee was constituted with an External Expert, which met to decide on the desirable technical specifications and performance of the instrument. Based on the recommendations of the Technical Committee, an indent was submitted and a Tender Notice advertised. However, only one company responded, and therefore, a second notice was issued. The results of this second round are currently awaited. Meanwhile the procedure for renovation of a small room on the second floor to house the major equipment has been initiated. Overall, more than Rs. 1 crore for purchase of consumables and about Rs. 2.5 crore for equipment purchase, have been distributed among the scientists.

- *Preparation of functional tRNA import complexes:* We have previously shown that RNA Import Complex (RIC) isolated from the inner mitochondrial membrane of *Leishymania tropica* is biologically active: it is taken up by cultured cells, targeted to intracellular mitochondria, where it induces uptake of endogenous tRNAs and restores respiration of mitochondria bearing a mutant tRNA gene (Mahata et al., *Science* **314**, 471-474, 2006). Preparation of the complex by this method requires the culturing and handling of large amounts of the parasite, and the preparations are invariably contaminated with minor amounts of mitochondrial and cytosolic proteins, as shown by mass spectrometry of individual subunit bands (Mukherjee et al., *EMBO Rep.* **8,** 589-595, 2007). Therefore, we prepared complexes reconstituted in vitro from recombinant subunits expressed in *E. coli*. This method has been shown to yield complexes active for import in vitro (Mukherjee et al., *EMBO Rep.* **8,** 589-595, 2007). Complexes were reconstituted with 6 (R6) or 8 (R8) nucleus-encoded subunits (RIC1, RIC3, RIC4A, RIC5, RIC6, RIC8A, RIC8B and RIC9). These were added to cultures of LB64, a cybrid line containing mitochondria with a point mutation in the tRNALys gene, as a result of which mitochondrial translation is inhibited and respiration is at baseline levels. After 5 d of treatment, the O2 uptake was measured (Table 1).

CELL TYPE	RESPIRATION RATE (fmole/min/cell)
LB 58	4.52
LB 64	0.63
LB 64+ NATIVE RIC	3.63
LB 64+ RIC 8 COMPLEX	3.3
LB 64 + RIC 6 COMPLEX	3.1
LB 64+ RIC 7 (- 8A)	0.65

This experiment showed that the native complex (isolated from *L. tropica*) as well as the synthetic complexes R6 and R8, restored respiration of LB64, and were thus biologically active.

- *A cellular model for mitochondrial deletion disorders*: Cytoplasmic hybrid (cybrid) cell lines LB64 and FLP32.39, which are homoplasmic for a point mutation in the mitochondrial tRNALys gene, and a 1.9 kb-deletion between COI and ND4L respectively, were maintained in monolayer cultures. These are cellular models for testing the efficacy of mitochondrial RNA or DNA targeting procedures. There is a large body of evidence correlating the presence of deletions of mitochondrial DNA with a number of complex disorders in humans, as well as with the 'normal' process of aging in humans and experimental animals. However, no cellular model representing heterogeneous mitochondrial deletions is currently available for testing procedures intended to correct the deletion phenotype. To this end, we have cultured HepG2 tissue culture cells, containing wild-type mitochondria, with limited doses of ethidium bromide, a DNA intercalating drug that induces mitochondrial deletions. In the resultant cell line, designated EB1, three major mitochondrial genomes were detected, with varying amounts of deletions. By Southern hybridization with a panel of probes spanning the entire genome, these deletions were mapped to different regions of mitochondrial DNA, confirming the heterogeneity of the mitochondrial population in this culture. In parallel, the O2 consumption rate of EB1 fell to ~25% of HepG2, as expected from the predominant presence of the non-functional deletion genomes.

- *Mitochondrial abnormalities in POAG patients*. One of our intents is to find out the mitochondrial abnormalities in POAG patients. Towards this goal we have collected blood samples from 100 primary open angle glaucoma patients and 100 control subjects with detail clinical characterization. The genomic DNA has been prepared from the samples. Sequencing of the mitochondrial DNA will be undertaken soon.

- We plan to investigate that whether mutations in candidate genes of glaucoma (*e.g.*-MYOC, CYP1B1) have any effect on mitochondrial function. Towards that goal we have generated a few clones (by site directed mutagenesis) which contain naturally occurring mutations in POAG patients. These clones will

be used in *ocular cell model* to examine potential involvement of mutant protein in alteration mitochondrial function

- Models for *in vivo* growth of *Plasmodium yoelii* in BALB/c mice, and *in vitro* culture of *Plasmodium falciparum* were established.
- A *rat model for Indomethacin-induced acute gastric ulcer and healing* was established.
- A rational, reproducible and progressive *animal model of the neurdegenerative disease, Parkinson's disease (PD)*, was obtained employing intracranial infusion of the potent mitochondrial electron transport chain complex I inhibitor, rotenone.
- To create an *in vitro model of PD*, the human neuroblastoma cell line SH-SY5Y was differentiated and treated with rotenone. On staining by immunofluorescence, it was observed that treatment with rotenone led to the formation of aggregates containing alpha-synuclein and ubiquitin in the neurons. Hence rotenone-treated neurons could be used to model the protein aggregation associated with PD *in vitro* and to test potential drugs that could reverse the defect prior to using animal models.
- Standardization and quantification of reactive oxygen species of mitochondrial origin by flow cytometry were performed.
- A series of *[(aryl)arylsufanylmethyl] pyridines (AASMP)* have been synthesized and these are found to be antimalarial in nature. These compounds inhibited hemozoin formation and the inhibition of hemozoin formation may develop oxidative stress in *P. falciparum* due to the accumulation of free heme. AASMP – mediated oxidative stress caused mitochondrial dysfunction by decreasing mitochondrial potential (m) in malaria parasite. Cytotoxicity testing of the active compounds showed selective activity against malaria parasite with selectivity indices greater than 100. AASMP also exhibited profound antimalarial activity *in vivo* against chloroquine resistant *P. yoelii* (MDR). Thus, *AASMP represents a novel class of antimalarial, which inhibits P. falciparum growth damaging mitochondria.*
- Detoxification of free heme by heme oxygenase (HO) system is a very common phenomenon by which it catabolizes free heme to form bilirubin as an end product. Interestingly, malaria parasite, *Plasmodium falciparum* lacks HO system, but it forms hemozoin mainly to detoxify free heme. We have found that bilirubin significantly induces oxidative stress by effectively inhibiting hemozoin formation. Furthermore, results indicate that bilirubin inhibits parasite growth and induces caspase – like protease activity, up-regulates the expression of apoptosis related protein (Gene ID PFI0450c) and reduces the mitochondrial membrane potential ($\Delta\psi m$). These findings suggest that bilirubin through the development of oxidative stress induces *P. falciparum* cell death and malaria parasite lacks HO system probably to protect itself from bilirubin–induced cell death as a second line of defense. Thus, data clearly indicate that induction of mitochondrial dysfunction by stimulating oxidative stress would be rationale to develop new antimalarial.
- Non-steroidal-anti-inflammatory drug (NSAID) develops severe gastropathy by activating gastric mucosal apoptosis. However, the role of mitochondria in gastric mucosal apoptosis *in vivo* during NSAID treatment is largely unclear. Preliminary studies indicate that indomethacin (a NSAID), by stimulating the generation of intra-mitochondrial hydroxyl radical (OH) induces mitochondrial pathology in gastric mucosal cell by disrupting mitochondrial structure and function, which ultimately leads to the activation of mitochondrial death pathway.
- We have standardized the *streptozotocin-induced diabetes model* and we will isolate mitochondria from the insulin target tissues of these animals. Clinicians have been contacted for type 2 diabetic patients' samples. Mainly we will collect patients' adipose tissue and blood samples and we will in the process of ethical clearance. The isolation of mitochondria from cells and tissues has been standardized.

- Study was performed to ascertain whether treatment with herbal antioxidant *Quercetin intercalated in mannosylated liposomal drug delivery vehicle* exert any protective against cerebral ischemia- reperfusion evoked damage in young or aged rat brain cell mitochondria. Cerebral ischemia- reperfusion induced a decrease of mitochondrial membrane viscosity both in young and old rat brain cells. Maintenance of mitochondrial membrane microviscosity, *i.e.,* reciprocal of membrane fluidity of young and old rat neuronal cells could be achieved by the protective action of Quercetin in galactosylated liposomes.
- Even though the human parasite *Leishmania donovani* encounters tremendous oxidative burst during macrophage invasion, a set of parasites survive and proliferate intracellularly leading to transformation from promastigote to amastigote form and disease manifestation. The striking shift of temperature (from 22C in the insect gut to 37C in the mammalian host) and pH (7.2 in the insect gut to 5.5 in the parasitophorous vacuole of macrophages) are the key environmental triggers for differentiation as these cause an arrest in the G1 stage of cell cycle and initiate transformation. We wanted to study whether differentiation-triggering environment induces parasite resistivity through a signaling network involving mitochondria. Cyclic nucleotide signaling is associated with differentiation coupled events and a correlation between intracellular cAMP with parasite mitochondria have been found as cAMP plays significant part in inducing resistance against oxidative damage. Several regulators of cAMP signaling in the parasite have been identified, cloned and characterized. Constructs and strains required for determining the role of cAMP response in regulating kinetoplast activity in the parasite have been prepared. Initial study regarding impact of cAMP in modulating kinetoplast activity has been carried out including examination of free radical generation, membrane depolarization, cardiolipin release *etc*.
- *Thyroid hormone induced cardiac hypertrophy in rat* was generated as routine procedure in our laboratory and the mitochondrial dysfunction was assessed by monitoring pathways to mitochondrial gene expression related to energy supply. The central players in mitochondrial gene expression such as peroxisome proliferator alpha (PPAR) and its upstream regulator, PGC1 regulate fatty acid oxidation in cardiac myocytes. The mRNA levels of PPAR and PGC1 in hyperthyroid induced hypertrophied heart was checked by real time RT PCR analysis. The expression of PPAR and PGC1 was significantly ($P<0.01$, $n=3$) reduced in hypertrophied heart tissue compared to control indicating the impaired biogenesis of mitochondria in hypertrophied condition. Furthermore, the expression of carnityl palmityol transferase (CPT1) mRNA was also reduced indicating altered fatty acid oxidation which may contribute to mitochondrial dysfunction in hypertrophied heart.

R&D Outputs during the first year (2007-2008):

Patents: 1 (one)

Total Number of Publications: 5 (five)

No. of Project Assistants engaged: 6 (six)

2. **Title:** Engineering Peptides & Proteins for New Generation Therapies.

Project: Nodal Net Work [NWP-005]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Microbial Technology (IMT), Chandigarh

Institute of Genomics and Integrative Biology (IGIB), Delhi

Centre for Cellular and Molecular Biology (CCMB), Hyderabad

Central Drug Research Institute (CDRI), Lucknow

Objectives:

[a] To engineer defensins of lesser complexity and enhanced anti-microbial properties.

[b] Designing and development of some novel small anti-microbial peptides with reduced toxicity.

[c] Development of peptidomimetics to block protein-protein interaction at the same time membrane penetration capability and increasing bioavailability.

[d] To study protein mis-folding and aggregation through engineering protein that does not mis-fold and aggregate.

[e] To engineer small peptides, which are equivalent to larger transcription factor-with Protein Transduction Domains for cell entry.

[f] Designing and development of recombinant proteins with much more stability and reduced toxicity, which can be used to cure certain life threatening diseases.

[g] New engineering techniques will be developed to produce proteins with new activities: implication in vaccine developments.

[h] To develop process for production of engineering protein.

[i] To engineer streptokinase having weaker immune response towards increasing their utility.

Significant achievements made during the first year (2007 – 08):

[i] The antifungal activity of C-terminal segments of human defensins-1-3 has been investigated. Antifungal activity has been observed for these peptides. Also, their activities were less salt sensitive and not lost in the presence of energy depleting agents unlike the parent defensins.

[ii] Bioinformatic analysis of defensin sequences: approach to study disulphide connectivities in defensins in promoting folding.

[iii] Detailed analysis was carried out on defensin sequences. From the analysis, it was evident that there is considerable positional preference for several amino acids. Also, the positional preferences for amino acids are different in β-defensins as compared to α-defensins.

Defensins have three β-strands across the primary sequence. The C-terminal β-strands have most of the cationic residues. This region has been shown to be an important determinant of antimicrobial activity. In order to determine the origin of this motif, an algorithm was developed to extract such β-strands from protein crystal structures.

Human β-defensins HBD-1-3 and their C-terminal analogs Phd1-3: Comparison of various aspects of their antifungal activity against *Candida albicans.*

We have investigated the antifungal activity of the C-terminal analogs of human β-defensins (Phd1-3) against *C. albicans* and compared the effect of salts and metabolic inhibitors with the parent defensins HBD-1-3.

Phd1-3 showed activity against *C. albicans*, but with slightly lower potency as compared to HBD-1-3. An important observation was: Phd1-3 kill *C. albicans* by energy independent mechanisms unlike HBD-1 and HBD-2. Also, the activities of Phd1-3 were attenuated to a lesser extent in the presence of salts, unlike HBD-1-3.

[iv] We have designed several novel analogs of cathelicidin-derived bovine anti-microbial peptide BMAP –27 with reduced toxicity but similar antibacterial activity.

[v] Because of structural and chemical similarity to proteins, a peptide based mimic of the protein may easily integrate many of the important functions of a DNA-binding protein. We have attempted the design and chemical synthesis of α-amino-isobutyric acid substituted, conformationally constrained, helical

mimics of Cro protein from bacteriophage λ. The monomeric peptide is self cross-linked through one introduced sulfhydryl group to produce a symmetric dimer. The protein mimic binds to operator OR3 with good affinity and single base-pair discrimination specificity approaching that of the protein. It appears that single base-pair discrimination capability is achievable by dimeric helical peptidomimetics. Due to ease of synthesis and design, incorporation of Aib into recognition helices at suitable positions may offer a good way of creating DNA-binding protein mimics and pave the way for new applications based on them.

[vi] A α-helical peptide was selected from AMA1 (Malaria Vaccine) residue (191-203) SPMTLDEMRHFYK. To maintain α-helicity of this peptide we have substituted some residues by Aib. This peptide sequence is as follows SPMTXDEMXHFXK (X= Aib).

Chicken ovalbumin (323-339) ISQAVHAAHAEINEAGR is an immuno-dominant T-cell epitope.

[a] SPMTXDEMXHFXK

[b] ISQAVHAAHAEINEAGRKKSPMTXDEMXHFXK

Mice (BALB/c) were immunized with above two peptides.

[vii] Arginine inhibits aggregation of BSA at pH 7.5. Interaction of arginine with tryptophan residues is suggested. Arginine increases the co-operativity of the unfolding transition (presumably because of its interaction with the unfolded states) leading to inhibition of the accumulation of the intermediate states.

[viii] We've replaced the active surface of a thermophile protein by that of a homologous mesophile protein through structure-guided 'protein surface grafting'.

[ix] We've expressed, purified, refolded and characterized a putative lysophospholipase from Pyrococcus furiosus, and shown retention of structure and lipase/esterase activity in the presence of water-miscible organic solvents at high temperatures.

[x] We've shown dimorphic aggregation behavior of a fusion polypeptide incorporating a stable protein domain (EGFP) with an amyloidogenic sequence (retroCspA).

[xi] We've identified and characterized a spontaneously aggregating amyloid-forming variant of human PrP((90-231)) through phage-display screening of variants randomized between residues 101 and 112.

[xii] We've designed a soluble mini-protein through tandem duplication of the minimally engineered beta hairpin 'tongue' motif of alpha-hemolysin.

[xiii] We've studied the conformational behavior of polypeptides derived through simultaneous global conservative site-directed mutagenesis of chymotrypsin inhibitor 2, and shown that sequences using similar amino acids at similar positions fold in similar ways.

[xiv] We've established that partial destabilization of native structure by a combination of heat and denaturant facilitates cold denaturation in a hyperthermophile protein.

[xv] We've shown that PhoP-PhoP interaction at adjacent PhoP binding sites is influenced by protein phosphorylation.

[xvi] Enhanced the stability of the cockroach allergen extract used for diagnosis and therapy of allergic disorders.

[xvii] Recombinant protein expression, purification and functional characterization of 12 kDa protein (Cur l 3) from *Curvularia lunata.*

[xviii] Crossreactivity studies of the 12 kDa protein (Cur l 3) with fungi and grass pollen allergens.

[xix] Raising of antibodies against 12 kDa protein (Cur l 3) in mice.

[xx] Identification & synthesis of 5 B cell and 5 T-cell epitopes for Cur l 3 using bioinformatic approaches.

[xxi] Peptide P6 behaved as B cell epitope having maximum IgE binding.

[xxii] A 26 kDa protein from *Alternaria alternata* was expressed and purified from *E. coli.*

[xxiii] In pharmacological studies, it was found that chimeric peptides were not able to produce analgesia but also prevented the development of tolerance by morphine.

[xxiv] Chimeric peptides are interacting with both opioid receptors and anti-opioid receptors were corroborated by physiological studies.

[xxv] Chimeric peptides showed only vasodepressive effect (opioid) and there was no cardio excitatory action.

R & D Outputs during the first year (2007-2008):

Total Number of Publications: 32 (thirty two)

Patents with reference: 2 (two)

No. of Project Assistants engaged: 27 (twenty seven)

3. Title: Development of diagnostics and target-based molecular medicines against allergy, bronchial asthma and chronic obstructive pulmonary disease

Project: Nodal Net Work [NWP-033]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Institute of Genomics and Integrative Biology (IGIB), Delhi

Indian Institute of Chemical Technology (IICT), Hyderabad

Industrial Toxicology Research Centre (ITRC), Lucknow

Indian Institute of Integrative Medicine (IIIM), Jammu

Objectives:

[a] Development of animal model for asthma for evaluation of lead molecules in vivo.

[b] Testing 2-3 lead molecules for anti-asthma activity

[c] To synthesize NCEs for the biological evaluation as PDE-4 inhibitors.

[d] Toxicological and safety evaluation of lead molecules with anti-asthmatic activity; and evaluation of drug efficacy by plethysmography

[e] Basic research on the role of Stat3 and Socs3 in asthma pathogenesis.

[f] Determination of Pharmacokinetics, Absorption/ Transport, Biotransformation, and Distribution studies.

Significant Achievements made during the first year (2007-2008):

[a] Mouse model of asthma based on two cycles of sensitization and 4cycles of challenge with ovalbumin has been developed. Asthmatic status of mice was monitored by histopathological analysis of the airways tissues and pulmonary function by measuring methacholine induced specific resistance of airways (sRaw) using small animal plethysmograph. These animals will be used for the evaluation of the efficacy of the lead molecules.

[b] ICB D8 shows inhibition of methacholine induced hyperreactivity in vivo.

[c] Due to the significant bioactivity of two of the NCEs, namely **IICT-TA67** and **IICT-TA49**, work was initiated for their multigram preparation for taking up the toxicity studies.

[d] Initiated acute oral toxicity and subacute oral toxicity of IICB-11-D8.

[e] Pharmacokinetics of TA-67 was performed 0-24 hrs after oral dosing of 20 mg/ kg of TA-67 in mice. Non-compartmental analysis of the data showed a Cmax of 107 ng/ml and Tmax of 3 hrs. Other pharmacokinetic constants were as follws: The half-life (T1/2 of 4.26 hrs; AUC, 502.75 ng. hr/ml; clearance (CL), 66.1 ml.min, and volume of distribution (Vd) 474 L. After i.v. dosing of 10 mg/ kg of TA-67 in mice showed AUC 357.71 ng/hr.ml; T1/2, 0.93 hrs; CL, 466 ml/min and Vd 37.5 L.

Absolute bioavailability (F) was found to be 0.703.

R & D Outputs during the first year (2007-2008):

Total published paper during this tenure: 7 (seven)

No. of Project Assistants engaged: 20 (twenty)

4. Title: New Insights in Cancer Biology: Identification of Novel Targets and Development of Target Based Molecular Medicine

Project: Inter Agency [IAP-001]

Nodal Laboratory: Indian Institute of Chemical Biology (IICB), Kolkata

Participating CSIR Institutes:

Indian Institute of Chemical Technology (IICT), Hyderabad
Centre for Cellular and Molecular Biology (CCMB), Hyderabad
Central Drug Research Institute (CDRI), Lucknow
Institute of Genomics and Integrative Biology (IGIB), Delhi
Central Glass & Ceramic Research Institute (CGCRI), Kolkata
National Inst. for Interdisciplinary Science & Tech. (NIST), Thiruvananthapuram

Participating Non-CSIR Institute:

National Center for Cell Sciences (NCCS), Pune

Objectives:

[a] Identification of new lead molecules from herbal and synthetic sources against specific cellular targets using high throughput approaches.

[b] Identification of novel anticancer targets based on the knowledge gained from molecular analysis of tumorigenic processes.

[c] Generation of library of small molecules by diversity-oriented chemistry.

[d] Deciphering the regulation of expression of target genes in normal and cancer cells.

[e] Understanding the molecular interactions between target proteins and their partners.

[f] Nano-structered calcium phosphate-based ceramics as drug carrier for the treatment of hepatocellular carcinoma in animal model.

[g] Multi-agent-based simulations of collective cell behaviors with application to cancer.

Significant achievements made during the first year (2007 – 2008):

Objectives 1 & 3

The medicinal plants were selected based on their folklore and ethnomedical use. During this period eight medicinal plants (ICB/12/A001–ICB/19/A001) were extracted at IICB.

The following scaffolds have been identified for the project:

1. Costunolides
2. Alkamides
3. Diterpenes & Triterpenes
4. Naphthaquinones
5. Isoflavones
6. Icetexatrienes

Accordingly 17 compounds belonging to these scaffolds have been isolated from the respective plants and 50mg each of them were supplied by IICT to the nodal laboratory.

After initial screening of 82 compounds by CDRI, 43 showed > 80% growth inhibition against different cell lines and were thus selected for the second screening using serial 2-fold dilutions. Out of 43 molecules, 13 were found 'inactive' according to the selection criteria and 27 showed 'general cytotoxicity' for all the cell lines (including Vero). Only 3 compounds were active *in vitro* for different cancer types. The IC50 of these compounds were determined.

Objectives 2, 4 & 5

Interplay between p53 mutation and HPV infection in Head and Neck cancer

Tumor suppressor gene p53 is mutated in more than half of human primary tumors and thus is a natural target for the development of anticancer agents. It is known that p53 inactivated both by direct mutation in the gene as well as by indirect mechanisms. In head and neck cancer, we have found that about 20% of the primary tumors has mutation in the gene. But about 70% of the HNSCC tumors harbor HPV infection, which is known to inactivate p53. We proposed that genetic and epigenetic alteration of *p53* follow distinct pathways during the development of HNSCC from normal epithelium via dysplasia. p53 mutation and HPV mediated p53 inactivation possibly constitute two independent pathways of tumorigenesis.

Differential expression of Matrix metalloproteinases during endometriosis

Matrix metalloproteinases are a series of Zn dependent proteolytic enzymes that are key enzymes in tumorogenesis and cancer metastasis. Reports are scanty on the regulation of MMPs in cancers of breast, endometrium and ovary and, pathogenesis of endometrial cancers that forms in the tissue lining the uterus remains unclear. Because both endometriosis and endometrial cancers are characterized by cell invasion and abnormal cell growths, we have primarily looked at MMP profile in endometriosis. Endometriosis was generated in mice and endometriotic tissues were tested for MMP-9 activity. In addition, human endometriotic tissues possessing varying degrees of severity were examined for expression of MMPs and tissue inhibitors of metalloproteinase (TIMP)-1. Results show significant upregulation of secreted and synthesized proMMP-9 activity with duration and severity of endometriosis. Along with upregulation of activity, the expression of

proMMP-9 was found increased while TIMP-1 expression followed an inverse trend. The effect of melatonin, a major secretary product of the pineal gland, on endometriosis was examined in preventive and therapeutic models in mice. Melatonin downregulated proMMP-9 activity and expression while protecting and regressing peritoneal endometriosis. Moreover, the attenuated activity and expression of proMMP-9 were associated with subsequent elevation in the expression of TIMP-1. Our study reveals for the first time the expression ratio of proMMP-9 versus TIMP-1, as a novel marker for assessing severity and progression of endometriosis.

Target molecule identification in childhood acute lymphoblastic leukaemia

Childhood acute lymphoblastic leukaemia (ALL) is a malignant transformation of lymphoblasts, representing the single commonest type of cancer in paediatric population. Exploring the preferential affinity of the *Achatina fulica* lectin Achatinin-H, towards 9-*O*-acetylated sialoglycoproteins (Neu5,9Ac2-GPs), an enhanced disease-associated cell surface expression of the Neu5,9Ac2-GPs molecules have been established on the lymphoblasts (Neu5,9Ac2-GPs+) of childhood ALL, irrespective of the lineage (B or T), indicative of defective sialylation associated with this disease. The expression of this biomarker decreases with successful treatment and reappears with clinical relapse.

Using Neu5,9Ac2-GPs as one of the biomarkers, along with other B/T lineage CD antigens, we have successfully monitored minimal residual disease (MRD) in the patients continuing treatment, the sensitivity of detection being 1 cancerous lymphoblast among 10,000 normal lymphocytes (10-4). High MRD at any point of treatment is associated with relapse.

We have also reported that the Neu5,9Ac2-GPs molecules are functionally active signalling molecules. An increased nitric oxide production is seen in Neu5,9Ac2-GPs+ cells on exposure to IFN-ã, with an increased viability suggesting the protective role of this glycotope.

Disease-specific anti-Neu5,9Ac2-GPs antibodies, with altered glycosylation profile, found in the patient plasma, are incapable of exerting a few Fc glycosylation sensitive effector functions, hinting towards a disbalanced homeostasis. Therefore, considering the protective role of Neu5,9Ac2-GPs and their antibodies promoting the survival of lymphoblasts in ALL and enabling them to escape host defense, it may be hypothesized that both the antigen and antibody might be potential target for further studies of the cancer biology of childhood ALL and its treatment. Enzymes involved in modulating these targets will also investigated.

ChIP-on-chip experiments to find global binding sites in order to understand the mechanism of the metastasis suppression by NM23-H2

Prior studies in our lab showed involvement of a particular DNA structural motif (G-quadruplex or G4 DNA) in transcription of the oncogene c-MYC. Our experiments opened up the possibility that a tumor suppressor protein NM23-H2 induces c-MYC by binding to the structural motif inside cells. NM23-H2 is one of the best studied metastasis suppressors; however, there is almost no understanding of the molecular mechanism of NM23-H2-mediated metastasis suppression. As a part of the current project, in the last one year we have standardized experiments to find out the global binding sites of NM23-H2 using chromatin immunoprecipitation coupled to genome-wide tiling hybridization. We have used Affymetrix tiling arrays which present the promoters of more than 22000 annotated human genes. Preliminary experiments and analysis done in lung carcinoma A549 cells shows more than 600 promoters that have enriched binding of NM23-H2. Leads from the genome-wide experiment will be used to investigate the molecular role of NM23-H2 in metastasis suppression.

Objective 6

Hydroxyapatite nano particles were synthesized by wet chemical method. Synthesis of HAp nano particles by this method is schematically represented in Fig. 1. The powder was thoroughly characterized for its phase composition, percent crystallinity *etc*. by X-ray diffraction (XRD) method and further by the Fourier transformed

infrared (FTIR) spectrophotometer. Stability of the formed phase was checked through DTA-TGA (differential thermal analysis-thermogravimetric analysis) up to a temperature as high as 1300°C. Particle size, shape, morphology formed at different temperatures were checked through FESEM (Field emission scanning electron microscopy) and compared for different formation temperature. The surface charge of the formed crystal were also checked for further investigation of drug inculcation with the calcium phosphate granules, while transmission electron microscopy (TEM) studies were carried out to check the crystal size, morphology *etc*. after calcinations at 800°C.

Objective 7

Conceptual Model for Cancer Development

Literature survey indicates that understanding of the mechanism of cancer is in a state of flux. A number of new concepts are emerging which show that understanding cancer would need inputs from a number of different areas like embryonic development, immunology, cell adhesion and migration in addition to the traditional realm of cancer research – that of the cell cycle and the mutations that lead to aberrations of the cell cycle. Tissue integrity is maintained by the co-operative action of a large number of different types of cells – cancer occurs due to disruption of this co-operative process. Therefore:

[i] In order to simulate cancer we must simulate the collective behavior of different types of cells.

[ii] Simulation of cancer must begin with simulation of the dynamic processes by which a normal tissue maintains itself.

[iii] The simulation should include rules for cell division, differentiation, migration and adhesion and death.

[iv] The immune response to cancer should be included.

This model is in need of continuous iteration.

The Choice of system for simulation

One of the most dynamically maintained tissue systems is the intestinal epithelium which completely renews itself within 3-4 days. Maintenance of a stem cell niche, regulated division, differentiation, migration, and cell death are involved in the normal maintenance of the intestinal epithelium. Considerable amount of data is also available on this tissue. Therefore we chose this system for simulation

Preliminary Code: Initial Simulation results The initial system was allowed to evolve with cells migrating, dividing, differentiating and dying. A steady state population was seen to evolve.

R & D Outputs during the first year (2007-2008):

Patents (Indian & Foreign): 1 (one)

Total Number of Publications: 15 (fifteen)

No. of Project Assistants engaged: 17 (seventeen)

PARTNER NETWORK PROJECTS OF IICB

Partner Network Projects	Objectives
Discovery, development and commercialization of new bioactives and traditional preparations (COR-023)	➢ To revisit Indian biodiversity and Indian Systems of Medicine in the light of current day knowledge in search of therapeutic principle(s) under four disease areas of national importance, namely, Leishmaniasis, Gastric ulcer, Immunomodulation, and Parkinson's disease.
Drug target development using in-silico biology (CMM-017)	➢ In silico analysis of genome/proteome architectures of various pathogenic bacteria, parasites and fungi for identification of virulence determinants ➢ Studies on mouse and human genome characteristics in an attempt to detect the host factors regulating or regulated by the pathogen invasion.Clustering of some host-parasite interaction pathways with a view to identify some of the networks crucial for the host-parasite interplay. ➢ Development of novel software/algorithms relevant to the study
Comparative genomics and biology of non-coding RNA in human genome (NWP-036)	➢ To investigate posttranslational control mechanisms involving such RNAs, ➢ To identify co-regulated gene networks using siRNA, ➢ To develop new RNA-based methods for influencing gene expression in subcellular compartments such as mitochondria, andto investigate the structural basis of the interactions between non-coding RNAs and their protein targets
Exploitation of India's rich microbial diversity (NWP-006)	➢ To develop state of the art molecular genetics approach to address the relationship between metal microenvironment and microbial communities.
Zero emission research initiative (NWP-044)	➢ To identify &scale up of technology and their extension for minimizing environmental risks from leather sector to near zero values.
Diabetes mellitus – New drug discovery R&D, molecular (NWP-032)	➢ To understand the basic mechanism of insulin resistance and defect in signaling of type 2 Diabetes. ➢ To identify possible drug targets . ➢ To develop drug against those targets.
Identification and validation of drug targets for selected pathogens of national importance (NWP-038)	➢ Identification of pathogen-specific, differentially-expressed proteins of Leishmania donovani. ➢ Validation of identified protein as drug targets. ➢ Development of target-specific assays and screening of available synthetic/natural libraries.

Biological and chemical transformation of plant compounds for production of value added products of therapeutic / aroma value (NWP-0009)	➢ Up-scaled isolation of parent anti-cancer molecules targeted for chemical and biological transformation ➢ Chemical transformation of selected phyto-molecules for value addition.
Pathway engineering and system biology approach towards homologous and heterologous expression of high-value phytoceuticals (NWP-008)	➢ Elucidation of the naturally occurring pathways of podophyllotoxin biosynthesis. ➢ Metabolic engineering of podophyllotoxin pathway in a suitable host ➢ Metabolic engineering of isoflavone biosynthesis pathway ➢ Reprogramming of reprogramming of these metabolic pathways in the selected host perhaps using synthetic transcription factors ➢ Creation of novel genetic switches for use in synthetic biology. ➢ Standardization of purification of the compound from metabolically engineered organism
Nanomaterials and nano-devices for application in health and disease (NWP-035)	➢ To synthesize, purify, characterizeand and study suitable linear and denditric peptides for producing and stabilizing metal nanoparticles and cadmium sulfide (CdS) nanoparticles (semiconductor quantum dots). ➢ To examine the cell entry of peptide capped cadmium sulfide (CdS) quantum dots using selective cell lines like normal cell lines (ordinary T-lymphocyte) and diseased cell line (fibroblast T-lymphocyte) and to check the locations of the quantum dots inside the cell , if the nanoconjugate (i.e. peptide capped CdS quantum dots).To explore self-assembling synthetic peptide based new nanoporous materials and to vary the pore size by varying the peptide based molecular building blocks for achieving the selective gas adsorption properties from a mixture of gases of different molecular dimensions. ➢ To check the biodegradability of these peptide based nanoporous materials. ➢ To fabricate pseudopeptide based nanofibers by peptide capped gold and silver nanoparticles and to study the important electrical and other material properties of these nano-materials. To study the self-assembling synthetic peptide based various nanostructures like nanofibrils, nanorods and nanotubes and to use these peptide nano-structures as templates for the production of gold/silver nanowires and nanocrystals.
Plasma proteomics in health, environment and disease (NWP-004)	➢ To identify disease specific biomarkers in easily accessible body fluids, which would constitute safe, effective and non-invasive methods for development of new diagnostic and prognostic approaches. ➢ Plasma proteome profiling in the areas of Arsenicosis, Leismaniasis, Cardiac diseases and ALL will be undertaken.

Publication & Information And Planning, Monitoring & Evaluation

Dr. Pijush K. Das, Dr. K.P. Mohanakumar, Dr. Aparesh Bhattacharya, Dr. Uday S. Chowdhury, Dr. Moonmoon Bhaumik, Dr. Tanmoy Mukherjee, Dr. Prasanta Chakraborty, Dr. Siddhartha Majumder, Sekhar Mukherjee, Arupesh Majumder, Swadesh K. Sahoo, Binayak Pal, Nikhil K. Das, Pratima Banerjee, Lily Das, Sukhendu Biswas, Gopal C. Sarkar, Pallab Mukherjee, Nishikanta Naskar, Bideshi Nayak

The scientific management of the different R&D activities of the institute is the primary focus of this division. The diverse activities of this division have been carried out successfully by seven major sections, e.g. [a] Publication & Information; [b] Planning, Monitoring & Evaluation; [c] Art & Photography; [d] ISTAD-IICB; [e] Intellectual Property Management Cell; [f] Business Development Group; and [g] Human Resource Group. The details of the scientific management activities of the individual sections are given below separately for the reporting year.

PUBLICATION & INFORMATION SECTION

Dr. Tanmoy Mukherjee and group

This section is basically catering the diverse informational activities, publication and monitoring of reports. The major contribution of this section lies in assisting scientists in day to day maintenance of the institute activities and innovations, project profiles, publication records and research utilization data. The section is involved in the following wide spectrum of programmes during the report year.

- Management of Eleventh Five-Year Plan (2007 – 2012).
- Preparation of Annual Plan (2008-09) and Budget.
- Preparation of IICB Annual Report (2006-07) and half-yearly reports.
- Preparation of documents released during events.
- Dissemination of information to scientific milieu on relevant subjects.
- Documents on IICB inputs for “CSIR Annual Report” and “CSIR Research Output 2007”.
- Assistance to scientists, fellows and staff members for participation in seminars, symposia and conferences.
- Preparation of minutes of RC meetings and other task force meetings to enable the members to follow the guidelines and proposals for future directions.
- Maintenance of database for testing and calibration.
- Total management of all technical queries.
- Public relations, advertisement and news and views forum.
- Organization display of exhibition and science news dissemination.
- Advice and comments for management of parliament queries and other related crucial matters of institute.

Management of Exhibition

P&I Section have participated in five (5) exhibitions during 2007-08 in and around Kolkata and also outside Kolkata organized by various organizations. Mr. Sekhar Mukherjee, a senior member of this section looks after the exhibition cell. He also arranged one exhibition at IICB premises on the occasion of CPYLS programme. List of exhibitions are given below.

EXHIBITIONS PARTICIPATED

No.	Date	Theme	Organized by
1.	Sept. 07 – 14, 2007	11th National Science Expo. Theme : Contribution to our National Progress	Central Calcutta Science Culture Organization for Youth, held at Rajdanga Samanway Play Ground, Kolkata – 700 107.
2.	Dec. 08 – 17, 2007	4th Jatiya Sanhati Utsab–O–Bharat Mela, 2007	Bangiya Seva Samity, held at Gobindanagar School Ground, Taldi, South 24-Parganas
3.	Dec. 20 – 29, 2007	Sundarban Kristi Mela–O–Loko Sanskriti Utsab-2007	Milontirtha Society at Kultali, Basanti, South 24-Parganas
4.	Jan. 03 – 07, 2008	Bharat Uday Expo. 2008	95th Indian Science Congress, held at Andhra Pradesh University, Visakhapattanam, AP
5.	Feb. 28 – 29, 2008	Science Exhibition, 2008	5th WB State Science & Technology and Bengal Engineering & Science University, held at Shibpur, Howrah

EXHIBITIONS ARRANGED

No.	Date	Theme	Organized by
1.	Dec. 28 – 29, 2007	CPYLS – 2007	IICB

Management of Laboratory Visit for Students

On the occasion of CSIR Foundation Day (2007) celebration, the members of this section have actively helped for the arrangement of 'OPEN HOUSE' programme where students from various schools/colleges/universities within and around Kolkata visited IICB. A large number of students from about fifteen schools and colleges with their teachers visited various laboratories and interacted with the scientists expressing great interest and enthusiasm. Members of this section also arranged the laboratory visit for students of outside Kolkata colleges and universities. A total of seven (07) numbers of visits were organized throughout the year (2007-08) as listed below.

No.	Date	Institution
1.	1.04.2007	Bajkul Milani Mahabidyalaya, Purba Medinipur, WB
2.	02.11.2007	College of Basic Science & Humanities (Orissa University of Agriculture & Technology, Bhubaneswar)
3.	04.12.2007	DM College of Science, Imphal, Manipur
4.	31.12.2007	Department of Life Science, Dibrugarh University, Assam
5.	04.01.2008	Department of Zoology, North Eastern Hill University, Shilong
6.	11.01.2008	Bajkul Milani Mahabidyalaya, Purba Medinipur, WB
7.	18-19.03.2008	Vidyasagar University, Midnapore, WB

Scientist Visit & Events

The P&I Section is also responsible for the announcement and arrangement of seminars for the national and international scientists who often visit the institute and like to share their research activities with IICB faculties. A list of 'Scientist Visitors' is given in a separate page.

The Institute also organized several significant events with the assistance of this section and 'List of Events' is also shown separately for the reporting year.

Sectional Members

Dr. Uday S. Chowdhury, Mr. Sekhar Mukherjee, Mr. Arupesh Majumdar, Mr. Nikhil K. Das, Mr. Pallab Mukherjee.

PROJECT MONITORING & EVALUATION SECTION

Dr. Prasanta Chakraborty and group

PME is basically involved in the management of the institute's Network as well as externally funded R & D Projects. There are fourteen numbers of Network projects and quite a few numbers of externally funded projects at IICB. Proper management of all these may lead to successful completion of those projects and steady growth of the institute. PME is also supposed to be the leading information centre of any CSIR laboratory regarding projects and therefore, PME of IICB like other CSIR laboratory is actively involved on the following activities:

- Preparation of databases for all extramural research projects (EMR) and calculation of ECF. Data/Information provided for unstarred Rajya Sabha questions regarding External Cash Flow (2007-08). Data/Information provided for Parliament question (2007-08). Data/Information provided for creating database by RDPD at CSIR Hq. (2007-08).
- Dissemination of information regarding call for National & International research project proposal/ awards/fellowship and correspondences with National & International project sponsors.
- Guiding new scientists for project proposal submission.
- Catering to different Scientific Audit queries. Data/Information provided to the Principal Director of Audit, Scientific Deptt., Kolkata Branch (2007-08).
- Data/Information provided to Internal Audit Cell (CSIR Hq.) (2007-08).

- Participation in institute's annual plan, budget preparation.
- Project expenditure monitoring of all network projects (2007-08).

Sectional Members
Mr. Sukhendu Biswas, Mr. Ramdas Ravidas

ART & DRAWING SECTION

Dr. Aparesh Bhattacharya and group

Art Section under the supervision of Mr. S.K. Sahoo has rendered full support to all the staff members during scientific seminars/symposia and all national events by preparing displays, illustrations, posters, exhibits, and slides. Diagrams, charts, graphs for publication in national and international journals are prepared in this section. They are working in collaboration with the photography Section for making each exhibition a great success to highlight the institute achievement. The section also participated in preparing artwork and cover design for Hindi Day and Hindi Report. This section also carried out work for decoration of floor, dias, institute during various scientific and official programmes.

Photography Section under the able guidance of Mr. Binayak Pal has been successful in procuring a digital camera for coverage of all events taking place in the institute. The section is continuously supplying all the photos for publications, Annual Reports, Journals and other related documents. Beside they are also assisting the scientists of the institute. Apart from that they also handled photographs of scientific activities and experiments slides for publication in different international journals.

Sectional Members
Mr. Swadesh K. Sahoo, Mr. Binayak Pal, Mr. Nishikanta Naskar

ISTAD SECTION

- Diverse activities of this section were personally supervised by the Head of the Division, Dr. Pijush K. Das with the active help of Dr. Samir K Dutta.

Intellectual Property Management Cell

Dr. Tanmoy Mukherjee and group

Intellectual Property Management (IPM) cell in IICB is working in close alliance with Business Development Group (BDG) in IICB and Intellectual Property Management Division (IPMD) of CSIR. With the help of a new Comprehensive Patent Database prepared by this cell, now any information about a patent filed by IICB, since 1990 is just a click away.

This cell has continuously maintained liaison with Scientists of IICB and IPMD, CSIR to protect Intellectual Properties of IICB/CSIR. The IPM cell, IICB provided all information, clarifications, explanations and reports to IPMD, CSIR regarding new patent applications, granted patents and renewal or lapsing of existing patents in consultation with concerned inventors within corresponding time-limit. During the reporting period, a large number of correspondences were made with IPMD, CSIR, a significant amount of responses were sent for different patent applications and a considerable number of communications were made with IICB scientists regarding patent queries to provide necessary information to IPMD, CSIR to obtain productive results. The IPM Cell always extended co-operation to the scientists, IICB in writing and filing patent applications. This cell has prepared, maintained and disseminated all information regarding patent application, status of the application, renewal etc as, when and where it was required. IPM cell, IICB has provided all necessary information to Business Development Group of IICB for licensed out patents; sent information on patent and technology transfer to IPMD, CSIR regarding Parliamentary Question; prepared necessary document on patents licensed out by IICB; prepared year wise documents on total Patents of IICB filed and granted; prepared Commercial Working Report of IICB Patents for IPMD, CSIR; approved number of Declaration forms for non patentability of publication and sent Renewal / Lapse recommendations of IICB patents for 2008-09 to IPMD, CSIR

During the reporting period 7 National Patents and 6 International Patents were filed by IPM Cell, IICB while 1 national patent and 6 International Patents were granted throughout the year.

FILED ABROAD

S. No.	NFNO	Lab	Title	Inventors	Country	Complete Filing Date
1	0076NF2006/WO	IICB	DNA vaccine as an immunoprophylactic agent against leishmaniasis	Rajatava Basu, Syamal Ray	WORLD	27/04/2007
2	0148NF2006/NP	IICB	Hybrid cell vaccine against kala-azar	Suniti Bhaumik, Rajatava Basu, Kshudiram Naskar, Syamal Roy	NEPAL	15/06/2007
3	0148NF2006/WO	IICB	Hybrid cell vaccine against kala-azar	Suniti Bhaumik, Rajatava Basu, Kshudiram Naskar, Syamal Roy	WORLD	15/06/2007

S. No.	NFNO	Lab	Title	Inventors	Country	Complete Filing Date
4	0148NF2006/BD	IICB	Hybrid cell vaccine against kala-azar	Suniti Bhaumik, Rajatava Basu, Kshudiram Naskar, Syamal Roy	BANGLA-DESH	17/06/2007
5	0314NF2005/DE	IICB	A herbal extract and herein a molecule, from murraya koenigii for treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	DENMARK	06/03/2008
6	0019NF2006/EP	IICB	A pharmeceutical composition useful for the treatment of prostate cancer	Sinha Swati, Pal Bikas Chandra, Bhattacharya Samir	EUROPE	26/03/2008

FILED IN INDIA

S. NO.	NFNO DATE	LAB	Title	Inventors	FILING
1	0273NF2006/IN	IICB	Soluble protein antigen vaccine as immunoprophylaxis and immunotherapy against kala-azar	Tripti De, Siddhartha Kumar Bhaumik	03/05/2007
2	0079NF2007/IN	IICB	Acaciaside-b: a prophylactic contraceptive for human immuno-deficiency virus infection/acquired immune deficiency syndrome"	Syed Nazrul Kabir, Heramba Nanda Ray, Bikash C Pal, Debashis Mitra	01/06/2007
3	0012NF2007/IN	IICB	Anti-leishmanial activity of para-momycin entrapped in cationic liposomal formulation	Nahid Ali, Antara Banerjee	01/06/2007
4	0160NF2007/IN	IICB	Methanolic extract of piper betel leaves for the treatment of human malignancies by inducing oxidative stress	Santu Bandyopadhyay, Bikas Chandra Pal, Jayashree Bagchi Chakraborty, Srabanti Rakshit, Labanya Mandal, Kausik Paul, Nabendu Biswas, Anirban Manna,	17/12/2007
5	0033NF2007/IN	IICB	Novel amino quinoline compounds	Sukdeb Banerjee, Nahid Ali, Partha Palit, Priyankar Paira, Abhijit Hazra, Nb Mondal	17/03/2008
6	0157NF2007/IN	IICB	Bioactive fraction of goltu kola l useful for antileishmanial activity	Tripti De, Siddhartha Kumar Bhaumik, Manoj Kumar Singh,	31/03/2008
7	0051NF2008/IN	IICB	An anti-leukemic composition comprising withaferin a	Chitra Mandal, Chandan Mandal, Avijit Dutta, Asish Mallick, Laxminarain Misra, Rajender Sangwan	31/03/2008

GRANTED ABROAD

S. No.	Title	Inventors	Country Date	Grant No.	Patent
1	Herbal extract and compound lupinoside and its analogues as anti-diabetic type II drugs from plant Pueraria tuberosa	Debleena Dey, Swapan Kumar Mandal, Mohua Mukherjee, Bikash Chandra Pal, Tanushree Biswas, Malabika Datta , Sib Sankar Roy, Arun Bandyopadhyay, Samir Bhattacharya, Bir Bhanu Giri, Santu Bandopadhyay, Aditya Konar	USA	02/10/2007	7276258
2	Anti-peptic ulcer activity of an extract of a flower of Woodfordia fruticosa	Pratap K. Das, Niranjan P. Sahu, Sukdeb Banerjee, Suchandra Sett, Suchandra Goswami, Samir Bhattacharya	USA	06/11/2007	7291353
3	A herbal extract and herein a lupinoside as potential anti-diabetic type ii drug from pueraria tuberosa	Prof Samir Bhattacharya, Dr. B.C Pal, Dr.Arun Bandopadhyay, Dr. Sib Sankar Roy, Mr. Swapan Kr Mandal, Mr. B.B Giri, Ms.	SOUTH AFRICA	28/11/2007	2006/5690
4	Herbal composition for treating CD^{33+} acute and chronic myeloid leukemia and a method thereof	Santu Bandyopadhyay, Keshab Chandra Roy, Mitali Ray, Goutam Banerjee, Bikash Chandra Pal, Tanusree Biswas, Samir Bhattacharya	USA	11/12/2007	7306817
5	Highly cost-effective analytical device for performing immuno-assays with ultra high sensitivity	Tarun K. Dhar, Arindam Pal	USA	25/12/2007	7312028
6	A herbal molecule as potential anti-leukemic drug	Santu Bandyopadhyay, Bikas Chandra Pal, Samir Bhattacharya, Keshab Chandra Roy, Gautam Bandyopadhyay	RUSSIA	10/01/2008	2314096

GRANTED IN INDIA

S. NO.	TITLE	INVENTORS	GRANT DATE	PATENT NO.
1	A process for the isolation of umbelliferone and apiorylskuminin	Bikas Chandra Pal	29/03/2008	217908

Sectional Members
Mr. Arupesh Majumdar, Mr. Nikhil K. Das

BUSINESS DEVELOPMENT GROUP

Dr. K.P. Mohanakumar and group

MAJOR ACTIVITIES OF THE GROUP:

1. Liaison with private Industries/ R&D Institutes/ Academic Institutions/ other potential clients
2. Negotiating Business Plans with Industries and drawing agreements and MOUs
3. Matters related to Service Tax (registration and filing returns)
4. Customer Satisfaction Evaluation activities
5. Conducting meetings (Industry-Institute meet; Introduction of new schemes, Arrangement of visitors and their interactions with scientists, *etc*.)
6. Parliamentary related matters – Responses to Parliamentary questions, *etc*.
7. Responses to Audit queries
8. Until 2006 – handled the budget (10th FYP; Annual Budget preparation, *etc*).
9. Matters related to investment of idle funds available in the institute timely & appropriately, distribution of money earned under royalties, *etc*.
10. Periodic preparation of lists of knowledgebase/products available, dissemination of information on technologies, *etc*.

COMMERCIALIZATION OF TECHNOLOGY DURING THE REPORT PERIOD

Sl. No.	Name of the company	Nature of agreement	Date of commercial release of the product
01	M/s East India Pharmaceutical Works Limited, Kolkata	Patent license agreement for utilizing the technology in connection with the treatmentand remedy of prostate cancer from herbal formulation	Dec 07 2007

Both Dr. T. Mukherjee and Dr. K. P. Mohanakumar, scienrtsist from the Division attended 3-day programme on 'Leveraging Intellectual Property for Business Development' from 6th to 8th August, 2007 organized by the Human Resource Development Centre (CSIR) in Ghaziabad.

HUMAN RESOURCE GROUP

Dr. Siddhartha Majumdar and group

Human resources Group (HRG), IICB has been set up in April 2005 to organize and nucleate Human Resources Management activities at IICB. HRG's mission is to promote professional Human Resources Management in this institute by evolving and implementing HR development plan.

Activities, Guidance and Initiatives:

- Defining & assessing institutes specific training needs and designing, developing to meet these.
- Coordinates academic & administrative affairs concerning Research Fellows/Associates holding independent fellowship and linkages with other organization/Agencies/Institutes.
- The office collects and disseminates comprehensive data and information to assist in strategic planning for IICB & CSIR.
- To advance the academic mission of the institute, the Office of HRG (Academic Affairs) provides leadership for continuous improvement in academic programs, support facilities and services.
- Maintaining and updating the databases of research fellows, summer students & Academic affairs.
- Selection and placement of the summer trainees/project trainee of different post graduate students studying in different Universities, Institutions and colleges all over the country.Ê
- Coordinate the in-house two semesters PhD Course WorkÊfor the IICB PhD research fellows as a part of the **Academic Affairs** of the Institute.
- To assist in the process for nominating Scientists and Officers by the Director, IICB in different training programme/workshop [*viz*. R&D Management, Leadership Development and personal skills up gradation programmes *etc*. organized by CSIR, HRDC and other national level institutes].
- Human Resources have established a range of training and support for research students to assist them with their professional and career development. This training and support is provided free of charge to them.
- Coordinates different awareness programme in relation to training, fellowship, etc.

Programs: Guidelines, Information & Initiative

Ph.D. Programme
The major objective of the programme is to generate adequate and trained human resource in the different fields of Biology and Chemistry, and related areas for meeting the requirement of cutting edge research. The duration of this programme is generally five years.

Eligibility criteria: For admission to the PhD program of the institute, the CSIR-NET qualified candidates / UGC-NET/ ICMR fellows/ DBT fellows can directly join the institute in their area of interest subject to consent from the institute's faculty to be the candidate's supervisor and director's approval.

Junior Research Fellowship for GATE qualified engineering graduates (CSIR_JRF-GATE):
CSIR has introduced a new research fellowship in 2002 for the GATE qualified candidates with B.E., B.Tech,

B.Arch, B.Pharm degree to pursue research leading to Ph.D. Each CSIR laboratory engaged in biological/biochemical research can have maximum 10 such JRF-GATE fellows.
Besides the adhoc fellowship, IICB advertises for recruiting research fellows to work in grant-in-aid projects and different research schemes.

At a Glance: Research Fellow
Number of existing (during December 2008) Research Fellows

Funding Agency	JRF & SRF	RA
CSIR	128	10
UGC	28	0
DST	14	01
DBT	08	0
ICMR	11	05
CLP	01	0
ESP	02	02
NMITLI	01	0

Career Opportunities: Research/Training

Ph.D. Course Work

The HRG & Academic Affairs Committee has been organizing Ph.D. course work in two-semester since 2005. The main objective of this courses are to make the students acquainted with modern modern biological sciences, chemistry and chemical biology along with Statistical Analysis, Instrumental Analysis and basic computer courses . The course work is mandatory for students registering Ph.D. degree.

The duration of this course is normally 120 hours. The course comprises of two major disciplines, namely **Basic Course** with [a] Computer Applications; [b] Instrumental Analysis; [c] Statistical Analysis; [d] Basic Biology (for Chemistry students); and [e] Basic Chemistry (for Biological Sciences students); and **Advanced Course** with: [a] Advanced Biology (for students engaged in Biological Sciences Laboratory); and [b] Advanced Chemistry (for Chemistry Laboratory students).

Number of IICB Ph.D. Course work (2008) Students: 58

Summer Training / Project Work / Dissertation Work

The Human Resource Group, IICB provides an excellent environment for training the next generation of researchers and is proud to support training towards partial fulfillment of the respective postgraduate degrees. IICB has imparted training in the state–of –the-art techniques to several summer students from different universities & Institutes. The aim is to let young minds feel the thrill and excitement of science by working on a project requiring application and critical appreciation of scientific principles. It also aims at active participation in the learning process through experimentation and putting into practice the knowledge acquired in the classrooms.

Students pursuing M. Sc. /M. Tech. /M. Pharm. etc. from various universities/institutes of the country get short-term training in different laboratories of this Institute. Under this programme, the Institute conducts training of short duration in various disciplines and is absolutely free of any cost. The courses comprise both lectures and practical with emphasis on practical R&D aspects in a particular discipline. The duration of this training programme / Project Work is generally two- three months and maximum six months duration during March and August every year.

Year 2008: Number of Summer Trainee/Project Trainee/Short term-trainee: 105

Other Activities and initiatives: Nomination in Training & Workshop

- To assist in the process for nominating Scientists and Officers by the Director, IICB in different training programme/workshop [viz. R&D Management, Leadership Development and personal skills up gradation programmes etc. organized by CSIR, HRDC.

Participants in different Training programme:

- Dr. Ashok Kr. Dasgupta, Technical Officer III(5), Computer Division participated in the"First Advanced Training Programme on Cyber Laws, Information Security and Computers for Scientists and Technologists" during June 9-15, 2008 at New Delhi, S&T Departments of Govt. of India
- Dr. Snehasikta Swarnakar, Scientist has been nominated for his participation in the "Work life balance for women scientists" held at HRDC, Ghaziabad during 23 – 25 October. 2008.
- Mr. A. K.Jha,S.O(F&A) has been nominated for his participation in the "Sciemnce Audit for senior Scientists & senior Administrators Symposium by the Dept. of S&T ,Govt of India, New Delhi during May 26 -30 , 2008
- Mr.U.S.Das , SPO has been nominated for his participation in the CSIR Leadership Programme (LDP) organized by the HRDC, CSIR during **Oct, 2008** at Ghaziabad
- Dr. P.Jaisankar, Scientist has been nominated for his participation in the" Decision Support Tools and Techniques for senior scientists" organized by DST, GOI during 2nd April to 6th April 2007 at ASCI, Hyderabad.
- Dr.Siddhartha Majumdar, Technical Officer Gr-III (6) & Head, HRG has been nominated for his participation in " Workshop on Strategic Management of Human Capital" organized by the HRDC, CSIR during **12th to 14th Oct, 2007** at Ghaziabad

Sectional Members

Ms. Lily Das, Ms. Pratima Banerjee, Sri. B. Nayak

Scientist Visitors

No.	Date	Speaker	Title of Seminar
1.	22.04.2007	Dr. Bhaswati Pandit Mount Sinai School of Medicine. Nu York, USA.	Dysregulated Ras signaling: A path to Cardiac abnormalities.
2.	25.05.2007	Dr. Atanu Basu. NIV, ICMR, Pune. India.	Electron Microscopy in Modern Infectious Disease Research : New Frontiers and Challenges.
3.	23.07.2007	Dr. Subrat K Panda AIIMS, New Delhi	Replication of HEV : the localization at Sub-cellular site.
4.	24.07.2007	Dr. Supratik Das Albert Einstein College, USA.	Multimerization of the tumor suppressor INI 1 : Implications in HIV -1 . Replication and transcription regulation.
5.	27.7.2007	Dr. Nikhil K Basu NIH, Maryland, USA	Phosphorylation of UDP-glucuronosyltransferase (UGT) : Its functional impact on drug metabolism and detoxification.
6.	01.08.2007	Dr. Ambar K Choudhury	Development of methodologies and synthesis of new organic molecules for specific studies.
7.	06.08.2007	Prof. B. Mukherjee Uni. of Connecticut Health Sc.	Engineering T-cells with tumour epitope specific TcR for tumour immunity.
8.	22.08.2007	Dr. Indranil Biswas Uni. of South Dakota. USA.	Streptococcal Pathogenesis : Unraveling the role of CovR in virulence Regulation.
9.	05.09.2007	Dr. Subhendu Sekhar Bag Nihon University, Tamura Koriyama, Japan.	Targeting the DNA : design and synthesis of enediynes as DNA- cleaving agents and novel base-discriminating fluorescent (BDF) oligonucleotide Probes for SNPs genotyping.
10.	11.10.2007	Dr. Samir K Maji California, USA.	Amyloid aggregation : from dark side to novel therapeuties.
11	29.10.2007	Dr. Saikat Chakraborty National Institute of Health Bethesda, Maryland, USA.	Towards understanding of structural functional and evolutionary diversities among proteins.
12.	07.11.2007	Prof Harish Padh, Director PERD, Ahmedabad.	Pharmacogenetics variation in drug response in Indian pollution.

No.	Date	Speaker	Title of Seminar
13.	08.11.2007	Dr. Sanjeev Das Harvard Medical school, USA.	Living with p53, dying of p53 ; The Hzf connection.
14.	15.11.2007	Dr. Tapas Manna Worcester, USA.	Regulation of microtubule dynamics by stathmin and its phosphorylated isoforms.
15.	20.11.2007	Dr. Mark McDowall Strategic Business Manager, Proteomics, Water Corporation.	The Integration of ion Mobility Spectrometry and Mass Spectrometry for high Definition Analysis of Proteins, Modified Peptides and Metabolities.
16.	21.11.2007	Dr. Dibyendu Bhattacharya Uni. of Chicago, USA.	Deciphering Translational ER Sites
17.	23.11.2007	Dr. Apurba Kumar Das University of Manchester, UK.	Nanostructured Materials by Enzyme Assisted Self-Assembly.
18.	20.12.2007	Dr. Subha Ranjan Das Carneige Mellon Univ. USA.	Chemo-genetic analysis of Ribozyme Function.
19.	24.12.2007	Dr. Anirban Basu NBRC, Gurgaon, India	Aberrant microglial response in Japanese Encephalities : from mechanism to intervention.
20.	24.12.2007	Dr. Jyoti Kusari	Brimonidine & Memantine Inhibit Diabetic Retinopathy.
21.	26.12.2007	Prof. William W. AU Univ. of Texas, Galveston.	Biomarkers, risk factors and molecular intervention of cancer.
22.	28.12.2007	Prof. Sumantra Chatterjee TIFR, Bangalore.	Why does stress cause emotional problems.
23.	25.01.2008	Prof. Shantanu Bhattacharya IIT, Kanpur.	Bio-MEMS and Lab on Chip Approaches for Analysis of Nucleic Acids.
24.	04.02.2008	Dr. Pravat K. Mandal Uni. of Pittsburgh, U.S.A.	"Spectroscopic Investigation of Neurodegenerative Diseases (Alzheimer's Parkinson and Dementia with Lewy Body)"
25	05.02.2008	Dr. Asim Kumar Debnath N.Y. Blood Centre, USA.	Rational Design of a Cell - Penetrating Peptide as HIV - 1 Assembly Inhibitor
26.	06.02.2008	Samrat Mukhopadhyay Scripps Res. Inst. USA	Illuminating the Pathway to Prion Amyloid.
27.	07.02.2008	Dr. Arijit Banerjee Uni. of Oxford, UK.	Unnatural aminoacid mutagenesis Using nonsense codon suppression: Getting proteins with desired structure and function

No.	Date	Speaker	Title of Seminar
28.	08.02.2008	Prof. Dipak K. Banerjee Uni. of Puerto Rico. USA.,	Glycotherapeutics in Breast Cancer.
29.	21.02.2008	Dr. Biswadip Banerjee Biopolis, Singapore.	Targeting Cancer : From Small Molecule to Natural Products As Inhibitors.
30.	11.03.2008	Prof. Subhash C. Basu Uni. of Notre Dame Indiana.	Structures of Carbohydrates and Glycocojugates.
31.	12.03.2008	- Do -	Biosynthesis and Regulations of Glycoproteins and Glycolipids.
32.	13.03.2008	- Do -	Apoptotic Signals in Nor4mal and Cancer Cells.
33.	28.03.2008	Prof. Dipankar Roy Northwestern University Chicago, USA.	Ubiquitination : roll in the maintanence of genomic integrity.

MONTHLY COLLOQUIUM SEMINAR 2007 - 08

1.	24.05.2007	Prof. Rahul Roy. Dept. of Medi. Biophysics & Biology Boston University school of Medicine.	"Group specific component - a protein that wears multiple hats."
2.	23.10.2007	Prof. K. P. Chang Dept. of Microbiology/ Immunology Rosalind Franklin University, North Chicago, University.	Prophyric Leishmania as suicidal mutants for photodynamic vaccination.
3.	28.02.2008	Prof. Johann Gasteiger Universiteat Erlangen – Nuernberg Germany.	Chemiinformatics in Drug Design.

Events 2007 – 2008

Date	Salient Details
April 02, 2007	IICB Foundation Day celebration. Prof. S.K. Pal, Director, Indian Statistical Institute (ISI), Kolkata was the Chief Guest. Prof. R.J. Simpson, LICR/WEHI, Australia delivered the XXth J.C. Ray Memorial lecture. A popular lecture entitled "Malaria – Ek Buddhijibi Porojibi" was delivered by Dr. Uday Bandyopadhyay, Scientist, IICB.
May 16, 2007	KVYP Programme held at IICB premises. About 46 students from various parts of India participated this programme. Prof. Siddhartha Roy, Director, IICB delivered a popular lecture entitled "Genes and Evolution". Dr. H.K. Majumder, Scientist, Director-Grade, delivered a lecture entitled "DNA topoisomerases : The hidden treasures".
August 15, 2007	Independence Day celebration.
September 14, 2007	Hindi Day celebration. Chief Guest was Mr. S.L.S. Purti, Deputy Director, Hindi Teaching Scheme, Ministry of Home, Govt. of India, Nizam Palace, Kolkata.
September 26, 2007	CSIR Foundation Day celebration. Welcome address was given by Prof. Siddhartha Roy, Director, IICB. Inaugural address was delivered by Prof. B.B. Biswas, Ex-Director, Bose Institute, Kolkata. Dr. G.C. Mishra, Director, NCCS, Pune delivered the Foundation Day lecture on "Dancing the immunological two step synapse ! Who orchestrates the music … … … the antigen or the costinulation".
November 05, 2007	Inaugural Ceneramony of National Institute of Pharmaceutical Education & Research (NIPER), Kolkata.
December 28 & 29, 2007	CSIR Programme on Youth for Leadership in Science (CPYLS-2007) was celebrated. Prof. Ashok Ranjan Thakur, Vice-chancellor, West Bengal University of Technology was Guest-in-Chief. Welcome address was delivered by Dr. H.K. Majumder, Director-Grade Scientist, IICB, and Dr. Kunal Roy delivered a popular lecture.
February 28, 2008	National Science Day celebration. A scientific lecture was delivered by Prof. Johann Gasteiger, University of Erlangen, Nuremberg, Germany on 'Chemiinformatics in Drug Design'.


NATIONAL INSTITUTE OF PH
AT IN


INAUGURAL CEREMON
OF
NATIONAL INSTITUTE OF PHARMACEUTICAL EDUCATION & R
AT INDIAN INSTITUTE OF CHEMICA
4, RAJA S.C. MULLICK ROAD
MONDAY, NOVEMBER 05
KOLKATA

Computer Division

Mr Debasis Paul, Dr. Asoke Das Gupta & Mr. Ashutosh Mukherjee

i) Upgrading of I.T. Facilities

The IT facility have been upgraded with latest technology like Radius Server, X Gen Mailing Software, Bandwidth Management, NMS Open View etc. Besides these, 300 Desktops PCs, Laptops and Printers. have been procured and distributed to the staff members including Scientists, Technical Officers. The WIFI Technology has been introduced at IICB Campus as well as at NIPER Office and NIPER hostel with 6.8 GHz RF link. About 200 users are having the facility of using WIFI technology throughout its range. High End CISCO Switches and POE Switches have been installed for IICB Network and WIFI Network. Recently, the bandwidth of IICB network has been upgraded from 4MBPS to 25MBPS for fast data communication.

ii) In house Maintenance

The division looks after about 500 nodes with various problems, like Hardware, Software and Network problems. IICB Website has been modified from time to time on regular basis. Internet website has been introduced for internal use, which includes various types of official work, Administrative matters, Office Memos, News etc. The Intra Website is updated from time to time on regular basis.

iii) Scientific Activities

The SPERMA, sperm motility analyzer, a unique computer based instrumental system has been developed for the first time to determine sperm motility (velocity), using a spectrophotometer for clinical and biological applications. The main purposes of this new project is to calibrate and standardize this unique instrumental system, SPERMA, and correlate the vertical motility parameters experimentally with fertilizing ability of the spermatozoa. The other purpose of this project is to upgrade the SPERMA by incorporating multi-cuvette (multi-sample) and multi-height exposures of the spermatozoa sample in the present instrumental system to make it more user friendly and market friendly. In order to acquire the intellectual property right, this unique work has already been filed for National (1605DEL2004) and International (WO-PCT/IB05/02541-26/08/2005) Patents.

Proposed instrumental upgradation will develop a simple but unique device for objective assessment of sperm motility. It provides both qualitative as well as quantitative assessment of spermatozoa. As sperm motility is essential for the fertilization efficiency of the male gametes, this equipment will be extremely beneficial for determining the fertility status of human males as well as bulls of various species of mammals. Consequently, this equipment has a great market potential for the human infertility clinics as well as in the animal / cattle breeding centres all over the world. This instrumental system will be useful in laboratories that are engaged in conservation of endangered species of animals. Further, this instrumental system may be useful in various other fields of basic sciences. It is also expected that several other applications will be relieved, once this instrumental system gets National and International exposures.

Research Scholars: Dr. Sudipta Saha (Research Associate, CSIR) and Ms. Abhi Das* (Junior Research Fellow, DST)*

Library & Documentation Division

Mr. N. C. Ghosh, Mrs. P. Chatterjee, Mr. S. Bhakta, Mr. S. K. Naskar, Mrs. S. Ganguly, Mr. P. K. Das, Mr. T. K. Mukherjee, Mr. M. Halder, Mr. S. Nath, Dr. B. K. Ghosh.

The Library & Documentation Division has been marked with the remarkable growth in respect of collection, systems, facilities and services during the period under review. Keeping pace with the information need of the Institute and modernization of Library and Information Services the books and other Library Documents have been selected and added to its holdings. Apart from a good number of books (text and reference) it has a very good collection of journals (print + online), technical reports, thesis, reprints and ADONIS Off Line CDROM databases containing about 743 scholarly journals in full text from 1991 to 2002. CSIR E-Journal Consortium is a CSIR Network Project under 10th Five Year Plan being implemented by NISCAIR providing access about 4500 world class STM Journals and online databases like Web of Science, DII, Delphaon to the CSIR family including the Library & Documentation Division of the Indian Institute of Chemical Biology.

Collections	2007-2008	Total
Books including Hindi Books (OLIC)	603	12847
No. of Titles of Journals (including titles on-line of SD, Springer, Blackwell, ACS, John Wiley, OUP, RSC, Taylor & Francis, Emerald, Nature, Cell Press, Science & CSIR E-Journal Consortium)		4600
Bound volumes of journals	1895	31574
Annual Reports	52	3766
Monographs (including WHO Monographs)	21	2058

The services rendered from the division are like reading room facilities, on-line and off-line literature search information services through CD-ROM database – ADONIS, lending facility, reference and referral services, reprographic and resource sharing etc. On-line availability of the journals of High Impact Factor through CSIR E-Journal Consortium enhanced the services tremendously.

The division is basically to provide library information services to the S & T personnel, staff members, research scholars and others associated with the Institute. However, outside users like academicians, bonafide research scholars, bonafide students etc. are also allowed to make use of Library information services.

IICB is the institutional member of the British Council Library, Kolkata. The users can avail the BCL services by borrowing materials in addition to its own.

The services rendered by the Division are not only confined to the resources available of its own, even from the resources available in CSIR family as a whole and sometimes from other libraries of same nature on resource sharing basis.

Library & Documentation Division organized a users training-cum-awareness programme in view to get them acquainted with the library collections- off-line & on-line available in Library and how to retrieve the required information for their research work. Library also organized a training session on web OPAC, for effective searching the library holdings and utilization of other facilities available there.

The division has LIBSYS 4.0 software installed on Linux (Red Hat Enterprise Edition) platform for facilitating access to the library catalogue through Web-OPAC. The computerization programme of the division is on the way in full swing. The computerized catalogue of the books in collection is now available on the web.

Central Instrumentation

Dr. S.K. Dana, Mr. Tapan K. Mukherjee, Mr. Kalyanmay Datta, Mr. Utpal Halder, Mr. Surojit M. Roy, Mr. Ajoy K. Pramanik, Mr. Tarak P. Nandi

The Central Instrumentation Division takes care of the repair and maintenance of all scientific instruments of the institute. In addition, the division is actively involved in developing the infrastructure and basic amenities for major equipments of the institute. The division supports the operation of Centrifuge, Ultracentrifuge, UV/VS spectrophotometers and Lypholyzer. The regular maintenance support is provided on small and essential instruments which are of high demand like fraction collector, electrophoresis apparatus, high voltage power supplies, voltage stabilizer and high vacuum systems to mention a few. The division also supports the audio-visual systems, video conferencing system in the institute during several meeting, seminar and conferences held throughout the year. In addition, the division initiated R&D efforts in developing new biomedical equipments and also investigations on experimental chaos synchronization in electronic circuits.

A group of scientists, technical officers and skilled technicians assist in the operation, repair and maintenance of scientific instruments used by different group in life science and chemistry of the institute. A few research scholars are working towards Ph.D. degrees on nonlinear dynamics using theoretical as well as experimental approaches.

Research and Development

Research and development have been initiated in the instrument division with the purpose of developing new apparatus for biological research. Another important R&D initiative is related to develop new understanding of dynamical behaviors in biological and physical systems and to search for their applications. Nonlinear dynamical approach is mainly adopted for understanding living systems' behaviors like cardiac arrhythmia, neuronal interaction in the brain under pathological condition. Trends of research are set around the world in recent years to understand these aspects using concept of synchronization in nonlinear oscillators and complex networks. The focus of our current research is to investigate some of these aspects using mainly experiment on chaotic electronic circuits and with appropriate numerical studies of paradigm models. The basic idea is to set a trend of interdisciplinary research bringing together the knowledge of physics, electronic and biology to explore complex dynamics of natural systems. A few fundamental aspects of chaos synchronization, namely, anomalous phase synchronization and phase flip bifurcation, robust antisynchronization and amplification of chaos phase synchronization has been explored and their experimental evidences in electronic circuits are also reported.

New initiative is undertaken using radio-telemetric EEG/ECG measurement and data analysis to understand rat's brain function under drug-induced condition in collaboration with the neurobiology group of the institute.

Collaboration with many national and international institutions has been established. Some of the premier institutions in the country like Presidency College, Kolkata, School of Physical Sciences, JNU, New Delhi, Department of Physics and Astronomy, Delhi University, Institute for Plasma Research, Gandhinagar and Physical Research Laboratory, Ahmedabad, are participating in joint research. Institutions from abroad like the Institute of Physics, University of Postdam, Germany; Department of Mathematics and Computer Sciences, Elizabeth State University, North Carolina, USA, Institute of Physics, Academia Sinica, Taiwan and Faculty of Bioengineering, University of Pharmacy and Medicine, Iasi, Romania and Nizhny Novogord State University, Russia have started collaboration.

Research Fellows

Mr. Ranjib Banerjee, Mr. Sourav K. Bhowmick, Mr. Chittaranjan Hens

Extramural Research Activities

An international collaboration between IICB and University of Medicine and Pharmacy, Iasi, Romania is continued on control and synchronization of chaos supported by the Department of Science and Technology (DST), India and Ministry of Education and Research, Romania.

Invited Lectures

(1) Invited as a faculty to lead a session on electronic experiments in the 2-week's Winter School on Hands-on-Research on Complex systems, Institute for Plasma Research, 2008 sponsored by the Abdus Salam International Centre for Theoretical Physics, Trieste, Italy.

(2) A series of lectures on experimental nonlinear dynamics was delivered in the one-month DST-SERC school held in the Indian Institute of Science, Bangalore, 2008.

(3) Invited talk "Antiphase synchronization of chaotic oscillators" in the International conference on Dynamical Systems and Turbulence held in the Indian Institute of Science, Bangalore, 2008

External Funding

Project Title	:	Synchronization nonlinear systems: Theory and Experiment
Funding Agency	:	Department of Science and Technology, New Delhi
Total Fund	:	16.56 lakh
Duration	:	2006-2009
Principal Investigator	:	Dr. Syamal Kumar Dana
Co-Investigators	:	Dr. Prodyot K. Roy, Department of Physics, Presidency College, Kolkata Prof. Abhijit Sen, Institute for Plasma Research, Gandhinagar, Gujarat Dr. Gautam C. Sethia, Institute for Plasma Research, Gandhinagar, Gujarat

Honours and Awards

Reviewer of International Journals: CHAOS, Physics Letters A, European Journal of Physics.

Publications

Journal

1. I.Grosu, E.Padmanaban, P.K.Roy, S.K.Dana, Designing coupling for synchronization and amplification of chaos, Phys.Rev.Lett. 100, 234102 (2008).

2. A.Prasad, S.K.Dana, R.Karnatak, J.Kurths, B.Blasius, R.Ramaswamy, Universal occurrence of phase-flip bifurcation in time delay coupled systems, CHAOS 18, 023111 (2008).

3. I.T.Tokuda, S.K.Dana, J.Kurths, Detecting Anomalous phase synchronization from time series, CHAOS 18, 023134 (2008).

4. S.K.Dana, P.K.Roy, Bursting near homoclinic bifurcation in two coupled Chua oscillators, Int.J.Bifur.Chaos, 17(10), 3437(2007).

Book

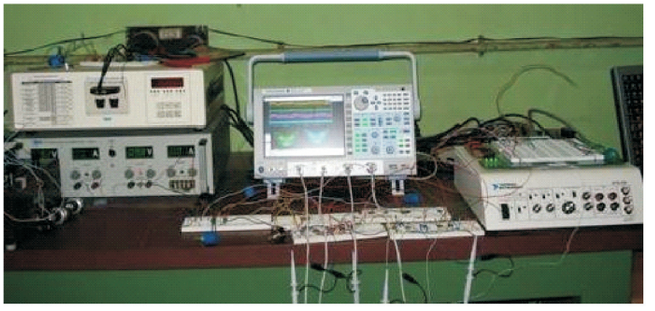
1. S.K.Dana, P.K.Roy, J.Kurths (Eds.), Complex Dynamics in Physiological Systems: From Heart to Brain, Springer, Complexity series, 2008.

Conference

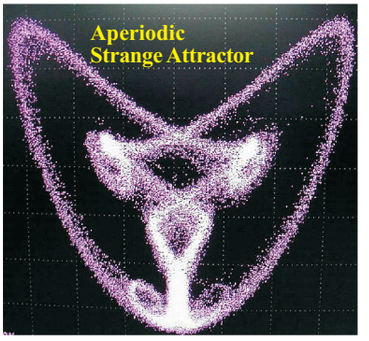
(1) S.K.Dana presented a paper in the Experimental Chaos Conference, Catania, Italy, in June, 2008

(2) Ranjib Banerjee attended one-month workshop on Complex networks, Max-Planck Institute of Physics for Complex Systems, Dresden, Germnay, May, 2008 and presented a poster.

(3) Sourav K.Bhowmick attended the 2-week's Winter school on Hands-on-Research on Complex systems, Institute for Plasma Research, 2008 sponsored by the Abdus Salam International Centre for Theoretical Physics, Trieste, Italy.



Experimental Set-up for studies of chaotic dynamics



Experimental picture of
Aperiodic strange attarctor

Animal House

Dr. A. Konar, Dr. H. Ray, Mr. S. S. Verma, Mr. R.K. Sarkar, Mr. A. Das, Mr. J. Middya, Mr. P. Middya, Mr. T. Sarkar, Mr. A. Sardar , Mr. G.C. Mondal

The animal facility in IICB is registered with CPCSEA (Registration No 147/1999/CPCSEA). It is identified as an important source of laboratory animals used in biomedical research. The supply of animals for the institutional projects is being made from the in-house breeding colony. Only a few special strains of mouse were purchased from outside. Some research organizations having their CPCSEA registration also collect animals from the facility for their IAEC approved research projects.

The environment of the animals rooms are maintained scientifically (Room Temp. 24 , ±2 ^{0}C ; relative humidity 55 – 60%; light and dark schedule 12:12hrs; illumination 350-400 lux at 1 mt above the floor, and 10 – 12 air-cycles/hr). The house keeping of the facility received high appreciation not only from the scientists but also the representatives of CPCSEA, representative of different NGOs and private entrepreneurs, visiting scientists and students.

The animal carcasses and other biological wastes, used syringes and needles, etc. are disposed through a Pollution Control Board (Govt. of India) approved agency. This procedure has been proved to be user friendly, hygienic as well as cost effective.

The proper utilization of animals is strictly monitored and estimation for animal production is made in such a manner, that the number of unutilized animals be minimum but the scientists get their animals as and when they require. An account of animal produced/supplied from the animal house in the year 2007-08 is given in the following table :

Species	Stock on 1st April 2006	No. of animals		Total (A)	No. of animals issued		No. of animals issued		Total (B)	Stock (=A-B) on 31.3. 2007
		Produced	Purchased		Produced	Purchased	Died in stock	Supplied to other R&D organi-zations		
Mouse	2102	5786	45	7933	5568	45	x	80	5693	2240
Rat	1916	4921	x	6837	4426	x	x	159	4385	2452
Hamster	303	1167	x	1470	939	x	x	x	939	531
Rabbit	102	51	x	153	20	x	x	22	42	111
Guinea pig	26	13	x	39	x	x	x	04	04	3

Essential Services Unit (ESU)

Dr.J.Rajan Vedasiromoni, Mr.S.Saha, Mr.U.K.Barua, Mr.D.P.Das, Mr.S.Roy, Mr.B.Jayakumar, Mrs.N.Bage, Mr.S.Basak, Mr.M.B.Malakar,Mr.G.Malik,Mr.D.K.Ghosh, Mr.S.N.Mondal,Mr.S.Pradhan, Mr.S.Biswas, Mr.S.R.Tudu, Mr.D.Banik, Mr.S.Nath, Mr.S.Mazumder, Mr.A.Pal, Mr.K.C.Das, Mr.B.Das and Mr.S.Ghosal

The Engineering Services Unit (ESU) is comprised of the Civil Engineering, Electrical and Air-conditioning & Refrigeration sections.

i. Civil Engineering section:

The Civil Engineering Section renders service in the broad areas of infrastructure development, renovation of laboratories & common facilities, maintenance of campus, sewerage and drainage systems, cleaning & housekeeping work and disposal of biological including radioactive waste.

List of major works carried out during this period:

1) Repair, renovation & up-gradation of different laboratories and store Section.
2) Repair, renovation & up-gradation of all Toilets.
3) Repair & renovation of NIPER Office at IICB Campus.
4) Renovation & up-gradation of Corridors.
5) Renovation & up-gradation of a portion of R.C.C. Road.
6) Replacement of pipelines for water supply distribution system.
7) Renovation of Seminar Rooms
8) General cleaning and housekeeping work.
9) Tendering process for development of new campus at Salt Lake.

The following Civil & Structural Engineering works are in progress or in proposal stage:

1) Renovation of Auditorium
2) Structural repair of overhead water tank
3) Water proofing treatment of roofs of auditorium, library & main building.
4) Construction of central A C Plant room
5) Repair, renovation & up-gradation of different laboratories and offices.
6) Annual maintenance of IICB campus.
7) Replacement of Barbed wire fencing at IICB Campus & Scientists' apartment Campus.
8) Repair, renovation & up-gradation of CSIR hostels at P. A. Shah Road.
9) Renovation of Library
10) Renovation of lift machine room & lift well for Lift near the canteen.
11) Installation of modular furniture in different laboratories.

12) Construction in new campus at Salt Lake.

13) Vertical expansion of IICB building and construction of Animal House.

14) Repair & maintenance of CSIR Scientists' Apartment complex at P. A. Shah Road.

15) General cleaning and housekeeping of CSIR Scientists' Apartment complex at P. A. Shah Road

ii. Electrical section:

The Electrical Section renders essential service and infrastructural support to R&D activities and other public utilities of the Institute. The section maintains and supplies steady power supply through 2MVA power sub-station of the institute and provides uninterrupted power supply from CESC source as well as emergency power through available source of DG-sets including their operation and maintenance. The section also takes care of water system management, internal communication system and incineration of dead animals and animal house waste.

List of major works carried out during the year:

1. Improvement of power supply system including erection and commissioning of 2MVA, 6KV Automatic Voltage Regulator.
2. Electrification of stores and the laboratories that have been renovated.
3. Provision of power source for emergency power line in different labs.
4. Renovation of electrical installations in two seminar rooms and lift room.
5. Breakdown maintenance of 6.6 KV HT OCB's of power substation of IICB.
6. Electrification of NIPER office and area lighting in IICB campus.

The following electrical works are in progress or in proposal stage:

1. Electrification of hostel building and area lighting in Scientists' apartment campus.
2. Renovation of LT distribution system of sub-station.
3. AMC for campus lighting and for internal & external electrification.
4. Proposal for procurement of 2 x 500 KVA DG-sets for emergency power.
5. Feeder connections of LT cubicle panels and allied works of power sub-station.

iii. Airconditioning and refrigeration section:

This section looks after the AC facility in all the laboratories, library, auditorium, administrative wings and most importantly the animal house. It also takes care of the refrigerators and deep freezers in the laboratories, maintains the cold rooms and constant temperature rooms and is responsible for the maintenance of the lifts.

List of major works in the past one year:

1. Annual maintenance of window and split AC units.
2. Annual maintenance of 2 x 80 TR AC plant for animal house.
3. Annual maintenance of 3 x 7.5 TR package type AC units for administrative wing.

4. Annual maintenance of 7.5 TR ductable split AC unit.
5. Maintenance of cold and constant temperature rooms.
6. Installation of 2 modular cold rooms and two constant temperature rooms.

The following works are in progress or in proposal stage:

1. Modernization of the passenger lift near the canteen.
2. Renovation and refurbishing of the central AC plant is in progress to cater for the library and auditorium.
3. Work has been taken up for making a clean room for installation of Protein Micro Array facility.
4. Proposal for providing 24 hrs AC facility for the server in library.
5. Proposal for installation of 15 TR ductable split AC system for the administrative wing.

Administration

The Administration takes care of the day-to-day activities required for smooth functioning of the Institute. The Administration is divided into three Divisions :

A. GENERAL ADMINISTRATION

General Administration comprises of the following Sections :

[i] *Recruitment & Committee*

This Section takes care of the recruitment and promotion of all Scientific, Technical and Administrative staffs. It also arranges for engagement of Project Assistants for different projects.

[ii] *Establishment*

This Section maintains the personal files of all the employees of the Institute.

[iii] *Bill & Cash*

All works related to preparation of salary bills and other advances as well as disbursement of cash are taken care of by this Section.

[iv] *General Section*

This Section takes care of all miscellaneous types of work including Works & Services.

[v] *Vigilance & CR Cell*

This Section keeps a vigil eye on all activities of the Institute. The confidential reports of all the employees are also maintained by this Section.

[vi] *Legal Cell*

The Legal Cell takes care of all legal activities related to the functioning of the Institute.

[vii] *Security*

The safety & security aspects of the Institute are taken care of by this Section.

B. FINANCE & ACCOUNTS

This Division takes care of all financial matters of the Institute which is of the tune of more than Rs. 20 crores per year.

C. STORES & PURCHASE

This Division takes care of purchase of materials from the country as well as from abroad.

Official Language activities of the Institute

The Institute has seen various activities of the Official Language in the Institute. Few employees had been awarded for working in the Official Language in their day to day work.

The workshops for Hindi passed employees as well as administrative officers who need Hindi for their day-to-day work had been successfully completed throughout the year.

The Hindi week of this year was observed from 10th to 14th September, 2007. The whole week saw Hindi written competitions like essay, noting & drafting poetry & extempore competition and wining of prizes. The Chief guest for this occasion was Dr. S.L.S. Purti, Deputy Director, Hindi Teaching Scheme, Home Ministry, Nizam Palace, Kolkata. Sri S.K. Pandey, Senior Training Officer, Central Translation Bureau, Kolkata, was invited as one of the judges for the competitions held on the Hindi Day i.e 14th September, 2007.

Hindi workshop was held on 28th April, 2007. The workshop was conducted by R.S. Gupta, Hindi Officer, Indian Oil Corporation. Another workshop was held on 14th December, 2007 on Hindi Implementation. It was conducted by Shri S.P. Dubey, Hindi Officer, Eastern Railway, Kolkata. A cultural programme was held on 14th September by Rangakarmee named Anataryatra directed by noted dramatist Usha Ganguly.

Extramural Activities

INFECTIOUS DISEASES AND IMMUNOLOGY

Invited Lectures

Dr. H. K. Majumder

Topic : DNA topoisomerases: The hidden treasures
Venue : KVPY Programme at IICB, Kolkata
Date: 16 May 2007

Topic : DNA topoisomerases: Fusion of the genes for bisubunit topo I of *Leishmania* forms an active enzyme with conserved type IB properties
Venue : IISc, Bangalore
Date : 13 June 2007

Topic : Excitements in DNA topoisomerase research in "Leishmania"
Venue : RGCB in the TRENDY's-2007 at Thiruvananthapuram
Date : 28-29 September 2007

Topic : Indian kala-azar: Advances in molecular medicine
Venue : Inauguration of the Department of Medical Biotechnology and Biochemistry at STM, Kolkata
Date : 14 November 2007

Topic : The large subunit of unique bi-subunit topoisomerase I in *L. donovnai* functions as a navigator in type IB topoiosmerase
Venue : 10th A IMBN Conference at ICGEB, New Delhi
Date : December 3-4, 2007

Topic : Excitements in DNA topoisomerase Research
Venue : GRC-2007 at Vedic Village and Sunderban
Date : 18-22 December 2007

Topic : DNA topoisomerase targeted molecular therapy against *L. Donovani*
Venue : US-India Joint Training program workshop on Global Infectious Disease, Jointly organized by JNU, New Delhi and University of Washington at ISB, Hyderabad
Date : 21-24 January 2008

Topic : Heterodimeric type IB topoisomease of *Leishmania*: which subunit is the molecular steer?
Venue : India Brazil Meeting on Infectious Disease 2008 at JNCASR, Bangalore
Date : January 27-28, 2008

Topic : Molecular medicine 'Science Express' off-board Scientific programme. A collaborative presentation of IACS, DST, Science Commuter's forum, BASF, E.Rly and BITM
Venue : Concourse of platform 23, Howrah Stn. (New Complex)
Date : 08 February 2008

Topic : DNA topology & DNA topoisomerases
Venue : UGC Refresher course at Calcutta university, Department of Biochemistry
Date : 07 March 2008

Topic : Molecular Biology of *L. donovani*
Venue : UGC: Refresher course at Calcutta university, Department of Zoology
Date : 10 March 2008

Topic : DNA, DNA topoisomerase and *Leishmania*
Venue : One day seminar on "Present scenario on Chemical an Biochemical research in Kolkata at Presidency College
Date : 18 March 2008

Topic : Solving the topological problems of kDNA of Leishmania, a protozoan parasite by the wonder enzyme DNA topoisomerases
Venue : Vidyasagar College, Kolkata on the occasion of 100th year celebration of the Department of Physics & Chemistry
Date : 19 March 2008

Dr. Pijush K. Das

Topic : Targeted drug delivery for macrophage-associated diseases using visceral Leishmania as model macrophage disease
Venue : International Symposium of Control Release in Infection and Cancer, CDRI, Lucknow.
Date : 18 June 2007

Topic : Immunomodulator of natural origin for macrophage associated diseases.
Venue : RNC 90th Birthday Celebration Symposium, CGCRI, Kolkata.
Date: 03 August 2007

Topic : Robust immunomodulatory activity of a natural triterpene from licorice root for macrophage associated diseases.
Venue : 34th Indian Immunology Society Conference, National Aids Research Institute (NARI), Pune.
Date : 16-18 December 2007

Topic : Role of intracellular cAMP in differentiation coupled induction of resistance against oxidative damage in *Leishmania donovani.*
Venue : 8th International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules, CCMB, Hyderabad.
Date : 21-25 January 2008

Topic : Phosphodiesterase mediated regulation of cAMP pool in *Leishmania donovani* stress response.
Venue : Molecular Immunology Fourm, IMTECH, Chandigarh.
Date : 14-16 March 2008

Dr. Chitra Mandal

Topic : 9-O-Acetylated GD3 in Leukemia
Venue : Institute of Biological Chemistry, Academic Sinica, Taipei, Taiwan.
Date : 8-12 July 2007

Topic : Structural analysis of a bacterial 9-*O*acetylated sialoglycoprotein found in patients suffering from visceral leishmaniasis in the Indian subcontinent
Venue : Luebeck, Germany.
Date : 2-7 September 2007

Topic : 9-O-acetylated sialic acids on haematopoietic stem cells of childhood acute lymphoblastic leukaemia.
Venue : Organized by CNCI held at Science city, Kolkata.
Date : 1-3 November 2007

Topic : Identification of a glycosylated bacterial ABC-type phosphate transporter from patients with Visceral Leishmaniasis.
Venue : Centre for Cellular and Molecular Biology, Hyderabad.
Date : 21-25 January 2008

Topic : Glycoproteomics of *Pseudomonas aeruginosa*, an opportunistic Pathogen.
Venue : Cairns, Queensland, Australia.
Date : 22-26 June 2008

Dr. Syamal Roy

Topic : Membrane biophysics in Leishmania donovani infection
Venue : Dormy House II Meeting, University of York
Date : 26 September 2007

Topic : Membrane biology of Leishmania infection.
Venue : Sir William Dunn School of Pathology, Oxford
Date : 30 September 2007

Topic : Inhibition of ABC transporters abolishes antimony resistance in *Leishmania* infection at trypanosomiasis, leishmaniasis and malaria meeting
Venue : British Society of Parasitology, Newcastle University, UK
Date : March 2008

Topic : Hybrid cell vaccination cures late stage *L. donovani* infection revealing contra-suppressive role of CD8+T cells in Th2 locus cytokine regulation
Venue : INDO-Brazil meeting, Bangalore
Date : January 2008

Dr. Nahid Ali

Topic : Drug-induced differential immunomodulation in kala-azar: implications for the development of PKDL
Venue : Guha Research Conference (GRC), Vedic Village (Kolkata) and Sunderbans, West Bengal
Date : 18-22 December 2007

Dr. Malini Sen

Topic : Wnt signaling in rheumatoid arthritis pathogenesis
Venue : Orthopedic Research Society Meeting, CA, USA
Date : 1-4 March 2008

Chairing a session

Dr. H. K. Majumder

Title: Excitements in DNA topoisomerase research in "*Leishmania*" – lecture delivered at RGCB in the TRENDY's-2007 at Thiruvananthapuram on September 28-29, 2007 and also chaired the session.

Dr. Pijush K. Das

Chaired a session on Cell Biology at the 76th Meeting of Society of Biological Chemists, Sri Venkateswara University, Tirupati on November 25-27, 2007.

Chaired a session on Immunoregulation and Immunomodulation at 34th Indian Immunology Society Conference, NARI, Pune on December 17, 2007

Dr. Chitra Mandal

Chaired a session in the conference "The Molecular Immunology of Complex Carbohydrates-3 (MICC-3)" at Institute of Biological Chemistry, Academic Sinica, Taipei, Taiwan during 8-12 July 2007.

Dr. Syamal Roy

Session on: Intervention (Dormy House II meeting) University of York , September 27, 2007.

Dr. Mridula Misra

Session on: 'Radiopharmacy and Radiochemistry' on 9th December 2007 at 39th Annual Conference of "Society of Nuclear Medicine India", held on 6th to 9th December 2007 at Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow.

Academic Performance: Teaching, examining and training

Dr. H. K. Majumder

a) Guest Professor, Department of Biophysics, Molecular Biology and Genetics, Calcutta University,
b) NIPER, Kolkata.

Dr. Pijush K. Das

Guest Professor, M.Sc. (Biophys & Mol. Biol), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) of Calcutta University, M.Tech (Biotech) of Jadavpur University and M.Tech (Biotech) of West Bengal University of Technical Education for teaching Biochemistry and Cell Biology.

Examiner in the M.Sc. (Biochemistry), M.Sc. (Biophysics & Molecular Biology), M.Sc. (Biotechnology), M.Sc. (Microbiology), M.Sc. (Genetics) at Calcutta University and M.Tech. (Biotech) at Jadavpur University.

Dr. Chitra Mandal

Guided a project of a summer research fellow, Mr. Srinivas R for the partial fulfillment of M.Sc, Annamalai University sponsored by the Indian Academy of Sciences, Bangalore from April to July 2007.

Guided a project of a summer research fellow Anubhab Nandy, a student of biochemistry from Calcutta University during his project from 23rd May- 23rd July 2007.

Guided a project of a summer research fellow, Ms Pujarini Dutta, student of Jadavpur University, Department of LifeScience and Biotechnology for a three-month period from July to September 2007.

Guided a project of a summer research fellow, R. Viswanathan, doing M.Sc Biochemistry in Bharathidasan University for the partial fulfillment of M.Sc, Thrichirapalli from December 2007 to May 2008.

Guided a project of a summer research fellow, Ms Neelima Kumar, for the partial fulfillment of M.Sc (Genomics), Madurai Kamaraj University, Madurai sponsored by the Indian Academy of Sciences, Bangalore during April-July 2008.

Teaching Immunology (Stem cells) in the course work offered to PhD student of IICB, Kolkata.

Teaching College teacher on Status and scope of Stem cells, 7th March Science College.

Dr. Nahid Ali

Teaching Immunology in the course work offered to Ph.D. students of IICB.

Evaluated research proposals submitted to CSIR and ICMR.

External examiner of Ph.D. thesis and viva-voce of Devi Ahilya Viswa Vidyalaya, Indore.

Supervised six students (Paulomi Biswas, Kalayani University; Rajani Gupta, Calcutta University; Saheli Chakraborty, Bethune College; Saswati Ghosh, Anna University; Abhishek Kumar, Sathyabama University; Saurav Rawal, University of Rajasthan) in the mandatory project work as part fulfillment of their various degrees like M.Sc., M.Phram., B.Tech. and B.E.

Dr. Rukhsana Chowdhury

Examiner in M.Sc. (Biochemistry), M.Sc. (Genetics), M.Sc. (Biotechnology) Calcutta University

Member of Ph.D committee, West Bengal University of Health Sciences

Reviewer for Nucleic Acids Research, BBA-Proteins and Proteomics, FEBS Lett.

Dr. Rupak K. Bhadra

Acted as an external examiner of Ph.D. viva voce examination of Jadavpur University, Kolkata.

M.Sc examiner of Department of Microbiology, Bijoygarh College.

Examiner of PhD thesis, JNU, New Delhi and Kerala University.

Evalutated research proposals submitted to DST, DBT, CSIR etc. for funding

Supervised students (Archana Bharti, Bhagalpur University; Roshni Roychoudhury, Madurai Kamraj University) in dessertation work as part of fulfillment of their M.Sc. and M.Tech degrees.

Dr. Tripti De

Examiner - M.Sc. Part II, Department of Biochemistry and Biophysics, University of Kalyani

Deputation Abroad

Dr. Chitra Mandal

To deliver a lecture and chair a session in the symposium on "The molecular immunology of complex carbohydrates-3 (MICC-3)" at Institute of Biological Chemistry, Academic Sinica, Taipei, Taiwan during 8-12 July 2007.

Deputation from 1-7 September 2007 to Lubeck, Germany for delivering an invited talk and attending a conference in the symposium on "EUROCARB 14"

Attend the Joint Symposium of the 4th Asian and Oceania Human Proteome Organization (AOHUPO) and the 2nd Pacific-Rim International Conference on Protein Science (PRICPS) during 22-26 June 2008 at Cairns, Queensland, Australia and deliver an invited talk.

Dr. Syamal Roy

Round Table Meeting on "Novel approach to the immunotherapy of leishmaniasis", Berlin, June 25-26, 2007

Dormy House II Meeting- September 24-27, 2007 University of York, York, UK

Leish-Risk Workshop, November 12-14, 2007, Institute of Tropical Medicine, Antwerp, Belgium

British Society of Parasitology Meeting, Newcastle University, March 29-April 1, 2008

Papers / Abstract presented in the Conference

Dr. Chitra Mandal

Chandan Mandal, *Avijit Dutta, Asish Mallick, Laxminarain Misra, Rajender Sangwan, Sarmila Chandra and Chitra Mandal. A novel anti-leukemic pure natural compound, induces mitochondria dependent apoptosis of lymphoblasts in the childhood acute lymphoblastic leukemia (ALL) by activating p38 MAP kinase signaling cascade. 8th International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules' Centre for Cellular and Molecular Biology, Hyderabad, India, 21-25 January, 2008.

Angana Ghoshal, Bibhuti saha, and *Chitra Mandal. Antibodies directed against O-acetylated sialoglycoconjugates triggers programmed cell death in erythrocytes of visceral leishmaniasis. 8th International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules' Centre for Cellular and Molecular Biology, Hyderabad, India, 21-25 January, 2008.

Susmita Mondal, Chandan Mandal, Sarmila Chandra and Chitra Mandal. Differential expression of sialyltransferases in childhood acute lymphoblastic leukemia. 8th International Symposium on Biochemical Roles of Eukaryotic Cell Surface Macromolecules' Centre for Cellular and Molecular Biology, Hyderabad, India, 21-25 January, 2008.

Suchandra Chowdhury, Suman Bandyopadhyay, Chandan Mandal, Sarmila Chandra and Chitra Mandal. · Mobilization of lymphoblasts from bone marrow to peripheral blood in childhood acute lymphoblastic leukaemia - role of 9-O-acetylated sialoglycoproteins governing the egress 8th International Symposium on Biochemical

Roles of Eukaryotic Cell Surface Macromolecules' Centre for Cellular and Molecular Biology, Hyderabad, India, 21-25 January, 2008.

Chowdhury S, Bandyopadhyay S, Mandal C, Chandra S and Mandal C. Flow-cytometric monitoring of disease-associated expression of 9-O-acetylated sialoglycoproteins in combination with known CD antigens, as an index for MRD in children with acute lymphoblastic leukaemia: a two-year longitudinal follow-up study" in "CME 2007: Scientific Meet on Haemato-Oncology", Kolkata 07 –09 September 2007.

Dr. Nahid Ali

Mazumder, S., Ravindran, R., Banerjee, A. and Ali N. Non-coding pDNA bearing immunostimulatory sequences: development of a new adjuvant against visceral leishmaniasis. U.S. India Joint Research Training Programme, Training on intracellular pathogens workshop, Hyderabad, Janunary 21-24, 2008.

Dr. Rupak K. Bhadra

Sangita Shah, Bhabatosh Das and Rupak K. Bhadra on 'Molecular characterization of the cgtA gene function in Vibrio cholerae' at the Symposium on Frontiers in Biological Research' held during August 3-5, 2007 at Viswa Bharati, Shantiniketan, West Bengal, India.

Kalpataru Halder, Bhabatosh Das and Rupak K. Bhadra on 'Genetic organization of CTX prophage in relation to evolution of new pathogenic Vibrio cholerae strains' (in Bengali) at the West Bengal State Science and Technology Congress held during February 28-29, 2008 at Bengal Engineering Science University, Sibpur, Howrah, West Bengal, India.

Sangita Shah, Bhabatosh Das and Rupak K. Bhadra on 'Characterization of an essential small G-protein coding gene cgtA of Vibrio cholerae' at the West Bengal State Science and Technology Congress held during February 28-29, 2008 at Bengal Engineering Science University, Sibpur, Howrah, West Bengal, India.

Dr. Tripti De

Immuno stimulating glycophosphosphingolipid antigen from leishmania donovani is recognized by visceral leishmaniasis patient sera. 8th ISCSM, January 2008, Hyderabad, India.

UDP-Gal: N-Acetylglucosamine â1-4 galactosyltransferase expressing live attenuated parasites as vaccines for Leishmaniasis. 8th ISCSM, January 2008, Hyderabad, India.

Dr. Mita Chatterjee Debnath

K. K. Halder, S. Pal, M. Chatterjee Debnath. Rapid diagnosis of myocardial cell damage in rats by novel radiotracer. 39th Annual Conference of Society of Nuclear Medicine, India, Lucknow, December 6-9, 2007.

B. Mandal, K. K. Halder, S. K. Dey, L. K. Ghosh, and M Chatterjee Debnath. Evaluation of chloramphenicol loaded PLGA Nanoparticles. 1st Pharm Tech IAPST Internal Conference on Drug Delivery and Drug Targeting Research, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, Janauary 19-20, 2008.

Dr. Mridula Misra

Susmita Chandra, Kakali De, Mridula Misra. "Solid phase synthesis of 99mTc peptide radiopharmaceutical using Fmoc chemistry for scintigraphic imaging"at 39th Annual Conference of "Society of Nuclear Medicine India", held on December 6-9 2007.

Kakali De, Susmita Chandra, Mridula Misra. "The Effect of Bacopa Monnieri extracts on biodistribution of technetium-99m labeled radiopharmaceuticals" at 39th Annual Conference of "Society of Nuclear Medicine India", held on December 6-9, 2007.

Conference/ Symposia / Workshops Organized

Dr. Mridula Misra

As convener of Radioactive, Chemical Safety and Bio-Safety Committee a "Training Programme and Workshop on Laboratory Safety" (Chemical Safety, Radioactive Safety and Bio-Safety) has been organized on 20th September 2007 for the students and staff of IICB, Kolkata.

Major Infrastructural facilities

Dr. (Mrs.) Chitra Mandal

Helped in developing Proteomic center.

Dr. Rupak K. Bhadra

Establishment of functional BSL-3 laboratory facility.

Maintenance of Scanning Electron Microscope (Tescan, Model VEGA II LSU) facility

Dr. (Mrs) Mridula Misra

Implementing the radiation safety aspects in research application of ionizing radiation.

As convener of the Radioactive and Chemical Safety Committee of IICB a booklet "Radiation Safety Guideline" and another booklet "Guidelines for Chemical Safety" as a co-author has been prepared for the students and staff members of IICB for the safe use of radioisotopes, which will be distributed in all the laboratory of IICB.

Procurement and distribution of radioactive materials for research from BARC, Mumbai and abroad like Amersham, NEN etc., Maintenance of the Central Radioactivity Facility of IICB, TLD badge service and radioactive waste disposal facility for the radioisotope user scientists/technical staff/fellows.

CELL BIOLOGY & PHYSIOLOGY

Invited Lectures

Dr. Sib Sankar Roy

Topic : Pitx2, a multifunctional transcription factor in ovary: its implication in hypothyroidism associated ovarian dysfunction.
Venue : 6th Congress of AOSCE, held at North Bengal University, India.
Date : December 10-14, 2007

Dr. Tuli Biswas

Topic : Morphological alterations in erythrocytes promote development of anemia in human population exposed to arsenic through drinking water in West Bengal
Venue : National Symposium on " Problems of Anemia in India : Genetics and Environment", In connection to the Platinum Jubilee Celebration of Ramkrishna Mission Seva Pratishthan ; Vivekananda Institute of Medical Sciences at Kolkata.
Date : November 30- December 02, 2007

Dr. Syed N. Kabir

Topic : Experimental galactose toxicity in rats produces bio-inactive isoform(s) of FSH and induces ovarian refractoriness to gonadotropins
Venue : Molecular and clinical aspects of gonadal and non-gonadal actions of gonadotropins, All India Institute of Medical Sciences, New Delhi, India.
Date : February 7-9, 2008

Topic : The rate of follicular atresia inversely correlates with the prevailing size of ovarian follicular reserve.
Venue : 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE) North Bengal University, Siliguri, India
Date : December 10-14, 2007

Topic : Projections of anti-HIV potential of Acaciaside-B: Hope for the development of prophylactic contraceptive for prevention of HIV epidemic.
Venue : 95th Indian Science Congress, Andhra University, Visakapatnam, India.
Date : 2-7 January 2008,

Topic : Acaciaside B, a prospective candidate molecule towards development of prophylactic contraceptive for HIV epidemic.
Venue : Recent trends in Reproductive Health Research, Hyderabad, India.
Date : 20-22 February 2008

Dr. Arun Bandyopadhyay

Topic : Molecular Mechanism of glucocorticoid-induced cardiac malfunction in rat
Venue : 6th Congress of the Asia and Oceania Society for Comparative Endocrinology, University of North Bengal.
Date : December 10-14, 2007.

Topic : Mechanism of dysfunction of cardiac myocytes by glucocorticoid in rat heart
Venue : XIIIth All India Congress of Cytology and Genetics and International Symposium on Genomic and proteomic Approaches to Decipher the Molecular Basis of Pathogenesis, Osmania University, Hyderabad.
Date : December 28-30, 2007

Topic : Molecular Mechanism of Disease Process: Current Approach
Venue : Hanyang Asia Science Forum (in Life Sciences), Seoul, S. Korea
Date : February 28-March 1, 2008.

Chairing sessions:

Dr. Sumantra Das chaired a session on Autism in the International Symposium on Advances in Neuroscience and Silver Jubilee Conference of Indian Academy of Neuroscience 2007 held at Benaras Hindu University during November 22 – 24, 2007.

Academic Performance: Teaching, examining and training

Dr. Tuli Biswas

Teaching of Physiology in the Coursework offered to PhD students of IICB, Kolkata.

External examiner of PhD thesis and viva-voce of Calcutta University.

Supervised the project work of Ms. Joyita Ghosh from Calcutta University (MSc-Biochemistry).

Dr. Sib Sankar Roy

UGC visiting teacher at Tripura University, Agartala to teach a course in Molecular Biology and Genetics for MSc students.

Teacher of course-work for the PhD students in IICB, Kolkata.

Examiner in the MSc (Biochemistry), MSc (Microbiology) at Calcutta University, MSc (Life Science) at Tripura University, Agartala.

Acted as external examiner for the PhD (Sc) Viva Voce examination of Jadavpur University for 4 PhD students of different Institute.

Supervised the project work of two students from Calcutta University (MSc-Biochemistry) and one student from West Bengal University of Technology (Department of Biotechnology) who have worked as summer trainee during March-July, 2007.

Dr. Syed N. Kabir

Guest lecturer and Examiner, M.Sc, Physiology, Calcutta University.
Guest lecturer and Examiner, M.Sc, Physiology, Vidyasagar University.
Guest lecturer, M.Sc, Physiology, Krishnath College, Murshidabad.
Guest lecturer, M.Sc, Physiology, Kalyani University.
Guest lecturer, M.Sc, Physiology, Rammohan College, Kolkata.
Examiner, M.Sc, Physiology, Presidency College, Kolkata.
Examiner, M.Sc, Zoology, Kalyani University.
Examiner, M.Sc, Zoology, Maulana Azad College, Kolkata.

Dr. Tushar Chakraborty

Resource Person & Lecturer on M Sc Course in Science Communication conducted by the National Council of Science Museum & BITS, Pilani, 2007.

Lecturer and Examiner of NIPER, Kolkata.

Delivered a Talk on History of Biochemistry in 20th Century at Asiatic Society, Calcutta as a part of History of Science Course.

Supervised the project work of two M. Sc. students working as Summer Trainee.

Dr. K. P. Mohanakumar

Supervised the project works of Mr. O. A. Stephen, Lecturer, Ladoke Akintola University of Technology, Nigeria for ten months w.e.f 29.01.2008 under the Research Training Fellowship for Developing Country Scientists (RFTDCS), Mr. A. Vijayakumar, a student of Dr. O. P. Agarwal, Emeritus Scientist and Hony. Prof. of Pharmacology, DIPSAR, New Delhi for one month from 29th July, 2007, Mr. Pijus Kanti Barman of Guru Nanak Deb University, Amritsar as a Summer Trainee from 28th May, 2007 to 20th July, 2007, Ms Preeti Solanki, a student of Dr. Shashi Bala Singh, Additional Director of Defence Institute of Physiology and Allied Sciences, Defence Research and Development Organisation, Delhi for training in HPLC-ECD for a period of 9 days from 22.07.07. Also guided Mr. R. Saravana, a student of Dr. Nibedita Lenka, NCCS, Pune, for completing the behavioural and immunohistochemical studies for two weeks from 29.07.2007 and Mr. Pankaj Dixit, Project Associate in the laboratory of Dr. S. N. Umathe, Asst. Professor, Pharmacology of Rashtrasant Tukdoji Maharaj Nagpur University, Nagpur on micro-punch technique of brain nuclei for five days w.e.f. 12th March, 2008.

Dr. Sumantra Das

Delivered a course of lectures on Neurobiology as part of curriculum (Special paper) for second year M. Sc. students of the Department of Biochemistry as well as first year M. Sc. students of the Department of Neuroscience, Calcutta University.

Lecturer and Examiner of NIPER, Kolkata

External examiner & Question setter for M. Sc. / Ph.D in Neuroscience at the National Brain Research Centre, Manesar, Haryana.

Ph. D. Thesis examiner (external) at the Banaras Hindu University.
Supervised the project work of two M.Sc. students working as Summer Trainee.

Deputation Abroad

Dr. Arun Bandyopadhyay worked as a visiting scientist in the Department of Life Science, Gwangju Institute of Science and Technology, Gwangju, S. Korea during March 1-21, 2007.

Conference / Symposium / Workshops

Dr. Syed N. Kabir served as a member of the Organizing Committee of the International Conference on Molecular & Clinical Aspects of Gonadal and Nongonadal Actions of Gonadotropins, AIIMS, New Delhi, 7-9 February 2008.

Papers / Abstract presented in the Conference

Bandyopadhyay A, Ghose Roy S, De, P, Chander V. Molecular Mechanism of glucocorticoid-induced cardiac malfunction in rat, presented at the 6th Congress of the Asia and Oceania Society for Comparative Endocrinology, University of North Bengal, December 10-14, 2007.

Bandyopadhyay A, De P, Ghose Roy S. Mechanism of Dysfunction of Cardiac myocytes by Glucocorticoid in Rat Heart presented at the XIIIth All India Congress of Cytology and Genetics and International Symposium on Genomic and proteomic Approaches to Decipher the Molecular Basis of Pathogenesis, Osmania University, Hyderabad, December 28-30, 2007.

Samir Kumar Saha, Shyam Sundar Nandi, Pamela Ghosh, Samir Bhattacharya and Sib Sankar Roy. A parallel and compensatory pathway of collagen metabolism is activated in hypothyroid ovary. 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE), December 10-14, 2007, North Bengal University.

Pamela Ghosh, Shyam Sundar Nandi, Samir Kumar Saha, Sudarshan Bhattacharya, Samir Bhattacharya and Sib Sankar Roy. Pitx2, a multifunctional transcription factor in ovary: Its implications in hypothyroidism associated ovarian dysfunction. 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE), December 10-14, 2007, North Bengal University.

Debleena Dey, Anirban Bhattacharya, Dipanjan Basu, Pomy Barma, Malabika Datta, Sib Sankar Roy, Arun Bandyopadhyay and Samir Bhattacharya. Fatty acid induced downregulation of insulin receptor gene is linked to PKCe and HMGA1 phosphorylation. 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE), December 10-14, 2007, North Bengal University.

Tanima Kundu and Sib Sankar Roy. Interactions of Cytokines and Matrix Metalloproteinases in epithelial ovarian cancer. 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE), December 10-14, 2007, North Bengal University.

Pomy Barma, Anirban Bhattachrya, Anindita Biswas, S. S. Roy, B.C. Pal, S. Bhattacharya. A parallel and compensatory pathway of collagen metabolism is activated in hypothyroid ovary. 6th Congress of the Asia and Oceania Society for Comparative Endocrinology (AOSCE), December 10-14, 2007, North Bengal University.

P Ghosh, S. S. Nandi, S. K. Saha, S. Bhattacharya and S. S. Roy. Pitx2, a multifunctional transcription factor in ovary. SBC symposium on “Frontiers in Biological Research”, held at Visva Bharati University, Santiniketan, August 3-4, 2007.

S. Biswas, S. Tarafdar, D. Pal, P. Chakraborty, S.N. Kabir The size of ovarian follicular reserve inversely modulates the rate of follicular atresia. Symposium on Recent Trends in Reproductive Health Research & 18th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, at Hyderabad, India on February 20-22, 2008.

P. Chandran, B. C. Pal, S.N. Kabir. Spermicidal potential of Acaciaside-C, a novel triterpene glycoside isolated from Acacia auriculiformis. Symposium on Recent Trends in Reproductive Health Research & 18th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, at Hyderabad, India on February 20-22, 2008.

P. Chakraborty, S. Biswas, B.N. Chakravarty, S.N. Kabir. Early postnatal androgenization of female rats: further evidence in support of its suitability as a working model of polycystic ovarian disease. Symposium on Recent Trends in Reproductive Health Research & 18th Annual Meeting of the Indian Society for the Study of Reproduction and Fertility, at Hyderabad, India on February 20-22, 2008.

S.N. Kabir, H.N. Ray, B.C. Pal, D. Mitra. Acaciaside-B: a prospective candidate molecule for development of prophylactic contraceptive for HIV epidemic. 23rd Annual Meeting of The European Society of Human Reproduction and Embryology, Lyon, France, July 1-4, 2007.

J. Chakrabarti, S. Banerjee, D. pal, S. Aditya, S.K. Goswami, B.N. Chakravarty, S.N. Kabir. The rate of ovarian follicular atresia is modulated by the size of follicular pool. 23rd Annual Meeting of The European Society of Human Reproduction and Embryology, Lyon, France, July 1-4, 2007.

Gangopadhyay P. K, Borah A, Samanta A and Mohanakumar K. P. Homocysteine and cognition International Symposium on Advances in Neurosciences and Silver jubilee Conference of Indian Academy of Neurosciences, Nov. 22-25, 2007, Banaras Hindu University, varanasi, India.

Varghese M, Hareendran S, Borah A Navneet A. K and Mohanakumar K. P. Inclusion body formation in rotenone model,s of Parkinson,s disease in vitro and in vivo: Effect of quercetin, IBRO world Congress of Neuroscience, Melbourne, July 12-17, 2007, Australia.

Tathagata Sengupta, C. Pal, D Nandi, P Jaisankar and K. P. Mohanakumar: “An Ayurvedic preparation possesses novel ingredients active against experimental Parkinson’s disease”, 3rd International Symposium on “Neurodegeneration & Neuroprotection” and Society for Neurochemistry (India) Meeting, 2007.

MOLECULAR & HUMAN GENETICS

Invited lectures

Dr Samit Adhya

Topic : Use of a parasite-derived protein complex to modulate the function of mitochondria in human cells, Strategies for Engineered Negligible Senescence (SENS3),
Venue : Queen's College, Cambridge, UK
Date : September 6-10, 2007.

Invited lectures

Dr. Keya Chaudhuri

Topic : Repeat number variation in the promoter region of XRCC5 gene associated with increased susceptibility to oral cancer.
Venue : Symposium on Recent Trends in Cancer Research & Treatment at Science City, Kolkata.
Date : November 2, 2007

Invited lectures

Dr. Kunal Ray

Topic : Molecular Genetic Studies on Human Pigmentary Disorder
Venue : SBC Kolkata chapter meeting at Visvabharati, Santiniketan
Date : August 3-5, 2007

Topic : Studies on Glaucoma Genetics
Venue : CME on Dry Eye & Glaucoma from Community Eye Health Angle at Hotel Larika, Digha, Purba Midnapur, W.B.
Date : August 15, 2007

Topic : Genetics of Wilson's Disease
Venue : Bangur Institute of Neurology & Psychiatry
Date : August 18, 2007

Topic : Molecular Genetic Studies on Human Diseases
Venue : Annual Meeting West Bengal Academy of Science and Technology, CGCRI, Kolkata,West Bengal
Date : August 2007

Topic : Potential Functional Diversity of CYP1B1 in the Context of Glaucoma
Venue : Symposium on Trends in Human Genetics at Toshali Sands, Puri, Bhubaneswar.
Date : August 20-21, 2007

Topic : Molecular genetic studies on oculo-cutaneous albinism: a disorder related to human pigmentation.
Venue : Guha Research Conference at Vedic Village & Sunderbans
Date : December 18-22, 2007

Topic : Molecular diagnosis of Wilson Disease using prevalent mutations and informative single nucleotide polymorphism markers.
Venue : XIIIth All India Congress of Cytology and Genetics & International Symposium at Osmania University, Hyderabad
Date : December 28-30, 2007.

Topic : Genetics of Wilson's Disease: Kolkata Experience
Venue : National Conference on Wilson's Disease at Christian Medical College, Vellore
Date : February 6, 2008

Invited lectures

Dr. A.K. Giri

Topic : Arsenic Induced Health Problems in India: Involvement of Genetic Susceptibility and Chromosome Aberrations.
Venue : 5th International Conference on Environmental Mutagens in Human Populations at Talya, Turkey
Date : May 20 - 24, 2007.

Topic : Cytogenetic Damage and Genetic Variants in Individuals Susceptible to Arsenic-Induced Cancer.
Venue : 38th Annual meeting of EMS, USA at Atlanta, Georgia, USA
Date : October 20-24, 2007.

Topic : "Invited Symposium talk at the 1st Asian Conference on Environmental Mutagens"
Venue : Kitakyushu International Conference Centre, Japan.
Date : November 29-30, 2007.

Topic : "Deficiency in DNA Repair May be the Prime Contender for Arsenic Susceptibility: Evidence from Challenge Assay"
Venue : The 13th All India Congress of Cytology and Genetics, at the Osmania University Hyderabad.
Date : December 28-30, 2007.

Topic : "Arsenic Induced Toxicity and Genetic Damage: Genetic variants and Sub-optimal DNA Repair may Lead to Arsenic Susceptibility"
Venue : Aligarh Muslim University, Aligarh
Date : January 1-3, 2008.

Invited lectures

Dr. Susanta Roychaudhury

Topic : Influence of cytokine gene polymorphism in *Helicobacter pylori* mediated gastroduodenal disease, National Seminar on "Genome analysis perspective in the post-genomic era and its relevance to society."
Venue : Mahatama Gandhi National Institute of Research and Social Action, Hyderabad.
Date : October 26-28, 2007.

Topic : Insight into Spindle assembly checkpoint defects in human cancers: CDC20 overexpression leads to aneuplodization in oral cancer.
Venue : 2nd International Symposium on Translational Research on Natural products and cancer, Society of Translational Cancer Research, Lonavala, Mumbai.
Date : December 9-12, 2007

Topic : Genetic polymorphism in p53 related genes modulates the risk of tobacco associated leukoplakia and oral cancer
Venue : XIIIth All India Congress of Cytology and Genetics, Osmania University, Hyderabad.
Date : December 28-30, 2007.

Topic : Mechanistic Insight into Spindle Assembly Checkpoint of Cell Cycle
Venue : 95th Indian Science Congress, Visakhapatnam
Date : January 3-7, 2008

Topic : Spindle assembly checkpoint: a frequent target for causing aneuploidy in tumor cell.
Venue : National Centre for Biological Sciences, Bangalore.
Date : February 23-25, 2008

Topic : Pro-inflammatory cytokine IL1B down regulates the expression of gastric acid stimulating hormone gastrin.
Venue : Annual Meeting of Molecular Immunology Forum-2008 at Institute of Microbial Technology, Chandigarh.
Date : March 14-16, 2008

Session Chairman

Dr. Kunal Ray chaired a session in the Annual Meeting of the Indian Eye Research Group at LV Prasad Eye Institute, Hyderabad (July 28-29, 2007).

Dr. Kunal Ray chaired a session in the XIIIth All India Congress of Cytology and Genetics & International Symposium on "Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis" organized by Osmania University, Hyderabad (December 28-30, 2007)

Dr. A. K. Giri chaired a Symposium Session at the XXXIII Annual Conference of Environmental Mutagen Society of India (EMSI) which was held at the Aligarh Muslim University, Aligarh (January 1-3, 2008)

Academic Performance / Teaching

Dr. Samit Adhya

Honorary lecturer department of biophysics Molecular biology and genetics Calcutta University

Dr. Keya Chaudhuri

Examiner of the M.Sc. (Biotechnology), Calcutta University.
Reviewer of papers in DNA and Cell Biology, BMC Genomics, Gene

Dr. Kunal Ray

An honorary lecturer and examiner of the M. Sc. (Biotechnology), M. Sc. (Genetics), M. Sc. (Microbiology), and M. Sc. (Neuroscienes), Calcutta University. Teaches Medical Genetics.

Delivers lectures in the UGC sponsored courses in Calcutta University

Member (External Expert) of a committee to perform function of Postgraduate Board for M.Sc. course in Genetics

Member of Monitoring Committee for National Fund for Basic & Strategic Research (NFBSRA)

Evaluates research proposals submitted to DST, DBT, CSIR etc. for funding.

Supervised eight students in the mandatory project work as part fulfillment of their various degrees like BTech, MSc and MTech.

Associate Editor, Journal of Genetics, Springer

Reviewed papers for (i) Investigative Ophthalmology & Visual Sciences, (ii) Molecular Vision, (iii) BMC Genetics, (iv) BMC Molecular Biology, (v) Archives of Ophthalmology, (vi) Journal of Biosciences, (vii) Journal of Investigative Dermatology, (viii) Journal of Genetics

Dr. A.K. Giri

Working as a Teacher and also as an Examiner at the Genetic Department, Centre of Advanced Study, Department of Botany, University of Calcutta.

Dr. Susanta Roychowdhury

Cell Biology course in M. Sc. (Biophysics, Molecular Biology & Genetics), Calcutta University.

Cancer Genetics course in M.Sc. (Biotechnology), Calcutta University.

Cancer Genetics course in integrated Ph.D, West Bengal University of Technology, Kolkata.

Human Genetics course in integrated M.Sc. curriculum of Indian Institute of Science Education and Research, Kolkata.

Dr. Samir Dutta

M. Tech Classes (Cal. Univ), M. Pharm (J. U.) dissertation examination etc.

Papers/Abstracts presented in the Conference

Rajdeep Chowdhury, Suchandra Chowdhury, Paromita Roychoudhury, Chitra Mandal and Keya Chaudhuri. 'Menadione (Vitamin K) enhances sodium arsenite induced apoptosis through ROS generation and modulation of survival signaling pathways I malignant melanoma A375 cells'. A symposium organized by the Society of Biological Chemists (India)-Kolkata Chapter at Santiniketan, West Bengal.

Pratim Chaudhuri, Sanjay Nag and Keya Chaudhuri. 'Mutation of gsk1 gene in *Vibrio cholerae* causes pleiotropic changes in virulence properties of the pathogen'. A symposium organized by the Society of Biological Chemists (India)-Kolkata Chapter at Santiniketan, West Bengal.

Susri Roychoudhury, Ranjan Rashmi Paul and Keya Chaudhuri. 'Status of GST and CYP genes in Oral Submucous Fibrosis - a precancerous condition'. In SSRR Satellite India 2008 Conference, held on February 11-12, 2008. Organized by Department of Biochemistry, All India Institute of Medical Sciences, New Delhi.

Bhattacharjee, M. Acharya, S. Mookherjee, D. Banerjee, A. Bandopadhyay, S.K.D. Thakur, A. Sen and K. Ray; Evaluation of the Role of *CYP1B1* in POAG Pathogenesis, Annual Meeting of The Association for Research in Vision and Ophthalmology (May 6-10, 2007) at Fort Lauderdale, Florida, USA. [Poster presentation].

Kunal Ray, Moumita Chaki, Mainak Sengupta, Indian Genome Variation Consortium; Genomic variation in the pigmentation genes among indians with special reference to oculocutaneous albinism, 12th Human Genome Meeting organized by HUGO (May 21-24, 2007), Montreal, Canada.

Deblina Banerjee, Ashima Bhattacharjee, Moulinath Acharya, Suddhasil Mookherjee, Sanjay KD Thakur, Arun K Bandyopadhyay, Abhijit Sen and Kunal Ray; Leu432Val Polymorphism in CYP1B1 as a Potential Susceptible Factor towards Predisposition to Primary Open Angle Glaucoma, SBC meeting at Shantiniketan on 'Frontiers of Biological Research' (Aug 3-5, 2007).

Mainak Sengupta, Ananya Ray, Moumita Chaki, Mahua Maulik, Kunal Ray, SNPs in Genes with Copy Number Variation: A Question of Specificity, SBC meeting at Shantiniketan on 'Frontiers of Biological Research' (Aug 3-5, 2007) [Oral presentation].

Moulinath Acharya, Ashima Bhattacharjee, Suddhasil Mookherjee and Kunal Ray; Functional Evidence of *CYP1B1* Involvement in Primary Open Angle Glaucom, Alberta Vision Science Symposium 2007 (August 31-Sep 1, 2007), at the University of Alberta, Edmonton, Alberta, Canada.

Babli Halder, Udayan Bhattacharya, Sibabrata Mukhopadhaya and A. K. Giri (2007) Black Tea Polyphenols Induced Apoptosis through mitochondria Mediated Death Cascade. Poster presented at the XIIIth All India Congress of Cytology and Genetics (AICCG) and International Symposium on Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis which was organized by the Department of Zoology, Osmania University, Hyderabad, Andhra Pradesh from December 28-30, 2007.

Sujata De Chaudhuri, Pritha Ghosh, Kunal Ray, Susanta Roychoudhury and A. K. Giri (2007) Genetic Variants Associated with Arsenic Metabolism and Susceptibility. Poster presented at the XIIIth All India Congress of Cytology and Genetics (AICCG) and International Symposium on Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis which was organized by the Department of Zoology, Osmania University, Hyderabad, Andhra Pradesh from December 28-30, 2007.

Nilanjana Banerjee and A. K. Giri (2007) Chronic Arsenic Exposure Impairs Macrophage Functions and Alters Inflammatory Cytokine Profile. Poster presented at the XIIIth All India congress of Cytology and Genetics (AICCG) and International Symposium on Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis which was organized by the Department of Zoology, Osmania University, Hyderabad, Andhra Pradesh from December 28-30, 2007.

Manjari Kundu, Sujata De Chaudhuri, Susanta Roychoudhury and A.K.Giri (2007) Arsenic Induced Toxicity: Involvement of p53 variant in Arsenic Susceptibility. Poster presented at the XIIIth All India congress of Cytology and Genetics (AICCG) and International Symposium on Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis which was organized by the Department of Zoology, Osmania University, Hyderabad, Andhra Pradesh from December 28-30, 2007.

Mayukh Banerjee and A. K. Giri (2007) Deficiency in DNA Repair: A Clue to Arsenic Susceptibility. Poster presented at the XIIIth All India congress of Cytology and Genetics (AICCG) and International Symposium on Genomic and Proteomic Approaches to Decipher the Molecular Basis of Pathogenesis which was organized by the Department of Zoology, Osmania University, Hyderabad, Andhra Pradesh from December 28-30, 2007.

Udayan Bhattacharya, Babli Halder, Sibabrata Mukhopadhaya and A.K. Giri (2008) Mechanisms of Black Tea Polyphenols Induced Apoptosis in Human Skin Cancer Cells. Poster presented at the International Symposium on the Predictive, Preventive and Mechanistic Mutagenesis and XXXIII EMSI Annual Meeting which was held at the Aligarh Muslim University, Aligarh from January 1-3, 2008

Susanta Roychoudhury, Meenakshi Chakravorty, Dipanjana Datta De, and Abhijit Choudhury IL1B Promoter Polymorphism Regulates The Expression Of Gastric Acid Stimulating Hormone Gastrin. HGM 2007, Montreal, Canada. May 21-24, 2007.

Susanta Roychoudhury, Swati Bajaj, M. Chakraborty, S. Mukhopadhayay**.** Dual approach for screening of chemotherapeutic agents for the restoration of tumor suppressor function of mutant p53 in tumors. 2nd International Symposium on Translational Research on Natural products and cancer, Society of Translational Cancer Research., Lonavala, Mumbai. December 9-12, 2007.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Invited Lectures

Dr. J. R. Vedasiromoni

Topic : Pharmacotherapeutic studies with black tea: from above the ground to underground
Venue : 95th Indian Science Congress, Andhra University, Visakhapatnam,
Date : January 3-7, 2008.

Topic : Anti-neoplastic studies with black tea: from above the ground to underground
Venue : 40th Annual Conference of Indian Pharmacology, Mohali,
Date : December 1-3, 2007.

Topic : Role of Pharmacy in drug Development
Venue : Guru Nanak Institute of Pharmaceutical Science & Technology, Kolkata-700114.
Date : 29th March, 2008

Dr. Pratap K. Das

Topic : Screening of Indian biodiversity and Indian Systems of Medicine in search of gastric anti peptic ulcer principle(s)
Venue : 95th Indian Science Congress, Section of Medical Sciences, Visakhapatnam, Andhra University
Date : January 3-7, 2008

Topic : On gastric ulcer, *Ayurveda* and Indian biodiversity
Venue : Narendrapur Ramakrishna Mission, Kolkata (National Conference on '*Ayurveda*' in Health Care and Its Socioeconomic Impact')
Date : March 29-30, 2008

Topic : On challenges and opportunities in pharma education and research
Venue : Calcutta Institute of Pharmaceutical Technology
Date : March 3, 2008

Dr. Snehasikta Swarnakar

Topic : Metalloproteinases and gastric inflammation
Venue : University of Connecticut Health Center, Farmington, Connecticut, USA,
Date : July 2007.

Topic : Role of matrix metalloproteainases on gastric ulcer
Venue : Lerner Research Institute, Cleveland, Ohio, USA
Date : July 2007.

Topic : Are matrix metalloproteinases potential target for gastric inflammation?
Venue : CME on Haematology and oncology, Kolkata.
Date : September 2007.

Topic : Targeting Matrix Metalloproteinases for Prevention of Gastric Inflammation
Venue : International Drug Discovery Science and Technology, Xi'an, China.
Date : Nov 2007.

Topic : *Azadirachta indica* leaf extracts in preventing gastric ulceration via matrix metalloproteinases
Venue : World Neem Conference, Coimbatore, India.
Date : Nov 2007.

Topic : Targeting metalloproteinases in protecting endometriosis
Venue : ROCG-SAFOG Conference, Kolkata.
Date : Dec 2007

Topic : New insights into gastric inflammation: Identification of novel targets
Venue : Indian Science Congress, Vizak.India.
Date : Jan 2008.

Topic : Bio-molecules in arresting endometriosis via metalloproteinases
Venue : SFRR-Satellite Meeting, New Delhi.
Date : Feb 2008

Dr. Nirmalendu Das

Topic: Nanocapsule as a vector for tissue targeted drug delivery
Venue : International conference on pharmacology and experimental therapeutics at Jadavpur University, Kolkata
Date : January 10-12 2008.

Dr. Anil K. Ghosh

Topic : Antiapoptotic role of S-adenosyl-L-methionine against hydrochloric acid induced cell death in *Saccharomyces cerevisiae.*
Venue : 31th AICBC meeting in BHU, Banaras
Date : December 14 – 16, 2007

Dr. Sharmila Chattopadhyay

Topic : Indian medicinal plant to combat visceral leishmaniasis
Venue : Prof. R.N. Chakraborty 90th Birth Anniversary Celebration: Symposium on Natural Products, CGCRI, Kolkata,
Date : 3rd August, 2007.

Topic : *Nyctanthes arbor-tristis* Linn. – Spectrum of its bioactivity potential. International Conference of the Society of Medicinal Plant Research (Germany) and 55th Annual Meeting,
Venue : Graz, Austria.
Date : 2-6 September 2007.

Topic : Indian Medicinal Plants and its Potential,
Venue : Division of Pharmacognosy, Section Metabolomics, IBL, Leiden University, The Netherlands
Date : September 10, 2007.

Chairing session

Dr. Snehasikta Swarnakar

Chaired a session in International Drug Discovery Science and Technology on "Better drugs by mastering medicinal chemistry", Xian China, Oct 2007.

Academic Performance/Teaching

Dr. Tarun Kumar Dhar

Reviewer of papers to be published in Analytica Chimica Acta, Analytical Chemistry.

Reviewer of project proposals submitted for funding to DST, New Delhi.

Reviewer of Joint R& D projects under Global Innovation and Technology Alliance promoted by DST & CII, India Habitat Centre, New Delhi.

Dr. J. R. Vedasiromoni

Member, Editorial Board of Indian Journal of Pharmacology since 1992.

Reviewer for Life Sciences, Indian Journal of Experimental biology, Indian Journal of Biochemistry & Biophysics, Indian Journal Medical Research, Natural Product Radiance and Journal of Ethnopharmacology.

Member, PG Expert Committee in Physiology, Presidency College, Kolkata.

Nominated as DBT representative on the Institutional Biosafety Committee (IBSC) of National Institute of Cholera and Enteric Diseases (NICED), Kolkata.

Member, Academic Committee of the School of Natural Product studies, Jadavpur University.

Attended the Brainstorming Session on "Seabuckthorn- Problems, Prospects & Need for Biotechnological Intervention" held on 7th September, 2007 in Department of Biotechnology, Ministry of Science & Technology, New Delhi as an invited participant.

Dr. Pratap K. Das

Visiting Faculty in the Department of Bioscience & Engineering, Jadavpur University

Guest Faculty in the Department of Biochemistry, Manipur University

Dr. Snehasikta Swarnakar

M.Sc examiner of Dept. of Microbiology and Biochemstry Calcutta University

Visiting Faculty of M.Sc. course in Environmental Sc., Calcutta University

Question setter of Biology Section of JBNST Examination

Editorial Board member of International Journal of Biomedical Science

Board member of SFRR-ASIA

Reviewer of project proposals submitted for funding to CSIR, New Delhi.

Dr Nirmalendu Das

External Expert, M.Sc Biochemistry Examination 2008 at Kalyani University
External Expert Selection Committee Lecturer Microbiology Dept Scottish Church College, Kolkata.
Nominated as a member of Academic Advisory Council Biotechnology and Microbiology Department at St. Xavier College, Kolkata

Dr. Suman Khowala

Ph. D. examiner of Biochemistry Department, Anna Malai University, Department of Genetics, Madurai Kamraj University.
Reviewer for Applied Biochemistry and Biotechnology, Bioresource Technology, Current Microbiology, Current Trends in Biotechnology and Pharmacy, Biotechnology Progress and Electronic journal of Biotechnology.

Dr. Sharmila Chattopadhyay

Thesis examiner of M.Sc (Biotech), Birsa Agricultural University, Ranchi, Jharkhand.
Reviewer of a project proposal on Plant derived drug development for Senior Research
Reviewer of project proposals submitted for funding to DST, New Delhi
Reviewer of project proposals submitted for funding to CSIR, New Delhi
Reviewer of papers to be published Phytochemistry and Food and Chemical Toxocology.

Deputation abroad

Dr. Snehasikta Swarnakar

Visiting Faculty, Department of Surgery, University of Connecticut, Farmington, Connecticut, USA (from June'07 to Aug'07)

Papers/Abstracts presented in the Conference

Ghosh, P., Besra, S.E., Mitra, S and Vedasiromoni, J. R. 'Apoptogenic effect of tea (*Camellia sinensis* var.*assamica*) root extract (TRE) and two of its steroidal saponins TS1 and TS2 on human leukemic cell lines K562 and U937 and on cells of CML and ALL patients' presented at the XVIII Annual State Conference of Indian Pharmacological Society, West Bengal Branch, Kolkata, December, 14-15, 2007.

Das, T., Vedasiromoni, J.R. and Gomes, A. 'Antileukemic activity of partially purified fraction from Indian spectacled cobra *Naja naja* venom fraction against human leukemic cell lines' presented at the XVIII Annual State Conference of Indian Pharmacological Society, West Bengal Branch, Kolkata, December, 14-15, 2007.
Roy, S., Besra, S.E., Banerjee, B. and Vedasiromoni, J.R. 'Anti-proliferative, cytotoxic and apoptotic activities of *Sweitenia mahagoni* leaf extract in Ehrlich's Ascites carcinoma model in mice' presented at the XVIII Annual State Conference of Indian Pharmacological Society, West Bengal Branch, Kolkata, December, 14-15, 2007.

Mallick, S., Nandi, D., Besra, S. E. and Vedasiromoni, J. R. 'Studies on anti-inflammatory and analgesic activities of *cassia fistula* (Golden shower) fruit extract' presented at the XVIII Annual State Conference of Indian Pharmacological Society, West Bengal Branch,Kolkata, December, 14-15, 2007.

Das Gupta,S., Vedasiromoni, J.R., Gomes, A. Antileukemic activity of Indian black scorpion (*Heterometrus bengalensis* Koch) venom against human leukemic U937 and K562 cells' presented at the XXXX Annual Conference of the Indian Pharmacological Society, NIPER, Mohali, November, 1-3, 2007.

Goswami, S., Pal, A., Annalakshmi, C., Bhakuni R. S., Das, P.K. and Khanuja, S.P.S. 'Anti *Helicobacter pylori* activity of artemisinin derivatives' presented at the 95th Indian Science Congress, Section of Biological Sciences (New Biology), Andhra University, January 3-7, 2008.

Ghanta, S., Banerjee, A., Kumar, A., Chakraborty, A., Bhattacharyya, D. and Chattopadhyay, S. "Production of high value compounds through genetic transformation of pudina" presented at the Symposium on natural products, past, present and future (NPPPF) CGCRI, Kolkata, 3rd August, 2007.

Ghanta, S., Kumar, A. and Chattopadhyay, S. "Tissue-specific overexpression of glutathione in plant system- a dietary supplement" presented at the Society for Biological Chemists (Kolkata Chapter) Shantiniketan, 3rd to 5th August 2007.

Chakraborty, A. and Chattopadhyay, S. "Strategies for the improvement of menthol production in *Mentha piperita* cell culture" in the Society for Biological Chemists (Kolkata Chapter) Shantiniketan, 3rd to 5th August 2007.

Ghanta, S., Chakraborty, A. and Chattopadhyay, S. "Transgenic *Mentha arvensis* overexpressing ã-ECS and/or GS gene" in the National Symposium on Plant Biotechnology for Conservation, Characterization and Crop Improvement & 29th Annual Meeting of Plant Tissue Culture Association (India), Mohanlal Sukhadia University, Udaipur, 8th to 10th February 2008.

Banerjee, A., Bhattacharyya, D. and Chattopadhyay, S. "Development of transgenic *Phyllanthus amarus* by A*grobacterium*-mediated transformation for value addition" presented at the in the National Symposium on Plant Biotechnology for Conservation, Characterization and Crop Improvement & 29th Annual Meeting of Plant Tissue Culture Association (India), Mohanlal Sukhadia University, Udaipur 8th to 10th February 2008. Chakraborty, A., Ghanta, S., Kumar, A., Banerjee, A., Bhattacharyya, D. and Chattopadhyay, S. "Development of transgenic pudina- a heavy metal tolerant" presented at the 15th West Bengal State Science & Technology Congress, Shibpur Bengal Engineering College, 28th to 29th Febrauary 2008.

Conferences / Symposia / Workshops Organised

Dr. (Mrs) Suman Khowala

Convener, Symposium on 'Frontiers in Biological Research' at Visva Bharati, Santiniketan under Society of Biological Chemists (India) during 3rd to 5th August 2007.

Dr. Pratap K. Das

Member, Sectional Committee of the Biological Sciences (New Biology) at 95th Indian Science Congress Association.

CHEMISTRY

Invited Lecture

Dr A. K. Sen (Jr.)

Topic : Studies on the oligosaccharide from the lipopolysaccharide of *Vibrio Parahae molyticus* O3: K6; Identification of a novel sugar 5,7- diacetamido–8- amino- 3,5,7,8,9-pentadeoxy-D-glycero-D-galacto-non- 2- ulosonic acid
Venue : CARBO-XXII, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab- 160 062.
Date : December 13-15 ,2007

Dr. G. Suresh Kumar

Topic : Nucleic acid binding natural alkaloids: An overview of structural and thermodynamic aspects of interaction
Venue : National Seminar on Current Trends in Chemistry, Cochin University of Science and Technology, Cochin, Kerala
Date : January 18-19, 2008

Dr. P. Jaisankar

Topic : Indium trichloride : An efficient catalyst for the Synthesis of broad spectrum of Heterocycles
Venue : Polish Chemical Society and Polish Association of Chemical Engineers and Nicolaus Copernicus University, Toruñ, Poland .
Date : September 9-12, 2007.

Dr. P. Jaisankar

Topic : Indium trichloride : An efficient catalyst for the Synthesis of broad spectrum of Heterocycles
Venue : Department of Chemistry, Jadavpur University, Kolkata
Date : August 02, 2007.

Dr. P. Jaisankar

Topic : A Search for Safe Drugs from Nature
Venue : Centre for Medical Biology of PAS, Lódz, Poland
Date : 28th September 2007

Dr. Arindam Banerjee

Topic : Nanomaterials in Biology
Venue : Department of Biotechnology, IIT, Khagarpur
Date : September 05, 2007

Dr. Arindam Banerjee

Topic : Synthetic, self-assembling peptides and pseudo-peptide in Nanosciences
Venue : Department of Biotechnology, B.M.S. College of Engineering, Bangalore
Date : October 05-06, 2007

Dr. Arindam Banerjee

Topic : Synthetic self-assembling peptides and pseudopeptides in Nanosciences
Venue : Department of Chemistry IIT, Kharagpur
Date : February 27, 2008

Dr. Arindam Banerjee

Topic : Synthetic Self-assembling Peptide based Nanomaterials
Venue : IICT, Hyderabad
Date : March 18, 2008

Dr. R. C. Yadav

Topic : Emerging Trends in Physics
Venue : P.G. Department of Physics, R.K.College Madhubani, Bihar
Date : December 17-19,2007.

Session Chairman

Dr. G. Suresh Kumar

Chaired a session at National Seminar on Current Trends in Chemistry, Cochin University of Science and Technology, Cochin, Kerala, during 18-19 January 2008.

Dr A. K, Sen (Jr.)

Chaired a Technical Session at the XXII Carbohydrate Conference, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab- 160062, 13-15 December, 2007.

Dr. R. C. Yadav

Chaired a National Seminar cum Conference on Emerging Trends in Physics held in the P.G. Department of Physics, R. K.College Madhubani, Bihar from December 17-19,2007.

Academic Performance / Teaching

Dr. V. S. Giri

Served as Ph. D. Examiner of Jadavpur University, Punjabi University, Patiala. and Pune University.
External examiner for MSc (Envir. Sc.), Calcutta University.
Guest faculty member, NIPER, Kolkata.

Dr. Partha Chattopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Chemistry, Scottish Church College, Kolkata.

Acting as a Reviewer of *Journal of Organic Chemistry*, American Chemical Society, 2007 and *Tetrahedron Letters* (Elsevier Science Ltd.), 2007.

Honorary guest faculty member NIPER, Kolkata.

Member of the Editorial Board of Referees ARKIVOC, USA.Year 2008

Dr. A. K. Sen, Jr.

Guest faculty member NIPER, Kolkata..

Ph.D. thesis examiner Burdwan University and CFTRI, Mysore.

Guest Faculty, M.Tech. at the Raja Bazar Science College, Calcutta University, January-February, 2008.

Dr. G. Suresh Kumar

Editor, International Journal of Physical Sciences (Academic Journal).

Member, Editorial Advisory Board, African Journal of Biochemistry Research (Academic Journal).

Reviewer for papers published in International Journal Biological Macromolecules and Bioorganic Medicinal Chemistry (Elsevier).

Dr. G. Suresh Kumar

Mr. Prateek Pandya, Research Scholar, Dayalbagh Educational Institute, Agra was given training in characterizing drug-DNA complexes by various physico-chemical techniques during 17.8.07 to 27.9.07.

Dr. R.C. Yadav

Delivered a series of lectures on "Instrumental Techniques in Chemical Analysis" for the PG Diploma Course of Department of Adult Continuing Education & Extension, Jadavpur.

Dr. S. Mukhopadhyay

Honorary guest faculty member for Post Graduate Teaching, Department of Organic Chemistry, Calcutta University.

Examinar of Ph. D. Thesis, Osmania University and Viswabharati

Dr. A. K. Banerjee

Acting as a Reviewer of *Organic Letters* and *Journal of Organic Chemistry*, American Chemical Society.

Acting as a member of the Board of Examiners in Chemistry for M. Sc. Part-II, Calcutta University and examiner in M.Sc Chemistry, Jadavpur University

Dr. Chinmay Chowdhury

Acting as a Reviewer of *Organic Letters* and *Journal of Organic Chemistry*, American Chemical Society.

Trainings Received

Dr. A. K. Sen, Jr.

Programme on 'Valorization of R & D' for Senior Scientists from 12.03.08 – 14.03.08, HRDC(CSIR), Ghaziabad.

Programme on ' Science Audit', 6.10.07 – 12.10.07, Administrative Staff College of India (ASCI), Hyderabad.

Dr. P. Jaisankar

Programme on Decision Support Tools And Techniques for Senior Scientists from 02.04.2007 – 06.04.2007, Administrative Staff College of India (ASCI), Hyderabad

Programme on Entrepreneurship Development - for CSIR Scientists, from 07.01.2008 – 12.01.2008, HRDC (CSIR), Ghaziabad

Conferences/Symposium/Workshops

Dr. A. K. Sen, Jr.

Convener, CSIR Programme on Youth for Leadership in Science, CPYLS-2007.

Elected as Hon. Secretary of the Association of Carbohydrate Chemists & Technologists (India) 2007-2008.

Papers/Abstracts presented during Seminar/Symposium

Dr. P. Jaisankar

Pal, C., Dey, S., Nandy , D., Giri, V. S., Jaisankar, P. Eco-friendly synthesis and study of new plant growth promoters: 3,3- Diindolylmethane and its derivatives: "11th EuCheMS International Conference on Chemistry and the Environment and 50th Anniversary Polish chemical Society & Polish Association of Chemical Engineers congress" organized by Polish Chemical Society and Polish Association of Chemical Engineers and Nicolaus Copernicus University, Toruñ, Poland,. September 9-12, 2007.

Dey, S., Pal, C., Nandy, D., Giri, V. S., Zaidlewicz, M., Krzeminski, M, Jaisankar, P. Synthesis of chiral phosphazene bases and their applications in catalytic asymmetric transformation:. " 10th Anniversary of CRSI National Symposium in Chemistry (NSC-10)" organized by Indian Institute of Science, Bangalore, India, February, 1-3, 2008

Dr. A. K. Sen, Jr.

Koushik Mazumder, Choudhury, B. P.,Nair,G.B., Sen, Asish K Studies on the oligosaccharide from the lipopolysaccharide of *Vibrio parahaemolyticus* O3K6; Identification of a novel sugar 5,7-diacetamido-8-amino-3,5,7,8,9-pentadeoxy-D-glycero-D-galacto-non-2-ulosonic acid at the CARBO-XXII, National Institute of Pharmaceutical Education and Research (NIPER), Mohali, Punjab- 160 062, 13-15 December, 2007.

Conveor, CSIR programme on Youth Leadership in Science, CPYLS-2007.

Dr. G. Suresh Kumar

Islam, Md. M. and Suresh Kumar, G. 'RNA targeting by small molecule alkaloids: Studies on the binding of palmatine and berberine to polyribonucleotides and comparison to ethidium'. National Symposium on Biophysics: Biophysics in Medicine and Biology, PU, IBS-2007-08, Chandigarh, November 15-17, 2007.

Hossain, M., Giri, P. and Suresh Kumar, G. A comparative binding and thermodynamic characterization of DNA intercalation by quinacrine and methylene blue' National Symposium on Biophysics: Biophysics in Medicine and Biology, PU, IBS-2007-08, Chandigarh, November 15-17, 2007.

Pandya, P., Suresh Kumar, G. and S. Kumar. 'Facilitation of DNA binding of vinblastine and its analogues by methylene linker: Fluorescence and NMR studies'. National Symposium on Biophysics: Biophysics in Medicine and Biology, IBS-2007-08, PU, Chandigarh, November 15-17,2007.

Giri, P. and Suresh Kumar, G. 'Binding of phototoxic cytotoxic plant alkaloid sanguinarine with double stranded poly(A): Spectroscopic and calorimetric studies'. National Symposium on Biophysics: Biophysics in Medicine and Biology, IBS-2007-08, PU, Chandigarh, November 15-17, 2007.

Adhikari, A., Maiti, M. and Suresh Kumar, G. Thermodynamics of sanguinarine-DNA complexation: Influence of base composition, ionic strength and temperature. National Symposium on Biophysics: Biophysics in Medicine and Biology, IBS-2007-08, PU, Chandigarh, November 15-17, 2007.

Bhadra K., Maiti, M. and Suresh Kumar, G. Interaction of protoberberine alkaloid palmatine with deoxyribonucleic acids; Binding heterogeneity, conformational and thermodynamic aspects. National Symposium on Biophysics: Biophysics in Medicine and Biology, PU, IBS2007-08, Chandigarh, November 15-17, 2007.

Islam, Md. M. and Suresh Kumar, G**.** RNA binding alkaloids: studies on the binding of some protoberberine alkaloids to polyribonucleotides. National Symposium on Current Trends in Chemistry, Kalyani, March 04, 2008,

Hossain, M. and Suresh Kumar, G. DNA intercalation by quinacrine and methylene blue: New insights into structural aspects and thermodynamics of binding. National Symposium on Current Trends in Chemistry, Kalyani, March 04, 2008,

Dr. R. C. Yadav

R.C.Yadav, R.Banerjee, Md.Monirujjaman and S.K.Dana 'Nonlinear Approaches towards Cardiovascular Diseases', published in the proceedings of the Conference on "Perspectives in Nonlinear Dynamics" held during July 16-27,2007 at International Centre for Theoretical Physics (ICTP) Trieste, Italy.

R.C.Yadav *et al* 'Multiscroll in Coupled Double Scroll Type Oscillatiors' published in the proceedings of 3rd International IEEE Scientific Conference on Physics and Control (PhysCon,2007**)** held from Sept. 3rd-7th 2007, at the University of Potsdam, Germany.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Invited Lectures

Prof. Siddhartha Roy

Venue : Hokkaido University, Sapporo, Japan;
Topic : Methods in Protein Structure Analysis(MPSA)

Dr. Chitra Dutta

Topic : Genome Projects & Beyond
Venue : National Institute of Technology
Date : March, 2008

Dr. Chitra Dutta

Topic : Pattern Recognition in Genome Architecture
Venue : St. Xaviers College, Kolkata
Date : September 30, 2007

Dr. Debasish Bhattacharyya

Topic : 'Kinetic stability of proteins: A case study with bromelain'
Venue : Department of Biochemistry, Calcutta University (refresher's course)
Date : 15 Jan 2008

Dr. Debasish Bhattacharyya

Topic : 'Stability of proteins'
Venue : Departmnet of Chemistry, Lady Brabourne College, Calcutta University
Date : 24th Feb. 2008

Dr. Nanda Ghoshal

Topic : Identifying Anticancer Drug Candidates Using Feature-Shape Pharmacophore of Biologically Active Conformation : A case Study with CDK2/CyclinA
Venue : "Recent Topics in Organic Chemistry", in the Department of Chemistry, University of Calcutta
Date : March 28, 2008

Session Chairman

Dr. Debasish Bhattacharyya "Acted as Chair Person of a session of the Annual conference of Indian Spectrophysics Association, held on 1st - 2nd February, 2008 at Pachaiyappa's College, Madras.

Academic Performance/Teaching

Dr. M. C. Bagchi

Guided project of Miss. Payel Ghosh for the partial fulfillment of M. E. (Biomedical Engineering) of Jadavpur University during 2007-08.

Acted as a Guest Faculty Member, Paper setter and Examiner in Biostatistics for the M.S.(Pharm) course of National Institute of Pharmaceutical Education and Research (NIPER), Kolkata.

Served as a reviewer for Journal of Theoretical and Computational Chemistry, Medicinal Chemistry Research, Chemical Biology & Drug Design and Indian Journal of Experimental Biology.

Evaluated proposal for funding by Department of Science & Technology, New Delhi.

Acted as a coordinator of Statistics course for Ph.D. students of IICB.

Dr. Chitra Dutta

Guest Lecturer and Examiner, M. Sc. (Genetics, Microbiology, Neuroscience, Biotechnology) Calcutta University NIPER, Kolkata

Dr. Debasish Bhattacharyya

Served as a guest lecturer at the Department of Biotechnology, Jadavpur University, Calcutta (M.Sc. BioTech.).

Served as a guest lecturer at the Department of Zoology, Bethune College, University of Calcutta (M.Sc. Part I, Proteins and Enzymology).

Served as a guest lecturer at the Department of Botany, University of Tripura, Agartala. (M.Sc. Part I, Proteins and Enzymology).

Dr. Nanda Ghoshal

Acted as Examiner for M.Pharm. final (thesis and corresponding oral) examination, J.U. (of one candidates), held in June, 2007 at Pharmaceutical Technology Div., J.U.

Teaching at NIPER, Kolkata, as a Guest Faculty Member (for the Academic Year 2007- 08).

Evaluated manuscripts to be published in J. Med. Chem., Eur. J. Med. Chem.

Delivered Lectures in the Department of Biotechnology, Visva – Bharati, Shantineketan to M.Sc. Biotechnology students and interacted with them (March 4, 2008).

Lecture Topics: “Drug – An Overview” and “Drug – Like Properties’Evaluated a Research Project Proposal entitled, “The role of water in flap opening dynamics of HIV-I protease”, submitted to CSIR for funding.

Dr. Krishnananda Chattopadhyay

Fluorescence Spectroscopy, Department of Biotechnology, Kolkata University

Dr. Saumen Datta

X-ray crystallographic courses (Basic and Advanced) in Ph. D course work at IICB

Dr. Subrata Adak

Examiner in M.Sc (Microbiology) and M. Sc (Biochemistry) of Calcutta University.
Examiner in M.Sc (Biotechnology) of Uttar Banga University

Deputation Abroad:

Dr. Saumen Datta

Research on membrane protein crystallography with Senior Research Fellowship from University of Limerick, Ireland.

Papers/Abstract Presented in the Conference:

Nandi S., Bagchi M. C "QSAR of Nitrofuranyl Amides Utilizing Calculated Molecular Descriptors: Statistical and Neural Network Approach", February 22-24, 2008 at "International Conference on the Interface of Chemistry-Biology in Biomedical Research" organized by the Indian Society of Chemists and Biologists (ISCB) at Birla Institute of Technology and Science, Pilani, India.

Dutta, A. Paul, S. Bag, S.K. Das, S. Dutta C. "Genomic signatures of adaptation in different *Prochlorococcus* strains" at "ISCBC 2008" on 22^{nd}-24^{th} Feb, 2008, BITS, Pilani, Rajasthan

Chakrabarty, P.D. De, D. Bhattacharyya, D. Spectroscopic studies of Human placental extract used as wound healer. Invited lecture at the Annual meeting, Indian Spectrophysics Society, 1^{st}-2^{nd} Feb. 2008, Pachaiyappa's College, Chennai-600030.

Bhattacharya, R. Bhattacharyya, D. Kinetic stability of Bromelain National Symposium on Biophysics (Indian Biophysical Society) held at Punjab University, Chandigarh, 15-17, Nov. 2007, Oral Presentation-09.

Sengupta, N. Brahma, A. Datta S. and Bhattacharyya D. UDP-galactose 4-epimerase from Kluyveromyces fragilis: Interactions of substrates and analogs at the catalytic site. National Symposium on Biophysics (Indian Biophysical Society) held at Punjab University, Chandigarh, 15-17, Nov. 2007, Poster Presentation-14.

Saha D. Bhattacharyya D. Solution properties of BSA as revealed from scattering mode of a spectrofluorimeter' National Symposium on Biophysics (Indian Biophysical Society) held at Punjab University, Chandigarh, 15-17, Nov. 2007, Poster Presentation-13.

Bhutoria, S. Ghoshal, N. An Efficient Virtual Screening Protocol for the Search of Adenosine Kinase Inhibitors". *4th joint Sheffield conference on Chemoinformatics, Sheffield, U.K.,* June 18-20, 2007.

Vijayan, R.S.K. Ghoshal, N. A Fast *In-silico* Protocol for Identification of Anti Epileptic Drug Leads", *Neuro 2007*, The 30th Annual Meeting of the Japan Neuroscience Society (JNS), The 50th Annual Meeting of the Japanese Society for Neurochemistry (JSN), The 17th Annual Meeting of the Japanese Neural Network Society (JNNS), *Pacifico Yokohama (Yokohama-shi, Kanagawa), Japan,* September 10-12, 2007.

Mascarenhas, N. M. Ghoshal N. Structural Determinants of CDK4 Inhibition : A Molecular Dynamics Study", *School on Biomolecular Simulations,* Nov 6 –16, JNCASR, Bangalore, India,. 2007.

Mascarenhas, N. M. Ghoshal N. Dissecting the activity profile of pyrido[2,3-d]pyrimidin-7-ones as CDK4 inhibitors : a QSAR study " *The interface of Chemistry – Biology in Biomedical Research* , Feb 22 -24, BITS, Pilani, Rajasthan, 2008.

Bhutoria, S., Ghoshal, N. Clustering of Adenosine Kinase Inhibitors-Study for their different binding modes", *12th International Conference on "The Interface of Chemistry- Biology inBiomedical Research" Pilani, Rajasthan, INDIA*, February 22-24, 2008.

Vijayan.R.S.K, Nahren.M, Prabu. M, Ghoshal, N. comprehensive Structure Based Virtual Screening Protocol using BACE as a test system: *The Keystone Symposia meeting on Computer- Aided Drug Design, Colorado. USA,* March 29 - April 3, 2008.

Yadav, R.K., Dolai, S., Pal, S. and Adak, S. Role of tryptophan-208 residue in cytochrome c oxidation by ascorbate peroxidase from *Leishmania major*: presented at 76th annual meeting of Society of Biological Chemists (India) meeting at Tirupati in Nov. 2007.

Dolai, S., Yadav, R.K., Pal, S. and Adak, S. *Leishmania major* ascorbate peroxidase overexpression protects cells against reactive oxygen species-mediated cardiolipin oxidation: presented at 76th annual meeting of Society of Biological Chemists (India) meeting at Tirupati in Nov. 2007

Conferences / Symposium / Workshops

Dr. Debasish Bhattacharyya

Nominated and attended the 'Proteomics Short Course' held at Bangalore (30th June – 2nd July, 2008) offered by Waters India Ltd.

Dr. Nanda Ghoshal

Invited to join the "Brainstorming session on Virtual Centre for Chemo-bio-informatics", organised by Indian Association for Cultivation of Science (as part of Indo-US initiative) at Seminar Hall, Department of Biophysics, Molecular Biology & Genetics, University College of Science (Rajabazar Campus), held on Jan. 14, 2008.

Organised a "One day International Seminar on Computational Solutions for Challenges in Drug Discovery", sponsored by M/S Schrodinger, Bangalore, on Aug. 3, 2007.

External Funding

INFECTIOUS DISEASES AND IMMUNOLOGY

Principal Investigator	:	Dr. H. K. Majumder
Project Title	:	*Leishmania donovani* unusual bi-subunit topoisomerase I: Solving the new twist in topoisomerase research related to evolution, functional conservation and preferential sensitivity to the specific inhibitors of type IB family
Funding Agency	:	DBT, Govt. of India
Total Fund	:	Rs. 21.98 lakhs only
Duration	:	June 9, 2006 to June 8, 2009

Principal Investigator	:	Dr. Pijush K. Das
Project title	:	Cyclic nucleotide signaling in the infectivity of an eukaryotic intracellular pathogen like *Leishmania*
Funding Agency	:	DST, Govt. of India
Total Fund	:	Rs. 22.00 lakhs
Duration	:	November 2006 to November 2009

Principal investigator	:	Dr. Chitra Mandal
Project Title	:	"9-O-Acetylated Sialic acid in Regulating the Lifespan of Erythrocytes in Childhood Acute Lymphoblastic Leukaemia"
Funding Agency	:	DST, Govt. of India
Total Funds	:	Rs. 21.37 lakhs
Duration	:	2005-08

Principal investigator	:	Dr. Susanta Roychoudhury
Co-Investigator	:	Dr. Chitra Mandal
Project Title	:	Identification of new molecular targets for the development of anti-cancer agents"
Funding Agency	:	DBT, Govt. of India
Total Funds	:	Rs. 162.65 lakhs
Duration	:	2007-2012.

Principal Investigator	:	Dr. Tripti De
Project Title	:	Protective efficacy of galactose terminal glycoconjugates of Leishmania donovani.
Funding Agency	:	DST
Total Fund	:	Rs. 20 Lakhs
Duration	:	April 2006 – March 2009

Principal Investigator	:	Dr. Malini Sen
Project Title	:	Role of WISP3 in Maintenance of Cartilage Integrity.
Funding Agency	:	DST
Total Funds	:	
Duration	:	March 2008 to February 2011

Principal Investigator : Dr. Mita Chatterjee Debnath
Project Title : Kit formulation of thiolate complexes of technetium –99m using S-thiomethyl as a novel protecting group for SH-containing ligands.
Funding Agency : ICMR
Total Funds : Rs. 1,99,000/-
Duration : March 2007 to February 2008

Principal Investigator : Dr. Mita Chatterjee Debnath
Project Title : Rapid Diagnosis of myocardial cell damage by a novel radiotracer.
Funding Agency : DST
Total Funds : Rs. 19, 86,000/-
Duration : August 2004 – November 2007

Principal Investigator : Dr. (Mrs.) Mridula Misra
Project Title : "Development of New Radiopharmaceuticals for Nuclear Brain Imaging : Pharmacokinetics and Mechanism of action."
Funding Agency : ICMR, Govt. of India
Total Fund : Rs. 28 Lakhs
Duration : January 2005 – December 2008

CELL BIOLOGY & PHYSIOLOGY

Principal Investigator : Dr. Sib Sankar Roy
Project Title : The role of Pitx2 homeodomain transcription factor to regulate ovarian function
Funding Agency : DST, Govt. of India
Total Fund : Rs. 23.536 lakhs.
Duration : 2007 – 2010

Principal Investigator : Dr. Sib Sankar Roy (multi-Institutional project)
Project Title : Development of a herbal drug for non-insulin dependent Diabetes mellitus
Funding Agency : DST, Govt. of India
Total Fund : Rs. 58.27 lakhs.
Duration : 2004 – 2007

Principal Investigator : Dr. Sib Sankar Roy (CoPI)
Project Title : Isolation, molecular characterization and biological evaluation of anti-diabetic principles from a few Indian medicinal plants
Funding Agency : DST, Govt. of India (with industry-institute tie up)
Total Fund : Rs. 20.26 lakhs.
Duration : 2007 – 2010

Principal Investigator : Dr. Sandhya Rekha Dungdung
Project Title : Purification and characterization of sperm motility inhibiting protein factor from goat epididymal plasma and fertility management.
Funding Agency : ICMR, Govt. of India
Total Fund : Rs.8.41 lakhs.
Duration : 2007 – 2010

Investigator	:	Dr. K. P. Mohanakumar (collaborative project with Dr. N. Lenka, National Centre for Cell Sciences, Pune)
Project Title	:	In vitro targeting and functional characterization of ES cell derived dopaminergic neurons and exploration of their therapeutic potential.
Funding Agency	:	Department of Biotechnology
Total Funds	:	Rs. 65.80 Lakhs
Duration	:	2004-2007

Investigator	:	Dr. Sumantra Das (CoPI)
Project Title	:	Limbal stem cell culture and transplantation of cultivated Corneal epithelial stem cells in ocular surface disorders.
Funding Agency	:	Department of Biotechnology
Total Fund	:	Rs. 24.456 lakhs
Duration	:	November 2005 – October, 2008

MOLECULAR & HUMAN GENETICS

Principal investigator	:	Dr. Samit Adhya
Project Title	:	Role of two proteins in mitochondrial tRNA import
Funding Agency	:	DST
Total Funds	:	Rs. 15.68 lakhs
Duration	:	August 2005 - July 2008

Principal investigator	:	Dr. Keya Chowdhury
Project Title	:	Malignant potentiality of precancerous oral submucous fibrosis and its association with expression of collagen types
Funding Agency	:	DST
Total Fund	:	Rs. 19.23 lakhs
Duration	:	2005-2008

Principal investigator	:	Dr. A. K. Giri
Project title	:	PRAMA Project under UKIERI
Funding Agency	:	University of Manchester, U.K.
Total Fund	:	£ 14,000
Duration	:	2008-2010

Principal Investigator	:	Dr. Susanta Roychoudhury
Project Title	:	Identification of new molecular targets for the development of anti-cancer agents.
Funding Agency	:	DBT, Govt. of India
Total Fund	:	Rs. 162.65 lakhs
Duration	:	2006-2011

Principal Investigator	:	Dr. Susanta Roychoudhury
Project Title	:	Identification of susceptibility alleles for the development of head and neck cancer in Indian population
Funding Agency	:	DBT, Govt. of India
Total Fund	:	Rs. 44.51 lakhs
Duration	:	2006-2009

Principal Investigator	:	Dr. Samir Dutta
Project title	:	Biochemical characterization and molecular cloning of a chymotrypsin/ trypsin inhibitor from winged bean seeds
Funding agency	:	DST, Govt. of India, New Delhi
Total fund	:	Rs. 18,51,595/-
Duration	:	2003-2007

Principal Investigator	:	Dr. A. K. Giri
Project title	:	Molecular Edidemiology and Environmental Health
Funding agency	:	Fogerty International Training Programm, NIH, USA
Total fund	:	US $ 34550
Duration	:	2005-2008

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Principal Investigator	:	Dr.(Mrs.) Aparna Gomes
Co-investigator	:	Dr. J. R.Vedasiromoni
Project Title	:	Evaluation of scorpion venom as an anticancer agent.
Funding Agency	:	DST, Govt. of India
Total Fund	:	Rs. 15.16 lakhs
Duration	:	2004-2007

Principal Investigator	:	Dr.(Mrs.) Aparna Gomes
Co-investigator	:	Dr. J. R.Vedasiromoni
Project Title	:	Pharmacological and molecular actions of Snake venom anticancer protein fraction (s) on experimental animals and on leukemic cell lines
Funding Agency	:	ICMR, Govt. of India
Total Fund	:	Rs. 23.8 lakhs
Duration	:	2007-2009

Cooordinator	:	Dr. Pratap K. Das (A Collaborative Project of DST Dey's Medical IICB Visva Bharati)
Project Title	:	Chemical standardization and biological evaluation with a view to increase efficacy of herbal medicines
Funding Agency	:	DST, Govt. of India & Dey's Medical Mfg. Co. Ltd.
Total Fund	:	Rs. 45.81 lakh (IICB Component)
Duration	:	2005-2008.

Principal Investigator	:	Dr. Snehasikta Swarnakar
Project Title	:	Effect of omeprazole on regulation of matrix and remodeling of extracellular matrix in gastroduodenal ulcer.
Funding Agency	:	ICMR
Total Fund	:	Rs. 18.70 lakhs.
Duration	:	2005-2008

Principal Investigator	:	Dr. Suman Khowala
Project Title	:	Conversion of cellulose and hemi-cellulose into sugars and ethanol
Funding agency	:	CSIR, (NMITLI) Govt. of India
Total Cost	:	Rs. 59.8 lakhs
Duration	:	2007-2010

Principal Investigator	:	Dr. Sharmila Chattopadhyay
Project Title	:	Role of Glutathione as a signaling molecule
Funding agency	:	DST., Govt. of India.
Total Cost	:	Rs. 23 lakhs
Duration	:	2007-2010

Principal Investigator	:	Dr. Sharmila Chattopadhyay
Project Title	:	Indian Medicinal Plants to combat kala-azar"
Funding agency	:	ICMR, Govt. of India.
Total Cost	:	Rs. 28.5 lakhs
Duration	:	2007-2010

CHEMISTRY

Principal Investigator	:	Dr. Asish Kumar Sen
Project Title	:	Immunomodulation and anti-microbicidal activity: effect of Bael (*Aegle marmelos*) exudate gum, and mucilage and other polysaccharides from semi-ripe Bael fruit .
Funding Agency	:	DBT, Govt. of India.
Total Fund	:	Rs. 18.62 lakhs
Duration	:	2004-2007

Principal Investigator	:	Dr. Asish Kumar Sen
Project Title	:	Chemical Characterization and modification of coir fiber for enhanced longevity, and their physico-chemical studies
Funding Agency	:	COIR BOARD, Govt. of India..
Total Fund	:	Rs. 29.48 lakhs
Duration	:	Nov 2006-Oct 2009

Principal investigator	:	Dr. B. C. Pal and Prof. S. Bhattacharya
Title of Project	:	Isolation, molecular characterization and biological Evaluation of anti-diabetic principle(s) from Indian Medicinal Plants
Funding agency	:	DST (Date of Sanction 1.03.2007)
Total Fund	:	Rs. 158.56 lakhs (IICB Rs. 20.26 lakh and Visva-Bharati, Santiniketan Rs. 73.20 lakhs and East India Pharmaceuticals Works Ltd. Rs. 65.10 lakh)
Duration	:	2007-2010

Principal Investigator	:	Dr. P. Jaisankar
Project Title	:	Development of Chiral Catalysts for Asymmetric Organic Synthesis
Funding Agency	:	DST
Total Fund	:	Rs. 6.5 lakhs (IICB component)
Duration	:	2006-2009

EXTERNAL FUNDING

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Co Investigator	:	Prof. Siddhartha Roy
Project Title	:	Structure function analysis of Tumor suppressor, P53 interacting protein: Structural basis of p53 activation.
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 7.02 lakhs
Duration	:	2006-2009

Co Investigator	:	Prof. Siddhartha Roy
Project Title	:	Development of Anti-Viral Agent against Chandipura Virus.
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 10.7 lakhs
Duration	:	2005 –2008

Principal Investigator	:	Dr. M. C. Bagchi
Project Title	:	Anti-tuberculosis Drug Design by Calculated Molecular descriptors: A QSAR Approach.
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 12.07 lakhs
Duration	:	2006-2009

Principal Investigator	:	Dr. Chitra Dutta
Project Title	:	Establishment of Sub-DIC at IICB
Funding Agency	:	Department of Biotechnology, (Govt. of India) New Delhi.
Total Funds	:	Rs. 53 lakhs
Duration	:	2002-2007 (extended up to 2012)

Principal investigator	:	Dr. Debasish Bhattacharyya
Project title	:	Regulation of activity and assembly of multineric proteins
Funding agency	:	DST
Total funds	:	Rs. 20.00 lakhs
Duration	:	2006 (December) – 2009 (November)

Principal investigator	:	Dr. Debasish Bhattacharyya
Project title	:	Biochemical characterization of the drug 'Placentrex
Funding agency	:	M/s Albert David Ltd
Total funds	:	Rs. 8.00 lakhs
Duration	:	2007 (November) – 2009 (October)

Principal investigator	:	Dr. Saumen Datta
Project title	:	Structural Insights into the Type III Secretion System (TTSS) of Pathogenic Bacteria
Funding agency	:	DST
Total funds	:	Rs. 22.51 lakhs
Duration	:	2007-2010

Principal Investigator	:	Dr. Subrata Adak
Co-Investigator	:	Dr. Alok K. Datta
Project Title	:	Molecular and functional characterization of ascorbate peroxidase from *Leishmania major*.
Funding Agency	:	DST, Govt. of India
Total Funds	:	Rs. 21.77 lakhs
Duration	:	2006-2009


65th CSIR FOUNDATION DAY CELEBRATION
WEDNESDAY, SEPTEMBER 26, 2007
INDIAN INSTITUTE OF CHEMICAL BIOLOGY
4, RAJA S.C. MULLICK RD., JADAVPUR, KOLKATA-32

Publications

INFECTIOUS DISEASES AND IMMUNOLOGY

BoseDasgupta, S., Das, B. B., Sengupta, S., Ganguly, A., Tripathi, G. and Majumder, H. K. Amino acids 39-456 of large subunit and 210-262 of small subunit constitute the minimal, functionally interacting fragments of the unusual heterodimeric topoisomerase IB of *Leishmania. Biochem J.* **409:** 481-489, 2007.

Roy, A., Das, B. B., Ganguly, A., BoseDasgupta, S., Khalkho, N. V., Pal, C., Dey, S., Giri, V. S., Jaisankar, P., Dey, S. and Majumder, H. K. An insight into the mechanism of inhibition of unusual bi-subunit topoisomerase I from *Leishmania donovani* by 3,3'-diindolylmethane, a novel DNA topoisomerase I poison with a strong binding affinity to enzyme. *Biochem J.* **409:** 611-622, 2007.

BoseDasgupta, S., Ganguly, A., Roy, A., Mukherjee, T. and Majumer, H. K. A novel ATP-binding cassette transporter, ABCG6 is involved in chemoresistance of *Leishmania*. *Mol. Biochem. Parasitol.* **158:** 176-188, 2007.

Ganguly, A., Das, B., Roy, A., Sen, N., BoseDasgupta S, Mukhopadhayay, S. and Majumder, H. K. Betulinic acid, a catalytic inhibitor of topoisomerase I, inhibits reactive oxygen species-mediated apoptotic topoisomerase I-DNA cleavable complex formation in prostate cancer cells but does not affect the process of cell death. *Cancer Res.* **67:** 11848-11858, 2007.

BoseDasgupta, S., Ganguly, A., Das, B. B., Roy, A., Khalkho, N. V. and Majumder, H. K. The large subunit of *Leishmania* topoisomerase I functions as the 'molecular steer' in type IB topoisomerase. *Mol. Microbiol.* **67:** 31-46, 2008.

BoseDasgupta, S., Das, B. B., Sengupta, S., Ganguly, A., Roy, A., Dey, S., Tripathi G, Dinda, B. and Majumder, H. K. The caspase-independent algorithm of programmed cell death in *Leishmania* induced by baicalein: the role of LdEndoG, LdFEN-1 and LdTatD as a DNA 'degradesome'. *Cell Death Differ.* **15:** 1629-1640, 2008.

Das, R., Roy, A., Dutta, N. and Majumder, H. K. Reactive oxygen species and imbalance of calcium homeostasis contributes to curcumin induced programmed cell death in *Leishmania donovani*. *Apoptosis* **13:** 867-882, 2008.

Misra, P., Khaliq, T., Dixit, A., Sengupta, S., Samant, M., Kumari, S., Kumar, A., Kushawaha, P. K., Majumder, H. K., Saxena, A. K., Narender, T. and Dube, A. Antileishmanial activity mediated by apoptosis and structure-based target study of peganine hydrochloride dihydrate: an approach for rational drug design. *J. Antimicrob. Chemother.* **62:** 998-1002, 2008.

Roy, A, Ganguly, A., BoseDasgupta, S., Das, B. B., Pal, C., Jaisankar, P. and Majumder, H. K. Mitochondria-dependent reactive oxygen species-mediated programmed cell death induced by 3,3'-diinodlylmethane through inhibition of F0F1-ATP synthase in unicellular protozoan parasite *Leishmania donovani*. *Mol. Pharmacol*. **74:** 1292-1307, 2008.

Pramanick, S., Roy, A., Ghosh, S., Majumder, H. K. and Mukhopadhyay, S. Withanolide Z, a new chlorinated withanolide from *Withania somnifera*. *Planta Med.* **74:** 1745-1748, 2008.

Bhattacharya, A., Biswas, A. and Das, P. K. Role of intracellular cAMP in differentiation-coupled induction of resistance against oxidative damage in *Leishmania donovani*. *Free Radical Biol. Med.* **44:** 779-794, 2008.

Ghosh, S., Bandyopadhyay, S., Mukherjee, K., Mallick, A., Pal, S., Mandal, C., Bhattacharya, D. K. and Mandal, C. *O*-acetylation of sialic acids is required for the survival of lymphoblasts in childhood acute lymphoblastic leukemia (ALL). *Glycoconjugate J.* **24:** 17-24, 2007.

Mukherjee, K., Chowdhury, S., Mondal, S., Mandal, C., Chandra, S., Bhadra, R. K. and Mandal, C. 9-*O*-acetylated GD3 triggers programmed cell death in mature erythrocytes. *Biochem. Biophys. Res. Comm.* **362:** 651-657, 2007.

Chowdhury, S., Bandyopadhyay, S., Chandra, S. and Mandal, C. Comparative analysis of differential expression of sialic acids and adhesion molecules on mononuclear cells of bone marrow and peripheral blood in childhood acute lymphoblastic leukaemia at diagnosis and clinical remission. *Indian J. Biochem. Biophys.* **44:** 357-365, 2007.

Mukherjee, K., Chava, A. K., Mandal, C., Dey, S. N., Kniep, B., Chandra, S. and Mandal, C. *O*-acetylation of GD3 prevents its apoptotic effect and promotes survival of lymphoblasts in childhood acute lymphoblastic leukaemia. *J. Cell. Biochem.,* **105:** 724-734, 2008.

Chowdhury, S., Bandyopadhyay, S., Mandal, C., Chandra, S. and Mandal, C. Flow-cytometric monitoring of disease-associated expression of 9-O-acetylated sialoglycoproteins in combination with known CD antigens, as an index for MRD in children with acute lymphoblasticl leukaemia: a two-year longitudinal follow-up study *BMC Cancer*, **8:** 40, 2008**.**

Dutta, A., Sarkar, D., Gurib-Fakim, A., Mandal, C. and Chatterjee, M. In vitro and in vivo activity of *Aloe vera* leaf exudate in experimental visceral leishmaniasis. *Parasitol. Res*. **102:** 1235-42, 2008.

Mandal, C., Dutta, A., Mallick, A., Chandra*, S.* Misra, L., Sangwan, R. and Mandal, C. Withaferin A induces apoptosis by activating p38 mitogen-activated protein kinase signaling cascade in leukemic cells of lymphoid and myeloid origin in a transcription-dependent manner through mitochondrial death cascade. *Apoptosis*. **13:** 1450-1464, 2008.

Basu, R., Bhaumik, S., Halder, A. K., Naskar, K., De, T., Dana, S. K., Walden, P. and Roy, S. Hybrid cell vaccination resolves *Leishmania donovani* infection by eliciting a strong CD8+ cytotoxic T-lymphocytes response with concomitant suppression of interleukin-10 (IL-10) but not IL-4 or IL-13. *Infect. Immun.* **75:** 5956-5966, 2007.

Basu, J. M., Mookherjee, A., Banerjee, R., Saha, M., Singh S., Naskar, K., Tripathy, G., Sinha, P. K., Panday, K., Sundar, S., Bimal, S., Das, P. K., Chaudhuri, S. K. and Roy, S. Inhibition of ABC transporters abolishes antimony resistance in *Leishmania* infection. *Antimicrob. Agents Chemother*. **52:** 1080-1093, 2008.

Chakraborty, D., Mookherjee Basu, J., Sen, P., Sundar, S. and Roy, S. Human placental extract offers protection against experimental visceral leishmaniasis: a pilot study for a phase-I clinical trial. *Ann. Trop. Med. Parasitol.* **102:** 21-38, 2008.

Mazumder, S., Ravindran, R., Banerjee, A. and Ali, N. Non-coding pDNA bearing immunostimulatory sequences co-entrapped with leishmanial antigen in cationic liposomes elicit almost complete protection against experimental visceral leishmaniasis. *Vaccine* **25:** 8771-8781, 2007.

Saha, S., Mondal, S., Ravindran, R., Bhowmik, S., Modak, D., Mallick, S., Rahman, M., Kar, S., Goswami, R., Guha, S. K., Pramanik, N., Saha, B. and Ali, N. IL-10 and TGF-β mediated susceptibility in Post-kala-azar-dermal leishmaniasis: The significance of amphotericin B in the control of *Leishmania donovani* infection in India. *J. Immunol.* **179:** 5592-5603, 2007.

Banerjee, A., Roychowdhury, J. and Ali, N. Stearylamine-bearing cationic liposomes kill *Leishmania* parasites through surface exposed negatively charged phosphatidylserine. *J Antimicrob. Chemother.* **61:** 103-110, 2008.

Palit, P. and Ali, N. Oral therapy with Amlodipine and Lacidipine, 1, 4-dihydropyridine derivatives, show antileishmanial activity against experimental visceral leishmaniasis. *Antimicrob. Agents and Chemother.* **52:** 374-377, 2008.

Bhowmick, S., Ravindran, R. and Ali N. gp63 in stable cationic liposomes confers sustained vaccine immunity to susceptible BALB/c mice infected with *Leishmania donovani*. *Infect. Immun*. **76:** 1003-1015, 2008.

Palit, P. and Ali, N. Oral therapy with sertraline, a selective serotonin reuptake inhibitor, shows activity against *Leishmania donovani*. *J. Antimicrob. Chemother.* **61:** 1120-1124, 2008.

Chatterjee A. and R. Chowdhury. Bile and unsaturated fatty acids inhibit the binding of cholera toxin and *Escherichia coli* heat-labile enterotoxin to GM1 receptor. *Antimicrob. Agents and Chemother.* **52:** 220-224, 2008.

Das, B., Halder, K., Pal, P. and Bhadra, R. K. Small chromosomal integration site of classical CTX prophage in Mozambique *Vibrio cholerae* O1 biotype El Tor strain. *Arch. Microbiol*. **188:** 677-683, 2007.

Das, B. and Bhadra R. K. Molecular characterization of *Vibrio cholerae* Δ*relA* Δ*spoT* double mutants. *Arch. Microbiol.* **189:** 227-238, 2008.

Bhaumik, S. K., Singh, M., Basu, R., Bhaumik, S., Roychoudhury, K., Naskar, K., Roy, S. and De T. Virulence attenuation of a UDP-galactose/N-acetylglucosamine β 1,4 galactosyltransferase expressing *Leishmania donovani* promastigote. *Glycoconjugate J.* **25:** 459-72, 2008.

Bhaumik S. K., Singh, M. K., Karmakar, S. and De, T. Immuno stimulating glycophosphosphingolipid antigen from *Leishmania donovani* is recognized by visceral leishmaniasis patient sera. *Mol. Biochem. Parasitol*. **159:** 121-129, 2008.

Kumar, S., Guha, M., Choubey, V., Maity, P., Shrivastava, K., Puri, S. K. and Bandyopadhyay, U. Bilirubin inhibits *Plasmodium falciparum* growth through the generation of reactive oxygen species. *Free Rad. Biol. Med.* **44:** 602-613, 2008.

Kumar, S., Das, S. K., Dey, S., Maity, P., Guha, M., Choubey, V., Panda, G. and Bandyopadhyay, U. Antiplasmodial activity of [(Aryl)arylsulfanylmethyl]Pyridine. *Antimicrob. Agents and Chemother*. **52:** 705-715, 2008.

Guha, M., Maity, P., Mitra, K., Reiter, R. J. and Bandyopadhyay, U. Melatonin inhibits free radical-mediated mitochondrial-dependent hepatocyte apoptosis and liver damage induced during malarial infection**.** *J. Pineal. Research* **43:** 373-381, 2007.

Sen, M. and Ghosh G. Transcriptional outcome of Wnt–Frizzled signal transduction in inflammation: Evolving concepts. *J. Immunol.* **181:** 4441-4445, 2008.

Miller, D. S. and Sen, M. Potential role of WISP3 (CCN6) in regulating the accumulation of reactive oxygen species. *Biochem. Biophys. Res. Comm*. **355:** 156-161, 2007.

Halder, K. K., Mandal, B., Chatterjee Debnath, M, Bera, H., Ghosh, L. K. and Gupta, B. K. Chloramphenicol-incorporated polylactide-co-glycolide (PLGA) nanoparticle formulation, characterization, Technetium-99m labeling and biodistribution studies. *J. Drug Targeting* **16:** 311-320, 2008.

CELL BIOLOGY & PHYSIOLOGY

Bhowal, S. K., Lala, S., Hazra, A., Paaira, P., Banerjee, S., Mondol, N. B. and Chakraborty, S. N. Synthesis and assessment of fertility-regulating potential of (2′′chloroacetamidobenzyl)-3-(3′indolyl) quinoline in adult rats as a male contraceptive agent. *Contraception* **77:** 214-222, 2008.

Biswas, D., Banerjee, M., Sen, G., Das, J. K., Banerjee, A., Sau, T. J., Pandit, S., Giri, A. K. and Biswas, T. Mechanism of erythrocyte death in human population exposed to arsenic through drinking water. *Toxicol. Appl. Pharmacol.* **230:** 57-66, 2008.

Borah, A. and Mohanakumar, K. P. Long-term L-DOPA treatment causes indiscriminate increase in dopamine levels at the cost of serotonin synthesis in discrete brain regions of rats. *Cell. Mol. Neurobiol*. **27:** 985-996, 2007.

Ghosh, M. and Das, S. Increased beta(2)-adrenergic receptor activity by thyroid hormone possibly leads to differentiation and maturation of astrocytes in culture. *Cell. Mol. Neurobiol.* **27:** 1007-1021, 2007.

Ghosh, P., Saha, S. K., Nandi, S. S., Bhattacharya, S. and Roy, S. S. Involvement of Pitx2, a homeodomain transcription factor, in hypothyroidism associated reproductive disorders. *Cell Physiol. Biochem.* **20:** 878-898, 2007.

Joardar, A. and Das, S. Effect of fatty acids isolated from edible oils like mustard, linseed or coconut on astrocytes maturation. *Cell. Mol. Neurobiol.* **27:** 973-83, 2007.

Kumar, S., Chatterejee, R., Dolai, S., Adak, S., Kabir, S. N., Banerjee, S. and Mondal, N. B. *Chenopodium album* seed extract-induced sperm cell death: exploration of a plausible pathway. *Contraception* **77:** 456-62, 2008.

Kumari, A., Sen, S. and Mohanakumar, K. P. Atropine, a muscarinic cholinergic receptor antagonist increases serotonin, but not dopamine levels in discrete brain regions of mice. *Neurosci.Lett.* **423:** 100-103, 2007.

Pandey, M., Varghese, M., Sindhu, K. M., Sen, S., Navneet, A. K., Mohanakumar, K. P. and Usha, R. Mitochondrial NAD^+-linked state 3 respiration and complex-I activity are compromised in the cerebral cortex of 3-nitropropionic acid-induced rat model of Huntington's disease. *J. Neurochem*. **104:** 420-434, 2008.

Sen, G., Biswas, D., Ray, M. and Biswas, T. Albumin-quercetin combination offers a therapeutic advantage in the prevention of reduced survival of erythrocytes in visceral leishmaniasis. *Blood Cells Mol. Diseases.* **39:** 245-254, 2007.

Senthilkumar, K. S., Saravanan, K. S., Chandra, G., Sindhu, K. M., Jayakrishnan, A. and Mohanakumar, K. P. Unilateral implantation of dopamine-loaded biodegradable hydrogel in the striatum attenuates motor abnormalities in the 6-hydroxydopamine model of hemi-parkinsonism. *Behav. Brain Res*. **184:** 11-18, 2007.

MOLECULAR & HUMAN GENETICS

Mukherjee, S., Basu, S., Home, P., Dhar, G. and Adhya, S. Necessary and sufficient factors for import of tRNA into the kinetoplast-mitochondrion. *EMBO Rep.* **8:** 589-595, 2007.

Basu, S., Mukherjee, S. and Adhya, S. Proton-guided movements of tRNA within the *Leishmania* mitochondrial RNA import complex. *Nucl. Acids Res.* **36:** 1599-1609, 2008.

Mukherjee, S., Mahata, B., Mahato, B. and Adhya, S. Targeted mRNA degradation by complex-mediated delivery of antisense RNAs to intracellular human mitochondria. *Hum. Mol. Genet.* **17:** 1292-1298, 2008.

Bandyopadhaya, A., Sarkar, M. and Chaudhuri, K. Human intestinal epithelial cell cytokine mRNA responses mediated by NF-κB are modulated by the motility and adhesion process of *Vibrio cholerae. Intl. J. Biochem. Cell. Biol.* **39:** 1863-1876, 2007.

Bandyopadhaya, A., Sarkar, M. and Chaudhuri, K. Transcriptional upregulation of inflammatory cytokines in human intestinal epithelial cells following *Vibrio cholerae* infection. *FEBS J.* **274:** 4631-4642, 2007.

Roychoudhury, P. and Chaudhuri, K. Evidence for heterogeneous nuclear ribonucleoprotein K overexpression in oral squamous cell carcinoma. *Br. J. Cancer.* **97:** 574-576, 2007.

Sarma, M. D., Ghosh, R., Patra, A., Chowdhury, R., Chaudhuri, K. and Hazra, B. Novel glycoconjugates of diospyrin, a quinonoid plant product: synthesis and evaluation of cytotoxicity against human malignant melanoma (A375) and laryngeal carcinoma (Hep2). *Org. Biomol. Chem.* **5:** 3115-3125, 2007.

Nag, S. and Chaudhuri, K. Differential regulation of inter-chromosomal copies of ToxR-induced genes. *Can. J. Microbiol.* **53:** 992-999, 2007.

Chatterjee, J., Mukherjee, A., Mukherjee, K., Dutta, P. K. and Chaudhuri, K. Statistical modeling of ultrastructural features of murine dermal collagen under chronic low-dose whole body X-irradiation. *FEBS Lett.* **581:** 5034-42, 2007.

Chowdhury, R., Dutta, A., Chaudhuri Ray, S., Sharma, N., Giri, A. K. and Chaudhuri, K. *In vitro* and *in vivo* reduction of sodium arsenite induced toxicity by aqueous garlic extract. *Food Chem. Technol.* **46:** 740-751, 2008.

Ray, K., Chaki, M. and Sengupta, M. Tyrosinase and ocular diseases: some novel thoughts on the molecular basis of oculocutaneous albinism type 1. *Prog. Retinal Eye Res.* **26:** 323-358, 2007.

Acharya, M., Mookherjee, S., Bhattacharjee, A., Thakur, S. K. D., Bandyopadhyay, A. K., Chakrabarti, S. and Ray, K. Evaluation of the Opticin gene in primary open angle glaucoma: functional significance of a silent change, *BMC Mol. Biol.* **8:** 21, 2007.

Bhattacharjee, A., Acharya, M., Mukhopadhyay, A., Mookherjee, S., Banerjee, D., Bandyopadhyay, A. K., Thakur, S. K. D., Sen, A. and Ray, K. Myocilin mutations and SNPs in Indian POAG patients. *Arch. Ophthalmol.* **125:** 823-829, 2007.

Sengupta, M., Chaki, M., Arti, N. and Ray, K. *SLC45A2* variations in Indian oculocutaneous albinism patients. *Mol. Vis.* **13:** 1406-1411, 2007.

Gupta, A., Maulik, M., Nasipuri, P., Chattopadhyay, I., Das, S. K., Gangopadhyay, P. K. and Ray, K. The Indian Genome Variation Consortium: Molecular diagnosis of Wilson disease using prevalent mutations and informative SNP markers. *Clin. Chem.* **53:** 1601-1608, 2007.

Biswas, A., Maulik, M., Das, S. K., Ray, K. and Ray, J. The Indian Genome Variation Consortium: Parkin polymorphisms: Risk for Parkinson's disease in Indian population. *Clin. Genetics* **72:** 484-486, 2007.

Gupta, A., Chattopadhyay, I., Dey, S., Nasipuri, P., Das, S. K., Gangopadhyay, P. K. and Ray, K. Molecular pathogenesis of Wilson disease among Indians: A perspective on mutation spectrum in ATP7B gene, prevalent defects, clinical heterogeneity and implication towards diagnosis. *Cell. Mol. Neurobiol.* **27:** 1023-33, 2007.

Ghosh, P., Banerjee, M., Chaudhuri, S. D., Chowdhury, R., Das, J. K., Mukherjee, A., Sarkar, A. K., Mondal, L. K., Baidya, K., Sau, T. J., Banerjee, A., Basu, A., Chaudhuri, K., Ray, K. and Giri, A. K. Comparison of health effects between individuals with and without skin lesions in the population exposed to arsenic through drinking water in West Bengal, India. *J. Exposure Sci. Environ. Epidemiol.* **17:** 215-223, 2007.

Banerjee, M., Sarkar, J., Das, J. K. and Mukherjee, A., Sarkar, A. K., Mondal, L. K. and Giri, A. K. Polymorphism in the ERCC2 codon 751 is associated with arsenic-induced premalignant hyperkeratosis and significant chromosomal aberrations. *Carcinogenesis* **28:** 672-676, 2007.

Ghosh, P., Banerjee, M., De Chaudhuri, S., Das J. K., Sarma, N., Basu, A. and Giri, A. K. Increased chromosome aberration frequencies in the Bowen's patients compared to non-cancerous skin lesions individuals exposed to arsenic. *Mut. Res.* **632:** 104-110, 2007.

De Chaudhuri, S., Ghosh, P., Sarma, N., Majumdar, P., Sau T. J., Basu, S., Roychoudhury, S., Ray, K. and Giri, A. K. Genetic variants associated with arsenic susceptibility: Study of purine nucleoside phosphorylase, arsenic (+3) methyl transferase and glutathione S-transferase omega genes. *Environ. Health Perspect.* **116:** 501-505, 2008.

Banerjee, M., Sarma, N., Biswas, R., Roy, J., Mukherjee A. and Giri, A. K. Deficiency in DNA repair leads to arsenic susceptibility:Evidence from Comet assay and challenge assay. *Int. J. Cancer* **123:** 283-287, 2008.

Banerjee, N., Banerjee, M., Ganguly, S., Bandopadhyay, S., Das, J.K., Bandopadhay, A., Chatterjee, M. and Giri, A. K. Arsenic induced mitochondrial instability leading to programmed cell death in the arsenic exposed individuals. *Toxicology* **246:** 101-111, 2008.

Biswas, R., Ghosh, P., Banerjee, N., Das, J. K., Sau, T. J., Banerjee, A., Roy, S., Ganguly, S., Chatterjee, M., Mukherjee, A. and Giri, A. K. Assessment of T Cell proliferation and cytokine secretion in the individuals exposed to arsenic. *Hum. Exp. Toxicol.* **27:** 381-386, 2008.

Biswas, D., Banerjee, M., Sen, G., Das, J. K., Banerjee, A., Sau, T. J., Pandit, S., Giri A. K. and Biswas, T. Mechanism of erythrocyte death in human population exposed to arsenic through drinking water. *Toxicol. Appl. Pharmacol.* **230:** 57-66, 2008.

Halder, B., Bhattacharya, U., Mukhopadhyay, S. and Giri A. K. Molecular mechanism of black tea polyphenols induced apoptosis in human skin cancer cells: involvement of Bax translocation and mitochondria mediated death cascade. *Carcinogenesis* **29:** 129-138, 2008.

Mitra, S., Banerjee, S., Mishra, C., Singh, R.K., Roy, A., Sengupta, A., Panda, C. K. and Roychoudhury, S**.** Interplay between human papilloma virus infection and *p53* gene alterations in head and neck squamous cell carcinoma of an Indian patient population**.** *J. Clin. Pathol.* **60:**1040-1047, 2007.

Singh, R. K., Indra, D., Mitra, S., Mondal, R. K., Basu, P. S., Roy, A., Roychoudhury, S. and Panda, C. K. Deletions in chromosome 4 differentially associated with the development of cervical cancer: evidence of slit2 as a candidate tumor suppressor gene**.** *Hum. Genet*. **122:** 71-81, 2007.

Sinha, S., Chunder, N., Mukherjee, N., Roy, A., Roychoudhury, S. and Panda, C. K. Frequent deletion and methylation in SH3GL2 and CDKN2A loci are associated with early- and late-onset breast carcinoma**.** *Ann. Surg. Oncol*. **15:** 1070-1080, 2008.

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Acharya, D., Saha, D., Roy, D., Jain, P. and Dhar, T. K. Filtration-based staining of proteins on membranes. *Anal. Biochem*. **379:** 121-123, 2008.

Goswami, S. and Das, P. K. Detection and quantification of ppb level potassium in biological samples in the presence of high sodium by ion chromatographic method. *J. Chromatogr.* B. **863:** 9-18, 2008.

Singh, L. P., Kundu, P., Ganguly, K., Mishra, A. and Swarnakar, S. A novel role of famotidine in downregulation of matrix metalloproteinase-9 during protection of ethanol-induced acute gastric ulcer. *Free Rad. Biol. Med.* **43:** 289-299, 2007.

Paul, S., Sharma, A. V., Das Mahapatra, P., Bhattacharya, P. and Swarnakar, S. Role of melatonin in regulating matrix metalloproteinase-9 via tissue inhibitors of metalloproteinase-1 during protection against endometriosis. *J. Pineal Res*. **44:** 439-49, 2008.

Basu, A., Chaudhuri, P., Malakar, D. and Ghosh, A. K**.** Co-purification of glucanase with acid trehalase–invertase aggregate in *Saccharomyces cerevisiae. Biotechnol. Lett.* **30:** 299-304, 2008.

Chaudhuri, P., Basu, A. and Ghosh, A. K. Aggregation dependent enhancement of trehalose-6-phosphate synthase activity in *Saccharomyces cerevisiae*. *Biochim. Biophys. Acta* **1780:** 289-297, 2008.

Malakar, D., Dey, A., Basu, A. and Ghosh, A. K. Antiapoptotic role of S-adenosyl-L-methionine against hydrochloric acid induced cell death in *Saccharomyces cerevisiae. Biochim. Biophys. Acta* **1780:** 937 –947, 2008.

Ghanta, S., Banerjee A., Poddar, A. and Chattopadhyay, S. Oxidative DNA damage preventive activity and antioxidant potential of *Stevia rebaudiana* (Bertoni) Bertoni, a natural sweetner. *J. Agri. Food Chem.* **55:** 10962-10967, 2007.

Poddar, A., Banerjee A., Ghanta, S. and Chattopadhyay, S. In vivo efficacy of calceolarioside A against experimental visceral leishmaniasis. Planta Med. **74**: 503-508, 2008.

CHEMISTRY

Sengupta, J., Mukhopadhyay, R.and Bhattacharjya, A. Bis- and trisuracil nucleosides with nucleobases anchored to 11-,12-, and 16-membered macrocyclic scaffolds: synthesis and aggregation Study. *J. Org. Chem.* **72:** 4621-4625, 2007.

Ray, A., Bhattacharya, S., Ghorai, S., Ganguly, T. and Bhattacharjya, A. Synthesis and trans–cis isomerization of azobenzene dendrimers incorporating 1,2-isopropylidenefuranose rings. *Tetrahedron Lett.* **48:** 8078-8082, 2007.

Tripathi, S., Roy, B. G., Drew, M. G. B. and Achari, B., and Mandal, S. B. Synthesis of oxepane ring containing monocyclic, conformationally restricted bicyclic and spirocyclic nucleosides from D-glucose: a cycloaddition approach. *J. Org. Chem.* **72:** 7427-7430, 2007.

Maity, J. K., Mukherjee, S., Drew, M. G. B., Achari, B. and Mandal, S. B. First example of 5/6-*O*-linked pseudosaccharides: synthesis of bicyclic nucleosides containing azido or extended carbohydrate moiety. *Carbohydr. Res.* **342:** 2511-2521, 2007.

Giri, P. and Suresh Kumar, G. Specific binding and self-structure induction to poly (A) by the cytotoxic plant alkaloid sanguinarine. *Biochim. Biophys. Acta* **1770:** 1419-1426, 2007.

Sinha R., Hossain, M. and Suresh Kumar, G. RNA binding small molecules: Studies on t-RNA binding by cytotoxic plant alkaloids berberine, palmatine and comparison to ethidium. *Biochim. Biophys. Acta* **1770:** 1636-1650, 2007.

Hossain, M., Giri, P. and Suresh Kumar, G. DNA intercalation by quinacrine and methylene blue: a comparative binding and thermodynamic characterization study. *DNA Cell Biol.* **27:** 81-90, 2008.

Giri, P. and Suresh Kumar, G. Spectroscopic and calorimetric studies on the binding of the phototoxic and cytotoxic plant alkaloid sanguinarine with double helical poly (A). *J. Photochem. Photobiol. A: Chemistry*. **194:** 111-121, 2008.

PUBLICATIONS

Islam, Md. M. and Suresh Kumar, G. RNA targeting by small molecule alkaloids: studies on the binding of berberine and palmatine to polyribonucleotides and comparison to ethidium, *J. Mol. Struct*. **875:** 382-391, 2008.

Bhadra, K., Maiti M. and Suresh Kumar, G., Thermodynamics of the binding of cytotoxic protoberberine molecule coralyne to deoxyribonucleic acids. *Biochim. Biophys. Acta* **1780:** 298-306, 2008.

Das, S. and Suresh Kumar, G. Molecular aspects on the interaction of phenosafranine to deoxyribonucleic acid: Model for intercalative drug-DNA binding. *J. Mol. Struct*. **872:** 56-63, 2008.

Bhadra, K., Maiti M. and Suresh Kumar, G Interaction of isoquinoline alkaloid palmatine with deoxyribonucleic acids: Binding heterogeneity and conformational and thermodynamic aspects. *Chem. Biodiver*. **5:** 575-590, 2008.

Jagadeesh, S., Sinha S., Pal, B. C., Bhattacharya, S. and Banerjee P. P. Mahanine reverses an epigenetically silenced tumor suppressor gene RASSF1A in human prostate cancer cells. *Biochem. Biophys. Res. Comm.* **362:** 212-217, 2007.

Kumar, V., Mukherjee, K., Pal, B. C., Houghton, P. J. and Mukherjee, P. K. Acetylcholinesterase inhibitor fron *Clitoria ternatea*. *Planta Medica* **73:** 973-974, 2007.

Dey, S., Pal, C., Nandi, D., Giri, V. S., Zaidlewicz, M., Krzeminski, M., Smentek, L., Hess Jr, B. A., Gawronski, J., Kwit, M., Babu, N. J., Nangia, A. and Jaisankar, P. Lewis Acid-catalyzed one-pot, three-component route to chiral 3,32-bipyrroles. *Org. Lett.* **10:** 1373-1376, 2008.

Roy, A., Das, B. B., Ganguly, A., Bose Dasgupta, S., Khalkho, N. V. M., Pal, C., Dey, S. Giri, V. S., Jaisankar, P. and Majumder, H. K. An insight into the mechanism of inhibition of unusual bi-subunit topoisomerase I from *Leishmania donovani* by 3,3′-diindolylmethane, a novel DNA topoisomerase I poison with a strong binding affinity to the enzyme. *Biochem. J.* **409:** 611-622, 2008**.**

Sarkar, S., Saha, M., Roy, D., Jaisankar, P., Das, S., Roy, L. G., Gachhui, R., Sen, T. and Mukherjee, J. Enhanced production of antimicrobial compounds by three salt-tolerant actinobacterial strains isolated from the Sundarbans in a niche-mimic bioreactor. *Marine Biotech.* **10:** 518-526, 2008.

Pal, C., Dey, S., Mahato, S. K., Vinayagam, J., Pradhan, P. K. Giri, V. S., Jaisankar, P., Hossain, T., Baruri, S., Ray, D. and Mandal Biswas, S. Eco-friendly synthesis and study of new plant growth promoters: 3,3′-Diindolylmethane and its derivatives. *Bioorg. Med. Chem. Lett.* **17:** 4924-4928, 2007.

Dutta, A., Ghosal, A., Mandal, D., Mondal, N.B., Banerjee, S., Sahu, N.P. and Mandal, C. Racemoside A, an anti-leishmanial, water soluble, natural steroidal saponin, induces programmed cell death in *Leishmania donovani*. *J. Med. Microbiol.* **56:**1196-1204, 2007.

Bhowal, S. K., Lala, S., Hazra, A., Paira, P., Banerjee, S., Mondal, N. B. and Chakrabarty, S. Synthesis and assessment of fertility regulating potential of 2-(2"-chloroacetamidobenzyl)-3-(3'-indolyl) quinoline in adult rats as a male contraceptive agent. *Contraception* **77:** 214-222, 2008.

Hazra, A., Paira, P., Sahu, K. B., Banerjee, S., Mondal, N. B. and Sahu, N. P. Moleculer iodine: an efficient catalyst for the synthesis of symmetrical and unsymmetrical tri-indolylmethane (TRIM). *Cat. Commun.* **9:** 1681-1684, 2008.

Majhi, T. P., Achari, B. and Chattopadhyay, P. Advances in the synthesis and biological perspectives of benzannulated medium ring heterocycles. *Heterocycles* **71:** 1011-1052, 2007.

Neogi, A., Majhi, T. P., Achari, B. and Chattopadhyay, P. Palladium-catalyzed intramolecular C-O bond formation: A chiron approach to the synthesis of medium ring oxygen heterocycles. *Eur. J. Org. Chem*. 330-336, 2008.

Bose, P. P., Drew, M. G. B. and Banerjee, A. Decoration of Au and Ag nanoparticles on self-assembling pseudopeptide based nanofiber using a short peptide as a capping agent for metal nanoparticles. *Org. Lett*. **9:** 2489-2492, 2007.

Bose, P. P., Das, A. K., Hegde, R., Shamala, N. and Banerjee, A. pH sensitive nanostructural transformation of a synthetic self-assembling water-soluble tripeptide: nanotube to nanovesicle. *Chem. Mater.* **19:** 6150-6157, 2007.

Palui, G., Simon, F. X., Schmutz, M., Mesini, P. J. and Banerjee, A**.** Organogelators from self-assembling peptide based dendrimers: Structural and morphological features. *Tetrahedron* **64:** 175-185, 2008.

Guha, S., Drew, M. G. B. and Banerjee. A. Dipeptide nanotubes, with N-terminally located omega-amino acid residues, which are stable proteolytically, thermally, and over a wide range of pH. *Chem. Mater.* **20**: 2282-2290, 2008

Banerjee, A., Palui, G. and Banerjee, A. Pentapeptide based organogels: the role of adjacently located phenylalanine residues in gel formation. *Soft Matter* **4:** 1430-1437, 2008.

Naskar, J., Drew, M. G. B., Deb, I., Das, S. and Banerjee, A. A water-soluble tripepide Ab (9-11) forms amyloid-like fibrils and exhibits neurotoxicity. *Org. Lett.* **10**: 2625-2628, 2008.

Mazumder, K., Choudhury, B. P., Nair G. B. and Sen, A. K. Identification of a novel sugar 5,7-diacetamido-8-amino-3,5,7,8,9-pentadeoxy-D-glycero-D-galacto-non-2-ulosonic acid present in the lipooligosaccharide of *Vibrio parahaemolyticus* O3:K6. *Glycoconjugate J*. **25**: 345-354.2008.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

PUBLICATIONS

Polley, S., Guha, S., Roy, N. S., Kar, S., Sakaguchi, K., Chuman, Y., Swaminathan, V., Kundu, T. and Roy, S. Differential recognition of phosphorylated transactivation domains of p53 by different p300 domains. *J. Mol. Biol.* **376:** 8-12, 2008.

Nandi, S., Marjan, V. and Bagchi, M.C. Anticancer activity of selected phenolic compounds: QSAR studies using ridge regression and neural networks. *Chem. Biol. Drug Design* **70:** 424-436, 2007.

Ghosh, P., Marjan, V., Chattopadhyay, A. K. and Bagchi M. C. On application of constitutional descriptors for merging of quinoxaline data sets using linear statistical methods. *Chem. Biol. Drug Design* **72:** 155-162. 2008.

Bag, S. K., Paul, S. Ghosh, S. and Dutta, C. Reverse polarization in amino acid and nucleotide substitution patterns between human-mouse orthologs of two compositional extrema. *DNA Res*. **14**: 141-54, 2007.

Paul, S., Bag, S. K., Das, S., Harvill, E. and Dutta, C. Molecular signature of hypersaline adaptation insights from genome and proteome composition of prokaryotes *Genome Biology* **9:** R70, 2008.

De, D. and Bhattacharyya, D. Secondary emissions from spectrofluorimeters. *Curr. Sci.* **93**: 911-914, 2008

Mandal, S. and Bhattacharyya, D. Two L-amino acid oxidase isoenxymes from Russell's viper (*Daboia russelli russelli*) venom with different mechanisms of inhibition by substrate analogs. *FEBS J.* **275:** 2078-2095, 2008.

Bhutoria, S. and Ghoshal, N. A Novel approach for the identification of selective anticonvulsants Based on differential molecular properties for TBPS displacement and anticonvulsant activity: An integrated QSAR modeling, *QSAR Comb. Sci*, **27:** 876-889, 2008.

Yadav, R. K., Dolai, S., Pal, S. and Adak S. Role of tryptophan-208 residue in cytochrome c oxidation by ascorbate peroxidase from Leishmania major-kinetic studies on Trp208Phe mutant and wild type enzyme. *Biochim. Biophys. Acta* **1784:** 863-871, 2008.

Kumar, S., Chatterjee, R., Dolai, S., Adak, S., Kabir, S.N., Banerjee, S. and Mondal, N.B. Chenopodium album seed extract-induced sperm cell death: exploration of a plausible pathway. *Contraception* **77:** 456-462, 2008.

Publications (2007-2008) at a Glance

Total Number of Publications	**…**	**127**
Average Impact Factor	**…**	**3.34**

BOOKS/REVIEWS/POPULAR ARTICLES

INFECTIOUS DISEASES AND IMMUNOLOGY

Sen, N. and Majumder, H. K. Mitochondrion of protozoan emerges as potent therapeutic target: exciting drugs are on the horizon. *Current Pharm. Design* **14:** 839-846, 2008.

Das, B. B., Ganguly, A. and Majumder H. K. DNA topoisomerases of *Leishmania*: The potential targets for anti-leishmanial therapy. *Adv. Exp. Med. Biol.* **625:** 103-115, 2008.

Sen, N., Banerjee, B. and Majumder, H. K. Molecular analysis of programmed cell death by DNA topoisomerase inhibitors in kinetoplastid parasite *Leishmania. In*: *Programmed cell death in protozoa*, (Ed. Jose Manuel Perez Martin), Landes Biosceince Publishers, Sprigner, USA, pp. 49-58, 2008

Bhadra, R. K. and Das, B. Coordinated regulation of gene expression in *Vibrio cholerae*. *In: 'Vibrio cholerae: Genomics and Molecular Biology*, (Eds. S.M. Faruque and G. B. Nair), Caister Academic Press, UK, pp. 153-167, 2008.

Roychoudhury, J. and Ali, N. Sodium stibogluconate: Therapeutic use in the management of leishmaniasis. *Indian J. Biochem. Biophys*. **45:** 16-22, 2008.

Ghoshal, A., Mukhopadhyay nee Bandyopadhyay, S. and Mandal, C. Sialoglycotherapeutics in protozoal diseases**.** *Mini-Reviews in Medicinal Chemistry*, Bentham Science Publishers, **8:** 358-369, 2008.

MOLECULAR & HUMAN GENETICS

Chaudhuri, K. and Chatterjee, R. MicroRNA detection and target prediction: Integration of computational and experimental approaches. *DNA Cell Biol.* **26:** 321-37, 2007.

De Chaudhuri, S., Kundu, M., Banerjee, M., Das, J. K., Majumdar, P., Basu, S., Roychoudhury, S., Singh, K. K. and Giri, A. K. Arsenic-induced health effects and genetic damage in keratotic individuals: involvement of p53 arginine variant and chromosomal aberrations in arsenic susceptibility. *Rev. Mut. Res.* **659:** 118-125, 2008.

CHEMISTRY

Maiti, M. and Suresh Kumar G. Molecular aspects on the interaction of proto-berberine, benzophenanthridine and aristolochia group of alkaloids with nucleic acid structures and biological perspectives. *Med. Res. Rev*. **27:** 649-695, 2007.

Maiti, M. and Suresh Kumar, G. Protoberberine alkaloids: Physicochemical and nucleic acid binding properties. *In: Top. Heterocycl. Chem.* Springer-Verlag, Berlin Heidelberg, Vol. 10: pp. 155-209, 2007.

Doctorates from the Institute

Name of Ph. D awarded candidate	*Name of supervisor*

INFECTIOUS DISEASES AND IMMUNOLOGY

Dr. Aruna Biswas	Dr. Pijush K. Das
Dr. Dipyaman Ganguly	Dr. Santu Bandopadhyay
Dr. (Mrs.) Srabanti Rakshit	Dr. Santu Bandopadhyay
Dr. Samiran Saha	Dr. Nahid Ali
Dr. Antara Banerjee	Dr. Nahid Ali
Dr. Sanjib Banerjee	Dr. Rukhsana Chowdhury
Dr. Amalendu Ghosh	Dr. Rukhsana Chowdhury

CELL BIOLOGY & PHYSIOLOGY

Dr. Asmita Dasgupta	Dr. Sumantra Das & Dr. P. K. Sarkar
Dr. Ishani Deb	Dr. Sumantra Das
Dr. Jana Chakrabarti	Dr. Syed N. Kabir
Dr. Kaushik Das	Dr. G. C. Majumder & Dr Sandhya R. Dungdung
Dr. Pamela Ghosh	Dr. Sib Sankar Roy & Prof. S. Bhattacharya
Dr. Samir Kumar Saha	Dr. Sib Sankar Roy & Prof. S. Bhattacharya
Dr. Debalina Dey	Dr. Sib Sankar Roy

Name of Ph. D awarded candidate	*Name of supervisor*

MOLECULAR & HUMAN GENETICS

Dr. Arnab Gupta	Dr. Kunal Ray
Dr. Moumita Chaki	Dr. Kunal Ray
Dr. Paromita Roychoudhury	Dr. Keya Chowdhury
Dr. Gourish K. Mondal	Dr. Sushanta Roy Chowdhuri
Dr. Meenakshi Chakravarti	Dr. Sushanta Roy Chowdhuri

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. Anindita Debnath	Dr. Aparna Gomes
Dr. Suchandra Goswami	Dr. Pratap K. Das
Dr. Dipankar Malakar	Dr. Anil K. Ghosh
Dr. Akhilesh Kumar	Dr. Sharmila Chattopadhyay
Dr. Anindita Ray	Dr. P. C. Banerjee & Dr. A. K. Ghosh
Dr. Arghya Basu	Dr. Anil K. Ghosh

CHEMISTRY

Dr. Prasun Kanti Pradhan	Dr. V. S. Giri
Dr. Nilendu Panda	Dr. N. B. Mandal
Dr. Debayan Mandal	Dr. N. B. Mandal
Dr. Debraj Mukherjee	Dr. U. S. Chowdhuri & Dr. P. Chatterjee

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Dr. Sabyasachi Das	Dr. Chitra Dutta
Dr. Gargi Maity	Dr. Debasish Bhattacharyya
Dr. Sangeeta Nath	Dr. Debasish Bhattacharyya

Honours and Awards

INFECTIOUS DISEASES AND IMMUNOLOGY

Dr. H. K. Majumder

Member of the Institutional Ethical Committee, Institute of Post Graduate Medical Education & Research (IPGMER), Kolkata. 2007-till date.

Member of the Research Advisory Committee of the Central Sericulture Research & Training Institute, Berhampur, Murshidabad, West Bengal.

Member of the Selection Committee for SRF/RA of CSIR.

Member of the Section Committee (VII) of Indian National Science Academy (FNA)

Member of the Fellowship Scrutiny Committee of National Academy of Sciences, India (FNASc)

Prof. Jnan Chandra Ghosh Memorial Award by Science Association of Bengal for excellent contribution in the field of science & technology, research promotion and development in India and abroad in 2007.

Prof. B. K. Bachhawat Memorial Lecture Award by National Academy of Sciences, India in 2007.

Chairman of the NASI, Allahabad Kolkata Local Chapter (NASI), w.e.f. 31.12.2007.

Chairman, Expert Committee for State Innovation Award, Govt. of West Bengal.

Chairman, State Level Climatic Change Committee**,** Govt. of West Bengal.

Working Chairman of the West Bengal State Council of Science & Technology-2004 onwards.

Edited a book on. 'Drug targets in kinetoplastid Parasites 'published by Landes Bioscience publishers, springer, USA 2007.

Dr. Pijush K. Das

Senior Scientist Oration Award from Indian Immunology Society (IIS) for outstanding work in Immunology at 34th Annual Meeting of IIS held in December 16-18, 2007 at National Aids Research Institute (NARI), Pune.

Member of the American Association of Immunologists.

Departmental Core Committee Member of the Recruitment and Assessment Board (RAB) of CSIR.

Member of Board of Studies of Calcutta University

Reviewer of National & International journals

Dr. Syamal Roy

"Shri Rajendra Prasad Oration", RMRI, Indian Council of Medical Research, Patna Dec 3, 2007.

Dr. Nahid Ali

Reviewer of papers to be published in Medical Microbiology and Immunology, European Journal of Biopharmaceuticals & Biopharmaceutics, Journal of Biosciences, Chemistry and Physics of Lipid, Vaccine, Drug development and Industrial Pharamacology, and Acta Tropica.

CELL BIOLOGY & PHYSIOLOGY

Dr. K. P. Mohanakumar

Reviewer of Brain Research (USA), Behavioural Brain Research (Germany), European Neuropsychopharmacology (Netherlands), Nitric Oxide (USA), Neuroscience Research (Ireland), Neurochemical Research (USA), Life Science (England), Journal of Diabetes and Its Complications (USA), The Journal of Agricultural Science (UK), BMC Neuroscience (England), Journal of Neuroscience Research (USA), Journal of Tissue Research (India), Indian Journal of Pharmacology (India), Current Science (India), Indian Journal of Biochemistry and Biophysics (India).

Advisor for the Institute for Communicative & Cognitive Neuro Sciences (ICCNS), Kerala under the Ministry of Health Sciences, Department of Public Health, Government of India.

Nominated member (D.G's representative) of the Research Council of the Central Drug Research Institute, Lucknow beginning from 1st April, 2007.

Member of the 10th Meeting of the Scientific Advisory Committee (SAC) of NBRC held during 17th and 18th April, 2007 at Manesar, Haryana.

Member of the Planning Committee for conducting and monitoring DST- SERC School in Neurosciences on 25th of April, 2007 at INSA, New Delhi.

IICB representative at the CSIR-Industry Meet and Annual Business Meet during 17th to 19th May 2007 held at IICT, Hyderabad.

Attended a 3-day programme on 'Leveraging Intellectual Property for Business Development' from 6th to 8th August, 2007 in Ghaziabad organized by the Human Resource Development Centre (CSIR).

Attended the International Society for Neurochemistry's symposium on "Neuroinflammatory Processes and Therapeutic Measures in Parkinson's Disease" during the 21st Biennial Meeting held at Cancun, Mexico.

Invited by Dr. R. V. Omkumar, Organizing Secretary of Trendys 2007 to give a lecture at Trendys 2007 which was held at Rajiv Gandhi Centre for Biotechnology during 28 and 29 of September, 2007.

Co-convener of Guha Research Conference-2007 held during December 18-22, 2007 in Kolkata.

Dr. Sib Sankar Roy

Appointed as a UGC visiting teacher by Tripura University, Agartala.

CSIR Raman Research Fellowship Award in 2008.

Dr. S. N. Kabir

Appointed as a member of the editorial Board of the "Proceedings of the Zoological Society of India"

MOLECULAR & HUMAN GENETICS

Dr. Samit Adhya

Member RAP/SAC for DNA Finger Printing and Diagonistics, Hyderabad.
Member RAP/SAC, Bose Institute, Kolkata.
Member RAP/SAC, National Institute of Immunology, New Delhi.

Dr. Kunal Ray

Elected as an Associate Editor of Journal of Genetics published by Springer (2008).
Elected as a member of *Guha Research Conference,* 2007

DRUG DEVELOPMENT, DIAGNOSTICS & BIOTECHNOLOGY

Dr. J. R. Vedasiromoni

Nominated for Col. R. N. Chopra Oration by the Indian Pharmacological Society and delivered the oration in the XXXX Annual Conference of the Indian Pharmacological Society, NIPER, Mohali, November, 1-3, 2007.

Dr. Snehasikta Swarnakar

National Bioscience Award 2007 by Govt. of India, Ministry of Science and Technology, Department of Biotechnology, India

CHEMISTRY

Dr. G. Suresh Kumar

Elected Member, National Academy of Science, India

Dr. A. K. Banerjee

Convenor / Director, NIPER, Kolkata

Dr. A. K. Sen, Jr.

Elected as Hon. Secretary of the Association of Carbohydrate Chemists & Technologists (India) 2007-2008.

STRUCTURAL BIOLOGY & BIOINFORMATICS DIVISION

Prof. Siddhartha Roy

Awarded "Prestigious Tata Innovation Fellowship 2007 – 2008

Dr. Debasish Bhattacharyya

Selected as one of the top-ranking reviewer of the 'Journal of Chromatography B' for the year 2007.

Dr. Chitra Dutta

Member, Editorial Board, International Journal of Soft Computing & Bioinformatics

Member, Board of Studies, Dept of Biotechnology, National Institute of Technology (Deemed Univ.) Durgapur, W. B.

Reviewer, Nucleic Acids Research, DNA Research, Bioinformatics, BMC Genomics, BMC Evolutionary Biology, Microbiology etc.

Staff List of IICB as on 31.03.2008

Staff Strength at a Glance

Director	…	…	1
Scientist, Gr. IV	…	…	77
Engineer	…	…	4
Technical, Gr. III	…	…	53
Technician, Gr. II	…	…	37
Helper, Gr. I	…	…	20
Ministerial Officer	…	…	11
Ministerial Staff	…	…	54
Gr. D (Non-Technical)	…	…	17
Canteen Staff	…	…	10
TOTAL	**…**	**…**	**284**

Detailed Staff List

Scientific and Technical

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
1.	Prof. Siddhartha Ray	489	DIRECTOR
2.	Dr. H.K. Majumdar	23	SCIENTIST GR. IV(6)
3.	Dr. Samit Adhya	37	DO
4.	Dr. Pijush K. Das	40	DO
5.	Dr. V.S. Giri	39	SCIENTIST GR. IV(5)
6.	Sri Debashish Pal	43	DO
7.	Dr. K.P. Mohanakumar	77	DO
8.	Dr. Tarun K. Dhar	63	DO
9.	Dr. S.B. Mondal	76	DO
10.	Dr. (Mrs.) M. Mukherjee	47	DO
11.	Dr. A.K. Sen (Jr)	65	DO
12.	Dr. (Mrs.) Chitra Mandal	60	DO
13.	Dr. J.R. Vedasiromoni	53	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
14.	Dr. B.C. Pal	64	DO
15.	Dr. Anil K. Ghosh	68	DO
16.	Dr. Syamal Roy	93	DO
17.	Dr. (Mrs.) Keya Chaudhuri	83	DO
18.	Dr. Sumantra Das	87	DO
19.	Sri Ajoy Kr. Banerjee	85	DO
20.	Dr. Partha Chattopadhyay	81	DO
21.	Dr. S.B. Mukhopadhyay	80	DO
22.	Dr. Santu Bandyopadhyay	97	DO
23.	Dr. Manish Ch. Bagchi	78	DO
24.	Dr. S.N. Kabir	90	DO
25.	Dr. (Mrs.) Chitra Dutta	95	DO
26.	Dr. Ashok Kumar Giri	402	DO
27.	Dr. Debashish Bhattacharya	96	DO
28.	Dr. Shyamal Kumar Dana	86	DO
29.	Dr. Ashish Kr. Sen (Sr)	55	SCIENTIST GR. IV(4)
30.	Dr. Aparesh Bhattacharya	59	DO
31.	Dr. U.S. Chowdhury	84	DO
32.	Dr. (Mrs.) Aparna Gomes	91	DO
33.	Dr. Nirmalendu Das	100	DO
34.	Dr. (Mrs.) Nahid Ali	103	DO
35.	Dr. G. Suresh Kumar	105	DO
36.	Dr. Susanta Roychowdhury	98	DO
37.	Dr. (Miss) Moonmoon Bhowmik	110	DO
38.	Dr. Kunal Ray	415	DO
39.	Dr. Samir Kr. Dutta	111	DO
40.	Dr. Sukdeb Bandopadhyay	102	DO
41.	Dr. Nirup Bikash Mondal	107	DO
42.	Dr. (Mrs.) Tuli Biswas	109	DO
43.	Dr. P. Jaisankar	112	DO
44.	Dr. (Mrs.) Rukhshana Chowdhury	115	DO
45.	Dr. S.N. Chakraborty	94	DO
46.	Dr. Ram Chandra Yadav	154	DO
47.	Dr. Ranjan Mukhopadhyay	114	DO
48.	Dr. Asish Kr. Banerjee	116	DO
49.	Dr. (Mrs.) Nanda Ghoshal	119	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
50.	Dr. Arun Bandyopadhyay	445	DO
51.	Dr. Rupak Kr. Bhadra	124	DO
52.	Dr. (Mrs.) Suman Khowala	118	DO
53.	Dr. (Miss) Chhanda Mitra	51	SCIENTIST GR. IV(3)
54.	Dr. Pratap Kr. Das	62	DO
55.	Sri U.K. Barua	464	DO
56.	Dr. Binayak Das	108	DO
57.	Dr. Tushar Kanti Chakraborty	99	DO
58.	Dr. (Mrs.) Padma Das	117	DO
59.	Dr. (Mrs.) S.R. Dungdung	120	DO
60.	Dr. Tanmoy Mukherjee	125	DO
61.	Mrs. N.V.M. Khalko	122	DO
62.	Dr. (Mrs.) Debjani Mondal	123	DO
63.	Dr. (Mrs.) Tripti De	433	DO
64.	Dr. Aditya Konar	441	DO
65.	Dr. Sibsankar Ray	443	DO
66.	Dr. Soumen Datta	503	DO
67.	Dr. Chinmay Chowdhury	520	DO
68.	Dr. Uday Bandopadhyay	521	DO
69.	Dr. K.N. Chattopadhyay	523	DO
70.	Dr. Mrinal Kanti Ghosh	524	DO
71.	Dr. Arindam Banerjee	526	DO
72.	Dr. (Mrs.) Malini Sen	527	DO
73.	Dr. Anindya Dasgupta	531	DO
74.	Dr. Bijon Kumar Ghosh	404	SCIENTIST GR. IV(2)
75.	Dr. (Mrs) Sarmila Chattopadhyay	447	DO
76.	Dr. Subrata Adak	472	DO
77.	Dr. (Miss) Snehasikta Swarnakar	473	DO
78.	Dr. Saraswati Garai	528	SCIENTIST GR. IV(1)
79.	Dr. (Mrs.) Mridula Misra	142	TECHNICAL OFFICER GR. III(7)
80.	Dr. (Mrs.) Krishna Das Saha	143	DO
81.	Sri H.N. Roy	152	DO
82.	Dr. (Mrs.) S.E. Besra	145	DO
83.	Sri Tapan Kumar Mukherjee	140	DO
84.	Sri Kalyan Kr. Sarkar	147	DO
85.	Sri Sailendra Nath Dey	148	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
86.	Sri Kalyanmay Dutta	153	DO
87.	Sri Tapan Kr. Chakraborty	159	DO
88.	Sri A.K. Das	151	DO
89.	Sri Subodh Kr. Roy	156	DO
90.	Dr. (Mrs) Mita Chatterjee Debnath	432	DO
91.	Sri S.K. Sahoo	163	DO
92.	Dr. S. Majumdar	164	DO
93.	Sri Sandip Saha	494	Ex. Engineer Gr. III(5)
94.	Sri Susanta Ray	514	ASSISTANT EXEC. ENGINEER
95.	Sri B. Jayakumar	517	DO
96.	Mrs. Nirali Bage	466	JUNIOR ENGINEER, GR. I
97.	Sri Mohan Lal Jana	167	TECHNICAL OFFICER GR. III(5)
98.	Dr. Prashanta Kr. Chakraborty	169	DO
99.	Dr. Kalidas Paul	168	DO
100.	Sri Shekhar Ghosh	467	DO
101.	Sri A.K. Bairagi	165	DO
102.	Sri Samir Kr. Roy	171	DO
103.	Dr. Ashok Kumar Dasgupta	172	DO
104.	Sri Narayan Ch. Ghosh	499	DO
105.	Sri Surajit Mohan Roy	166	DO
106.	Sri Gautam Gupta	170	DO
107.	Sri Binayak Pal	448	DO
108.	Mrs. Aparna Laskar	449	DO
109.	Dr. Sankar Kumar Maitra	174	DO
110.	Dr. (Mrs) Gayatri Tripathi	462	DO
111.	Dr. Ardhendu Kr. Mandal	175	DO
112.	Dr. Tapas Sarkar	177	DO
113.	Dr. Subhagata Ghosh Miss	179	DO
114.	Sri Arupesh Majumdar	180	DO
115.	Sri Kshudiram Naskar	162	TECHNICAL OFFICER GR. III(4)
116.	Sri Rajat Bandopadhyay	181	DO
117.	Dr. Ramdhan Majhi	184	DO
118.	Sri R.N. Mandi	185	DO
119.	Sri P. Gangopadhyay	186	DO
120.	Sri Asish Mullick	187	DO
121.	Mrs. Dipika Roy	188	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
122.	Mrs. Purnima Chatterjee	173	DO
123.	Mrs. Banasri Das	176	DO
124.	Sri Diptendu Bhattacharya	178	DO
125.	Sri E. Padmanaban	496	DO
126.	Sri Sekhar Mukherjee	477	DO
127.	Sri Pratap Ch. Kayal	182	DO
128.	Sri Utpal Halder	157	TECHNICAL OFFICER GR. III(3)
129.	Sri Sandip Chowdhury	411	TECHNICAL ASSISTANT GR. III(2)
130.	Dr. (Mrs) Shampa Sarkar	461	DO
131.	Mrs. Arti Khetrapaul	463	DO
132.	Sri Swapan Kr. Mondal	465	DO
133.	Sri Jishu Mandal	495	TECHNICAL ASSISTANT GR. III(1)
134.	Sri Debashis Banik	513	DO
135.	Sri Sandip Chakraborty	516	DO
136.	Sri Asutosh Mukherjee	193	TECHNICIAN GR. II(4)
137.	Sri Ajoy Kr. Pramanik	195	DO
138.	Sri M.B. Malakar	219	DO
139.	Sri S.K. Basak	220	DO
140.	Sri Phelaram Dhank	309	DO
141.	Sri Goutam Malik	224	DO
142.	Sri Gopal Ch. Sarkar	234	DO
143.	Sri P.K. Chanda	236	DO
144.	Sri S.N. Mondal	237	DO
145.	Sri S.K. Prodhan	239	DO
146.	Sri S.C. Das	241	DO
147.	Sri S.R. Tudu	251	DO
148.	Sri Swapan Kumar Naskar	244	DO
149.	Md. Ayub Shah	344	DO
150.	Sri Sheo Shankar Verma	242	DO
151.	Sri Tapas Chowdhury	246	DO
152.	Sri Pradip Mondal	383	DO
153.	Sri A.K. Sen	478	DO
154.	Sri Tarak Prasad Nandi	247	DO
155.	Mrs. Sutapa Ganguly	248	DO
156.	Sri Sanjib Biswas	249	DO
157.	Sri R.P. Gorh	250	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
158.	Sri Sarit K. Sarkhel	245	DO
159.	Sri Nishikanta Naskar	252	DO
160.	Sri Pallab Mukherjee	253	DO
161.	Sri Ranjit Das	345	DO
162.	Sri Abhijit Paul	450	TECHNICIAN GR. II(2)
163.	Sri Anirban Manna	410	DO
164.	Sri Samir Majumder	426	DO
165.	Md. M. Ahmed	360	DO
166.	Sri Paresh Sarkar	409	DO
167.	Sri Sujit Kr. Majumdar	416	DO
168.	Mrs. Mahua Bhattacharjee	419	DO
169.	Sri Prabir Kr. Das	418	DO
170.	Sri Atanu Maitra	417	DO
171.	Sri Tapan Das	460	DO
172.	Sri Ujjal Roy		TECH. ,GR,II(1)
173.	Sri R. Mahato	258	HELPER GR. I(4)
174.	Sri Tapan Kumar Mukherjee	267	DO
175.	Sri Sunil Nath	272	DO
176.	Sri R.N. Jana	274	DO
177.	Sri Prahlad Das	275	DO
178.	Sri Bhaskar Basu	440	DO
179.	Sri Brihaspati Das	347	DO
180.	Sri Shyamal Das	279	HELPER GR. I(3)
181.	Sri Sasthi C. Sil	356	DO
182.	Sri Madan Halder	479	DO
183.	Sri Amerika Das	280	DO
184.	Sri Nimai Charan Prodhan	282	DO
185.	Sri Sambhu Raul	351	DO
186.	Sri Suresh Balmiki	353	DO
187.	Mrs. Uma Biswas	455	DO
188.	Sri Nandalal Routh	352	HELPER GR. I(2)
189.	Sri S.K. Banik	361	DO
190.	Sri Ashoke Sardar	501	HELPER GR. I(I)
191.	Sri Ram Kumar Sarkar	502	DO
192.	Sri Shyamal Nath	519	DO

Administration

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
1.	Sri S.K. Chaudhuri	497	ADMINISTRATIVE OFFICE
2.	Sri S.K. Das	498	F & A OFFICER
3.	Sri U.S. Das	515	STORES & PURCHASE OFFICER
4.	Sri Subhas Ch. Dutta	290	SR. SECURITY OFFICER
5.	Sri Kausik Bhattacharjee	492	SECTION OFFICER (GENERAL)
6.	Sri H.N. Bonia	483	DO
7.	Sri Siddhartha Dey	485	DO
8.	Mrs. Shampoo Sengupta	525	DO
9.	Sri Asim Kr. Jha	518	SECTION OFFICER (F&A))
10.	Sri Basudev Bhattacharya	459	PRIVATE SECRETARY
11.	Sri S.K. Chhatui	312	DO
12.	Sri Kanu Mondal	392	ASSISTANT (GENERAL) GR. I (ACP)
13.	Sri K.C. Das	302	ASSISTANT (GENERAL) GR. I
14.	Mrs. Ratnabali Adhikari	304	DO
15.	Sri D.R. Chakraborty	306	DO
16.	Mrs. Anjana Mandi	308	DO
17.	Sri Ratan Bag	397	DO
18.	Mrs. Sanhita Ganguly	427	DO
19.	Mrs. Monalisa Mukhopadhyay	428	DO
20.	Mrs. Rita Sikdar	326	DO
21.	Miss Lily Das	330	DO
22.	Sri P.K. Saha	468	DO
23.	Sri Paritosh Purkait	339	DO
24.	Mrs. Indira Kundu	331	DO
25.	Sri R.N. Hansda	334	ASSISTANT (GENERAL) GR. II
26.	Sri Prem Singh	335	DO
27.	Sri D.K. Kisku	340	DO
28.	Sri Alok Ray	396	DO
29.	Sri Jayanta Pal	510	ASSISTANT (GENERAL) GR. III
30.	Sri Tarun Kr. Sinha Roy	508	DO
31.	Sri Raju Pal	507	DO
32.	Sri Ranjit Debnath	509	DO
33.	Sri Saugata Das	511	DO
34.	Sri Sukhendu Biswas	512	DO

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
35.	Sri Mrinal K. Ghosh	299	ASSISTANT (F & A) GR. I
36.	Sri A.K. Chanda	327	DO
37.	Mrs. Banani Dutta	476	DO
38.	Sri Sanjoy Mukhopadhyay	343	DO
39.	Mrs. P.L. Saha	332	ASSISTANT (F & A) GR. II (ACP)
40.	Sri Asit K. Roy	336	ASSISTANT (F & A) GR. II
41.	Sri M.K. Dutta	338	DO
42.	Sri Vishal Agarwal	506	ASSISTANT (F&A) GR. III
43.	Sri Tapan Kr. Mitra	320	ASSISTANT (S & P) GR. I
44.	Sri Panchanan Naskar	322	DO
45.	Sri A.B.S. Roy	328	DO
46.	Sri R.L. Bhattacharya	329	DO
47.	Sri Bisweswar Das	342	ASSISTANT (S & P) GR. II
48.	Mrs. Bula Pal	363	DO
49.	Sri Pradipta Sarkar	505	ASSISTANT (S&P) GR. III
50.	Sri Arnab Sen	504	DO
51.	Mrs. Ambalika Nag	321	SR. HINDI TRANSLATOR
52.	Sri Mangala Prasad Banerjee	469	SR. STENOGRAPHER (ACP)
53.	Sri Debdas Guhathakurta	313	DO
54.	Sri Nikhil Kumar Das	315	DO
55.	Sri Sankar Prasad Dutta	316	DO
56.	Sri Dipak Kr. Guin	318	DO
57.	Sri Asim Roy	323	SR. STENOGRAPHER
58.	Mrs. Pratima Banerjee	324	DO
59.	Sri Shankar Bhakta	325	DO
60.	Sri Rabindranath Das	393	DO
61.	Sri Saibal Giri	405	DO
62.	Sri Gautam Saha	453	JR. STENOGRAPHER
63.	Sri Sudip Ghosh	454	DO
64.	Sri Sankar Santra	490	DO
65.	Smt Moumita Majumdar	491	DO
66.	Sri U.N. Mandi	358	RECORD KEEPER
67.	Sri Ashok Ram	348	GR-D (NT) (UPGRADED under ACP)
68.	Sri Bideshi Nayak	349	DO
69.	Sri N.N. Prodhan	354	DO
70.	Mrs. Chaina Devi Nayak	366	GR-D (NT) (UPGRADED)

Sl. No.	EMPLOYEE'S NAME	EMP. ID	DESIGNATION
71.	Sri Kailash Chandra Nayak	365	DO
72.	Mrs. Gita Ghosh	364	DO
73.	Mrs Soma Devi Sharma	401	DO
74.	Sri Gopal Ch. Mandal	412	DO
75.	Sri Asit Mitra	413	DO
76.	Sri Janmanjoy Midya	431	DO
77.	Sri Pasupati Midya	430	DO
78.	Sri P.C. Dehury	414	GROUP-D (NT)
79.	Sri Shyamal Kr. Ghosal	423	DO
80.	Sri Tapan Sarkar	424	DO
81.	Sri Manoranjan Adhikary	425	DO
82.	Sri Dinesh Mehali	451	DO
83.	Sri Tarun Dutta	367	ASSTT. MANAGER-CUM-STORE KEEPER
84.	Sri Amal Dutta	369	COUPON CLERK
85.	Sri Balaram Panda	368	HALWAI-CUM-COOK
86.	Sri Sudhangshu Halder	373	TEA MAKER
87.	Sri Bimal Das	372	BEARER
88.	Sri Ashok Sadhukhan	371	BEARER
89.	Sri Badal Haldar	370	BEARER
90.	Sri Jagabandhu Biswas	374	WASH BOY
91.	Sri Mantu Das	376	SWEEPER
92.	Sri Nirapada Halder	375	SWEEPER

Positional Strength

Director	…	1
Scientist Gr. IV	…	77
Engineering	…	4
Technical Gr. III	…	53
Technician Gr. II	…	37
Helper Gr. I	…	20
Ministerial Officer	…	11
Ministerial Staff	…	54
Gr. D (Non-tech)	…	17
Canteen Staff	…	10
TOTAL	**…**	**284**

Retirement List from April 01, 2007 to March 31, 2008

SL. NO.	NAME OF THE STAFF MEMBER	DESIGNATION	DATE OF RETIREMENT
1.	Dr. Anup Bhattacharjya	Scientist Gr. IV(5)	April 30, 2007
2.	Shri Ramdas Ravidas	Helper	July 31, 2007
3.	Shri Debi Prasad Das	Exec. Engineer	August 31, 2007
4.	Dr. P.K. Bhattacharjee	Scientist Gr. IV(5)	October 31, 2007
5.	Shri Ujjal Baran Sarkar	Technical Officer	October 31, 2007
6.	Dr. Smita Mitra	Scientist Gr. IV(4)	December 31, 2007
7.	Shri D.P. Thakur	Private Secretary	January 31, 2008
8.	Shri D.K. Ghosh	Technician	January 31, 2008

New Appointment from April 01, 2007 to March 31, 2008

SL. NO.	NAME OF THE STAFF MEMBER	DESIGNATION	DATE OF APPOINTMENT
1.	Dr. Malini Sen	Scientist Gr. IV(3)	July 12, 2007
2.	Shri Ujjal Ray	Technician Gr. II(1)	October 22, 2007
3.	Dr. Saraswati Garai	Scientist Gr. IV(1)	October 24, 2007
4.	Dr. Anindya Dasgupta	Scientist Gr. IV(3)	February 27, 2008


ME ON
N SCIENCE
BIOLOGY,JADAV
8,2007
MERI,Durgap


CSIR PROGRAMME ON
YOUTH FOR LEADERSHIP IN SCIENCE
CPYLS-2007
INDIAN INSTITUTE OF CHEMICAL BIOLOGY,JADAVPUR
DECEMBER 27 & 28,2007
In Association With:
CG&CRI,Kolkata * CSIR,New Delhi * CMERI,Durgapur
DR. ASISH K. SEN
PROF. A. R. THAKUR
DR. H.K. MAJUMDER

Research Council 2007-2008, IICB

Dr. Seyed E. Hasnain, Chairman
Vice-Chancellor
University of Hyderabad
Hyderabad - 500 046

Dr. A. N. Bhisey
Former Director
Cancer Research Institute
7, Yug Prabhat Society
Naryan Pathara Marg, Mahim
Mumbai - 400 016

Dr. K.N. Ganesh
Director
Indian Institute of Science Education and Research (ISER)
900, NCL Innovation Park
Dr. Homi Bhabha Road
Pune - 411 008

Prof. R.V. Hosur
National Facility for High Field NMR
Tata Institute of Fundamental Research
Homi Bhabha Road, Navy Nagar
Mumbai – 400 005

Prof. K. Muniyappa
Head, Department of Biochemistry
Indian Institute of Science
Bangalore – 560 012

Dr. P. Bhatnagar
Senior Vice President
New Drug Discovery Research
Ranbaxy Laboratories Limited
Plot No. 20, Sector-18, Udyog Vihar, Industrial Area
Gurgaon – 122 015

Dr. Sukhdev Sinha
Adviser
Department of Biotechnology
Block-2, 7th Floor, CGO Complex
Lodi Road
New Delhi - 110 003

Dr. Gopal Pandey
Scientist F
Centre for Cellular & Molecular Biology
Uppal Road
Hyderabad - 500 007

Dr. Girish Sahni
Director, Institute of Microbial Technology
Sector 39-A
Chandigarh 160 036

Dr. Naresh Kumar
Head, RDPD
Council of Scientific & Industrial Research
Anusandhan Bhawan, Rafi Marg
New Delhi 110 001

Prof. Siddhartha Roy, Member
Director, India Institute of Chemical Biology
4, Raja S. C. Mullick Road, Jadavpur, Kolkata - 700 032
Fax : 033 2473 5197
Tel : 033 2413 1157 / 2473 5638 (O); 033 2429 8795 / 2412 1261 (Res.)
E-mail : siddhartharoy@iicb.res.in

Dr. Kunal Roy, Secretary
Scientist, Indian Institute of Chemical Biology
4, Raja S. C. Mullick Road, Jadavpur, Kolkata - 700 032
Fax : 033 2473 5197
Tel : 033 2473 0492/3491/3493 (O); 033 2432 8022 (Res.)
E-mail : kray@iicb.res.in

Special Permanent Invitee

Prof. B. Bhattacharyya
Department of Biochemistry, Bose Institute,
Centenary Building, P-1/12 C. I. T. Scheme VII M,
Kolkata 700 054

Prof. D. J. Chattopadhyay
Pro-Vice-Chancellor (Academic Affair)
Department of Biotechnology
B. C. Guha Centre for Biotechnology and Genetic Engineering
University of Calcutta
35, Ballygunge Circular Road
Kolkata - 700 019

Prof. Chanchal DasGupta
Department of Biophysics, Molecular Biology and Genetics,
University College of Science, 92 A.P.C. Road,
Kolkata 700009, India

Management Council 2007-2008, IICB

Prof. Siddhartha Roy
Chairman
Director, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: director@iicb.res.in;siddhartharoy@iicb.res.in

Dr. H. S. Maiti
Director, Central Glass & Ceramic Research Institute
196, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-5829/3469/3476-77/3496
Fax: (033) 2473 0957
E-mail: director@cgcri.res.in;hsmaiti@cgcri.res.in

Dr. K. P. Mohana Kumar
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. MullicV Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: mohankumar@iicb.res.in

Dr. J. Rajan Vedasiromoni
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: vedasiromoni@iicb.res.in

Dr. (Mrs.) Tuli Biswas
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: tulibiswas@iicb.res.in

Dr. Rupak Kr. Bhadra
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: rupakbhadra@iicb.res.in

Dr. Sibsankar Roy
Scientist, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: sibsankar@iicb.res.in

Dr. Asoke Kumar Das Gupta
Technical Officer, Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967
E-mail: asokedg@iicb.res.in

Finance & Accounts Officer
Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967

Administrative Officer
Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur, Kolkata - 700 032
Phone: (033) 2473-0492/3491/3493/6793
Fax: (033) 2473 5197, 2472 3967