CSIR

CSIR-Indian Institute of Chemical Biology

Technology & Translation

IICB TRUE
Translational Research Unit of Excellence

सी एस आई आर - भारतीय रासायनिक जीवविज्ञान संस्थान

CSIR-Indian Institute of Chemical Biology, Kolkata

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4 राजा एस.सी. मल्लिक रोड,कलकाता- 32
सी एन- 6 , सेक्टर-V, सल्ट लेक,कलकाता- 91

Asmon

A CSIR-IICB product for Asthma Patients

Technology

Inhibits oxidation of arachidonic acid in ex vivo blood assay wherein blood cells are stimulated by calcium ionophor or known stimulator to enhance their oxidative activity.

Application

- Effective against all cases of bronchial asthma except cardiac asthma.
- Purely herbal drug derived from plants; no side effect.
- Fast relief.
- Can be used as a capsule or as a syrup

Status of the Technology

The technology has been licensed and the product is in the market

Looking for other potential licensees in India and abroad.

PROSTALYN

A herbal extract for treatment of benign prostate hyperplasia

Technology

A herbal composition useful for the treatment of benign prostate hyperplasia.

The herbal composition includes a therapeutically effective amount of the compound mahanine, or its derivatives, or analogues, or pharmaceutically acceptable salt there of.

Applications

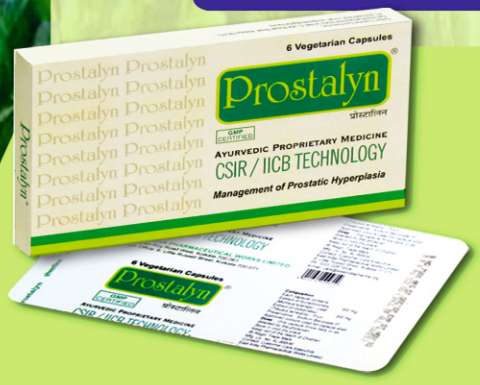
This invention is developed as a pharmaceutical composition for the treatment of prostate hyperplasia in patients

Intellectual Property

Patents granted in Europe, Britain, China and Germany.

Status of the Technology

- Technology has been licensed in 2006
- Product launched in the market in 2007.
- Receiving royalty from the licensee.



Looking for potential licensees abroad

A herbal product with

Anti-leukemic Activity

Technology

The present invention provides a synergistic pharmaceutical composition for treatment of acute and chronic myeloid leukemia.

It is comprised of an effective amount of chlorogenic acid (CA) and 3-o-p-Coumaryl quinic acid (PCQ), isolated from Piper betel plant.

Applications

- Purely herbal formulation derived from Piper betel leaves
- No side effect.
- Effective against solid tumors including lymphomas.
- Provides oral, intravenous, intramuscular or subcutaneous routes for administration.

Intellectual Property

Patent granted in India.

Status of the Technology

Technology licensed to
Nicholas Piramal India Limited (NPIL)
Awaiting product Launching

Looking for potential licensees in India and other nations

A Promising Therapeutic Lead from Medicinal Plant: Hope for Targeting Cancer and Cancer stem-like cells

Edible Plant

Abundantly available across India in all seasons
Lead molecule: Carbazole Alkaloid (CM-5)
Medicinal values reported in Charaka Samhita

In vitro studies with CM-5

- Induces apoptosis in different cancer types with various mutations and also in cancer stem-like cells.
- Exhibits cell death even in hypoxic condition.
- Shows synergistic activity with a few clinically used cancer drugs .

Mechanism of Apoptosis induced by CM-5

- Produces reactive oxygen species by blocking complex-III of mitochondrial electron transport chain, Inhibits mTORC1/C2.
- Inhibits Autophagy.
- Arrest cell cycle at G0/G1 phase.
- Inhibits migration & invasion and sensitize cancer cells to Anoikis.

Toxicity of CM-5

- Non toxic to $CD34^{+}$ progenitor cell, normal blood cells and astrocytes, normal lung/kidney cell lines from human and monkey.
- Showed NO acute and chronic toxicity towards normal mice.

In vivo and ex vivo studies with CM-5

- Reduces tumour mass in glioblastoma, pancreatic, melanoma, ovarian, breast and lung cancers in animal models.
- Induces cell death in primary cells isolated form cancer patients.

APPROVED US PATENT

Herbal extract enriched with CM-5

- Shows anti-proliferative activity against cancer cells (in vitro/ex vivo/in vivo)
- Exhibits NO toxicity in mice (14, 28 and 90 days)

Technology licensed to Kudos

Biomarker for Rheumatic Heart Disease (RHD)

RHD

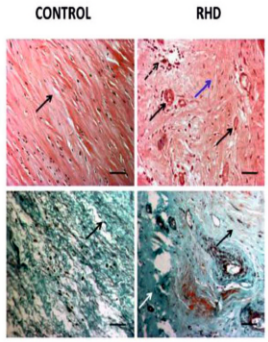
Rheumatic heart disease is the result of valvular damage caused by abnormal immune response to group A streptococcal infection, usually during early childhood.

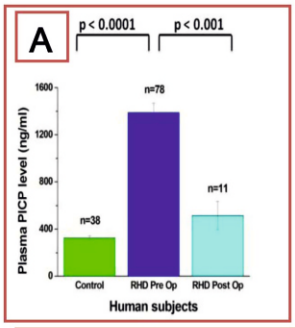
Disease Prevalence

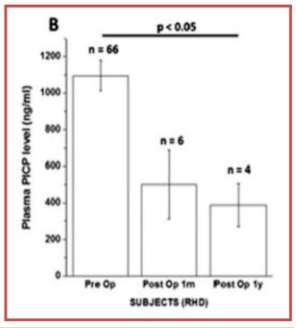
Estimated to be 15.6 million people world wide. Every year 470, 000 new cases are diagnosed and 233,000 deaths attributed to this disease. In India, the disease is responsible for 30 to 40% of cardiovascular disease related hospital admissions and is a common indication for cardiac surgery.

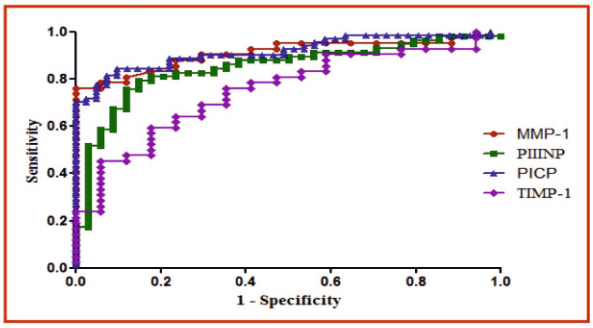
Salient Features of CSIR-IICB biomarker

- It is a protein based biomarker
- It is detected in serum and urine
- Patented Know-how by CSIR









Why it is important

RHD is diagnosed by ECG. No biochemical marker is available for management of RHD. We have found that PICP is robustly increased in RHD patients. Based on this Prototype of the lateral flow is developed. This test kit would help measurement of clinical activity in quiescent rheumatic heart disease, post penicillin treatment and overall management of the disease.

ArobustPlasmabiomarker
Well defined Cut off value
Sensitivity: 90 %
Specificity: 89 %
AUC: 0.998
Likelihood Ratio: 37.03

Prototype

Application

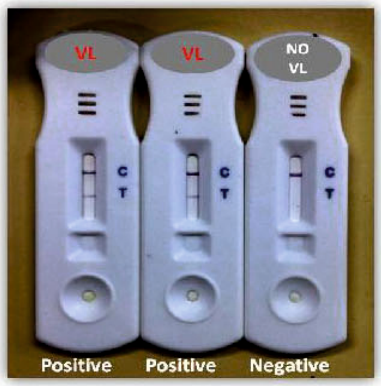
Measurement of clinical activity in RHD, prognosis and overall management of rheumatic heart disease.

Rapid Diagnostic Kit for Detection of Kala-azar from Serum and Urine Samples

Lateral Flow Technology

Dipstick transformed into Colloidal Gold-Based Lateral Flow Technology for field adaptable, easy and non-invasive diagnosis of Kala-azar.

Result can be seen by the naked eyes in two minutes without the use of any sophisticated instruments

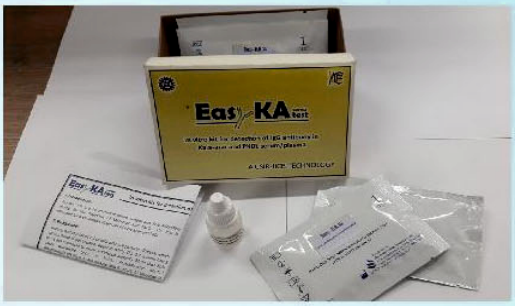


Applications

- Capable of detecting anti-leishmanial IgG antibodies in kala-azar serum and urine
- Could be useful for test of cure

Advantages

- Simple and easy to use tests
- Highly sensitive and specific for kala-azar
- Equally effective for PKDL diagnosis
- Does not cross react with *cutaneous leishmaniasis*



Stage of Development

The technology has been developed at lab scale and multicentre validated. CSIR-IICB has signed secrecy agreement with three Indian biotech companies, Ubio Biotechnology Systems, Kochi, Medsource Ozone Biomedicals Pvt. Ltd., Faridabad, and Tulip Diagnostics Pvt. Ltd., Goa for prototype development.

Intellectual Property status

Patent Filed

Achievements

Inventor received Gold Medal at "Innovators Competition" for DST-Lockheed Martin India Innovation Growth Program 2015 for the serum-based dipstick technology.

Serum dipsticks validated in India, Nepal, Sri Lanka, Brazil, Ethiopia, Spain and UK.

Business Model

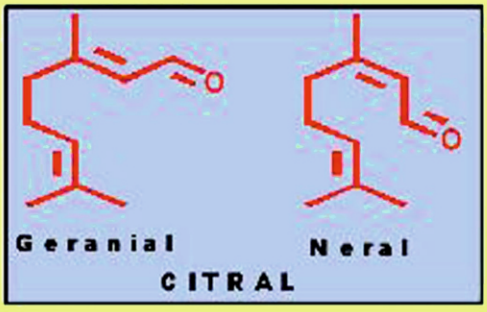
CSIR-IICB is looking for industrial partners to commercialize this technology. Also looking for Joint Venture formation.

Handheld Electronic Device for Estimating Citral Content in Lemongrass Oil : Empowerment of Farmers

Hand held portable device for quantitative estimation of citral in lemongrass and other essential oils towards empowerment of farmers

- **Lemongrass oil is widely used in perfumery industry.**
- **Perfumary industries procure lemon grass oil directly from farmers, Farmers are deprived of good price for lack of knowledge about the percentage of citral content based on which the price is fixed.**

Conventional techniques used are GC-MS and HPLC : Accurate but costly, time consuming, require special operator, not handy



Demonstration of the device to Shri Giriraj Singh Hon'able Minister of State (Independent Charge) for Micro, Small and Medium Enterprise, Government of India during his visit to Kisan Mela at CSIR-CIMAP, Lucknow on 31-01-2018

Status of Technology

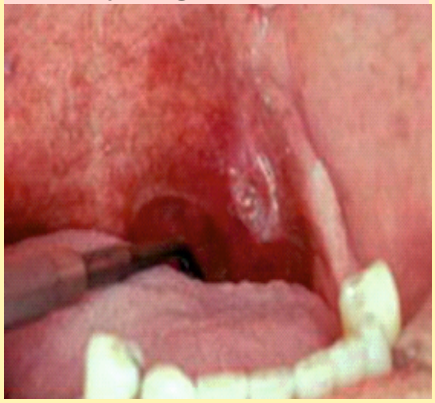
Patent filing in progress

A Gene Chip Based Predictive Biomarker for Oral Cancer Metastasis

Technology

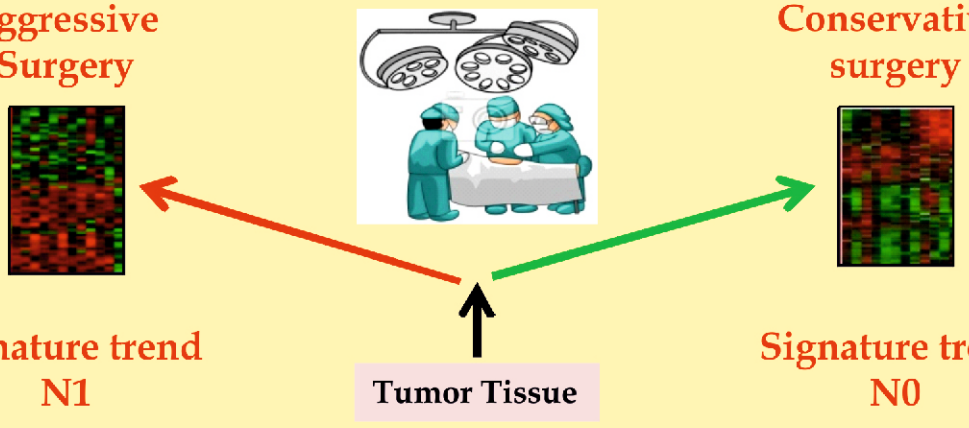
A gene expression chip comprised of 34 genes that predict nodal metastatic subset of early stage oral cancer with high specificity

Patient diagnosed with early stage Oral Cancer



Oral cancer is the most common cancer type in India. Age-adjusted rates of oral cancer in India is 20 per 100,000 population and accounts for over 30% of all cancers in the country.

Procedure Decision



Application

- Will allow to detect whether or not an early stage oral tumor has nodal metastasis.
- This will help onco-surgeon to decide whether not to do aggressive surgery.
- Approximate number of early stage oral cancer patient would be 75,000/year
- Projected market value would be Rs.150 Cr/year (assuming an assay cost of Rs.20,000/-)

Status of technology : Patent filed in 2018

Potent TLR9-selective and TLR9/7 dual antagonists

A series of novel and potent inhibitors of toll-like receptor (TLR) 9 as well as dual antagonists of TLR9 and TLR7, with potential application in autoimmune disease and metabolic syndrome.

- ❑ **Potent (nano to low micromolar IC_{50}) inhibitors of TLR9 and TLR7: 'ABODINIBS' and 'ADADINIBS'**
- ❑ **Demonstrated efficacy in human immune cells and pharmacokinetics in preclinical rodent model**
- ❑ **Demonstrated efficacy in a preclinical model of psoriasis**

Challenge/Application domain

Activation of toll-like receptors (TLRs) on immune cells is one of the critical mechanisms for self-nonself discrimination by the host immune response[1]. Interestingly, aberrant TLR9 activation is implicated in the pathogenesis of a number of autoimmune diseases[2] (viz. psoriasis, systemic lupus, scleroderma, rheumatoid arthritis, type 1 diabetes etc.) as well as in different components of metabolic syndrome[3] (obesity-associated type 2 diabetes, fatty liver disease, atherosclerosis). TLR9 is established as an important therapeutic target in these different clinical contexts. But inhibitors of TLR9 are yet to be available for clinical use.

Technology

The present invention relates to a lead series of small molecule compounds for inhibiting TLR9 or both TLR9 and TLR7[4,5], developed through rational design driven by well characterized SAR in human primary immune cells (Table 1). The lead series includes molecules with oral bioavailability, documented target-binding, favourable pharmacokinetics and in vivo efficacy for TLR9/7 antagonism in preclinical rodent pharmacodynamics studies as well as a preclinical disease model of the autoimmune disease psoriasis (Figure 1).

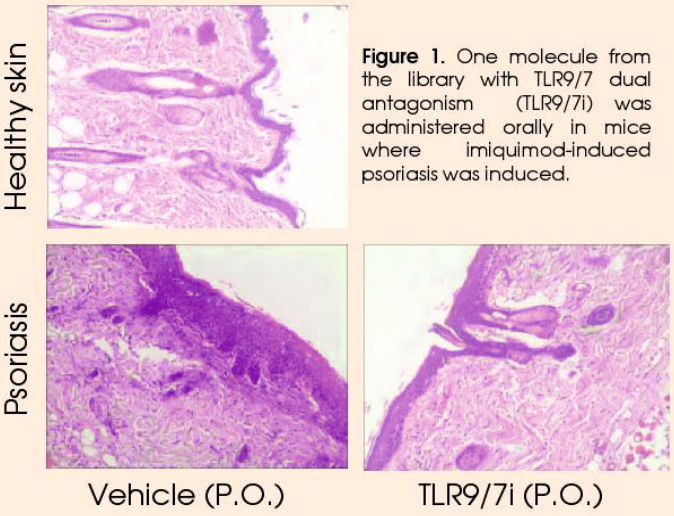


Figure 1. One molecule from the library with TLR9/7 dual antagonism (TLR9/7i) was administered orally in mice where imiquimod-induced psoriasis was induced.

Opportunity

CSIR-Indian Institute of Chemical Biology is seeking to transfer the technology of this advanced lead series of TLR9/7 inhibitors to an pharmaceutical industry entity (with global footprint and past experience with clinical trial for drugs toward global regulatory approval for human use) for further preclinical development and nomination of clinical candidate/s for evaluation in clinical trials.

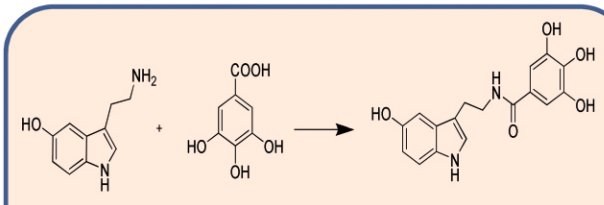
References

1. Talukdar A et al., Patent WO2017163264 A1.

2. Gilliet Met al., Nat Rev Immunol, 2008. 8(8):594.
3. Ganguly D et al., Nat Rev Immunol, 2013, 13(8):566.
4. Ganguly D, Trends Immunol, 2018. 39 :28.
5. Roy S et al., Eur J Med Chem, 2017. 134 : 334.
6. Paul B et al., Eur J Med Chem, 2018. 159 :187.

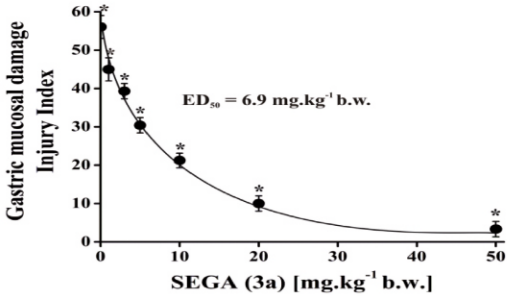
Designing of a novel serotonin-gallic acid hybrid (SEGA) to prevent gastric ulcer

Synthesis

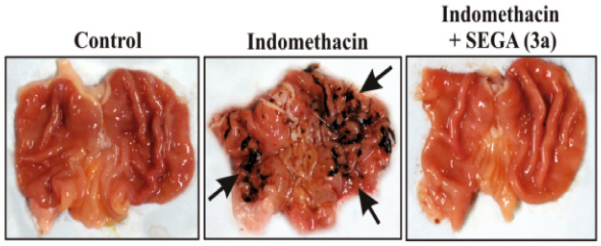


Serotonin Gallic acid SEGA (MWt 328.32)

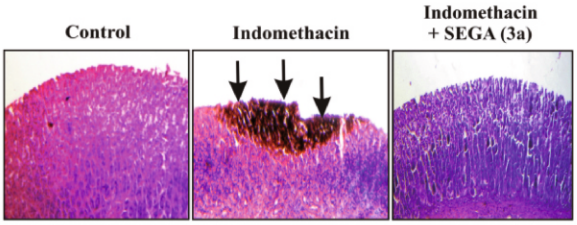
In vivo activity



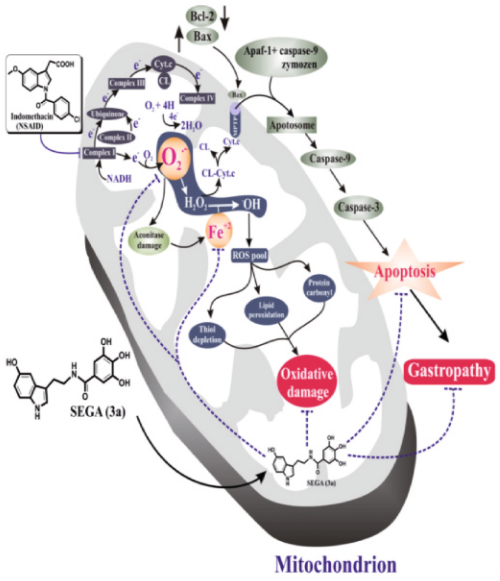
In vivo dose-response effect against gastric ulcer induced by Indomethacin (a non-steroidal antiinflammatory drug)



Morphological evidence for antiulcer effect



Histological evidence for antiulcer effect



Mechanism of action

- Prevents mitochondrial oxidative stress.
- Chelates intramitochondrial free iron.
- Blocks epithelial cell death induced during ulceration

Summary

- ✓ NSAID-induced gastropathy is the consequence of mitochondrial oxidative stress.
- ✓ Mitopatholoy involves electron leakage, generation of ROS.
- ✓ SEGA, a mitochondrially targeted, antioxidant, iron chelating molecule would be effective in treating mitochondrial oxidative stress induced pathology.

Immense therapeutic potential of SEGA against NSAID-induced gastric ulcer/injury

Bandyopadhyay. U, et al United States Patent No *8,901,317,* Grant date: December 2, 2014
Bandyopadhyay. U, et al European Patent 2616439, , Grant date: December 16, 2015

Identification of disease causing genetic variations in Indian patients: A translational approach towards diagnostics, genetic counseling and a better quality of life

BACKGROUND

The Indians represent one-sixth of the world population and India consists of ethnically, geographically and genetically diverse populations with several thousand endogamous groups. In some community the load of genetic disorder is relatively high due to consanguineous marriage practiced in the community. This database has been created to keep track of mutations in the causal genes for genetic diseases common in India and help the Physicians, Geneticists and other professionals related to genetic disorders to retrieve and use the information for the benefit of the families affected with the disorders.

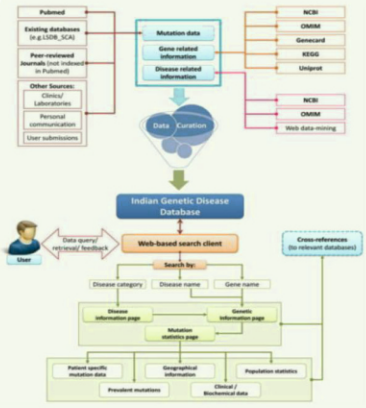
GOALS

- To reduce genetic disease load by identifying ethnicity/religion specific causal genetic variations across Indian population.
- To identify pre-symptomatic individuals at the earliest so that therapeutic intervention could help prevent disease progression.
- To identify carriers of recessive diseases which when associated with premarital genetic counseling could help reduce the spread of disease
- To develop a gene chip for specific disease based on prevalent mutations.
- IGDD is the first step towards all these goals.

SIGNIFICANCE OF IGDD

- IGDD could be a major source of information on genetic disorders prevailing in India
- It will provide comprehensive information to geneticists, genetic counselors, clinicians and heath policy makers for Indians all over the world.
- IGDD will ideally provide starting knowledge for molecular diagnostics for prevalent genetic/metabolic diseases in India.

METHODOLOGY



Tools used:

1. **Oracle9i** for Database Design
2. **VB.net** for Web Site Development
3. **SQL Loader** for Data Entry
4. **Visual Studio** for Frontend Design

System Configuration:

1. **Windows Server with IIS** (Internet Information Services)

Data Structure :

1. Relational database with inter connected elements and their attribute tables like disease, gene, mutation, support groups for patients.

DOCUMENTATION

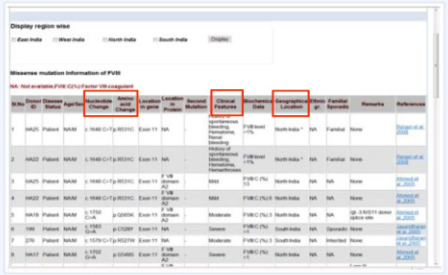
IGDD Homepage

Database URL : http://www.igdd.iicb.res.in/

(Database being Updated and Redesigned)

Gene TABLE

Mutation TABLE

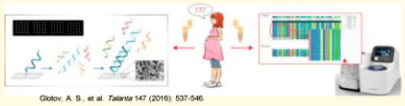


IGDD Contents as on 2016

Name of Disease	Number of Patients	Number of Carriers	Number of Mutations
Renal Cysts and Diabetes (RCAD) Syndrome	-	1	1
Chronic Pancreatitis	412	7	501
Duchenne Muscular Dystrophy	369	-	369
Non-syndromic Hearing Loss (DFNB1A)	313	24	549
Beta Thalassemia	271	3339	3851
Haemophilia A	178	-	185
Primary Congenital Glaucoma (PCG)	154	-	236
Spinocerebellar ataxia 2 (SCA 2)	132	-	132
Gilbert Syndrome	129	-	210
Macular Corneal Dystrophy	129	-	249
Haemophilia B	128	-	129
Cystic Fibrosis	125	-	188
Wilson Disease (WD)	96.00	-	136
Granular corneal dystrophy Type I	75	2	87
90 More diseases	...	...	...
Total: 104 Diseases	3458	3493	8233

ANTICIPATED PRODUCTS & PROCESSES OF TECHNOLOGICAL & SOCIO-ECONOMIC RELEVANCE

- The comprehensive and upgraded version of IGDD would be the primary product.
- Meta-analysis of allele and genotype frequencies for different ethnic groups or geographical regions of India with mutation statistics and graphical representation
- Cross-links to various disease support groups and other relevant databases may serve as valuable resources for patients and their relatives.
- Possible development of Microarray or Gene Chip based Mutation Detections



Glotov, A. S., et al. *Talanta* 147 (2016): 537-546.

UPDATES AND FUTURE GOAL

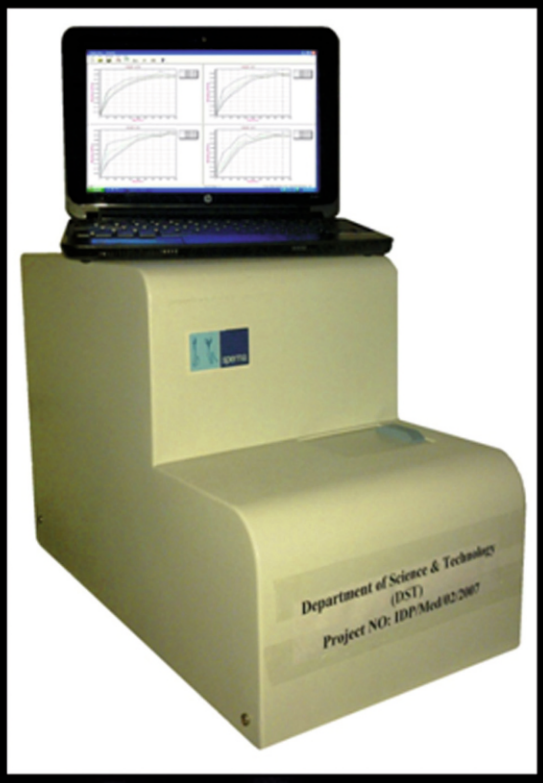
- Regular database updates with additional data on recorded as well as newly identified genetic disorders in India
- A completely new module to include genetic information on common genetic diseases like **(a) all the Mendelian disorders reported from India to date, (b) major complex diseases with special emphasis on cancer, (c) Mitochondrial diseases, and d) chromosomal abnormalities**
- Genotype-phenotype correlation based on clinical, biochemical and structural data
- Software upgrade and better data submission & retrieval system directly through web.

SPERMA

SPERM "VERTICAL VELOCITY" ANALYSER: A NOVEL COMPUTER ASSISSTED INSTRUMENT FOR ANALYSING SPERM QUALITY

Technology:

- A Novel Technology to analyze the sperm motility in vertical direction against the gravity.
- "Vertical Velocity" is expected to be a better index to predict the health and fertilizing ability of sperm sample.



Advantages:

- ✓ Multiple samples can be analyzed at a time
- ✓ Best quality semen samples can be selected
- ✓ Very low cost (Approx. Rs. 25000)
- ✓ Small and portable
- ✓ No special infrastructure required

Applications:

- ➢ Human infertility clinics & sperm banks
- ➢ Animal breeding centers & poultries
- ➢ Animal conservation laboratories
- ➢ Universities and research organizations

Stage of Development:

- ❖ The technology has been developed at CSIR-IICB in collaboration with Indian Association for the Cultivation of Science and Elico Ltd., Hyderabad as industrial partner.

CONTRIBUTION OF CSIR-IICB TO COMBAT ARSENIC DISASTER AND MITIGATION IN WEST BENGAL

CONTRIBUTION TO SOCIETY

In the last 15 years, CSIR-IICB has provided medical advice, essential medicine and milk to about 30,000 individuals and 2,000 children in Murshidabad and about 35,000 adults and 10,000 children in East Midnapur district

Expert physicians are examining arsenic affected individuals to identify the arsenicosis patients

CSIR-IICB has measured arsenic in drinking water and urine free of cost and reports were given to about 2500 families.

Skin lesions, skin cancers, peripheral neuropathy, respiratory disorders and eye problems were identified by the expert physicians and were informed to the patients.

CSIR-IICB has identified about 135 arsenic induced skin cancer patients. Out of these 135 patients, we have operated 89 skin cancer patients at free of cost in Kolkata.

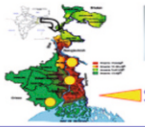
In an India-UKIERI joint research program, CSIR-IICB has identified that rice is a potential source of arsenic exposure

UKIERI
UK-India Education and Research Initiative

PRAMA

Rice- as potential source of arsenic exposure

CSIR-IICB has also reported that arsenic through rice alone can induce genetic damage in human.



SCIENTIFIC REPORTS
Banerjee et.al.; 2013, 3: 2195.
doi: 10.1038/srep02195

WORLD NEWS COVERAGE OF ARSENIC IN RICE
(after publication in Nature- Group Journal *Scientific Report* in 2013)

NATURE WORLD NEWS
Arsenic in Rice Linked to Genetic Damage

High levels of arsenic in rice have been shown to be associated with elevated genetic damage in humans, a new study has found. Over the last few years, researchers have reported high concentrations of arsenic in several rice-growing regions around the world. Now, University of Manchester scientists, working in collaboration with scientists at CSIR-Indian Institute of Chemical Biology in Kolkata, have proven a link between rice containing high levels of arsenic and chromosomal damage, as measured by micronuclei in urothelial cells, in humans consuming rice as a staple. The researchers discovered that people in rural West

ABC Science

High arsenic levels in rice linked to DNA damage

http://www.abc.net.au/science/articles/2013/07/23/3809133.htm

Eating large daily helpings of rice tainted with high levels of arsenic has been linked to genetic damage that heightens the risk of cancer, a study suggests. Scientists have been worried about rice grown in contaminated groundwater, but this is the first time they have found evidence of a risk. Researchers at Britain's University of Manchester and the Indian Institute of Chemical Biology in Kolkata studied 417 villagers from India's West Bengal.

MANCHESTER 1824
The University of Manchester

Health risks from arsenic in rice exposed

http://www.manchester.ac.uk/discover/news/article/?id=10424

High levels of arsenic in rice have been shown to be associated with elevated genetic damage in humans, a new study has found. Over the last few years, researchers have reported high concentrations of arsenic in several rice-growing regions around the world. Now, University of Manchester scientists, working in collaboration with scientists at CSIR-Indian Institute of Chemical Biology in Kolkata, have proven a link between rice containing high levels of arsenic and chromosomal damage, as measured by micronuclei in urothelial cells, in humans consuming rice as a staple. The researchers discovered that people in rural West

HNGN

High Levels of Arsenic in Rice Linked to Elevated Genetic Damage in Humans

The high level of arsenic in many rice growing regions has led to genetic damage in humans, a new study found

By Sam Goudsen | Jul 24, 2013 07:20 AM EDT

http://www.hngn.com/articles/6442/20130724/high-levels-arsenic-rice-linked-elevated-genetic-damage-humans.htm

Researchers have recently raised concerns about the high level of arsenic in many rice growing areas across the world. In a new study conducted by University of Manchester scientists, working in collaboration with scientists at CSIR-Indian Institute of Chemical Biology in Kolkata, researchers exposed the health risks of consuming excessive arsenic. He went on to clarify that without contamination, rice is an important source of essential energy, vitamins and fiber. Dr Ashish K. Giri, who led the Indian research team, clarified that while high levels of arsenic in rice can pose a threat to human health, there is no need to panic. Proper precautions can be taken to avoid such contamination. One of them includes using right agricultural techniques.

ASIAN SCIENTIST
News and information from the asian scientific community

Exposed: Health Risks From Arsenic In Rice

High levels of arsenic in rice is associated with elevated genetic damage in humans, according to new research.

Asian Scientist Newsroom | July 30, 2013 | Health Read more from Asian Scientist Magazine

http://www.asianscientist.com/2013/07/health/exposed-health-risks-arsenic-rice-2013/

Asian Scientist (Jul. 30, 2013) - High levels of arsenic in rice is associated with elevated genetic damage in humans, according to new research. Now, researchers from India and the UK have found a link between rice containing high levels of arsenic and chromosomal damage in the tissues of people consuming rice as a staple. The researchers discovered that people in rural West Bengal eating rice as a staple with greater than 0.2 mg/kg arsenic showed higher frequencies of micronuclei than those consuming rice with less than this concentration of arsenic. "One CSIR institute in India has already identified a number of Indian rice varieties which accumulate lower concentrations of arsenic, so we can easily address future human health risks with proper mitigation strategies."

India Science

High arsenic concentration in rice results in genotoxicity

https://indiascience.org/news/2013/high-arsenic-concentration-in-rice-results-in-genotoxicity

Scientists at CSIR - Indian Institute of Chemical Biology (IICB), Kolkata have reported surprisingly high levels of arsenic in locally grown rice, resulting in genotoxicity. Arsenic is a very common component of various pesticides used in agricultural fields. The risk of increasing arsenic levels in ground water and soil, due to its prolonged agricultural use, has been known for a while now. However, arsenic levels in rice have only recently come into the picture. A.K. Giri at IICB and his team have conducted a thorough study in rural West Bengal and conclusively demonstrated genotoxicity as a result of high arsenic content in rice.

JAPANTODAY

Scientists sound new warning for arsenic in rice

http://old_archives.newsgabel.net/detail.php?date=2013-07-24&nid=58330

Rice tainted with high levels of arsenic has been linked to genetic damage that heightens the risk of cancer, a study published on Monday said. Naturally-occurring arsenic in drinking water is a long-known health hazard, especially in Bangladesh, where tens of millions of people depend on wells drilled in the 1970s. Scientists have also fretted about rice grown in contaminated groundwater, but this is the first time they have found proof of a risk. Researchers at Britain's University of Manchester and the Indian Institute of Chemical Biology in Kolkata carried out a probe with the help of 417 villagers in India's West Bengal.

In the Fogarty international training program with University of California, Berkeley, USA we have trained 98 national and 32 international researchers

National participants				International participants			
West Bengal	61	Delhi	4	Bangladesh	14	U.K.	2
Bihar	7	Maharashtra	3	Thailand	6	USA	1
Punjab	6	Assam	3	Nepal	2	China	1
Tamil Nadu	6	Andhra Pradesh	3	Vietnam	2	Nigeria	1
Uttar Pradesh	4	Rajasthan	1	Iran	2	Pakistan	1

CSIR-IICB has distributed new and old clothes to approximately 2500 men, women and children who belong to below poverty line

Night jasmine: An efficient source for *kala-azar* treatment

TECHNOLOGY

An efficient pharmaceutical composition against chronic visceral leishmaniasis

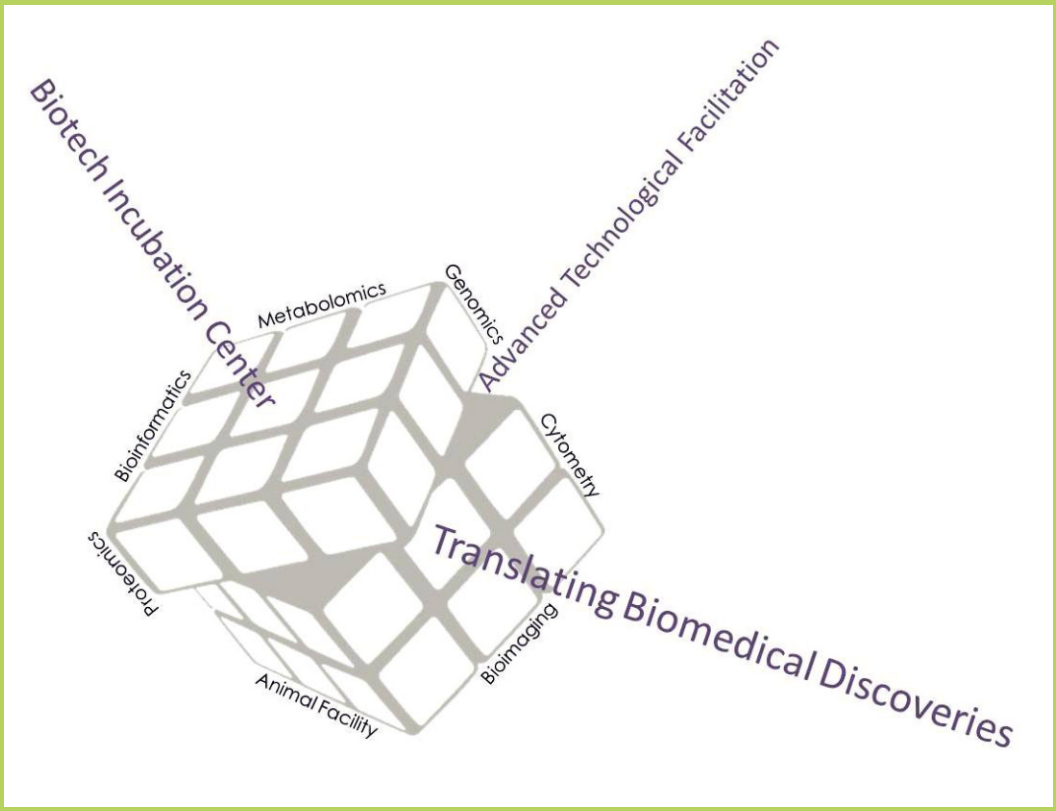
This therapeutically effective composition is a bioactive herbal extract derived from Night jasmine leaves, predominating with Calceolarioside A, along with SAG (5mg/Kg BW) and 0.5% Piperine as pharmacuetically acceptable doses as leishnamicidal agent

APPLICATIONS

This invention is a combination therapy and efficient pharmaceutical composition for the treatment of chronic visceral leishmaniasis

INTELLECTUAL PROPERTY

Patent granted in India
Awaiting for PCT countries



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