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वार्षिक प्रतिवेदन

ANNUAL REPORT

2009-10

Central Drug Research Institute, CSIR

Central Drug Research Institute

(Council of Scientific & Industrial Research)

Chattar Manzil Palace, M.G. Marg, Lucknow-226001

www.cdriindia.org


CSIR
TECHNOLOGY AWARD FOR INNOVATION - 2009
Awarded to the team at CDRI, Lucknow
for
Development of Synthetic Endoperoxide Antimalarials as
Substitute to Artemisinine Derivatives
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Council of Scientific & Industrial Research
Anusandhan Bhawan, Rafi Marg, New Delhi - 110001
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केन्द्रीय औषधि अनुसंधान संस्थान
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद्)
छत्तर मंजिल पैलेस, महात्मा गांधी मार्ग, लखनऊ

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HIGHLIGHTS OF ACHIEVEMENTS

◆ Prestigious Award Received (2009)	:	CSIR Technology Award for Innovation 2009
◆ Technologies Licensed to Industries (Feb. 2009 - Jan. 2010)	:	03
◆ Publications (2009)	:	289
- Average Impact Factor	:	2.591
- Publications with >5 Impact Factor	:	20
◆ Book Chapters (2009)	:	07
◆ Instruction Manual (2009)	:	01
◆ Patents (Feb. 2009 - Jan. 2010)		
- Filed Abroad	:	09
- Filed in India	:	05
- Granted Abroad	:	15
- Granted in India	:	12
◆ Ph.D. Thesis Submitted (2009)	:	59
◆ Contract Research Undertaken (Feb. 2009 - Jan. 2010)	:	02
◆ Grant-in-Aid Projects Initiated (Feb. 2009 - Jan. 2010)	:	21
◆ Total External Budgetary Resources (April 2009 - Jan. 2010)	:	Rs. 18.23 Crore

THE CHARTER

- Development of new drugs and diagnostics
- Cellular and molecular studies to understand disease processes and reproductive physiology
- Development of contraceptive agents and devices
- Systematic evaluation of medicinal properties of natural products
- Development of technology for drugs, intermediates and biologicals
- Dissemination of information in the field of drug research, development and production
- Consultancy and development of technical manpower

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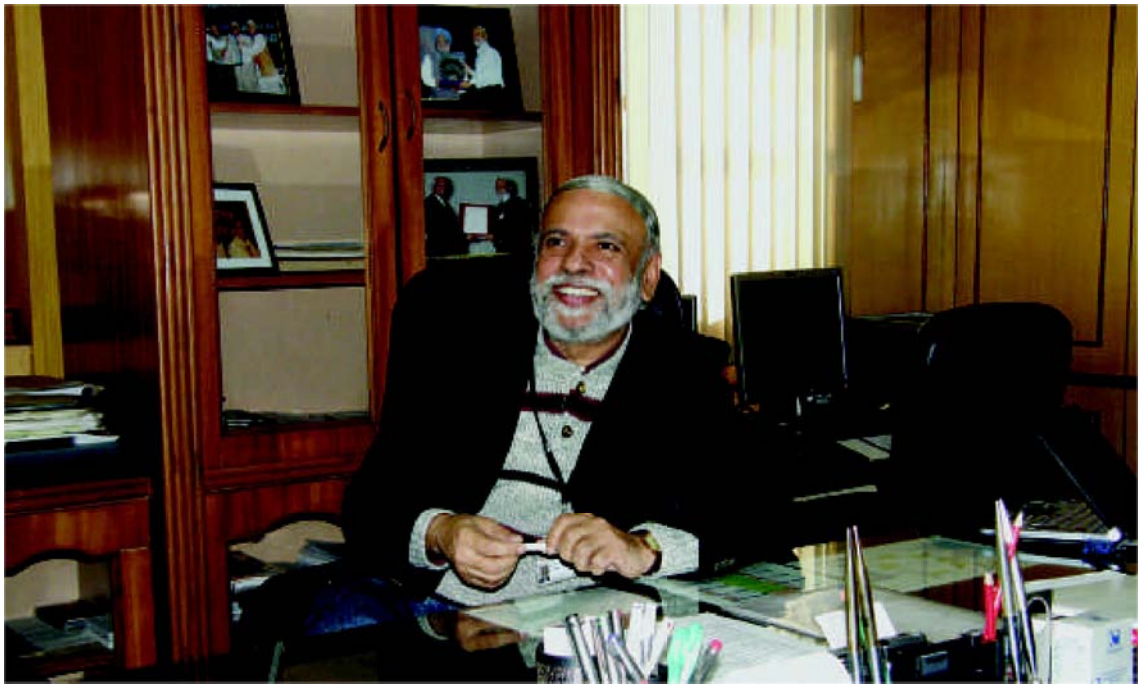
निदेशक की कलम से



संस्थान की वर्ष 2009-2010 की वार्षिक रिपोर्ट आपके सम्मुख प्रस्तुत करते हुए मुझे अत्यधिक हर्ष हो रहा है। इस वर्ष की समाप्ति, संस्थान के अस्तित्व के 60वें वर्ष के प्रारंभ होने का संकेत है। यह वर्ष विश्व में तेजी से बदल रही प्रौद्योगिकी, कठिन अर्थव्यवस्था और भविष्य की अकल्पित चुनौतियों को सामने ला रहा है।

पिछले दस वर्षों का सिंहावलोकन करने पर, भारत सरकार द्वारा दी गयी आर्थिक सहायतों से नई अनुसंधान सुविधाएं, उपकरण और तकनीक में अभूतपूर्व परिवर्तन किए गए हैं जिससे संस्थान की आधारिक संरचना विश्व के किसी भी स्थान के समकक्ष हो चुकी है। अनुभवी और नए वैज्ञानिकों की भर्ती से उपलब्ध क्षमता में सुधार आया है। इस प्रकार, लक्ष्य आधारित औषधि अनुसंधान के नतीजों, गुणवत्ता, प्रकाशनों और पेटेण्ट में परिणामी सुधार हुआ है। एक लम्बे अंतराल के बाद, संस्थान से अनेकों पदार्थ, मानव कल्याण के लिए विभिन्न बीमारियों के उपचार हेतु कतार में हैं।

संस्थान में अनुसंधान कार्यों के प्रति वचनबद्धता जारी रही और नई चुनौतियों का सामना करना पड़ा। एक चुनौती, संस्थान के नए परिसर के निर्माण को तेजी से पूरा करना और उसको कार्यात्मक प्रयोगशाला में परिवर्तित करना है। नए परिसर के विभिन्न ब्लॉक क्षितिज पर दिखने लगे हैं। विकास गति में शीघ्रता लाने की आवश्यकता को ध्यान में रखते हुए डॉ० नागेश अय्यर, निदेशक, स्ट्रक्चरल इंजीनियरिंग रिसर्च सेण्टर, चेन्नई की अध्यक्षता में एक नई समिति का गठन किया गया है ताकि नए परिसर को शीघ्रताशीघ्र पूर्ण किया जा सके। मैं डॉ० अय्यर का नई समिति में हार्दिक स्वागत करता हूँ।

लम्बे अंतराल से संस्थान के अनुसंधान एवं विकास के क्रियाकलाप, समस्यामूलक बीमारियों, विषयों और प्रौद्योगिकी क्षेत्रों में कार्यरत थे। संस्थान में अब तक 12 अनुसंधान क्षेत्रों में कार्य किया जाता रहा है और इनमें से अधिकांश क्रियाकलापों में

परस्परव्याप्ति हो रही थी। इन क्षेत्रों को नियंत्रित करने के लिये इनकी संख्या घटाकर 6 कर दी गई - ''**सुरक्षा और क्लीनिकल विकास**'', ''**कैंसर और संबंधित क्षेत्र**'', ''**सी.वी.एस., सी.एन.एस. और संबंधित विकृतियाँ**'', ''**मलेरिया और अन्य परजीवी विकृतियाँ**'', ''**प्रजनन स्वास्थ्य अनुसंधान, मधुमेह तथा ऊर्जा चयापचय**'' तथा ''**यक्ष्मा और सूक्ष्मजीवी संक्रमण**''। यद्यपि यह पुनर्गठन, संस्थान के क्रियाकलापों की विभिन्नता को प्रभावित नहीं करता।

उपुर्यक्त अनुसंधान क्षेत्रों में हुई प्रगति से स्पष्ट है कि नई लीड्स के साथ-साथ वर्तमान पाइपलाईन उत्पादों के सभी महत्वपूर्ण चरणों में अभूतपूर्व प्रगति हुई है। विभिन्न मोर्चों पर महत्वपूर्ण उपलब्धियाँ इस प्रकार हैं : 2153 रिकार्ड यौगिकों का संश्लेषण; 20 प्राकृतिक उत्पादों का शुद्धिकरण; पश्चिमी हिमालय, पूर्व एवं मध्य क्षेत्रों से 69 पादप सामग्रियों का एकत्रीकरण/पुनः एकत्रीकरण, उनका प्रमाणीकरण, प्रलेखन; आई.एन.डी. फाइलिंग हेतु हर्बल मेडिकोमेंट के आँकड़ों का जनन; पादप संख्या 1020 की सक्रियता निर्देशित फ्रैक्शन एफ147 में एल.सी.एम.एस./एम.एस. द्वारा सक्रिय अस्थियोंजेनिक मार्कर का विश्लेषण और क्वान्टीफिकेशन; तीन मार्कर की औषधि निर्माण गति प्रोफाइलिंग; एक मार्कर के तीन समरूप पी.जी.आई.एम.आर., चण्डीगढ़ में मलेरिया रोधी यौगिक 97-78 में प्रथम चरण की परीक्षण सुविधा का प्रारंभ; 50 स्वैच्छिक कार्यकर्ताओं में एकल खुराक अध्ययन की समाप्ति, सी.डी.आर. 134डी123 (मधुमेहरोधी) का स्वरूप और मधुमेहग्रस्त रोगियों में परीक्षण के आँकड़ों की विपणन की अनुमति हेतु ''आयुष'' को प्रस्तुतीकरण; चूहों में शाइजोफ्रोनिया अल्ज़ाइमर्स माडल हेतु के उपयोग से छानबीन के लिए *सी. ऐलिगैन्स* का उपयोग; खरगोश में मायोकार्डियल पोस्ट ऐन्तियोप्लास्टी त्वरित एथेरॉस्क्लेरोसिस हेतु नए जन्तु मॉडल का विकास; 99-373 अस्थि सुषुप्तरोधी को प्रथम चरण के क्लीनिकल परीक्षण मुख्य हैं। इसके अतिरिक्त, अस्थ्योप्लास्ट ऐक्टिवेशन के माध्यम से अस्थि स्वास्थ्य हेतु नवीन अभिकर्मकों का अध्ययन, मेडीकार्पिन स्काफोल्ड यौगिकों का संश्लेषण किया गया जिससे अस्थि फ्रैक्चर में शीघ्र लाभ प्राप्त किया जा सके।

क्षय रोग संबंधी अनुसंधानों में फास।। के विरुद्ध युक्तिपूर्वक अभिकल्पित 80 यौगिकों की *एम. औरम* में जाँच की गयी जिनमें से 4 यौगिकों ने जीवाणु क्षमता में 85% कमी प्रदर्शित की और दो ने वीटागाल इन्ड्यूसिविलिटी अमापन में सकारात्मकता क्रियाशीलता प्रदर्शित की। कालाज़ार रोग के निवारण संबंधी अनुसंधानों में *एल. डोनोवानी* एस.एस.जी. प्रतिरोधक जीन्स की क्लोनिंग की गयी। सीक्वेन्सिंग ऐक्टिन ने डी.एन.ए. में निक्स उत्पन्न करने में और के-डी.एन.ए. नेटवर्क से के-डी.एन.ए. मिनी और मैक्सी सर्किल को निकालने में महत्वपूर्ण भूमिका प्रदर्शित की। मलेरिया के औषधि विकास लक्ष्य को पाने के लिए ट्रांस्केटोलेज का मान्यकरण कार्य सफलतापूर्वक पूर्ण हुआ। रीसस मॉडल में अपनी रक्षात्मक भूमिका के मूल्यांकन हेतु रिकाम्बिनेन्ट मेरोजॉइट सरफेस प्रोटीन-1 (एम.एस.पी.-1) और *पी. साइनोमौलगी* और *पी. वाईवैक्स* सर्कम्स्पोरोजॉइट प्रोटीन (सी.एस.पी.) पर कार्य जारी है।

संस्थान में सी.एस.आई.आर. द्वारा समन्वित तीन नेटवर्क परियोजनाएँ व एक सूप्राइन्सिटीट्यूश्नल परियोजना कार्यरत हैं जिसमें परजीवी बीमारियाँ और सूक्ष्मजीवी संक्रमण, चयनित रोगजनक के औषधि लक्ष्यों की पहचान, मान्यकरण, वैकल्पिक मॉडलों का विकास और मधुमेह रोग संबंधी मॉलीक्युलर प्रक्रियाओं का अध्ययन, जेनेटिक और एपिडेमिआलोजिकल कारकों पर कार्य सम्मिलित है। नेटवर्क परियोजनाओं के परिणामस्वरूप विभिन्न सुविधाओं की रचना संभव हो सकी। इस

वर्ष, *सी. एलैगेन्स* मॉडल का उपयोग करके कार्यात्मक जेनामिक्स की सुविधाओं का विकास किया गया तथा नियामक औषधि प्रभावगति केन्द्र को सुदृढ़ किया गया। यह सुविधाएँ मूलभूत अनुसंधान और उत्पाद विकास में आवश्यक आँकड़े निर्मित करने में मद्दगार सिद्ध होंगी।

राष्ट्रीय और अन्तर्राष्ट्रीय मानकों के अनुसार कार्य करते हुए संस्थान के प्रत्येक वैज्ञानिक से वाह्य निधि प्राप्ति हेतु प्रस्तावों को प्रस्तुत करने का आह्वान किया गया है। वर्ष के दौरान, संस्थान में 21 सहायता अनुदान परियोजनाओं की संख्या में असाधारण वृद्धि हुई है। उद्योगों द्वारा प्रायोजित परियोजनाएं केन्द्रीभूत समस्याओं को समझने का महत्वपूर्ण साधन है। इसके अतिरिक्त ऐसी परियोजनाएं संसाधन और क्षमता जुटाने का राजस्व भी है और इस क्षेत्र में इनको उच्च प्राथमिकता दी जाती है। मुझे यह सूचित करते हुए अपार हर्ष हो रहा है कि कई वर्षों के उपरांत, दीर्घकालिक प्रयासों से निधिबद्ध परियोजनाओं की संख्या में वृद्धि हुई है। नई और पुरानी वाह्य निधिबद्ध परियोजनाओं की संख्या 51 है। तीन विदेशी सहायता प्राप्त परियोजनाएँ वर्ष के दौरान जारी रहीं जिनमें प्रमुख भूमिका विश्व स्वास्थ्य संगठन, डी.एन.डी.आई. तथा यूरोपियन यूनियन की रही। सभी स्रोतों से प्राप्त संपूर्ण धनराशि 18.23 करोड़ रुपये थी।

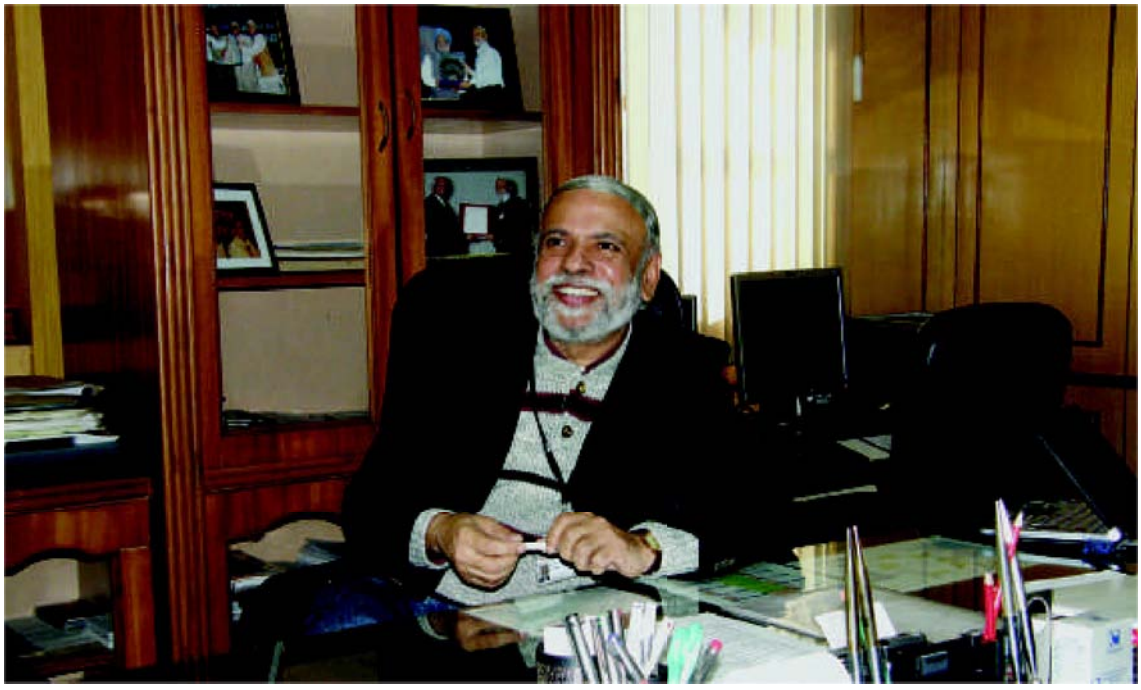
संस्थान का कार्य प्रदर्शन का संकेतक उच्च स्तरीय जर्नलों में 289 प्रकाशनों द्वारा प्रतिबिंबित है (औसत आई.एफ.: 2.591)। इस वर्ष 14 पेटेण्ट फाइल किये गये तथा 59 थीसिस प्रस्तुत की गईं। पेटेण्ट फाइल करने की नियमों में परिवर्तन किया गया है। उन्हीं अनुसंधानों को पेटेण्ट किया जाएगा जिनमें व्यावसायिक प्रयोग के प्रति वचनबद्धता है।

पिछले वर्षों की भाँति अनेक वैज्ञानिकों को उनके योगदान के लिये पुरस्कारों और उपाधियों से सम्मानित किया गया। **सी.एस.आई.आर. प्रौद्योगिकी पुरस्कार-2009**, लगातार दूसरे वर्ष संस्थान को प्राप्त हुआ। मैं सभी पुरस्कार प्राप्तकर्ताओं को उनके कार्य के लिए और टीम सी.डी.आर.आई. को प्रौद्योगिकी पुरस्कार के लिये बधाई देता हूँ।

तुषार चक्रवर्ती

(तुषार कान्ति चक्रवर्ती)

FROM THE DIRECTOR'S DESK



It gives me great pleasure to present the institute's Annual Report for the year 2009-2010. This not only marks the completion of the year, but also the commencement of the 60th year of the institute's existence, an era unfolding fast changing technologies on the horizon, harder economy and unconceivable future challenges!

In retrospect, over the past ten years or so, the Government funding has made it possible to introduce new research facilities, tools and techniques bringing the institute's infrastructure at par with the best anywhere in India or abroad. Recruitment of experienced hands and new blood has further improved the available capability thus effecting target based drug discovery and consequential improvement of research output, quality of publications and patents. Also, after prolonged gap, the pipeline generated now holds promise of some success.

As the institute's legacy of dedicated work continues, new challenges confront us. One of the challenges is to fast complete the new campus and transform it into an operational laboratory. The various blocks of the new campus have already appeared on the skyline. The pace of development is expected to increase further following the constitution of a new committee under the Chairmanship of Dr. Nagesh Iyer, Director, SERC, Chennai. I extend Dr. Iyer a warm welcome to the new committee and look forward to the speedy completion of the project under his able guidance.

For long, Institute's R&D activity had been carried out under the titles of problem diseases and disciplines and technology areas, totaling twelve major areas, many having overlapping activities. To effect manageability of these areas it was considered prudent to reduce their numbers to six viz. "**Safety and Clinical Development**", "**Cancer and Related Areas**", "**CVS, CNS and Related Disorders**", "**Malaria and Other Parasitic Diseases**", "**Reproductive Health Research, Diabetes and Energy Metabolism**", "**Tuberculosis and Microbial Infections**". This, however, does not affect institute's overall diversity of activities.

As is evident from the milestones reached under the above areas, significant progress has been made on all fronts including progress in all existing products in pipeline as well as new leads. Significant achievements made on various fronts are: synthesis of a record 2153 compounds; purification of 20 natural products; collection/recollection of 69 plant materials from Western Himalayas, Eastern and Central regions, their authentication and documentation; data generation on Herbal Medicaments (anti-stroke) for IND filing; analysis and quantification of active osteogenic markers by LC MS/MS in activity guided fraction (F147) of the plant 1020, and pharmacokinetic profiling of three markers, and one marker's three analogues; initiation of phase I trial facility for Compound 97-78 (antimalarial) at PGIMER, Chandigarh, and completion of single dose study in 50 volunteers; submission of data on trials of CDR 134D123 (anti-diabetic) in healthy and diabetic patients to AYUSH for fast track marketing permission; development of new animal models for schizophrenia (mice), Alzheimer (*C. elegans*), myocardial post-angioplasty accelerated atherosclerosis (rabbit); pushing 99-373 (anti-osteoporotic) to phase-I clinical trials; studies on novel agents for bone health through osteoblast activation; synthesis of chemical series using medicarpin scaffold, and one of the compounds showing rapid healing of bone fractures.

Out of 80 rationally designed compounds against FASII pathway screened in *M. aurum,* 4 compounds showed over 85% reduction in bacterial viability and two also showed positive in β-gal inducibility assay. Cloning and sequencing of *L. donovani* SSG resistant genes was carried out. Recombinant leishmania actin showed a role in generating nicks in DNA and consequential release of K-DNA mini and maxi circles from K-DNA network. Validation of transketolase as a potential drug target for malaria has been carried out and work continued on recombinant merozoite surface protein-1 (MSP-1) and *P. cynomolgi* & *P. vivax* circumsporozoite protein (CSP) for evaluation of their protective role in rhesus model.

The institute is involved in one supra-institutional and three network projects funded by CSIR, covering parasitic diseases and microbial infections; identification & validation of drug targets of selected pathogens; validation of identified and development of alternative models; and *diabetes mellitus* - molecular mechanisms,

genetic and epidemiological factors. Creation of several facilities has been made possible as a result of network projects. During the year, facilities of functional genomics using *C. elegans* as a model, regulatory pharmacology & toxicology and center for pharmacokinetics were strengthened. These facilities together, will immensely help in creating data required for basic research and product development.

Pursuing a policy of enhanced collaboration, both nationally and internationally, each and every scientist in the institute is called upon to submit proposals for external funding. During the year, institute had phenomenal increase in 21 grant-in-aid projects, though sponsored projects stagnated at two. Industry sponsored projects are an important means to attend to focused problems, besides as a source of revenue to build resources and capacity, this area currently receives high priority. After several years, sustained efforts have led to building up an increasing number of externally funded projects; the total strength of new and old external funded projects number 51. The three foreign aided projects (WHO, DNDi & EU) continued during the year. The total EBR, generated from all sources, amounts to Rs.18.23 crores.

The institute performance indicators as reflected through 289 publications in high impact factor journals (average IF: 2.591); 14 patents filed and 59 theses submitted are no small means. The downslide of patents lies in the policy to restrict patenting of only those inventions which hold greater promise of commercial application.

Likewise the preceding years, several scientists were recognized for their contributions through awards and honours. For the second consecutive year, the institute received CSIR Technology Award for Innovation, the award has been given for new synthetic endoperoxide antimalarial. I congratulate all awardees for recognition of their work and the "Team-CDRI" for the technology award.

(Tushar K. Chakraborty)

Significant Achievements

To combat the fast changing scenario of drug research worldwide, the Institute concentrated on reorganizing its research activities so as to produce quality research and develop newer products at par with globally acceptable norms and become a world class center for drug research in India. Since quite long, the new drug development program of CDRI had 12 project areas. In order to avoid overlapping of activities, strengthen the work force, effective monitoring and reallocation of resources; they have been restructured into 5 disease areas and 1 safety and clinical development area. The theme behind restructuring is to achieve synergism in the discovery of new drugs in disease areas of national relevance. It also envisages a strong commitment for exploiting natural resources so that the problem is approached holistically and multilaterally along with multifaceted infrastructure developments.

CDRI scientists receiving the prestigious CSIR Technology Award for Innovation – 2009 from Hon'ble Shri Prithviraj Chavan, Vice President, CSIR and Minister of State (Independent Charge) for Science & Technology and Earth Sciences.

We report with pride that the Institute received the prestigious **CSIR Technology Award for Innovation**, for the second consecutive year. The award has been bestowed towards discovery and development of new synthetic endoperoxide antimalarials as synthetic substitute for drugs based on Artemisinin, derived from the plant *Artemisia annua.* Publication of a bi-annual CDRI Newsletter has been initiated during the year and the first issue was formally released on September 26, 2009. During the year under review, impressive scientific returns have been achieved and their brief summary is presented below:

1. Business Development and Contract Research

Likewise the previous years, the Institute continued to give top priority to business development activities in terms of new projects, collaboration with industry, licensing of products/technologies. Major agreements executed during the year are as follows:

1.1 CDRI entered into a MoU with Department of Clinical Pharmacology, Seth GS, Medical College and KEM Hospital, Mumbai for setting up a Phase-I clinical trial unit for molecules developed by CDRI and also to carry out Phase-I studies for other government organizations and pharmaceutical industries. The unit would accelerate such trials in future.

1.2 CDRI licensed the improved patented process of synthesis of Ormeloxifene (Centchroman) to M/s HLL Life Care Ltd., Thiruvananthapuram for developing and marketing the drug as an oral contraceptive.

1.3 CDRI entered into a sponsored project agreement with M/s HLL Life Care Ltd., Thiruvananthapuram for generating various data for registration of Ormeloxifene (Centchroman) in Brazil as per ANVISA guidelines and inclusion in WHO medicine list.

1.4 Towards boosting public-private partnership for research and development, CDRI and Biocon executed an agreement for the development of a novel, non-infringing process patents for the synthesis of Bivaluridin, a 20-mer polypeptide used as thrombin inhibitor under a sponsored project.

Dr. Vanita Sabahit, Deputy Manager, Strategic Project Coordinator, Biocon Ltd., Bangalore presenting the first installment of premium to Dr. T.K. Chakraborty, Director, CDRI.

1.5 CDRI licensed the know-how for the plant 1020 F147 to M/s Natural Remedies Private Ltd., Bangalore for further development and marketing the product as neutraceutical and dietary supplement for optimum bone health.

Dr. Rajendra Prasad signing the agreement with Mr. Anurag Agarwal, Chief Operating Officer, Natural Remedies Private Ltd., Bangalore.

1.6 Launching of Memory Sure

(**B**acosides **E**nriched **S**tandardised **E**xtract of **B**acopa)

CDRI has developed **BESEB -** a single plant based unique natural memory enhancer formulation and patented its technology. **Memory Sure** is being launched by CDRI Licensee - Lumen Marketing Co., Chennai and Zaar Distributors Pvt. Ltd., New Delhi for extensive marketing in India for all age groups particularly ADHD (Attention Deficit Hyperactivity Disorder) children, elderly persons with AAMI (Age Associated Memory Impairment), for those with emotional stress from relationship or stress, tension, anxiety from work/study and for the prevention & early treatment of dementia. The clinical trials on BESEB were successfully conducted by CDRI in India and by Lumen in Australia at Swinburne University of Technology's Brain Sciences Institute and University of Wollongong**.** It is being exported to following countries:

Country	Brand Name
New Zealand & Australia*	Keenmind, Membac
Malaysia, Philippines & Singapore	Memo Plus Gold
France & Germany	Memory Perfect

*First drug approved by "**Therapeutic Goods Authority, Australia"** for memory enhancing.

2. Progress in R&D Activities

A complete restructuring of the Institute's research programs was initiated this year. Five disease areas viz. Tuberculosis & Microbial Infections; Reproductive Health Research, Diabetes & Energy Metabolism; Malaria & other Parasitic Diseases; CVS, CNS & other Related Disorders and Cancer & Related Areas and one Safety & Clinical Development area were formed. During the year 2009, a record number of 2153 compounds were synthesized and 20 natural products were purified for different biological activities in the Medicinal and Process Chemistry Division. The Botany Division conducted 4 tours and collected 10 repeat and 59 new plant materials from Western Himalaya, eastern and central regions of the country. These samples were authenticated, documented and submitted for follow-up as well as in primary biological screening program of the Institute. 158 New and 81 repeat samples of marine organisms were received from 8 participating centers. After documentation of data, samples were distributed to the concerned biologists for confirmation of identified activities and general biological screening.

2.1 Safety and Clinical Development

2.1.1 Pharmaceutics

One project was finalized with HLL Lifecare for generating data required for product registration in other countries and for development of novel formulations using

Ormeloxifene. Data for IND application of Herbal Medicament were generated and handed over to M/s Themis Medicare Ltd. A formulation of compound 99-411 was developed. Chitosan based nanoemulsion showed improved survival of septic animals (using *E. coli* serotype) and suppression of LPS and cytokine level in the blood. Layer-by-layer (LBL) based ultrathin polyelectrolyte nanoreservoir has also been developed for the delivery of insulin which was able to prevent its enzymatic degradation in presence of trypsin and chymotrypsin. The system has been tailored in a manner that makes it suitable for oral delivery. LBL based system has also been used for the delivery of Kaempferol which showed enhanced bioavailability in both blood and bone marrow. The formulation exhibited improved osteogenic activity in animals when compared with plain solution.

2.1.2 Pharmacokinetics and Metabolism

Principal component analysis and absolute quantification of five biologically active osteogenic markers K051, K052, K054, K080 and K095 in activity guided fraction F147 of plant 1020 has been established by LC MS/MS. Comparative plasma pharmacokinetic data on three markers K054, K080 and K095 from F147 and on three promising synthetic analogs of K095, S-006-1709, S-007-1500 and S-008-399 was generated in female SD rats by oral and intravenous routes for establishing the pharmacodynamic correlation.

Principal component analysis and absolute quantification of 4 biologically active markers K012, K058, K068 and K100 in activity guided fraction of plant 914 has been accomplished by LC MS/MS. Plasma pharmacokinetic data on the most active marker K058 has also been generated in female SD rats by oral and intravenous routes for establishing the pharmacodynamic correlation.

To accelerate in-house drug development program, rapid and highly sensitive bio-analytical assay procedures for the quantification of Lumefantrine, an antimalarial and Ormeloxifene, a contraceptive, in rat plasma by LC MS/MS have been established. These procedures will be extremely useful in evaluating drug – drug interaction potential with other drugs.

2.1.3 Regulatory Toxicology

Regulatory Toxicity studies have been carried out on CDRI candidate drugs and products from outside agencies. Compound 99-411 has been screened for various preclinical safety profiles. Besides, several basic studies were also conducted, which include test for early detection of renal toxicity, damage and hepatotoxicity using biofluids (urine) on the platform of metabonomics through NMR so as to develop a noninvasive, time and cost intensive test system. Studies related to evaluation of rotenone on different brain regions, mechanistic exploration of rotenone induced effect on glial cells, evaluation of effect of melatonin on rotenone induced cell death and oxidative stress in glial cells using rat glioma cell line C6, SNP analysis in squamous cell carcinoma of head neck and breast cancer and *in vitro* hepatotoxicity with special emphasis on mechanism of INH induced toxicity were carried out.

2.1.4 Clinical Trials

Clinical trials continued on CDRI candidate drugs. During the year, phase III clinical trials of Picroliv (hepatoprotective) in patients of tuberculosis on MDT has been completed at CSMMU, Lucknow and Seth G.S. Medical College, Mumbai and the data is being compiled for analysis. New phase-I clinical trial facility for compound 97-78 (antimalarial) was inaugurated by DG, CSIR at PGIMER, Chandigarh, where single dose tolerance study was completed in 50 healthy male volunteers. The data of clinical trials of CDR134 D123 (anti-diabetic) in healthy male volunteers and type-2 *Diabetes mellitus* patients together with summary of preclinical data submitted to AYUSH for fast-track marketing. The IEC of PGIMER, Chandigarh cleared the plan and protocol for phase-I clinical trials, already approved by DCG(I) for compound 99-373 (anti-osteoporotic).

2.2 Cancer and Related Areas

During the period under report, 110 marine extracts and 256 synthetic molecules were tested for anticancer activity. Of these, 124 hits were identified and tested further at serial dilutions to determine IC_{50} values.

A chemical library of chalcones was synthesized and screened for anticancer activity in the cancer cell lines PA1, MCF-7, KB, C33A, and VERO. Compounds S-007-533, S-007-540, S-007-541 have shown good anticancer profile with IC_{50} values in the range of 1-2 μM. Compound S-009-837 was found to be most active compound out of sixty compounds synthesized in this series. Further, the compound showed activity against all the tested cancer cell lines. This compound also showed lowest IC_{50} value of 3.33 μg/ml against KB cells followed by C33A (4.73 μg/ml), A549 (7.61 μg/ml), and MCF-7 (10.27 μg/ml), respectively. Ten novel benzocoumarin Schiff's Bases were synthesized and screened for anticancer activity against MCF-7 cell lines. Compounds S-006-1555, S-006-1558 and S-006-1559 showed IC_{50} value 3.8- 7.9 μM which is lower than tamoxifen (11.8 μM).

Staurosporine (STS), a protein kinase inhibitor from *Streptomyces sp*., was evaluated to induce apoptosis in human papillomavirus positive oral carcinoma cells (KB) and it was established that STS induces mitochondria-mediated KB cell apoptosis at G2/M phase by altering cell cytoskeletal network.

Studies on the effect of Ormeloxifene along with an EGFR inhibitor on squamous cell carcinoma of the head and neck (SCCHN) suggest that the combination therapy has a synergistic effect and could possibly serve as a useful therapeutic intervention in SCCHN, by reducing the (STAT)-3 phosphorylation pathway.

Studies on ectopic expression of C/EBPs (Enhancer Binding Proteins) have shown that C/EBPs induce apoptosis and growth arrest in breast cancer cells. The induced apoptosis in these cells is associated with caspase mediation. Among C/EBPs, C/EBP alpha is the prominent isoform and that it induced apoptosis and growth arrest in a dose dependent manner.

2.3 CVS, CNS and Related Disorders

During the reporting period, suitable animal models and *in vitro* tests were used to evaluate synthetic compounds (179), plant and marine extracts/fractions (443), for their biological efficacies. Some new models such as a mice model of schizophrenia, *C. elegans* model of Alzheimer's disease, rat myocardial infarction model and a rabbit model of accelerated atherosclerosis following balloon angioplasty, were also translated and validated. Several promising lead molecules which exhibited antiulcer, neuroprotective and memory enhancing activities, have been identified. A blood pressure lowering compound and a hypolipidemic compound isolated from plant source have been selected for investigation of their mechanism of action. Studies on an antithrombotic compound (S-007-867) have helped to identify its mechanism of action against collagen induced platelet activation. Investigations were also undertaken to delineate the molecular mechanisms involved in the above mentioned pathologies. Studies on the animal models of dementia suggested important role of neuronal angiotensin converting enzyme and insulin receptor associated signaling, while role of various AIF binding proteins and other important mediators was explored in the cerebral ischemia. Significant information has been generated to delineate the role of IRAK in macrophage foam cell formation. Role of signalling proteins in PMA mediated neutrophil extracellular traps release, have been delineated, while involvement of CDK2 nitrosylation, interaction with cyclin E and increase in its activity were found to mediate the HL-60 cells proliferation following treatment with NO donors. Involvement of PPAR-γ and glucocorticoid receptor in the amelioration of inflammatory responses in pioglitazone mediated gastric ulcer healing was also delineated.

2.4 Malaria and other Parasitic Diseases

2.4.1 Malaria

Bioevaluation of over 650 novel synthetic compounds representing thirty different prototypes and nearly 1200 natural products derived from terrestrial plants / marine extracts / microbial and fungal extracts was conducted against *Plasmodium falciparum in vitro* model to generate promising leads for further validation. Several compounds have been identified with IC_{50} values below 50 ng/ml. Representative compounds from amongst these identified leads were evaluated against *in vivo* models. Lead optimization studies with the previously identified pyrrolidino-aminoalkane prototype compounds have shown curative response at 100 mg/kg/day. Bioassay guided fractionation trial with two plant extracts NBR-0012 and IHB-1418 have resulted in identification of active sub-fractions which may lead to isolation of new chemical moieties for SAR studies. Phase-I clinical trials with the identified endoperoxide 97-78 are underway at PGIMER, Chandigarh while the pre-clinical dossier compilation for the other compound 99-411 is in progress. TEM studies with liver samples from malaria infected mice demonstrated marked alterations in the mitochondrial morphology of hepatocytes.

For validation of transketolase as a potential drug target for malaria, homology modeling of *P. falciparum* transketolase using the crystal structure of yeast as a template was carried out and the model refined through molecular dynamic simulations. Recombinant Merozoite Surface Protein-1 (MSP-1) and Circumsporozoite protein (CSP) of *P. vivax* and *P. cynomolgi B* are being generated for evaluation of protective potential in *P. cynomolgi* rhesus monkey model system. The optimum conditions for expression of $MSP\text{-}1_{19}$ gene were standardized and purified protein showed high reactivity in ELISA with monoclonal antibodies thereby suggesting that the recombinant protein is in conformational form.

Studies on the identification and analysis of proteins, involved in *Plasmodium falciparum* apicoplast DNA replication and organization, have been carried out. Recent studies have demonstrated that the ~12 μm plDNA circle is packed into a ~0.3 μm organelle through condensation by a DNA-compaction protein PfHU which is capable of mediating DNA stiffening, intermolecular

bundling and formation of DNA bridges followed by assembly of condensed DNA networks. Studies on the molecular aspects of the apicoplast translation process demonstrated the functional interaction of two translation factors encoded by different cellular compartments in mediating a critical process in the apicoplast.

Studies on the role of variations in host immune regulatory and adhesion molecules including complement receptors on malaria susceptibility have shown that CR1/CD35 levels on erythrocytes and related CR1 polymorphisms have been associated with response to falciparum malaria in populations inhabiting malaria endemic regions. While low CR1 levels correlated with susceptibility to severe malaria in the non-endemic region, high CR1 levels were associated with manifestation of disease in the endemic region.

2.4.2 Leishmaniasis

Novel synthetic moieties comprising 356 compounds representing seventeen different prototypes and 280 natural product extracts were evaluated against *in vitro* macrophage - amastigote model for lead identification. Based on the leads, a total of 36 synthetic compounds representing four different prototypes were evaluated *in vivo* against *L. donovani* – Golden hamster model. Nine of these compounds have shown moderate (52-79%) activity. Combination therapy comprising immunomodulator CpG ODN with antileishmanial drug miltefosine was found to enhance the efficacy of miltefosine which correlated with increased production of toxic oxygen metabolites and increased CMI responses. For characterization of drug resistant parasites, *L. donovani* SSG resistant related genes (LdSSG-I and II) were cloned and sequenced. SSRG-I exhibited significant homology with protein kinase homologue while SSRG-II showed homology with NLI gene. Proteomic analysis of differentially expressed proteins in membrane-enriched and cytosolic fractions of Sodium Stibogluconate (SSG) sensitive and resistant parasites revealed identification of some major and novel proteins.

Characterization and validation studies are underway with several potential drug targets for leishmania drug discovery. Assay for Squalene Synthase (LdSSN) was standardized and Zaragozic acid A, a fungal metabolite and a potent inhibitor of mammalian and fungal SQSs, inhibited recombinant *Ld*SSN (IC_{50} - 100 nM). The 3D model of Triose Phosphate Isomerase LdTIM revealed an active site similar to that of *L. mexicana* with conservation of the catalytically important residues. The recombinant Arginase was partially purified and found to be catalytically active. Folding stability of recombinant trypanothione reductase was characterized wherein reactivation and cross-linking experiments demonstrated that the loss of activity at lower urea and GdmCl concentrations did not coincide by dimer dissociation or structural unfolding. Docking studies of dipeptidyl-carboxypeptidase with captopril and molecular electrostatic potentials revealed several minor but potentially important structural differences in the active sites of three enzymes namely LdDCP, EcDCP and ACE.

Studies for immunoprophylaxis against Leishmania are continuing and seven out of 18 soluble *L. donovani* proteins that were identified as major immunostimulatory proteins through proteomics have been cloned, over expressed and recombinant proteins have been evaluated for the validation of their bio-active potential to stimulate cellular responses *in vitro* in cured *L. donovani* infected hamsters.

Studies with recombinant *Leishmania* actin have shown that this protein by itself is capable of generating nicks in the DNA, which eventually results in relaxation of supercoiled plasmid DNA and release of k-DNA mini and maxi circles from the k-DNA network. *Leishmania* coronin gene has been successfully knocked out and cellular effects have been analysed after reduction in protein levels. Depletion of coronin resulted in generation of bipolar cells due to intrusion of growing microtubule ends in to the daughter cell corsets thereby restricting their separation.

2.4.3 Filariasis

A total of 1600 natural products and 1481 synthetic compounds were evaluated *in vitro* against *B. malayi*. Moderate adulticidal activity has been observed in a few agents against *B. malayi* / rodent model while others are under *in vivo* evaluation. Several vital enzymes of *B. malayi* viz. *B. malayi* Hexokinase (BmHk), DEAD box RNA Helicase (BmL3-Helicase), Co-factor independent Phosphoglycerate mutase (Bm*i*PGM) and Trehalose-6-phosphate phosphatase (BmTPP), acetylcho-linesterase were cloned, expressed and characterized to validate their potential as antifilarial drug targets. The 3D structures of BmHk and BmL3-Helicase were constructed; mutations were incorporated at the G6P binding site in BmHk sequence and mutant protein expressed. BmL3-Helicase gene was successfully knocked down by specifically designed and chemically synthesized small sized siRNA of <20 bp by electroporation as well as soaking, former method being relatively more efficient. The diminished helicase gene expression had significant adverse effect on the *in vitro* release of microfilariae from adult females as well as on their viability. Bm*i*PGM produced a mixed Th1/Th2 immune response in host while BmTPP elicited

a Th1 biased response and protected the rodent host mastomys against an infective larval challenge.

Nitric Oxide (NO) stimulating fraction B8 (45.2-48.6kDa) of adult *B. malayi* conferred protection against L_3 induced infection (61% reduction in adult worm recovery with suppressed microfilaremia) in *M. coucha* by up-regulation of NO production, cellular proliferation, IgG, CD4+ T cells and down-regulation of TGF-β production. Presence of immunostimulatory proteins identified by MALDI TOF in the fraction further substantiated the protective potential of the fraction. A ~34 kDa BMT-5 antigen molecule present in the mitochondrial rich fraction (MT) of adult *B. malayi* offered significant protection in *Mastomys coucha* conferred through Th1 driven milieu. A few immunoreactive *B. malayi* proteins viz. Repetitive antigen (BML3 R15), HSP60 and Calponin were cloned and expressed for further molecular characterization. Entrapment of recombinant myosin increased its protective efficacy and alum adsorbed myosin conferred marginally superior protection than FCA emulsion in *B. malayi* / jird model.

2.5 Reproductive Health Research, Diabetes and Energy Metabolism

2.5.1 Reproductive Health Research

Preliminary *in vivo* vaginal safety of S-003-296 (a novel synthetic compound being developed as a vaginal contraceptive) was evaluated in rats in comparison to nonoxynol-9. Rats treated vaginally with 10 mg dose of S-003-296 for 24 hours bore normal vaginal histological features comparable to controls, which was in sharp contrast to erosion of the lining of vaginal epithelium and "washing-off" effect caused by the strong detergent action of N-9. Studies are underway to establish the vaginal safety of compound in rabbits. In another approach, nanoparticles composed of biocompatible, biodegradable material, which cross the cervical barrier when instilled into the vagina, were tested for contraceptive efficacy in female mice. No significant reduction in conceptions per estrus cycle was observed.

Inhibition of endogenous GnRH pusatility by exogenous pulsatile delivery of testosterone through transdermal patches to fertile male rats strongly suggested contraceptive efficacy at significantly lower doses than literature reports. A computation model describing the rates of decline and recovery of pituitary gonadotrophe populations on imposition and removal of GnRH suppression was developed.

37 Synthetic compounds were tested for anti-implantation cum early post-implantation interceptive activity in adult female rats when administered on days 1-7 post-coitum, by oral route. Of these, five compounds showed 100% contraceptive activity.

With a view to identify natural products for optimum bone health, total ethanolic extract derived from a plant and its fraction was evaluated for attainment of peak bone in growing rats, and bone loss in ovariectomized rats (post-menopausal bone loss simulation). The latter was found to be more effective than the former. A novel flavonoid, 6-C-β-D-glucopyranosyl-(2S,3S)-(+)-3',4',5,7-tetrahydroxy-flavanone was identified and isolated that alleviated ovariectomy induced bone loss in rats. Two more compounds, Naringenin-6-C-ß-D-glucopyranoside and (2S,3S)-(+)-4',5,7-trihydroxyd-ihydroflavonol-6-C-ß-D-glucopyranoside, were also isolated that promoted osteoblast function and inhibited adipogenesis. On the other hand, 8,8"-biapigeninyl, a condensation product of two apigenin molecules stimulated osteoblast function and inhibited osteoclast and adipocyte functions in murine bone cells *in vitro*. This phyto-compound exhibited potent osteoprotective activity in ovariectomized mice. Osteoprotective effects were also identified from the stem-bark of another plant, two methoxylated daidzeins (cladrin and formononetin) and medicarpin. Using the medicarpin scaffold, a chemical series was synthesized and three compounds (S-006-1709, S-007-1500 and S-008-399) were found to exhibit promising activity *in vitro* as well as *in vivo*. Further studies have indentified promising activity of S-007-1500 in rapid healing of bone fractures.

2.5.2 Diabetes and Energy Metabolism

Nearly 400 new molecules based on the selected antidiabetic drug targets i.e. DPP-IV, PTP1b and GLP-1, alpha-glucosidase, glucose-6-phosphatase, glycogen phosphorylase, and aldose reductase were synthesized and evaluated against their putative targets. Three new molecules showed inhibition against PTP1b, whereas nine new molecules showed inhibition against DPP-IV. One of glucose-6-phosphatase and two α-glucosidase inhibitors showed antihyperglycaemic activity on streptozotocin-induced diabetic rats. In addition, eight promising antidiabetic molecules were further explored for their *in vivo* efficacy in models of type 2 *Diabetes mellitus* i.e. high fructose high fat fed-low streptozotocin-treated and neonatally streptozotocin treated diabetic rats. Among the 71 trerrestrial plants explored for the isolation of antidiabetic compounds, few compounds showed significant antihyperglycaemic activity on streptozotocin-induced diabetic rats and db/db mice.

2.6 Tuberculosis and Microbial Infections

Among two thousand compounds that were screened for anti-TB activity, 16 synthetic molecules showed an MIC ≤ 3.12 μg/ml; eight of these compounds were found non-toxic and pursued for *in vivo* screening in mouse model. Nearly 80 in-house compounds, rationally designed against mycobacterial FASII elongation pathway, were screened using recombinant *M. aurum* strain of which four showed >85% reduction in viability counts in *M. aurum* and two of them was also confirmed with β-gal inducibility assay. Assays for AHAS activity and mycolic acid have also been developed. Using 3D-QSAR models in combination with virtual screening and molecular docking, potential hits were idenified against *M. tuberculosis* Enoyl acyl carrier protein reductase (MtENR). Ligand and receptor based virtual screening approaches were used to identify potential virtual screening hits targeting type II dehydroquinase from *M. tuberculosis,* an effective and validated antimycobacterial target. A highly polymorphic VNTR locus, identified in *M. tuberculosis* H37Rv, was found to alter the expression of rv3303c (lpdA) in different mycobacteria depending on its copy number. Proteolytic inactivation of PKC-α by PknG helped mycobacteria avoid phagocytosis and killing by macrophages, while knocking down PknK enhanced the multiplication of BCG. A *M. smegmatis* Δ*sigF* mutant was created and its phenotype was analysed during different physiological conditions and upon exposure of various stress conditions. Deletion of *sigF* resulted in loss of carotenoid pigmentation and increases the susceptibility of mutant towards H_2O_2 induced oxidative stress. There is an enrichment of *sigH* subfamily and seven *sigH* paralogs are reported in *M. smegmatis* genome. Expression of *sigH* paralogs at different stages of growth and under various stress conditions were examined and it was found that *sigH1* expression is increased several folds in response to different antimycobacterial drugs *viz*. isoniazid, ethambutol, rifampicin and streptomycin. NMR solution structure of ΔRv0603 from *M. tuberculosis* H37Rv showed a novel α,β-fold.

534 Compounds, including plant extracts, were screened for antifungal and antibacterial activity. Synthetic compounds S-008-1633, -995, -997, -1355, -1478, S-009-0307, -155 and -160 were found to be active against fungi (MIC in the range of 0.19-1.56 μg/ml). Two monoclonal antibodies, 10D2 and 2A11, generated against *C. albicans*, showed specificity to *C. albicans* and did not exhibit any cross reactivity against other yeast and mycelial pathogen fungi. Anti-HIV-RT screen system was used for screening of in-house synthesized compounds.

3. New Facilities Created

3.1 National Facility for Regulatory Pharmacology and Toxicology

A state-of-art National Facility for Regulatory Pharmacology and Toxicology has been established in the Pharmacokinetics Division, to generate safety and toxicity data that may help in preclinical development of a candidate molecule.

State-of-Art Animal Facility for Regulatory Pharmacokinetic, Toxicology and Safety Pharmacology studies

3.2 National Centre for Pharmacokinetic and Metabolic Studies

This facility was established to generate the desired pharmacokinetic data that may help in selection of right candidate drug for the preclinical development.

Functional Highthroughput Facility for Drug Metabolic & Pharmacokinetic studies

3.3 Laboratory of Functional Genomics and Molecular Toxicology

The laboratory of Functional Genomics and Molecular Toxicology has created model system *Caenorhabditis elegans* towards identifying genetic modulators/targets of various human diseases employing transgenic and knock out mutant strains of model system *C. elegans.*

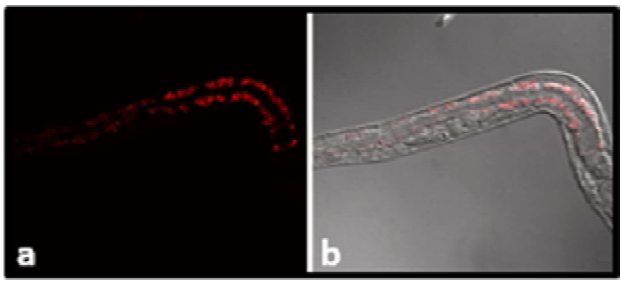


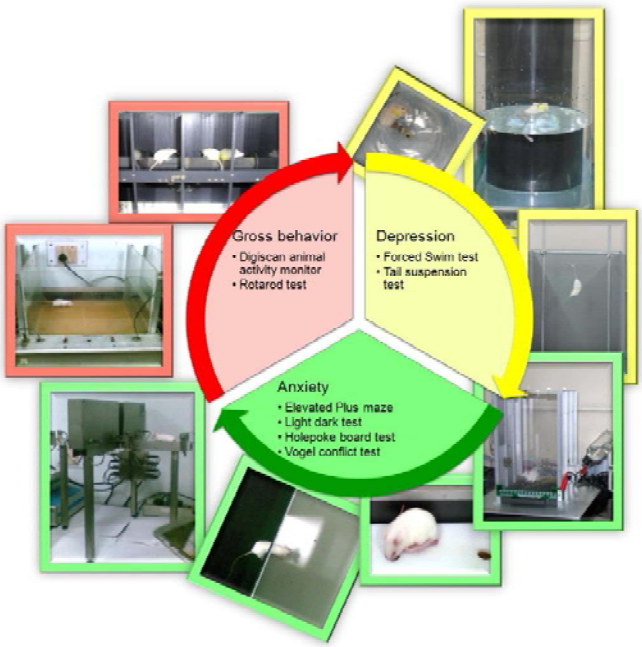
Image of *C. elegans* stained with Nile Red for localization of lipid deposits. a) Fluorescence microscopy image b) Image using DIC optics merged with fluorescence image.

Image of a GFP tagged transgenic strain of *C. elegans.* a) Control, b) After treatment with a toxic protein, c) 100X image of nematode treated with toxic protein.

3.4 Neuro-behavioural Laboratory

The facility comprises of *in vivo* microdialysis and equipments for testing antianxiety, antidepression and anticataleptic effects of compounds.

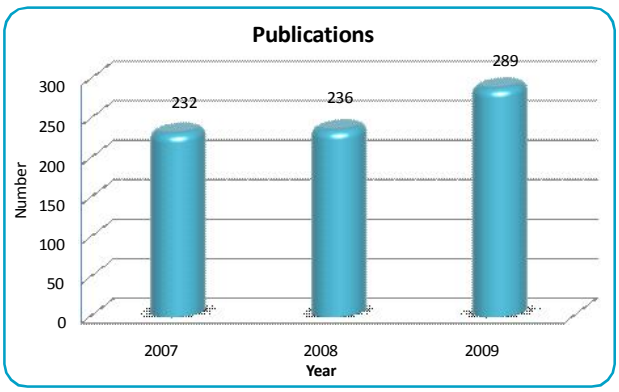
***In vivo* microdialysis setup**

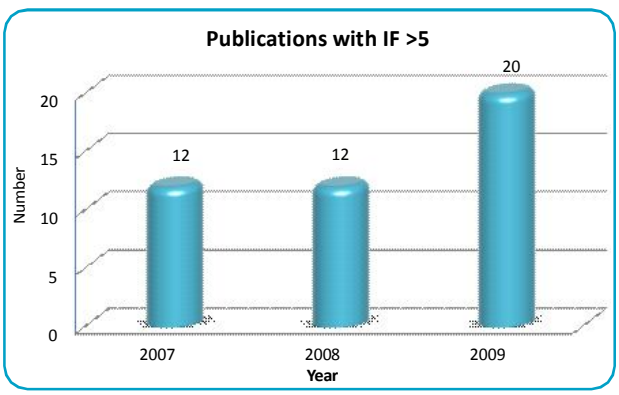


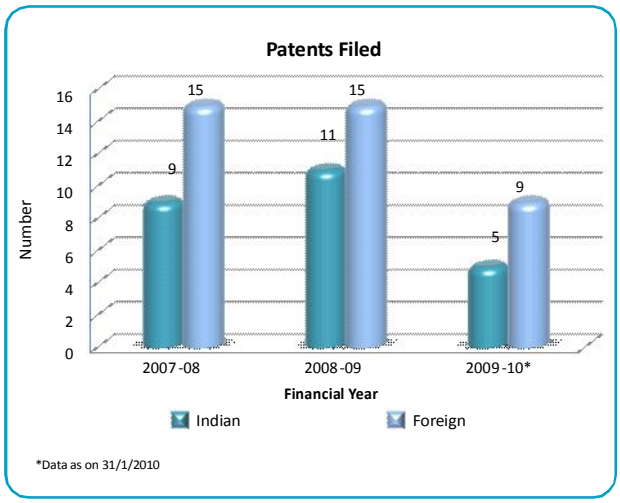
Models of neurobehavioural studies

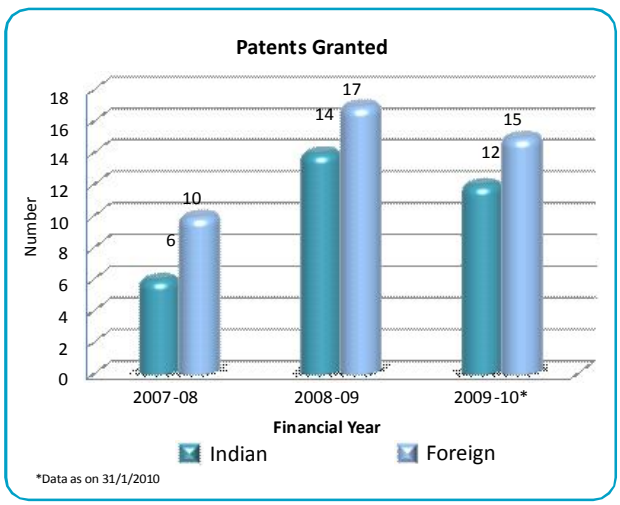
4. Publications and Patents

During the reporting year, 289 research papers were published in different national, international periodicals and 7 book chapters and an instruction manual **"How to Handle Inventions"** was published by IPR Cell of the Institute. Besides, several papers and posters were presented in different national and international symposia/ conferences. This year, a total of 5 Indian and 9 foreign patents were filed and 12 Indian and 15 foreign patents were granted.









5. Technical Services Provided

Sophisticated Analytical Instrument Facility extended its services to scientists and other users from academic institutes, R&D laboratories and industries to enable them to carry out R&D work. During the year, the Centre carried out analyses of 6987 external and 39414 internal samples. Users were from Universities, Colleges, National Laboratories, Government Organization and Industries. The Institute continued to provide the *in vitro* and *in vivo* screening facilities to R&D institutions,

academic organizations, universities, industries, etc. on payment basis. CDRI Knowledge Resource Center provided computerized information services and subscribed to J-Gate Custom Content for Consortia (JCCC). The facility was made operational in May 2009 for the scientists in CSIR and DST laboratories. All activities of the Center are fully computerized and conform to the norms of e-governance. The Center organized 5 user training programs and 2 workshops during the reporting year. It manages, maintains and updates the CDRI website and institutional repository.

National Laboratory Animal Centre supplied defined and healthy laboratory animals for research as per requirement of institutional user scientists and outside agencies. This year, over 46000 laboratory animals were supplied out of which total 4553 animals were supplied to various academic institutions, pharmaceutical industries and research organizations.

Instrumentation Division continued to provide repair, maintenance and upkeep of sophisticated analytical, bio-medical, electronic and laboratory instruments. Division maintained uninterrupted smooth power supply to all the divisions. In cases of non-availability of imported components, equivalent indigenous substitutes were installed to ensure smooth functioning of instruments.

6. Human Resource Development

Under the CSIR program, **Faculty Training & Motivation and Adoption of Schools & Colleges by CSIR Labs,** CDRI adopted 3 local Colleges viz. Govt. Jubilee Inter College, Govt. Husainabad Inter College and Govt. Girls Inter College. Several activities, such as popular science lectures by eminent scientists, visit of students to local laboratories and Regional Science Centre were organized.

An open policy was pursued to reorient and train staff in all disciplines. During the year, 36 scientists were extended trainings in diversified areas while 1 newly recruited scientist was provided orientation training at Human Resource Development Centre of CSIR. This year, several scientific workers were imparted training at CDRI. These include: 3 scientists from CIMAP, Lucknow (in bio-informatics), 2 technical personnel from Sipra Labs. Ltd., Hyderabad (in cell line culture), 1 from PGMIER, Chandigarh (in microbiology) while 15 students of B. Pharma. From BITS, Pilani were provided 6 months training in different research areas. During the calendar year, 242 postgraduate students from 81 Universities/Colleges, all over the country, were imparted training in various disciplines for 2 to 12 months duration.

Fourteen scientists of the Institute were deputed abroad for specialized training in their areas of research. Under foreign trainees, 4 candidates received extensive training in different divisions of the Institute. This year, 59 research fellows submitted their thesis for the award of Ph.D. degree.

7. Memorable Events

7.1 CDRI Annual Day

The Institute celebrated its 58th Annual Day on February 17, 2009. In a glittering ceremony, Dr. T.K. Chakraborty, Director, enumerated the achievements made by the Institute during last year. He informed the audience that multi-centric clinical trials have been concluded on Arteether, an antimalarial drug for pediatric use as the data on 235 cases are very promising and provides evidence for its suitability and efficacy. He highlighted that marketing permission for this product is likely to be obtained soon. Chief Guest of the function was Prof. S. Chandrasekaran from Indian Institute of Science, Bangalore while Prof. N.K. Ganguly, Former Director General, ICMR, presided over the function. They called on the scientists to enhance the quality and quantity of their research outputs and mend them in a way so that it should be beneficial for the society.

(Top) View of 58th Annual Day Celebrations of CDRI on February 17, 2009 (Bottom) Release of Annual Report 2008-09

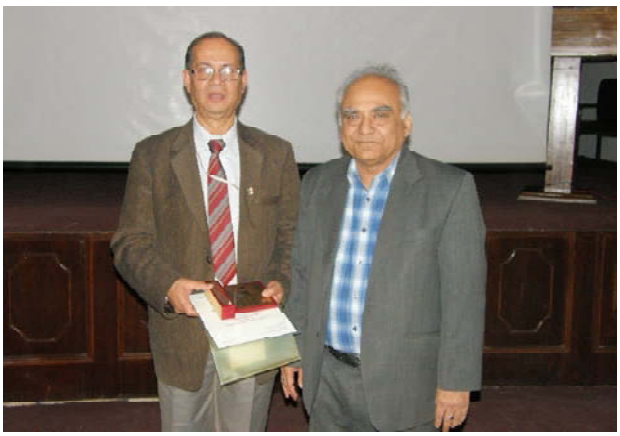
Several employees, completing 25 years of continuous service, were felicitated on the occasion. Audience was informed that Dr. Saman Habib got a research proposal of Rs. ≈ 1.9 crore from European Commission. Academic Incentive Awards were given to several scientists for publishing their research findings in high impact journals and filing / grant of foreign patents. Dr. M.M. Dhar Memorial Prize 2008 was given to 2 research fellows for best thesis presentations. Large number of dignitaries and galaxy of scientists, including former Directors from different CSIR laboratories graced the function. Dr. (Ms.) Ranjana Srivastava, Senior Deputy Director and Head, Microbiology Division proposed a vote of thanks.

Earlier during the day, Annual Prize Distribution Function of CDRI Club was organized and Dr. T.K. Chakraborty, Director and President, presided over while Dr. (Mrs.) Susmita Chakraborty graced the occasion as Chief Guest. She distributed prizes to the winners of different sport and field events, held at the Institute as a part of Annual Day celebration functions.

View of Annual Prize Distribution Function of CDRI Club during 58th Annual Day Celebrations on February 17, 2009

7.2 Mellanby Memorial Lecture

As a part of the 58th Annual Day Celebrations of CDRI, the 34th Mellanby Memorial Oration was delivered by Dr. Vishwa Mohan Katoch, Director General, ICMR, New Delhi. The topic of his presentation was **Drug Resistant Tuberculosis**. He informed the audience that multi-drug resistance has presented a scary situation for victims. He presented mind blowing data on drug resistant tuberculosis in Northern India and emphasized on expanding the coverage of DOTS and DOTS Plus. Prof. N.K. Ganguly, Former Director General, ICMR, presided over the function.



View of 34th Mellanby Memorial Oration delivered by Dr. V.M. Katoch, DG, ICMR, New Delhi

7.3 National Science Day Celebrations

National Science Day is celebrated every year on 28th February - the day when Raman's Effect was invented by Prof. C.V. Raman at Indian Institute of Science, Bangalore in 1928. As a part of the National Science Day celebrations, a science quiz competition was organized on February 27, 2009. The occasion was used to lure young minds into the scientific fields. The participants in the quiz were research scholars, project assistants and

project trainees. Prizes, certificates and mementos were given to the winners.

(Top) A View of National Science Day Celebrations at CDRI, February 28, 2009 (Bottom) Winners of various competitions with organizers

7.4 CSIR Program on Youth for Leadership in Science (CPYLS)

A 2-day program, CPYLS, was organized at the Institute on March 18 and 19, 2009. Dr. T.K. Chakraborty, Director welcomed meritorious students from Uttar Pradesh and encouraged them to adopt science as a career to reveal the secrets of science for the welfare of mankind. He expressed his concern on the face that the percentage of the school students opting for science has consistently declined over the years. Medical and engineering still continue to attract top class students but the majority of the extraordinarily talented students are reluctant to opt science as their career. Therefore, CSIR has initiated such programs to inculcate interest in science amongst the talented youths towards the fascinating world of science. He also stressed upon great opportunities and avenues available in the field of science. Prof. V.D. Gupta, Dean, Faculty of Sciences, Integral University, Lucknow graced the occasion as Chief Guest while Dr. Ashok Sharma, Scientist, CIMAP, Lucknow explained the genesis of the program. In all, 15 students participated in the function. Eminent scientists from CDRI and IITR, Lucknow delivered their presentations. Later the day, students visited different laboratories, where they interacted with bench scientists about the excitements associated with science.

(Top) Views of CPYLS program organized at CDRI on March 18, 2009 (Bottom) Participants of the programme

7.5 The Earth Day Celebration

The Earth Day Celebration 2009 was organized at CDRI under the sponsorship of Ministry of Earth Sciences, Govt. of India, New Delhi. The event was marked by the participation of different groups of children drawn from 16 schools of the town. They made drawings and paintings on the themes (1) The environment around you (Class 5th and below) (2) global warming in your eyes (Class 6 to 9) (3) The violent earth (Class 10 to 12).

The prizes were distributed by Dr. (Mrs.) S. Chakraborty to the winners in all the three categories. Further, the award winning drawings from all 45 centers were adjudged by the National Committee at Ministry of Earth Sciences, New Delhi and Master Pranjal, Kendriya Vidyalaya, Aliganj, Lucknow, who stood first in Class V and below category was awarded IIIrd prize in this category, at national level.

(1) View of Earth Day Celebrations, (2) Competition held and (3) Prize Distribution function

7.6 Director General's Visit to CDRI

Prof. Samir K. Brahmachari, Director General, CSIR and Secretary to Government of India, Department of Scientific and Industrial Research, New Delhi visited CDRI on March 26, 2009. He addressed all the staff members of the Institute. Later, in a separate meeting, he addressed all Head of Departments and Area Coordinators of the Institute. During his deliberations, he stressed upon the need for the overall development of leadership among the senior scientists. In order to generate more revenue, he emphasized that the technologies and products should be marketed in a more professional manner. The DG also met the younger scientists of the Institute and asked to improve the quality and quantity of the research work and publish papers in high impact factor journals.

(1) DG, CSIR Addressing the CDRI Staff, (2) Head of Divisions & Scientists 'G' and (3) Interacting with CDRI staff

7.7 CDRI Awards - 2009

CDRI award was instituted in the year 2004 to recognize excellence in contribution of Indian researchers below 50 years of age to the broad areas of drug research. A presentation ceremony of this award for the year 2009 for excellence in drug research was organized on June 12, 2009. Prof. Sandeep Verma from Indian Institute of Technology, Kanpur was selected and honored on this day. He delivered their award oration "**Peptide Soft Structures: Application in Drug Discovery and Gene Delivery"**. Dr. Nitya Nand, Former Director, CDRI presided over the function.

7.8 Special Meeting of MoES Project

A Special meeting of MoES Project 'Drugs from the Sea' was organized in CDRI on 10th Sept. 2009 chaired by Dr. Shailesh Nayak, Secretary, Ministry of Earth Sciences, New Delhi. Dr. Ram Raghubir, PI, MoES Project presented detailed highlights and achievements of the programme. Thereafter, Mr. Kural also made presentation on the database application developed by CDRI for project coordination among various centers. Dr. Nayak also formally inaugurated the database application system. He was satisfied with the progress of the programme.

7.9 CSIR Foundation Day

The Institute celebrated the 67th CSIR Foundation Day on September 26, 2009. During the day, a Science Exhibition was organized in the CDRI Museum and was inaugurated by the chief guest Prof. U.N. Dwivedi, Vice Chancellor, Lucknow University. The exhibition remained open and a large number of scientists from academic institutes, students and general people visited it and discussed their concern with experts.

During his deliberations, Prof. Dwivedi recalled his association with CSIR as he started his career with NCL, Pune before joining Biochemistry Department of Lucknow University. Later he felicitated CDRI staff members who completed 25 years of their service in CSIR and also presented a certificate, wrist watch and a shawl to the employees who superannuated between September 2008 and August 2009. Besides, prizes and cash awards were given to children of staff members for winning essay/ quiz competitions and securing meritorious positions in different all India examinations and securing admissions in medical / management courses.

For the second consecutive year on this eventful day, CDRI proudly received the **CSIR Technology Award - 2009** on "**Development of Synthetic Endoperoxide Antimalarials as Substitute to Artemisinine Derivatives**". The award carries a cash award of Rs. 2.00 lakh, a plaque and a citation. A short video film on the subject was exhibited on the occasion. For the first time in the history of CDRI, a competition was organized for preparing a suitable logo of the Institute. Out of the several entries received, one was selected for inclusion in official documents, letter heads etc. Further, a bi-annual CDRI

(1) A view of 67th CSIR Foundation Day celebrations at CDRI on the occasion of 67th CSIR Foundation Day, September 26, 2009 (2) A view of inauguration of exhibition by Prof. U.N. Dwivedi, Vice Chancellor, Lucknow University (3) A view of students visiting the exhibition (4) Dr. (Mrs.) Susmita Chakraborty presenting a memento to Prof. U.N. Dwivedi

(1) A view of 67th CSIR Foundation Day celebration jointly organized by CDRI, IITR, CIMAP and NBRI at Scientific Convention Center, Lucknow (2) Dr. T.K. Chakraborty, Director, CDRI addressing the audience (3) Prof. Ram Rajasekharan, Director, CIMAP presenting a memento to Dr. Nitya Nand, Former Director, CDRI (4) Dr. T.K. Chakraborty, Director, CDRI presenting a memento to Dr. T. Ramasami, Secretary, DST, New Delhi

Newsletter was released by the chief guest Prof. U.N. Dwivedi.

The main function was organized at Scientific Convention Center, Shahmeena Road, Lucknow where all the four CSIR laboratories viz. CDRI, IITR, CIMAP and NBRI jointly participated in the CSIR Foundation Day Celebrations. Dr. Nitya Nand, Former Director, CDRI, in his keynote address stressed upon the need of coordinated research work since individual concepts and divergent working might not yield adequate results. Dr. T. Ramasami, Secretary, Department of Science and Technology, New Delhi presided over the function. In his address he emphasized upon the need for linking the scientific investments with national and social benefits and complimented scientists for concentrating their research activities with national needs and goals. Dr. T.K. Chakraborty, Director, CDRI proposed a vote of thanks to the dignitaries present on the occasion.

7.10 CSIR Technology Award for Innovation - 2009: Felicitation of Team Members

CDRI, in its quest for innovations, has set a milestone by bagging, 2nd time in succession, the prestigious "**CSIR Technology Award for Innovation - 2009**".

(Top) Dr. Nitya Nand, Former Director, CDRI felicitating a team member with certificate of appreciation (Bottom) Dr. Nitya Nand presenting a memento to Prof. Geoffrey A. Cordel

The cohesive and most coordinated efforts of drug discovery and development teams of CDRI have accomplished the preclinical development of two potential antimalarial compounds 97-78 and 99-411 in a relatively fast track mode, in collaboration with IPCA Laboratories, Mumbai, as the Pharma Partner. Compound 97-78 is currently under Phase I clinical trials at PGIMER, Chandigarh. The other compound 99-411 has also completed pre-clinical studies.

To commemorate the occasion, institute organized a function on 14 October 2009 to felicitate the team members who were associated with the development of technology. Prof. Geoffrey A. Cordel, University of Illinois, USA, was the chief guest and Dr. Nitya Nand, Dr. B.N. Dhawan and Dr. V.P. Kamboj were guests of honor of the event. The chief guest and guests of honor felicitated all the team members with a plaque and certificate of appreciation.

7.11 Vigilance Awareness Week - 2009

In accordance with the guidelines of Central Vigilance Commission, a one week program was organized at the Institute, as Vigilance Awareness Week, during 3.11.09 to 7.11.09. Sri Sulkhan Singh, IPS & Inspector General (Prison), Uttar Pradesh delivered an interesting talk on the subject. All members of the staff took a pledge to ensure transparency, identify root causes of corruption and eradicate it from the society at all cost to the best of their abilities. During the course of Awareness Week, several programs were organized which included a lecture, a debate competition and an essay competition. Winners of the events were suitably given prizes during the valedictory function held on November 9, 2009.

7.12 Faculty Training & Motivation and Adoption of Schools/Colleges by CDRI

With an aim to take up training and motivational programs for selected science teachers; to upgrade their knowledgebase and skills in new and emerging areas of science; to raise the standard of science education; and learning capabilities of students in selective schools/ colleges to nurture a cadre of the most brilliant and gifted youths to take up science as a career, HRDG, CSIR has initiated ***Faculty Training & Motivation and Adoption of Schools & Colleges by CSIR Labs.*** program. Under this scheme, Central Drug Research Institute adopted 3 local Colleges viz. **Govt. Jubilee Inter College, Govt. Husainabad Inter College and Govt. Girls Inter College.** Various activities viz. popular science lectures by eminent S & T personages, visit of students to local National Labs and Regional Science Center to get the handholding experience; thrill and excitements, associated with the scientific research; workshop/orientation program for science teachers; update the science laboratories of these colleges by providing them the essential scientific materials and equipments; strengthen the library with some popular scientific books, periodicals and science magazines and to provide selected students/teachers lab facilities at the institute for the project work of their interest.

CDRI formally launched the above program on 29th October, 2009 in a function attended by Principals, teachers and large number of students of the adopted colleges. Dr. U.N. Dwivedi, Vice Chancellor, Lucknow University graced the occasion as Chief Guest and Dr. T.K. Chakraborty, Director, CDRI presided over the function.

As part of the above function, CDRI organized Science Quiz and Essay Competitions on 27th October 2009 at Govt. Jubilee Inter College Lucknow. About sixty students from all 3 adopted colleges participated in both the events and winners were given awards and the certificates.

Continuing the scheme, a **Popular Lecture Series** was initiated on 30th Nov, 2009 at Govt. Jubilee Inter College, Lucknow. The inaugural lecture was delivered by Mr. Pradeep K. Srivastava, Scientist, CDRI on "**Global Warming and the Climate Change".**

7.13 Communal Harmony Campaign Week

In accordance with the guidelines of National Foundation for Communal Harmony, the Institute celebrated Communal Harmony Campaign Week from 19-25 November 2009. The main objective of the program was to promote communal harmony and national integration. All members of the staff took a pledge on this occasion to effectively promote the values of communal harmony and national integration amongst the people.

8. Conferences / Seminars / Symposia / Workshops

8.1 World Congress on Leishmaniasis

The 4th World Congress on Leishmaniasis was held on February 2-7, 2009 at Scientific Convention Center, Lucknow. The meet was organized in the honor of Late Prof. A.N. Bhaduri, ex Director, Indian Institute of Chemical

View of the inaugural function of World Congress on Leishmaniasis

Biology, Kolkata. The main theme of the conference was **'Translational Health Science'** (bench to bedside for management of Leishmaniasis). The conference served as an appropriate platform for this theme and evoked meaningful discussions amongst the delegates. For the students, it aptly served as an interesting and informative experience. Six hundred and sixty two Indian and foreign delegates participated for five days of interactive deliberations and discussions. Seven hundred and fifty one presentations were made, covering nearly all aspects of Leishmaniasis research. A rich collection of papers by contributors were presented which were also showcased as posters.

8.2 National Symposium on Animal Models in Biomedical Research: Ethical and Welfare Issues

A two days national symposium on **Animal Models in Biomedical Research: Ethical and Welfare Issues** was organized on February 25-26, 2009 in collaboration with the CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals), Ministry of Environments and Forest, Govt. of India and LASAI (Laboratory Animal Science Association of India) at the institute. The main theme of the symposium was on Animal Models for Biomedical Experimentations, Ethical and Welfare Issues in Management of Laboratory Animals, Health Monitoring and Disease Control Program, Quality Control and Strain Characterization including Genetic Monitoring, and Animal House Health Hazards and Safety Precautions. Luminaries from academic institutions, scientists, medical professionals and administrators participated in this program. The inaugural address was delivered by Sri Anjani Kumar, Director, Animal Welfare and Member Secretary, CPCSEA. Presidential remarks, as Guest of Honor, were delivered by Dr. C.M. Gupta, Distinguished Biotechnologist and Former Director, CDRI. Dr. S.K. Puri, Chairman, Animal House Advisory Committee, CDRI gave a presentation on Guidelines for Managing Animal Facility while Dr. K.R. Bhardwaj, the President of LASAI, gave an overview on laboratory animals in India. The symposium was well attended by a large number of participants from different parts of country. The two-day meet was divided in six scientific sessions, including a poster presentation session and a LASAI General Body Meeting. The valedictory function was organized in the evening of February 26, 2009 and Dr. V.P. Kamboj, Former Director, CDRI delivered valedictory address. Over Seventy persons participated and twenty-one lectures were delivered by honorable speakers on several topics.

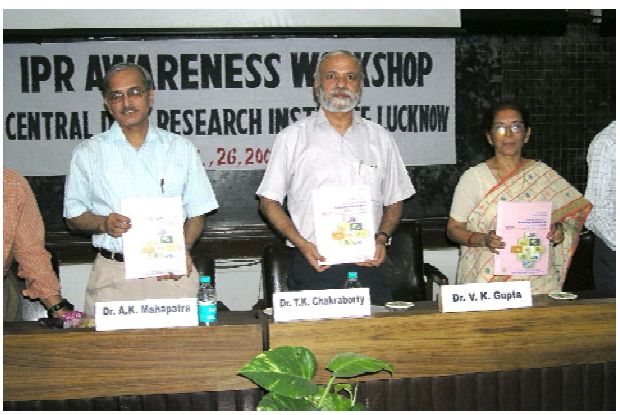
8.3 Symposium on Medicinal Chemistry and Pharmaceutical Sciences

With the growing demand of the skilled personnel for drug discovery, Union Cabinet felt the need and accorded approval for setting up 6 new NIPERs out of which NIPER, Rae Bareli is being mentored by CDRI. A symposium on Medicinal Chemistry and Pharmaceutical Sciences was organized at CDRI on March 25 and 26, 2009. The organization of this symposium was a joint effort of CDRI and NIPER to bring the pharma students and scientific community to a common platform to discuss and share current state-of-art of research being conducted in different disease areas. The inaugural function was organized on in the evening of Tuesday, 24th March 2009. Dr. D.K. Dikshit, Senior Deputy Director, CDRI welcomed the participants and dignitaries and T.K. Chakraborty, Director, CDRI presented an overview about **Mentoring NIPER (RBL): A Challenge**. Dr. J.M. Khanna, Executive Director – S&T, Jubilant Organosys Ltd., USA delivered the inaugural lecture entitled **Pharmaceutical Industry and Changing Environment**. Dr. Nitya Nand, Former Director, CDRI presented the presidential remarks. The 2-day symposium was split into several sessions. The

first session was devoted to Therapeutic Peptides and Proteins while the second one to Drug Discovery and Approaches. Third and fourth sessions focused on Drug Delivery and Pharmacokinetics respectively followed by two sessions on Life Style Related Disorders. A poster session was organized by the participating students where they highlighted their research findings. Several eminent speakers presented their views and research data in their area of specialization. Over 300 participants participated in the symposium. Prizes were given to several fellows. Neeti Mishra from Institute of Foreign Trade and Management won the first prize in poster competition in the area of pharmaceutical sciences and Neelima Uniyal from B.R. Nahta College of Pharmacy, Mandsaur (MP) won the first prize in medicinal chemistry. Ravi Dharmika from NIPER, Hajipur and Sujeet Gupta from Rajiv Academy of Pharmacy, Mathura won the Jury's award during the valedictory function of the symposium.

8.4 IPR Awareness Workshop

World Intellectual Property Organization (WIPO) declared April 26th as the World Intellectual Property Day. On this occasion, a half day IPR Awareness Workshop was organized on 26.4.09 at the Institute. Focal theme of the workshop was traditional health systems. Besides organizing lectures on the theme, a special supplement of Drugs and Pharmaceuticals: Industry Highlights was published. Scientific and technical staff of CDRI and other Lucknow based academic institutions attended the workshop.



8.5 WHO-TDR Training Workshop on OECD Principals of Good Laboratory Practice

Good Laboratory Practice is being implemented in different divisions of the Institute for making the test facilities and safety studies to be GLP compliant. These divisions include: Toxicology, Pharmaceutics, Pharmacokinetics & Metabolism, Pharmacology, Biometry & Statistics, Instru-mentation, Computer Cell and Division of Laboratory Animals. A WHO-TDR Training Workshop on OECD Principals of Good Laboratory Practice was organized at CDRI from October 27 – 29, 2009 in which 29 scientific workers, involved in GLP studies, were provided extensive training. External GLP trainers were Dr. Deepak Agarwal from IITR, Lucknow and Dr. Sudhir Srivastava, Dr. Rakesh Shukla and Dr. J.K. Saxena. Certificates were presented to participants by Dr. T.K. Chakraborty, Director, CDRI.

8.6 Workshop on Rational Approaches in Drug Designing - Application of Tools & Techniques of Bioinformatics

As a part of Bioinformatics activities, funded by DBT (under BTISNET Project), a one day workshop on "Rational Approaches in Drug Designing - Application of Tools and Techniques of Bioinformatics" was organized on 30th October, 2009. The workshop provided hands-on training on bioinformatics tools applied in drug discovery process on genome for drug discovery; structural biology and its application in drug design and computer aided modeling. Faculty included senior scientists from IGIB, New Delhi, CDRI and IIT, Kanpur.

8.7 Training Program Basics & Application of Sophisticated Analytical Instruments

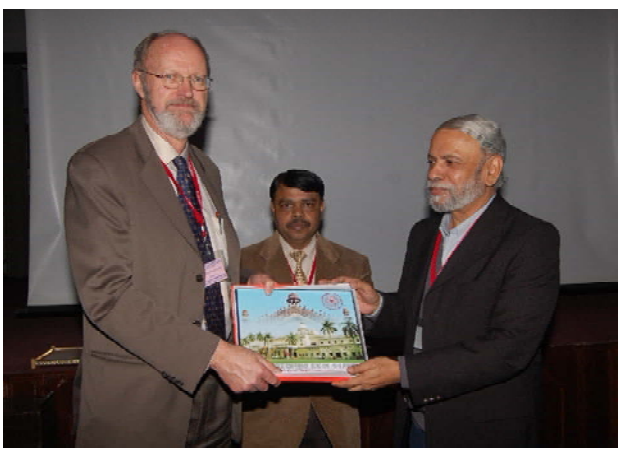
Sophisticated Analytical Instrument Facility (SAIF) organized a five days training program from 8.12.09 to 12.12.09 for Ph.D. students (Chemistry) of SAIF users on sophisticated Mass and NMR instruments. The objective was to appraise the SAIF users about the latest developments in the area of Mass and NMR and to train in these areas. Fifteen students from different universities participated in this training program. Series of lectures on hardware and software and their capabilities of all the instrumental techniques, available in SAIF, were delivered by the respective area experts. Experiments were planned and onsite demonstrations were provided on all the instruments of Mass and NMR.

8.8 14th ISCB International Conference on Chemical Biology for Discovery: Perspectives and Challenges

Indian Society of Chemists and Biologists, India organized its 14th International Conference on "Chemical Biology for Discovery: Perspectives and Challenges" at the Central Drug Research Institute from January 15-18, 2010. Dr. P.M.S. Chauhan, General Secretary of the ISCB was organizing secretary. Prof. David St. C. Black, Secretary General, IUPAC was chief guest of the function. Prof. Robert H. Grubbs, Nobel Laureate delivered a special lecture. Prof. Nancy B. Jackson, Elected President of American Chemical Society, Prof. Colin J. Suckling, UK, Prof. Michael D. Threadgill participated in valedictory function.

Approximately 550 delegates from India and abroad participated in this conference. Several scientists presented their deliberations on different aspects of drug research.

The renowned pharma company and industries viz. THINQ Pharma (USA), Jubilant Chemsys Limited, Ranbaxy, ZydusCadila, Orion Pharma, Nicholas Piramal, GVK Biosciences Pvt. Ltd., Torrent Pharmaceuticals Ltd., Wockhardt, etc. participated in this conference. The four days scientific programs include 9 plenary lectures, 50 invited lectures and 16 oral presentations.



(Top) A view of the inaugural function. (Bottom) Dr. T.K. Chakraborty, Director, CDRI presenting a memento to Prof. Robert H. Grubbs Nobel laureate

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10. Honors and Awards

CDRI received the prestigious **CSIR Technology Award for Innovation – 2009**, for the second consecutive year. The award was conferred towards discovery and development of new synthetic endoperoxide antimalarials as synthetic substitute for drugs based on Artemisinin, derived from the plant *Artemisia annua.*

Dr. C.M. Gupta received the Distinguished Biotechnology Research Professorship Award from DBT. Dr. S.K. Puri was elected Fellow of National Academy of Sciences, India while Dr. C. Nath was elected as a Fellow of Indian Academy of Neurosciences. Dr. Ashim Ghatak was conferred the Dr. Coelho Memorial Oration in Experimental Medicine – 2009 from the Association of Physicians of India. Dr. Sanjay Batra received the Most Cited Paper 2006-2009 Award from Tetrahedron. Indian Chemical Society of India honored Dr. Atul Goel by giving him the Ghanshyam Srivastava Memorial Award – 2007 and Dr. Renu Tripathi got Dr. G.D. Bhalerao Award - 2009 from Zoological Society of India. Besides, several research fellows of the Institute received honors for their research contributions, details thereof are given in the relevant section of this Report.

11. CDRI Newsletter

In order to highlight the activities of CDRI, it was decided to publish a bi-annual **CDRI Newsletter**, which would give a glimpse of the institutional activities. First issue of this document was formally released on CSIR Foundation Day, September 26, 2009.

12. Other Activities

Staff Club actively organized various sports, cultural, literary and welfare activities. In view of the active interest and the increasing numbers of players in Table Tennis, Staff Club purchased a new TT table. After qualifying the zonal tournament, 9 players of the Institute participated in the Shanti Swaroop Bhatnagar Tournament (Indoors) held at NGRI, Hyderabad during 20-22 February 2009. The Institute also participated in the SSBMT (outdoor cricket and volleyball) Zonal at NPL, New Delhi from 27-29 December 2009. Children of the staff members participated in various events organized by CDRI Club and the winners were suitably awarded.

Year 2009 Vol. 1 No. 1 April - September

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CDRI Newsletter

Central Drug Research Institute, CSIR

From the Director's Desk

I am privileged to present before you the first issue of CDRI Newsletter. Ever since my joining CDRI as Director in December 2008, I was keen to bring out a document, which would provide an overview of our activities. The first issue of the Newsletter gives an idea of the Institute's reforms during the last 6 months i.e. April 2009 to September 2009. CDRI has a very productive past and its contributions, in terms of new drugs released for marketing, process technologies licensed for commercialization, human resource development, national and international collaborations, generation of new knowledge, etc. have been greatly appreciated world-wide. However, during this period, we have reorganized our research activities so as to produce quality research and develop newer substances at par with globally acceptable regulations and GLP guidelines and become a world class center for drug research in India.

World Intellectual Property Organization (WIPO) declared April 26th as the World Intellectual Property Day. To commensurate the occasion, an IPR Awareness Workshop was successfully organized. Focal theme of the workshop was traditional health systems. Besides organizing lectures on the theme, a special supplement of Drugs and Pharmaceuticals Industry Highlights was published. During the period of report, CDRI has done exceptionally well in terms of high quality research publications, grant of international and national patents. Several prestigious projects were initiated and new ones got sanctioned. Important new leads have been identified for further development as drugs. Besides, many of our scientists have won several national and international awards for their scientific contributions. I congratulate all of them and wish them and others for many more such prizes in the coming days.

September 26, 2009, the Foundation Day of CSIR, had a special occasion in the history of CDRI as we were bestowed with the prestigious CSIR Technology Award for Innovation 2009. I compliment all of my colleagues, both in scientific laboratories and in administration, for their wholehearted support for presenting CDRI as one of the best laboratories in India. We feel immensely proud of our institute. Best wishes.

(Tushar Kanti Chakraborty)

CSIR Technology Award for Innovation - 2009

CDRI received the Technology Award for the year 2009 towards the discovery and development of two new synthetic endoperoxidic antimalarials as synthetic substitute for drugs based on Artemisinin, derived from the plant *Artemisia annua*.

Artemisinin based combination therapy has been recommended by WHO for the treatment of *Plasmodium falciparum* malaria. A synthetic derivative of artemisinin will be a major breakthrough in cost effective management of falciparum malaria and multi drug resistant falciparum malaria in clinical practice. The compound is being developed to meet the new global challenges of the malaria incidence covering 300-600 million patients every year including the Indian population of around 3 millions.

The compounds 97/78 and 99/411 are found to be safe in animals. Phase I clinical trials of compound 97/78 is being carried out at PGIMER, Chandigarh in order to assess its safety and tolerability after getting the necessary approval from DCG(I). So far, 29 healthy male volunteers have completed phase I single oral dose trial out of 50 cases. The preclinical studies of compound 99/411 have been completed and the data is being compiled for IND (Investigational New Drug) submission to DCGI in order to obtain the permission to initiate Phase I clinical trials in human.

For further development and commercialization of these drugs at affordable price to common people, CDRI has already obtained its patent rights and licensed the technology to Ipca Laboratories Ltd., Mumbai.

A Newsletter from
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केन्द्रीय औषधि अनुसंधान संस्थान
(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद)
छत्तर मंजिल, चेटर बाग़ ला-173 लखनऊ-226 001

The First Issue of CDRI Newsletter

1. Safety and Clinical Development

Coordinator:
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Assistant Coordinator:
Dr. Amit Misra

Area Leaders:
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The major objective of this area is to conduct regulatory studies of candidate drugs for clinical development. The studies include:

- Pharmaceutical Information: Active ingredients, Physiochemical Data Validations, Stability, Formulations
- Pharmacokinetics: Absorption, Distribution; Metabolism; Excretion
- Safety Pharmacology: Essential Safety Pharmacology Studies
- Toxicity Studies: Systemic Toxicity, Special Toxicity Studies
- Clinical Studies: Clinical Trials

1.1 Pharmaceutics

1.1.1 Delivery System for Septic Shock

Novel emulsion based formulations have been prepared by incorporating cationic charge with chitosan. Gel retardation studies indicate existence of direct interaction with Lipopolysaccharide (LPS) and nanoemulsion as there was change in electro mobility shift of LPS when it was incubated with nanoemulsion. The prototype formulation (chitosan based nanoemulsion) showed improved survival of septic animals (using *E. coli* serotype) and suppression of LPS and cytokine level in the blood. This provides evidences for efficacy of developed formulation in animals against septic shock.

1.1.2 Development of LBL Based Nanoreservoir

Layer-by-layer (LBL) based ultrathin polyelectrolyte nanoreservoir has been developed for the delivery of Kaempferol. The developed system showed increased circulation in blood and simultaneously provided higher level (1.6 times) of Kaempferol in bone marrow as well as in the blood when compared with solution. The formulation also showed improved osteogenic activity in animals when compared with plain solution.

1.1.3 Development of LBL Based Nanoreservior for Delivery of Insulin

LBL based ultrathin polyelectrolyte nanoreservoir has also been developed for the delivery of insulin. It has been established that the developed system was able to prevent enzymatic degradation of insulin in the presence of trypsin and chymotrypsin. The system has been tailored in a manner that it releases only 10% of insulin at pH 1.4 which makes it suitable for oral delivery.

1.1.4 Quality Control and Stability Studies

Ormeloxifen is one of CDRI's flagship drugs and is currently being manufactured by HLL Life Care Ltd., Trivandrum and they are interested to export it. Necessary data is being generated for its registration in Brazil and other countries under sponsored project.

Quality control and stability studies on Herbal Medicament (HM), CDR 134F194 and compounds 99-373, 99-411 & S-007-1558 are continuing. Data for IND application in respect of HM were generated and handed over to M/s Themis Medicare Ltd., Mumbai. Compound S-007-724 has been purified by preparative HPLC. A new formulation of compound 99-411 has been developed. HPLC method for S-004-1032, S-007-1558, S-008-399, S-006-1709, S-007-1500, S-006-703, S-007-867, S-008-833 and S-007-1261, with proper resolution of the starting materials, has been developed. HPLC method for estimation of R & S isomers of S-001-469 has also been developed.

1.2 Pharmacokinetics & Metabolism

1.2.1 Compound 99-411 (Antimalarial)

(a) Assay procedures

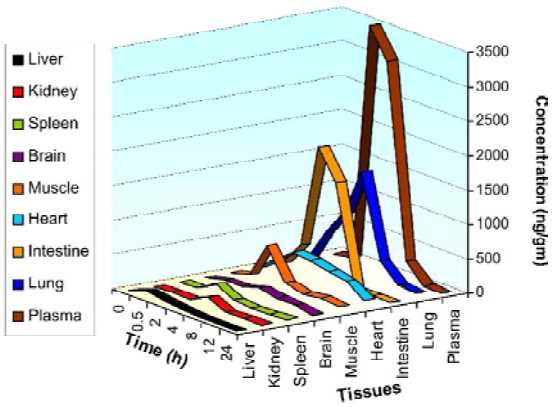
Sensitive and selective LC MS/MS assay procedures were developed for the quantification of 99-411 in rat feces, urine and tissues (liver, brain, heart, lung, spleen, kidney, intestine and muscles).

(b) Excretion studies

Excretion studies have been completed in male SD rats. 0.02-0.08% of unchanged 99-411 was excreted in feces till 96 hours post oral administration whereas 0.00063-0.0024 % was excreted in urine over a period of 60 hours at single oral dose of 12 mg/kg.

(c) Tissue distribution studies

Tissue distribution studies have been completed in liver, brain, heart, lung, spleen, kidney, intestine and muscles of male SD rats at single oral dose of 12 mg/kg. ~4.52 % of the total dose was found to be distributed in the tissues in comparison to absolute oral bioavailability of 49.68%.



(d) *In vitro* metabolite profiling

A sensitive and selective LC MS/MS assay procedure has been developed for the simultaneous detection of 99-411 and its metabolites in rat S-9/ microsomal milieu. *In vitro* metabolic studies with rat S-9 and microsomes revealed the formation of mono- and di-hydroxy metabolites and their respective glucuronides. Further work is in progress.

1.2.2 Compound 97-78 (Antimalarial)

Validated bio-analytical LC MS/MS method for simultaneous quantification of 97-78 and its metabolite 97-63 in human plasma has been developed which will be helpful in undertaking clinical pharmacokinetic studies in human volunteers during Phase-II clinical trials.

1.2.3 Compound S-007-1500 and S-008-399 (Anti-osteoporotic)

A highly sensitive and selective bio-analytical LC MS/MS method was developed for the quantification of S-007-1500 and S-008-399 in rat plasma. Plasma pharmacokinetic studies were conducted in female SD Rats by oral and intravenous route.

1.2.4 Compound : S-001-469 (Antidiabetic)

Sensitive and selective assay procedure was developed for the quantification of S-001-469 in rat feces and urine. Following oral administration of 25 mg/kg of S-001-469, parent along with two metabolites (M-1 and M-2 with molecular weight 399 and 415 respectively) were detected in faeces and urine.

1.2.5 Compound 99-373 (Anti-osteoporotic)

Stability studies of 99-373 have been completed in Simulated Gastric Fluid (SGF) and Simulated Intestinal Fluid (SIF). The compound was found to stable in the both the milieus.

1.2.6 Plant 1020 F147 (Anti-osteoporotic - Osteogenic)

(a) Principal component analysis and absolute quantification of 5 active markers K051, K052, K054, K080 and K095 in F147 by LC MS/MS has been completed.

(b) Sensitive and selective bio-analytical LCMS/MS method has been developed for the quantification of marker components K054 and K080 in rat plasma.

(c) Plasma pharmacokinetic studies of K054 and K080 were done in female SD rats by oral and intravenous route of administration.

1.2.7 Plant 914 K058 (Anti-osteoporotic - Osteogenic)

Plasma pharmacokinetic studies were done in female SD rats by oral (5 mg/kg) and intravenous (1 mg/kg) route.

1.2.8 New Leads

(a) **Antithrombotic**: Sensitive and selective bio-analytical LC MS/MS assay methods for the simultaneous quantification of isomers S-004-1032 and S-007-1558 (isomers of S-002-333) has been developed in rabbit plasma.

(b) **Antimalarial**: Plasma pharmacokinetic studies of anti-malarial lead molecule S-006-1055 were done in male SD rats.

(c) **Anti-prostate hyperplasia**: CDRI compound S-007-972.

- A sensitive and selective HPLC-UV assay method has been developed for the determination of S-007-972 in rat plasma.
- Stability studies in rat serum, Simulated Gastric Fluid (SGF) and Simulated Intestinal Fluid (SIF) have been completed.
- Plasma pharmacokinetic and prostate uptake studies have also been completed in male SD rats.

1.2.9 Other Studies

a. Established a validated rapid, sensitive and selective method for the determination of Lumefantrine in rat plasma by liquid-liquid extraction using LC-MS/MS. It will be useful for evaluating pharmacokinetics of Lumefantrine-trioxane combinations.

b. Established a validated, rapid, sensitive and selective liquid chromatography tandem mass spectrometry method for quantification of Ormeloxifen in rat plasma. It will be useful for conducting interaction studies with other class of drugs which may require co-administration with Ormeloxifen.

1.3 Safety Pharmacology

Five new promising compounds for anti-dementia (AP-20am 15 & AP-20am 16), anti-thrombotic (S-007-867 & S-007-333) and fracture healing (S-007-1500) are scheduled for essential safety pharmacology studies.

1.4 Regulatory Toxicology

1.4.1 In-house Candidate Drugs

Compound 99-411	:	Single dose toxicity studies in rat and mice completed and found safe.
Compound 99-373	:	Reprotoxicity- teratogenicity study in rats and in rabbits completed and found safe.
Herbal Medicament; CDR 267F018; CDR 134F194	:	Studies related to genotoxicity - chromosomal aberration, micronucleus test and reprotoxicity-male fertility studies completed found safe.

1.4.2 Samples from Outside Agencies

AP76-P	:	28 days repeat dose toxicity study in rat by oral route has been completed and found safe.
Ras Sindoor; Vasant Kusumakar; Kajjali Yoga	:	90 days repeat dose toxicity study in rat by oral route completed and found safe.

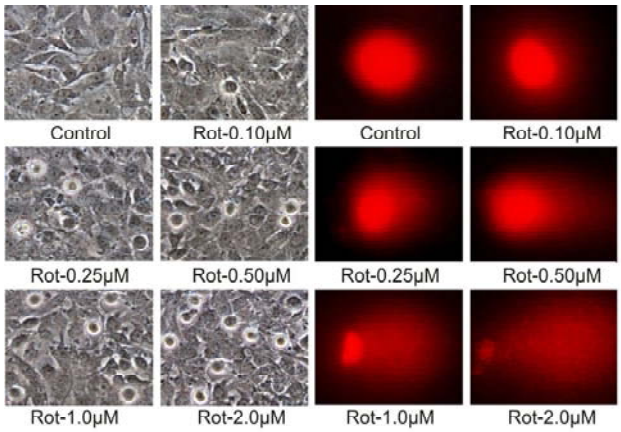
1.4.3 Experimental Toxicology (Basic Studies)

In addition to regulatory toxicity studies, basic research is conducted to understand molecular mechanisms of organ toxicity and to develop alternative test systems to reduce cost and time, and can also reduce, refine or replace the use of animals in toxicity testing.

1.4.3.1 Neurotoxicity: Evaluation of rotenone induced effects on neurons and glia

(a) Mechanistic exploration of rotenone induced effect on glial cells

Evidences of environmental toxins like insecticides, mycotoxin, glutamate and dopaminergic neurotoxins induced adverse or toxic effects on neurons have been



Glial cell viability with increasing concentration of rotenone

DNA damage assessed by single cell gel electrophoresis

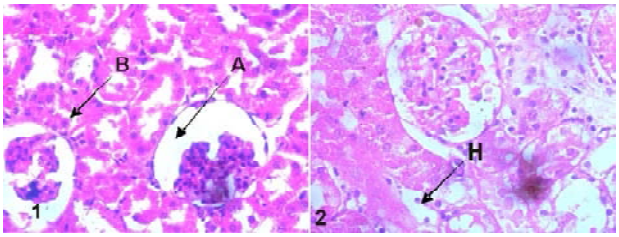
documented but its effect on glial cells are not well explored. Rotenone a known pesticide induces neurotoxicity along with activation of glial cells. Its effect on glial cells is not well explored therefore mechanistic exploration of rotenone-induced effects on glial cells has been done. Rotenone exposure led to significant decrease in glial cell viability and DNA damage via reactive oxygen species and mitochondria mediated pathway.

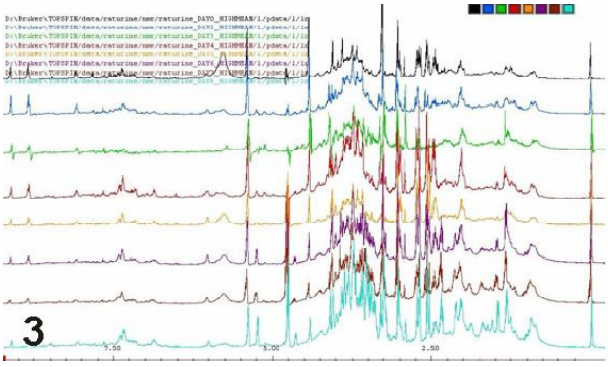
(b) In vitro studies

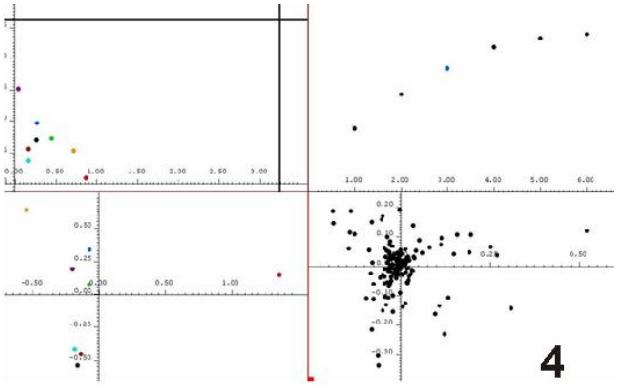
Melatonin, a pineal hormone is an efficient free radical scavenger and being used in therapeutics. The effect of melatonin in preventing neurotoxin induced cell death is not well explored in astroglial population. The effect of melatonin was evaluated on rotenone, a neurotoxin, induced cell death and oxidative stress in glial cells. Rat glioma cell line C6, was co-incubated with rotenone and melatonin. The different parameters viz. cell viability, levels of reactive nitrogen and oxygen species and nuclear fragmentation were estimated. Rotenone exposure caused significant decrease in cell viability, increased ROS, super oxides and nitrite levels and alteration in nuclear morphology. Melatonin offered significant protection against rotenone induced adverse effects.

1.4.3.2 Test for early detection of renal toxicity and damage using bio-fluids (Urine) on the platform of Metabonomics using NMR.

Rats were treated with various doses (100, 150 and 200 mg/kg body weight) of gentamicin through i.m. route for seven consecutive days. Urine was collected one day prior to the commencement of gentamicin treatment followed by daily collection during treatment till day 7 for routine, microscopic and for NMR spectroscopic analysis. On 8th day, these rats were sacrificed and observations were made followed with the collection of blood sample for renal function tests. Kidneys were also collected for gross examination and histopathology. The results revealed that only at 150 & 200 mg/kg dose levels, gentamicin affected more to the proximal tubule than glomerulai.







1. ***High Magnification of same Photomicrograph showing Glomerulai and tubules. (H&E 400X)***
2. **PCT showing Hydropic Changes (Vacuolation, 'H'). (HD. Gp. Rat # 3; H&E 400X)**
3. **Stack Plot of a High Dose Group rat from day '0' to day '7'.**
4. ***Principal Component Analysis (PCA) of the spectra***

1.4.3.3 SNP analysis in squamous cell carcinoma of head neck and breast cancer

SNPs are considered to be the best genetic markers inhabiting the genome due to their wide

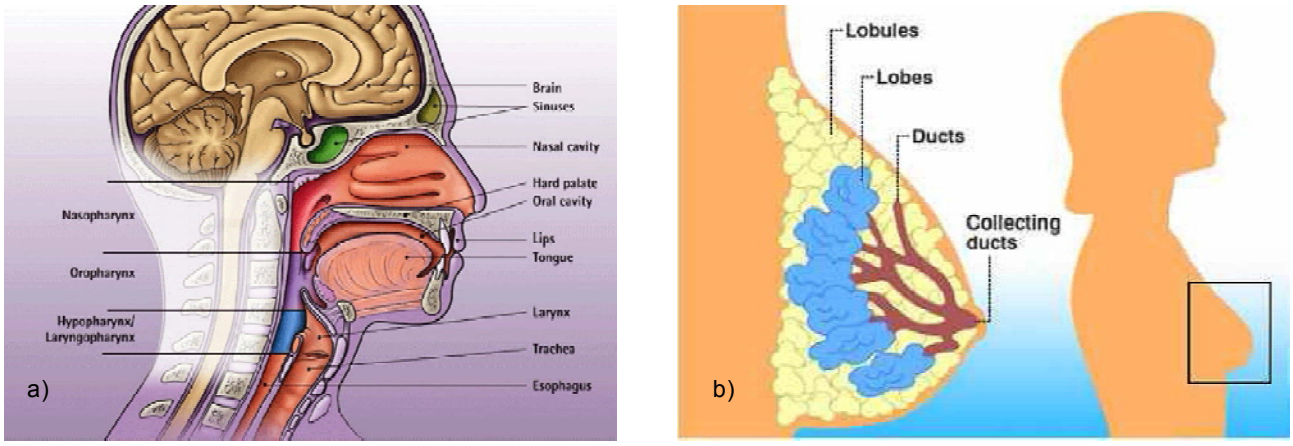
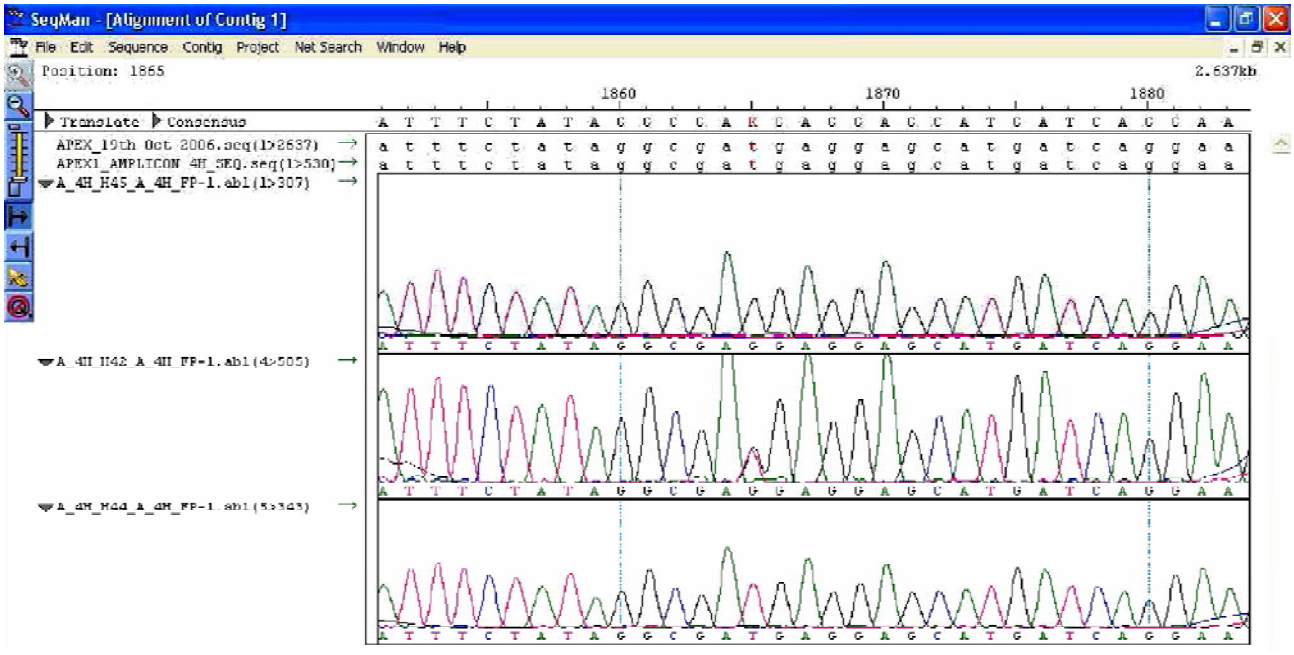
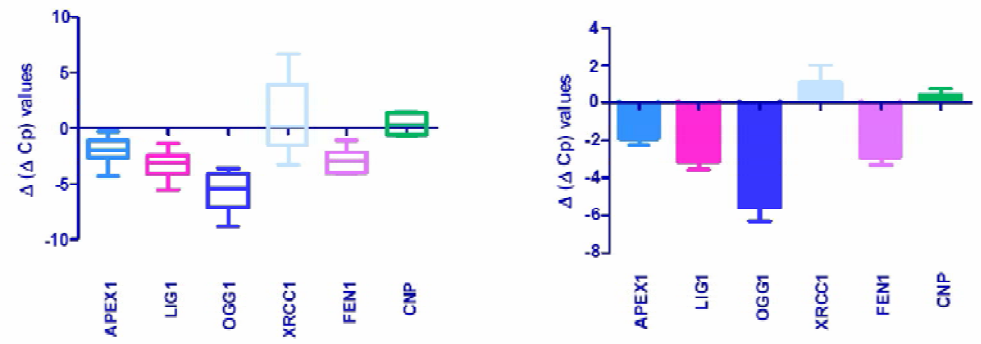


Fig: a- Representative regions of squamous cell carcinoma of head and neck; b- Breast cancer



Gene expression analysis in SCCHN cases and controls using quantitative RT-PCR



Box plot and Histogram representing relative gene expression levels of the genes selected for study among SCCHN cases compared to normal healthy controls, inferred on the basis of corresponding ΔΔCp values

ΔΔCp>0 denotes over expression, while ΔΔCp=0 demonstrates decrease in gene expression among SCCHN cases compared to controls

prevalence, easier automation for scoring, highly polymorphic & biallelic nature, co-dominance, easy reproducibility and their presence in both exonic as well as intronic regions of genes. SNPs are primarily responsible for differences between individuals that may serve as causative variations for simple and complex genetic diseases or can be indirectly associated to a diseased state by serving as linked markers for localizing a disease on the human genome map. Genotoxicity lab is primarily involved in identifying and analyzing such genetic variation in DNA repair genes with respect to Squamous cell carcinoma of head neck (SCCHN) and breast cancer.

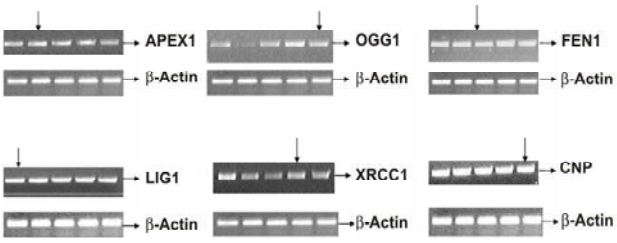
Mutations in DNA repair genes in form of single nucleotide polymorphism are suggestive to involve in reduced repair capacity and aberrant gene function leaving genomic instability and resulting in complex disease such as cancer. Number of studies reported from different world populations suggesting different level of risk with cancer. Different non synonymous polymorphism from different genes of DNA repair pathway have been selected and studied using polymerase chain reaction - restriction fragment length polymorphism (PCR-RFLP) and DNA sequencing analysis. Gene expression analysis of DNA repair genes in cases and controls were also performed to observe differential expression of genes. Genes involved in human DNA repair (APEX1, FEN1, LIG1, XRCC1, hOGG1, ERCC2 and CNP) were selected for the study mainly on the basis of their relevance as functional candidates in many cancers.

Statistically significant association for homozygous mutant (CC), and heterozygous (AC) of SNP (rs13181) in ERCC2 gene was observed. Conversely, significant protective association with SCCHN risk was observed among homozygous mutant (GG) of the SNP (rs1130409) in APEX1, heterozygous (CA), homozygous mutant (AA) of SNP (rs20580) in LIG1, heterozygous (CG), homozygous (GG) of SNP (rs1052133) of OGG1 gene, (AA), heterozygous (GA) of SNP (rs25487) of XRCC1 gene and homozygous mutant (TT) and heterozygous (CT) of SNP (rs1799782) in the XRCC1 gene. No association was observed for the mutant genotypes of the polymorphism of SNP (rs2070106) of CNP gene. Sequence analysis and SNP detection was done by using Seqman module of Lasergene v6.0 (DNA STAR).

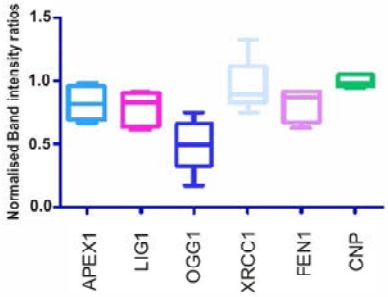
Similarly **s**tatistically significant association were observed between homozygous mutant (GG) and heterozygous TG for SNP (rs1130409) in APEX1gene, homozygous mutant (CC), heterozygous (AC) of SNP (rs13181) in ERCC2 gene and homozygous mutant (AA) of SNP (rs25487) in XRCC1 gene. On the contrary, protective association was exhibited by homozygous mutant (TT), heterozygous (CT) of SNP (rs1799782) of XRCC1 gene and homozygous mutant (AA), heterozygous (CA) SNP (rs20580) of LIG1 gene. No association was observed between rs4989588 (FEN1) genotypes with breast cancer risk.The polymorphisms rs4989586/G3259A (FEN1) and rs4989587/C3315T (FEN1) were not found in any of the breast cancer or control subjects.

1.4.3.4 Gene expression analysis

Consistent down regulation of gene expression profiles of the genes APEX1, FEN1, LIG1 and OGG1 between SCCHN cases and controls. The gene XRCC1 showed upregulation although there was a huge inter-sample difference in gene expression values which may be a consequence of the fact that functional studies conducted so far on XRCC1 have suggested that the rs25487 and rs1799782 variant alleles are associated with contrasting roles.



Control samples in each gel are represented with an downward arrow (↓) sign while rest are all SCCHN cases



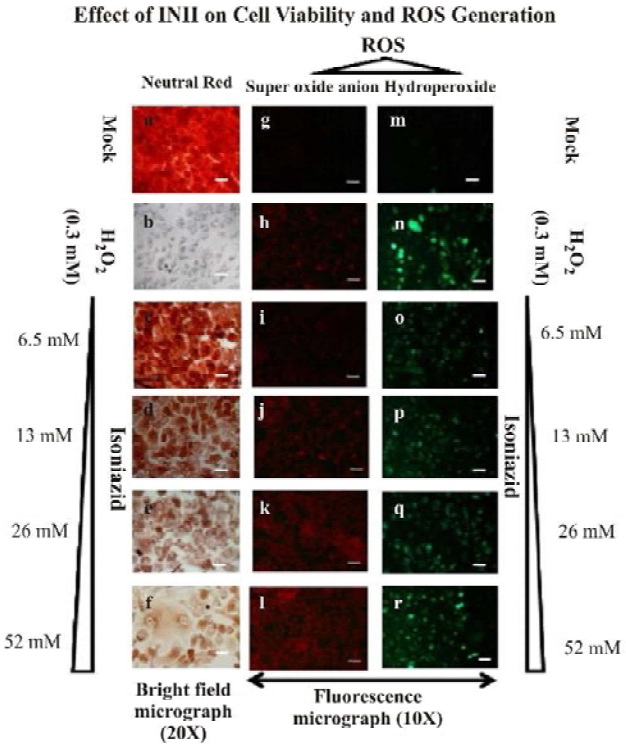
Box plot depicting relative expression of selected DNA repair genes in SCCHN cases compared to controls obtained using semi-quantitative RT-PCR and represented in terms of normalised relative band intensity values

Gene expression analysis in SCCHN cases and controls using semi-quantitative RT-PCR

1.4.3.5 *In vitro* hepatotoxicity, with special emphasis on mechanism of INH induced toxicity

Isoniazid is a first-line antibiotic used in the treatment of infections caused by *Mycobacterium tuberculosis*. However, it has a serious limitation of being hepatotoxic. The study was aimed at identifying the key components/pathways of the INH induced apoptotic pathway using Hep G2 cells. The findings indicate that

INH exposure causes increased ROS generation along with alteration in levels of enzymatic antioxidants such as superoxide dismutase, catalase and glucose-6-phosphate dehydrogenase. Altered Bcl-2/Bax content cytochrome-c translocation, caspase activation and DNA fragmentation emphasized involvement of apoptosis. This model can be used for screening of hepatotoxicants and studying their mechanism of action.



1.5 Clinical & Experimental Medicine

1.5.1 Compound 99-373 (Anti-osteoporotic)

- Plan and protocol for phase I clinical trials are cleared by IEC, PGIMER, Chandigarh.
- Investigators' brochure prepared.

1.5.2 Herbal Medicament (Anti-stroke)

Preclinical data is being compiled by Themis Medicare Ltd. for IND application.

1.5.3 Picroliv (Hepatoprotective)

- Phase III clinical trial in patients of tuberculosis on multi drug therapy have been completed at CSM Medical University, Lucknow and Seth G.S. Medical College, Mumbai.
- Data is being compiled for statistical analysis.

1.5.4 Compound 97-78 (Antimalarial)

- New Phase I clinical trial facility (CP Unit) inaugurated by DG, CSIR in July, 2009 at PGI, Chandigarh.
- Single dose tolerance study completed in 50 healthy male volunteers.

1.5.5 Compound 99-411 (Antimalarial)

- Preclinical data sent to Ipca Lab. Ltd.
- Investigational New Drug application is being submitted in collaboration with Ipca Lab. Ltd., Mumbai.

1.5.6 Arteether (Antimalarial)

A presentation on clinical trials with Arteether in children suffering from *P. falciparum* malaria was made at Drugs Controller General (India) Office. Queries received from DCG (I) Office. The respective participating centers being contacted for formulating the reply.

1.5.7 CDR 134D123 (Antidiabetic)

The Phase-I multiple dose clinical trial completed in 36 diabetic subjects. Data has been compiled and submitted to Department of AYUSH for marketing permission.

1.5.8 CDR 134F194 (Antidiabetic)

The requisite additional data, investigator's brochure and their consent has been submitted to IND Expert Committee of DCG (I) for obtaining permission to initiate phase I clinical trials. The approval from DCG (I) is awaited.

1.5.9 Compound 80-574 (Hypolipidemic)

Cadila Pharma, Ahmedabad has prepared and sent a dossier for submitting to DCG (I) for extended Phase-III clinical trial of the combination of 80-574 and Atorvastatin. The Dossier with comments has been sent to Cadila Pharma.

1.5.10 CU 001 (Puffer Fish Oil) (Hypolipidemic)

The answers to DCG (I) IND Expert Committee queries are being prepared along with data generated at Calcutta University, Kolkata.

2. Cancer and Related Areas

Coordinator:
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Assistant Coordinator:
Dr. D.P. Mishra

Area Leader:
Dr. Rakesh Maurya

The objectives of this project area include:

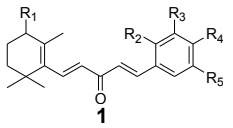
- Design, synthesis and evaluation of new chemical entities for anticancer activities using different cancer cell types on high throughput screening platform.
- To elucidate mechanism of action of known and generated lead molecules by molecular and cell biology approaches.
- To develop nude and SCID mice models to evaluate efficacy of these compounds *in vivo*.

2.1 Screening of Compounds

The screening was performed using human tumour cell lines (procured from American Type Culture Collection) for oral, lung, breast and cervical cancers. A non tumorogenic mouse embryo fibroblast, NIH3T3, is included in cell line panel to see selective activity of test samples towards cancer cells. Standard cell viability based protocol and sulforhodamine B assay, recommended by National Cancer Institute is being followed. The screening is a two stage process, beginning with the evaluation of all samples at a single dose of 50 μg/ml. Samples showing >"80% growth inhibition were considered as "hits". One hundred ten marine extracts and 256 synthetic molecules were tested for anticancer activity. Out of 366 samples, 124 hits were identified and tested further at serial dilutions to determine IC_{50} values. None of the 124 hits showed selective activity.

2.1.1 Chemical scaffolds under Investigation

During the period under report, chemical scaffolds 1-3 were selected for lead optimization and SAR studies. These scaffolds are inspired either from natural products with promising anticancer activity or from screening of in-house synthetic compounds. During this period a chemical library of chalcones exemplified by **1** was synthesized and screened for anticancer activity in the cancer cell lines PA1, MCF-7, KB, C33A, and VERO. Compounds S-007-533, S-007-540, S-007-541 have



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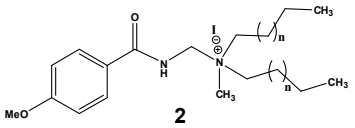

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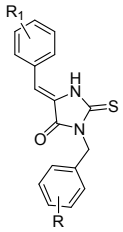
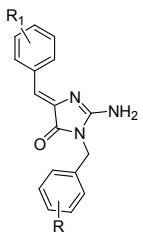


3A



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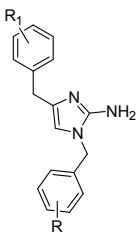


3C

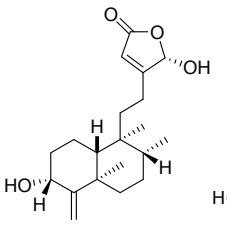
shown good anticancer profile with IC_{50} values in the range of 1-2 μM. One of the compounds S-007-541 was synthesized on gram scale and is being followed-up.

Marine sponges are still the main source of bioactive natural products. Complex natural products isolated from marine sponges have been the basis for many clinical leads. Isonaamine C, a 2-aminoimidazole alkaloid, was isolated from marine sponge *Leucetta chagosensis* collected from Australian Bougainville Reef. Only biological activity known for this alkaloid is it's cytotoxicity against HM02, HepG2, Huh7 tumour cell lines with GI_{50} values of 5.3, 2.2 and 2.1 μg/mL, respectively. Inspired by these findings, during this period, 60 analogues of Isonaamine C were synthesized and evaluated for anticancer activity against KB (oral squamous cell

carcinoma), MCF-7 (breast cancer), A549 (lung carcinoma), C33A (cervical carcinoma). Compound S-009-837 was found to be most active against all the tested cancer cell lines. This compound also showed lowest IC_{50} value of 3.33 μg/ml against KB cells followed by C33A (4.73 μg/ml), A549 (7.61 μg/ml), and MCF-7 (10.27 μg/ml), respectively. It was also found to be 5.18 times more selective towards KB cells in comparison to that of NIH3T3 mouse embryonic fibroblast cells. Selectivity against all other cell lines was in the range of 3.6 – 1.7. Compound (S-009-843**)** was cytotoxic against C33A cells with IC_{50} 8.85 μg/ml and was 4.98 times more selective in comparison to NIH3T3 cells. S-methyl derivatives of the thiohydantoins (S-009-856 to S-009-865) were also screened for cytotoxicity but were found to be inactive.

Ten novel benzocoumarin Schiff's bases were synthesized and screened for anticancer activity against MCF-7 cell lines. Compounds S-006-1555, S-006-1558 and S-006-1559 showed IC_{50} value 3.8- 7.9 μM which is lower than Tamoxifen (11.8 μM). These compounds induced cell cycle arrest at G0/G1 phase, nuclear DNA fragmentation and enhanced annexin binding suggestive of apoptosis through caspase-3 activation. Based on this data, thirteen compounds of the same series (S-009-1381 to S-009-1393) were synthesized and submitted for anticancer screening. Twenty coumarin-chalcone derivatives were synthesized and screened for anticancer activity against four cancer cell lines. Three compounds S-009-0131 to S-009- 0133 were found to be active especially against cervical carcinoma (C33A) cell lines (IC_{50} value 1.5- 3.28 μg/ml).

Two new clerodane diterpens and cycloortane triterpene were isolated from *P. longifolia* var. *pendula* **[*Natural Product Research*, (*DOI: 10.1080/10236240902765301*)]**. These compounds have shown promising anticancer activity in a variety of cell lines. Compounds **4** and **5** exhibited activity against oral (IC_{50} 29.7, 23.0 μg /ml), cervical ((IC_{50} 14.3, 10.4 μg /ml), ovarian (IC_{50} 13.4, 11.8 μg/ml), and breast cancer (IC_{50} 28.0, 24.0 μg/ml) cell lines respectively. A new labdane diterpene **6,** 13-*epi-sclareol* has been isolated from plant *Coleus forskohlii*. This compound showed antiproliferative activity in breast and uterine cancers *in vitro* and it also exhibited concentration dependent increased apoptotic changes in the breast cancer (MCF-7) cell line.



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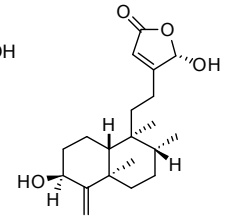

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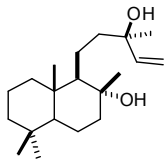


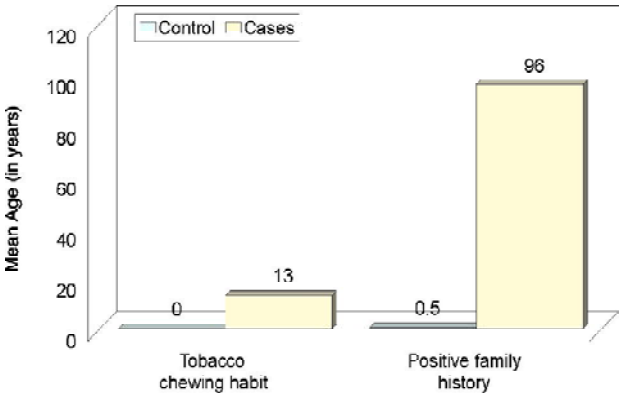
6

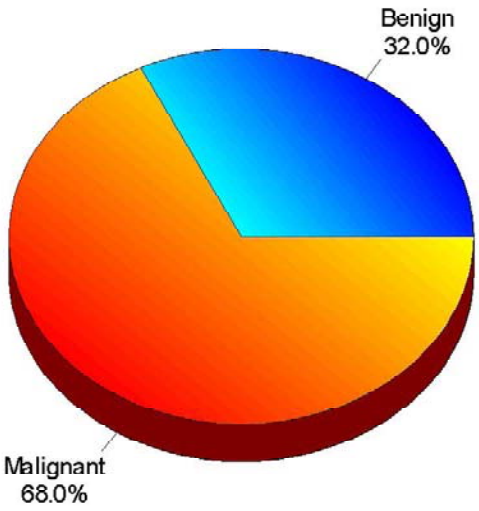
Earlier, two plant extracts (4499 and 4655) had shown anticancer activity. As a follow up study on the isolated active compounds, analogs of K029 were prepared and studied for anticancer activity. One of the compounds (K029 D9) showed significant *in vitro* activity and *in vivo* studies in progress.

2.2 Basic Research in Cancer Biology

2.2.1 Cytokine gene polymorphism in breast cancer

Interleukins and cytokines are important regulator of the aetio-pathogenesis of the majority of cancers. Mechanistic role of IL-1RN and IL-4, particularly in breast





Distribution of subjects in the study

carcinogenesis, is well documented. However, the role of polymorphisms of IL-1RN and IL-4 combinations associated with risk of breast cancer is not reported. The IL-1RN and IL-4 gene polymorphisms were genotyped with VNTR-PCR in 100 patients (benign tumour *n*=32 and breast cancer *n*=68) and 200 normal healthy control subjects with normal mammogram. Genotype distribution and allelic frequencies between patients and controls were compared and odds ratios (OR) with 95% confidence intervals (CI) were calculated using SPSS software (version 12.0). There were no significant differences in the genotype distributions of both IL-1RN and IL-4 polymorphisms between cases and controls.

Similarly, sub-group analysis showed that there is no significant association for pre- and post-menopausal women. However, BB genotype of IL-1RN is significantly differs among benign and malignant stages of breast cancer. IL-1RN and IL-4 polymorphisms, alone or in combination, are not associated with risk of breast cancer in Indian patients. The association of IL-1RN with malignant stages may indicate its possible role in progression of breast cancer. Further studies in other population are in progress to confirm our findings and to elucidate the role of IL-1RN in progression of breast cancer.

2.2.2 Dissection of molecular mechanism of GPS2 mediated growth arrest and A20 mediated drug resistance in breast cancer

G Protein Pathway Suppressor 2 (GPS2) is an enigmatic protein that has been initially identified as a suppressor of yeast pheromone response when expressed ectopically. Further, GPS2 has been known to be a coactivator for tumour suppressor protein p53 and is known to cause growth arrest in breast cancer cells via induction of p21 tumour suppressor protein. GPS2, has been identified as an interacting protein for oestrogen receptor (ER) and the bile acid receptor FXR. The role of ER in breast cancer is well known and FXR has recently been found to play multiple roles in breast cancer progression and survival. Role of GPS2 in breast cancer and its molecular mechanism of action in respect to ER and FXR is being investigated. In this context, tetracycline inducible stable MCF-7 cell over-expressing GPS2 have been constructed and are currently being investigated for the role of GPS2 in these cells.

A20/TNFAIP3 is a TNF alpha inducible protein, if ectopically expressed, can render breast cancer cells drug resistant. Therefore, information about the detailed regulation of this gene can give invaluable insight into drug resistance of breast cancer. This protein has been found to be up-regulated by oestrogen receptor related receptor alpha and are dissecting the molecular mechanism of its regulation. Since this gene is regulated by inflammatory responses, it is imperative to study its regulations under non-stress conditions. Therefore, construction of adeno associated virus expression cassettes have been undertaken.

2.2.3 Studies on pro-apoptotic effect of staurosporine on oral cancer cell line

Staurosporine (STS), a protein kinase inhibitor from *Streptomyces sp.* was evaluated to induce apoptosis in human papillomavirus positive oral carcinoma cells (KB). Growth inhibition studies revealed an IC_{50} value of approximately 100 nM. STS induced marked nuclear fragmentation and inter-nucleosomal cleavage, compared to untreated cells. It also caused dose dependent disruption of mitochondrial membrane potential and activation of caspase-3, indicating involvement of mitochondria mediated cell death signaling in KB cell apoptosis. Results revealed time-dependent arrest of the KB cells at G2/M phase of cell cycle (Figure-1). Using fluorescence microscopy, it was demonstrated that STS treatment disrupts microtubules and reorganizes F-actin after 6 h exposure. Taken together, the results suggest that STS induces mitochondria-mediated KB cell apoptosis at G2/M phase by altering cell cytoskeletal network.

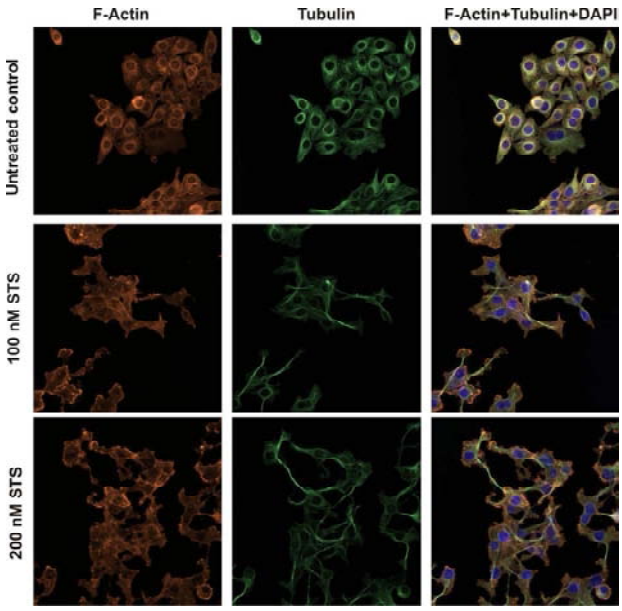


Figure-1

2.2.4 Studies on the effects of ormeloxifene on squamous cell carcinoma of the head and neck

Squamous cell carcinoma of the head and neck (SCCHN) is a leading cause of cancer deaths world wide. In SCCHN conditions, there is a persistent over expression of a critical transcription factor i.e. signal transducer and activator of transcri-ption(STAT)-3.Therefore, the targeted disruption of the constitutive (STAT)-3 activation in SCCHN could possibly serve as a therapeutic target. Therefore, using SCC HN cell lines (HN5 and HN6), a selective estrogen receptor modulator Ormeloxifene has been shown to inhibit (STAT)-3 phosphorylation while DNA binding activity down regulates anti-apoptotic protein expression, induces caspase activation resulting in apoptosis. In related studies, SCCHN cells treated with a specific epidermal growth factor receptor (EGFR) inhibitor along with Ormeloxifene further reduced (STAT)-3 phosphorylation and enhanced the apoptotic effect. However, combination studies with the other mitogen activated protein/extracellular signal regulate kinase (MEK1/2) inhibitors or the Janus kinase (JAK)-1 and JAK2 inhibitors had no significant effect on the (STAT)-3 phosphorylation status in SCCHN cells. These results suggest that the combination therapy of a SERM (ormeloxifene) along with an EGFR inhibitor could possibly serve as a useful therapeutic intervention in SCCHN.

2.2.5 Resveratrol regulation of antiproliferative activity of Centchroman vis-à-vis CYP 1B1 in MCF-7 human breast cancer cells

CYP 1B1 is reportedly implicated in the progression of breast cancer in various ways. Therefore, the present study was undertaken to enunciate the role of Resveratrol (RES), a phytoestrogen, in ameliorating the antineoplastic activity of Centchroman (CC) using MCF-7 Human Breast Cancer Cells (HBCCs) in relation to CYP 1B1. The role of RES (1-200 μM) and CC (1-25 μM) added separately and together in the MCF-7 cell culture was investigated. CC & RES separately were found to exhibit the IC_{50} of 10 & 100 μM respectively. When added together, the IC_{50} was found to be 38.0 μM. Keeping the concentration of CC at 1, 5, 10, 15 & 20 μM respectively, the dose of RES was varied from 10,25,50,75,100 & 150 μM. It was found that RES at 100 μM enhances the cytotoxic efficacy of CC at 10 μM. However, the preliminary results also indicate that RES at lower doses (10 μM) in combination with CC (10 μM) evinced slight up-regulation of cytotoxicity.

2.2.6 Understanding induced apoptotic and differentiation pathways in myeloid Leukaemia (Mol. Cell Biochem., October 23, 2009 [E-pub ahead of print])

In-house and commercially available cytostatic compounds, based on their stability and solubility were selected for screening their potential to induce differentiation and apoptosis in myeloid leukemia cell (U937, HL60 and K562). In preliminary screening, one "Hit", which seems to induce differentiation and apoptosis in these AML cells, was observed. Further, to characterize the mechanism of differentiation and apoptosis elicited by the hit molecule using various biochemical and cell biology techniques is under investigation. These assays are assessment of differentiation markers CD11b, CD14, GCSFR, CD61 and C/EBPalpha by FACS flow cytometer and at mRNA (quantitative real time PCR) and protein (western blotting) levels.

2.2.7 Ectopic expression of C/EBPs

CCAAT Enhancer Binding Proteins (C/EBPs) are well known to induce apoptosis and growth arrest in various cell types due to their tumor suppressor activity. Based on this, role of ectopically expressed C/EBPs in MCF7 and MDA-MB231 cells was assessed and the data indicates that C/EBPs indeed induce apoptosis and growth arrest in breast cancer cells. The induced apoptosis in these cells is associated with caspase mediation. Among C/EBPs, C/EBPalpha is the prominent isoform and that it induced apoptosis and growth arrest in a dose dependent manner.

2.2.8 Role of oestrogen(s) induced oxidative stress in breast carcinogenesis

The present work was undertaken to delineate underlying molecular mechanism/pathways through which oestrogen(s) induced oxidative stress causes initiation and progression of breast cancer. Further, to target these pathways using specific inhibitors/blockers for preventing breast carcinogenesis. The information, so obtained, will provide lead information for cure of breast cancer.

2.2.9 Development of fission yeast as model system for identifying drug target

The fission yeast *S. pombe* is a good model system for the studies of the cell cycle events. Most of the yeast proteins, which are involved in basic cellular processes are conserved between yeast and human.

Hence target identification in yeast can be relevant for cancer, which at the simplest level is a disorder of proliferation or checkpoint control due to the accumulation of mutations. Drug compound, which can cause in viability in conjunction with those checkpoint mutants that are already known to exist in different kinds of cancers, can be a potential anticancer drug. Decreased expression of the human gene *MAD2L1* has been reported in a breast cancer cell line exhibiting chromosome instability and aneuploidy. Mad2, a spindle checkpoint protein has also been found mutated in some bladder cancer cells. Using genetics approaches, attempts are being made to identify extragenic mutations that can nullify the effect of null or truncated *mad2* gene product and hence could serve as a good drug target for anticancer drug. To perform the screen, mad2 gene has been cloned in the suitable vector to identify its extrageneic suppressors. Furthermore, experiments related to identification of some other orthologs such as hypoxia induced factor 2 (HIF2) in fission yeast that can also be used for genetic screen to identify its role in cell cycle regulation are in progress.

3. CVS, CNS and Related Disorders

Coordinator:
Dr. Madhu Dikshit

Assistant Coordinator:
Dr. K.V. Sashidhara

Area Leaders:
Dr. Ram Raghubir
Dr. Gautam Palit

The research activities in this research area include:

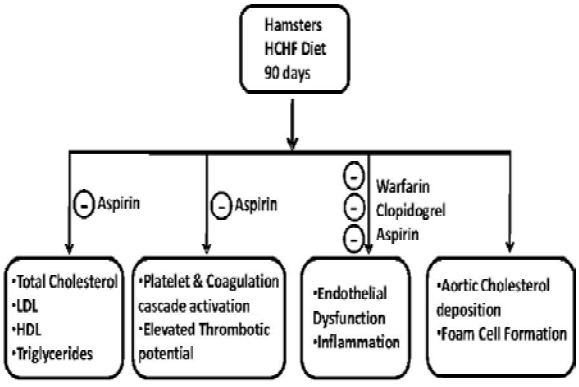
- Design, synthesis and development of new drugs from synthetic compounds, plant and marine extracts or fractions to treat pathologies of: **cardiovascular system** *(hypertension, dyslipidemia, atherosclerosis, thrombosis* and *myocardial infarction)*; **central nervous system** *(anxiety, depression, psychosis, dementia* and *stroke)* and **other related disorders** *(stress, gastric ulcers* and *inflammation).*
- Development of suitable animal models and *in vitro* tests (isolated cells, cell lines and enzymes assays) to mimic the pathologies of CVS-CNS and related disorders. Researches to delineate the molecular mechanisms of these pathologies are being carried out so as to identify suitable targets for the new drug discovery, as well as to analyze the possible mechanism(s) of action of the candidate drugs.

3.1 Basic Studies

3.1.1 Cardiovascular System

3.1.1.1 Atherosclerosis, inflammation and athero-thrombotic events in hyperlipidemic hamsters

High cholesterol high fat (HCHF) fed golden Syrian Hamsters were susceptible to thrombosis due to endothelial dysfunction, activation of platelets, coagulation cascade and inflammation after 90 days of HCHF feeding. Reduction in acetylcholine induced relaxation (endothelial dysfunction) in HCHF group was significantly recovered after aspirin (30 μM/kg) clopidogrel (30, 100 μM/kg) or warfarin (0.1 mg/kg) treatment. Aspirin significantly reduced circulating lipid levels but warfarin and clopidogrel had no effect. Platelet (adhesion/ aggregation) and thrombin activation was normalized in aspirin or clopidogrel treated hamsters but not in warfarin treated group. Hamster is warfarin tolerant, hence no change was observed in the coagulation parameters (TT, aPTT and PT). mRNA expression of pro-inflammatory cytokines (TNF-α and IFN-γ) in the spleenocytes was significantly reduced ($p<0.05$), while iNOS and anti-inflammatory cytokines, IL-10 and TGF-β, were not altered on warfarin and clopidogrel treatment. Increase in TNF-α transcript on HCHF treatment was also significantly reduced on clopidogrel 100 μM ($p<0.05$) pretreatment. Aspirin however prevented increase in all the inflammatory cytokines.

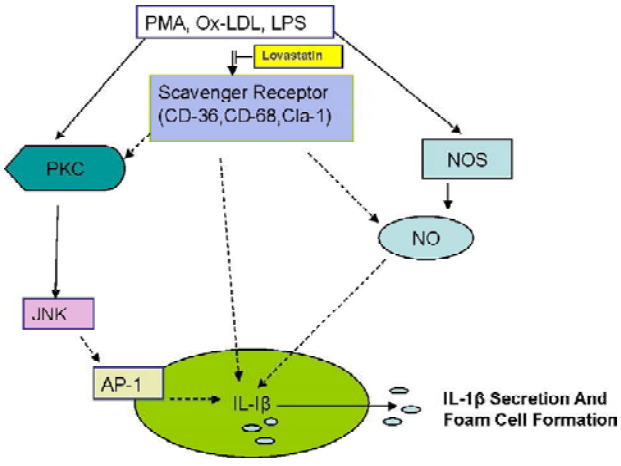


Effect of anti-thromotic drugs in hamsters

Studies conducted in this model indicate that protective effect of warfarin was independent of its anti-coagulant effect, while aspirin and clopidogrel exerted anti-atherothrombotic effect by preventing platelet activation, inflammation, endothelial dysfunction and thrombin generation.

3.1.1.2 PMA and Ox-LDL induced IL-1β secretion - exploration of mechanism involved

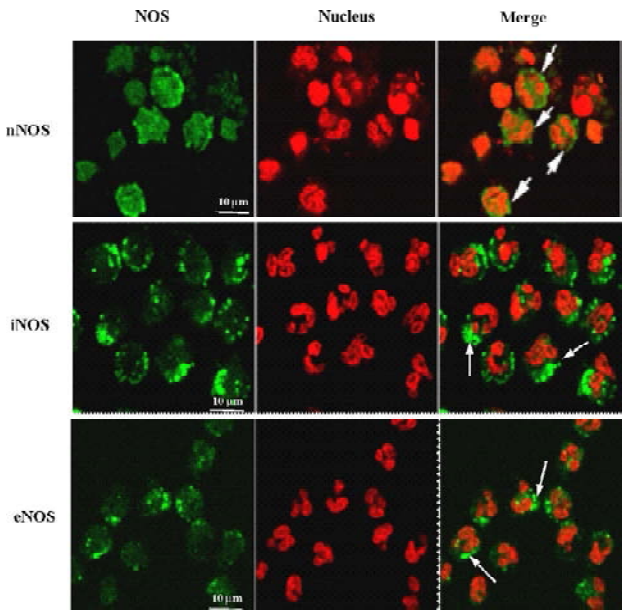
Atherosclerosis involves series of events that are accompanied with hyperlipidemia and inflammation. Ox-LDL induces inflammatory response during atherosclerosis progression and IL-1β is one of the important pro-atherogenic cytokines involved in such a phenomenon. Studies have therefore been initiated to explore the mechanisms involved. A time dependent increase in IL-1β secretion was observed in PMA or Ox-LDL treated human monocytic THP-1 cells. An increase in scavenger receptor expression on PMA or OX-LDL treatment was also observed, which was prevented by Lovastatin. Up-regulation of NOS/NO synthesis was also found after LPS treatment. Expression of TLR-2 and CD-36 was increased after Ox-LDL treatment. Pretreatment with inhibitors of JNK, PKC-δ, Src-kinase or IL-1receptor antagonist, significantly reduced Ox-LDL induced IL-1β secretion. Pretreatment with p38MAPK inhibitor or PI3K inhibitor had no significant effect on Ox-LDL induced IL-1β secretion. Although Ox-LDL augmented AP-1 and NF-kB activity, both small molecule and peptide inhibitor of NF-kB failed to prevent Ox-LDL induced IL-1β secretion, indicating role of NF-kB independent pathway. Since Ox-LDL induced JNK phosphorylation was inhibited by rottlerin, a PKC-δ inhibitor, indicating its downstream position. Results obtained so far indicate that PKC-δ, JNK, Src kinases play an important role in IL-1β secretion.



Mechanisms involved in foam cell formation

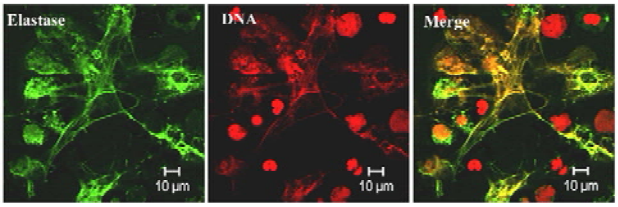
3.1.1.3 Studies on neutrophils/HL60 cell lines

(a) NOS expression, catalysis and localization in human neutrophils: NO modulates several important functions of neutrophils (PMNs). Previous studies have demonstrated regulation of NO dependent neutrophil free radical generation and presence of NOS isoforms (nNOS and iNOS) and its interacting protein in rat neutrophils, however NOS distribution, expression and biochemical characterization remains least defined in human PMNs. Studies were undertaken to explore status of NOS in human PMNs. Real time PCR demonstrated high copy number of nNOS than iNOS. nNOS possessed PDZ domain and was catalytically active, vinyl-L-NIO (nNOS inhibitor), significantly reduced NO generation as compared to 1400W (iNOS inhibitor) , which correlated with higher nNOS expression in PMNs. eNOS protein was very less, while we failed to detect the eNOS mRNA signal in PMNs. Immunocytochemical studies exhibited distribution of nNOS, eNOS and iNOS in cytoplasm and nucleus. In human PMNs nNOS, thus seems to contribute to calcium dependent activity and most of the NO generation.



Localization of NOS isoforms in PMNs

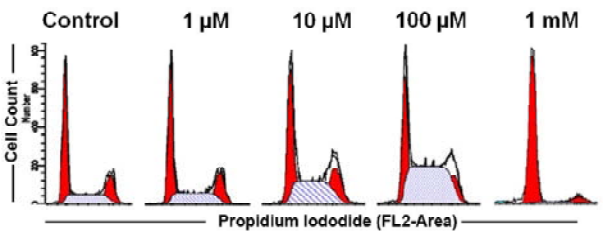
(b) Role of p38 MAPK in PMA induced neutrophil extracellular traps (NETs) release: Neutrophils, release NETs to bind and kill the extracellular microorganisms. Studies have identified NO as a new mediator of NETs release. Role of signaling molecules/proteins, involved in PMA induced reactive oxygen species (ROS) generation and NETs formation have therefore been initiated. PMA



PMA induced NETs release

induced the protein tyrosine phosphorylation and phosphorylation of p38 MAPK and ERK1/2 in PMNs in a time and concentration dependent manner. Pre-treatment of PMNs with SB202190 did not significantly reduce PMA induced free radical generation, but prevented the formation of NETs. Pre-treatment of PMNs with DPI completely blocked the p38 MAPK phosphorylation, free radical generation and NETs release, suggesting that p38 MAPK activation is downstream to the free radical generation. Delineation of the molecular mechanisms involved in NETs release by PMA and NO is in progress.

(c) Nitric oxide dependent biphasic effect on HL-60 cell cycle [Free Rad. Biol. Med., in press, 2010]: Effect of NO was explored on promyelocytic HL-60 cell proliferation and apoptosis. NO donor (DETA-NO) modulated HL-60 cell cycle in a biphasic manner. DETA-NO at lower concentrations (1-100 µM) had proliferative effect as investigated by ^{3}H-thymidine incorporation, BrdU labelling and cell cycle analysis, while cells treated with higher concentrations (250 µM-1mM) showed apoptosis, mitochondrial membrane potential loss, enhanced caspase-3 activity and dUTP nick end labeling. The proliferative effect of DETA-NO was NO dependent and redox sensitive as the effect was abolished by cPTIO and DTT pre-treatment respectively. Expression of various cell cycle regulators such as Cdk2, cyclin B, cyclin E expression was significantly augmented in cells treated with 10-50 µM DETA-NO. Proliferative effect of NO was blocked by roscovitine, a Cdk2 inhibitor. S-Nitrosylation of Cdk2 and an increase in the Cdk2 associated kinase activity was observed for the first time in DETA-NO treated cells. DETA-NO thus mediated biphasic effect on HL-60 cells which was dependent on Cdk2 nitrosylation/activation and loss of mitochondrial potential at low and high concentrations respectively.



Modulation of cell cycle by NO

3.1.1.4 Microbial heparinases to generate novel LMWHs

During this year, two isolates were processed for heparinase production in stirred tank bioreactor. The experimental results of CCD were analysed by second order polynomial regression for the estimation of linear, quadratic and interaction effects of the agitation and aeration for heparinase production. In the optimized production medium at optimized stirred tank fermentation conditions, the maximum specific heparinase production rate of the crude cell extract and volumetric heparinase productivity by *A. calcoaceticus* was found to be 278 U/g of cell/hour and 713 U/l/hour, respectively. Membrane entrapped heparinase from *A. calcoaceticus* was used for the generation of low molecular weight heparins (active oligosaccharides) by incomplete depolymerization (<30%) of heparin in a bubble column bioreactor for 24 hours. The different fractions of oligosaccharides were collected by size exclusion chromatography and were evaluated for uronic acid formation, aPTT, anti-Xa and anti-IIa activity.

3.1.2 Central Nervous System

3.1.2.1 Basic studies on learning and memory

(a) Cerebral circulation in dementia: Evidences suggest that AD and other types of dementia are associated with reduced cerebral blood flow (CBF) due to vascular amyloidosis, oxidative stress and endothelial dysfunction. Cerebral microcirculatory impairment might initiate pathophysiological changes that play a role in the progression of AD. It was found that intracerebral (IC) or intracerebro ventricular (ICV) administration of streptozotocin (STZ) reduced cerebral blood flow. Administration of curcumin and quercetin restored the cerebral blood flow and prevented the memory deficit.

(b) Role of renin-angiotensin system: Renin-angiotensin system, besides blood pressure regulation, affects learning and memory as evidenced by improvement of cognition in hypertensive patients being treated with angiotensin converting enzyme (ACE) inhibitors. The ongoing studies explored role of ACE in model of memory deficit induced by intracerebroventricular (ICV) STZ in rats. Results obtained indicate that ACE plays a facilitatory role in STZ induced memory deficit and ACE inhibition improved memory decline by scavenging free radicals and improving the cerebral blood flow and cholinergic system.

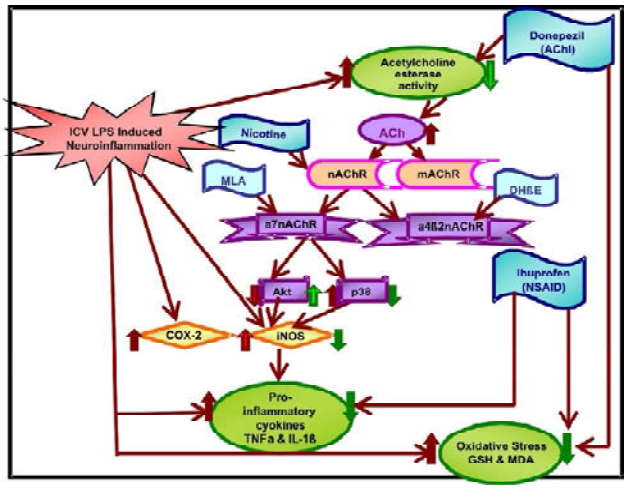
(c) Involvement of brain insulin receptor (IR): The IR protein expression in brain areas (hypothalamus, hippocampus, cerebral cortex and cerebellum) of adult

male and female rats (4-6 months) showed similar pattern, while in aged female rats (20-22 months), IR protein expression was 31% and 34% higher in hippocampus and cerebral cortex respectively and 27% lower in hypothalamus than that of aged male rats. The IR protein expression was decreased in hypothalamus, hippocampus and cerebral cortex of male (20–30%) rats and hypothalamus and cerebellum of female (20–45%) rats with aging. These observations might have relevance to possible linkage of brain IRs with gender and age related functions.

(d) IR signaling in rat hippocampus: IR gene expression in CA1, and CA3 sub-regions of hippocampus was up-regulated but not in DG in the trained rats (Morris water maze test). The significant increase in phosphorylation of Shc, Erk1/2, IRS-1 and Akt in CA1 and CA3 regions after training suggest that both IR/Shc/Erk and IR/IRS-1/Akt pathways might be involved in the regulation of memory functions. ICV administration of STZ (3 mg/kg) in rats showed memory deficit and significant decrease in IR gene and protein expressions only in CA3 region. Phosphorylation of IRS-1 and Akt was also reduced in CA3 region but Shc and Erk1/2 phosphorylation remains unaffected in STZ treated group. The STZ induced changes in IR signaling was reversed by pre and post-treatment of melatonin (20 mg/kg) but donepezil (5 mg/kg) was effective only against memory deficit. Thus the study indicates that only IR/IRS-1/Akt pathway in CA3 region is associated with STZ induced memory deficit, oxidative stress and IR signaling in hippocampus. Curcumin pretreatment prevented reduction in AChE, IR, oxidative stress and offered protection against STZ induced dementia.

(e) Cholinesterase inhibitors and neuronal apoptosis: An interrelationship between AChE and mitochondria in the neuronal apoptosis after STZ (ICV) administration was investigated. A significant increase in AChE activity, ROS generation and Ca^{++} influx was observed in the mitochondria isolated from brain, while apoptosis was confirmed by TUNEL and fluoro jade-C staining. Tacrine and donepezil (5 mg/kg) significantly attenuated the neurodegenerative effects of STZ but did not influence enhanced ROS generation and Ca^{++} influx. Tacrine and donepezil due to cholinesterase inhibition prevented ROS mediated elevation of intra-mitochondrial Ca^{++} and neuronal death. Melatonin (10 mg/kg), prevented STZ induced elevation of Ca^{++} and ROS in the mitochondria and neuronal apoptosis.

(f) Cholinergic regulation of neuroin-flammation: LPS induced neuroinflammation attenuated Akt phosphorylation. Treatment with nicotine or donepezil normalized the levels of phosphorylated Akt, suggesting the role of the PI3K-Akt signaling in the inhibitory effect of nicotine and donepezil. LPS induced augmentation in p38 MAPK phosphorylation, was however normalized only by nicotine and not by donepezil. Nicotine thus seems to regulate the neuroinflammatory cascade through diverse pathways.



Neuroinflammatory regulatory mechanisms

(g) Oxidative stress and neuroinflammation: MPTP induced neuroinflammation in rat astrocytoma cell line C6 augmented nitrite release, ROS formation, MDA levels, COX-2, IL1β, and TNF-α expression, reduced intracellular GSH, IL-1β and IL-6 expression, translocated NF-kB to the nucleus but had no effect on GFAP expression. Pretreatment of cells with melatonin modulated MPTP induced neuroinflammatory changes in astrocytoma cell line suggesting role of oxidative stress in neuro-inflammation.

3.1.2.2 Japanese Encephalitis virus (JEV) infection in rats: Altered monoamine and locomotor response [Brain Res. 2009, *1292*, 136-147]

12 Days old Wistar rats inoculated with an intracerebral dose of 3×10^6 pfu JE, virus exhibited significant reduction in spontaneous locomotor activity and grip strength. Norepinephrine, dopamine, 3,4-dihydroxyphenylacetic acid, homovanillic acid, and serotonin contents were also significantly reduced in the thalamus, midbrain, corpus striatum and frontal cortex as compared to control, suggesting the possible involvement of different brain regions in altered locomotor activity in the rats.

3.1.2.3 Cerebral stroke

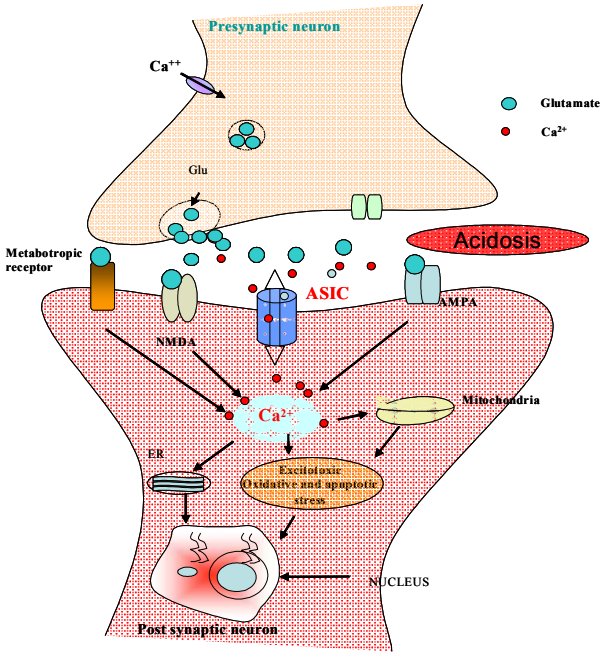
Studies have been undertaken to decipher the major pathways leading to neuronal death following cerebral stroke, a most common life threatening disorder.

Involvement of NMDA receptor, acid sensing ion channels, glutamate transporters, NADPH oxidase dependant oxidative stress and NFκB mediated inflammation are being analysed in the rat MCAO model of stroke.

(a) Glutamate transporter 1 (GLT-1): The modulation of GLT-1, a major glutamate transporter protein, offers neuroprotection in various models of ischemic injury. Therefore, an attempt was made to explore the effect of ceftriaxone, a GLT-1 modulator in cerebral ischemia/ reperfusion (I/R) injury. An increase in the expression and activity of GLT-1 following treatment with ceftriaxone was observed which led to significant protection against glutamatergic excitotoxicity.

(b) NADPH oxidase: Generation of reactive oxygen species (ROS) by NADPH oxidase contributes to the pathophysiology of cerebral ischemia. A biphasic increase in NADPH oxidase activity was observed. It increased immediately after MCAO in striatal and cortical regions and returned to the basal level, but it was again upregulated after 7 days of MCAO. The results obtained suggest that early rise in NADPH oxidase activity contributed to the oxidative stress, while later rise possibly triggered survival mechanisms, requiring further elucidation.

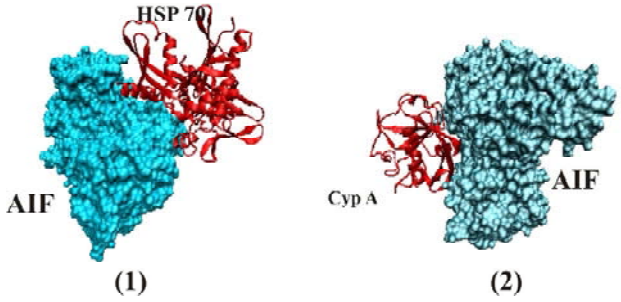
(c) ASIC in cerebral I/R injury: Calcium overload responsible for the neuronal death subsequent to cerebral stroke was considered to be mainly glutamate driven but recently acid sensing ion channels (ASIC's), activated following acidosis were also found to promote neuronal Ca^{++} influx. Treatment with flurbiprofen, an ASIC inhibitor, exhibited significant improvement in all neurological and biochemical parameters following MCAO and significantly inhibited calcium influx in the isolated rat brain synaptoneurosomes. Results obtained suggest that ASIC's has a prominent role in the pathology of cerebral stroke.



Mechanisms involved in neuronal injury

(d) NF-κB in pathophysiology of cerebral stroke in diabetic rats: NF-κB, a transcription factor, which is involved in the regulation of cell survival and inflammation, was explored for the possible involvement in ischemic injury in hyperglycaemic rats. These animals showed marked increase in neurological deficit and infarct size as compared to normoglycemic rats. Furthermore, increased phosphorylation of IκBα, an indirect measure of NF-κB activation, suggested that in hyperglycaemic rats MCAO led to the activation of NF-κB which could be detrimental in the exacerbation of cerebral infarct.

(e) Binding domains of AIF: Docking studies followed by co-immunoprecipitation assays, were performed to deduce interaction pattern of HSP70, PARP-1, cyclophilin A (cyp A) and calpain-1, the major regulator proteins of caspase independent apoptosis. Sequence data of these proteins were subjected to molecular docking using Hex 5.1 docking tool, applying only shape and shape/ electrostatic complementarities and were visualized by VMD, a molecular visualization tool. Considering both parameters i.e. shape and shape/electrostatic correlations, it was found that both HSP70 and cyp A exhibited strong binding affinity with AIF and their binding domains in AIF were different from each other. The binding pockets for HSP70 fall in the region between amino acids Ser266-Arg272 and Ser416-Ser501, while for cyp A it was located in Gln532 to Ser539 residues. On the other hand PARP-1 and calpain-1 demonstrated comparatively poor interaction with AIF. Results obtained demonstrate high affinity of AIF with cyp A and HSP70, which could be utilised to generate novel strategies to prevent uncontrolled apoptosis following cerebral ischemia.



AIF-interactions with HSP70 & CYP A

3.1.2.4 Studies on acute and chronic unpredictable stress models

(a) Role of dopamine and D1 receptors [Neurochem. Res., 2010, *35*, 22-32]: Acute stress (AS) significantly reduced dopamine (DA) levels in the striatum and hippocampus, while DA levels were significantly augmented in the frontal cortex. Chronic unpredictable stress (CUS), however, reduced DA level in these brain parts, providing insights into the differential regional response of dopaminergic system during AS and CUS. Involvement of D1 receptor was also examined by using A68930, a D1 selective agonist, which prevented reduction in DA following AS and CUS in most of these parts of the brain. Moreover, radio-ligand binding assays revealed a significant decrease in the number of D1-like receptors in the frontal cortex during CUS. A68930 pre-treatment prevented the increase in D1-like receptors, but failed to affect D2-like receptors in the striatum and hippocampus. Neurochemical and behavioural effects of D1 agonist thus helped to assess the modulatory role of D1 receptor under stressful episodes.

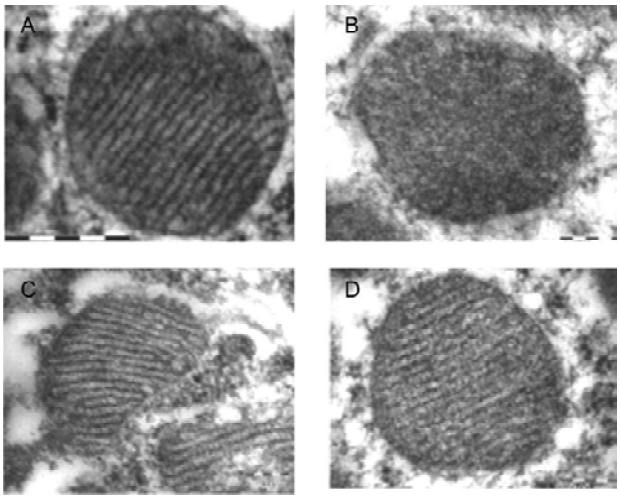
(b) Involvement of tyrosine hydroxylase, HSP-70 and glucocorticoid receptor expression: Modulatory effect of AS and CUS on the dopaminergic neurons fibre density and number of TH positive neurons were explored. CUS reduced the TH positive neurons in the striatum, medial forebrain bundle (MFB) and substantia nigra (SN) as compared to control, thus substantiating the reduction in dopamine levels following stress. HSP-70 expression was also significantly enhanced in all these brain regions following AS and CUS. Moreover, CUS caused a significant reduction in the expression of glucocorticoid receptor (GR) in the striatum, cortex and hippocampus with no change in amygdala suggesting a region specific response. Results obtained, so far, suggest that persistent increase in corticosterone during CUS led to GR down regulation.

3.1.3 Other Related Disorders

3.1.3.1 Basic studies of gastric ulcers

(a) Role of PPAR-γ in ulcer healing [Eur. J. Pharmacol. 2009, *609*,118-125]: Peroxisome proliferator-activated receptor-gamma (PPAR-γ) a member of the nuclear receptor super family, has gained importance as a potential therapeutic target in the management of gastrointestinal inflammation. Pioglitazone suppressed the expression of inflammatory mediators like, TNF-α and IL-1β during chronic gastric ulcer healing leading to the repression of NF-κB transcriptional activity. This might be mediated through the combined upregulation and interaction of PPAR-γ and glucocorticoid receptor resulting in amelioration of gastric ulcer. Thus, PPAR-γ along with the co-operation of glucocorticoid receptor might repress overlapping distinct subsets of inflammatory response genes during chronic gastric ulcer healing. Results obtained implicate both PPAR-γ and glucocorticoid receptor in the amelioration of inflammatory responses in pioglitazone mediated gastric ulcer healing.

(b) Role of mitochondria in indomethacin-induced gastropathy [J Biol Chem. 2009, *284*, 3058-3068]: Indomethacin treatment led to structural distortion of mitochondria in the rat stomach, parts of mitochondrial outer membrane were disintegrated, mitochondria in the moderately ulcerated stomach (ulcer index (UI) 25-35) showed more disintegration of cristae and in the outer membrane, while in severely ulcerated stomach (UI= 100 nm) complete disintegration of cristae was observed (bar = 200 nm). DMSO and PBN (ROS scavengers bar = 100 nm) restored indomethacin-induced alterations in the mitochondrial ultrastructure (control bar = 200 nm).



A: Control, B: Indomethacin (UI 40-55) C/D: DMSO/PBN + indomethacin (UI 7-12)

(c) Melatonin and experimental reflux oesophagitis [J. Pineal Res. 2009, *46*, 207-213]: Melatonin offered protection against experimental reflux esophagitis (RE) by scavenging the free radicals and subsequently improving the antioxidant status of esophageal mucosa. In addition, melatonin displayed significant anti-inflammatory activity as evident by suppressed Th1-mediated immune responses in melatonin treated animals. The antioxidant and anti-inflammatory functions of melatonin appeared to be receptor independent as melatonin receptor antagonist, luzindole failed to prevent RE induced esophageal injury.

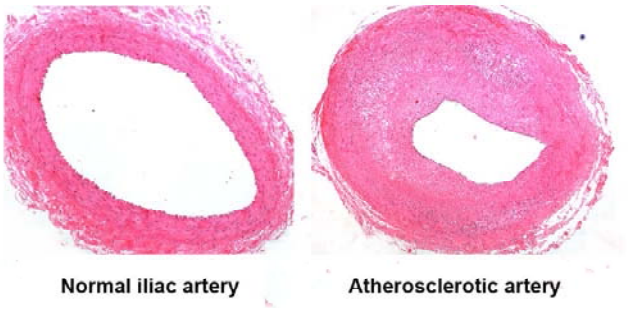
3.2 Experimental Models of CVS-CNS Disorders

During the reporting period, new/well accepted models have been selected for the standardization/ translation in the labs. These animal models shall be used for secondary or tertiary screening to delineate the efficacy of active molecules under development mode, while *C. elegans* could be very useful for primary screening to test the new molecules.

3.2.1 Cardiovascular System *(Myocardial Infarction* and *Atherosclerosis)*

(a) MI/RP in hypertriglyceridemic rats: Insulin resistance (IR), a well-known risk factor for cardiovascular disease was developed in Wistar rats by feeding fructose enriched diet for 12 weeks. Fructose diet induced hypertriglyceridemia, hyperinsulinemia, insulin sensitivity (reflected by high homeostasis model assessment and low quantitative insulin-sensitivity check index), oxidative stress and inflammation (CRP), which were significantly ameliorated by Atorvastatin (ATV) treatment. The results obtained demonstrate that fructose diet feeding for 12 week aggravated MI/RP (Infarct size 30%±2 vs.18%±2], plasma LDH, CK-MB and tissue MPO activity, which was restored by ATV treatment. Moreover, in ATV treated MI/RP myocardial rats nitrite content, expression of iNOS was significantly increased in comparison to the sham operated hypertriglyceridemic rats. The results obtained, so far, suggest that fructose diet feeding aggravated the MI/RP injury and ATV administration ameliorated insulin resistance in hypertriglyceridemic rats. This model will be useful in the evaluation of hypolipidemic and cardioprotective compounds.

(b) Rabbit model of accelerated atherosclerosis: Male New Zealand White rabbits were kept on high cholesterol high fat diet consisting of cholesterol and peanut oil. After seven days, anesthetized animals were subjected to balloon injury to mimic post angioplasty injury using Fogarty embolectomy catheter in the iliac artery. These rabbits were maintained on the high cholesterol diet for the next 4 weeks. Acetaminophen and ampicillin were given for 3 to 5 days. At the end of study period (5 weeks), the animals were euthanized and assessment of various parameters (plasma lipids, platelet activation, vasoreactivity, histology of the normal and injured artery) were carried out. Immunostaining studies to characterize the monocyte/macrophage, smooth muscle cells, important signaling molecules, NOS and/or important cell cycle regulatory proteins are in progress. This model will be useful to predict the efficacy of lipid lowering, anti-proliferative as well as for the identification of anti-thrombotic molecules.



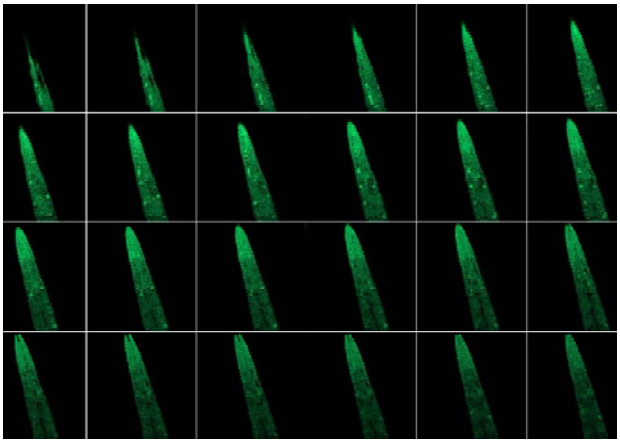
Normal iliac artery Atherosclerotic artery

3.2.2 Central Nervous System *(Schizophrenia, Alzheimer Disease)*

(a) Psychosis model in mice: An animal model of schizophrenia has been standardized by using Ketamine (100 mg/kg), a NMDA antagonist to mice. Locomotor activity, forced swimming and passive avoidance were subsequently evaluated, which exhibited positive, negative and cognitive symptoms respectively. Ketamine administration for ten days produced significant 'hyperactivity', stereotypy and enhanced the immobility period during the forced swim test, reduced the latency period in the passive avoidance test, which persisted even after the withdrawal of ketamine. Haloperidol (0.25 mg/kg for 10 days) improved the positive symptoms but did not affect negative and cognitive deficits. Fluoxetine, an antidepressant drug, ameliorated the positive and negative symptoms only. In contrast, pre-treatment with atypical antipsychotic drugs, clozapine (10 mg/kg) and risperidone (0.025 mg/kg) for the same duration improved all the symptoms.

(b) *Caenorhabditis elegans:* The model system *C. elegans* is aimed towards screening of potential pharmacological agents. *C. elegans* models of - Alzheimer's disease (Source: Link lab. University of Colorado, USA) that expresses 'human' amyloid beta, model of,Parkinson's disease expressing 'human' alpha synuclein (Source: *C. elegans* Genetics Center, Minnesota, USA) and several other mutants and transgenic strains that would be used for carrying out in-depth studies on neurochemical, neurophysiological and neurogenetics aspects of neurobehavioral diseases have been obtained. Various strains of *C. elegans* that are currently being maintained include:

- N2 (var Bristol) Wild type
- CL2006 – Transgenic strain expressing human amyloid beta
- QC47 - pRF4 + pRIC-19::GFP – Strain expressing the RIC-19::GFP fusion protein under the ric-19 promoter in all neurons.
- LX929 [unc-17::GFP] – Strain expressing GFP in all cholinergic neurons.
- BZ555 - egIs1[Pdat-1::GFP], GFP expressed in dopamine neuronal soma and processes.
- TJ356 - Integrated DAF-16::GFP roller strain.
- NL2099 – Homozygous rrf-3 deletion allele; strain exhibiting enhanced effect of RNAi mediated gene silencing.



Transgenic *C. elegans* model of Alzheimer's disease, showing amyloid beta expression

3.3 Bioevaluation of Test Substances

3.3.1 Cardiovascular System

3.3.1.1 Antihypertensive activity

Various plant and herbal extracts were evaluated for their blood pressure (BP) lowering efficacy. Both anaesthetized as well as conscious rats (normotensive and spontaneously hypertensive) were used to assess BP lowering effect of crude extracts and active fractions. Active compounds were subsequently tested for their direct effect on the vasoreactivity of isolated rat vascular rings and angiotensin converting enzyme. One BP lowering compound, from a plant source, has been selected for investigation its mechanism of action.

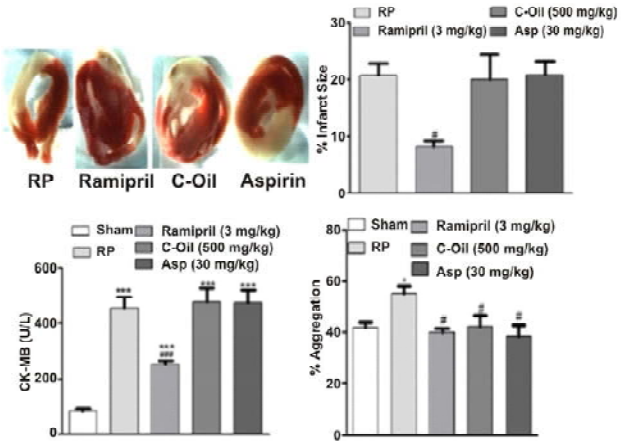
3.3.1.2 Anti-thrombotic activity

During this period, 58 compounds were screened for the anti-thrombotic efficacy against collagen and adrenaline induced thrombosis in mice as well as for their effect on bleeding time. Several of them exhibited better or aspirin like effect in this model of thrombosis.

Two synthetic compounds (S-002-333 and S-007-867) were picked up for the drug development mode due to their selective inhibition of collagen induced platelet activation (adhesion and aggregation), efficacy in various thrombosis models, reduction in the inflammatory mediators, reversal of platelet activation and endothelial dysfunction in high fat fed hamsters, less deleterious effect on bleeding time and no effect on the coagulation cascade (TT, PT, aPTT). Effect of S-007-867 was also evaluated *in vitro* on collagen induced ATP and TxB_2 release from human platelets, thrombin generation in human platelet rich plasma and human/mice platelet adhesion on collagen coated surface.

3.3.1.3 Cardioprotective activity

Herbal medicament (HM)/Curcuma Oil (C oil), ramipril, aspirin and S-002-867 have been evaluated for the cardioprotective activity in the coronary artery induced myocardial ischemia model. Ramipril (3 mg/kg) offered significant protection against myocardial infarct size, CK-MB release, neutrophil migration and enhanced platelet aggregation. HM (500 mg/kg), aspirin (30 mg/kg) and S-007-867 (30 and 100 µM/kg) did not offer protection against MI in the rat, both the compounds however prevented platelet activation in the doses used. Compound 93-478 is currently being evaluated. Three plants extracts, tested in rat heart Langendorff preparation, did not affect ionotropic and chronotropic activities evaluated in this model.



Effect of test agents on MI/RP induced injury

3.3.1.4 Anti-dyslipidemic activity

In dyslipidemic hamsters, 21 natural products, 25 NWP, 4 synthetic compounds and 93 marine samples were tested for the hypolipidemic activity. Thirty materials were evaluated in the rat Triton model, while 28 were screened in 3T3-L1 mouse cell line. A herbal formulation was also evaluated and presently its activity is being confirmed, as initial data had shown interesting trends. Further studies are in progress.

3.3.2 Central Nervous System

3.3.2.1 Rotenone induced oxidative stress and anti-stroke activity

Thirty two synthetic molecules were tested using rotenone induced oxidative stress in rat brain. Compounds were given orally 1 hour prior to rotenone challenge. One hour later, MDA and GSH contents in the brains were monitored. Only four compounds prevented change in brain MDA and GSH level. The activity of these will be reconfirmed and subsequently their anti-stroke potential be evaluated.

Neuroprotective effect of *Withania* was explored on neuronal morphology and DNA fragmentation. The novel leads from *Withania* exhibited neuroprotective as well as anti apoptotic activity.

3.3.2.2 Anti-dementia activity

Sixteen synthetic molecules were tested for their anti-dementia activity (Passive avoidance test in mice) and 35 molecules are under evaluation for beta-amyloid aggregation inhibitory activity in *C. elegans*.

3.3.2.3 Anti-anxiety activity

Among the crude extracts and its fractions received for the bio-evaluation for anti-anxiety activity, CSM/1570/P03/321/C001/F002 exhibited appreciable anti-anxiety activity in the elevated plus maze model.

3.3.2.4 Anti-psychotic activity

Two compounds, 70/343 and 74/243 were evaluated against positive, negative and cognitive dysfunctions to assess the anti-psychotic activity and found to be effective against acute and chronic models.

3.3.2.5 Anti-stress activity

Nine plant extracts and 12 synthetic compounds were screened against acute stress (AS) model. Five extracts and four compounds were effective in restoring AS induced changes. When these extracts were further evaluated against chronic unpredictable stress, only one was found effective.

3.3.3 Other Related Disorders

3.3.3.1 Anti-Ulcer Activity

Seventy synthetic compounds were tested and 3 of them exhibited appreciable protection against animal models of ulcers and associated changes in the acidity and mucin secretion. Their possible protective mechanisms were also explored by evaluating the proton pump inhibitory effect or cytoprotective potential by assessing the mucin secretion. Natural product, WGI 76P, ethanolic extract of *Tectona grandis* and its fractions as well as a marine sample were also evaluated in various animals models of ulcers.

(a) WGI 76P: A natural product, WGI76P (batch no. 18), from Arya Vadiya Sala, showed promising anti-ulcer activity against acute gastric and duodenal ulcer models in rats and guinea pigs. It potentiated mucin secretion, indicating the cytoprotective potential, while significant inhibition of H^+K^+ATPase in gastric microsomes, demonstrated its anti-secretory activity. In addition, ulcer healing effect along with attenuation in the gene expression of proinflammatory cytokine, TNF-α and augmentation of growth factor, VEGF was also evident in chronic gastric ulcer model in rats.

(b) 4483C003: One fraction F010 showed potent anti-ulcer activity against acute gastric and duodenal ulcer models in rats and guinea pigs, which was comparable to standard anti-ulcer drugs. Moreover, 4483C003 and 4483F010 significantly increased mucin secretion and inhibited the enzymatic activity of proton pump in gastric microsomes. Six compounds were isolated and one of them significantly reduced proton pump activity.

(c) CDR-134: Fraction from marine sample CDR134 F234 showed significant anti-ulcer activity against acute gastric and duodenal ulcer models in rats and guinea pigs, which was comparable to the standard anti-ulcer drugs.

3.3.3.2 Anti-inflammatory Activity

Nineteen synthetic compounds were tested against carrageenan induced paw oedema model in rats, none was more active than the standard drug, ibuprofen. While 124 samples (NWP-37) were evaluated for TNF inhibition activity in THP cell line, only one sample exhibited mild activity.

4. Malaria and other Parasitic Diseases

Coordinator:
Dr. S.K. Puri

Assistant Coordinator:
Dr. Saman Habib

Area Leaders:
Dr. Shailja Bhattacharya
Dr. Anuradha Dubey

Malaria, Leishmaniasis and Filariasis are the three main parasitic disease areas being vigorously pursued at the Institute. Researchers at the Institute address issues pertaining to design and development of novel drug molecules as well as optimization and preclinical development of lead molecules and combination therapy regimens, besides investigation of novel drug delivery systems. A significant basic research component of the programme focuses on identification and characterization of novel drug targets, understanding mechanisms of drug action and drug resistance, investigation of aspects of parasite biology and host-parasite interaction, immunoprophylaxis and immuno-diagnosis. The contribution of host genetic factors in malaria susceptibility in Indian populations is also under investigation. The structural biology component of the programme aids in molecular modeling and X-ray structure determination.

4.1 Malaria

4.1.1 Synthesis and Screening

4.1.1.1 Synthesis

Novel synthetic moieties comprising nearly 850 compounds representing several prototypes viz. endoperoxides, β-carbolines, indoloquinolines, phenanthridines, pteridines, pyridines, pyridopyrazines, pyrrolidines, imidazopyridines, quinazolines, quinolines, aminoalkanes, annulated quinolines, quinoline-peptide hybrids, furanones, acridines, thiourea derivatives, 2-amino imidazoles, benzamidazoles, indozilinoindoles, benzamidoles, pyranone derivatives, substituted indoles, substituted triazines, pyrazoles, pyrazole-pyrimidines, fatty acid synthesis inhibitors, tetratrahydropyridines, phenylcyclopropyl methanones, chalcones, fibrifugine analogs, azoles, etc. were synthesized during the year for evaluation against *in vitro* or *in vivo* experimental malaria models. In addition, 47 extracts/fractions from natural sources were prepared and evaluated for antimalarial activity.

4.1.1.2 Screening against *Plasmodium falciparum in vitro*

A total of 820 new synthetic compounds were screened against *Plasmodium falciparum* (strain 3D7) *in vitro* at various concentrations ranging between 1-50 µg/ml to determine the concentrations inhibiting the intracellular maturation of schizonts. Potential compounds with MIC <1 µg/ml were processed for determining concentration response profile employing SYBR green nucleic acid dye based micro-fluorimetric assay. Several compounds have been identified with IC_{50} values below 50 ng/ml. Screening of 195 samples of marine fauna against *in vitro* model yielded 2 crude extracts with MIC values at 10 µg/ml. In addition, nearly 1000 samples of natural origin comprising plant, fungal or bacterial extracts were evaluated under a CSIR coordinated network programme and 5 plant extracts showing schizont maturation inhibition at 10 µg/ml concentration were identified for follow up studies.

4.1.1.3 Screening against *Plasmodium yoelii* (N-67) – Swiss mice model

Thirty synthetic compounds from 5 different prototypes, identified after activity response against *P. falciparum in vitro*, were evaluated against chloroquine resistant *P. yoelii* (N-67) – Swiss mice model. Several quinoline triazine and quinoline peptide hybrid derivatives exhibited above 90% parasite clearance after 4-day treatment regimen. None of the 5 plant extracts evaluated against the same model showed any promising activity up to 500 mg/kg dose. Bioassay guided fractionation studies with a previously identified plant extract NBR 1220 have led to isolation of active single molecules. Likewise, active sub-fractions for another plant extract IHB 1418 have been identified.

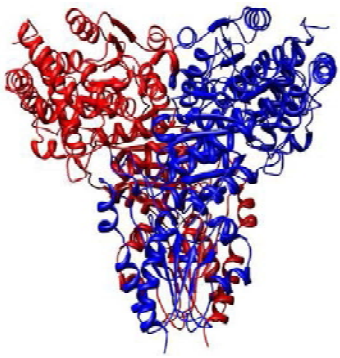
4.1.1.4 Screening against *Plasmodium yoelii* (MDR) – Swiss mice model

Lead optimization studies were conducted with identified pyrrolidone amino alkane derivatives. Thirty seven compounds were evaluated against multi drug resistant *P. yoelii nigeriensis* in Swiss mice. Lead compound S-008-1263, earlier found curative at 50 mg/kg dose, showed 80% efficacy at lower dose of 25 mg/kg. Four other compounds, S-008-462, -464, -236 and -270 showed activity at 100 mg/kg dose while the lower dose of 50 mg/kg was suppressive.

4.1.2 Basic Studies

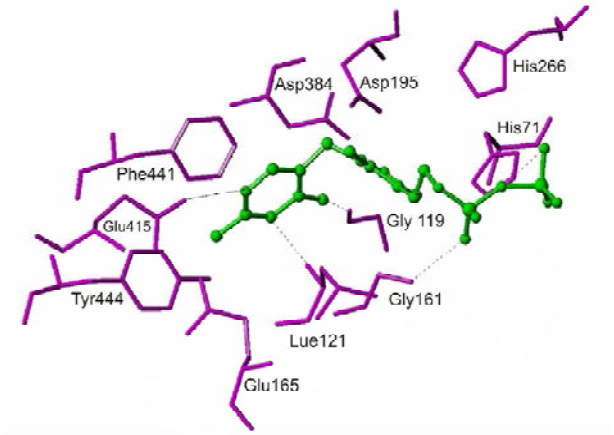
4.1.2.1 *Plasmodium falciparum* transketolase as a drug target

The enzymes of Pentose Phosphate Pathway (PPP) have been shown to be one of the most promising targets for the chemotherapy of parasitic protozoa. Previously it has been reported that the non-oxidative arm of PPP is active in malarial parasites and the transketolase is the key enzyme of non-oxidative branch. The thiamine diphosphate (ThDP) dependent enzyme transketolase (Tk; D- sedoheptulose-7-phosphate: D-glyceraldehyde-3-phosphate glycolaldehydetransferase, EC 2.2.1.1.) catalyzes the cleavage of a C-C bond adjacent to a carbonyl group in keto sugars and transfers a ketol moiety to aldo sugar. In malaria parasites, it plays an important role in the generation of ribose molecules that are essential for nucleic acid production. The transketolase gene of *P. falciparum* has been cloned, over-expressed and characterized. The purified recombinant protein of malarial parasite was competitively inhibited by the transketolase inhibitors p-hydroxyphenyl pyruvate and oxythiamine pyrophosphate under *in vitro* condition and exhibited antimalarial activity *in vivo* against *P. yoelii.*



Dimeric model structure of PfTk. built on the basis of homologue transketolase of *S. cerevisiae* (ID: 1TRK, 2.0 Å resolution).

Homology modeling of *P. falciparum* transketolase, using the crystal structure of yeast as a template, was carried out and the model refined through molecular dynamic simulations. Using this homology model, efforts have been made for the identification and prioritization of potential compounds targeted against *Plasmodium falciparum* transketolase. For this, an integrated pharmacophore and structure-based virtual screening was performed using CDRI small molecule database. Subsequently interaction patterns from known actives to the substrate (fructose-6-phospahte) and thiamine pyrophosphate (ThDP) were applied for scoring and ranking the virtual screening hits using UNITY module of SYBYL 7.1. The eight compounds, selected after virtual screening on the basis of ThDP and thirteen compounds obtained after screening on the basis of fructose-6-phosphate, were further screened biologically. Finally, one compound, in case of ThDP based screening and three compounds in case of fructose-6-phosphate based screening, were found active against PfTk.



Docking of ligands into active site of PfTk: Docking of thiamine pyrophosphate into ThDP binding site of PfTk. These ligands were docked into their respective sites using the FlexX program interfaced with SYBYL7.1

4.1.2.2 Mechanism of resistance to artemisinine derivatives

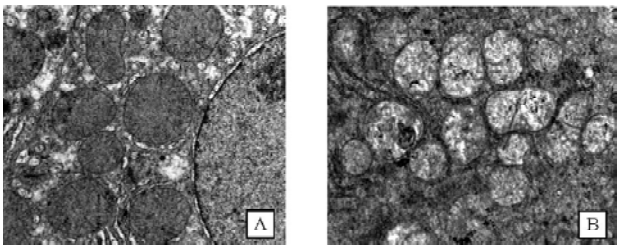
PfATP6, the only SERCA-type Ca^{2+} ATPase, a membrane transporter protein of *P. falciparum*, has been implicated as a probable target for the action of artemisinine derivatives since artemisinin completely inhibits PfATP6 activity by high specificity. Moreover, polymorphism in this gene has been associated with *in vitro* resistance to artemether in the *P. falciparum* field isolates. Studies have been initiated on comparative genomic and proteomic of SERCA in *P. vinckei* arteether sensitive and experimentally selected resistant parasites to explore its role in resistance to arteether. SERCA gene was amplified with gene specific primers and cDNA of arteether sensitive *P.vinckei* as SERCA 1, SERCA 2 and SERCA 3. Amplified fragments of SERCA were cloned in TA cloning vector and sequenced. Cloned gene fragment of *P.vinckei* SERCA have shown >85%homology with other *Plasmodium* SERCA. A gene fragment of SERCA with length of 717bp was cloned in bacterial expression system and purified recombinant *Plasmodium* SERCA was used for production of antibodies. Cloning and sequencing of SERCA from arteether resistance *P. vinckei* parasites is in progress.

4.1.2.3 Drug targeting

Optimization studies are underway to target erythrocytes for antimalarial drug delivery through nanoparticles. Nanoparticles containing antimalarial agents, including CDRI compound 97-63 or chloroquine free-base, were prepared and the processes partially optimized. These particles target the erythrocyte Glucose Transporter (GLUT-1) and also, possibly the hexose transporter expressed by the parasite on the erythrocyte membrane (e.g. PfHT-1). Evidence of targeting was obtained in experiments designed to block the glucose transporters using the specific inhibitors phloretin and cytochalasin, as well as glucose, the natural ligand of these transporters.

4.1.2.4 Mitochondrial pathology in malaria infection (Free Radical Biol. Med., 2009, *46*, 271-281)

TEM study demonstrated marked alterations in the mitochondrial morphology of hepatocytes of malaria infected mice. TEM studies clearly showed (A) intact mitochondria, with the double membrane clearly visible, cristae structurally intact, and intra-mitochondrial matrix consisting of electron-dense granules in control hepatocytes. In hepatocytes from infected mice (B), however, the mitochondrial double membrane is absent



and leaky, with distorted cristae that are far fewer in number than in controls, and the matrix appears extracted with an appreciable reduction in electron-dense granules in the intra-mitochondrial matrix.

4.1.2.5 Role of drug metabolizing enzymes

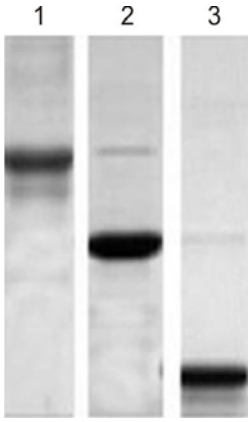
Estimation of drug metabolizing enzymes was studied in liver homogenates obtained from *P. berghei* (ANKA strain) infected Swiss mice at different levels of parasitaemia. The activities of aminopyrine-N-demethylase and aniline hydroxylase were dependent on an adequate supply of microsomal cytochrome P_{450}. With a decrease in the activity of cytochrome P_{450}, aniline hydroxylase showed a decrease of 45.3% and aminopyrine-N-demethylase decreased by 40.7% in comparison to the uninfected control samples. At the highest parasitaemia level, GST also showed a reduction of 30.1%. The steady decline in enzyme activity is attributed to the disruption of hepatic microsomal system, which is the site of localization of these enzymes. Administration of ketoconazole, a known cytochrome P_{450} inhibitor in combination with antimalarial α/β arteether in mice, has been shown to reduce the required curative dose for arteether. Monitoring of the levels of cytochrome P_{450} in liver samples and parasite preparations from combination treated groups indicated that ketoconazole inhibited the enzyme activity in the parasites while the parasites which were exposed to only α/β arteether showed an induction of the enzyme activity.

4.1.2.6 Characterization of MSP-1 of *P. vivax* and *P. cynomolgi*

Plasmodium vivax is the second most important malaria parasite that infects humans outside Africa and causes severe clinical symptoms and morbidity. The lack of *in vitro* culture system and requirement of specialized monkey model system for *in vivo* testing are some of the major challenges for development of *P. vivax* vaccines. *P. cynomolgi bastianelli*, a parasite of rhesus monkeys, is closely related to *P. vivax* as there is high homology of prime vaccine candidates (CSP, MSP1, AMA1 and EBA) between these two parasites. Therefore, the Merozoite

Surface Protein-1 (MSP-1) and Circum Sporozoite Protein (CSP) of *P. vivax* and *P. cynomolgi B* were selected for cloning, expression and evaluation of protective potential in *P. cynomolgi* rhesus monkey model system. The MSP-1_{42} antigen of *P. vivax* and *P. cynomolgi B* malaria parasites have been previously cloned and expressed. The recombinant MSP-1_{42} antigens from *P. vivax* and *P. cynomolgi B* showed high reactivity with monoclonal antibodies and immune monkey sera (from protected monkeys). In order to find out whether the monkey sera and monoclonal antibodies react with MSP-1_{19} fragment (containing the protective epitope), we have cloned and expressed the 19 kDa fragment of *P. cynomolgi B*.

The *P. cynomolgi bastainelli* MSP-1_{19} fragment was PCR amplified using gene specific primers. The sequencing of PCR product revealed that the amplified fragment is of *P. cynomolgi* B MSP-1_{19} gene. The cloned gene was excised using *Bam*HI and *Not*I and ligated to the compatible site of pGEX6P1 expression vector. The optimum conditions for expression of MSP-1_{19} gene was standardized and maximum expression was obtained at 0.1mM IPTG at 37°C. The expressed fusion protein was in soluble fraction and purified using GST affinity column on AKTA prime protein purification system and a GST fusion protein of 45 kDa was observed on SDS-PAGE. In order to

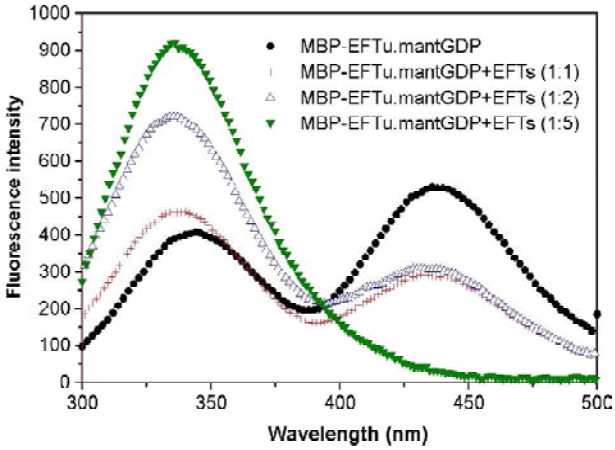


SDS-PAGE pattern of purified *Plasmodium cynomolgi MSP* 1-19 recombinant protein. 1=Fusion protein; 2=GST; 3=MSP-1_{19}

get MSP1_{19} recombinant protein free of GST, the fusion protein was cut with specific protease and the recombinant MSP1_{19} was further affinity purified as shown in figure. The purified Pc-MSP-1_{19} protein (free of GST) showed high reactivity in ELISA with monoclonal antibodies thereby suggesting that the recombinant protein is in conformational form. The purified *P. cynomolgi* MSP-1 recombinant protein will be characterized using immune sera from protected monkeys. The subcloning and expression of *P. cynomolgi B* CSP gene fragment (1.3 kb) showed fusion protein of 72 kDa on SDS-PAGE. As the fusion protein was localized in the inclusion bodies efforts were made to solubilize and purify the fusion protein, but the recovery was very low. The *P. cynomolgi B* CSP gene fragment will be sub-cloned in other expression vector to obtain better recovery of fusion protein.

4.1.2.7 Translation in *Plasmodium* apicoplast

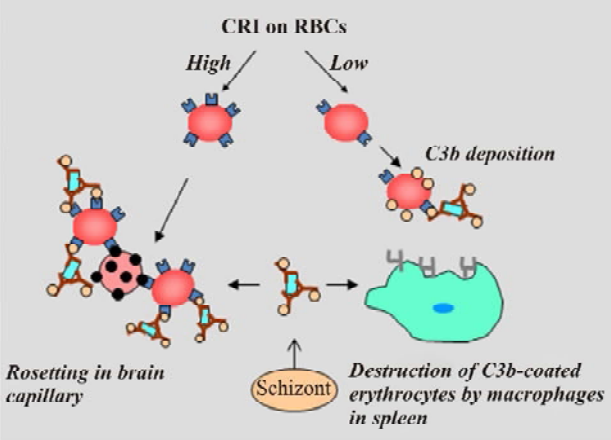
Protein translation in the plastid of the malaria parasite is a target for several antibiotics whose anti-malarial activity has been demonstrated. However, there is little information on molecular aspects of the apicoplast translation process. The function and interaction of two critical translation elongation factors was investigated. Apicoplast-encoded EF-Tu was characterized as a GTPase that interacts with nuclear-encoded apicoplast-targeted EF-Ts and the kinetics of interaction was determined. The effect of an antibiotic that targets EF-Tu function in bacteria was analysed on PfEF-Tu. Structure-function analysis by molecular modeling indicated structural alterations in the PfEF-Tu GDP binding pocket upon interaction with PfEF-Ts that result in release of GDP for the next round of GTP binding and EF-Tu-mediated catalysis of aminoacyl-tRNA entry into the ribosome. Our results demonstrate the functional interaction of two translation factors encoded by different cellular compartments in mediating a critical process in the apicoplast and provide an experimental system to study the effect of prokaryotic translation inhibitors on the *Plasmodium* apicoplast.



Apicoplast targeted EF-Ts mediates GDP release from EF-Tu

4.1.2.8 Genetic variation and pathogenesis of malaria (Hum. Immunol., 2009, *70*, 244-250)

Complement receptor 1 (CR1/CD35) levels on erythrocytes and related CR1 polymorphisms have been associated with response to falciparum malaria in



populations inhabiting malaria-endemic regions. Differences in disease association profiles of its low expression alleles have been observed in populations from different regions of the world. We analyzed the influence of CR1 levels and associated SNPs on susceptibility/resistance to falciparum malaria in Indian populations. Two CR1 SNPs [exon 22 (A/G) and intron 27 (A/T)] define the low expression (L) CR1 allele in populations inhabiting a *P. falciparum*-endemic and a non-endemic region of India. Populations of the endemic region have very low RBC surface CR1 levels and higher frequencies of the exon 22 and intron 27 mutant L alleles.

While low CR1 levels, correlated with susceptibility to severe malaria in the non-endemic region, high CR1 levels were associated with manifestation of disease in the endemic region. Additionally, the exon 22 L allele was a risk factor for severe malaria in the non-endemic region. Absence of correlation between levels of TNF-α, IFN-γ, and IL-6 with CR1 levels in severe patients indicated that RBC CR1 levels in individuals are not the major determinants of pro-inflammatory cytokine release during infection. Our results indicate context-specific differences in the pathogenesis of severe malaria in the malaria-endemic and non-endemic region.

4.2 Leishmaniasis

4.2.1 Synthesis and Screening

4.2.1.1 Synthesis

Synthetic compounds representing several prototypes viz. quinolines, imidazolopyrimidines, triazines, β-carbolinopyrimidines, chromano-chalcones, alkylated pyridinium salts, terpenyl chalcones, pyrazoles, pyrimidines, styryl pyrimidines, trizinopyrimidine, indoles, pyrazolines, quinazolines, aryloxylazoles, aryloxylazolyl chalcones and oximinoetherazoles, were synthesized for bioevaluation against experimental models.

4.2.1.2 Screening against *in vitro* model

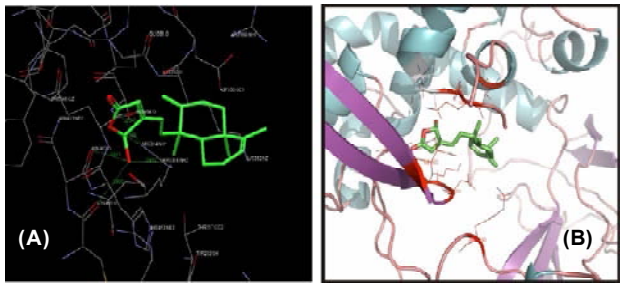
More than six hundred compounds and 280 natural product extracts were evaluated at 40 μM concentration against *in vitro* macrophage-amastigote model for lead identification. 83 Compounds showing significant activity (80-100 % inhibition in parasite growth) were reevaluated for their IC_{50} and CC_{50} responses. Selected on the basis of significant IC_{50} response and high selectivity index (SI), 36 compounds were identified for *in vivo* efficacy evaluation. Likewise 9 marine extracts and 4 plant extracts / fractions which showed high SI values, were identified for *in vivo* trials against hamster model.

4.2.1.3 Screening against *in vivo* model

Thirty six synthetic compounds were evaluated against *L. donovani* / hamster model. Out of these, 9 samples exhibited moderate inhibitory activity (52-79% inhibition). One of the 8 plant extracts screened against *in vivo* model has also shown moderate activity (54-79% inhibition).

4.2.1.4 Follow-up studies with 4555K009 (British Journal of Pharmacology, 2010, *in press*)

Bioassay guided fractionation studies with plant extract 4555 led to isolation of a pure compound K009 as a non-cytotoxic orally active antileishmanial. Compound K009 inhibits recombinant DNA topoisomerase I with the ultimate induction of apoptosis. Molecular docking studies, conducted with DNA topoisomerase I to identify the binding interactions responsible for activity, suggested five strong hydrogen bonding interactions and hydrophobic interactions of K009 with LdTopo1. The data reveals this compound as a potent and safe antileishmanial. Several

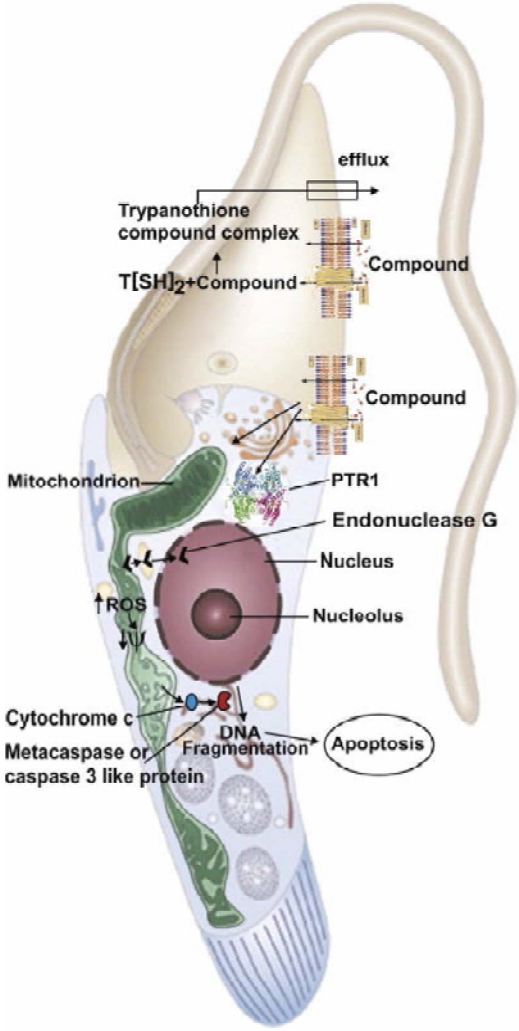


(A) Docking of 16α-hydroxycleroda-3, 13 (14)Z-dien-15,16-olide (1) **into the active site of *Leishmania donvani* DNA-topoisomerase (Ld-topo-I) (green dotted line represents hydrogen bonding). (B) superimposition of K9 in to the active site display as Ribbon form.**

pharmacophores of the above compound are under evaluation for their antileishmanial potential.

4.2.1.5 Evaluation of monastrol for Leishmania chemotherapy (Exp Parasitol., 2009, *123,* 258-264; Parasitol Res., 2009,*105*,1317-1325)

Monastrol is an established Kinesin Spindle Protein (KSP) inhibitor for human cancer therapy, which inhibited the proliferation of amastigotes of *L. donovani* clinical isolate in infected macrophage cultures with no host cytotoxicity. It has been shown that in experimental animals, effective oral administration gives therapeutic strength to monastrol for use as a potent antileishmanial in human visceral leishmaniasis cases. Monastrol has been shown to inhibit the pteridine metabolic pathway in *Leishmania* parasites. Our earlier target based drug discovery studies identified dihydropyrimidine (DHPM) analogues as potent antileishmanials targeting pteridine reductase 1 (PTR1), an enzyme of the folate biosynthetic pathway in *Leishmania* parasites. DHPMs, known to be orally active, represent a diverse family of biologically active compounds with antiviral, antitumor, antibacterial and anti-inflammatory properties and for the first time have been shown to exhibit antileishmanial activity.

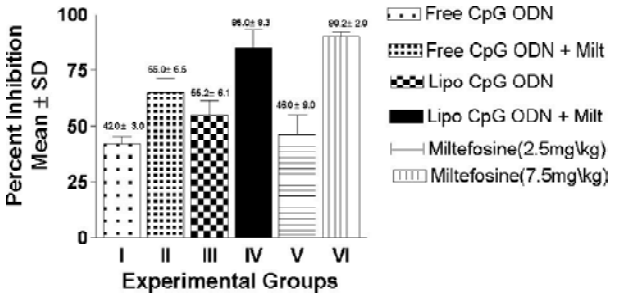


Proposed mechanism for dihydropyrimidine (DHPM) analogues induced apoptosis in *L. donovani* promastigotes.

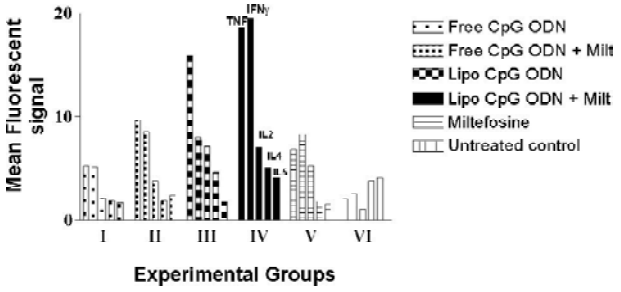
Elucidation of the X-ray crystal structure of monastrol in complex with PTR1 enzyme and the substrate confirmed that enzyme PTR1 is the target for the antileishmanial property of monastrol. Further confirmatory evidence was obtained by the PTR1 recombinant enzyme inhibition assay. This target specificity of monastrol to *Leishmania* parasites suggests that this anticancer molecule may have a role in leishmania chemotherapy.

4.2.1.6 Combination therapy with Miltefosine and CpG-ODN against experimental Visceral Leishmaniasis (VL)

The progression of VL often results in down regulation of host's immune system. To combat this situation, we have explored a combination of CpG-ODN and Miltefosine for treatment of experimental VL where enhancement of adaptive immunity and simultaneous decrease of parasitic burden can be achieved. CpG ODN is bacterial Oligodeoxy- nucleotide containing CpG motifs,



Combination therapy of free and liposomised CpG ODN with miltefosine in *L. donovani*mice model

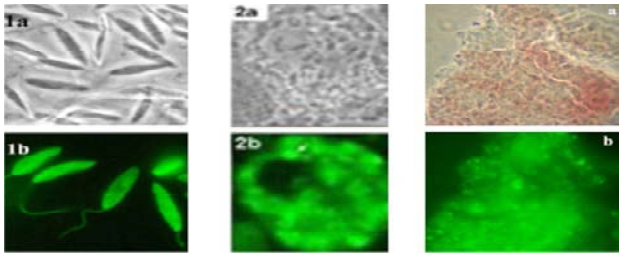


Th1/Th2 cytokine response in mice

which is known to promote the innate immunity by activation of TLR-9 receptors. For the present study, experiments were carried out in BALB/c mice and hamsters, infected with *L. donovani* infection. CpG-ODN was administered in infected animals at various dosages in single and multiple shots by intraperitoneal (i.p.) route. The dose showing best antileishmanial activity was tried as free and liposomised form with miltefosine. Animals co-administered with liposomised CpG-ODN & Miltefosine have shown better inhibitory effect (85%) as compared to those treated with free CpG-ODN & Miltefosine (65%), Miltefosine (46%), free CpG-ODN alone (42%) and liposomised CpG-ODN alone (55.2%). Monitoring of immunological parameters in animals treated with liposomised CpG-ODN and Miltefosine have shown significant enhancement in Th1 cytokines, NO production and ROS along with higher H_2O_2 production. Remarkable increase in phagocytosis index was also observed indicating overall immunological support to antileishmanial activity of Miltefosine by CpG-ODN.

4.2.1.7 Generation of stable Green Fluorescent Protein (GFP) transfectant cell lines (J. Ant. Chem., 2009, *64*, 370–374)

Several Leishmania strains with episomal expression of GFP require constant drug pressure for its continuous expression and hence limit its use for *ex vivo* or *in vivo* system. The aim of this study was to alleviate this problem by stably integrating the GFP gene into the parasite genome so as to use these transfectants for *ex vivo* and *in vivo* drug screening. The GFP gene was integrated at downstream of 18S ribosomal promoter region. The GFP expressing parasites both sodium stibogluconate (SAG) susceptible and resistant isolates after initial selection were grown without adding G 418. A constitutive and enhanced expression of GFP in promastigote and amastigote stages was achieved for about 12 months without any need of drug pressure. The parasites were highly infective to macrophage cell lines as well as to hamsters as observed by fluorescence microscopy and flow cytometry (FACS). GFP tagged promastigotes as well as intracellular amastigotes were found to be highly susceptible to all antileishmanial drugs viz. miltefosine, amphotericin B and pentamidine in a concentration-dependent manner except SAG which was inactive against the GFP-Promastigotes as well as SAG resistant intracellular amastigotes correlating well with earlier reports. The GFP-transfectants were found suitable for FACS-based *ex vivo* screening assays. These were also infective to hamsters up to day 60 and 90 post-infection.



GFP expressing *L. donovani* (1) Promastigotes and (2) Amastigotes

4.2.2 Elucidation of Drug Resistance Mechanism

4.2.2.1 Follow-up studies with sodium stibogluconate resistant genes

A few genes exhibiting up-regulation in SAG–resistant clinical isolates were identified previously using micro array technique. These genes were arbitrarily named as SRRG1, SRRG2 and SRRG3 (SAG resistance related gene-1, gene II, gene III). Amplified segments of two of these genes, SRRG-I and SRRG-II were cloned and sequenced. SSRG-I exhibited significant homology with protein kinase homologue while SSRG-II showed homology with NLI gene.

4.2.2.2 Biochemical and molecular mechanism of sodium stibogluconate resistance in Leishmania under field conditions

Earlier it was shown that the non-responsive isolates exhibited varying fold of resistance to SAG under laboratory conditions. Promastigotes of non-responsive isolates exhibited increased levels of intracellular thiols, which corresponds to the increased level of trypanothione and amplification of MRPA and TR genes. Real time PCR assay further confirmed the increased expression of MRPA and TR in resistant isolates as compared to sensitive ones.

4.2.2.3 Amplified fragment length polymorphism (AFLP) analysis (Acta Tropica, 2009, 110, 80-85)

The Leishmania strains belonging to cutaneous leishmaniasis (CL) and visceral leishmaniasis (VL) have been reported to possess close homology in genome profiles. To confirm this on genetic basis, an attempt was made to differentiate clinical isolates (SAG sensitive as well as resistant) of *L. donovani, L. major, L. tropica* genetically using amplified fragment length polymorphism (AFLP)-a high throughput DNA fingerprinting technique. The objective of this research work was to identify DNA markers of CL and VL. Ten combinations of selective primers detect several informative AFLP markers. Analysis

based on polymorphic AFLP markers, revealed considerably high genetic variation among the genome of these species, which was sufficient to distinguish between CL and VL.

4.2.3 Identification, Characterization and Validation of Novel Drug Targets

4.2.3.1 Nucleoside diphosphate kinase B (NDKb)

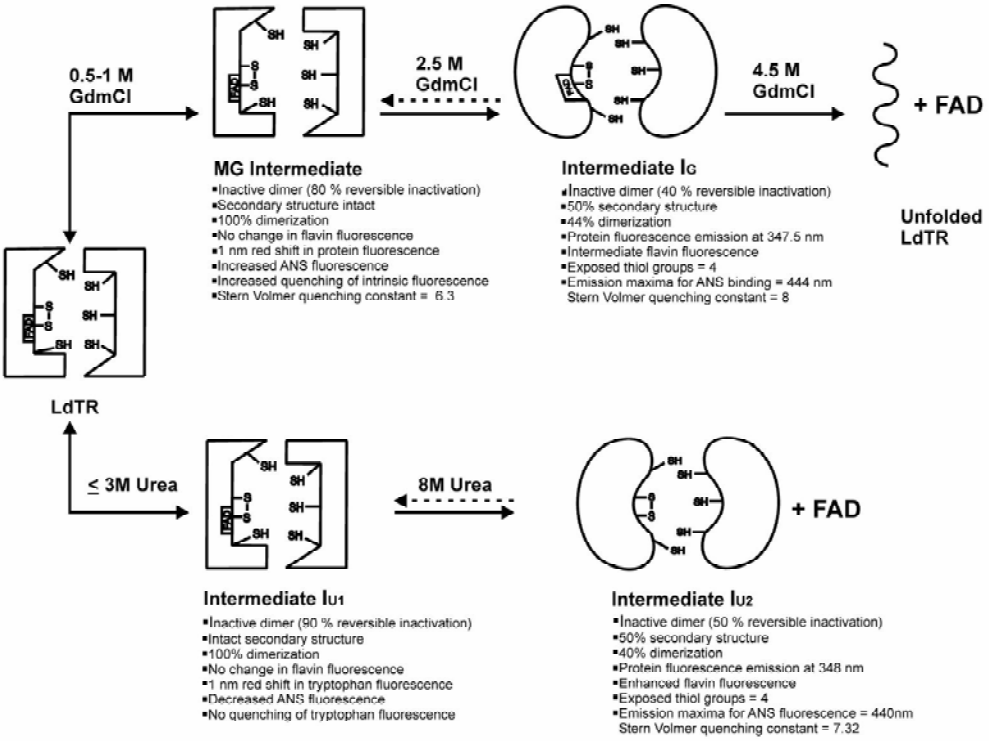
Protozoans are unable to synthesize purines *de novo* from amino acids and rely upon the salvage of these compounds from host cells. NDKs are involved in salvage pathway of these parasites and they have importance in the maintenance of intracellular ratios of NTPs and dNTPs. NDKs have a molecular mass of 15-18 kDa and are conserved during evolution. A 456bp amplicon of NDKb has been cloned and over-expressed (Acc. No. EU867388). The purified protein has molecular weight of approximately 18kDa on SDS-PAGE. The antibody has been raised against recombinant NDKb and further characterization of its activity is underway.

4.2.3.2 Dipeptidylcarboxypeptidase

DNA microarray expression profiling approach identified a gene encoding dipeptidylcarboxypeptidase enzyme for the kinetoplast protozoan *Leishmania donovani* (LdDCP) that was differentially expressed in two stages of the parasite life cycle. Three-dimensional model of LdDCP was generated based on crystal structure of *Escherichia coli* DCP (EcDCP) by means of comparative modelling and assessed using PROSAII, PROCHECK and WHATIF. Captopril docking with htACE, LdDCP and EcDCP and analysis of molecular electrostatic potentials suggested that the active site domain of three enzymes has several minor but potentially important structural differences. These differences were exploited to identify selective inhibitor of LdDCP by virtual screening. Screening of CDRI compound library against the homology models of LdDCP led to identification of five compounds, which significantly inhibited LdDCP.

4.2.3.3 Trypanothione reductase (TR) (BBA, 2009, *1794,* 1474-1484)

TR is a NADPH-dependent disulfide oxidoreductase, unique to kinetoplastid parasites including *Trypanosoma* and *Leishmania*, is a validated target for the design of improved drugs. TR is a stable homodimer with a FAD molecule tightly bound to each subunit. Urea induced unfolding was non-reductive in nature and led to the formation of partially folded



Diagrammatic representation of the differential modes of unfolding of LdTR by GdmCl and urea.

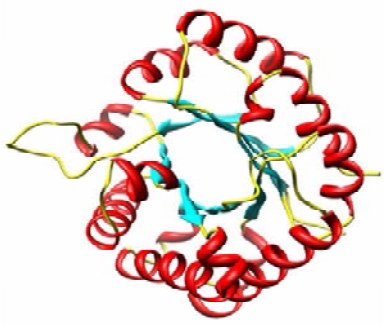
intermediate. This intermediate species lacks catalytic activity and characteristic conformation of native LdTR but has significant secondary structure and could be partially reactivated. Reactivation and cross-linking experiments clearly demonstrated that the loss of activity at higher denaturant concentrations was coincided by dimer dissociation or structural unfolding. To demonstrate the formation of intermediates, during unfolding, binding characteristics towards hydrophobic probe 1, 8 anilino–naphthalene sulfonate (ANS) and acrylamide quenching studies were carried out. Lower concentrations of urea resulted in the formation of a native-like intermediate (I_{UI}) with only disturbed hydrophobic interactions but at higher concentrations, a partially folded intermediate (I_{U2}) accumulates. Treatment with GdmCl at lower concentrations resulted in formation of molten globule intermediate (0.5-1M) which has well ordered secondary structures but the tertiary structure is perturbed due to an increase in hydrodynamic radius and exposure of hydrophobic patches. Further increase in the concentrations of GdmCl led to a progressive unfolding of structure and conformation and a second intermediate state (I_G) is populated around 2.5 M GdmCl. However, higher concentrations of GdmCl are able to unfold this compact stable intermediate leading to complete unfolding of the protein.

4.2.3.4 Arginase

Arginase, an important enzyme for polyamine biosynthesis, from *L. donovani* was cloned and sequence submitted to NCBI gene bank. Further studies with the enzyme have shown that the GC content in whole ORF is 60.37 %. LdArg shows 40.30%, 39.39%, 18.78%, 97.27% identity with Human, Mouse, *T. cruzi,* and *L. mexicana* respectively. In *L. donovani* the glycine was found at position 288, instead of glutamic acid in all other available sequences. This glutamic acid with His-154 is responsible for L-arginine interaction. The recombinant Arginase (LdArg) was partially purified and found catalytically active. The enzyme was biochemically characterized and it was observed that heat inactivation enhanced the arginase activity. The LdArg activity showed different responses in presence of different cations at varying pH and temperature.

4.2.3.5 Triose phosphate isomerase (LdTIM)

Triose phosphate isomerase from *Leishmania donovani* has been cloned, over-expressed, purified and biochemically characterized. Gel filtration chromatography studies suggest that LdTIM is a homodimer. Loss of LdTIM activity with respect to unfolding of protein in presence of



Model structure of LdTIM

denaturants (urea and GdmCl) was studied and it was found that at 3 M denaturants concentration the activity of LdTIM was completely lost. The LdTIM was found to be more sensitive to s-Methyl methanethiosulfonate than other reported trypanosomatids. The energy minimized and refined 3D structure of the LdTIM was built by using homology modeling based on the known crystal structure of Triose Phosphate Isomerase from *L. mexicana* (PDB code 1AMK) as a template. The model of LdTIM revealed an active site similar to that of the 1AMK with conservation of the catalytically important residues.

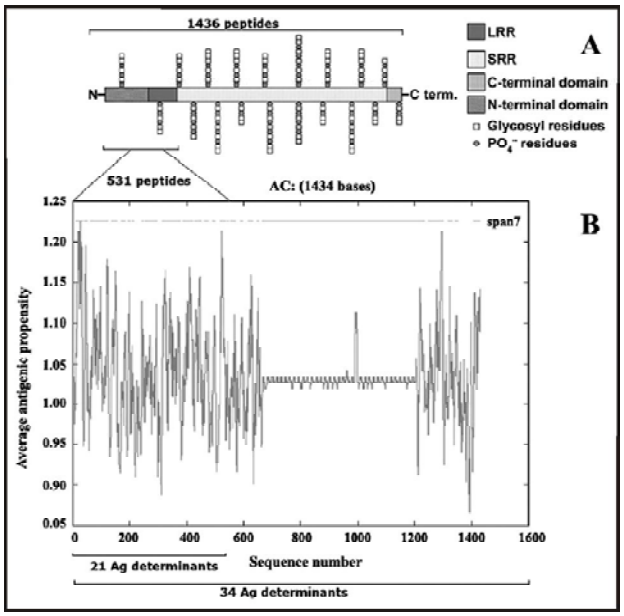
4.2.4 Immunological Studies

4.2.4.1 Identification of Th1 stimulatory proteins for immunoprophylactic potential

Studies conducted earlier led to the identification of a fraction of *L. donovani* soluble promastigote antigen belonging to 97.4–68 kDa for its ability to stimulate Th1-type cellular responses in cured VL patients as well as in cured hamsters. These Th1-stimulatory antigenic fractions of soluble *L. donovani* promastigotes and amastigotes offered long-lasting protection against experimental visceral leishmaniasis. MALDI-TOF–MS/MS analysis of these subfractions further revealed that of the 19 identified immunostimulatory proteins, Elongation factor-2, p45, Heat shock protein-70/83, aldolase, enolase, triosephosphate isomerase, disulfideisomerase and calreticulin were the major ones in these subfractions. Out of these identified Th1 stimulatory proteins, seven recombinant proteins viz. elongation factor-2, p45, aldolase, enolase, triosephosphate isomerase, protein disulfide isomerase and calreticulin were developed and their molecular and biochemical characterization has been carried out.

4.2.4.2 Immunization with the DNA encoding N-terminal domain of proteophos-phoglycan (PPG) of *L. donovani* (J. Immunol.; 2009, *183,* 470-479)

Leishmania produces several types of mucin-like



The schematic structure of PPG (*A*) and Antigens (Ag) determinants in *ppg* using Ag determination software (*B*).

glycoproteins called proteophosphoglycans (PPGs). These exist as secretory as well as surface-bound forms in both promastigotes and amastigotes. We earlier demonstrated the differential expression of PPG in sodium stibogluconate sensitive and resistant clinical isolates of *L. donovani*. For elucidation of the structure and function of *ppg* gene of *L. donovani*, a partial sequence of its N-terminal domain of 1.6 kb containing majority of antigenic determinants, was successfully cloned and expressed in prokaryotic as well as mammalian cells. The evaluation of DNA encoding N-terminal domain of *ppg* gene, as a vaccine, was done in golden hamsters (*Mesocricetus auratus*) against the *L. donovani* challenge. The results suggested N-terminal domain of *L. donovani ppg* as a potential DNA vaccine against visceral leishmaniasis.

The localization and expression of N-terminal gene in Leishmania parasite has been done. Cloning and characterization of 2.7 kb ppg gene and validation of expression profile of N-terminal domain of *ppg* gene (1.6 kb) ppg through antisense technology are underway.

4.2.4.3 Photodynamic vaccination of hamsters with inducible suicidal mutants of *L. amazonensis* (European Journal of Immunology 2009, *39(1)*, 178-191)

Leishmania, naturally residing in the phagolysosomes of macrophages, is a suitable carrier for vaccine delivery. Genetic complementation of these trypanosomatid protozoa to partially rectify their defective heme-biosynthesis renders them inducible with d-aminolevulinate to develop porphyria for selective photolysis, leaving infected host cells unscathed. Delivery of released "vaccines" to antigen-presenting cells is thus expected to enhance immune response, while their self-destruction presents added advantages of safety. Such suicidal *L. amazonensis* was found to confer immunoprophylaxis and immunotherapy on hamsters against *L. donovani*. Neither heat-killed nor live parasites without suicidal induction were effective. Photodynamic vaccination of hamsters with the suicidal mutants reduced the parasite loads by 99% and suppressed the development of disease. These suppressions were accompanied by an increase in Leishmania-specific delayed-type hypersensitivity and lymphoproliferation as well as in the levels of Splenic iNOS, IFN-γ, and IL-12 expressions and of Leishmania-specific IgG2 in the serum. Moreover, a single intravenous administration of T cells from vaccinated hamsters was shown to confer effective cellular immunity against *L. donovani* challenges. The absence of lesion development at vaccination sites and parasites in the draining lymphnodes, spleen and liver further indicates that the suicidal mutants provide a safe platform for vaccine delivery against experimental visceral leishmaniasis.

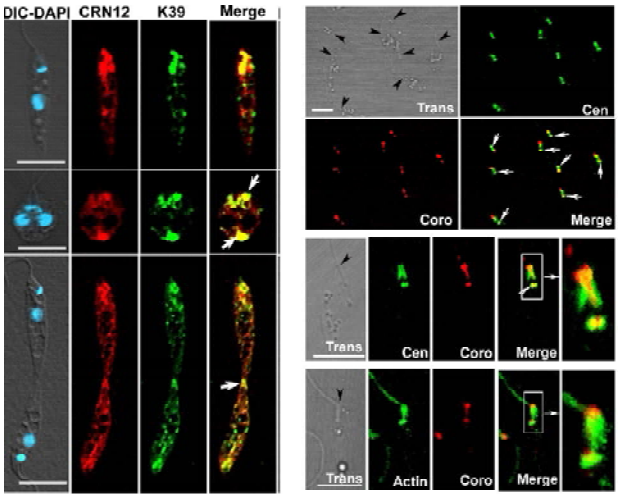
4.2.5 Cell Biology Studies

4.2.5.1 Actin-network of *Leishmania donovani*: functional characterization of actin / actin-binding proteins

Actin is the most abundant, highly characterized and indispensable cytoskeletal element in eukaryotes. However, the trypanosomatid parasite *Leishmania*, suffers from poor knowledge about this component. For the first time, it is demonstrated that actin is abundantly present and distributed throughout the cell including nucleus and kinetoplast. Further studies revealed that most of the toxins that are known to alter structure and function of conventional-actins are insensitive for *Leishmania*-actin. This unconventional behavior of actin-network in *Leishmania* parasites has therefore received attention as a potential target for therapeutic intervention against leishmaniasis. Analyses of this network includes study of actin itself as well as various actin-binding proteins e.g., coronin, ADF/cofilin, myosin etc., that modulate functions of this cytoskeletal component in the eukaryotic cells.

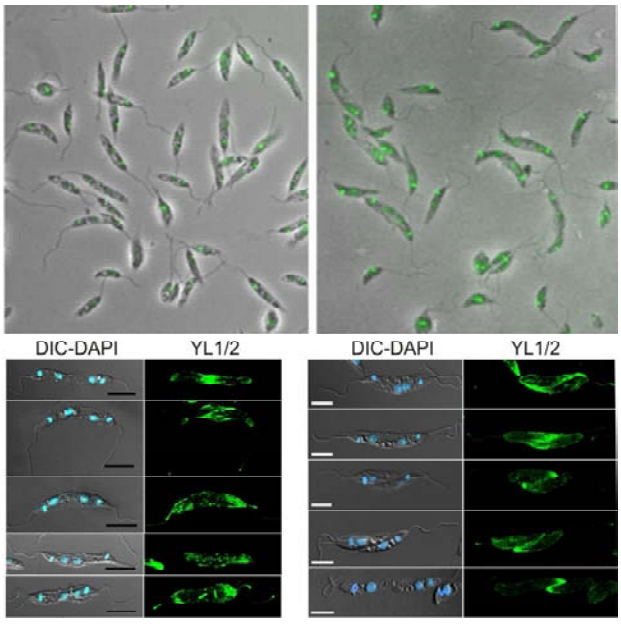
4.2.5.2 Ancient *Leishmania*-coronin (CRN12) is involved in microtubule remodeling during cytokinesis

Previously it was shown that an F-actin binding protein, coronin (Coro), decorates and stabilizes filamentous structures of actin in the *Leishmania* promastigotes. To further analyze functions of coronin in these parasites, we generated coronin-gene knockout mutants and performed detailed cell biological analyses of the phenotypes obtained.



Co-localization of CRN12 with K39 and Centrin

The study shows that besides F-actin, coronin interacts with a microtubule-based motor, kinesin-K39, and regulates dynamics of corset-microtubules during cytokinesis. This protein is also located at the basal body region marked by "Centrin" (Cen) in the cytoskeletal fraction, strengthening the possibility of its interactions with tubulin-based structures.

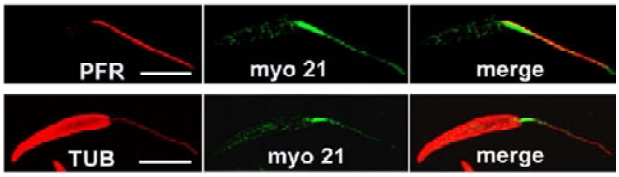


Formation of bipolar cells in CRN12$^{+/-}$ mutants

Depletion of coronin results in generation of bipolar cells due to intrusion of growing microtubule ends in to the daughter cell corsets thereby restricting their separation. However, such cells appear to acquire a unique mode of cytokinesis for the daughter cell separation. Since coronin null mutants could not be obtained and in spite of that an aneuploid population survived, it was concluded that coronin is essential for the survival of these parasites.

4.2.5.3 Flagellar localization of a novel isoform of myosin, myosin XXI, in *Leishmania* (Mol. Biochem. Parasitol. 2009)

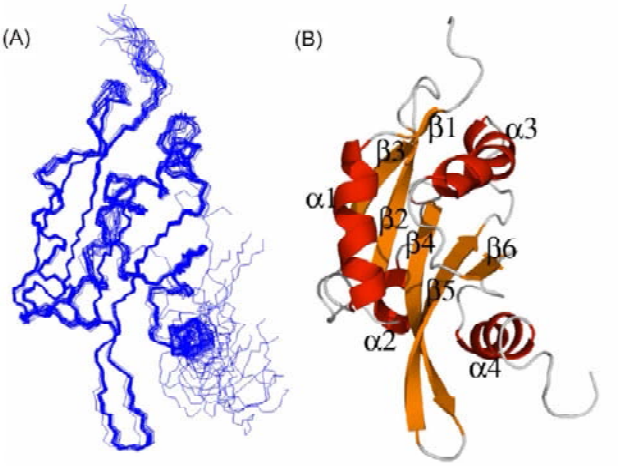
Leishmania cells harbor two myosin genes and recently it has been shown that only one of them i.e., myosinXXI, is detectable in promastigote and amastigote stages. Interestingly, myosinXXI predominantly localized in the proximal region of the flagellum and its expression is greatly reduced in the amastigote stage, which indicated its role in motility and flagellar biogenesis.



Localization of my021 with tubulin and PFR

4.2.5.4 Solution structure and dynamics of ADF/cofilin from *L. donovani*

L. donovani ADF/cofilin (LdCof) is a novel member of ADF/cofilin family. LdCof depolymerizes, but does not co-sediment with, rabbit muscle actin filaments. Its F-actin depolymerizing activity is pH independent. Further, it possesses weak F-actin severing activity. To understand the structural basis of its characteristic properties, we have characterized the solution structure and dynamics of LdCof, and have studied its interaction with actin, using NMR spectroscopy. LdCof possesses a conserved ADF/cofilin fold with a central mixed β-sheet consisting of six β-strands, which is surrounded by four α-helices. Model-free analysis of ^{15}N-relaxation data shows that LdCof exists as a monomer in solution (τ_m = 9.047 ± 0.03 ns). LdCof binds to actin with 1:1 stoichiometry and with high affinity (K_d ~ 0.2 μM). LdCof structure has conserved G/F-actin binding site, and consists of the characteristic long kinked



(A) Superimposition of backbone traces from final ensemble of 20 structures with lowest target function. (B) Ribbon diagram of lowest energy structure of LdCof showing 6 stranded mixed β-sheet surrounded by 4 α-helices. The individual β strands and α helices are labeled. PDB ID: 2KD5.

μ-helix (α3). The α-actin binding site is more open and flexible in LdCof leading to its low F-actin severing activity.

4.3 Filariasis

4.3.1 Synthesis and screening

4.3.1.1 Screening against *in vitro* model

A total of 250 novel entities representing synthetic compounds and natural products from marine or terrestrial sources were evaluated to identify new leads for chemotherapy of filarial worms. Bio-evaluation of 41 fused cyclo-alkylamino pyrimidines derivatives against *B. malayi* adult worms and microfilariae (mf) identified three compounds (S-009-1119, S-009-1120 and S-008-724) affecting both motility and MTT reduction of adult worms at 5-10 μg/ml while higher concentrations (20-40 μg/ml) killed microfilariae (mf).

In addition, 1440 synthetic compounds' outsourced under CDRI–WHO collaboration, were also evaluated for new lead generation. Forty-four of these samples were active *in vitro* at 10 μM concentration against microfilariae while 9 on adult *B. malayi*. Five of these samples acted against both adult and mf. Screening of 264 marine extracts against adult *B. malayi* at 15.6 μg/ml, identified 31 samples for follow up. Minimum effective concentrations for these samples ranged between 1.9 and 15.6 μg/ml and CC_{50} against vero cell line was > 50 μg/ml. Four out of the eight fractions of IIC-857A001, identified earlier, exhibited activity at a minimum concentration of 15.6 μg/ml. Six, out of the 46 new plant extracts evaluated, were also found to be active *in vitro* at 15.6 μg/ml, while the CC_{50} values were >300 μg/ml. Besides, none of the 1290 natural products screened under a CSIR network project for *in vitro* activity against *B. malayi* adult worms and mf at 62.5 μg/ml, did not show any promising response. A pure compound K002 obtained from the fraction F001 of plant extract NBR 0014 P04 was found to be active on adult worm at 31.25 μg/ml.

4.3.1.2 Screening against *in vivo* model

Three previously identified plant extracts 4722A001, 4723A001 and 4726A001 were evaluated *in vivo* against *B. malayi - Mastomys coucha* model after oral administration at 500 - 1000 mg/kg in 5 day regimen. 4723A001 showed low antifilarial action *in vivo* in mastomys while 4726A001 exerted ~42.8% adulticidal action over control with no female worm sterility, while 4722A001 demonstrated moderate adulticidal (44%) activity at 1g/kg, p.o. x 5 days in *B. malayi*-mastomys model. Bioassay guided fractionation studies to identify leads are also underway with plant extracts MAP 2443 P03, ICB 1851 P01, IHB 1429 P14.

4.3.1.3 Antifilarial activity of marine sponge (Parasitol. Res., 2009, *105*, 1295–1301)

The crude methanol extract and n-butanol-soluble fraction of marine sponge *Haliclona exigua* killed adult *Brugia malayi* at 31.25 μg/ml concentration while chloroform fraction was lethal at 15.6 μg/ml. The activity could be located in a single molecule araguspongin C, which brought about mortality of worm at 15.6 μg/ml. *In vivo* the crude extract (5×500 mg/kg orally) and the chloroform fraction (5×250 mg/kg orally) in *B. malayi* infected mastomys, led to reduced microfilarial densities apart from adulticidal action which was more pronounced in the chloroform fraction (50.2%) with moderate adverse effect on the reproductive potential of female worm. The antifilarial action could be attributed to the presence of compound araguspongin C.

4.3.2 Identification, Characterization and Validation of Drug/Vaccine Targets

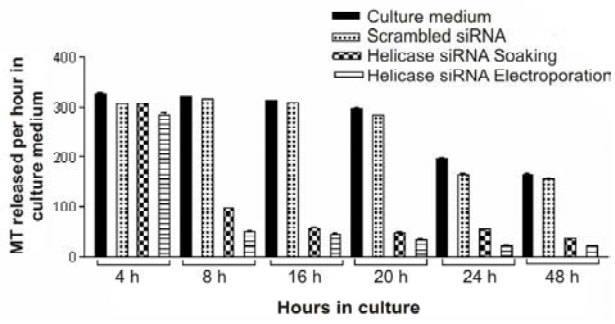
4.3.2.1 *B. malayi* hexokinase

Hexokinase (ATP: D-hexose-6-phospho-transferase, EC 2.7.1.1.) is the key regulatory enzyme of glycolytic pathway catalyzing the transfer of a phosphoryl group from ATP to glucose to form glucose-6-phosphate. Full length cloning and characterization of *Brugia malayi*

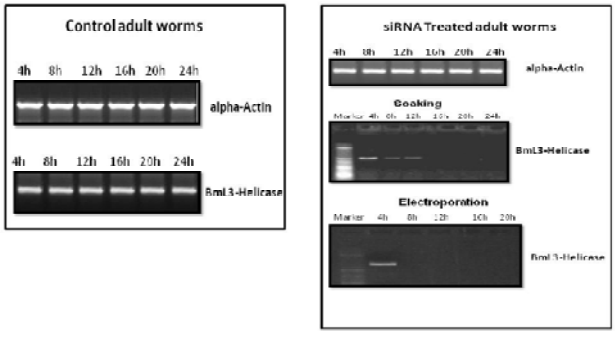
hexokinase was reported earlier. Changes in the molecular dimension of the protein were studied by size exclusion chromatography. With the aim to explore the structural similarity of BmHk with existing hexokinases, a 3D-homology model of BmHk was also constructed which was similar to the 3D-structure of HuHk I. The refined model when validated by a series of tests for its internal consistency and reliability clearly suggested the backbone conformations of our BmHk model to be nearly as good as those of template. Mutant BmHk was developed by carried out mutations at two sites of G6P binding motifs (DLGG**T**^{120}NLRV and II**A**^{262}TG). At one mutation site, threonine (Thr^{120}) was replaced by serine (Ser) and at other mutation site alanine (Ala^{262}) was replaced by glycine (Gly). The mutations were incorporated at the G6P binding site in BmHk sequence using sense and anti-sense primers. The mutant BmHk was sequenced and checked for incorporation of mutations at appropriate sites and the mutant protein was expressed and purified. The enzyme activity of mutant protein was monitored in presence of G6P, which showed some change in fold activation as compared to wild BmHk.

4.3.2.2 *B. malayi* DEAD box RNA helicase

The DEAD/H box families of RNA Helicases are a multifunctional group of proteins involved in unwinding of inter- and intra-molecular base-paired regions. DEAD box RNA Helicase gene (BmL3-Helicase) of human lymphatic filarial parasite *B. malayi* was successfully knocked down by specifically designed and chemically synthesized small sized siRNA of <20 bp by electroporation as well as soaking, former method being more efficient. The diminished helicase gene expression adversely affected the *in vitro* release of microfilariae (87.5% reduction) from adult females and also their viability (98%). The male worms died within 20 hours of exposure to siRNA while motility of the female parasites reduced to half and proved detrimental to intrauterine development of embryos and phenotypic deformities *in utero*. RT-PCR of siRNA treated worms confirmed complete knockdown of BmL3-Helicase transcription after 16 hours.

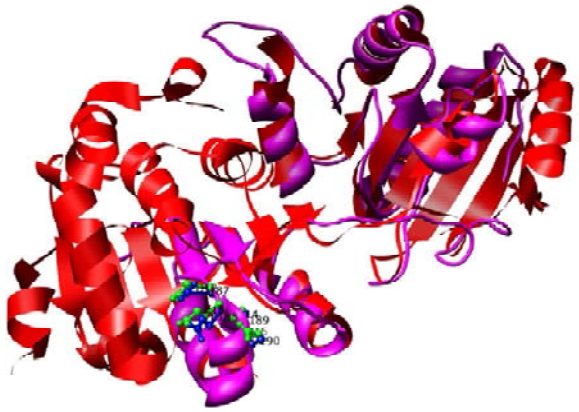


Effect of SiRNA on Mf release



RT-PCR confirmation of gene silencing

The 3D structure of BmL3-Helicase was constructed to further ease the *in silico* screening and synthesis of specific enzyme inhibitors. The sequence of *B. malayi* RNA helicase cDNA was translated in all three reading frames and frame 3 was selected for homology modeling as its probability of representing the protein was enhanced by the presence of highly conserved DEAD and SAT domains. Several crystal structures of DEAD box RNA helicases from various sources have been reported, however, no reports contain data regarding the 3-dimensional structure of RNA helicases from any helminth species including *C. elegans* or filarial species. Of the various BLAST hits, the highest scoring human RNA helicase with 25% sequence identity and 48% sequence similarity was chosen as a structural template for homology modeling. Superposition of the BmL3-helicase homology model on the template also revealed a close structural resemblance, which, along with non-variant similarities in DEAD and SAT domains of both the proteins, indicated the high conservation.



The 3-D model of *B. malayi* RNA Helicase constructed by homology modeling [The conserved domains are marked with red which includes DEAD and SAT domains responsible for ATP hydrolysis and RNA unwinding. BmL3-Helicase model (purple) was superimposed with the *Homo sapiens* RNA Helicase crystal structure (red)].

4.3.2.3 Filarial acetylcholinesterase

PCR amplification of gene coding for filarial AchE using primers designed from the conserved sequences of AchE from related organisms was earlier attempted, however, the clones showed homology to esterase but not significant homology to specific AchE sequence. Polyclonal antibody produced against the electric eel AchE (eAchE) was cross-reactive with filarial AchE and therefore used to immunoscreen *B. malayi* lgt11 cDNA expression library. Four cDNA clones were purified and gene was amplified using AchE specific and lambda primers in combination to obtain PCR products of 0.9 kb, 0.3 kb from two cDNA clones and 0.6 kb from other two cDNA clones which have been sub-cloned and sequenced for characterization. In order to identify the full-length Ache gene, primers were designed from the C terminal region of the known AchE sequences. Different primer pairs tried in combination in PCR using *S. cervi* genomic DNA and *B. malayi* cDNA. Two AchE gene fragments of 0.8 and 0.4 kb were obtained with *Setaria* genomic DNA and 1.8 kb with *B. malayi* cDNA which were subcloned and sequenced. The 0.4 kb PCR product from *S. cervi* showed homology to carboxylesterase type B signature sequence which is a highly conserved sequence in AchE from different sources. Efforts are under way to get the complete sequence of 1.8 kb *B. malayi* cDNA.

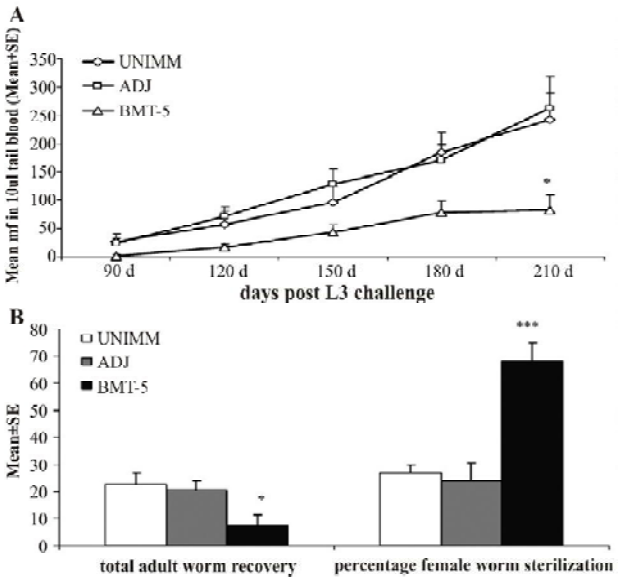
4.3.2.4 *B. malayi* Co-factor independent phosphoglycerate mutase and trehalose 6 phosphate phosphatase (TPP)

Both TPP and *i*PGM are absent from mammals making these two enzymes as promising antifilarial drug vaccine target. TPP and *i*PGM enzymes of adult *B. malayi* were cloned, expressed and purified as ~60 kDa and ~58 kDa proteins respectively and their expression was confirmed on western blot using anti-His antibody. The recombinant proteins were found cross-reactive with various categories of human bancroftian sera. For immunological characterization, both recombinant proteins were individually administered along with FCA/ FIA in Balb/c mice. Various immunological parameters were accessed by flow cytometry. Immunization with Bm*i*PGM resulted in to Th1/Th2 type of mixed immune response however it was more Th1 biased in case of TPP. A significant rise in IgG antibody level was observed along with specific increase in IgG1, IgG2a, and IgG2b isotypes showing a mixed response. An increase in both anti-inflammatory and pro-inflammatory cytokines was also noticed. The proteins also stimulated murine macrophages as evidenced by an increased ROS generation. The resistant serum caused *in vitro* adherence of peritoneal cells (ADCC) to the surface of microfilariae (mf) and infective larvae (L3) of *B. malayi* causing cytotoxicity and their immobility and death. Their immunoprophylactic potential was assessed after one month of infective larvae challenge in mastomys vaccinated with rBm-TPP and rBm-*i*PGM along with adjuvant FCA and FIA achieving 64.48% and 45.47% reductions in adult worm establishment in rBm-TPP and rBm-*i*PGM respectively post *B. malayi* L3 challenge. The immunized-challenged animals showed increased Treg cell population, their activation ligand CTLA4 with expansion in CD4+ and CD8+ cell population and decrease in T cell activation markers CD45+/CD30+ with enhanced production of both pro-inflammatory and anti-inflammatory cytokines.

4.3.3 Immunological Studies

4.3.3.1 *B. malayi* ~34 kDa (BMT-5) antigen offers protection against challenge (Journal of Helminthology, 2009, *83*, 83–95; Parasitology International, 2009, *58*, 346-35).

Mitochondria rich (MT) fraction of adult *B. malayi* was earlier reported to offer sizeable protection in mastomys. To locate the protective molecules in this fraction, MT was subjected to further fractionation and one of the eight sub fraction (BMT-5) with a molecular mass of ~34 kDa produced utmost cellular proliferation and therefore exploited for vaccination study. BMT-5 emulsified in Freund's adjuvant produced discernible protection causing 69 and 67% reductions in microfilaraemia and adult worm burden respectively along with sterilization of 68% of the recovered female parasites.



Significant levels of filaria-specific and non-specific lymphoproliferation along with enhanced release of Th1 cytokines (TNF-α, IFN-γ and IL-2) by splenocytes were observed in the vaccinated mastomys in addition to elevated levels of antigen-specific IgG, IgG2a, IgG2b and IgA. The peritoneal macrophages of immunized animals also revealed enhanced nitric oxide production in the presence of BMT-5 suggesting the immunoprophylactic efficacy of MT rich fraction was due to presence of ~34 kDa BMT-5 molecules which generated a Th1 biased milieu in the host.

4.3.3.2 Vaccination with recombinant *B. malayi* heavy chain myosin using various adjuvant and delivery system

Three adjuvants viz. Freund's complete and incomplete adjuvant, montanide and alum FCA/FIA were employed to assess vaccine efficacy of recombinant heavy chain myosin of *B. malayi*. Both the human compatible adjuvants (montanide and alum) could not provide an edge over FCA/FIA adjuvant in terms of degree of protection against infective larval challenge in mastomys model, however, myosin in combination with alum adjuvant provided protection more or less akin to that of antigen+Freund's adjuvant. In addition, alum adsorbed myosin conferred better protection in jird model as compared to FCA. To improve the vaccination efficacy of recombinant myosin, the protein was entrapped in egg-PC liposomes and *E. coli* lipid liposomes (escheriosome). Liposome enhanced the immunization efficacy of myosin over FCA group while escheriosome revealed still better protection in two antigen doses at a reduced protein concentration of 10 µg/animal.

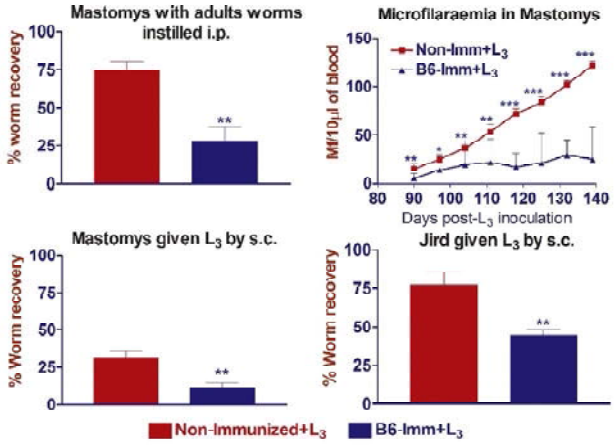
4.3.3.3 Identification and characterization of *S. cervi* antigen equivalent to filarial circulating antigen

Circulating parasite antigens are the key modulators or targets of immune system. Previously *S. cervi* antigen (recognized by monoclonal antibody against filarial circulating antigen) was purified and used for the production of polyclonal antibodies. Out of the four cDNA clones, identified by immuno-screening of *B. malayi* lgt11 cDNA expression library with polyclonal antibodies (against purified antigen), one cDNA clone was sub-cloned and expressed as fusion protein of 55 kDa. As the recombinant protein was present in the inclusion bodies, the bacterial cells were lysed by sonication and the lysate was used for the purification of recombinant protein employing Ni-NTA affinity column. The purified protein showed high ELISA reactivity with filarial patients sera and was recognized by filarial patients serum pool but not by the non-filarial serum pool in immunoblotting. The immunoreactivity of the recombinant protein was tested in ELISA using individual sera from filarial and non-filarial patients as well as non-endemic control sera. Significantly high IgG and IgG4 antibody responses were detected in filarial patient's sera. No significant reactivity of recombinant protein was observed with non-filarial patient's sera. The diagnostic potential of recombinant protein will be evaluated using large number of filarial patients' sera.

4.3.3.4 Characterization of inflammation-modulating molecules of *B. malayi*

(a) Pro-inflammatory mediator stimulating fraction induces a Th1/Th2- immune response and confers protection (Vaccine, 2009, *27*, 4263-4271)

Filarial parasite antigens modulate the immune response through inflammatory mediators, which eventually protect the parasite or host from the parasite or produce pathology. However, the precise identity of such potential molecules is not known. Earlier studies revealed that a pro-inflammatory cytokine stimulating fraction B6 (54.3-67.8kDa) of *B. malayi* adult extract demonstrated protective efficacy against L_3 establishment in *M. coucha* through Th1/Th2 type of responses with greater predisposal towards Th1 response. Presently, protective efficacy of the fraction was validated against L_3-induced *B. malayi* infection in jird, as indicated in the figure. A remarkable reduction in intraperitoneally implanted adult worms in immunized *M. coucha* was found to be associated with upregulation of NO, TNF-α and IL-6 but not IL-10 release in macrophages/splenocytes. The findings further suggest that elimination of parasites

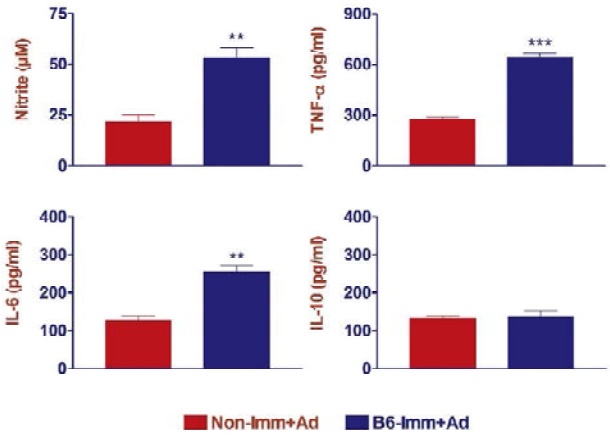


Microfilaremia profile and worm recovery in immunized animals

largely depends on Th1 response. One of the immunostimulatory proteins (HSP60) identified earlier by MALDI TOF in B6 fraction was cloned and expressed. Purification and characterization of the protein is in progress.

(b) Nitric oxide (NO)

NO is a multi-faceted molecule with regulatory roles including toxic defense against infectious organisms including filarial parasites. To identify the precise identity of NO inducing molecules of filarial parasites, three NO stimulating fractions of *B. malayi* adult worm extract were identified. *M. coucha* were immunized with the fractions and challenged with L_3. Fraction B8 (45.2-48.6kDa) was found to offer protection against the larvae demonstrating 60-75% reduced microfilarial density and 61% decrease in adult worm establishment in *M. coucha* over non-immunized controls. Immunological findings revealed that the fraction effectively suppresses parasite establishment by inducing favorable protective responses as evidenced

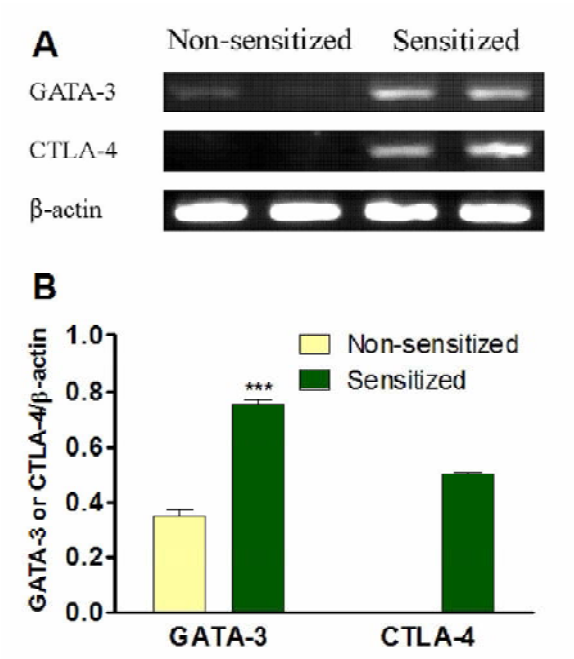


Response of nitric oxide, IL-6, TNF-α and IL-10 in macrophages/ splenocytes of B6-immunized *M. coucha* infected with adult worms of *B. malayi* in peritoneal cavity.

by up-regulation of NO production, cellular proliferation, IgG, CD4+ T cells and down-regulation of TGF-β production.

(c) Anti-inflammatory fraction facilitates survival and development of parasites in the hostile peritoneal cavity of *Mastomys coucha*

Anti-inflammatory cytokine (IL-10 and TGF-β) network plays an important role in modulation of effector mechanisms of the host against parasite survival/ invasion in filarial infection. BmAFI, a sephadex G-200 fraction of *B. malayi* adult worm and IL-10 release stimulating potential was earlier reported to facilitate survival and development



Gene expression for GATA-3 and CTLA-4 normalized to β-actin expression (A) and densitometric analysis (B)

of infective larva (L_3) in the peritoneal cavity (p.c.). Presently we have initiated immune characterization of host responses to the fraction using various parameters with an aim to get an insight into the immune function responsible for supporting parasite survival and development. Sensitization with the fraction upregulated Th2 cytokine release (TGF-β, IL-10), and specific IgG1 and IgG2b but not IgE, and downregulated cellular proliferation, inflammatory cytokine and nitric oxide production. GATA-3 and CTLA-4 mRNA expression was significantly increased in sensitized animals (Fig. above A,B). The results indicate that a Tr1 response evoked by the fraction facilitates parasite development and survival in the hostile p.c. of *M. coucha*.

4.3.3.5 Immuno-modulators from plants for use as immuno-prophylactant and/or chemotherapy adjunct against parasitic infections

Immunomodulators of natural, synthetic and recombinant origin can stimulate host defense mechanisms for the prophylaxis and as novel adjunct treatment to established antimicrobial, antiviral and antiparasitic or antifungal therapies. These have also been shown to adversely affect various infections when used prophylactically or when used in combination with chemotherapeutics or vaccines. A few plant extracts and synthetic compounds were assayed for their effect on the

various immune parameters of Balb/c mice viz. proliferation of T/ B lymphocytes, production of ROS, expansion of CD4+, CD8+ and CD19+ cells and Th1/Th2 cytokine responses. The crude extract from plant extract 4738 A001was found to stimulate mouse immune responses at various doses (3, 10 and 30 mg/kg) when administered orally for 14 consecutive days. The activity was localized in two fractions F002 and F003. Two other plants 4740A001 and 4743A001 showed dose dependent immunostimulation while 4741A001 was not that effective and exerted effective immune-stimulant only at 10 mg/kg. A001 and A002 preparations from plant 4742, on contrary, revealed a dose dependent immunosuppressive action. *Tinospora cordifolia* polysaccharide was highly effective showing highest immunostimulation *in vivo* at 1.0 mg/kg. The crude ethanol extracts of *Withania coagulans* and plant 3833C002 were ineffective. The extract from *Ashwagandha nagori* variety also did not show any convincing immunomodulation at 3, 10 or 30 mg/kg in Balb/c mice on oral administration for 14 days.

5. Reproductive Health Research, Diabetes & Energy Metabolism

Coordinator:
Dr. Naibedya Chattopadhyay

Assistant coordinators:
Dr. Gopal Gupta
Dr. Sabyasachi Sanyal

Area Leader:
Dr. Arvind Srivastava

- Designing and synthesizing novel molecules/isolates from natural sources and evaluating them for their bioactive potential, generating new leads for developing them as female or male contraceptives, spermicides with anti-STI properties, agents for the management of post-menopausal osteoporosis and other endocrine disorders; evaluating traditional remedies for fertility regulation and endocrine disorders; understanding the mode of action of promising agents and undertaking basic research to generate new knowledge on female and male reproductive endocrinology relevant to fertility regulation;
- Discovering of targeted therapeutic leads in type II diabetes mellitus (T2DM) and hyperlipidemic conditions for potential preclinical development;
- Understanding pharmacological basis of actions of existing and potential therapeutics in T2DM and hyperlipidemic conditions.

5.1 Reproductive Health Research

5.1.1 Preliminary Safety Assessment of a Vaginal Contraceptive

Preliminary *in vivo* vaginal safety of S-003-296 was evaluated in rats by following a standard method. 10 mg of S-003-296 or nonoxynol-9 (N-9) was delivered in the vagina of young adult female rats with the help of a 16 G syringe-needle. Control rats received vehicle only. The animals were autopsied after 24 hours of treatment and vaginae were fixed in 10% buffered formaldehyde and later embedded in paraffin wax. 5 micron sections were cut using a microtome and stained with eosin-hematoxylin. S-003-296 did not cause any detectable damage to vaginal epithelium (Fig. 1B) at 10 mg vaginal dose (50 times the minimum effective contraceptive dose). Rats treated vaginally with 10 mg S-003-296 for 24 hours bore normal vaginal histological features comparable to controls (Fig. 1A). On the other hand, N-9 at 10 mg caused distinct

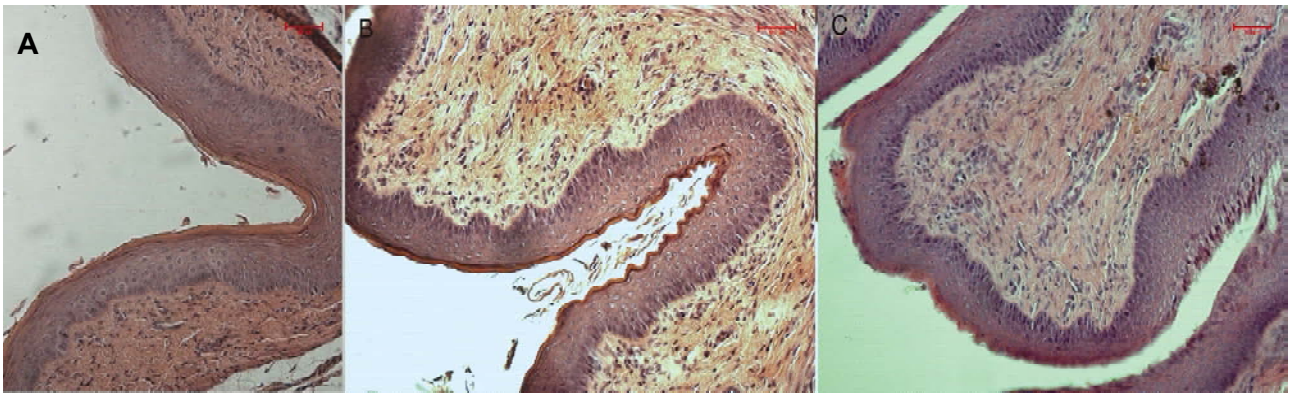


Fig.1: Rat vaginal histology indicating the safety of S003-296 as a vaginal contraceptive over N-9

erosion of the lining of vaginal epithelium and exhibited conspicuous "washing-off" effect due to detergent action (Fig. 1C).

5.1.2 Rationally Designed Testosterone Delivery System for Male Contraceptive/Hormone Supplementation

Selected transdermal formulation delivering pulsatile testosterone to fertile male rats strongly suggested contraceptive efficacy with significantly smaller doses than that reported in literature. The work also enabled partial testing of a hypothesis that pulsatile stimulation by gonadotropin-releasing hormone (GnRH) is essential for function/survival of mature pituitary gonadotrophes as well as differentiation/maturation of their precursors. Massive apoptosis was observed in the anterior pituitary when endogenous GnRH pulsatility was inhibited by exogenous pulsatile testosterone delivery through transdermal formulation. A computation model describing the rates of decline and recovery of pituitary gonadotrophe populations on imposition and removal of GnRH suppression was developed.

5.1.3 Nanoparticles as Self-administered Contraception for Women

Nanoparticles composed of biocompatible, biodegradable material, which cross the cervical barrier when instilled into the vagina, were tested for contraceptive efficacy in female mice. No significant reduction in conceptions per estrus cycle was observed, implying that such nanoparticles would not function as stand-alone contraceptive agents.

5.1.4 Development of Anti-Implantation and Early Post-Implantation Pregnancy Interceptive Agents

5.1.4.1 Evaluation of RBA for estrogen receptors

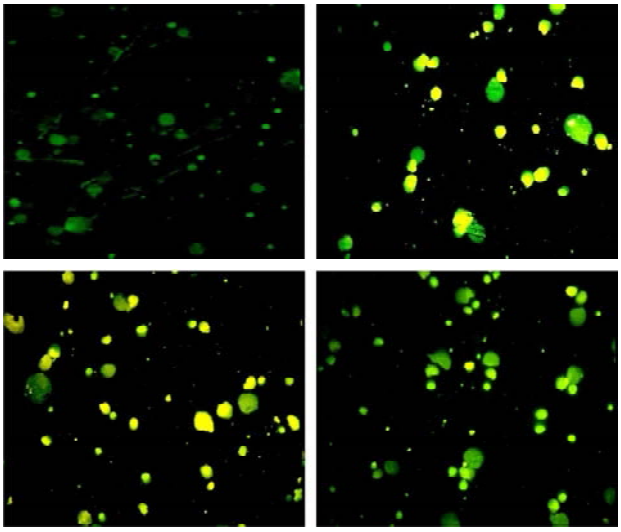
In an ongoing program on development of selective estrogen receptor modulators as anti-implantation/ anticancer agents for the treatment of breast cancer, the relative binding affinity of 16 compounds was evaluated for uterine estrogen receptor (ER). Results revealed that compounds S-008-701, -971, -1255 and -1480 showed RBA of 0.01 to 0.1 %., S-008-700, -703, -704, -705, -706, -707, -971 and -972 showed RBA of 0.1% to 0.5% of estradiol whereas compound S-008-702 showed the RBA of 1-2 % of estradiol. Rest of the compounds was inactive.

5.1.4.2 Evaluation of anti-implantation activity of synthetic compounds / natural products

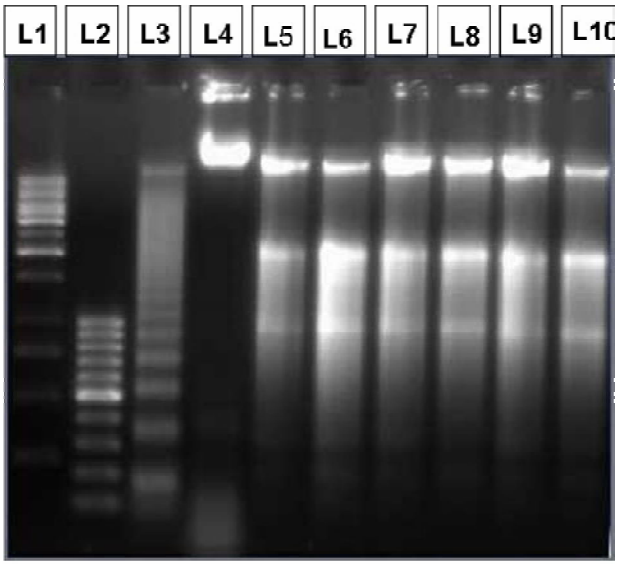
Thirty seven synthetic compounds and 31 extracts of natural origin were tested for anti-implantation-cum-early post implantation interceptive activity in adult female Sprague Dawley rats when administered on days 1-7 post-coitum by oral route. Of these, four synthetic compounds S-008-413, -414, -514 and -700, showed 100% activity at 10 mg/kg dose while compound S-008-702 showed similar activity at 5 mg/kg dose. None of the plant/marine extracts showed desired efficacy.

5.1.5 Studies on 2,3-Diaryl-2H-1-Benzopyran Derivatives as Therapeutic Agents for Endometrial Hyperplasia / Endometrial Cancer

Benzopyran derivatives exhibit significant anti-estrogenic activity and inhibit uterine growth and proliferation of endometrial cancer cells. The present study was undertaken to explore the mechanism of anti-proliferative action of three derivatives (85/287-I, II and III) in human endometrial cancer cells. Results revealed that these derivatives induced apoptosis of endometrial cancer cells in a concentration dependent manner. Derivatives I, II and III induce apoptosis in ishikawa cells through caspase-9 mediated (intrinsic) pathway. These compounds also decreased the XIAP expression and interfered with Akt activation leading to decreased Bcl2: Bax ratio. Results suggest that these benzopyran derivatives are selective apoptosis inducer in endometrial



Induction of apoptosis in Ishikawa endometrial cancer cells in response to benzopyran derivatives I, II and III, as observed by TUNEL assay



DNA fregmentation in Ishikawa cells under the influence of derivatives I, II and –III. Electrophoresis of genomic DNA (2 X 106 cells/lane) on 1% agarose gel. (L1 and L2, DNA marker; L3, positive control; L4, control; L5, I -10 µM; L6,I-15 µM; L7, II-10 µM; L8,II-15 µM; L9; III-10 µM; L10,III-15µM

cancer cells and can be potent therapeutic agents in endometrial cancer of uterus.

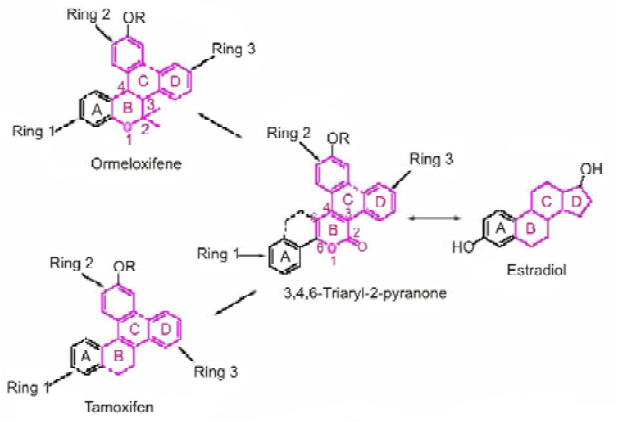
5.1.6 Development of Anticancer Agents for Treatment of Breast Cancer

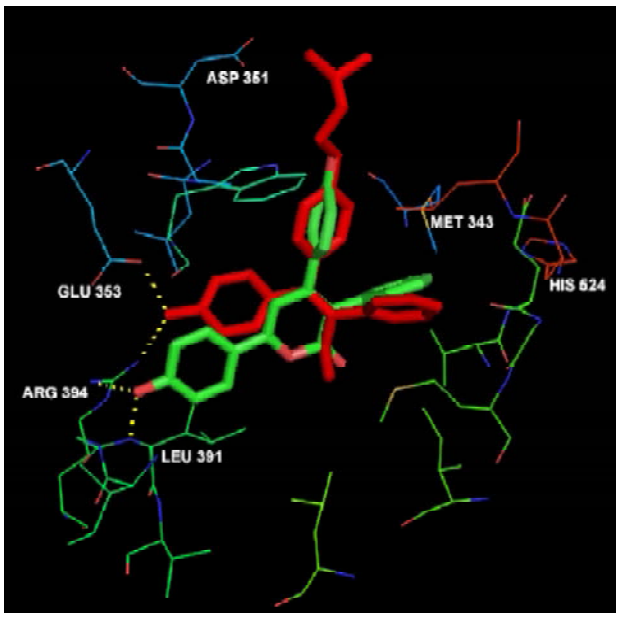
5.1.6.1 Screening

Forty compounds, belonging to two different prototypes, were evaluated for anti-proliferative activity in human breast cancer cells. Four compounds viz. S-008-702, -707, S-009-613 and -637 were found to be active. Among these, two lead compounds, viz. S-009-613 and S-009-637 showed IC_{50} of 8 µM in MCF-7 cells and 3-6 µM in MDA-MB cells and appear to be safer in comparison to Tamoxifen in terms of general cytotoxicity. Both compounds caused induction of apoptosis and cell cycle arrest at G1 phase.

5.1.6.2 Triaryl pyranones as new class of compounds for treatment of breast cancer

A series of 3,4,6-triaryl-2-pyranones, have been synthesized as a structural variants of cyclic triphenylethylenes by replacing the fused benzene ring with pendant phenyl ring to mimic the phenolic A ring of estradiol. Nine of these newly synthesized pyranones exhibited significant anti-proliferative activity in ER+ve and ER-ve breast cancer cell lines. Four active non-cytotoxic



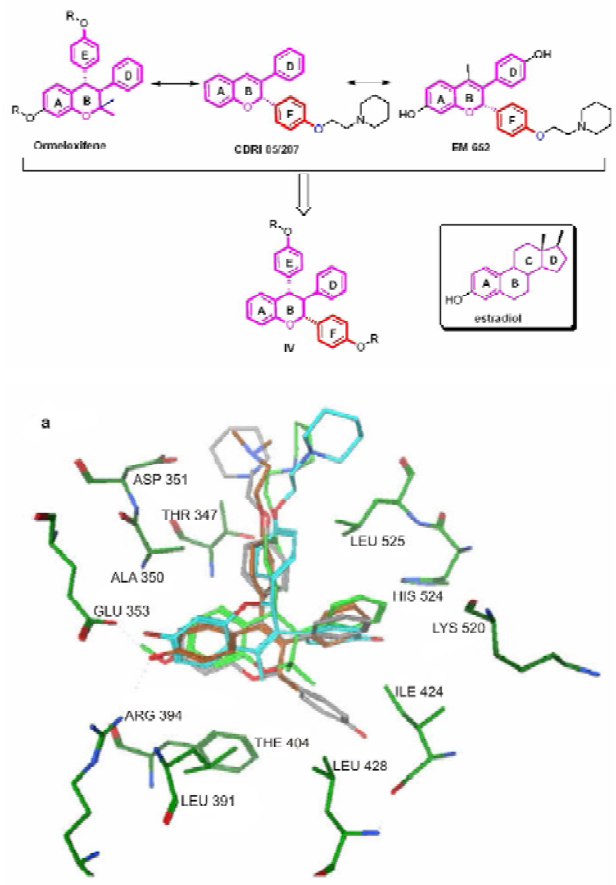


Structural resemblance of 3,4,6, triaryl-2-pyranones to tamoxifen, estradiol and ormeloxifene.

compounds S-007-153, -154, -155 and -158 showed specific and selective cytotoxicity and two compounds S-007-153 and -154 induced significant DNA fragmentation in MCF-7 and MDA-MB-231 cell lines. Based on RBA studies, the molecules probably act in an ER-independent mechanism. The involved pathway was observed as caspase-dependant apoptosis in MCF-7 cells. However, the particular caspases involved and the possible cellular target through which this series of compounds mediate cell death are not known.

5.1.6.3 2,3,4-Triarylbenzopyran derivatives for treatment of breast cancer

A novel class of 2,3,4-triarylbenzopyrans has been synthesized and were evaluated for their selective estrogen



Structural resemblance of 2,3,4-triaryl benzopyrans l to potential SERMs.

receptor modulation activity and as a therapeutic agent for treatment of breast cancer.

Among the compounds synthesized, compounds S-008-971 and S-008-165 exhibited 73.91% and 69.24% inhibition as estrogen antagonistic activity, respectively. Compound S-008-165 showed the lowest IC_{50} at 6.97 µM against MCF-7 and showed the lowest IC_{50} value of 5.6 µM against MDA-MB-231 cell line in spite of their low receptor binding affinity implicating these compounds probably act through ER independent mechanism.

5.1.6.4 Benzoxazepine derivatives for treatment of breast cancer

A series of new benzoxazepine derivatives substituted with different alkoxy and aryloxy group were synthesized and they specifically inhibited growth of breast cancer cell lines, MCF-7 and MDA-MB-231, but lack cytotoxicity to normal HEK-293 cells. The cell growth inhibition induced by the active compounds was due to cell cycle arrest at G0/G1 phase. The active compound could cause significant reduction in tumor volume of MCF-7 xenograft tumor in nude mice model and their activity was comparable to that of Tamoxifen citrate at 16 mg/kg dose at 30 days of treatment. The identified most active compounds of the series have specific advantages as anticancer agent in breast cancer than Tamoxifen.

5.1.7 Development of Agents for Management of Benign Prostatic Hyperplasia (BPH)

A series of twenty seven aryl/heteroaryl/aralkyl/aroyl piperazines were synthesized and evaluated for their effect on rat prostate. Most of these compounds reduced the prostate size in the range of 15-47%. Three compounds, S-007-967, -972 and S-008-315, showed better activity profile (decreased the size of prostate in rat by 47%, 43% and 39% respectively) than the standard drug finasteride (32%). QSAR study exhibited the positive influence of number of rotable bonds on activity. The phamcokinetic study of compound S-007-967 at an oral dose of 10 mg/kg suggested that these piperazines are well absorbed and insignificant amount of extrahepatic elimination takes place. Therefore, further lead optimization may yield a potent agent for the management of BPH.

5.1.8 Development of Anti-osteoporosis Agents

5.1.8.1 Identification of a fraction from the stem bark of plant 914 for optimum bone health

Objective of this study was to determine the skeletal effects of total ethanolic extract and its fraction from the stem bark of a plant, rich in C-glycosylated flavonoids, in growing rats [for peak bone (PB) achievement] and in ovariectomized (OVx) rats (for menopausal bone loss). In growing rats, both the extracts increased BMD, bone strength and bone formation rate suggesting higher PB achievement. OVx rats treated with either these extracts exhibited increased BMD at various anatomical positions and improved bone strength and trabecular architecture compared with OVx + vehicle group. Serum osteoclacin and urinary CTx levels in OVx rats treated with either TEE or BF were significantly lower than OVx + vehicle group. Neither TEE nor BF exhibited uterine estrogenicity. Analysis of marker compounds revealed significant enrichment of two bioactive markers in BF over TEE.

5.1.8.1 A novel flavonoid, 6-C-β-D-glucopyranosyl-(2S,3S)-(+)-3',4',5,7-tetrahydroxy-flavanone (GTDF)

Having demonstrated that a standardized extract from the stem-bark of plant 914 had beneficial outcome

on bone health of ovariectomized (OVx) rats, examination of GTDF/ Ulmoside A, a new compound isolated from the extract, was carried out so as to estabilish whether it has bone sparing effect in OVx rats. It was concluded that GTDF is a novel compound present in 914 extract that improves bone biomechanical quality through modifications of BMD, and trabecular microarchitecture without hyperplastic effect on uterus. Its prolonged systemic availability underscores additional benefit of GTDF for potential therapeutic use in postmenopausal osteoporosis.

5.1.8.2 Naringenin-6-C-β-D-glucopyranoside (NG) and (2S,3S)-(+)-4',5,7-trihydroxy-dihydroflavonol-6-C-β-D-glucopyranoside (TDFG)

NG at 100 nM promoted osteoblast differentiation and mineralization. At the same concentration, NG also inhibited differentiation of 3T3-L1 preadipocytes to mature adipocytes. Furthermore, when murine bone marrow cells were differentiated to mature adipocytes in the presence of a differentiation cocktail containing IBMX, insulin, dexamethasone and indomethasine, presence of 100 nM NG significantly inhibited differentiation of mesenchymal stem cells (MSCs) to adipocyte. NG, in addition, inhibited expression of mRNA levels of PPARγ, CEBP and aP2 in 3T3-L1 cells, indicating inhibition of adipocyte differentiation.

Very much similar to NG, TDFG also promotes osteoblast differentiation and inhibits adipocyte differentiation. TDFG at 100 nM promoted osteoblast differentiation and mineralization. At the same concentration, TDFG also inhibited differentiation of 3T3-L1 preadipocytes to mature adipocytes. Furthermore, when murine bone marrow cells were differentiated to mature adipocytes in the presence of a differentiation cocktail containing IBMX, insulin, dexamethasone and indomethasine, presence of 100 nM TDFG significantly inhibited differentiation of mesenchymal stem cells (MSCs) to adipocyte. TDFG, in addition, inhibits expression of mRNA levels of PPARγ, CEBP and aP2 in 3T3-L1 cells, indicating inhibition of adipocyte differentiation.

5.1.8.3 8,8"-Biapigeninyl stimulates osteoblast functions and inhibits osteoclast and adipocyte functions: Osteoprotective action of 8,8"-biapigeninyl in ovariectomized mice

8,8"-biapigeninyl (BA) is a condensation product of two apigenin molecules and is found abundantly in the nuts of *Cupressus sempervirens*. Effects of BA on murine bone cells *in vitro* and in ovariectomized (OVx) mice were investigated. BA at 10^{-10}M and 10^{-8}M, inhibited osteoclastogenesis of bone marrow cells (BMCs) and displayed concentration dependence. BA at 10^{-8}M and 10^{-6}M inhibited differentiation of 3T3-L1 preadipocyte cells and BMCs to mature adipocytes. BA (10^{-10}M) stimulated osteoblast proliferation, differentiation and mineralization. In stimulating osteoblast function, BA was found to be 10^{4}-fold more potent than apigenin. The effect of BA in osteoblasts appeared to be mediated via estrogen receptors (ER) as antiestrogen ICI-182780 abolished BA-stimulated osteoblast differentiation. In OVx mice BA treatment given orally for 30 days (at 1.0, 5.0 and 10.0 mg/kg/day doses) dose-dependently inhibited mRNA levels of osteoclastic genes including tartrate resistant acid phosphatase, receptor activator of nuclear factor (RANK), tumor necrosis factor alpha, interleukin-6 and the RANK ligand/osteoprotegerin ratio in bones compared with OVx mice treated with vehicle. In addition, BA treatment to OVx rats dose-dependently stimulated production of osteoprogenitor cells in the bone marrow and increased mRNA levels of osteogenic genes core binding factor alpha-1, type I collagen and bone morphogenic protein-2 in bones compared with OVx + vehicle group. Microcomputed tomography revealed that BA treatment to OVx mice improved parameters of trabecular microarchitecure. BA exhibited no uterine estrogenicity. From these data, we conclude that BA exerts osteoprotective effect in OVx mice by multiple beneficial effects on bone cells.

5.1.8.4 Standardized fraction from the stem-bark of a plant has non-estrogenic osteoprotective action

Objective of this study was to determine the skeletal effects of the total extract (BTE) and its acetone soluble fraction (ASF), rich in methoxyisoflavones, in ovariectomized (OVx) rats, a model for postmenopausal bone loss. BTE (1.0 g/kg/day) and ASF (100 g/kg/day) were given orally for 12 weeks to adult OVx rats. Sham-operated and OVx + vehicle groups served as controls. Bone mineral density (BMD), osteoid formation (MAR and BFR), bone microarchitecture and bone turnover/resorption markers were studied. Bioactive marker compounds in BTE and ASF were analyzed by HPLC.

OVx rats treated with either BTE or ASF exhibited increased BMD in trabecular bones and improved trabecular architecture compared with OVx + vehicle group. Serum osteoclacin and urinary CTx levels in OVx rats treated with either BTE or ASF were significantly lower than OVx + vehicle group. ASF treatment led to increased MAR and BFR compared with OVx + vehicle group while BTE had no such effect. ASF was found to be devoid of any estrogenic effect in the uterus while BTE was found to be

slightly estrogenic. Analysis of marker compounds revealed significant enrichment of three bioactive markers in ASF over BTE. It is concluded that ASF at 10-fold lower dose than BTE was effective in preventing OVx-induced bone loss and stimulated new bone formation.

5.1.8.5 Osteoprotective effect of two methoxylated daidzeins, cladrin and formononetin is mediated via activation of Mek-Erk and p38 mapk pathways by an estrogen receptor-independent mechanism

Daidzein, a phytoestrogen, is known to have bone-sparing effects under estrogen deficiency. Following a lead from stem-bark extract of *Butea monosperma,* used for rapid fracture healing in traditional Indian medicine, two structurally related methoxydaidzeins; cladrin and formononetin were studied for their effects in osteoblasts *in vitro* and bone formation *in vivo*. Whereas, cladrin at 10 nM maximally stimulated both osteoblast proliferation and differentiation by activating MEK-Erk pathway; formononetin at 100 nM only stimulated osteoblast differentiation that involved p38 MAPK pathway. Unlike daidzein, none of these two compounds activated estrogen receptor in osteoblast nor had any effect on osteoclast differentiation. Daily oral administration of each of these compounds at 10 mg/kg/day doses was given to recently weaned female *Sprague Dawley* rats for 30 consecutive days. Compared with controls, both compounds dose-dependently increased bone mineral density at various anatomic positions studied while they had no effect on bone strength. Rats treated with cladrin exhibited increased mineral apposition rate and bone formation rate compared with control, while formononetin had no effect. Cladrin had much better plasma bioavailability compared with formononetin. None of these compounds exhibited estrogen agonistic effect in uterus. Our data suggest that cladrin is more potent in promoting parameters of peak bone mass achievement, which could be contributed to its better bioavailability. To the best of our knowledge, this work represents the first attempt to elucidate structure-activity relationship between the methoxylated forms of daidzein regarding their osteogenic effects.

5.1.8.6 Medicarpin has a direct and indirect effect on osteoclastogenesis *in vitro* and in ovariectomized mice

Medicarpin, a phytoalexin, was isolated from a plant extract. Effects of medicarpin on murine bone cells *in vitro* and in ovariectomized (OVx) mice were studied. At nanomolar concentrations, medicarpin suppressed osteoclastogenesis from bone marrow cells (BMCs) and displayed concentration dependence. Medicarpin also induced apoptosis of mature osteoclasts isolated from long bones. Effects of medicarpin in osteoclasts are not estrogen receptor (ER) dependent as ICI-180,782 did not reverse its actions. In co-culture system consisting of osteoblast and bone marrow, medicarpin treatment inhibited RANKL/OPG ratio and mRNA levels of osteoclast markers TRAP and RANK. Medicarpin inhibited the expression of tumor necrosis factor alpha (TNFα) in mouse calvarial osteoblasts. This effect was ER dependent as ICI-180,782 reversed the suppressive effect of medicarpin on TNFα mRNA levels in osteoblasts. In addition, like E_2, presence of medicarpin inhibited TNFα-induced upregulation of osteoclastogenic cytokines, interleukin-1, and -6 in osteoblasts. Furthermore, medicarpin inhibited nuclear factor kappaB (NF-kB) signaling assessed by TNFα-stimulated nuclear translocation of p65 subunit of NF-kB. In OVx mice, medicarpin treatment (10.0 mg/kg/day dose) given orally for 30 days presented with reduced formation of osteoclasts but increased formation of osteoprogenitor cells in BMCs compared with OVx + vehicle group. Microcomputed tomography revealed that medicarpin treatment to OVx mice improved parameters of trabecular microarchitecure. Medicarpin exhibited no uterine estrogenicity. Our findings point towards direct and indirect inhibitory effects of medicarpin on osteoclastogenesis *in vitro* that contribute to its bone sparing effect in OVx mice.

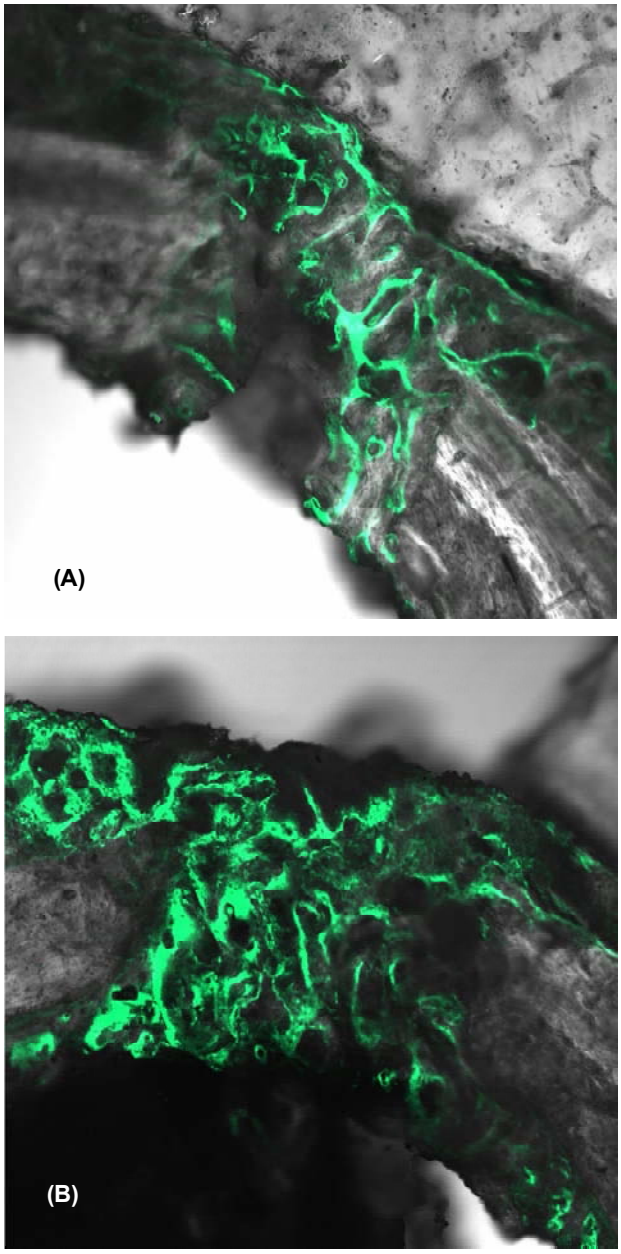
5.1.8.7 Novel analogs of medicarpin as osteogenic agents

Using medicarpin scaffold, a chemical series was synthesized. A series of 47 compounds were screened for *in vitro* osteogenic activity. Three compounds (S-006-1709, S-007-1500 and S-008-399) were found to be most active *in vitro* and had no estrogenicity or anti-estrogenicity. Data indicated that all three compounds have osteogenic effect *in vivo* and therefore, are suitable for use in postmenopausal osteoporosis.

5.1.8.8 S-007-1500 as rapid fracture healing agent

Fracture repair mimics processes of bone morphogenesis involving mesenchymal stem cells (MSCs). Bone morphogenetic proteins (BMPs) have crucial roles in this process. No oral drug is available for accelerating fracture healing. Very recently rhBMP-2 and BMP-7 have been approved by U.S. F.D.A. for local application in cases of spine surgery and open tibial fracture. Clearly, this is an interventional approach having limited use and there is a need for oral drug for accelerated fracture healing.

S-007-1500 stimulated osteoblast differentiation by stimulating several BMPs including BMP-2, -4, -6 and -7. Oral administration of S-007-1500 (1.0 mg/kg dose) to adult rats receiving fracture in femur resulted in 40% increase in bone formation at the fracture site, as shown in the figure. These data suggest that S-007-1500 has therapeutic potential as rapid fracture healing agent.



(A) S-007-1500 is synthesized based on medicarpin scaffold. (B) Calcein labeling, a surrogate of new bone formation at the site of fracture (made in femur) in rats receiving vehicle and (C) S-007-1500 (1.0 mg/kg dose) for 12 days.

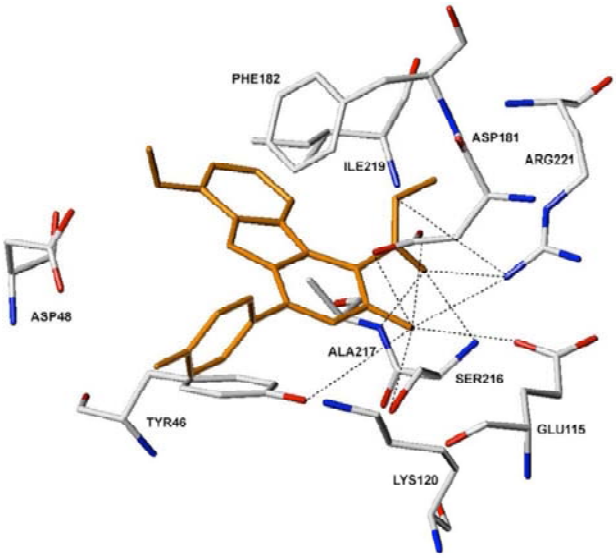
5.2 Diabetes and Energy Metabolism Research

5.2.1 Glucagon-like Peptide-1 (GLP-1) and Dipeptidyl Peptidase-4 (DPP-4) as Therapeutic Targets for T2DM

Efforts to increase GLP-1 half-life through the preparation of DPP-4 resistant analogues and efficacious GLP-1 receptor agonists are needed and are being pursued. Towards, this objective a program has been initiated for the development of physiologically more stable and potent congeners of GLP-1 as antidiabetic agents. During this period, three new analogs of GLP-1 have been prepared and their evaluation, in comparison to native GLP-1, is in progress. In addition, towards inhibiting DPP-IV enzyme, a Xaa-prolidide was used as prototype and peptidomimetic design was applied for the lead optimization. During this period, thirty new compounds were synthesized for DPP-IV inhibitory activity and they have shown 30-70% inhibition at 10 μM concentration. Further studies with these compounds are in progress.

5.2.2 Synthesis of PTP-1B Inhibitors

Based on molecular modeling studies, a new series of 4,5-dihydro-2H-benzo[e]indazoles has been identified as novel PTP1B inhibitors. Nearly 180 compounds were synthesized and screened. Nine compounds showed good *in vivo* antihyperglycemic activity. From recent synthetic as well as natural leads



Docked conformation of dibenzofuran (gold), showing interactions with neighbouring residues through H-bonding in the PTP1B catalytic site.

pyrocoumarine, isoxazole and benzo[e]indazole-based PTP1B inhibitors are being synthesized.

5.2.3 Synthesis of PPARγ Agonists

Peroxisome proliferator-activated receptorg (PPARγ) is an important target for the development of antidiabetic agents as agonists for this receptor are widely known to act as insulin sensitizers. However, this class of compounds exhibit liver toxicity. Several molecules have been designed with objective to minimize the toxicity and simultaneously improve the activity. During this period, 24 new compounds were synthesized. Some of the compounds have shown 30-40% blood glucose lowering effect in db/db mice.

5.2.4 Antidiabetic-cum-antidyslipidemic Agents from Natural Sources

Extracts from 71 terrestrial plants as well as 35 marine flora/fauna have been evaluated in validated animal models of T2DM and hyperlipidemia. Among the 17 antidiabetic plants explored for the isolation of antidiabetic compounds, several compounds have been isolated from 5 plants and they have shown significant antihyperglycaemic activity on *in vitro* tests and Streptozotocin induced diabetic rats and db/db mice respectively.

5.2.5 Antidiabetic-cum-antidyslipidemic Leads

Optical isomers of one of the synthetic antidiabetic compound have been prepared, evaluated in db/db mice and their PK profiles have been completed in albino rats. Results indicate fastest absorption, stability in SGF & SIF for 2 hours. Pharmacokinetic profile indicates high and prolonged systemic exposure and its oral bio-availability was 11.62%. In addition, the preclinical development of two other lead antidiabetic-cum-antidyslipidemic compounds is in progress.

6. Tuberculosis and Microbial Infections

Coordinator:
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Aims and objectives of the research area Microbial Infections focus on Tuberculosis, Fungal and Viral infections. Using different screening formats *viz. in vitro*, *ex vivo*, *in vivo* and BACTEC, screening of natural products and synthetic compounds for antitubercular, antifungal, antibacterial and antiviral activities is undertaken towards the identification of new lead molecules, validation of novel drug targets, developing rationale based screen system, resolving the structure of candidate mycobacterial proteins, analysing host-pathogen kinase interaction and sigma factors regulon to understand the molecular mechanisms of mycobacterial pathogenesis.

6.1 Tuberculosis

6.1.1 Screening

More than two thousand substances, including natural and marine extracts and in-house synthesized compounds, were screened for anti-TB activity using different screening formats. 4 Plant extracts showed an MIC of ≤ 50 μg/ml against *M. tuberculosis* H37Rv, while 16 synthetic molecules showed an MIC of ≤ 3.12 μg/ml. Eight of these compounds and two plant extracts were found to be non-toxic in Vero cells and mouse bone-marrow derived macrophages, screened *ex vivo* using mouse macrophages and were pursued for *in vivo* screening in mouse model. Treatment with the synthetic molecules S-009-227, S-006-830, -703 and S-007-1085 enhanced the mean survival time (MST) by 9, 7, 9 and 4 days respectively and nearly 100 fold reductions in viable bacterial counts in lungs. Both plant extracts enhanced MST by 4 days, percent survival (48% and 67%) and about 10 fold reduction in viable bacterial counts in lung. Ten compounds showed activity (MIC < 6.25 μg/ml) in the *in vitro* and BACTEC screening and were pursued for further evaluation.

Protective efficacy of S-006-227, a selected lead, was evaluated in combination with the suboptimal dose (0.1 mg per kg body weight per day for 30 days) of isoniazid. We observed 30-fold reduction in viable counts in the lungs of isoniazid (suboptimal) treated mice, whereas 50-fold reduction in viable counts in animals treated with INH+227. Similarly percent survivors were also higher in the combination treatment, i.e. 80% as compared to 66% in the INH only treated group.

6.1.2 Generation of Rationale Based Antimycobacterial Screen System

A recombinant *Mycobacterium aurum* strain is being used for screening compounds affecting FAS-II elongation pathway in mycobacteria. The recombinant *M. aurum* strain showed constitutive expression of *lacZ* reporter gene under the influence of *M. tuberculosis* H37Rv *kas* operon promoter, but the expression got enhanced after treatment with FAS-II pathway inhibitors. The inhibiting response of drugs is monitored by a simple β-gal enzyme assay. Screening of >80 in-house compounds, rationally designed for targeting FASII elongation pathway in mycobacteria, resulted in identification of 4 compounds showing >85% reduction in viability counts in *M. aurum* and two of them were confirmed with β-gal inducibility assay.

6.1.3 Studies on BCAA Pathway Enzymes as Drug Target

Acetohydroxyacid synthase (AHAS) is a thiamine diphosphate- (ThDP-) and FAD-dependent enzyme that catalyzes the first common step in the biosynthetic pathway of the branched-amino acids such as leucine, isoleucine

and valine and is a potential target for development of antimyco bacterial compounds. In *M. tuberculosis* genome, four ORFs (ilvB1, ilvB2, ilvG, ilvX) have been annotated as coding for catalytic subunit and one ilvN for regulatory subunit. We have cloned and overexpressed all five ORFs in pET28a in *E. coli* BL21(DE3). All the subunits were expressed as N-terminal hexahistidine-tagged fusion proteins. The IlvB1, IlvN were found in soluble fraction and were biologically active. The IlvB1 enzyme (catalytic subunit) showed AHAS activity which was enhanced in presence of IlvN, regulatory subunit. A microplate assay for AHAS activity has been developed.

6.1.4 Assay for Mycolic Acids

Mycolic acids and fatty acids were extracted, esterified and resolved by thin layer chromatography. Comparison of 2-D TLC patterns showed similarities in the mycolic acids / fatty acids profiles of *M. tuberculosis* strains H37Ra and H37Rv. In TLC profile, fading methoxy mycolic acid was observed after INH treatment. TLC patterns have been compared with the standard mycolic acid of *M. tuberculosis* obtained from Sigma.

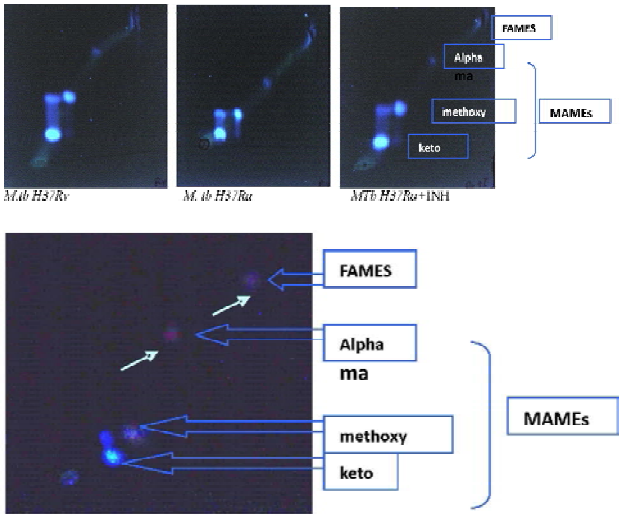


Fig. Resolution of mycolic acid and fatty acid methyl esters (MAMEs and FAMEs) by 2-D TLC.

6.1.5 Computational Approaches to Identify Mycobacterial Targets and Virtual Screening

6.1.5.1 Receptor based 3D-QSAR to identify putative binders of *Mycobacterium tuberculosis* Enoyl acyl carrier protein reductase (J. Mol. Model. 2009, *10*, 1007)

The applicability and scope of 3D-QSAR models (CoMFA and CoMSIA) to complement virtual screening using 3D pharmacophore and molecular docking was examined and applied to identify potential hits against *Mycobacterium tuberculosis*. Enoyl acyl carrier protein reductase (MtENR). Initially CoMFA and CoMSIA models were developed using series of structurally related arylamides as MtENR inhibitors.

The contour maps from 3D-QSAR models in combination with docked binding structures helped better interpretation of the structure activity relationship. Integrated with CoMFA and CoMSIA predictive models structure based (3D-pharmacophore and molecular docking) virtual screening were employed to explore potential hits against MtENR. A representative set of 20 compounds with high predicted IC_{50} values were sorted out in the present study.

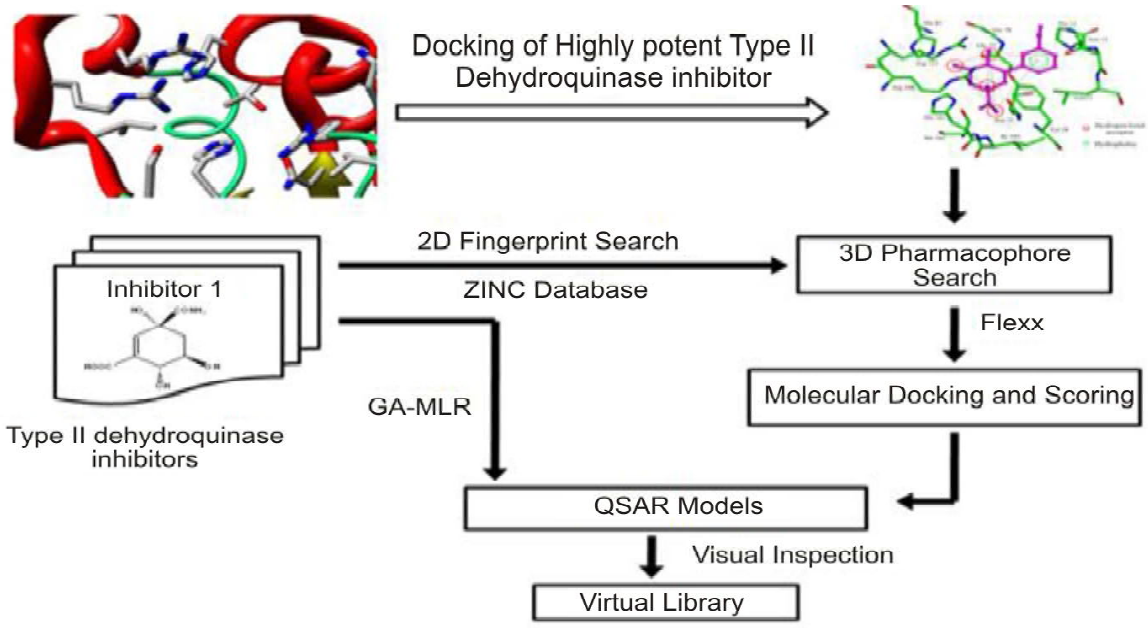
6.1.5.2 Identification of *Mycobacterium tuberculosis* InhA targeted virtual library using structure based virtual screening and receptor interaction fingerprints (Mol. Diversity 2010, *in press*)

A virtual screening workflow based on combination of 2D structural fingerprints, 3D pharmacophore and molecular docking was applied to identify compounds matching rigidly specific aspects of ligand bioactive conformation targeted against *M. tuberculosis* Enoyl acyl carrier protein reductase. The resulting compounds were then ranked and prioritized by a combination of scoring functions and knowledge based scores derived from the similarity of receptor interaction fingerprints for each docking solution to that of crystallographic inhibitor binding mode, in order to develop rational proposals for new chemical templates or new sets of potential ligands. Such library support hit-to-lead design efforts for tasks like follow-up from high-throughput screening hits or scaffold hopping from one hit to another attractive series.

6.1.5.3 New molecular scaffolds for the design of *Mycobacterium tuberculosis* Type II dehydroquinase inhibitors identified using ligand and receptor based virtual screening (J. Mol. Model. 2009, *10,* 1007)

Using ligand and receptor based virtual screening approaches we have identified potential virtual screening hits targeting type II dehydroquinase from *Mycobacterium tuberculosis,* an effective and validated *anti*-mycobacterial target.

Initially, we applied a virtual screening workflow based on combination of 2D structural fingerprints, 3D pharmacophore and molecular docking to identify compounds that rigidly match specific aspects of ligand bioactive conformation. Subsequently, resulting



compounds were ranked and prioritized using receptor interaction fingerprint based scoring and quantitative structure activity relationship model developed using already known actives.

6.1.6 Basic Research Using *M. tuberculosis* and other Mycobacterial Species

6.1.6.1 Dormancy and resuscitation

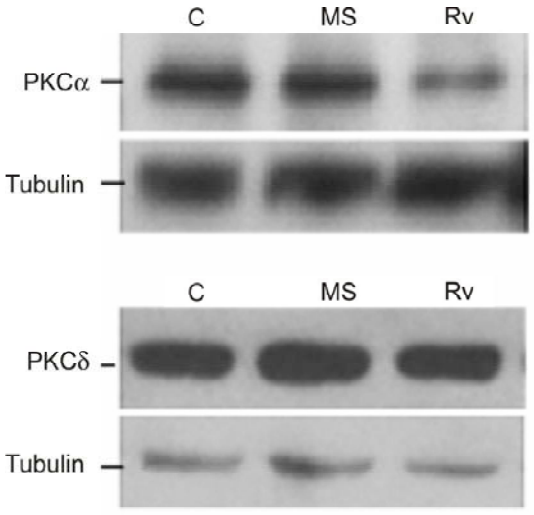
Prolonged incubation of BCG and *M. tuberculosis* in stationary phase induces a true dormancy generating non-culturable cells that have to be resuscitated before resuming active growth. Resuscitation is promoted by resuscitation promoting factor (Rpf) derived from *Micrococcus luteus, M. tuberculosis* or *M. bovis* BCG. To obtain an insight into the physiology of BCG during extended stationary phase and Rpf mediated resuscitation, whole genome expression profiling was done by microarray. A total of 765 genes were found to be upregulated and 814 genes down regulated in resuscitation phase versus extended stationary phase of growth. Twenty differentially regulated genes were selected and were validated by real time PCR.

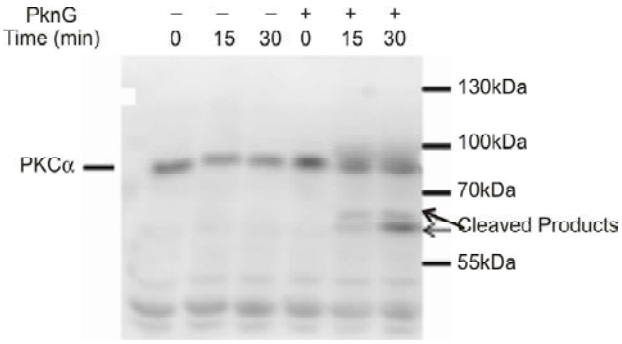
6.1.6.2 VNTR polymorphism (J. Med. Microbiol. 2009, *64(4)*, 774-781)

Polymorphism of VNTR 3690 locus located in the intergenic region between *rv*3304 and *rv*3303c (encoding the *glp*D2 and *lpd*A) was correlated with expression of rv3303c (lpdA) gene. The copy number of VNTR 3690 was found to vary among Indian clinical isolates of *M. tuberculosis* (1-12 copies), *M. tuberculosis* H37Rv (four copies) and BCG (1 copy). The expression of *lpd*A as measured by qRT-PCR was 12 fold higher in *M. tuberculosis* H37Rv than in *M. bovis* BCG indicating a correlation between copy number and transcription of *lpd*A.

6.1.6.3 Proteolytic inactivation of protein kinase C-α by PknG enhances the intracellular survival of mycobacteria (BMC Microbiology 2009, *9*, 271)

M. tuberculosis H37Rv and *M. bovis* BCG were reported to downregulate the expression of PKC-α during infection. When selectively knockdowned PKC-α level in macrophages by SiRNA, infection of PKC-α deficient cells resulted in the significant reduction in phagocytosis of

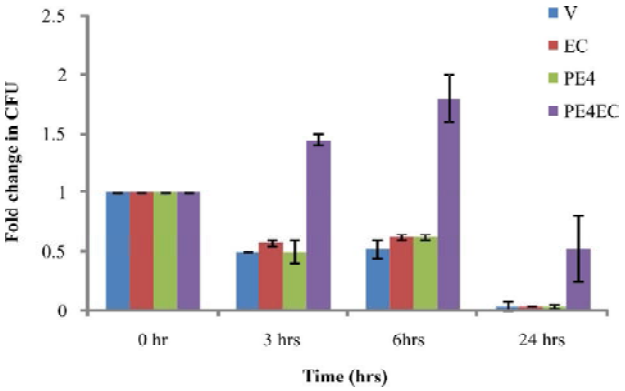


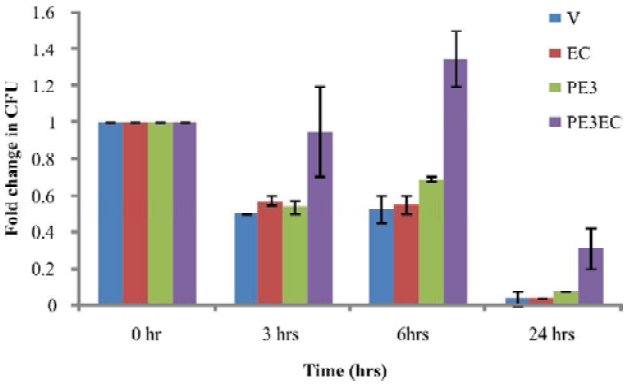


BCG and MS while their intracellular survival increased. Protein Kinase G (PknG) from pathogenic mycobacteria has been reported to increase intracellular survival of mycobacteria by inhibition of the phagosomal maturation and it was concluded that proteolytic inactivation of PKC-α by PknG help mycobacteria to avoid phagocytosis and killing by macrophages.

6.1.6.4 Proline-Glutamic acid rich proteins PE3 and PE4 are responsible for mycobacteria/ macrophage interactions

About 10% of the coding capacity of *Mycobacterium tuberculosis* (MTB) genome is devoted to the PE/PPE family of genes scattered throughout the genome. The function of the proteins encoded by these large gene families remains unknown, although they have been proposed to be the rich source of protective antigens involved in antigenic variation and have immune-pathogenic importance. The study investigates the characteristic of PE3 (Rv0159c) & PE4 (Rv0160c) and their associations with ESAT-6 & CFP-10 and finally their interactions with macrophage. PE3 and PE4 were cloned in a shuttle vector and expressed constitutively in *Mycobacterium smegmatis* MC²155 (MS) strain. The recombinant MS were grown in different conditions. The data showed a significant decrease in the growth of MS containing PE3 and PE4. To test the survival of various MS recombinants in macrophage, J774A.1 cell line was infected with these recombinants and the synergistic effect was observed in the survival rate of recombinant MS having ESAT-6, CFP-10 along with PE3 and / or with PE4 as compared to the MS and MS with ESAT-6 and CFP-10 alone.

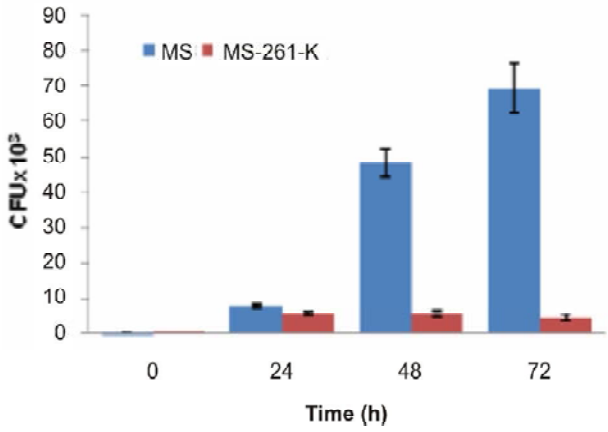


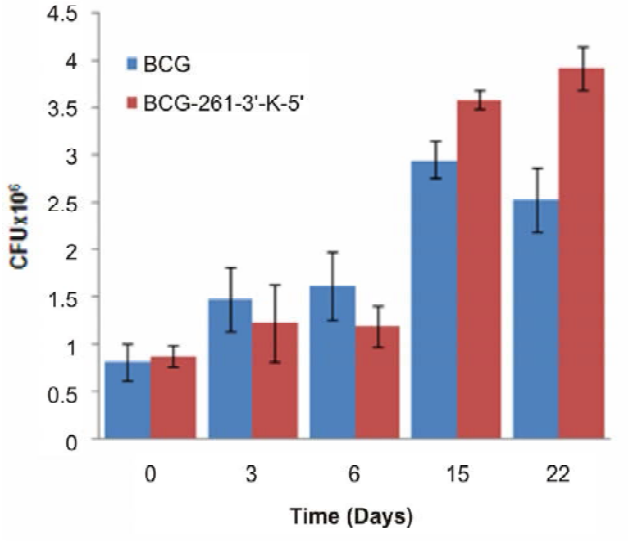


6.1.6.5 Cytosolic Serine Threonine Protein Kinase (STPK) is linked to the slow growth and increased survival of mycobacteria in macrophages

Protein Kinase K is present in slow growers or in pathogenic mycobacteria. The full length gene is present in MTB H37RV, H37RA, *M. bovis* BCG, and in *M. asiaticum*. This gene has been cloned, expressed and purified to homogeneity. The gene was further cloned in a Mycobacterial *E. coli* shuttle vectors (integrative as well as replicative) and electroporated into *M. smegmatis* (MS) Mc² 155 strain.

Different *M. smegmatis* strains, wild type MS, MS vectors only and MS containing PknK were cultured in different conditions. MS containing PknK grew slowly in comparison to other MS strains. To examine the intracellular role of these recombinant mycobacteria, J774A.1 macrophage cell line (1:10 MOI) was infected with MS wild type and recombinant strains and it was

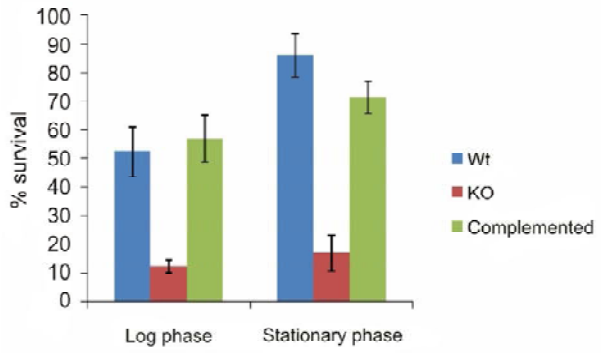




observed that MS containing PknK resides in macrophages for longer period of time as compared to wild type MS. Thus, it was concluded that PknK is responsible for increasing mean survival time of mycobacteria and might be responsible for the slow growth and increased pathogenesis of tubercular mycobacteria. Knocking down PknK enhanced the multiplication of BCG.

6.1.6.6 Generation and characterization of *Mycobacterium smegmatis* Sigma Factor, SigF mutant

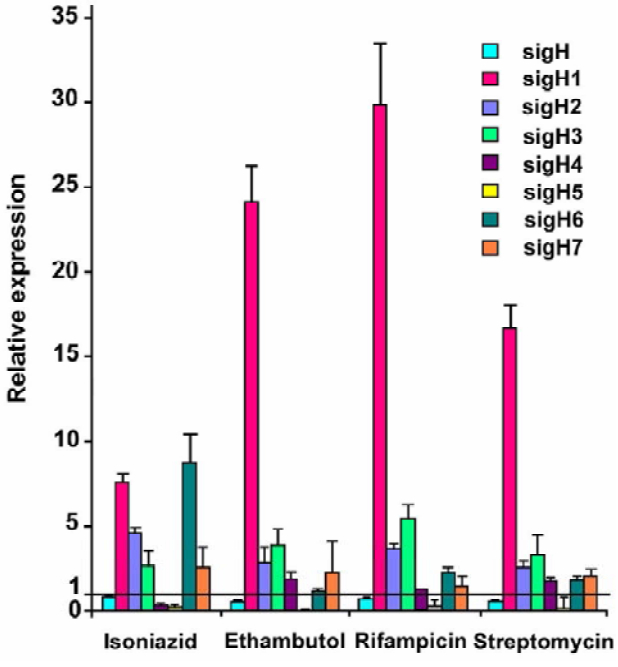
Alternative sigma factor, SigF was reported first time in *M. smegmatis* and its expression was analysed under varying growth conditions. We further generated a Δ*sigF* mutant and studied its phenotype during different physiological conditions in order to understand its role in *M. smegmatis* biology and it was observed that *M. smegmatis sigF* is dispensable for growth of bacterium under normal physiological conditions. Expression of *sigF* increases in response to cold shock, nutrient starvation and after treatment with anti-mycobacterial agents like isoniazid and ethambutol, but its absence does not affect the survival of the bacterium under these conditions.



Deletion of *sigF* resulted in loss of carotenoid pigmentation (shown below) and increases the susceptibility of mutant towards H_2O_2 induced oxidative stress (depicted above). SigF deletion also altered the structure of outer most layer of the *M. smegmatis* cell envelope.

6.1.6.7 *M. smegmatis* sigma factor SigH1 is highly expressed in response to antibiotic stress (J Bacteriology 2009, *191(8)*, 2888-2893)

Sigma factors play a major role in the regulation of bacterial gene expression and its content varies considerably in different mycobacterial genomes. Recently sequenced, *Mycobacterium smegmatis* genome is predicted to encode 26 sigma factors, which is twice the number present in *M. tuberculosis* (13 sigma factors). There is an enrichment of *sigH* subfamily and seven *sigH* paralogs are reported in *Mycobacterium smegmatis* genome. SigH is a key regulator of a transcriptional network that responds to oxidative and heat stresses in mycobacteria. Expression of *sigH* paralogs was examined at different stages of growth and under various stress conditions using quantitative real time RT-PCR and found that *sigH1* expression is increased several folds in response to different antimycobacterial drugs *viz*. isoniazid, ethambutol, rifampicin and streptomycin.



This protein finds high level of similarity (51%) with Bacillus SigW, which is known to regulate antibiosis regulon in *Bacillus subtilis*.

6.1.6.8 Structural analysis of proteins using NMR and X-ray crystallography

(a) Solution structure of matured exported protein Rv0603 from *Mycobacterium tuberculosis* H37Rv reveals a novel α, β protein fold

Protein Rv0603 from *M. tuberculosis* is a 102-residue protein and has no significant sequence or structural similarities with any protein with solved three-dimensional structure of known function. So far, no functional annotations are available for this protein. In order to understand the role of secretory proteins in molecular recognition and interactions, structural studies on signal sequence deleted mature exported Rv0603 protein (ΔRv0603) using NMR spectroscopy have been initiated and NMR solution structure of ΔRv0603 from *M. tuberculosis* H37Rv, which exhibits a novel α, β-fold has been reported.

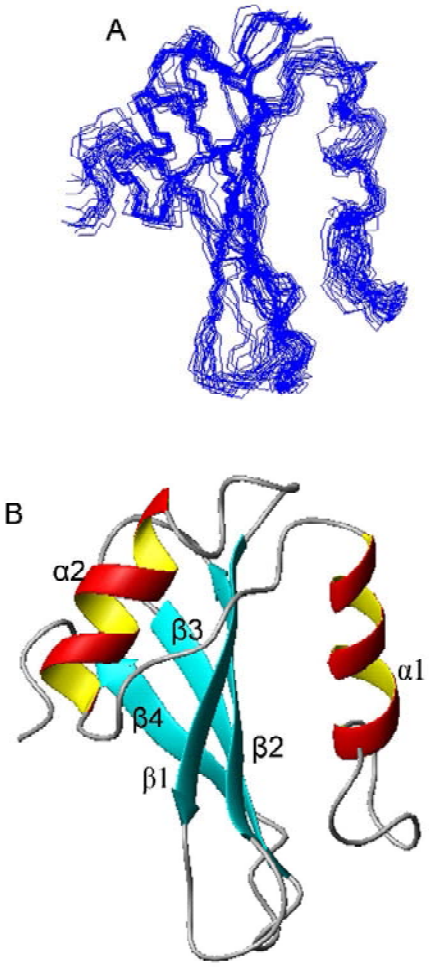
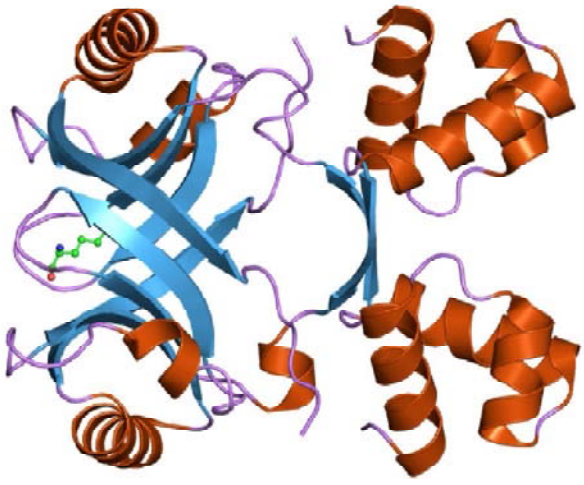


Figure: (A) Superimposition of backbone traces from final ensemble of 20 structures with lowest target function. (B) Ribbon diagram of lowest energy structure of Rv0603 showing 4 stranded antiparralel β-sheet surrounded by 2 α-helices. The individual β strands and α helices are labeled. PDB ID: 2KGY

(b) Ligand-induced structural transitions, mutational analysis, and 'open' quaternary structure of the *M. tuberculosis* feast/famine regulatory protein (Rv3291c) (J. Mol. Biol. 2009, *392*, 1007-1019)

Rv3291c is a member of the feast/famine regulatory protein family that is known to form stable protein-DNA complexes. A specific oligomeric transition between hexadecameric and octameric/lower-order oligomers in the presence of Phe, that supports an effector-mediated model for the disassembly of a nucleosome-like particle has generated two mutants, Gly102Thr and Glu104Ala, which are part of the essential 100-106 effector-binding loop. The Gly102Thr mutant adopts an unusual 'open' quaternary structure and offers interesting functional insights co-related to the binding of an effector. This is similar to the previously reported *Escherichia coli* Lrp co-crystallized in the presence of DNA where the interactions of the substrate with the N-terminal DNA binding domain presumably lead to symmetry deviations to the oligomeric association.

The present structure represents a direct evidence to support that changes made to the effector-binding domain at the C-terminus also result in a functionally relevant quaternary structural change. Conversely, the Glu104Ala mutant retains the closed quaternary association observed in the native protein and reveals nonsymmetrical interaction effects in the two subunits of the dimer. We also report that the native protein unexpectedly binds Lys but does not recognize Arg and



offers a structural explanation for it. Error-scaled difference distance matrix analysis suggests that the protein has a relatively flexible core that is presumably needed to mediate the structural changes necessary for the protein's regulatory functions.

(c) Interactions of the *M. tuberculosis* UsfX with the cognate sigma factor SigF and the anti-anti sigma factor RsfA (Biochem. Biophys. Acta 2009, *1794*, 541-553)

M. tuberculosis employs an exquisite cascade consisting of the cognate anti-sigma factor UsfX and anti-antisigma factors RsfA and RsfB to regulate the functions of the alternate sigma factor SigF. We have purified these proteins to characterize their molecular properties and interactions with UsfX. UsfX forms a stable complex with SigF that could be purified only after co-expressing the proteins in *E.coli*. Formation of the complex is nucleotide independent and apparently requires unknown *in vivo* factors. Fluorescence spectroscopy experiments suggest that the nucleotide binding sites of UsfX are distal to the protein-protein interaction interface. RsfA is a novel anti-antisigma factor whose binding to UsfX is triggered by the reduction of an intrachain disulphide bond between Cys73–Cys109. The reduction is accompanied by an increase in the hydrodynamic radius of the protein. The UsfX–RsfA complex exhibits a novel stoichiometry of 2:1 compared to the 2:2 stoichiometry reported for other anti-anti-sigma factors. The role of the disulphide bond in complex formation was explored using molecular dynamics simulations. These studies support specific conformational changes that occur upon reduction of the Cys73–Cys109 bond of RsfA. This leads to a rearrangement that increases the interactions of a conserved His107 of UsfX with Cys109 of RsfA.

6.2 Bacterial and Fungal Infections

6.2.1 Screening

A total of 316 synthetic compounds, 204 marine and 14 plant extracts were evaluated for *in vitro* antifungal and antibacterial activity by microbroth dilution method. Synthetic compounds S-008-1633, -995, -997, -1355 and -1478, S-009-0307, -155, -160 (MIC in the range of 0.19-1.56 μg/ml against fungi), marine extract CSM-4147A001 (MIC 15.6 and 7.8 μg/ml against *Staphyloccus aureus* (ATCC 25923) and *Klebsiella pneumoniae* (ATCC 27736) respectively), plant extract 4743A001 (MIC 0.9 μg/ml *C. albicans*, 1,9 μg/ml *Cryptococcus neoformans*, 1.9 μg/ml *Sporothrix schenckii* and 31.2 μg/ml *T. mentagrophytes*), 4483K006 (MIC 6.25 μg/ml against *Staphyloccus aureus* (ATCC 25923) and *Klebsiella pneumoniae* (ATCC 27736) were found to be active. One marine extract CDR 332F026 was evaluated *in vivo* against *A. fumigatus* infection in mice. Other extracts did not exhibit any significant activity.

6.2.2 Monoclonal Antibodies Against *Candida albicans* and *Aspergillus fumigatus*

The two monoclonal antibodies, 10D2 and 2A11, generated against *C. albicans* GPI anchored cell wall proteins were studied for their therapeutic potential. They are specific to *C. albicans* and did not exhibit any cross reactivity against other yeast and mycelial pathogen fungi. The *in vitro* candidacidal activity for 2A11 and 10D2 was found to be 93% and 98 % respectively. The candidacidal activity was further estimated using flow cytometry where 89% and 81% reduction in viability was observed in 2A11 and 10D2 respectively. The epitope localization for both MAbs 2A11 and 10D2 showed the presence of the epitope on the surface of *C. albicans* yeast and mycelial form. *In vivo* efficacy of these two purified MAbs was evaluated in BALB/c mice through intraperitoneal route (100 μg/day for 4 days) against intravenous challenge of $2x10^5$ cells of *C. albicans*. MAb 2A11 and MAb 10D2 caused 85% and 78% reduction in CFU/g kidney tissue of mice respectively. The light chain of one of the monoclonal antibodies (2A11) was amplified using RT PCR and sequenced.

6.2.3 Genetic Analysis of Amphotericin B Strain of *C. albicans*

Candida albicans resistant strain AMB-R, developed earlier, was further explored at genetic level. Two genes Erg11 and CSP37 were amplified and sequenced using DNA of both parent and resistant *C. albicans* strains. The sequences were analysed using pair wise alignment software CLUSTALW and mutations were observed at nucleotide level in AMB-R as compared to the gene sequence of its parent strain of *C. albicans*. The reduced expression level of Erg 11 in AMB-R was observed using RT PCR. The behaviour of both yeast and pseudohyphal form of resistant strain AMB-R against oxidative stress (H_2O_2 and menadione) were compared to its parent strain on the basis of activity of anti-oxidative enzymes (Catalase, Glutathione Peroxidase and Glutathione S Transferase). The enzymatic activities of anti-oxidative enzymes were significantly higher in AMB-R under control and oxidative stress conditions.

6.2.4 Studies of *Candida* Biofilm Formation

The biofilm formation capacity of *C. albicans* on silicone elastomer was estimated using confocal microscopy and XTT assay. The prostaglandin level in the presence of arachidonic acid and antifungal agents, fluconazole and terbinafine was estimated and compared for four *Candida* species *C. albicans, C. parapsilosis, C. tropicalis* and AMB-R. The *non-albicans* and amphotericin B resistant *Candida* showed the significant increase in the prostaglandin level in presence of arachidonic acid and antifungal agents. Further, glycoproteins from *C. albicans and* AMB-R biofilm cell wall and cytoplasm has been isolated using concanavalin A columns.

6.3 Viral Infections

6.3.1 *In vitro* Evaluation of Anti-HIV-1 RT Activity

Several viral targets have been identified to preclude the viral replication in the patient. Reverse transcriptase (RT) turned out to be an important target because this enzyme opens the gateway for HIV multiplication. Post viral penetration into the cell, the RT transcribes viral RNA genome into double stranded DNA, which gets integrated into the host genome for making viral transcripts which translate into viral proteins. Having synthesized all viral proteins, the virus acquires the envelope from the host cell membrane and the full viron is released to infect new cells.

HIV RT has two important sites where two different classes of inhibitors can successfully bind and inhibit RT activity. The HIV-RT inhibitors are: nucleoside reverse transcriptase inhibitors (NRTIs) that bind competitively and covalently to the active site of the enzyme, and inhibit polymerisation, while non-nucleoside reverse transcriptase inhibitors (NNRTIs), which bind non-competitively and non-covalently at allosteric site on the enzyme and different from its active site. The inhibitors against RT enzyme can be identified by *in vitro* HIV-1 RT assay. This assay is fast, sensitive and specific to HIV-1RT. The compounds found active in this assay, in majority, show anti HIV-1 activity in cell based assay system. Screening of anti-HIV-RT compounds is in progress.

Technical Services & Facilities

1. Division of S&T Management

In order to reflect diverse management functions performed by the erstwhile "Technical Information, Industrial Liaison and Planning Division", it was rechristened as **Division of S&T Management** (DSTM). The Division continued to serve its multifarious activities including Project Planning, Monitoring & Evaluation (PME), International Science & Technology Affairs, Intellectual Property Rights Protection (IPR) Management, Coordination of training program, Implementation of national schemes like CPYLS and KVPY, Coordination with CSIR and other funding agencies, etc. The collections and management of Institute's chemical library is also housed in this division.

1.1 Significant activities performed by DSTM are:

- Compiled and prepared Annual Plan 2010-11 of the Institute;
- Compiled Mid-Term Appraisal document for eleventh five year plan projects;
- Budget allocated and equipment prioritized for inhouse projects;
- IPR protection of innovative technologies;
- Coordinated the filing of Indian and foreign patents and interaction with granting agencies;
- Published an Intellectual Property Instruction Manual "How to Handle Innovations";
- Compiled and published first issue of CDRI Newsletter (April-September 2009) and CDRI Annual Report 2009-10;
- Organised quarterly/six monthly/annual project monitoring meetings and pursued reports compilation and follow-up of recommendations;
- Coordinated biological screening services;
- Coordinated training of 242 postgraduate students and 5 foreign students;
- Coordinated deputation of institute scientists abroad under different programs;
- Disseminated technical and non-technical information related to institute's programs and activities;
- Processed staff nominations for honours & awards and national & international fellowships;
- Processed requests of staff and research fellows for participation in conferences / seminars / symposia / workshops organized by various agencies;
- Organized "CSIR Program on Youth for Leadership in Science-2009" on March 18 and 19, 2009;
- Under the program on "Faculty Training & Motivation and Adoption of Schools & Colleges by CSIR Labs", Institute implemented programmes in 3 local Colleges, adopted earlier viz. Govt. Jubilee Inter College, Govt. Husainabad Inter College and Govt. Girls Inter College, Shahmina Road;
- Regularly updated database on staff, research fellows, budget, ECF, projects, awards, etc. and used it for preparation of various reports;
- Regularly updated and maintaned CDRI Chemical Library & managed databases of Institute's synthetic compounds, natural products and marine samples.

2. Business Management Unit

Business Management Unit continued to explore the business development opportunities by establishing liaison with national and multinational industries, academia government organizations, funding agencies and foreign bodies in order to have more public - private partnerships at the early stage of the development and to have collaboration with them for new leads. Major agreements executed during the year are :

SN	Details	Client	Date of Signing
Products Licensed to Industries			
1.	Process know-how for Plant 1020 F147 (For optimal bone health)	M/s Natural Remedies Private Ltd., Bangalore	13/01/10
2.	Improved patented process for synthesis of Centchroman	HLL Lifecare Ltd., Thiruvananthapuram	02/12/09
3.	Compound 80/574 + Atorvastatin formulation	Cadila Pharmaceuticals Ltd., Ahmedabad	25/02/09
Contract Research Undertaken			
4.	Generation of data on Centchroman as per ANVISA guidelines for registration in Brazil & inclusion in WHO medicine list	HLL Lifecare Ltd, Thiruvananthapuram	02/12/09
5.	Development of novel, non-infringing process patents for the synthesis of Bivaluridin	Biocon Ltd., Bangalore	06/08/09
6.	Amended contract agreement for lead identification for antileshmanial compound	DNDi, Geneva	04/03/09
Memorandum of Understandings for Joint R&D			
7.	Studies on impact of adipokene and chemokene gene polymorphism and its protein expression in metabolic syndrome	CSM Medical University, Lucknow	08/12/09
8.	Optimization of anticancer leads	CIMAP, Lucknow	27/10/09
9.	Development of siRNA therapeutics against myeloid cell infections by pathogens	Meharry Medical College, USA	23/10/09
10.	Establishment of international consortium on antivirals in India	International Consortium on Anti- Virals, Canada	04/10/09
11.	Synthesis, molecular modeling and development of ER dependent anticancer agents	Amity Institute of Pharmacy, Amity University, Lucknow	14/09/09
12.	Setting of Phase-I clinical facility	SGSMC-KEM Hospital, Mumbai	27/07/09
13.	Leishmania induced non coding RNA manipulations in phagocytes and keratinocytes	Meharry Medical College, USA	16/07/09
14.	Anti-osteoclastogenic effect of 99/373 and its mode of action	Department of Biotechnology, Govt. of India, New Delhi	02/06/09
15.	Association of CD36 locus with type II diabetes and related atherosclerosis	Lucknow University, Lucknow	19/05/09

Material Transfer Agreements			
16.	SNM-Luc and XNM-Luc plasmids	University Health Network, Ontario, Canada	09/09/09
17.	p 21-promoter luciferase construct	John Hopkins Medical Institution, USA	02/06/09
18.	Recombinant clone of SHMT of *L. donovani* and the methodology of overexpression of SHMT towards crystallographic studies	Indian Institute of Science, Bangalore	13/05/09
19.	cDNA clones for human BMPRIa, BMPRIb & BMPRII	Tsinghua University, Beijing, China	31/03/09
20.	pEt28b-Rv2875 expression vector	Indian Immunological Ltd., Hyderabad	25/02/09
Secrecy Agreements for exploration of collaboration			
21.	Exploration of collaborative setting of 'Centre of excellence in clinical trials' at CDRI, Lucknow	Vimta Labs, Hyderabad	25/07/09
22.	Evaluation of data on Plant 914 (osteogenic) for exploration of further development and commercialization	Supreem Pharmaceuticals, Mysore	15/07/09
23.	Evaluation of data on Plant 1020F147 (osteogenic) for exploration of further development and commercialization	Natural Remedies Pvt. Ltd., Bangalore	27/05/09
24.	Evaluation of data on Centchroman (alternative use in the treatment of breast cancer) for exploration of further development and commercialization	HLL Lifecare limited, Thiruvananthpuram	02/04/09

3. Sophisticated Analytical Instrument Facility (SAIF)

SAIF is one of the first four facilities set up by the Department of Science & Technology (DST), Government of India to fulfill the following objectives:

- Provide facilities of sophisticated analytical instruments to scientists and other users from academic institutes, R&D laboratories and industries to enable them to carry out measurements for R&D work;
- Acquire and develop capability for preventive maintenance and repair of sophisticated instruments;
- Organize short term courses/workshops on the use and application of various instruments and analytical techniques;
- Train technicians for maintenance and operation of sophisticated instruments;
- Development of new measurement/analytical techniques.

Newly installed Waters Alliance E-2695 Separation Module HPLC System

3.1 Testing/analytical services provided

During the period, the facility carried out analyses of 6987 external and 39414 internal samples. Users were from University/Colleges, National Labs./Govt. Organizations and industries. Details are as follows:

Name of the Instrument	External Samples	Internal Samples	Total no. of samples analyzed
Mass Spectrometry	2209	9185	11394
NMR Spectrometry	2304	15982	18286
IR Spectroscopy	1000	3825	4825
HPLC & GLC	194	1603	1797
Micro-analysis	1229	743	1972
Flow Cytometry	8	7030	7038
Electron Microscopy	14	226	240
Confocal Microscopy	29	820	849
Total	**6987**	**39414**	**46401**

4. National Laboratory Animal Center (NLAC)

NLAC ensured the supply of defined and healthy animals for biomedical research, supply of quarantined and tested Rhesus monkeys obtained from recognized animal suppliers, supply of tissues, organ, blood, sera samples of laboratory animals for research, health monitoring of laboratory animals through microbiological, parasitological, pathological screening, radiological monitoring of monkey, nutritional monitoring of laboratory animal feed, feed trial studies, production of special research diet like, high sucrose diet, high fat diet, high cholesterol diet, high fat and high cholesterol diet, etc. This facility is also involved with the HRD programme in laboratory animal science through conducting training courses, including care, breeding and management, health monitoring and quality control, nutritional monitoring, diagnosis and management of laboratory animal diseases.

4.1 Important activities carried out

Microbiological screening through samples	:	268
Parasitological screening through samples	:	970
Nonhuman primates purchased for experimentation	:	14
Nonhuman primate in rehabilitation & breeding	:	27
Tuberculin testing of monkeys performed	:	28
Chest radiography of monkeys undertaken	:	14

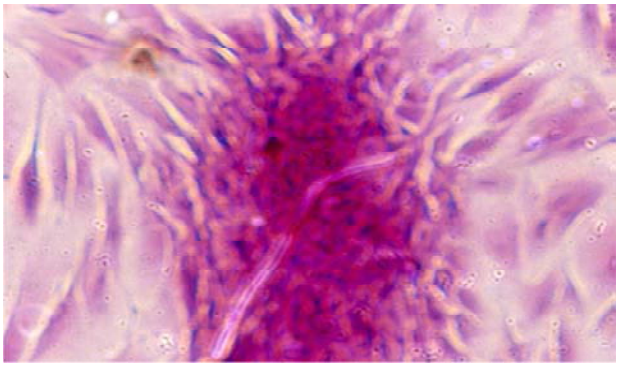
4.2 Services provided

During the reporting period, over 46,000 laboratory animals were supplied for research studies out of which 4553 animals were supplied to outside agencies like academic institutions, pharmaceutical industries and research organizations. Details are as follows:

Month	Mice	Rat	Hamster	Mastomys	Gerbil	G. pig	Rabbit	Total
December 08	1442	998	556	75	50	92	25	**3238**
January 09	1834	1963	651	100	20	125	54	**4747**
February 09	1015	1505	394	70	65	-	29	**3078**
March 09	1215	1662	567	100	23	06	19	**3592**
April 09	1362	1871	459	112	35	24	08	**3871**
May 09	1839	1973	489	100	35	120	23	**4579**
June 09	1669	1806	497	90	40	10	76	**4188**
July 09	1421	1699	461	85	45	80	48	**3839**
August 09	1533	1617	598	40	20	11	44	**3863**
September 09	1453	1470	628	100	50	-	75	**3776**
October 09	1915	1278	620	68	45	210	68	**4186**
November 09	1723	1206	431	50	10	-	07	**3427**
G. Total	**18421**	**19048**	**6333**	**990**	**438**	**678**	**476**	**46384**

5. Tissue & Cell Culture Facility

The Central Tissue Culture Facility has been established with an objective of development, maintenance, propagation, cryopreservation, revival of cell lines and extending the necessary support for research. During the reporting period, a new cell line H9c2 - Rat Myoblasts was included in the facility. Further, 120 T-25 cell culture flasks of various cell lines were provided to user scientists for research and development. Besides, facility continued to provide short term training to personnel from academic institutions and industries in techniques of tissue and cell culture.



Fibroblasts Emanating from Gingival Explant

5.1 Cell lines under maintenance

1	MCF-7	Human Breast Cancer ER +ve
2	MDA MB 231	Human Breast Cancer ER -ve
3	L 929	Mouse Connective Tissue Fibroblasts
4	THP 1	Human Monocyte
5	HEK 293	Human Embryo Kidney
6	ZR 75	Human Breast Cancer
7	Hep G2	Human Liver Carcinoma
8	Hep 3B	Human Liver Carcinoma
9	3T3 L1	Mouse Embryo Fibroblasts
10	J774 A.1	Mouse Macrophage
11	Vero C 1008	African Green Monkey Kidney
12	C 6	Rat Glioma
13	L 6	Rat Muscle
14	SHSY 5Y	Human Neuroblastoma
15	hGF	Human Gingival Fibroblast-Primary Culture
16	H9c2	Rat Myoblasts

6. S&T Knowledge Resource Centre (KRC)

The KRC has been established with an objective to provide biomedical information services. This state of art centre is regarded as a premier library in the country for the scientists and entrepreneurs involved in biomedical research and pharmaceutical industry.

KRC continued to provide computerized information services to its users and a total of 540 outside users utilized these services during the year. All activities of the centre are fully computerized and confirm to the norms of e-governance. Its present collection comprises of 22203 books and 70650 bound volumes of journals. Besides, the centre manages, maintains and updates the Institute website & Institutional Repository.

The centre publishes three periodicals viz. 'Drugs & Pharmaceuticals - Industry Highlights' (Monthly), 'Drugs & Pharmaceuticals - Current R & D Highlights' (Quarterly), and a new title 'Recent Patents on Bioinformatics In Drug Research' (Online bi-monthly). The subscribers largely appreciated the contents of these periodicals. The topics covered in four issues of Current R&D Highlights published during the year include - Diabetes, RNA & Drug Discovery, Genetic Basis of Diseases and Hepatitis. Besides 'Special Supplement on IPR Awareness' was published on the occasion of IPR Awareness Workshop organized in April 2009.

6.1 Training programs organized

User training programs and workshops organized by KRC include :

1. E-resources available at KRC, CDRI, Lucknow
2. JCCC@ INSTIRC
3. Web of Science
4. SciFinder
5. Indianjournal.com
6. IPR Awareness Workshop
7. Workshop on Rational Approaches in Drug Designing: Application of Tools & Techniques of Bio-informatics.

7. Biometry and Statistics

The division has an objective of assisting the scientists in planning and designing of experiments, analyse data and draw inferences.

7.1 Tasks carried out

- Modified the questionnaires in English and Hindi for the project *Rural School Health Education Program Integrating with Disease Inputs: Reaching the Unreached*.
- Laboratory data, obtained from various R & D divisions were analysed within stipulated time. The pie diagram depicts the proportional time spent for and works from various divisions over the reported period.
- A computer program was developed to randomize the animals in required groups.
- Postgraduate training was provided to two students from BITS Pilani.
- Acquired SYSTAT 12.0 which has extensively being used for data analysis work.

8. Information Technology Services

The ICT infrastructure was augmented to provide for fully redundant internet leased line connectivity with 2 Mbps (1:1) link from BSNL on optic fiber. A BSNL Broadband connection of bandwidth 1Mbps-Up to 8 Mbps was installed to provide for backup.

CDRI was connected to High Bandwidth low latency 'National Knowledge Network' to interconnect educational and research organisations of the country, facilitating high-end computing intensive research and related services.

MoES database application software was developed and implemented for online transaction between the participating institutes of the MoES sponsored project 'National program on development of potential drugs from ocean'.

The LAN was expanded to provide for wireless connectivity in a few departments. Infrastructure planning and implementation support was extended to NIPER Rae Bareli for its ICT setup.

9. Academic Affairs Unit

The unit primarily works as liaison centre for the award of Ph.D. degree to the research students who are registered with the Jawaharlal Nehru University, New Delhi.

9.1 Tasks carried out :

- Conducted examinations / interviews for the selection of students for CDRI-JNU Ph.D. Program.
- Liaised with JNU for timely registration, synopsis approval, thesis submission, etc.
- Conducted pre-Ph.D. course work as prescribed by JNU.

10. Drawing and Photomicrography

The unit continued to provide its services to the scientists of Institute and other scientific organizations in terms of preparing and providing photographs, power point presentations, exhibition display panels and posters, desgning of covers and layouts for various publications.

11. Instrumentation Division

Instrumentation Division continued to provide repair, maintenance & upkeep of sophisticated analytical, biomedical, electronics and laboratory instruments. Division maintained uninterrupted smooth power supply to all the divisions of the institute. In cases of non-availability of imported components, equivalent indegenous substitutes were installed to ensure the smooth functioning of equipments. Specifications & technical evaluations were also prepared for new equipments.

12. Central Archives and Document Control Unit (CADC)

The state of art GLP compliant CADC unit has been created for the archiving and retrieval of CDRI GLP documents, Standard General Formats, Standard Operating Procedures (SOP's), Floor Plans, Curriculum Vitae (CV's), details of equipment's facility, preclinical regulatory data, study reports, test items and test specimen samples. The unit facilitates implementation of GLP compliance in CDRI and will ultimately act as a central point of control for all GLP related activities. This facility is well equipped with MobiStack-LD2 compactors for dry archiving and Ultra Low Temperature deep freezers for wet archiving along with computer aided facility for electronic archiving. Therefore this unit will mainly function as Central Archives to preserve all data generated from preclinical regulatory studies conducted as per CDRI GLP directives.

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2008

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2009

Total Number of Publications in SCI journals	**: 274**
Number of Publications in Non-SCI journals	**: 15**
Average Impact Factor	**: 2.591**
No. of Publications with >5 Impact Factor	**: 20**
Book Chapters	**: 07**
Instruction Manual	**: 01**

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Book Chapters

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2. Sharma R and Raghubir R. Models for studying stem cell therapy. In Drug Screening Methods. Ed. SK Gupta Publication. Published by Jaypee Medical Publisher, Delhi. pp 82-94, 2009

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4. Raghubir R and Nath C. Neuropharmacology : Neuroscience in India. Eds Dhawan BN , Seth PK. Published by Indian Academy of Neurosciences and CSIR. 2009 pp 147-174

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Patents

I.	Patents Filed Abroad	09
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IV.	Patents Granted in India	12

I. Patents Filed Abroad

1. **US Patent Appl. No.:** 12/376909 **Filing Date:** 09/02/2009

   Title: **Antidiabetic and antidyslipidemic activities of S-(+)-7-[3N- substituted amino-2-hydroxypropoxy] flavones.**

   Inventors: Ram Pratap, Himanshu Singh, Alok Kumar Verma, Amar Bahadur Singh, Priti Tiwari, Mukesh Srivastava & Arvind Kumar Srivastava.

   Supporting Staff: Krishna Kumar Chaudhari & Suresh Yadav.

2. **PCT Appl. No.:** PCT/IN2009/000146 **Filing Date:** 03/03/2009

   Title: **A bioactive extract/fraction from *Ulmus wallichiana* and its compounds for prevention for treatment of osteo-health disorders.**

   Inventors: Rakesh Maurya, Preeti Rawat, Kunal Sharan, Jawed Akhtar Siddiqui, Gaurav Swarnkar, Geetanjali Mishra, Lakshmi Manickavasagam, Girish Kumar Jain, Kamal Ram Arya & Naibedya Chattopadhyay.

   Supporting Staff: Satish Chandra Tiwari, Abdul Malik Tyagi, Devi Dutt & Amruta Kendurkar.

3. **European Patent Appl. No.:** 7805638.9 **Filing Date:** 09/03/2009

   Title: **Antidiabetic and antidyslipidemic activities of S-(+)-7-[3N- substituted amino-2-hydroxypropoxy]flavones.**

   Inventors: Ram Pratap, Himanshu Singh, Alok Kumar Verma, Amar Bahadur Singh, Priti Tiwari, Mukesh Srivastava & Arvind Kumar Srivastava.

   Supporting Staff: Krishna Kumar Chaudhari & Suresh Yadav.

4. **PCT Appl. No.:** PCT/IN2009/000215 **Filing Date:** 31/03/2009

   Title: **Novel donor-accpetor fluorenes, fluorenones and their π-conjugated systems scaffolds: A process and uses thereof.**

   Inventors: Atul Goel, Sumit Chaurasia, Vijay Kumar, Sundar Manoharan & Raghubir Singh Anand.

5. **Viet Nam Patent Appl. No.:** 1-2009-00832 **Filing Date:** 27/04/2009

Title: **Novel 6-(1-aryl ethyl)-1,2,4-trioxanes, useful as antimalarial agents and a process for the preparation thereof.**

Inventors: Chandan Singh, Ajit Shankar Singh & Sunil Kumar Puri.

Supporting Staff: Shashi Rastogi, Akhilesh Srivastava & Kamlesh Singh.

6. **PCT Appl. No.:** PCT/IN2009/000285 **Filing Date:** 14/05/2009

Title: **Substituted benzfurochromenes and related compounds for the prevention and treatment of bone related disorders.**

Inventors: Atul Goel, Amit Kumar, Sumit Chaurasia, Divya Singh, Abnish Kumar Gautam, Rashmi Pandey, Ritu Trivedi, Man Mohan Singh, Naibedya Chattopadhyay, Lakshmi Manickavasagam, Girish Kumar Jain & Anil Kumar Dwivedi.

Supporting Staff: Abdul Malik Tyagi & Avinash Kumar.

7. **Australian Patent Appl. No.:** NG/0/2009/442 **Filing Date:** 13/08/2009

Title: **Novel substituted bis-1,2,4-trioxanes, useful as antimalarial agents and a process for the preparation thereof.**

Inventors: Chandan Singh, Ved Prakash & Sunil Kumar Puri.

8. **Australian Patent Appl. No.:** 2009212969 **Filing Date:** 07/09/2009

Title: **Herbal medicaments for treatment of neurocerebrovascular disorders.**

Inventors: Madhur Ray, Raghwendra Pal, Satyawan Singh & Nandoo Mal Khanna.

Supporting Staff: Jharna Arun & Madhuri Chaudhari.

9. **Viet Nam Patent Appl. No.:** 1-2009-01910 **Filing Date:** 10/09/2009

Title: **Novel substituted bis-1,2,4-trioxanes, useful as antimalarial agents, and a process for the preparation thereof.**

Inventors: Chandan Singh, Ved Prakash & Sunil Kumar Puri.

II. Patents Filed in India

1. **Patent Appl. No.:** 0384DEL2009 **Filing Date:** 27/02/2009

Title: **Polymeric nanomatrix associated delivery of Kaempferol in rats to improve its osteogenic action.**

Inventors: Prabhat Ranjan Mishra, Ritu Trivedi, Girish Kumar Gupta, Avinash Kumar, Varsha Gupta, Srikanta Kumar Rath, Kamini Srivastava, Naibedya Chattopadhyay & Anil Kumar Dwivedi.

Supporting Staff: Mahesh Chandra Tewari & Geet Kumar Nagar.

2. **Patent Appl. No.:** 0458DEL2009 **Filing Date:** 09/03/2009

Title: **Novel substituted spiro [indoline-heterocycle]-carboxylic acid derivatives as antidiabetic and metabolic disorder treating agents.**

Inventors: Atul Kumar, Ram Awatar Maurya, Arvind Kumar Srivastava, Amar Bahadur Singh & Akhilesh Kumar Tamrakar.

Supporting Staff: Tahseen Akhtar Ansari.

3. **Patent Appl. No.:** 2344DEL2009 **Filing Date:** 13/11/2009

Title: **A mercapto phenyl naphthyl methane compounds and preparation thereof.**

Inventors: Sangita, Atul Kumar, Man Mohan Singh, Girish Kumar Jain, Puvvada Sri Ramachandra Murthy & Suprabhat Ray.

4. **Patent Appl. No.:** 0080NF2009 **Filing Date:** 29/01/2010

Title: Novel di-spiro cycloalkanones useful as inhibitors of NAD^+ -dependant DNA ligase and antitubercular agents.

Inventors: Rama Pati Tripathi, Jyoti Pandey, Nimisha Singh, Divya Dube, Vandna Kukshal, Shalini Bhatnagar, Sudhir Sinha, Vinita Chaturvedi & Ravishankar Ramachandran.

5. **Patent Appl. No.:** 0082NF2009 **Filing Date:** 29/01/2010

Title: An antitubercular formulation of 4-alkoxy phenyl cyclopropyl alkanols.

Inventors: Rama Pati Tripathi, Prabhat Ranjan Mishra, Girish Kumar Gupta, Surendra Singh Bisht, Jyoti Pandey, Vinita Chaturvedi, Sudhir Sinha, Varsha Gupta & Anil Kumar Dwivedi.

III. Patents Granted Abroad

1. **Chinese Pat. No.:** ZL2802523.7 **Grant Date:** 28/01/2009

Patent Appl. No.: 2802523.7 **Filing Date:** 31/03/2003

Title: **Substituted 1,2,4-trioxanes useful as antimalarial agents and a process for the preparation thereof.**

Inventors: Chandan Singh, Pallvi Tiwari & Sunil Kumar Puri.

2. **Malaysian Pat. No.:** MY-137775-A **Grant Date:** 31/03/2009

Patent Appl. No.: PI 20023694 **Filing Date:** 10/03/2002

Title: **Synergistic antimalarial formulation.**

Inventors: Guru Prakash Dutta, Dharam Chand Jain, Ranjendra Singh Bhakuni, Sudhanshu Saxena, Sangeeta Dhawan, Suman Preet Singh Khanuja, Sushil Kumar, Renu Tripathi, Aseem Umesh, Nuzhat Kamal, Anil Kumar Dwivedi & Satyawan Singh.

3. **US Pat. No:** 7495025 **Grant Date:** 24/02/2009

Patent Appl. No.: 11/514453 **Filing Date:** 01/09/2006

Title: **Novel spiro 1,2,4 trioxanes as antimalarial agents and a process for the preparation thereof.**

Inventors: Chandan Singh, Heetika Malik & Sunil Kumar Puri.

Supporting Staff: Shashi Rastogi, Akhilesh K. Srivastava & Kamlesh Kumar Singh.

4. **European Pat. No.:** 1831172 **Grant Date:** 18/02/2009

Patent Appl. No.: 4816679.7 **Filing Date:** 28/12/2004

Title: **Substituted carbamic acid quinolin-6-yl esters as acetylcholinesterase inhibitors.**

Inventors: Neeraj Shakya, Zeeshan Fatima, Chandishwar Nath & Anil Kumar Saxena.

Supporting Staff: Zahid Ali & Bishambhar Nath.

5. **European Pat. No.:** 1684781 **Grant Date:** 11/02/2009

Patent Appl. No.: 03769719 **Filing Date:** 26/05/2006

Title: **Novel herbal composition for the treatment of gastric ulcer.**

Inventors: Janaswamy Madhusudhana Rao, Upparapally Sampathkumar, Boggavarapu Subrahmanya Sastry, Jhillu Singh Yadav, Kondapuram Vijaya Raghavan, Gautam Palit, Dwaraka Nath Bhalla, Deepak Rai, Panniyampally Madhavankutty Varier, Trikovil Sankaran Muraleedharan & Kollath Muraleedharan.

6. **Sri Lankan Pat. No.:** 14128 **Grant Date:** 30/04/2009

Patent Appl. No.: 14128 **Filing Date:** 20/06/2006

Title: **Process for isolation of saponin disogenin pentaglycoside.**

Inventors: Vijay Lakshmi, Kartikay Pandey, Raja Roy, Bhawani Shanker Joshi, Kunnath Padmanabhan Madhusudanan, Ramesh Chandra, Arvind Kumar Srivastava, Deepak Raina & Anil Kumar Rastogi.

Supporting Staff: Ashok Kumar Khanna.

7. **Sri Lankan Pat. No:** 14131 **Grant Date:** 30/04/2009

Patent Appl. No.: 14131 **Filing Date:** 20/06/2006

Title: **Improved process for isolation of Bisvittoside D from sea cucumber.**

Inventors: Vijay Lakshmi, Ajet Saxena, Kartikay Pandey, Kunnath Padmanabhan Madhusudanan, Mahendra Nath Srivastava, Zafar Kamal Khan, Pooja Jain, Gopal Gupta & Janak Dulari Dhar.

Supporting Staff: Jagdamba Prasad Maikhuri.

8. **Ukranian Pat. No.:** 86600 **Grant Date:** 12/05/2009
Patent Appl. No.: a200605416 **Filing Date:** 22/10/2003
Title: **Biodegradable, inhalable microparticles containing antitubercular drugs.**
Inventors: Himadri Sen, Suryakumar Jayanthi, Rakesh Sinha, Rolee Sharma & Pawan Muttil.

9. **Mexican Pat. No.:** 266702 **Grant Date:** 13/05/2009
Patent Appl. No.: PA/A/2004/05680 **Filing Date:** 11/06/2004
Title: **A composition for treating neurocerebrovascular disorders.**
Inventors: Madhur Ray, Raghwendra Pal, Satyawan Singh & Nandoo Mal Khanna.
Supporting Staff: Jharna Arun & Madhuri Chaudhari.

10. **Canadian Pat. No.:** 2512508 **Grant Date:** 09/06/2009
Patent Appl. No.: 2512508 **Filing Date:** 30/06/2005
Title: **An improved process for the synthesis of guggulsterones: A pharmacologically active constituent of gugulipid.**
Inventors: Ram Pratap, Dharmendra Pratap Singh, Raghwendra Pal & Satyawan Singh.

11. **European Pat. No.:** 1453528 **Grant Date:** 22/07/2009
Patent Appl. No.: 02781641.2 **Filing Date:** 15/06/2004
Title: **Herbal medicaments for treatment of neurocerebrovascular disorders.**
Inventors: Madhur Ray, Raghwendra Pal, Satyawan Singh & Nandoo Mal Khanna.
Supporting Staff: Jharna Arun & Madhuri Chaudhari.

12. **Chinese Pat. No.:** ZL200380110617.9 **Grant Date:** 05/08/2009
Patent Appl. No.: 200380110617.9 **Filing Date:** 28/04/2006
Title: **Novel herbal composition for the treatment of gastric ulcer.**
Inventors: Janaswamy Madhusudhana Rao, Upparapally Sampathkumar, Boggavarapu Subrahmanya Sastry, Jhillu Singh Yadav, Kondapuram Vijaya Raghavan, Gautam Palit, Dwaraka Nath Bhalla, Deepak Rai, Panniyampally Madhavankutty Varier & Trikovil Sankaran Muraleedharan.

13. **Great Britain Pat. No.:** ZL2827077 **Grant Date:** 19/08/2009
Patent Appl. No.: 2827077 **Filing Date:** 13/07/2004
Title: **Herbal medicaments for treatment of neurocerebrovascular disorders.**
Inventors: Madhur Ray, Raghwendra Pal, Satyawan Singh & Nandoo Mal Khanna.
Supporting Staff: Jharna Arun & Madhuri Chaudhari.

14. **US Pat. No.:** 7582653 **Grant Date:** 01/09/2009

Patent Appl. No.: 11/812251 **Filing Date:** 15/06/2007

Title: **Substituted mercapto phenyl naphthyl methane derivatives as SERM for the prevention and treatment of osteoporosis and other estrogen dependent disorders and as contraceptives.**

Inventors: Sangita, Atul Kumar, Man Mohan Singh, Girish Kumar Jain, Puvvada Sri Ramanchandra Murthy & Suprabhat Ray.

Supporting Staff: Vasi Ahmad, Abdul Haq Ansari, Mohini Chhabra & Govind Keshri.

15. **US Pat. No.:** 7601838 **Grant Date:** 13/10/2009

Patent Appl. No.: 11/023915 **Filing Date:** 28/12/2004

Title: **2-Alkyl/aryl sulphonyl-1,2,3,4-tetrahydro-9H-pyrido (3,4-b) indole-3-carboxylic acid esters/amides as antithrombotic agents.**

Inventors: Stuti Gaur, Zeeshan Fatima, Anshuman Dixit, Zahid Ali, William Rascan Surin, Kapil Kapoor, Kanta Bhutani, Mohd. Salim Ansari, Madhu Dikshit & Anil Kumar Saxena.

Supporting Staff: Arimardan Singh Kushwaha & Dayanand Vishwakarma.

IV. Patents Granted in India

1. **Patent No.:** 227532 **Grant Date:** 13/01/2009

Patent Appl. No.: 1062DEL2003 **Filing Date:** 28/08/2003

Title: **Herbal extracts of *Salicornia* species, process of preparation thereof, use thereof against tuberculosis.**

Inventors: Meena Rajnikanth Rathod, Bhupendra Dhanvantrai Shethia, Jayant Batukrai Pandeya, Pushpito Kumar Ghosh, Prakash Jagjivanbhai Dodia, Brahm Shankar Srivastava, Ranjana Srivastava, Anil Srivastava & Vinita Chaturvedi.

2. **Patent No.:** 227863 **Grant Date:** 22/01/2009

Patent Appl. No.: 2057DEL2004 **Filing Date:** 20/10/2004

Title: **Novel substituted 1,2,4-trioxanes.**

Inventors: Chandan Singh, Sunil Kumar Puri & Pallavi Tiwari.

Supporting Staff: Shashi Rastogi & Akhilesh Kumar Srivastava.

3. **Patent No.:** 229247 **Grant Date:** 16/02/2009

Patent Appl. No.: 02838DELNP2004 **Filing Date:** 22/09/2004

Title: **A composition for treating neurocerebrovascular disorders.**

Inventors: Madhur Ray, Raghwendra Pal, Satyawan Singh & Nandoo Mal Khanna.

Supporting Staff: Jharna Arun & Madhuri Chaudhari.

4. **Patent No.:** 231654 **Grant Date:** 07/03/2009
Patent Appl. No.: 1311DEL2001 **Filing Date:** 31/12/2001
Title: **Novel 6-[(cycloalkylphenyl) vinyl]-1,2,4-trioxanes useful as antimalarial agents.**
Inventors: Chandan Singh, Pallvi Tiwari & Sunil Kumar Puri.
Supporting Staff: Shashi Rastogi & Akhilesh Kumar Srivastava.

5. **Patent No.:** 231699 **Grant Date:** 08/03/2009
Patent Appl. No.: 0323DEL2001 **Filing Date:** 23/03/2001
Title: **An improved process for the synthesis of 3,4- disubstituted-1,5-dihydro-2H-3-pyrrolin-2-one.**
Inventors: Kalpana Bhandari, Vishnu Lal Sharma & Suprabhat Ray.
Supporting Staff: Radha Rani Gupta.

6. **Patent No.:** 232539 **Grant Date:** 18/03/2009
Patent Appl. No.: 1579DEL1999 **Filing Date:** 28/12/1999
Title: **Novel substituted 1,2,4-trioxanes useful as antimalarial agents.**
Inventors: Chandan Singh & Sunil Kumar Puri.

7. **Patent No.:** 233025 **Grant Date:** 25/03/2009
Patent Appl. No.: 1554DEL1999 **Filing Date:** 21/12/1999
Title: **Novel substituted 1,2,4 α-trioxanes as antimalarial agents.**
Inventors: Neena Goyal & Mukul Kumar Mittal.

8. **Patent No.:** 233470 **Grant Date:** 30/03/2009
Patent Appl. No.: 0260DEL2003 **Filing Date:** 10/03/2003
Title: **(-)-3S, 4S-trans -2,2- dialkyl -3-substituted phenyl-4-(hydroxy substituted phenyl) substituted chroman derivatives as useful intermediates for the synthesis of selective estrogen modulators.**
Inventors: Atul Kumar, Sangita & Suprabhat Ray.
Supporting Staff: Vashi Ahmad.

9. **Patent No.:** 233980 **Grant Date:** 24/04/2009
Patent Appl. No.: 0774DEL2002 **Filing Date:** 25/07/2002
Title: **Novel synthesis of organic carbamates.**
Inventors: Chandan Singh, Rani Kanchan & Sunil Kumar Puri.

10. **Patent No.:** 234487 **Grant Date:** 01/06/2009

Patent Appl. No.: 1364DEL2003 **Filing Date:** 06/11/2003

Title: **α-substituted naphthyloxy-ω- substituted alkyl/aryl amino substituted alkane derivatives as agents for the treatment or prophylaxis of diabetes and related metabolic disorders.**

Inventors: Devdutt Chaturvedi, Atul Kumar, Reema Rastogi, Arvind Srivastava, Priti Tewari, Rehan Ahmad, Ramesh Chander, Anju Puri, Geetika Bhatia, Farhan Rizvi, Anil Kumar Rastogi & Suprabhat Ray.

11. **Patent No.:** 235205 **Grant Date:** 29/06/2009

Patent Appl. No.: 1196DEL2001 **Filing Date:** 29/11/2001

Title: **A novel 1-arylalkyl-5-oxo-proline carboxamides.**

Inventors: Dinesh Kumar Dikshit, Madhu Dikshit, Stuti Srivastava & Prashant Sharma.

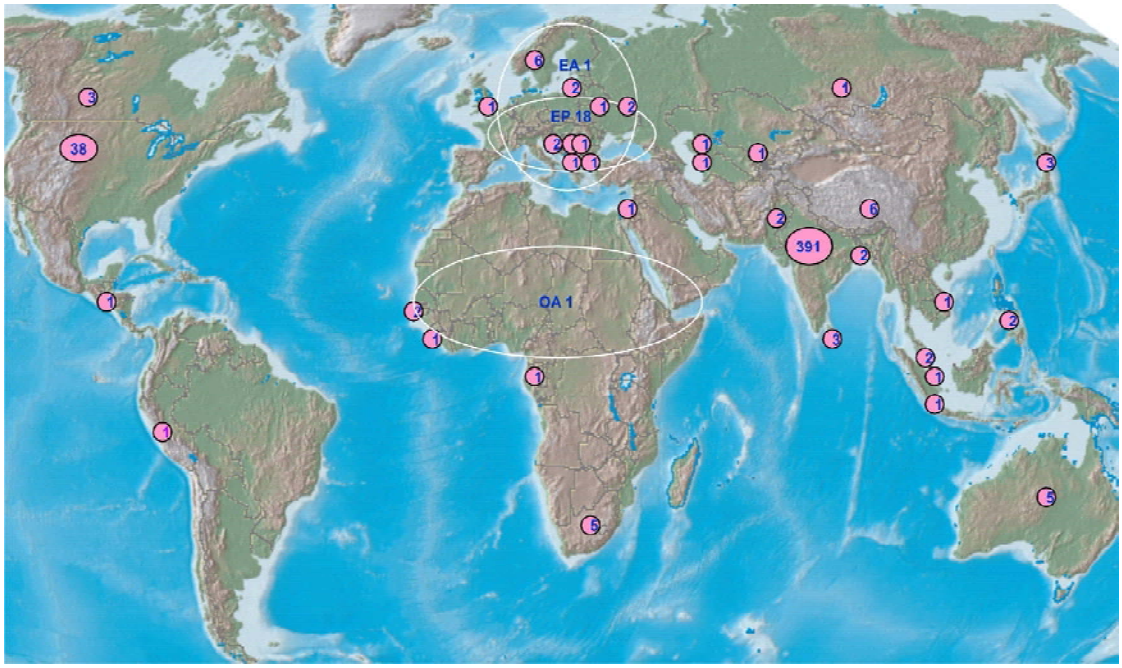
12. **Patent No.:** 237239 **Grant Date:** 10/12/2009

Patent Appl. No.: 05373DELNP2005 **Filing Date:** 23/11/2005

Title: **Heterologous expression of trypanothione reductase from *Leishmania donovani* in a prokaryotic system.**

Inventors: Neena Goyal & Mukul Kumar Mittal.

Global Distribution of Patents-in-force



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Peru	1	South Africa	5	Viet Nam	1

Papers Presented in Conferences

2008

(Not included in Annual Report 2008-09)

International Symposium on Advances in Neurosciences & 26th Annual Conference of Indian Academy of Neurosciences, Cochin (12-14 December)

Inhibition of pro-inflammatory cytokines via α7 nicotinic acetylcholine receptor in LPS induced neuoinflammation.
E. Tyagi, R. Agrawal, C. Nath & R. Shukla.

Correlation of oxidative stress with acetylcholinesterase activity in ICV STZ induced dementia model in rat.
R. Agrawal, E. Tyagi, C. Nath & R. Shukla.

Protective effect of donepezil on LPS-induced neuroinflammation in rat.
R. Shukla, E. Tyagi, R. Agrawal & C. Nath.

Anti-proliferation and antiinflammatory effect of Guggulipid on LPS stimulated human astrocytoma cell line U373MG.
R. Niranjan & R. Shukla.

International Symposium on Prognostic and Predictive Factors in Cancer Management: Clinical Applications, Lucknow (15-16 December)

Significant association of the Single Nucleotide Polymorphism (SNP) rs13181 in the gene ERCC2 with the risk of Squamous Cell Carcinomas of the Head and Neck (SCCHN) and breast cancer among north Indians.
A.K. Mitra, S.V. Singh, S. Agarwal, A. Zaidi, V.K. Garg, R. Chaturvedi, M. Sharma & S.K. Rath.

4th NOST Conference, Madurai (6-9 December)

Palladium-free lactone methodology to various donor-acceptor biaryl and heteroaryl scaffolds.
A. Kumar & A. Goel.

Indian Pharmacological Society Meeting, New Delhi (18-20 December)

Involvement of p53, p21 and BCl2 members in Centchroman induced apoptosis in MCF-7 and MDA MB231 human breast cancer cells.
M. Nigam, V. Ranjan, N. Singh, R. Sharma & A.K. Balapure.

Centchroman potentiates mitochondrial events leading to oxidative insult in human breast cancer cells.
V. Ranjan, M. Nigam , D. Zaidi, R. Sharma, S. Sundaram & A.K. Balapure.

2009

4th Indo-US Lecture Series on Discrete Mathematical Chemistry (With Applications to Drug Discovery, Environmental Protection, Genomics and Proteomics), Hyderabad (6–9 January)

The solubility challenge: A prospective and retrospective analysis.
S. Deshpande, M. Goodarzi, B.K. Sharma, S.B. Katti & Y.S. Prabhakar.

International Conference on Novel Updates in Reproductive Biology and Comparative Endocrinology and 27th SRBCE, Hyderabad (19-21 January)

Reproductive toxicological effects of artesunate and proguanil in male albino rats.
O.S. Akinsomisoye, R.K. Jain, V. Verma, A. Jain, R. Kumar, J.P. Maikhuri, Y. Raji, O.G. Ademowo & G. Gupta.

Timing feedback inhibition by testosterone: Disruption of spermatogenesis and induction of LH gonadotrope apoptosis.
R. Malik, S. Tondwal, K.S. Venkatesh, G. Gupta & A. Misra.

4th RBF Symposium on Current Trends in Pharmaceutical Sciences Advances in Cardiometabolic Research - Basic Science and Clinical Aspect, Ahmedabad (2-5 February)

Atherosclerosis and complications: The road ahead.
M.K. Barthwal.

Platelet and coagulation activation in high fat high fructose diet fed hyperlipidemic hamsters.
V. Singh, V. Khanna, T. Santosh, A. Puri, S. Bhadauria, M.K. Barthwal & M. Dikshit.

Effect of antithrombotic drugs on ferric chloride induced thrombosis in rats.
W.R Surin, P. Prakash, M.K. Barthwal & M. Dikshit.

Effect of aging on atherosclerosis progression in mice.
V. Singh, M. Jain, M. Dikshit & M.K. Barthwal.
Aspirin inhibits atherothrombotic events in hyperlipidemic hamsters.
M. Jain, V. Singh, P. Prakash, R.L. Tiwari, A. Mishra, R.S. Keshari, S. Singh, M. Dikshit & M.K. Barthwal.

Evaluation of herbal medicament for the antiplatelet effect in various experimental models of thrombosis.
W.R. Surin, A. Misra, P. Prakash, M.K. Barthwal & M. Dikshit.

4th World Congress on Leishmaniasis, Lucknow (3-7 February)

Cloning and expression of N-terminal domain of proteophosphoglycan (PPG) of *Leishmania donovani* and its evaluation as DNA vaccine candidate.
M. Samant, R. Gupta, P. Misra, P. Khare, P. Kushwaha & A. Dube.

Photodynamic vaccination of hamsters with inducible suicidal mutants of *Leishmania amazonensis* elicits T cell-transferable immunity against visceral leishmaniasis.
S. Kumari, M. Samant, P. Khare, P. Misra, S. Dutta, B. K. Kolli, S. Sharma, K.P. Chang & A. Dube.

Piper betel Linn. - a cultural plant with medicinal property: Antileishmanial efficacy in *Bangla mahoba* Landrace with high eugenol content mediated with apoptosis like cell death.
P. Misra, N. Singh, S. Gupta, A. Kumar, A. Jaiswal, R. Tandon, R. Baharia & A. Dube.

Triose Phosphate Isomerase (TPI) - a potential Th1 stimulatory protein: Cloning, expression, purification and assessment of its cellular response in Leishmania infected cured hamsters.
P.K. Kushawaha, R. Gupta, M. Samant, R. Tandon, R.K. Baharia & A. Dube.

Stable expression of GFP in Leishmania clinical isolates: a tool for *ex vivo* screening of natural products.
R. Gupta, N. Singh, A. K. Jaiswal, R. Tandon & A. Dube.

In vitro and *in vivo* efficacy of *Abutilon indicum* – a herbaceous Indian plant against *Leishmania donovani* infection.
P. Khare, P. Rastogi, P. Misra, S. Gupta, R. Maurya & A. Dube.

Development of novel nanocarrier for effective treatment of visceral Leishmaniasis.
M. Nahar, V. Dubey, P. Mishra, P. Khare, A. Dube & N.K. Jain.

A computational docking study of 5-hydroxy-4-[2-(1,2,4a,5-tetramethyl-1,2,3,4,4a,7,8,8a-octahydro naphthalen-1-yl)-5H-furan-2-one: A Leishmanial DNA topoisomerase I as a target for antileishmanial activity.
A.K. Saxena, S.S. Chaudhaerya, S.P. Singh, K. Sashidhara, P. Misra, R. Gupta, H.K. Majumdar & A. Dube.

Identification and analysis of differentially expressed proteins of sodium antimony gluconate sensitive and resistant clinical isolates of Leishmania.
A. Kumar, P. Misra, B.S. Sisodia, S. Sundar, A.K. Shasany & A. Dube.

Glycosomal targeting of hexokinase is essential in *Leishmania donovani*.
R. Kumar, S. Gupta & A.A. Sahasrabuddhe.

Immuno-chemotherapy of experimental visceral Leishmaniasis using Miltefosine in combination with CpG-ODN: A preliminary study.
S. Gupta, S.A. Sane, Nishi & W. Haq.

Therapeutic switching of primaquine in treatment of visceral Leishmaniasis in combination with oral drug Miltefosine and an immunomodulator.
N. Shakya, S.A. Sane & S. Gupta.

Antileishmanial efficacy of paromomycin and Miltefosine combined with the immunomodulator Picroliv.
S. A. Sane, Nishi & S. Gupta.

The antileishmanial activity of novel tetrahydronaphtyl azoles.
K. Bhandari, N. Srinivas, V.K. Marappu, S. Palne, Nishi & S. Gupta.

Experimental models for lead optimization of novel antileishmanial agents.
S.K. Puri & S. Gupta.

Cloning over expression and characterization of *L. donovani* squalene synthase.
U. Roy.

Alexander Von Humboldt Network Meeting, Konstanz, Germany (4-6 February)

Efficient synthesis of novel biaryl lactones and their atropo-enantio selective ring opening to axially chiral biaryl scaffolds.

A. Goel, T.A.M. Gulder, V. Kumar, M. Knauer, D. Goetz & G. Bringmann.

11th CRSI National Symposium in Chemistry, Pune (6-8 February)

Novel donor-acceptor fluoranthenes for yellow organic light emitting diodes.

V. Kumar, S. Chaurasia, R.S. Anand & A. Goel.

International Congress on Bio-immunoregulatory Mechanisms Associated with Reproductive Organs: Relevance in Fertility and in Sexually Transmitted Infections, New Delhi (9-13 February)

In vitro evaluation of *Sapindus* saponins as a microbicide using *Trichomonas* infected HeLa.

A. Jain, R.K. Jain, V. Vikas, R. Kumar, J.P. Maikhuri & G. Gupta.

Functional attenuation of human sperm by promising non-surfactant spermicides - precise targeting of membrane physiology without affecting its structure.

R.K. Jain, A. Jain, V. Verma, R. Kumar, J.P. Maikhuri & G. Gupta.

International Conference on Advances in Biosciences: From Darwin to Dolly and Beyond, Nanded (12-14 February)

Studies on susceptibility of Balb/c mice to *L. donovani* infection.

S. Mishra & S. Gupta.

NIPER-BMS International Drug Metabolism and Pharmacokinetics Symposium, Mohali (13-14 February)

Liquid–liquid extraction of strongly protein bound Lumefantrine from rat plasma followed by high-performance liquid chromatography/tandem mass spectrometry.

Wahajuddin, S.P. Singh & G.K. Jain.

28th Annual Convention of Indian Association for Cancer Research and International Symposium on Emerging Challenges and Approaches in Cancer Biology, Bangalore (21-24 February)

Glutathione S-transferase M1 and T1 polymorphisms in breast cancer patient.
H.K. Bid, P. Chaudhary, D. Chaudhary, N. Chattopadhyay, S.K. Tiwari, S. Kumar & R. Konwar.

In vitro anti-breast cancer activity of new synthetic benzocoumarins: Induction of cell cycle arrest and caspase-dependent apoptosis in MCF-7 Cells.
R. Konwar, R.K. Gara, K.V. Sashidhara, J.N. Rosaiah, N. Chattopadhyay & H.K. Bid.

Lack of association of VDR gene polymorphisms with risk of breast cancer in Indian population.
H.K. Bid, V.L. Nayak, D. Chaudhary, N. Chattopadhyay, S.K. Tiwari, S. Kumar & R. Konwar.

NIPER Second Winter School 2009– Nanotechnology in Advanced Drug Delivery, Mohali (24-28 February)

Inhalable poly lactide particles as drug carrier against tuberculosis.
R.K Verma & A. Misra.

National Symposium on Animal Models in Biomedical Research: Ethical & Welfare Issues, Lucknow (25-26 February)

Alternatives to laboratory animals in biomedical research.
R. Sharma & A.K. Balapure.

Health hazards associated with laboratory rodents.
D. Hansda, K. Rai, A.K. Srivastava & D.S. Upadhyay.

Practice of procuring routine feed and feed ingredients required for laboratory animals and their quality control.
D. Hansda, R. Singh & D.S. Upadhyay.

Various feed formulations fulfilling the need of laboratory animals under biomedical experimentations.
D. Hansda, R. Singh, K. Rai & D.S. Upadhyay.

Variability in pelleted feed components of laboratory animal feed: Implications on performance of model animal and decision making procedures.
D. Hansda, R. Singh & D.S. Upadhyay.

Common breeding practices for laboratory rodents.
K. Rai, D.S. Upadhyay & Dhananjoy Hansda.

Management of routine maintenance jobs in the laboratory animal facility.
A.K. Bhargava, D.S. Upadhyay & D. Hansda.

Impact of waste disposal practices for upkeep of hygienic status of laboratory animals facility.
A.K. Bhargava, D.S. Upadhyay & D. Hansda.

Effective management of *Myobia musculi* infestation in conventional mice colony by Amitraz (N-methylbis (2,4-xylyliminomethyl methylamin) and carbaryl dust.
S.N.A. Rizvi, K. Rai, D. Hansda & D.S. Upadhyay.

Breeding and management of albino S.D. Rat (*Rattus norvegicus*) for biomedical experimentation.
A.K. Srivastava, D. Hansda, K. Rai & D.S. Upadhyay.
Effect of commercial and in house feed on growth of S.D. rats.
R. Singh, D. Hansda & D.S. Upadhyay.

Comparative study of intestinal microbial flora in guinea pigs (*Cavia porcellus*) maintained on in house formulated diet and commercial diet.
R. Singh, S.N.A. Rizvi, D. Hansda & D.S. Upadhyay.

National Laboratory Animal Centre: Its' role in biomedical research and animal welfare.
D.S. Upadhyay.

Breeding of Albino Syrian Hamster (*Mesocricetus auratus*) at National Laboratory Animal Centre.
A.K Srivastava, K. Rai & D.S. Upadhyay.

Development of cross species microsatellite markers in Golden and Albino Hamster.
A. Gupta, S. Dayal & D.S. Upadhyay.

Setaria cervi as alternate model for human filarial parasite.
N.A. Kaushal, A. Tandon, S.K. Singh & D.C. Kaushal.

Plasmodium vivax antigens for evaluation of protective potential in *P. cynomolgi* rhesus monkey model system.
D.C. Kaushal, N. Kumar, S.K. Puri & N.A. Kaushal.

Estimation of ED_{50} for repeated measure observations in animal experiment: anti-diabetic studies.
M. Srivastava, M. Abbas & A.K. Srivastava.

Statistical assessment of bone quality of laboratory animals: Sprague-Dawley rats.
M. Srivastava, M. Abbas & M.M. Singh.

13th ISCB International Conference on Interplay of Chemical and Biological Sciences: Impact on Health and Environment, New Delhi (26 February-1 March)

Synthesis and bioevaluation of indole derivatives as antileishmanial agents.
S.S. Chauhan, M. Sharma, S. Gupta & P.M.S. Chauhan.

Synthesis and biological evaluation of (Z)-2-amino-4-methylene-1H-imidazole-5(4H)-one derivatives.
S. Khan, R. Kumar, J. Sarkar, S. Sinha, K. Srivastava, S. Gupta & P.M.S Chauhan.

HDP-A novel heme detoxification protein from *Plasmodium vinckei*.
A. Soni, S. Kumar & S.K. Puri.

Differential proteomic study revealed HPRT as a potential antimalarial drug target.
S. Kumar, A. Soni & S.K. Puri.

Macrofilaricidal efficacy of resin of *Moringa oleifera* Lam against *Brugia malayi in vitro* and *in vivo*.
V. Kushwaha, K. Saxena, S.K. Joseph, V. Dube, A. Sharma, S. Srivastava, S.K. Mishra, V. Lakshmi, R.K. Sharma & P.K. Murthy.

Excretion of the anti-ischemic and anti-hypertensive aryl piperazine derivative CDRI compound 93/478 in rats.
J. Lal, S.K. Pandey & R.C. Gupta.

Cloning of *Brugia malayi* transketolase.
A. Verma & J.K. Saxena.

A three-dimensional *in silico* pharmacophore model for substituted 1,2,4-trioxanes as potential antimalarial agents.
A.K. Gupta & A.K. Saxena.

Hypo Gen-based pharmacophore model development on structurally diverse carbamates as acetylcholinesterase inhibitors.
S.S. Chaudhaerya, K.K. Roy & A.K. Saxena.

3D-QSAR common feature pharmacophore model for protein-tyrosine phosphatases 1B inhibitors as antidiabetic agents.
S. Gupta & A.K. Saxena.

Design and synthesis of aryl-piperzines as possible agents for BPH management.
A. Sarswat, V.L. Sharma, R. Kumar, V. Verma, J.P. Maikhuri & G. Gupta.

Design and synthesis of 2-(pyrimidin-2-yl)-1-phenyl-2,3,4,9-tetrahydro-1H-β-carbolines as anticancer agents.
R. Kumar, S. Khan, J. Sarkar, S. Sinha & P.M.S. Chauhan.

Synthesis and biological evaluation of (Z)-2-amino-4-methylene-1H- imidazole-5(4H)-one derivatives.
S. Khan, R. Kumar, J. Sarkar, S. Sinha, K. Srivastva, S. Gupta & P.M.S. Chauhan.

Design and Synthesis of 2,3,4,9-tetrahydro-β-carboline dimers with potent anticancer activity.
L. Gupta, J. Sarkar, S. Sinha & P.M.S. Chauhan.

Synthesis of novel thiourea, thiazolidinedione and thioparabanic acid derivatives of 4-aminoquinoline as potent antimalarials
N. Sunduru, K. Srivastava, S.R. Kumar, S.K. Puri, J.K. Saxena & P.M.S. Chauhan.

Synthesis and bioevaluation of indole derivatives as antileishmanial agents.
S.S. Chauhan, M. Sharma, S. Gupta & P.M.S. Chauhan.

Synthesis and antimalarial activity of 4-aminoquinoline derivatives having oxalamide, triazine functionalities in the side chain.
M. Sharma, N. Sunduru, K. Srivastava, S.K. Puri & P.M.S. Chauhan.

20th International Symposium on Pharmaceutical & Biomedical Analysis, Agra (1-4 March)

In vitro drug metabolism: Data correlation and constraints.
S. Mishra & G.K. Jain.

High performance liquid chromatography – electrospray ionisation mass spectrometric method for analysis of medicarpin in rat plasma.
M. Lakshmi, A. Kendurkar, D. Dubey & G.K. Jain.

Development and validation of a sensitive and selective liquid chromatography-tandem mass spectrometry method for quantitation of a novel antidiabetic flavonoid in rat plasma and its application to pharmacokinetic study.
N. Gautam & S.K. Singh.

Optimization and validation of LC-MS/MS method with liquid-liquid extraction for determination of Curcumin in rat plasma: Application to pharmacokinetic study.
Wahajuddin, S.P. Singh & G.K. Jain.

HPLC method for determination of Kaempferol, quercetin and rutin from *Gingko biloba* extract in rat serum and tissues.
A.K. Dwivedi, V. Gupta, J. Madan, S. Kumar, A. Kumar, R. Trivedi & N. Chattopadhyay.

International Conference on "Advances in Free Radical Research: Natural Products, Anti-oxidants and Radioprotectors", Lucknow (19-21 March)

Expedient synthesis of some novel pregnane derivatives and their evolution as antioxidant and antidyslipidemic agents.
G. Bhatia, A. Sethi, A.K. Khanna, M.M. Khan, J.K. Saxena, A.K. Pandey, A. Maurya & D. Shukla.

Nitrite induced cell cycle progression in S phase in the promyelocytic cells without apoptosis.
S. Kumar, M.K. Barthwal & M. Dikshit.

Nitric oxide dependent release of neutrophil extracellular traps from adhered human neutrophils.
R.S. Keshari, A. Jyoti, S. Kumar, B.S. Srinag, A. Verma, H. Krishnamurthy, V.K. Bajpai, M.K. Barthwal & M. Dikshit.

Nitric oxide dependent free radical generation in human neutrophils: Role of NOS, NADPH oxidase and MPO.
A. Jyoti, S. Kumar, R.S. Keshari, A. Verma, M.K. Barthwal & M. Dikshit.

International Conference on "Open Source for Computer Aided Drug Discovery (OSCADD), Chandigarh (22-26 March)

In silico prediction of antileishmanial activity of marine and terrestrial substances.
R.K. Sharma, B. Rupani & R. Raghubir.

Identification and prioritization of potent antitubercular compounds using virtual screening and molecular docking.
M.I. Siddiqi.

1st CDRI-NIPER (RBL) Symposium on Medicinal Chemistry and Pharmaceutical Sciences, Lucknow (24-26 March)

A simple and selective HPLC-ESI-MS/MS assay for the simultaneous quantification of Curcumin and demethoxy-curcumin in rat plasma: Application to pharmacokinetic study.
S.P. Singh, Wahajuddin & G.K. Jain.

Optimization and validation of LC-MS/MS method with liquid-liquid extraction for determination of Curcumin in rat plasma: Application to pharmacokinetic study.
P. Kushal & Wahajuddin.

Bioanalytical method development and validation of 16-dehydropregnenalone in human plasma by LC-MS/MS: Application to pharmacokinetics study.
D.K. Dubey, Y.S. Chhonker, R.S. Bhatta, R. Pratap, A. Ghatak, O.P. Asthana & G.K. Jain.

Determination of S-000-20 in rabbit plasma by HPLC: Validation and its application to pharmacokinetic studies.
S. Pandey, S. Gupta, Y.S. Chhonker, D.K. Dubey, R.S. Bhatta, D.K. Dixit & G.K. Jain.

A sensitive and selective LC-MS/MS method for determination of S-002-333 using protein precipitation method in rabbit plasma.
Y.S. Chhonker, D.K. Dubey, S. Gupta, R.S. Bhatta, A.K. Saxena & G.K. Jain.

Quantitative determination of S-001-556 in rabbit plasma by liquid chromatography with electrospray ionization tandem mass spectrometry.
S. Gupta, S. Pandey, D.K. Dubey, Y.S. Chhonker, R.S. Bhatt, K. Raj & G.K. Jain.

In vivo pharmacokinetics in rodents.
C. Hardik & R.S. Bhatta.

Permeability and its role in new drug discovery and development.
Nidhi & J. Lal.

Regulatory guidelines of bioanalytical assays.
H. Kumar & S.K. Singh.

Role of *in vitro* metabolism in drug discovery and development.
C. Rathi & G.K. Jain.

National Seminar on Translational Health Research: Pathways to Discovery, Lucknow (28-29 April)

Computer-aided drug design: Identification and development of potent antitubercular compounds.
M.I. Siddiqi.

2nd International Conference on Drug Development for Third World. Trietse (1-5 June)

Knowledge based identification and prioritization of potent antitubercular compounds using structure-based virtual screening.
M.I. Siddiqi.

Training Course on Computer Design and Discovery of Potential Drugs for Developing Countries, Trieste (8-12 June)

Principles of QSAR and Selected case studies.
M.I. Siddiqi.

International Workshop on "Advanced Design and Development of Potential Drugs against Tuberculosis, Pretoria (3-5 August)

Rational identification and design of potent anti-mycobacterial agents using pharmacophore-based virtual screening, molecular docking and interaction fingerprints.
M.I. Siddiqi.

10th International Colloquium on Paratuberculosis, Minnesota (9-14 August)

In vitro susceptibility of *Mycobacterium avium* paratuberculosis to antibacterial drugs individually and in combination with the immunosuppressive drug 6-mercaptopurine.
M.Y. Krishnan, E.J.B. Manning & M.T. Collins.

International Conference on Enviornmental, Ocupational and Lifestyle Concerns: Transdisciplinary Approach, Bangalore (16-19 September)

Role of oxygen free radicals in chloroquine induced dose specific hepatotoxicity in mice model.
S.K. Mishra, P. Singh, A.K. Verma & S.K. Rath.

17th International Conference on Bioencapsulation, Groningen, Netherlands, (24-26 September)

Pulmonary delivery of microparticles in rhesus monkeys.
R.K Verma & A. Misra.

Ciprofloxacin surf-plexes as emulsion to improve antimicrobial efficacy.
P.R. Mishra, G.K. Gupta, V. Jain, G.B.S. Keshava & P.K. Shukla.

Encapsulated insulin in layer-by-layer assembly for effective per-oral delivery.
G.K. Gupta, A. Verma & P.R. Mishra.

Novel grafted co-polymer self assembled micelles as nanocarriers for amphotericin.
B.V. Kumar, Bholenath, P.R. Mishra & A.K. Dwivedi.

Short Term Training Program on Bioinformatics & System Biology, Lucknow (6-8 October)

Protein 3-D structure prediction and structure-based drug design.
M.I. Siddiqi.

5th Annual Conference of Indian Society of Bone and Mineral Research, Udaipur (8 October)

S-006-1709, a synthetic pterocarpan, promotes bone formation in ovariectomized rats: Ingeniously designed molecules target sperm precisely at concentrations that are inert to HeLa and *Lactobacillus in vitro*.
A.K. Gautam, D. Singh, B. Bhargavan, A. Kumar, M. Dixit, S.D. Dwivedi, N. Singh, L. Manickavasagam, G.K. Jain, A. Goel, S. Sanyal & N. Chattopadhyay.

Medicarpin is a new estrogen mimic in osteoblast, promotes acquisition of peak bone mass in rats.
B. Bhargavan, D. Singh, A.K. Gautam, A. Kumar, M. Dixit, D.K. Yadav, D. Dube, S.D. Dwivedi, N. Singh, L. Manickavasagam, G.K. Jain, R. Maurya, R. Ramachandran, A. Goel, S. Sanyal & N. Chattopadhyay.

Differential effects of cladrin and formononetin on osteoblast function, peak bone mass achievement and bioavailability in rats.
D. Singh, A.K. Gautam, B. Bhargavan, A.M. Tyagi, K. Srivastava, D.K. Yadav, M. Kumar, Akanksha, J.S. Mishra, A.B. Singh, S. Sanyal, R. Maurya, L. Manickavasagam, S.P. Singh, Wahajuddin, G.K. Jain & N. Chattopadhyay.

A biodegradable nanomatrix associated delivery of Kaempferol enhances its osteoprotective effect in rats.
A. Kumar, R. Trivedi, V. Gupta, P.R. Mishra, A.K. Dwivedi & N. Chattopadhyay.

Identification of Kaempferol regulated proteins in rat calvarial osteoblasts during mineralization by proteomics.
B. Changkija, A. Kumar, A.K. Singh, A.K. Gautam, M.P. Singh, D. Singh, N. Chattopadhyay & R. Trivedi.

Bone formation in ovariectomized rats by an orally active small molecule (CDROsteoid-C) by stimulation of transient parathyroid hormone release.
R. Trivedi, B. Changkija, A. Kumar, K. Srivastava, A. Malik, R. Pratap & N. Chattopadhyay.

Advanced Diagnostics and Drug Delivery at the Nanoscale: State of the Art and Possible Applications to Orphan Diseases, Trieste (13-15 October)

Computer-assisted drug design: Rational identification and design of antitubercular compounds.
M.I. Siddiqi.

The Annual Conference of Indian Association of Pathologists and Microbiologists, Lucknow (24 October)

Hypolipidemic activity of *Anthocephalus indicus* (fruits) in hyperlipidemic rats.
V. Kumar, P. Singh, R. Chander, F. Mahdi, R. Singh, S. Singh, A.K. Khanna, J.K. Saxena & R.K. Singh.

Workshop on Rational Approaches in Drug Designing: Application of Tools and Techniques of Bioinformatics, Lucknow (30 October)

Computer-aided molecular modeling: From protein ligand interaction to drug design.
M.I. Siddiqi.

Advanced School in Biotechnology in India-Biologics: From Discovery to Development, Gurgaon (29 October- 3 November)

Drug metabolism and pharmacokinetics in drug discovery and development.
Wahajuddin, S.P. Singh, K. Patel, D. Tewari & G.K. Jain.

78th Annual Meeting of Society of Biological Chemists (India) held at National Centre of Cell Science, Pune (30 October-1 November)

Apigenin produces oxidative stress in kidney of Swiss mice.
P. Singh, S.K. Mishra, P. Srivastava, S. Sharma & S.K. Rath.

Optimization of Inhaled Tuberculosis Therapies and Implications for Host-Pathogen Interactions, New Delhi (3-5 November)

Serum, tissue and intracellular concentrations following pulmonary delivery in rhesus macaques.
R.K. Verma, A.B. Yadav & A. Misra.

Validation of microarray transcription analysis of responses to treatment with inhalable microparticles containing anti-TB agents.
A.K. Singh, A.B. Yadav & A. Misra.

Serendipitous activation of mouse and human macrophages infected with *Mycobacterium tuberculosis* on treatment with inhalable microparticles.
R. Sharma, P. Muttil, A.H.B. Yadav, R.K Verma, A.K. Singh, M. Mohan & A. Misra.

10th International Symposium on Vectors and Vector Borne Diseases, Goa (4-6 November)

Miltefosine treatment of *Leishmania donovani* infected hamsters generates Th1 type of response as evidenced by real time PCR.
R. Gupta, P.K. Kushawaha, M. Samant, A.K. Jaiswal, R. Baharia & A. Dube.

Induction of Th1 type response by recombinant protein disulfide isomerase (PDI), a potential vaccine candidate against Visceral Leishmaniasis.
P.K. Kushawaha, R. Gupta, M. Samant & A. Dube.

Cloning, expression and purification of multi-drug resistance protein domain from *Plasmodium vinckei* that is homologous to *Plasmodium falciparum*.
A. Tripathi, A.J. Siddiqui, J. Bhardwaj & S.K. Puri.

Cloning, over-expression and purification of *Plasmodium vinckei* hypoxanthine-guanine phosphoribosyl transferase (HGPRT).
S. Kumar, A. Soni & S.K. Puri.

Cloning and expression of 19 kDa fragment of *P. cynomolgi* B merozoite surface protein-1.
N. Kumar, N.A. Kaushal & D.C. Kaushal.

International Congress on Veterinary Anatomy and Symposium on New Concept & Innovative Technologies in Veterinary Anatomy for Sustainable Livestock Production in the New Millennium, Lucknow (4-6 November)

Experimental animals as backbone of biomedical research: From structure function to the modern medical science.
D.S Upadhyay.

10th International Symposium on Vector and Vector Borne Diseases, Goa (4-6 November)

Transcriptomic analysis of murine host liver following exposure to *Plasmodium vinckei*.
S.K. Mishra, P. Singh, P. Mishra, A.K. Verma, S. Kumar, S.K. Puri & S.K. Rath.

36th Annual Conference of Association of Clinical Biochemists of India, Kochi (5-7 November)

Hypolipidemic activity of *Hibiscus rosa sinensis* (Root) in hyperlipidemic rats.
V. Kumar, R. Singh, S. Singh, S. Pandey, A.K. Khanna, R. Chander, P. Singh, F. Mahdi, J.K. Saxena, V.K. Singh & R.K. Singh.

American Association of Pharmaceutical Scientists - Annual Meeting 2009, Los Angeles (8-12 November)

Development and characterization of PLGA microspheres for the delivery of filarial immunogenic molecules in rodent hosts.
V Saini, P.K. Murthy & D.V. Kohli.

21st National Congress of Parasitology, Annual Congress of Indian Society of Parasitology, Chandigarh (14-16 November)

Actinomycetes extracts: A potent antitrypanosomal agent.
H. Dwivedi, S.K. Pandey, A. Rizvi & R. Tripathi.

Role of antioxidant system in drug resistance in malaria parasites.
A. Rizvi, H. Dwivedi, J.K. Saxena & R. Tripathi.

Role of folate in RPMI medium and its effect on DHFR inhibitors.
S. Gunjan, S.K. Pandey & R. Tripathi.

Lymph node pathology with special emphasis on mast cells status in *Mastomys coucha* sensitized with pro- and anti-inflammatory fractions of *Brugia malayi*.
S.K. Joseph, S.K. Verma, M.K. Sahoo, V. Kushwaha, K. Saxena & P.K. Murthy.

Antifilarial activity of some flavonoids.
V. Dube, V. Lakshmi, S.K. Joseph, S. Srivastava, S.K. Verma, M.K. Sahoo, S.K. Mishra & P.K. Murthy.

Evaluation of new aryloxy alkyl/arylalkyl imidazoles as antileishmanial agents.
A. Verma, V.K. Marrapu, N. Srinivas, S. Srivastava, Nishi, K. Bhandari & S. Gupta.

Antileishmanial activity of benzocycloalkyl azole oximino ethers.
S. Srivastava, V.K. Marrapu, N. Srinivas, A. Verma, S.A. Sane, K. Bhandari & S. Gupta.

Comparison of nitric oxide production and cytokine profile during infection with virulent and avirulent strain of *Plasmodium vinckei*.
A.J. Siddiqui, J. Bhardwaj, A. Tripathi & S.K. Puri.

Glutathione S-transferase may play a role in drug resistance in arteether resistant rodent malaria parasite *Plasmodium vinckei*.
A. Tripathi & S.K. Puri.

Role of antioxidant system in drug resistance in malaria parasites.
A. Rizvi, H. Dwivedi, J.K. Saxena & R. Tripathi.

Analysis of structure and function of *Leishmania donovani* trypanothione reductase in presence of miceller detergent, SDS.
B. Singh, S. Rai & N. Goyal.

Leishmania donovani trypanothione reductase: Role of urea and guanidine hydrochloride in modulation of functional and structural properties.
S. Rai, U.N. Dwivedi & N. Goyal.

Expression and purification of protein kinase homologue from *Leishmania donovani*.
M. Garg, Ashutosh & N. Goyal.

Leishmania donovani dipeptidylcarboxypeptidase: Overexpression in Leishmania and characterization.
S. Gangwar & N. Goyal.

Molecular characterization of triose phosphate isomerase of *L. donovani*.
K. Kumar.

3rd National Conference of Indian Academy of Tropical Parasitology, Chandigarh (16-19 November)

IgE, histamine and IL-13 mediated responses in the elimination of experimental *Brugia malayi* infection in *Mastomys coucha*.
S.K. Joseph, M.K. Sahoo, S.K. Verma, A. Sharma & P.K. Murthy.

International Conference on Frontiers in Prevention, Diagnosis and Therapy of Cancer, Allahabad (21-22 November)

Role of soluble Fas in the diagnosis of urinary bladder cancer.
A.K. Srivastava, P.K. Singh, P. Singh, S.K. Rath, D. Singh, S. Singh, D. Dalela, M.M. Goel & M.L.B. Bhatt.

11th ISMAS Triennial International Conference on Mass Spectrometry, Hyderabad (24-28 November)

Identification of cardiac glycoside using liquid chromatography tandem mass spectrometry.
S. Kanojiya, K.P. Madhusudanan & A. Khare.

Simultaneous quantification of formononetin and diadzein by LC MS/MS.
Wahajuddin, S.P. Singh & G.K. Jain.

Simultaneous determination of Biochanin A and Genistein by LC MS/MS.
S.P. Singh, Wahajuddin & G.K. Jain.

LC MS/MS assay for quantification of 97/78 and its metabolite 97/63, a promising trioxane antimalarial in human plasma.
H.N. Kushwaha, N. Gautam & S.K. Singh.

5th J-NOST, Kanpur (4-7 December)

Synthetic applications of 1-formyl-9H-β-carboline for generating β-carboline derivatives with D-ring.
S. Batra & V. Singh.

Molecular diversity oriented construction of aromatic scaffolds from flexible or rigid lactones.
A. Kumar & A. Goel.

40th Annual Conference ISNCON – 2009, Guwahati (4-6 December)

Pharmacological effect of antioxidant, immunostimulant, post heparin lipolytic activity and lipid lowering milk oligosaccharides as diet supplement for Crf patients.
A. Srivastava, R. Tripathi, D. Deepak, S. Bhattacharya & R.K. Sharma.

International Conference on Emerging Trends in Biotechnology and 6th Annual Convention of the Biotech Research Society, Varanasi (4-6 December)

Generation and characterization of *Mycobacterium smegmatis* sigma factor F mutant.
A.K. Singh, D. Dutta, R.K. Biswas & B.N. Singh.

APSN, IBRO-SNCI School & International Conference on Neurosciences Update, Cochin (7-14 December)

Modulation of ASIC by flurbiprofen in cerebral ischemia/ reperfusion injury.
V. Mishra, R. Verma & R. Raghubir.

Differential activity of NADPH oxidase following cerebral ischemic Injury.
N. Singh & R. Raghubir.

International Conference on Integrative & Personalized Medicine and 42nd Annual Conference of Indian Pharmacological Society, Kolkata (10-12 December)

Comparative evaluation of forced swim test and tail suspension test as models of negative symptoms of schizophrenia.
M. Chatterjee & G. Palit.

Involvement of PPAR γ and GR: A novel molecular approach in pioglitazone mediated chronic gastric ulcer healing.
S. Lahiri, S. Samanta, B. Gorain, T. Sen & G. Palit.

Role of glutamate transporter 1 (GLT-1) and its modulation in glutamate uptake drug ischemia.
R. Verma, V. Mishra & R. Raghubir.

Antiallergic activity of CDRI plant no. 4533.
A. Nath, C. Singh & R. Raghubir.

61st Indian Pharmaceutical Congress, Ahmedabad (11-13 December)

Reverse phase-HPLC method for determination of marker compounds in NP-1 an antiosteoporotic plant product from *Butea monosperma*.
V. Gupta, A.K Dwivedi, D.K. Yadav, M. Kumar and R. Maurya.

Development and validation of improved HPLC method for the quantitative determination of curcuminoids in herbal medicament.
R. Malasoni, R.R. Pandey, A. Srivastava and A.K. Dwivedi.

Annual Conference of Indian Academy of Neurosciences - 2009, Jaipur (17-18 December)

Differential expression and activity of NADPH oxidase following cerebral ischemia reperfusion injury.
N. Singh, A. Desai & R. Raghubir.

Possible involvement of NF-kB in pathophysiology of cerebral stroke in diabetic rats.
A. Desai, N. Singh & R. Raghubir.

27th Annual Conference of Indian Academy of Neurosciences, Jaipur (18–20 December)

Beneficial effect of melatonin on LPS induced neuroinflammation in rat.
E. Tyagi, R. Agrawal, C. Nath & R. Shukla.

Distribution of brain insulin receptors in rats.
R. Agrawal, E. Tyagi, R. Shukla & C. Nath.

Effect of curcumin on brain insulin receptors and memory functions in STZ (ICV) induced dementia model of rat.
R. Shukla, B. Mishra, R. Agrawal, E. Tyagi & C. Nath.

Melatonin attenuated MPTP-induced inflammatory mediators via inhibition of NF-KB and Pp-38 activation in rat astrocytoma cells, C6.
R. Niranjan & R. Shukla.

Neurophrmacological evaluation of okadaic acid (ICV) induced memory impairment in rats: A suitable experimental model to test antidementia activity.
P.K. Kamat, S.K. Tota, G. Saxena, R. Shukla & C. Nath.

3rd International Symposium on Translational Cancer Research Cell Signaling and Cancer Therapy, Bhubaneshwar (18-21 December)

Quantitative analysis of telomerase activity in exfoliated human urothelial cells and bladder transitional cell carcinoma.
P.K. Singh, A.K. Srivastava, P. Singh, D. Singh, M.L.B. Bhatt, D. Dalela, M.M. Goel, M.P.S. Negi & S.K. Rath.

Functional polymorphisms in PTGS-2 gene and risks of squamous cell carcinomas of upper aero digestive tract (UADT).
S.V. Singh, A.K. Mitra, P. Misra, S. Shukla, V.K. Garg, R. Chaturvedi, M. Sharma & S.K. Rath.

Quantitative detection of UCA1 expression in exfoliated human urothelial cells and bladder transitional cell carcinoma.
A.K. Srivastava, P.K. Singh, P. Singh, D. Singh, M.L.B. Bhatt, D. Dalela, M.M. Goel, M.P.S. Negi & S.K. Rath.

National Conference on *Diabetes mellitus* and Cancer (Dia-Can 2009), Annamalainagar (19-20 December)

Anti-hyperglycaemic activity of *Swertia chirayita* in validated animal models of diabetes.
S. Srivastava, S.P. Srivastava, R.K. Asthana, N.K. Sharma, R. Ahmad, D. Raina, P. Tiwari & A.K. Srivastava.

α-Glucosidase inhibitory potential of selected terrestrial antidiabetic plants.
N. Jaiswal, V. Lakshmi, T. Narender, R. Maurya & A.K. Srivastava.

Evaluation of antihyperglycaemic activity in marine flora and fauna.
N. Rahuja, V. Lakshmi, R. Raghubir & A.K. Srivastava.

Antihyperglycaemic activity in marketed herbal formulations, Madhuhari and Madhusunya.
A. Mishra, R. Srivastava, S.P. Srivastava & A.K. Srivastava.

Antidiabetic, antidyslipidemic and aldose reductase inhibitory effects of the *Tectona grandis* leaves and *Terminalia chebula* fruits.
S.P. Srivastava, V. Bhatia, R. Srivastava, A. Mishra, T. Narender & A.K. Srivastava.

Aldose reductase inhibitory and antidiabetic potential in *Acacia nilotica* and *Eclipta alba*.
V. Bhatia, S.P. Srivastava, T. Narender & A.K. Srivastava.

Antihyperglyaemic and antidyslipidaemic activity of *Coccinia indica* leaves.
R. Srivastava, S.P. Srivastava, A. Mishra, R. Maurya & A.K. Srivastava.

Inter-Agency Linkages

Title of the Project	Funding Agency	Principal Investigator
National project on development of potential drugs from the ocean.	Ministry of Earth Sciences, Govt. of India	Director, CDRI
Reproductive health research programme.	Ministry of Health and Family Welfare, Govt. of India	Director, CDRI
To supply the phytochemical reference standards (PRS) to Indian Pharmacopoeia Commission.	-do-	Dr. A.K. Saxena
Technological innovations for commercial exploitation of *Morinda citrifolia* (Noni) as livelihood option for islands farmers.	-do-	Dr. J.K. Saxena
Mass spectrum fingerprinting of Indian medicinal plant (as a special reference to anti-diabetic aspect).	-do-	Dr. Brijesh Kumar
Sophisticated Analytical Instrument Facility (SAIF).	Department of Science & Technology, Govt. of India	Director, CDRI
J.C. Bose Fellowship.	-do-	Dr. T.K. Chakraborty
Synthesis of small ring saturated heterocycles and cycloalkanes from 2,3-epoxy alcohols containing acrylic moiety by conjugate radical additions triggered by epoxide ring opening with Cp2TiCl: Application in the synthesis of natural products.	-do-	Dr. T.K. Chakraborty
Structural characterization of gamma -glutamylcysteine synthetase (gamma GCS) and glutathione synthetase (GS) from *Leishmania spp*.	-do-	Dr. J.V. Pratap
Diversity oriented organic synthesis of small but smart molecules in drug discovery research.	-do-	Dr. Gautam Panda
Isolation and characterization of proteo-phosphoglycans of *Leishmania donovani.*	-do-	Dr. Anuradha Dubey
Studies on synthesis of cyclic compounds using Baylis-Hillman chemistry.	-do-	Dr. Sanjay Batra
Expansion of facilities in national centre for pharmacokinetic and metabolic studies.	-do-	Dr. G.K. Jain

Title of the Project	Funding Agency	Principal Investigator
Identification and elucidation of novel signaling pathways involved in monocyte /macrophage activation, migration, differentiation, proliferation and death during dyslipidemia and atherosclerosis.	-do-	Dr. M.K. Barthwal
Osteogenic actions of a naturally derived NP-1 pure compound on bone.	-do-	Dr. Divya Singh
Proteomic analysis of drug resistance in *Leishmania donovani* clinical isolate.	-do-	Dr. Neeloo Singh
Identification and characterization protein(s) from Arteether sensitive and Arteether resistant rodent malaria parasites for elucidation of mechanism of resistance.	-do-	Dr. S.K. Puri
Design, synthesis and development of novel antileishmanial agents.	-do-	Dr. T. Narender
A systematic RNAi screen for identification of genetic modulators of HIV-NEF induced pathogenesis in a novel *Caenorhabditis elegans* model.	-do-	Dr. Aamir Nazir
Molecular diversity- oriented synthesis of aromatic scaffolds through ring transformation strategy.	DST (Ramanna Fellowship)	Dr. Atul Goel
Human cytochrome P450 1B1: implications in Centchroman treated hormone-mediated MCF-7 tumor cell metabolism as a novel target for therapeutic intervention.	DST (Women Scientist Scheme)	Dr. Neetu Singh
Structure based drug design of inhibitors targeting recombinant pteridine reductase 1 from *Leishmania donovani* clinical isolate.	Department of Biotechnology, Govt. of India	Dr. Neeloo Singh
Cloning, expression and characterization of filarial acetylcholine esterase.	-do-	Dr. N.A. Kaushal
Evaluation of *Mycobacterium* W as an immunomodulator for the management of visceral leishmaniasis and as an adjunct to antileishmanial vaccine/drug.	-do-	Dr. Anuradha Dube
Cloning and over-expression of Th1 stimulatory polyproteins identified through proteomics for their prophylactic potential against experimental visceral leishmaniasis.	-do-	Dr. Anuradha Dube
Up-gradation of the CDRI project on design synthesis and development of new molecules against MDR tuberculosis to a DBT centre of excellence of TB drug discovery.	-do-	Dr. Sudhir Sinha

Title of the Project	Funding Agency	Principal Investigator
Studies on neutrophil nitric oxide synthase: Isolation, molecular characterization and identification of interacting proteins.	-do-	Dr. Madhu Dikshit
New inhibitor design/drug development using novel protein targets: NAD+ dependent DNA ligases and Feast/famine regulatory proteins from *M. tuberculosis.*	-do-	Dr. R. Ravishankar
Studies on the structure and functions of actin cytoskeletal network in *Leishmania donovani.*	-do-	Dr. C.M. Gupta
Understanding the mechanism of mitotic/spindle checkpoint using genetics approaches in fission yeast *Schizosachromyces pombe*.	-do-	Dr. S. Ahmed
Anti-osteoclastogenic effect of 99373 and its mode of action.	-do-	Dr. N. Chattopadhyay
Expression profiling of major testis specific genes in human semen/spermatozoa for identification of the biological role of these genes, their diagnostic utility and identification of novel targets for infertility treatment/male contraception.	-do-	Dr. Rajender Singh
Development of new chemotherapeutic agents and drug combinations for the multi-drug resistant/service malaria treatment.	Indian Council of Medical Research, Govt. of India	Dr. Renu Tripathi
Synthesis of monosaccharide derivatives as potential antimycobacterial agents.	-do-	Dr. A.K. Shaw
Design and synthesis of novel SERMs for the management of osteoporosis and other estrogen related disorders.	-do-	Dr. Gautam Panda
Target based design and synthesis of novel compounds for treating diabetes and dyslipidemia.	-do-	Dr. Atul Goel
Cytokine gene polymorphism in breast cancer patients.	-do-	Dr. Rituraj Konwar
Synthesis of antimalarial agents and their combinatorial chemistry.	-do-	Dr. P.M.S. Chauhan
Development of bone anabolic agents from Indian medicinal plant.	-do-	Dr. N. Chattopadhyay
Effect of 2,3-diaryl-2H-1-enzopyran derivative on estrogen induced endometrial cell proliferations and uterine hyperplasic formation.	-do-	Dr. Anila Dwivedi
Design, synthesis and biological evaluation of HIV-1 RT inhibitors-4-thiazolidinone compound.	-do-	Dr. S.B. Katti

Title of the Project	Funding Agency	Principal Investigator
Design, synthesis and bioequivalence of new analogues of fluconazole for antifungal activity.	-do-	Dr. P.K. Shukla
DNA based tools for antimalarial drug screening against *Plasmodium falciparum.*	-do-	Dr. Kumkum Srivastava
Development of anti-ulcer drug from Indian medicinal plant *Tectona grandis.*	-do-	Dr. G. Palit
Effect of monoisoamyl 2,3-dimercaptosuccinic acid on cardiovascular and respiratory parameters in the rat.	Defense Research & Development Organization	Dr. Madhu Dikshit
Synthesis of biologically active molecules from carbohydrates based ligands for potential application in defense.	-do-	Dr. R.P. Tripathi
Mode of action of artemisinin based antimalarial drugs.	UPCST, Lucknow	Dr. J.K. Saxena
Pharmacological and genomic investigations on *Withania somnifera*-an Indian medicinal plant.	NMITLI (CSIR)	Dr. Shailja Bhattacharya
Lead identification for antileishmanial compounds.	DNDi, Geneva	Dr. S.K. Puri
Development of new macrofilaricidal and/or embryostatic agents.	WHO, Geneva, Switzerland	Dr. Shailja Bhattacharya
Targetting protein synthesis in apicoplast and cytoplasm of *Plasmodium*.	European Commission, Brussels, Belgium	Dr. Saman Habib
To develop a process for Bivalirudin	Biocon Ltd, Bangalore	Dr. W. Haq
Stability and formulation development studies of omeloxifene and authentification of cis & trans standards	HLL Lifecare Ltd., Thiruvananthapuram	Dr. A.K. Dwivedi

Human Resource Development

1. Training Programmes Attended by CDRI Staff

	Title of the program, Organizer and Date	Name of the Staff
1	Hands on Training "Whole Body Plethysmogragh" Buxco Research System, Micheldever, Winchester, UK, 21-24 Janaury 2009.	Dr. Manoj Kumar Barathwal
2	Induction Training Program for Newly Recruited Scientists, HRDC, Ghaziabad, 23-28 February 2009.	Dr. Aamir Nazir
3	Training program on "Science Communication: The Emerging Scenario", HRDC, Ghaziabad, 20-22 May 2009.	Dr. Gitika Bhatia Dr. Anju Puri Dr. Kumkum Srivastava
4	Summer Training on Techniques and Tools of Biotechnology and Bioinformatics-2009, CIMAP, Lucknow, 23 June - 22 July, 2009.	Dr. D.K. Mishra
5	Leadership Development Programs (LDP0903, LDP0904 and LDP0905) HRDC, Ghaziabad.	Dr. M.N. Srivastava Dr. K.K. Srivastava Dr. Sanjay Batra Dr. B.N. Singh Dr. R. K. Tripathi Dr. S.M. Rajendran Dr. D.S. Upadhyaya Dr. K.R. Arya Dr. K.V. Sashidhara Dr. Smrati Bhadauria Dr. D.P. Mishra Dr. Sarika Dr. S.R. Kulkarni
6	DNA Microarray Analysis and Applications, M.S. University, Tamil Nadu, 16-20 August 2009.	Dr. B. Maity
7	1st Biomics Hands on Workshop, CSIR-ISTAD Weizmann Institute of Sciences, Rehovot, Israel, 30 August - 4 September 2009.	Dr. Aamir Nazir Dr. Rajender Singh
8	Programme on R&D Management, IIT-Bombay, 17-19 September 2009.	Dr. D.N. Upadhayay Mr. Prem Prakash
9	FACS Area Training, BD Bioscience, San Jose, California, 5-9 October 2009.	Mr. A.L. Vishwakrma
10	Quantitative Analysis and Modelling in Animal Sciences, CCMB, Hyderabad, IISER, Pune, NCL, Pune and DST, New India, 6-11 October, 2009.	Mr. Wahajuddin
11	Technology Commercialization Program for Senior Scientists, ASCI, Hyderabad, 19-30 October 2009.	Dr. Neeraj Sinha
13	Advanced School in Biotechnology in India on "Biologics: From Discovery to Development", CGEB, New Delhi. RCBTE, New Delhi, IUBMB, USA and UNESCO, 27 October - 3 November 2009.	Mr. Wahajuddin

	Title of the program, Organizer and Date	Name of the Staff
12	Workshop Training on OECD Principles of Good Laboratory Practice (GLP), Central Drug Research Institute, WHO-TDR GLP Network Regional Coordination (Asia) and IITR, Lucknow, 27-29 October 2009.	Dr. A.K. Dwivedi Dr. M. Abbas Dr. D.S. Upadhyay Dr. A.K. Srivastava Dr. Gopal Gupta Dr. S.M. Rajendran Dr. P.R. Mishra Dr. D. Hansda Dr. Manoj Kumar Barthwal Dr. Aamir Nazir Dr. Sarika Sri S.N.A. Rizvi Sri A.K. Bhargava Sri Karunesh Rai Mrs M. Chaudhry

2. Ph.D. Thesis Submitted

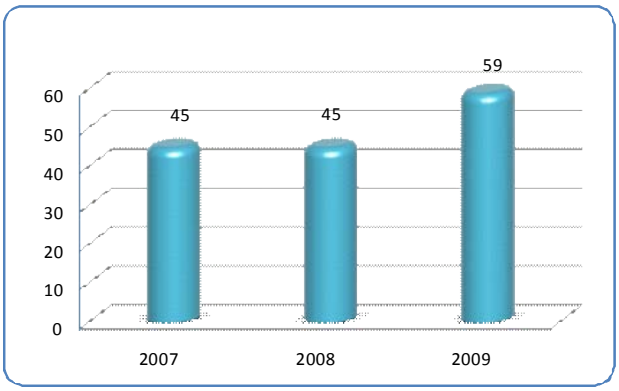
Name of the Research Fellow	Title of the Ph.D. Thesis	Name of the Supervisor	Name of the University
Amar Bhadur Singh	Biochemical and molecular targets of novel antidiabetic agents.	Dr. Arvind Kumar Srivastava	Jawaharlal Nehru University, New Delhi.
Amita Yadav	Studies of rpf (resuscitation promoting factor) genes of *Mycobacterium tuberculosis.*	Dr. Ranjana Srivastava	Jawaharlal Nehru University, New Delhi.
Anirudh Kumar Singh	Identification and characterization of sigma factor F of *Mycobacterium smegmatis.*	Dr. B.N. Singh	Jawaharlal Nehru University, New Delhi.
Ashutosh	Differential gene expression studies to explore the molecular mechanism of drug resistance in *Leishmania donovani* isolates.	Dr. Neena Goyal	Jawaharlal Nehru University, New Delhi.
Avadh Bihari Yadav	Transcriptional analysis of microphage response to tuberculosis infections on treatment with bio-degradable microparticals containing anti-TB drugs.	Dr. Amit Misra	Jawaharlal Nehru University, New Delhi.
Awanish Kumar	Expression proteomics and genomic fingerprinting studies in sodium antimony gluconate (SAG) sensitive and resistant clinical isolates of *Leishmania donovani.*	Dr. Anuradha Dube	Jawaharlal Nehru University, New Delhi.
Divya Dube	Identification and optimization of novel inhibitors against proteinaceous drug targets from pathogenic species using *in silico* approaches.	Dr. Ravishankar R.	Jawaharlal Nehru University, New Delhi.

Name of the Research Fellow	Title of the Ph.D. Thesis	Name of the Supervisor	Name of the University
G.B. Shiva Keshava	Secretory proteome analysis of *Candida albicans* for identification of potential target molecules.	Dr. P.K. Shukla	Jawaharlal Nehru University, New Delhi.
Gauri Misra	Structural studies on proteins involved in transit peptide mediated transport in *Plasmodium falciparum*.	Dr. Ravishankar R.	Jawaharlal Nehru University, New Delhi.
Geetika Kharkwal	A comparative study of estrogen receptor under the influence of CDRI 99/373 and SERMs.	Dr. Anila Dwivedi	Jawaharlal Nehru University, New Delhi.
Jyoti Pandey	Synthetic studies in carbohydrates and heterocycles: Development of new antitubercular agents.	Dr. R.P. Tripathi	Jawaharlal Nehru University, New Delhi.
K.S. Santha Ram	Characterization of myosin protein(s) of *Leishmania donovani.*	Dr. C.M. Gupta	Jawaharlal Nehru University, New Delhi.
Malaya Kumar Sahoo	Studies on immunogenecity and pathogenicity of certain molecules of *Brugia malayi* adult worms in rodent host.	Dr. Kalpana Murthy	Jawaharlal Nehru University, New Delhi.
Meghna Singh	Molecular cloning and characterization of functional antigen/s of human lymphatic filariid *Brugia malayi.*	Dr. Shailja Bhattacharya	Jawaharlal Nehru University, New Delhi.
Mohammad Hassam	Antimalarial 1,2,4-trioxanes: Synthesis and biological evaluation.	Dr. Chandan Singh	Jawaharlal Nehru University, New Delhi.
Naikade Niraj Krishna	Structurally simple synthetic peroxides: Synthesis and antimalarial assessment.	Dr. Chandan Singh & Dr. A.K. Saxena	Jawaharlal Nehru University, New Delhi.
Prabodh Kapoor	Functional and structural characterization of actin from *Leishmania donovani*	Dr. C.M. Gupta	Jawaharlal Nehru University, New Delhi.
Ram Awatar Maurya	Design and synthesis of MCR derived novel nuclear receptor modulators as therapeutic agents.	Dr. Atul Kumar	Jawaharlal Nehru University, New Delhi.
Ranjeet Kumar	Structural and functional studies on isocitrate lyase and malate synthase from *Mycobacterium tuberculosis.*	Dr. Vinod Bhakuni	Jawaharlal Nehru University, New Delhi.
Ravi Kumar	Design and synthesis of novel heterocycles as potent anticancer and antiinfective agents.	Dr. P.M.S. Chauhan	Jawaharlal Nehru University, New Delhi.
Rohitashw Kumar	Generation of monoclonal antibodies against covalently linked cell wall proteins of *Candida albicans*.	Dr. P.K. Shukla	Jawaharlal Nehru University, New Delhi.
Sachin Kumar	Role of nitric oxide in neutrophil maturation and function.	Dr. Madhu Dikshit	Jawaharlal Nehru University, New Delhi.

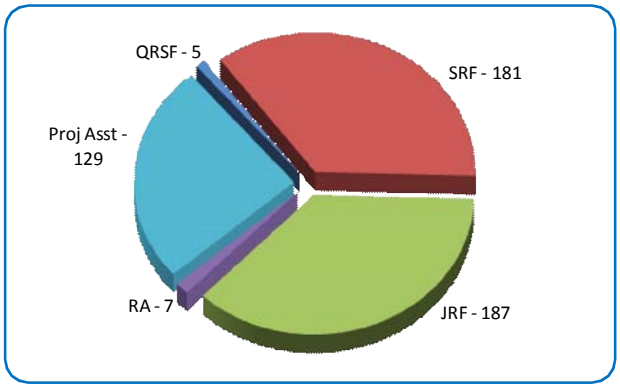
Name of the Research Fellow	Title of the Ph.D. Thesis	Name of the Supervisor	Name of the University
Santosh Kumar Maurya	Antidyslipidemic activity of *Curcuma longa* and *Glycyrrhiza glabra.*	Dr. Arvind K. Srivastava	Jawaharlal Nehru University, New Delhi.
Shailesh Kumar	Studies on diversity oriented synthesis of bioactive compounds.	Dr. D.P. Sahu	Jawaharlal Nehru University, New Delhi.
Shivendra Kumar Chaurasiya	Studies on the inter-relationship between protein kinases of macrophage and mycobacteria for their roles as determinant of pathogenicity.	Dr. K.K. Srivastava	Jawaharlal Nehru University, New Delhi.
Sumit Chaurasia	Studies on isolated or fused 2-pyranones and their nucleophile induced products.	Dr. Atul Goel	Jawaharlal Nehru University, New Delhi.
T.V. Satish Tammana	Functional and structural characterization of ADF/Cofilin homologue from *Leishmania donovani.*	Dr. C.M. Gupta	Jawaharlal Nehru University, New Delhi.
Timir Tripathi	Structural, functional and stability studies of redox active proteins from *Plasmodium* sp.	Dr. Vinod Bhakuni	Jawaharlal Nehru University, New Delhi.
Venkata Prasuja Nakka	Cellular and molecular studies on the endoplasmic reticulum mediated survival and death mechanism in cerebral ischemia.	Dr. Ram Raghubir	Jawaharlal Nehru University, New Delhi.
Vikas Jain	Colloidal delivery system bearing antibiotic for treatment of septic shock	Dr. R. Pal & Dr. P.R. Misra	Jawaharlal Nehru University, New Delhi.
Vishal Kumar Rajput	Synthesis of biologically active oligosaccharides and medicinally relevant sugar heterocycles hybrids.	Dr. B. Mukhopadhyay & Dr. B. Kundu	Jawaharlal Nehru University, New Delhi.
Anil Dangi	Characterization of protein profile of filarial parasite *Brugia malayi* after depletion of intracellular endosymbiotic bacteria Wolbachia through antibiotics and development of antibiotic delivery system for antifilarial targeting.	Dr. Shailja Bhattacharya	Chhatrapati Shahu Ji Maharaj University, Kanpur.
Ethika Tyagi	Relationship between central cholinergic system and neuroinflammation : A molecular pharmacological approach.	Dr. Rakesh Shukla	Chhatrapati Shahu Ji Maharaj University, Kanpur.
Richa Verma	Studies on phospholipid membrane interaction of peptides derived from the conserved segments of voltage gated potassium channels.	Dr. J.K. Ghosh	Chhatrapati Shahu Ji Maharaj University, Kanpur.
Shilpy Shakya	Purification and characterization of adult *Brugia malayi* antigen: Identification and immunoprophylactic evaluation of protective molecule(s).	Dr. Shailja Bhattacharya	Chhatrapati Shahu Ji Maharaj University, Kanpur.

Name of the Research Fellow	Title of the Ph.D. Thesis	Name of the Supervisor	Name of the University
Swati Gupta	Studies on hepatocarcinogenesis-promotion potential of certain antidiabetic PPAR-gama-agonists in rat.	Dr. P.S.R. Murthy	Chhatrapati Shahu Ji Maharaj University, Kanpur.
Leena Gupta	Synthesis of novel heterocycles as possible anticancer and antiparasitic agents.	Dr. P.M.S.Chauhan	Chhatrapati Shahu Ji Maharaj University, Kanpur.
N. Sundru	Synthesis of novel heterocycles as bioactive agents.	Dr. P.M.S.Chauhan	Chhatrapati Shahu Ji Maharaj University, Kanpur.
Ravi Shankar	Search of new lead bioactive molecules with potential for drug development.	Dr. Kanchan Hajela	Dr. B.R. Ambedkar University, Agra.
Sharad Porwal	Synthesis of heterocycles of biological interest and their combinatorial chemistry.	Dr. P.M.S. Chauhan	Dr. B.R. Ambedkar University, Agra.
Sunil Sharma	Design and synthesis of imidazole based biheterocycle derivatives of medicinal interest.	Dr. Bijoy Kundu	Dr. B.R. Ambedkar University, Agra.
Vandana Varshney	Synthesis of pharmacodynamic compounds.	Dr. D.P. Sahu	Dr. B.R. Ambedkar University, Agra.
J. Naga Rosaiah	Synthesis, reactivity and anticancer evaluation of novel derivatives of aromatic dicarbaldehydes.	Dr. K.V. Sasidhara	Acharya Nagarjuna University.
Kancharla Papi Reddy	Isolation, characterization, chemical transformation and total synthesis of natural products of biological importance.	Dr. T. Narendra	Acharya Nagarjuna University.
Nagarapu Srinivas	Design and synthesis of potential antileishmanial agents.	Dr. Kalpana Bhandari	Acharya Nagarjuna University.
P. Venkat Reddy	Studies on synthesis of stereochemically pure highly functionalized tetrahydrofurans of biological importance from carbohydrates.	D. A.K. Shaw	Acharya Nagarjuna University
Maloy Kumar Parai	Design, synthesis and evaluation of bioactive privileged structures for drug discovery.	Dr. Gautam Panda	Jadavpur University, Kolkata.
Shawon Lahiri	A study on the role of peroxisome proliferation activated receptor gamma (PPAR-gama) in gastric ulcer healing.	Dr. Gautam Palit	Jadavpur University, Kolkata.
Manisha Nigam	Study of the molecular mechanisms of anti estrogen Centchroman induced apoptosis in MCF-7 and NDA MB-231 human breast cancer cells.	Dr. Anil Balapure	Allahabad University, Allahabad.

Name of the Research Fellow	Title of the Ph.D. Thesis	Name of the Supervisor	Name of the University
Vishal Ranjan	Redox mechanisms in Centchroman mediated antineoplasticity in human breast cancer cells.	Dr. Anil Balapure	Allahabad University, Allahabad.
Mohammad Saquib	Design and synthesis of carbohydrate derived molecules of biological importance	Dr. A.K. Shaw	Lucknow University, Lucknow.
Shweta Joshi	Molecular and biochemical characterization of transketolase of *Plasmodium falciparum.*	Dr. J.K. Saxena	Lucknow University, Lucknow.
Rahul Agrawal	Molecular and pharmacological evaluation of central insulin receptors in behavioral responses.	Dr. C. Nath	Lucknow University, Lucknow.
Vineeta Singh	Isolation and characterization of antimicrobial metabolites from microbial isolates.	Dr. C.K.M. Tripathi	Uttar Pradesh Technical University, Lucknow.
Naila Rasheed	Role of central dopaminergic system in rats under various stressfull conditions in relation to neuro-endocrine and behavioral alterations.	Dr. Gautam Palit	Integral University, Lucknow.
Alok Ranjan Singh	Molecular and biochemical studies on hexokinase of filarial parasite.	Dr. J.K. Saxena	Banaras Hindu University, Varanasi.
Anchal Gusain	Studies on the potential role of calcineurin in cerebral ischemia / reperfusion injury.	Dr. Ram Raghubir	Jiwaji University, Gwalior.
Bipin Chandra Misra	Analysis of single nucleotide polymorphisms (SNPs) in some drug metabolizing genes in selected Indian sub-populations.	Dr. S.K. Rath	Deen Dayal Upadhyay Gorakhpur University, Gorakhpur.
Abhishek Chandra	Studies on characterization and significance of 33 kDa luminal fluid glycoprotein of mammalian epididymis in sperm functions and fertility.	Dr. Archana Srivastava	Dr. Ram Manohar Lohiya Awadh University, Faizabad.



Ph. D. Thesis Submitted



Research Fellows/Assistants Position

3. MS Thesis Submitted

Name of the Researcher	Title of the M.S. Thesis	Name of the Supervisor	Name of the University
Henna Rahman	Comparative evaluation of cytotoxicity profile of few root canal sealers: An *in vitro* analysis.	Dr. Rituraj Konwar	Chhatrapati Shahuji Maharaj Medical University, Lucknow.
Anika Dang	Analysis of single nucleotide polymorphisms association in peridontitis.	Dr. S.K. Rath	Chhatrapati Shahuji Maharaj Medical University, Lucknow.

4. Advance Training Imparted to External Aspirants

Under this programme, the institute conducts different kinds of advance training of short duration in various disciplines at CDRI against payment to scientists and technical persons working in industries, academic institutions and students who pursue post graduation courses from different universities / colleges in the country. Institute also provides training to foreigners either under the exchange programs of two countries or under the sponsored programs.

4.1 International training under bilateral cooperation

Long and short-term training was provided to following sponsored persons

Name and address of the Trainee	Supervisor	Duration
CSIR-TWAS Fellows		
Mr. Olumide Stephen Akinsomisoye Lecturer, Department of Physiological Sciences, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria	Dr. Gopal Gupta	24.08.08 to 09.03.09
Dr. Samuel Adetunji Onasanwo Lecturer, University of Ibadan, Nigeria	Dr. Ram Raghubir	23.09.08 to 22.09. 09
Ms. Olajumoke Omolaro Ojo Assistant Lecturer, Biochemistry Department, Faculty of Science, University of Ado Ekiti, Ekiti State, Nigeria	Dr. S.K. Rath	20.07.09 to 19.07.09
RTFDCS Fellow		
Dr. Akinmoladun A.C. Lecturer, Department of Biochemistry, Federal University of Technology, Akure, Nigeria	Dr. Ram Raghubir	09.05.08 to 26.04.09
INSA-JRD Tata Fellow		
Dr. O.A. Adaramoye Lecturer, Department of Biochemistry, University of Ibadan, Nigeria	Dr. Sudhir Sinha	15.03.09 to 14.06.09

4.2 Short term traning programme

A. Basics & application of sophisticated analytical instruments [08-12 December, 2009]

1. **Mr. Ahmad Husain**
   Dept. of Chemistry
   Aligarh Mulsim University, Aligarh
2. **Mr. S.L. Ashok Kumar**
   Department of Chemistry, NIT, Trichy
3. **Mr. Deepak Singh**
   M.S. University, Vadodara
4. **Mr. M. Saravana Kumar**
   Department of Chemistry, NIT, Trichy
5. **Mr. Atul Ranjan**
   Department of Chemistry
   Delhi University, Delhi
6. **Mr. Atul Kumar Gupta**
   Department of Molecular Biology,
   G.B. Pant University of Agriculture, Pantnagar
7. **Mr. Ajoy Pal**
   CMC Department
   IMMT, Bhubaneswar
8. **Mr. Biswanath Biswal**
   CMC Department, IMMT, Bhubaneswar
9. **Ms. Preeti Singh**
   39 Vasudev Bihar
   Awas Vikas, Jhansi
10. **Mr. R. Tamilarasan**
    Department of Chemistry,
    NIT, Trichy
11. **Mr. Gautam M. Patel**
    M.S. University, Vadodara
12. **Mr. Sundar S. Mety**
    Department of Botany
    Gulbarga University, Gulbarga
13. **Mr. Souvik Sur**
    Department of Chemistry,
    Delhi University, Delhi
14. **Mr. Dinesh Ch. Pathak**
    Department of Molecular Biology,
    G.B. Pant University of Agriculture,
    Pantnagar
15. **Ms. Priti Sinha**
    Department of Chemistry
    Banaras Hindu University, Varanasi

B. Experimental maintenance of *B. malayi* and vector rearing and breeding [18-20 November, 2009]

1. Mr. Md Ali. Senior Research Fellow Jamia Hamdard University, Delhi
2. Mr. Prashant Saini, Research Scholar, Vishwabharati University, Shantiniketan.

C. Training in tissue & cell culture techniques [17-27 August, 2009]

Under this program, 7 students from C.S.M. Medical University, Lucknow were imparted training.

4.3 Training under cooperation with Indian universities

Under this program, 15 students of B. Pharma. stream from Birla Institute of Technology and Science (BITS), Pilani were provided six months training in different desciplines of drug and pharmaceutical science.

4.4 Training to scientists, academia & technical personnel

Under this program, 3 scientists from CIMAP, Lucknow, in bioinformatics science; 2 technical personnel from Sipra Labs Ltd., Hyderabad in cell line culture; 1 technical person from PGMIER, Chandigarh in microbiology were imparted training.

4.5 Training to post graduate students

During the calendar year January to December 2009, a total of 242 Post Graduate students from 35 Universities and their affiliated colleges from all over the country were imparted training in various disciplines for 2 to 12 months duration. Details of trainees, from different Universities/Colleges are :

S.N.	Name of University / College	Number of Students
1.	A.N. College, Patna	2
2.	Aligarh Muslim University, Aligarh	3
3.	Allahabad Agricultural Institute , Allahabad	10
4.	Allahabad University, Allahabad	1
5.	Alpine Institute Management & Technology, Dehradun	2
6.	Amity University, Lucknow	9
7.	Amity University, Noida	10
8.	Baba Saheb Bhim Rao Ambedkar University, Lucknow	6
9.	Babu Banarasi Das College, Lucknow	12
10.	Banaras Hindu University, Banaras	2
11.	Banasthali Vidyapith, Rajasthan	24
12.	Bhagwant University, Ajmer	2
13.	Bhupal Nobles College of Pharmacy, Udaipur	1
14.	Birla Institute of Technology, Pilani	2
15.	Biyani Girls College, Jaipur	1
16.	Brahmananda College, Kanpur	1
17.	Bundelkhand University, Jhansi	2
18.	Centre for Food Technology, Allahabad	1
19.	College of Pharmaceutical Sciences, Behrampur	1
20.	CSJM University, Kanpur	4
21.	DAV College, Kanpur	1
22.	Deen Dayal Gorakhpur University, Gorakhpur	2
23.	DGPG College, Kanpur	5
24.	Dolphin Institute of Biomedical & Natural Science, Dehradun	2
25.	Doon College of Agriculture Science & Technology, Dehradun	2
26.	Dr. D.Y. Patil University, Mumbai	3
27.	Dr. Hari Singh Gaur University, Sagar	4
28.	Dr. R.M.L. Avadh University, Faizabad	4
29.	Gayatri College of Pharmacy, Sambalpur	1
30.	GICTS, Gwalior	2
31.	Govt. Model Autonomous Holkar Science College, Indore	1
32.	Guru Jambheshwar University, Hisar	4
33.	Gyan Vihar College, Jaipur	1
34.	H.P. University, Simla	1
35.	Indira Gandhi Institute of Pharmaceutics & Sciences, Bhubaneswar	3
36.	Institute of Allied Science & Computer Application, Gwalior	1

S.N.	Name of University / College	Number of Students
37.	Integral University, Lucknow	17
38.	International College for Girls, Jaipur	2
39.	IT College, Lucknow	1
40.	ITS Paramedical College (Pharmacy), Ghaziabad	7
41.	Jain College, Gwalior	2
42.	Jaipur National University, Jaipur	7
43.	Jamia Hamdard University, New Delhi	2
44.	Janta College, Etawah	1
45.	Jaypee Institute of Information & Technology, Noida	1
46.	Jiwaji University, Gwalior	2
47.	Kanak Manjari Institute of Pharmaceutical Sciences, Orissa	1
48.	Kanya Gurukula Mahavidyalaya, Haridwar	1
49.	KIIT University, Bhubaneswar	1
50.	Kumaun University, Nanital	1
51.	Lovely Professional University, Punjab	1
52.	Loyola College, Chennai	1
53.	Lucknow University, Lucknow	8
54.	Lyallaper Khalsa College, Jalandhar	1
55.	Mahatma Gandhi Institute of Applied Sciences , Jaipur	3
56.	MCMT, Varanasi	1
57.	MITS, School of Biotechnology, Bhubaneswar	3
58.	Modi Institute of Management & Technology, Kota	2
59.	Modi Institute of Technology & Science, Rajasthan	2
60.	NIMS University, Jaipur	2
61.	NIPER, Guwahati	1
62.	Northern India Engineering College, Lucknow	2
63.	PGIMER, Chandigarh	1
64.	University of Pune, Pune	2
65.	Raisoni Institute of Inter Disciplinary Sciences, Nagpur	1
66.	Rajendra Institute of Technology, Sirsa	1
67.	Rajiv Academy, Mathura	2
68.	Satra University, Thanjavur	1
69.	SD College of B. Pharmacy, Barnala	1
70.	Shivdan Singh Institute of Technology & Management, Aligarh	1
71.	Shobhit University, Meerut	4

S.N.	Name of University / College	Number of Students
72.	Sikshao Anusndhan University, Bhubaneswar	1
73.	Singhania University, Rajasthan	4
74.	SSITM, Aligarh	1
75.	St. John's College, Agra	3
76.	St. Josephs College, Tiruchirapalli	2
77.	University of Rajasthan, Jaipur	2
78.	Vardhman College, Bijnor	1
79.	VBS Purvanchal University, Jaunpur	1
80.	Vinayaka Missions College of Pharmacy, Salem	1
81.	VIT University, Vellore	6
	Grand Total	**242**

Honours and Awards

Team CDRI	CSIR Technology Award for Innovation - 2009 for Development of Synthetic Endoperoxide Anti malarials as Substitute to Artemisinine Derivatives.
	**Dr. C.M. Gupta** Distinguished Biotechnology Research Professorship Award, Department of Biotechnology, Government of India.
	**Dr. S.K. Puri** Fellow of National Academy of Sciences, India.
	**Dr. C. Nath** Fellow of Indian Academy of Neurosciences, India.
	**Dr. Ashim Ghatak** Dr. Coelho Memorial Oration in Experimental Medicine – 2009, The Association of Physicians of India.
	**Dr. Sanjay Batra** The Most Cited Paper 2006 - 2009 Award, Tetrahedron.

Dr. Atul Goel

Dr. Ghanshyam Srivastava Memorial Award - 2007, Indian Chemical Society of India.

Dr. Renu Tripathi

Dr. G.D. Bhalerao Award - 2009, Zoological Society of India.

Dr. N. Chattopadhyay

Member, Editorial Advisory Board, Biochemical Pharmacology, member, Editorial Advisory Board, American Journal of Physiology.

Dr. Ravishankar R.

Member, Advisory Board, Trends in Carbohydrate Chemistry.

Ms. Jyoti Pandey

DST-DFG Award for Participation in the Meeting of Nobel Laureates & Students - 2009, Lindau, Germany.

Ms. Gauri Misra

Eli Lilly Asia Outstanding Thesis Award - 2009 (First Prize), Eli Lilly & Company, USA.

Mr. Sumit Chaurasia

Eli Lilly Asia Outstanding Thesis Award - 2009 (Second Prize), Eli Lilly & Company, USA.

Mr. Vikash Verma

Best Poster Award, International Congress on Bio-immunoregulatory Mechanisms Associated with Reproductive Organs: Relevance in Fertility and in Sexually Transmitted infections, National Institute of Immunology, New Delhi.

Ms. Ankita Misra

Best Poster Award, Raman Bhai Foundation 4th International Symposium on Advances in Cardio-metabolic Research- Basic Science and Clinical Aspects, Zydus Research Centre, Ahmedabad, Gujarat.

Ms. Reema Gupta

Best Poster Award, 10th International Symposium on Vectors and Vector Borne Diseases, National Institute of Malaria Research, Panaji.

Mrs. Smita Rai

Young Scientist Award, 21st National Congress of Parasitology, 2009, held at Punjab University, Chandigarh.

Ms. Mansi Garg

Best Poster Award, 21st National Congress of Parasitology, 2009, Punjab University, Chandigarh.

Mr. Prashant Kumar Singh

Best Poster Award, 21st National Congress of Parasitology, 2009, Punjab University, Chandigarh.

Mr. Hari Narayan Kushwaha

Best Poster Award, 11th ISMAS Triennial International Conference on Mass Spectrometry, Hyderabad.

Lectures Delivered

Name of Scientist	Title of Lecture	Venue	Date
Dr. T.K. Chakraborty	Affordable healthcare: Drugs & pharmaceuticals: A CSIR perspective;	Swabhumi, Kolkata	10.12.09
	Developing new chemical entities, leads and drugs: From an organic chemist's perspective;	Institut de Chimie des Substances Naturelles, France	21.10.09
	Developing new chemical entities, leads and drugs: From an organic chemist's perspective;	Université de Picardie Jules Verne, France	23.10.09
	Developing new chemical entities, leads and drugs: From an organic chemist's perspective;	Banaras Hindu University, Varanasi	30.07.09
Dr. A.K. Saxena	Application of natural resources and traditional knowledge in search of potential leads for the treatment of osteoporosis;	NCL, Pune	22.11.09
	Basics and applications of computer aided drug design in drug discovery research;	Amity University, Lucknow	14.10.09
	A novel class of antipsychotic agents: Octa/decahydropyrazino-pyridoindoles;	North-West University (PUK), South Africa	25.09.09
	Applications of 2D and 3D QSAR to antihistamines H_1;	Bioinformatics Centre, Assam University, Silchar	17.09.09
	Homology modeling and docking studies on human histamine H_1-receptors;	Bioinformatics Centre, Assam University, Silchar	16.09.09
	Bioinformatics and its applications in drug designing;	Bioinformatics Centre, Assam University, Silchar	18.09.09
	Molecular modeling and docking studies on Hsp inhibitors;	Istanbul, Turkey	06.07.09
	Drug discovery research: Challenges and opportunities to medicinal chemists;	IIT Madras, Chennai	02.04.09
	Chemistry and biology of pyridocarbazoles;	Department Chemie, Universität Rostock, Germany	30.03.09
	Design and synthesis of potential PTP1B inhibitors for diabetes;	Erlangen-Nurnberg University, Erlangen Germany	27.03.09
	Chemistry and biology of pyridocarbazoles and related compounds;	Technische University, Dresden, Germany	26.03.09
	Applications of QSAR and molecular modeling in search of AChE inhibitors as potential anti-dementia agents. software, agents and services for business, research, and E-sciences;	Leipzig University, Germany	24.03.09

Name of Scientist	Title of Lecture	Venue	Date
	Design of agents for cardiovascular disorders – antihypertensives, anti-ischemics and antithrombotics;	Düsseldorf University, Germany	19.03.09
	QSAR in drug discovery research: Current scenario.	Sri Venkateswara College, University of Delhi, New Delhi	22.01.09
Dr. Ranjana Srivastava	Gene expression and its optimization;	Central Institute of Fisheries Education, Mumbai	10.12.09
	Expression of recombinant proteins of eukaryotic origin.	Central Institute of Fisheries Education, Mumbai	10.03.09
Dr. S.K. Puri	Development of synthetic endoperoxides as viable alternative for malaria chemotherapy.	Panjab University, Chandigarh	14.11.09
Dr. Ram Raghubir	Emerging targets for novel therapeutic strategies in ischemic stroke;	NIMS University, Jaipur	17.12.09
	The quest of drugs from marine environment.	Swabhumi, Kolkata	10.12.09
Dr. Gautam Palit	Drug discovery based on natural products: Identification and evaluation of functional leads for peptic ulcer disease;	University of Delhi, Delhi	07.01.10
	Scientific approaches for the development of potential drugs from medicinal plants;	Swabhumi, Kolkata	10.12.09
	New drug discovery and development: A collaborative approach.	Institute of Postgraduate Medical Education and Research, Kolkata	28.08.09
Dr. P.K. Murthy	Interface between immunomodulation and chemotherapy of filarial infections.	National Institute of Immunology, New Delhi	04.11.09
Dr. B. Kundu	The Pictet-Spengler reaction revisited.	Zydus Research Centre, Ahmedabad	09.09.09
Dr. R.K. Sharma	Bioinformatics in agriculture: Tools, technologies, opportunities;	N.D. University of Agriculture & Technology, Faizabad	09.12.09
	Application of *in silico* studies in the identification of targets for prevention and control of plant diseases;	N.D. University of Agriculture & Technology, Faizabad	09.12.09
	Bioinformatics in rational drug designing in role of chemo-informatics, pharmaco-informatics and bio-informatics in rational drug designing;	Biotech Park , Lucknow	08.10.09
	Bioinformatics in drug development: Application and current approaches;	Biotech Park, Lucknow	10.06.09
	Molecular modeling and drug designing;	Aligarh Muslim University, Aligarh	15.01.09
	Bioinformatics and proteins: An overview;	Aligarh Muslim University, Aligarh	15.01.09
	Sequencing and docking techniques, tools and case studies.	Aligarh Muslim University, Aligarh	16.01.09

Name of Scientist	Title of Lecture	Venue	Date
Dr. J.S. Srivastava	Ethics in the medical research;	CSMMU, Lucknow	13.10.09
	Introduction to Bioethics;	CSMMU, Lucknow	22.09.09
	Pharmacogenomics in depression;	Taj Hotel, Lucknow	05.07.09
	Ethical issues in clinical research;	PGIMER, Chandigarh	04.03.09
	Biomedical ethics.	CSMMU, Lucknow	13.02.09
Dr. Ashim Ghatak	High oxidant stress, depleted nitric oxide system and hyperhomocysteicysteinemia in Indian patients with hypertension.	International Convention Centre, Greater Noida	01.02.09
Dr. Madhu Dikshit	Flowcytometry to assess cell functions;	National Centre of Biology, Bangalore	17.12.09
	Neutrophils: Friend or foe;	Shivaji College, Delhi University, Delhi	24.11.09
	NO dependent biphasic effect on HL-60 cell cycle: Role of Cdk2-nitrosylation and loss of mitochondrial potential;	National Centre for Cell Science, Pune	31.10.09
	Intravascular thrombosis: Novel therapeutic targets for future anti-thrombotic drug development;	Pulmonary Vascular Research Institute, Chandigarh	22.10.09
	Human cardiovascular pathologies: Mechanisms and search for new drugs.	CDRI, Lucknow	26.03.09
Dr. Rakesh Shukla	Cholinergic mechanisms controlling inflammation in brain and their therapeutic implications in relation to neurodegenerative diseases;	NIMS University, Jaipur	18.12.09
	Protective effect of donepezil on LPS-induced neuroinflammation in rat;	Indian Academy of Neurosciences, Cochin	12.12.08
	Brain antiinflammatory cholinergic mechanisms in neurodegenerative diseases.	KIIT University, Bhubaneswar	13.11.09
Dr. J.K.Saxena	Structural biology of helminthes proteins.	Allahabad University, Allahabad	09.10.09
Dr. Sudhir K. Sinha	Drug discovery: An overview.	DM College of Science, Manipur University, Imphal	29.10.09
Dr. Naibedya Chattopadhyay	Drug development for bone health and osteoporosis;	DRDO, Delhi	23.11.09
	Studies on a rare disease translated into drugs: the story of calcium-sensing receptor;	CSJM Medical University, Lucknow	28.04.09
	Expression and function of calcium-sensing receptor in GnRH neurons.	University of Hyderabad, Hyderabad	19.01.09
Dr. R.P. Tripathi	Carbohydrates in medicinal chemistry: Our current studies;	LM College of Pharmacy, Jodhpur	07.12.09
	Design and development of new generation of antitubercular agents;	Pretoria, South Africa	03.08.09

Name of Scientist	Title of Lecture	Venue	Date
	Synthesis of biologically active molecules from carbohydrate based ligands;	DRDO, Gwalior	08.04.09
	Engineering monosaccharides to new chemotherapeutic agents;	University of Delhi, Delhi	04.03.09
	Engineering monosaccharides to new chemotherapeutic agents.	Allahabad University, Allahabad	08.02.09
Dr. Arvind K. Srivastava	A rat model for metabolic syndrome and type 2 diabetes mellitus.	Annamalai Nagar, Tamil Nadu	19.12.09
Dr. Y.S. Prabhakar	Feature selection in QSAR models;	Jaipur National University, Jaipur	22.08.09
	Properties of macromolecules - discrete mathematics in their characterization.	Nizam College, Hyderabad	08.01.09
Mr. Vinay Tripathi	Technology development / transfer / commercialization related aspects;	NIPER, Rae Bareli	30.10.09
	Patent filing and patent search;	Amity University, Lucknow	28.10.09
	Nuts and bolts of Copyrights and Trademarks.	NIPER, Rae Bareli	25.09.09
Dr. P.M.S. Chauhan	Solid support and microwave assisted synthesis of novel heterocycles and their antiinfective activity;	Nirma University, Ahemdabad	13.11.09
	Nitrogen heterocycles as antiinfective agents;	Glasgow, UK	03.08.09
	Nitrogen heterocycles as anti-infective agents.	University of Delhi, Delhi	27.02.09
Dr. Gopal Gupta	Targeting the male germ cell for contraception.	IITR, Lucknow	30.12.09
Dr. K.K. Srivastava	Cross talk between mycobacterial and macrophages serine threonine kinases: Subversions for survival.	National Habitat Centre, New Delhi	03.11.09
Dr. S.K. Singh	Important aspects of animal and human pharmacokinetics.	CDRI, Lucknow	23.09.09
Dr. Brijesh Kumar	Direct analysis in real time mass spectrometer DART MS and its applications;	CDRI, Lucknow	07.12.09
	Application of mass spectrometry for structure elucidation.	National University, Jaipur	22.08.09
Dr. Saman Habib	DNA organization and replication in the relict plastid of *Plasmodium falciparum;*	IICB, Kolkata	11.12.09
	Looking for cure in a parasite plastid: Novel avenues for drug target identification in malaria;	IITR, Lucknow	13.10.09
	Current advances in biological research;	IITR, Lucknow	02.02.09
	Indian science in the international context.	IIT, New Delhi	10.01.09
Dr. Amit Misra	The devil's advocacy: When and why inhaled therapies may not work;	India Habitat Centre, New Delhi	03.11.09
	Nanotechnology in the hospital pharmacy workspace;	Scientific Convention Centre, Lucknow	25.10.09

Name of Scientist	Title of Lecture	Venue	Date
	'Yes' and 'no' to nano for drug and antigen delivery systems;	Nanotech India, Cochin	14.08.09
	Route, timing, size and cost: Delivery systems for use in infectious diseases, contraception and diabetes;	University of Bradford, Bradford, UK	09.06.09
	Setting a pulse to catch a pulse: Non-invasive episodic intervention in the hypothalamo-pituitary-testicular axis for male contraception.	University of Hyderabad, Hyderabad	21.01.09
Dr. Jawahar Lal	Pharmacokinetics and bio-analytical method validation;	Anand College of Pharmacy, Agra	14.11.09
	Role of pharmacokinetics in drug research.	CDRI, Lucknow	22.09.09
Dr. Sanjay Batra	New dimensions to the synthesis of quinolines and polycyclic quinolines;	SGIT, Indore	23.07.09
	Adventures in the synthesis of aza-heterocycles;	BHU, Varanasi	25.02.09
	Quinolines and antimalarial chemotherapy: New developments.	BHU, Varanasi	25.02.09
Dr. Atul Goel	2-Pyranones: versatile precursors with unlimited synthetic potential;	Vellore Institute of Technology, Vellore	05.12.09
	Efficient synthesis of biaryl lactones and axially chiral biaryl scaffolds.	University of Wuerzburg, Germany	24.03.09
Dr. Jimut Kanti Ghosh	Identification, design and characterization of biologically active peptides from pore-forming toxin and antimicrobial peptides.	SRM University, Kattankulathur, Tamil Nadu	13.05.09
Dr. B.N. Singh	Genome organization and gene expression and comparative genomics;	Lucknow University, Lucknow	17.12.09
	Genomics driven approach to tuberculosis drug development;	Institute of Nuclear Medicine and Allied Science, Delhi	24.11.09
	Genetic regulation modeling.	CSJM Medical University, Lucknow	05.02.09
Dr. P.R. Mishra	Rational approach for LPS neutralization in sepsis: A case of severe systemic infection.	Jamia Hamdard, New Delhi	18.04.09
Dr. M.I. Siddiqi	Computer assisted drug design: Rational identification and design of antitubercular compounds;	Trieste, Italy	13.10.09
	Computer-aided molecular modeling: From protein ligand interaction to drug design;	CDRI, Lucknow	30.10.09
	Protein 3-D structure prediction and structure-based drug design;	University of Lucknow, Lucknow	07.10.09
	Rational identification and design of potent anti-mycobacterial agents using pharmacophore-based virtual screening, molecular docking and interaction fingerprints;	Pretoria, South Africa	03.08.09

Name of Scientist	Title of Lecture	Venue	Date
	Principles of QSAR and selected case studies: QSAR analysis;	Trieste, Italy	08.06.09
	Knowledge based identification and prioritization of potent anti-tubercular compounds using structure-based virtual screening;	Trieste, Italy	03.06.09
	Computer-aided drug design: Identification and development of potent antitubercular compounds;	CSJM Medical University, Lucknow	28.04.09
	Identification and prioritization of potent anti-tubercular compounds using virtual screening and molecular docking.	IMTECH, Chandigarh	24.03.09
Mr. Sanjeev Kanojiya	Role of mass spectrometers in metabolomics.	CDRI, Lucknow	07.12.09
Dr. S.R.Kulkarni	Intellectual property rights and related issues;	CDRI, Lucknow	01.12.09
	An insight into biotech patenting;	Amity University, Lucknow	28.10.09
	Series of lectures relating to IPR (PT 560);	NIPER, Rae Bareli	Aug-12.09
	Information source and its search methods.	CDRI, Lucknow	26.04.09

Distinguished Visitors and Lectures

Name and Address	Title of the Lecture	Date
Dr. Amitabha Bandyopadhyay Assistant Professor Dept. of Biological Sciences & Engineering Indian Institute of Technology, Kanpur.	Yin and Yang of Skeletal Development: Gene Hunting and Genetics	9.3.09
Dr. Bathula Surender Reddy UNC Chapel Hill, USA.	Development of Cancer Targeted Therapeutics	13.3.09
Prof. Dipak Dasgupta Head, Biophysics Division Saha Institute of Nuclear Physics Kolkata.	Chemical Biology of Two Anticancer Antibiotics with Additional Therapeutic Potential	25.3.09
Dr. Dipak Datta Department of Medicine Children's Hospital Harvard Medical School Boston, USA.	Pro-tumorigenic Signals of Calcineurin Inhibitors: Beyond Immunosuppression	27.3.09
Dr. Gopal C. Kundu Scientist National Center for Cell Sciences Pune.	Therapeutic and Diagnostic Significance of Osteopontin and other Associated Proteins in Regulation of Vascular Angiogenesis, Tumor Growth and Metastasis	30.3.09
Dr. Amit Singh University of Albama Birmingham, USA.	*Mycobacterium tuberculosis* Redox Sensing Mechanisms: Linking Environmental Cues and Virulence Pathways	9.4.09
Dr. R.K. Sunil Singh Institute of Molecular Medicine New Delhi.	Visualizing Transcription at a Genetic Locus	27.4.09
Dr. P.K. Jadhav Senior Research Fellow Lilly Research Laboratories USA.	Eli Lilly Asia Outstanding Thesis Awards: Eligibility and Selection Process	29.4.09
Prof. Simeon Arseniyadis Institute de Chimie des Substances Naturelles CNRS, Gif-sur-Yveette France.	The Domino and Chiral Pool Approaches as Problem Solving Tools in Biologically Active Natural Product Synthesis	5.5.09
Dr. Mukund S. Chorghade President, Chorghade Enterprises THINQ Pharma, USA.	Bridging the Innovation Deficit using Natural Products as an Inspiration: Reverse Pharmacology and Systems Approaches for Drug Discovery	22.5.09

Name and Address	Title of the Lecture	Date
Dr. Denis Martin Project Manager Drugs for Neglected Diseases Geneva.	DNDi: Advancing Research and Development Projects Through Partnership – Focus on Visceral Leishmaniasis	26.5.09
Dr. Ashoke Sharon Department of Applied Chemistry Birla Institute of Technology Mesra, Ranchi.	Structure Based Approach Towards Antiviral Drug Discovery	2.6.09
Prof. Sandeep Verma Department of Chemistry Indian Institute of Technology Kanpur.	Peptide Soft Structures: Application in Drug Discovery and Gene Delivery	12.6.09
Dr. Udayannath Aich Massachusetts Institute of Technology USA.	Development of Bio-therapeutic Agents against Influenza and Cancer Diseases by Bio-analytical, Structural Organic Synthesis and Biological Tools	22.6.09
Dr. Saurabh Singh Department of Molecular, Cellular and Craniofacial Biology University of Louisville Birth Defects Center Louisville, KY, USA.	Cellular and Molecular Mechanisms of Environmental Toxins in Development	1.7.09
Prof. Subho Mazumdar University of Delhi Delhi.	The Fascinating Science of Nanoparticle Technology: Synthesis to Drug Delivery	10.7.09
Mr. Sachchidanand Senior Research Scientist Institute of Life Sciences Hyderabad.	Finding HITS against Bromodomain and SIRT1	20.7.09
Dr. Ning Ke Head, Functional Genomics Acea Biosciences San Diego, USA.	Applications in Drug Discovery, RNAi Study, Cell Invasion / Migration	21.7.09
Dr. Barry M. Trost Professor of Chemistry Stanford University USA.	Cyclo-additions via TMM-Pd Intermediates: New Strategies for Asymmetric Induction and Total Synthesis	7.8.09
Dr. Ampapathi Ravi Sankar National Institute of Health Frederick, USA.	Structural Studies on Transcriptional Factor STAT4: Enzymatic Domain of Cholera Toxin	24.8.09
Dr. Robert Rice Scientist Qiagen, Germany.	High Resolution Melt Curve Analysis – Revolution in DNA Analysis for SNPs and Genotyping	2.9.09
Dr. Alexander Stadler Application Specialist Microwave Synthesis Anton Parr, Austria.	New Development in Microwave Assisted Synthesis in Organic Chemistry	9.9.09

Name and Address	Title of the Lecture	Date
Dr. Arunava Dasgupta Max Plank Institute for Infection Biology Berlin, Germeny.	Fight Against Tuberculosis, the Ancient Disease that has Taken a Deadly New Turn	17.9.09
Prof. H. Sakurai Institute of Molecular Science Japan.	Gold Nanocluster as Unique Catalyst under Aerobic Condition	23.9.09
Dr. N. Pratap Mukhopaydhyay CEO and Head R&D Gene Ombio Technologies Pvt. Ltd. Pune.	Custom DNA Sequencing and DNA Fingerprinting	6.10.09
Prof. Mohammed Ahmad Director Biotech Centre, University of West Indies, Kingston Jamaica, West Indies.	Business of Biotechnology: A Marketing and Management Perspective	8.10.09
Prof. Geoffrey A. Cordell University of Illinois USA.	Sustainable Drugs and Global Health	14.10.09
Ms. Neera Pandey Manager, Business Development Center for Genomic Applications New Delhi.	Applications and Infrastructure at The Center for Genomic Applications: Utility of These Platform in Scientific Research	24.11.09
Prof. S.S. Agarwal Former Director Sanjay Gandhi Post Graduate Institute of Medical Sciences Lucknow.	Role of Institutional Ethics Committee	24.11.09
Prof. Raymond C.F. Jones Department of Chemistry Loughborough University United Kingdom.	The Expected and the Unexpected: Adventures with 1,3-Dipoles	8.12.09
Prof. Shantanu Sinha Department of Radiology University of California San Diego, USA.	Role of Magnetic Resonance Imaging in Drug Discovery and Development	25.12.09
Prof. Ram Mohan Professor of Natural Sciences Department of Chemistry Illinois Wesleyan University Bloomington, USA.	Environmentally Friendly Organic Synthesis using Bismuth (III) Compounds	18.12.09
Dr. Utpal Banerjee Co-Director, Molecular, cell & Development Biology University of California Los Angeles, USA.	Drosophila Hematopoiesis: Stem Cells, Development and Stress Response	31.12.09

Membership of Scientific Societies and Committees

Name of Scientist	Membership Details
Dr. T.K. Chakraborty	**Member,** The American Chemical Society; **Life Member,** (a) Chemical Research Society of India (b) Indian Chemical Society (c) Indian Peptide Society; **Member,** (a) Chemical Sciences Sectional Committee, Indian Academy of Sciences (b) India-Taiwan Joint S&T Committee (c) Program Advisory Committee (Organic Chemistry), DST (d) Steering Committee of the National Bioresource Development Board, DBT (e) Sub-committee of Sponsored Schemes Research Committee, CSIR (f) Expert Committee of Drugs and Pharmaceuticals Research Programme, DST, Govt. of India (g) Drugs Technical Advisory Board; **Member**, Editorial Board, Indian Journal of Chemistry, Section B.
Dr. A.K. Saxena	**Member**, The American Chemical Society; **Patent Evaluator**, Current Drugs Ltd., U.K; **Member,** (a) Board of Directors' in American Bibliography Inc. USA (b) International Charitable Foundations (Scientific Partnership) Coordinating Board, Russia; **Life Member,** (a) Indian Chemical Society (b) Indian Association of Medicinal Chemists (c) UP Association for Science and Technology advancement; **Member,** (a) Expert Committee, Department of Pharmaceuticals, Ministry of Chemicals & Fertilizers, Govt. of India (b) IND Committee, Directorate General of Health Services, Office of Drugs Controller General (India) (c) Reach India Task Force, Department of Chemical and Petrochemicals, Ministry of Chemicals & Fertilizers, Govt. of India; **UGC Nominee**, Advisory Committee, Special Assistance Programme for (a) Department of Chemistry, Saurashtra University, Rajkot (b) Department of Chemistry, A.P.S University, Rewa; **Member**, Editorial Board, (a) Medicinal Chemistry Research (b) SAR and QSAR in Environmental Research (c) Online International journal ARKIVOC, ARKAT USA Inc (d) The Open Toxicology Journal.
Dr. Ranjana Srivastava	**Editor**, Indian Journal of Microbiology; **DBT Nominee,** (a) IBSC, IITR, Lucknow (b) IBSC, IIT, Kanpur.
Dr. S.K. Puri	**Vice President**, Indian Society for Parasitology; **Member,** (a) Academic Council, JNU, New Delhi (b) Institutional Animal Ethics Committee, Indian Animal Suppliers, Lucknow.
Dr. Zaka Imam	**Member**, Editorial Board, International Journal of Health Technology & Management, UK.

Name of Scientist	Membership Details
Dr. Ram Raghubir	**Member**, National Steering Committee, MoES Project: Drugs from the Sea, New Delhi; **Member**, Editorial Board, Annals of Neurosciences; **Secretary**, Indian Pharmacological Society, Lucknow Branch.
Dr. Gautam Palit	**Member,** (a) Fellowship Expert Group Committee, ICMR, New Delhi (b) IEC, Vivekananda Polyclinic & Institute of Medical Sciences, Lucknow.
Dr. S.B. Katti	**Member**, Editorial Advisory Board, The Open Natural Products Journal.
Dr. C. Nath	**Member,** (a) Advisory Committee for IND Permission, Drug Controller General of India, Ministry of Health, Government of India (b) Animal Ethics Committee, IITR.
Dr. Shailja Bhattacharya	**Member,** Scientific Advisory Committee, VCRC, Pondicherry; **Honorary Advisor,** German Academic Exchange Services (DAAD); **Member**, Advisory Board, J. Immunology and Immunopathology.
Dr. R.K. Sharma	**Member**, Research Advisory Committee, Govt. Homeopathic Medical Colleges.
Dr. J.S. Srivastava	**Member,** Institutional Ethics Committee, (a) SGPGI, Lucknow (b) CSMMU, Lucknow.
Dr. A. Ghatak	**Member,** (a) National Academy of Medical Sciences (b) American College of Clinical Pharmacology.
Dr. G.K. Jain	**Member,** Official Side of the Local Council of CSIR for Adoption of Central Civil Services (Recognition of Service Association) Rules, 1993 & for Establishment of Joint Consultative Machinery; **Life Member,** (a) UP Association for the Advancement of Science & Technology (b) Indian Pharmaceutical Association.
Dr. Rajendra Prasad	**Life Member**, UP Association for Advancement of Science & Technology.
Dr. A.K. Dwivedi	**Member**, Drugs Panel for New Drugs Manufacturing Licenses, Directorate of Medical & Health Services, U.P.; **Life Member**, UP Association for Advancement of Science & Technology, Indian Pharmaceutical Association; **Joint Secretary**, Indian Society of Chemists and Biologists, Lucknow.
Dr. Madhu Dikshit	**Vice President**, The Cytometry Society of India; **Council Member**, The National Academy of Sciences of India;

Name of Scientist	Membership Details
	Member, (a) Medicine Sectional Committee, Indian Academy of Sciences (b) Program Advisory Committee of DST (WOS-A), ICMR (c) Research Advisory Committee, SGPGI, Lucknow; **Member**, Editorial Board, (a) Annals of Neurosciences (b) Proceedings of the National Academy of Sciences India (Section B: Biological Sciences) (c) Indian Journal of Pharmacology.
Mr. S.K. Mallik	**Nodal Person**, CSIR e-Journal Consortium; **Member**, (a) Negotiation Committee, CSIR – DST e-Journal Consortium, (b) Task Force, DBT Electronic Library Consortium (c) Task Force, North Eastern Region Electronic Resource Committee.
Dr. Rakesh Shukla	**Member**, Task Force Committee, Pharmacological Studies of Homeopathic Drugs, Central Council for Research in Homoeopathy, New Delhi; **Treasurer**, Indian Academy of Neurosciences, Lucknow Branch.
Dr. J.K. Saxena	**Secretary**, The Indian Society for Parasitology; **Vice President**, Society of Biologists and Chemists; **Member**, Agriculture Research Service Examination Board.
Dr. Naibedya Chattopadhyay	**Member**, Editorial Board, (a) American Journal of Physiology (Endocrinol. Metab.) (b) Biochemical Pharmacology (c) The Open Physiology Journal.
Dr. Vinod Bhakuni	**Member,** (a) Board of Governors, IIT, Roorkee (b) Research Advisory Council, Sriram Institute of Industrial Research, New Delhi (c) Technical Advisory Committee, DBT (d) Technical Screening Committee of Small Business Innovation Research Initiative (SIBRI) DBT, New Delhi (e) Program Advisory Committee, Life Sciences, DST; **Member**, Editorial Board, International Journal of Integrative Biology.
Dr. R.P. Tripathi	**Excutive Member**, ACCTI(I); **Associate Editor**, Carbohydrate News Letter; **Member**, Editorial Board, (a) ARKIVOC (b) Trends in Carbohydrate Chemistry.
Dr. Neeraj Sinha	**Life Member**, (a) Society of Toxicology, India (b) ISCA (c) Laboratory Animal Science Association of India (d) Indian Society of Cell Biology, New Delhi (e) National Academy of Science, Allahabad (f) Society of Toxicologists of India, Izatnagar (g) Indian Science Congress Association, Calcutta (h) Laboratory Animal Science Association of India, Lucknow.
Dr. D.S. Upadhyay	**Member,** (a) CPCSEA sub Committee for Rehabilitation of Laboratory Animals, (b) Live Stock Feed, Equipments and System, Sectional Committee, FAD, Bureau of Indian Standard, New Delhi (c) Veterinary Council India (d) Institutional Animal

Name of Scientist	Membership Details
	Ethics Committee, IVRI, CIMAP, CDRI, IITR, Integral University and Animal Husbandry Department, Lucknow (e) CSIR Nominee, National Institute of Animal Welfare (f) U.P Veterinary Council, Lucknow; **Life Member**, Laboratory Animal Science Association of India, CDRI, Lucknow.
Dr. P.M.S. Chauhan	**Member**, Advisory Board, Future Medicinal Chemistry.
Dr. P.K. Shukla	**Associate Editor**, Asian Journal of Biochemistry, Academic Journals Inc., USA; **Member**, Editorial Board, (a) Research Journal of Biological Sciences, Medwell Online (b) Journal of Applied Bioscience, India.
Dr. D.N. Upadhyay	**Life Member**, Society for Advancement of Electrochemical Science & Technology.
Dr. Atul Goel	**External International Expert**, BEBUK Scholarship, University of Kinshasa, Africa; **Life Member,** (a) Indian Chemical Society (b) The UP Association for the Science and Technology Advancement, Lucknow.
Dr. A.K. Srivastava	**Life Member,** (a) UP Association of Science and Technology, (b) Indian Society of Parasitology (c) Laboratory Animal Science Association of India, CDRI, Lucknow.
Dr. Jawahar Lal	**Life Member**, Indian Society of Chemists and Biologists.
Dr. S.K. Rath	**Life Member,** (a) ADNAT (b) Genome Foundation (c) Indian Society of Cell Biology (d) Environmental Mutagen Society of India; **Member,** (a) Indian Genome Variation Data Base (b) Agricultural Committee, Organic Farming Awareness Programme, Mahima Research Foundation and Social Welfare, Varanasi.
Dr. Amit Misra	**Life Member**, Indian Pharmaceutical Association; **Founder Member**, Indian Nanoscience Society; **Member,** (a) Controlled Release Society, Indian Chapter (b) Consultative Committee on Drug Discovery and Delivery.
Dr. S.M. Rajendran	**Honorary Member**, Executive Council, Society of Ethnobotanists in India; **Member**, Editorial Board, Journal Phytotaxonomy, Botanical Survey of India, Kolkata.
Mr. Prem Prakash	**Life Member,** (a) UP Association for Advancement of Science & Technology (b) Indian Pharmaceutical Association.
Dr. Sanjay Batra	**Member**, Advisory Board of Editors, Anti-infective Agents in Medicinal Chemistry.

Name of Scientist	Membership Details
Dr. (Mrs.) Kumkum Srivasatava	**Life Member**, Society for Biological Chemists, India; **Member**, Executive Committee, Indian Society for Parasitology.
Dr. R.K. Singh	**Life Member,** (a) Society of Toxicology, India (b) Indian Society for the Study of Reproduction and Fertility, Mumbai (c) International Society of Applied Biology, India (d) Society for Reproductive Biology and Comparative Endocrinology, Chennai (e) Laboratory Animal Science Association of India, CDRI, Lucknow (f) National Academy of Science, Allahabad (g) International Society for Environmental Protection (h) Society of Bio Sciences (i) Society of Embryology India.
Dr. P.R. Mishra	**Member**, Advisory Board, IIPC, Bilaspur University; **Life Member**, Indian Pharmaceutical Association; **Founder Member**, Indian Nanoscience Society; **Member**, Editorial Board, Recent Patents in Drug Delivery and Formulations.
Dr. Dhananjay Hansda	**Life Member,** (a) Indian Association of Veterinary Microbiologists, Immunologists and Specialists in Infectious Diseases (b) West Bengal Veterinary Council (c) Laboratory Animal Science Association of India, CDRI, Lucknow.
Dr. Rajender Singh	**Managing Editor**, Special issue of Frontiers in Biosciences.
Dr. Aamir Nazir	**Life Member**, Indian Society of Cell Biology; **Member**, American Society of Genetics.
Dr. Akhilesh Tamrakar	**Life Member**, Society for Biological Chemists, India.
Dr. Rabi Sankar Bhatta	**Member**, Indian Pharmaceutical Association.
Mr. Naseem Ahmed Siddiqui	**Member**, All India Management Association, New Delhi.
Mr. Wahajuddin	**Life Member**, Indian Society for Mass Spectrometry.
Mr. Janki Prasad	**Associate Member**, Institution of Engineers, India; **Member**, Indian Institute of Chemical Engineers, Kolkata.

Visits Abroad

Name of Scientist	Place of Visit	Purpose of visit	Duration
Dr. T.K. Chakraborty	France	For discussion with Dr. Siriwardena Aloysius on collaborative project entitled "Design and Synthesis of Novel SAA Based Glycosidase Inhibitors".	16 - 25 October 2009
Dr. Anil Kumar Saxena	Germany	To attend 2nd International Conference on Bioinformatics and Systems Biology (BSB 2009);	23 - 25 March 2009
	Turkey	To participate in 5th International Symposium "Computational Methods in Toxicology and Pharmacology Integrating Internet Resources";	4 - 8 July 2009
	Germany	To discuss about 2 new Anti-thrombotic Compounds with Prof. T. Hohlfeld;	9 - 10 July 2009
	South Africa	To attend the 5th International Congress on Pharmaceutical and Pharmacological Sciences (ICPPS 2009).	23 - 26 September 2009
Dr. Ranjana Srivastava	France	To participate in the 8th ICAV International Symposium.	3 - 6 October 2009
Dr. S.K. Puri	Geneva	To attend Visceral Leishmaniasis Lead Optimization Team Meeting;	12 - 13 March 2009
	Holland	To present research proposal before MMV convened Expert Scientific Advisory Committee.	22 - 23 September 2009
Dr. Zaka Imam	Canada	To participate in the 6th International Congress on Peer Review and Biomedical Publications.	10 - 12 September 2009
Dr. D.K. Dikshit	France	To attend meeting of Consultative Committee for Amount of Substance: Metrology in Chemistry (CCQM) and its working Groups;	20 - 24 April 2009
	France	To attend 8th ICAV International Symposium.	3 - 6 October 2009

Name of Scientist	Place of Visit	Purpose of visit	Duration
Dr. Shailja Bhattacharya	Switzerland	To attend the joint meeting of the Expert Drug Discovery Advisory Committee and the Task Force on Helminthes Drug Initiative (HDI).	30 March - 1 April 2009.
Dr. Vinod Bhakuni	Hong Kong	6th Asian Biophysics Association Symposium;	11 - 14 January 2009
	S. Korea	To attend meeting on "International foreign collaborative research on the protein folding problem".	19 - 22 February 2009
Dr. N. Chattopadhyay	Greece	To attend 9th European Congress on Clinical and Economic Aspects of Osteoporosis and Osteoarthritis;	18 - 21 March 2009
	UK	To attend 8th European Congress on Menopause & Andropause;	16 - 20 May 2009
	Denmark	To take Ph.D. viva as external examiner and delivering lectures.	25 June - 3 July 2009
Dr. A.K. Srivastava	Greece	To attend 2nd International Conference on "Advanced Technologies and Treatment of Diabetes".	25 - 28 February 2009
Dr. Suman Gupta	Geneva	To attend Visceral Leishmaniasis Lead Optimization Team Meeting.	12 - 13 March 2009
Dr. Rama Pati Tripathi	South Africa	To participate in the programs on "Advanced Design and Development of Potential Drug against Tuberculosis".	3 - 5 August 2009
Dr. P.M.S. Chauhan	UK	To participate in 42nd IUPAC Congress at University of Glasgow.	2 - 7 August 2009
Mr. Pradeep Kumar	South Africa	To deliver a lecture on "Nanotechnology and Medical Science: Challenges Ahead".	18 - 21 February 2009
Dr. Saman Habib	Spain	To attend Project Meeting of MEPHITIS "Targeting protein synthesis in the apicoplast and cytoplasm of *Plasmodium*".	30 - 31 March 2009
Dr. Vinita Chaturvedi	USA	To attend workshop for the BSL3 Bio-safety officers in Albuquerque.	27 April - 02 May 2009
Dr. Amit Misra	U. K.	To conduct experiments in the laboratory of Prof. Peter York at IPI.	7 - 13 June 2009
Dr. Mohd. Imran Siddiqi	Italy	To participate in "Rational Drug Design & Development Sub-program" ICS, UNIDO;	10 May - 10 July 2009

Name of Scientist	Place of Visit	Purpose of visit	Duration
	South Africa	To participate in the programs on "Advanced Design and Development of Potential Drug against Tuberculosis";	3 -5 August 2009
	Italy	Advanced Diagnostics and Drug Delivery at the Nano-scale: State of the Art and Possible Applications to Orphan Diseases.	13 - 15 October 2009
Dr. Atul Goel	Germany	Alexander von Humboldt Fellowship, Institute of Organic Chemistry, University of Wuerzburg, Germany.	July 2008 – March 2009
Dr. R.K. Tripathi	Thailand	To attend workshop on "Design and Discovery of Drugs against HIV, Dengue Fever and Avian Influenza".	4 - 6 May 2009
Dr. P.R. Mishra	Netherlands	To participate in the XVII International Conference on Bio-encapsulation.	24 - 26 September 2009
Dr. Manoj Kumar Barthwal	U. K.	Training on "Whole Body Plethysmograph" to be used for regulatory respiration studies at Buxco Research Systems.	21 - 24 January 2009
Dr. Amir Nazir	Israel	To attend the 1st BIOMICS Workshop and Conference.	30 August - 4 September 2009
Dr. Rajender Singh	Israel	To attend the 1st BIOMICS Workshop and Conference.	30 August - 4 September 2009
Dr. S.K. Shukla	USA	To conduct research and obtain training in advance research techniques in Chemical Sciences.	May 2009 – May 2010
Dr. A.K. Tamrakar	Canada	BOYSCAST Fellowship, 2008-09 for conducting research/ undergoing training in advance research techniques in area of *Diabetes mellitus* and insulin resistance at The Hospital for Sick Children, Toronto.	27 April 2009 - 26 April 2010
Dr. Kalyan Mitra	USA	Indo-US Research Fellowship Award.	June 2008 – June 2009
Dr. Rabi Sankar Bhatta	USA	For 5500/4000QTRAP System Proteomics Operator Training Course on Protein Identification.	08 - 11 December 2009
Mr. A.L. Vishwakarma	USA	Invited to attend a training course at San Jose, California.	5 - 9 October 2009

Budget

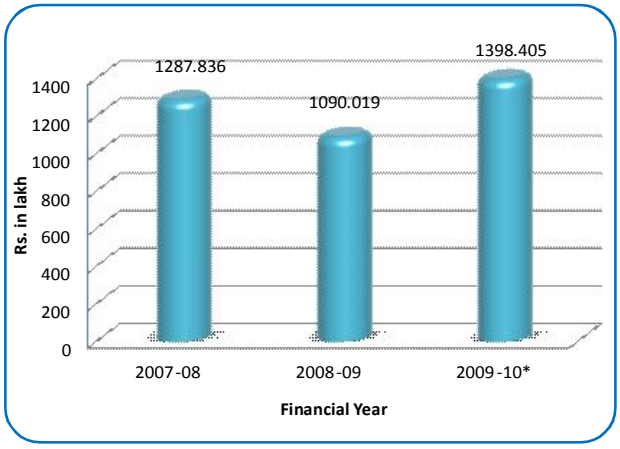
2009-2010 (Sanctioned Estimates)

(Rs. in lakh)

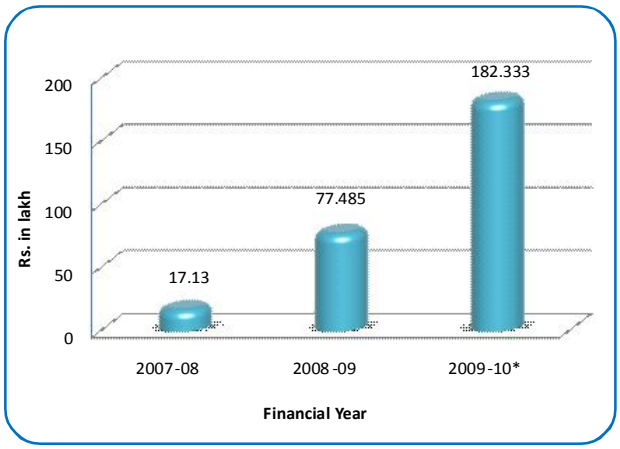
	Heads	CSIR Grant
(A)	**Recurring**	
	Pay & Allowances	4037.081
	Contingencies	215.000
	HRD	4.000
	Lab Maintenance	150.000
	Staff Quarter Maintenance	14.000
	Chemicals and Consumables	402.000
	Sub-Total	**4822.081**
(B)	**Capital**	
	Works & Services including Staff Quarter	60.000
	Apparatus and Equipments	128.000
	Office Equipments, Furniture and Fittings	9.000
	Library Books & Journals	215.000
	Sub-Total	**412.000**
	Total (A+B)	**5234.081**
(C)	SIP/NWP/IAP/FAC/CMM/SMM Projects	7542.239
	***Grand* Total (A+B+C)**	**12776.320**

2008-2009 (Actual Expenditure)

	Heads	CSIR Grant	LRF
(A)	**Recurring**		
	Pay & Allowances	2642.501	271.370
	Contingencies	210.000	0.991
	HRD	2.881	
	Lab Maintenance	140.00	5.546
	Staff Quarter Maintenance	13.993	
	Chemicals and Consumables	400.076	
	Sub-Total	***3409.451***	***277.907***
(B)	**Capital**		
	Works & Services including Staff Quarter	56.816	
	Apparatus and Equipments	325.000	19.112
	Office Equipments, Furniture and Fittings	9.962	
	Library Books & Journals	207.000	
	Infrastructure, Renovation and Refurbishing (ICT)	0.275	
	Infrastructure, Renovation and Refurbishing (Construction)	29.173	
	Sub-Total	***628.226***	***19.112***
	Total (A+B)	***4037.677***	
(C)	SIP/NWP/IAP/FAC/CMM/SMM Projects	4541.530	
	***Grand Total* (A+B+C)**	**8579.207**	**297.019**

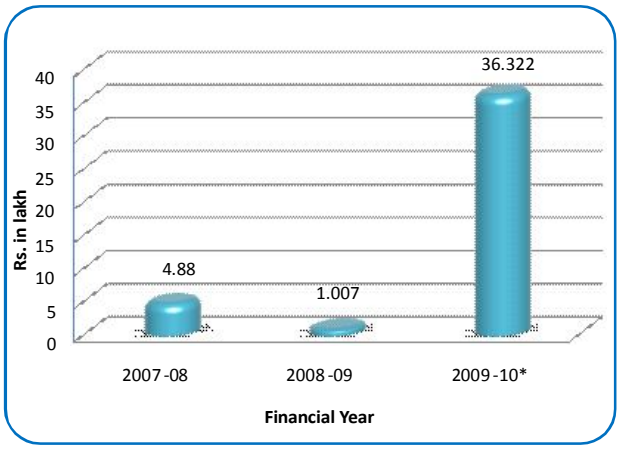


ECF - Industries

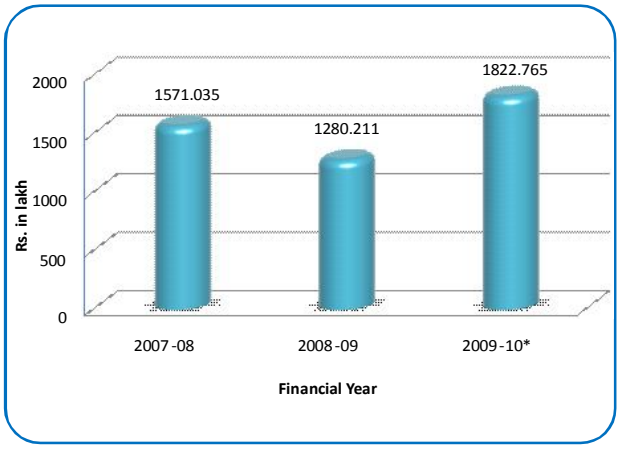


Total External Budgetary Resources

ECF - Government Agencies



ECF - Foreign Agencies



*Data as on 31-01-2010

Research Council

(April 2007 - March 2010)

Chairman

Prof. N.K. Ganguly
Former Director-General, ICMR
Translational Health Science & Technology Institute
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi – 110 067.

Members

Dr. A. Surolia
Director
National Institute of Immunology
Aruna Asaf Ali Marg
New Delhi – 110 067.

Dr. T.P. Singh
Professor and Head
Department of Biophysics
All India Institute of Medical Sciences
Ansari Nagar
New Delhi – 110 029.

Dr. Y.K. Gupta
Professor and Head
Department of Pharmacology
All India Institute of Medical Sciences
Ansari Nagar
New Delhi – 110 029.

Dr. M.D. Nair
Former Vice President
SPIC Pharmaceuticals
A-11, Sagarika, No. 15, 3rd Seaward Road
Valmiki Nagar, Thiruvanmiyur
Chennai – 600 041.

Prof. K. Muniyappa
Professor & Head
Department of Biochemistry
Indian Institute of Science
Bangalore – 560 012.

Dr. Surinder Singh
Drug Controller General (India)
Directorate General of Health Services
Ministry of Health and Family Welfare
Nirman Bhawan
New Delhi – 110 011.

Dr. Arun Bandyopadhyay
Scientist F
Head, Division of Cell Biology
Indian Institute of Chemical Biology
4, Raja S.C. Mullick Road, Jadavpur
Kolkata – 700 032.

Dr. Rakesh Tuli
Director
National Botanical Research Institute
Rana Pratap Marg
Lucknow – 226 001.

Dr. T.K. Chakraborty
Director
Central Drug Research Institute
Lucknow – 226 001.

Dr. Naresh Kumar
Head
Planning and Performance Division
Council of Scientific & Industrial Research
Rafi Marg
New Delhi – 110 001.

Secretary

Dr. S.B. Katti
Scientist G
Central Drug Research Institute
Lucknow – 226 001.

Management Council

Chairman

Dr. T.K. Chakraborty
Director
Central Drug Research Institute
Lucknow – 226 001.

Members

Dr. K.C. Gupta
Director
Indian Institute of Toxicological Research
Lucknow – 226 001.

Dr. Zaka Imam
Scientist Gr. IV(6)
Division of S&T Management
CDRI, Lucknow – 226 001.

Dr. S.P.S. Gaur
Scientist Gr. IV(5)
Clinical & Experimental Medicine
CDRI, Lucknow – 226 001.

Dr. Vinod Bhakuni
Scientist Gr. IV(5)
Molecular & Structural Biology Division
CDRI, Lucknow – 226 001.

Dr. (Smt.) Saman Habib
Scientist Gr. IV(4)
Molecular & Structural Biology Division
CDRI, Lucknow – 226 001.

Dr. Mohd. Imran Siddiqui
Scientist Gr. IV(2)
Molecular & Structural Biology Division
CDRI, Lucknow – 226 001.

Sh. Karunesh Rai
Technical Officer Gr. III(5)
Division of Laboratory Animals
CDRI, Lucknow – 226 001.

Controller of Finance & Accounts / Finance & Accounts Officer
CDRI, Lucknow – 226 001.

Member – Secretary

Controller of Administration / Administration Officer
CDRI, Lucknow – 226 001.

The Staff

DIRECTOR

Dr. Tushar Kanti Chakraborty, M.Sc., Ph.D. (IIT, Kanpur), FNA, FASc, FNASc

R & D DIVISIONS/UNITS

BIOCHEMISTRY

Scientists Group IV (5)
J.K. Saxena, M.Sc. (Lucknow), Ph.D. (Kanpur), *In-Charge*
Uma Roy, M.Sc., Ph.D. (Kanpur)
Gitika Bhatia, M.Sc., Ph.D. (Agra)
A.K. Srivastava, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientist Group IV (4)
Neena Goyal, M.Sc. (Lucknow), Ph.D. (Agra)

Scientist Group IV (3)
Anju Puri, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientist Group IV (1)
A.K. Tamrakar, M.Sc., Ph.D. (Jiwaji)

Technical Officer Group III (6)
A.K. Khanna, M.Sc. (Lucknow), Ph.D. (Kanpur)

Technical Officer Group III (4)
B. Maity, M.Sc. (Kanpur), Ph.D. (Rohilkhand)

Technical Assistants Group III (1)
Rima Ray Sarkar
Ishbal Ahmad

Technical Assistant Group II (4)
Suresh Yadav

Technical Assistants Group II (3)
B.R. Yadav
Ram Pal Rawat

Helpers Group I (4)
Ramesh Chandra
Noor Jehan

Jr. Steno
Vineet Pandey

BOTANY

Scientist Group IV (6)
R.K. Sharma, M.Sc., Ph.D. (Agra), *In-Charge*

Scientist Group IV (4)
M.N. Srivastava, M.Sc. (Kanpur), Ph.D. (Lucknow)

Scientists Group IV (3)
S.M. Rajendran, M.Sc. (Madurai Kamaraj), Ph.D. (Lucknow), Head, CADC Unit
K.R. Arya, M.Sc. (Kumaon), Ph.D. (Kanpur)

Scientist Group IV (2)
D.K. Mishra, M.Sc. (Vidyasagar), Ph.D. (Pune)

Technical Assistant Group III (1)
Savita Tripathi, M.Sc. (Kanpur)

Technical Assistant Group II (4)
J.K. Joshi, M.Sc. (Kanpur)

Helpers Group I (4)
Ram Jeewan
K.K. Yadav
Devi Dutt
Maiku Lal Lodh
Makhan Lal
Gopi
Satya Narain

Helper Group I (2)
R.C. Maurya

Helpers Group I (1)
Lakhana Devi
N.K. Khanduri
Ashok Kumar

Private Secretary
Sumit Srivastava, B.Com.

CLINICAL & EXPERIMENTAL MEDICINE

Scientists Group IV (5)
S.P.S. Gaur, M.B.B.S., M.D. (Lucknow), *In-Charge*
J.S. Srivastava, M.B.B.S., M.D. (Lucknow), D.M. (Chandigarh), M.H.Sc. (Toronto)
A. Ghatak, M.B.B.S., M.D. (Lucknow), MNAMS, FICP

Technical Officer Group III (7)
A.K. Nigam, M.Sc. (Kanpur) [Retired on 30/06/2009]

Technical Assistant Group III (1)
Shail Singh, M.Sc. (Jabalpur)

Technical Assistants Group II (4)
J.R. Gupta [Retired on 30/04/2009]
H.S. Dubey
Kishori Lal [Retired on 31/07/2009]

Helper Group I (3)
Umesh Kumar

DRUG TARGET DISCOVERY AND DEVELOPMENT

Scientist Group IV (5)
Sudhir K. Sinha, M.Sc. (Lucknow), Ph.D. (Kanpur), *In-Charge*

Scientists Group IV (4)
Neeloo Singh, M.Sc. (Lucknow), Ph.D. (Kanpur)
Vinita Chaturvedi, M.Sc., Ph.D. (Agra)

Scientist Group IV (3)
Sabyasachi Sanyal, M.Sc. (Viswabharati), Ph.D. (CNU, South Korea)

Scientists Group IV (2)
Anil N. Gaikwad, M.S. (Pharm.) (NIPER, Chandigarh), Ph.D. (JNU)
Y.K. Manju, M.Sc. (Calicut), Ph.D. (Kerala)
Arun Kumar Trivedi, M.Sc. (Varanasi), Ph.D. (Ludwik Maximillians)

Scientist Group IV (1)
Jayant Sarkar, M.V.Sc., Ph.D. (IVRI)

Technical Officer Group III (5)
S.L. Verma, B.Sc.

Technical Assistants Group III (1)
Ajay Singh Verma, M.Sc. (Aligarh)
Shyam Singh, M.Sc. (Agra)
Sanjeev Meena, M.Sc. (Rajasthan)

Technical Assistant Group II (4)
Chandramool

Technical Assistant Group II (3)
Lal Hori

Jr. Steno
Rekha Tripathi

ENDOCRINOLOGY

Scientists Group IV (5)
Naibedya Chattopadhyay, M.Sc. (Calcutta), Ph.D. (SGPGIMS), *In-Charge*
Archana Srivastav, M.Sc., Ph.D. (Lucknow)

Scientists Group IV (4)
Anila Dwivedi, M.Sc. (Lucknow), Ph.D. (Kanpur)
Gopal Gupta, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientists Group IV (3)
F.W. Bansode, M.Sc. (Nagpur), Ph.D. (Udaipur)
Durga Prasad Mishra, M.Sc. (Karnal), Ph.D. (Delhi)

Scientists Group IV (2)
Divya Singh, M.Sc. (Lucknow), Ph.D. (Lucknow)
Ritu Trivedi, M.Sc. (Lucknow), Ph.D. (SGPGIMS)
Rajender Singh, M.Sc. (Amritsar), Ph.D. (JNU)

Scientists Group IV (1)
Hemant Kumar Bid, M.Sc. (Avadh), Ph.D. (Kanpur)
Konwar Rituraj, M.V.Sc., Ph.D. (IVRI)

Technical Officer Group III (6)
J.P. Maikhuri, M.Sc. (Garhwal), Ph.D. (Jamia Hamdard)

Technical Officer Group III (5)
Mohini Chhabra, B.Sc., CLSc.

Technical Officers Group III (4)
Shakti Kitchlu, M.Sc. (Kanpur)
Balvir Singh, M.Sc. (Rohilkhand)

Technical Assistants Group III (1)
Lakshma Nayak V. [Transferred to IICT, Hyderabad on 10/07/2009]
Preeti

Technical Assistants Group II (4)
A.P. Dev
T. Firdaus
Kanak Lata [Retired on 31/12/2009]

Technical Assistants Group II (3)
P.K. Bhattacharya
Chattar Pal
Geet Kumar Nagar

Helpers Group I (4)
N.P. Misra
B.P. Mirsa
R.G. Pandey

Helper Group I (2)
Mahesh Chandra Tewari

Helpers Group I (1)
Nabbulal Kori
Ram Karan
Pradeep Singh

FERMENTATION TECHNOLOGY

Scientist Group IV (5)
C.K.M. Tripathi, M.Sc., Ph.D. (BHU), *In-Charge*

Scientist Group IV (4)
P.K. Shukla, M.Sc. (Lucknow), Ph.D. (Kanpur)

Technical Officer Group III (7)
A.K. Joshi, M.Sc. (Kumaon)

Technical Officers Group III (5)
Shyamendra Mehrotra, B.Sc.
Bikram Banerjee, B.Sc.
M.K. Srivastava, M.Sc. (Sagar) [Retired on 30/06/2009]
Malkhan Singh, B.Sc.
Agney Lal, B.Sc.

Technical Assistant Group II (4)
Kishan Singh

Technical Assistant Group II (3)
O.P. Gupta

Helpers Group I (4)
Lakshmi Prasad
A.N. Dixit

Private Secretary
H.K. Khulve

MEDICINAL AND PROCESS CHEMISTRY DIVISION

Scientists Group IV (6)
A.K. Saxena, M.Sc., Ph.D. (Lucknow), *In-Charge*
D.P. Sahu, M.E. Chem. Engg. (S.I.T., USA),
Ph.D. (IIT, Kharagpur) [Retired on 31/03/2009]
S.B. Katti, M.Pharm., Ph.D. (Mysore)
Bijoy Kundu, M.Sc., Ph.D. (Kanpur)
Ram Pratap, M.Sc., Ph.D. (BHU)

Scientists Group IV (5)
K.C. Agarwal, M.Sc., Ph.D. (Lucknow)
[Retired on 28/02/2009]
S.N. Suryawanshi, M.Sc., Ph.D. (Pune)
Kamlakar Avasthi, M.Sc., Ph.D. (Lucknow)
Rakesh Maurya, M.Sc., Ph.D. (Varanasi)
Kalpana Bhandari, M.Sc., Ph.D. (Lucknow)
R.P. Tripathi, M.Sc. (Gorakhpur), M.Phil, Ph.D.(Delhi)
Vijai Lakshmi, M.Sc., Ph.D. (Allahabad)
Kanchan Hajela, M.Sc., Ph.D. (Lucknow)
Y.S. Prabhakar, M.Sc. (Vishakhapatnam), Ph.D. (Pilani)
Arun K. Shaw, M.Sc., Ph.D. (Calcutta)

Scientists Group IV (4)
W. Haq, M.Sc., Ph.D. (Lucknow)
P.M.S. Chauhan, M.Sc., Ph.D. (Agra)
V.L. Sharma, M.Sc., Ph.D. (Lucknow)
Pradeep Kumar Srivastava, M.Sc. (Kanpur)
Atul Kumar, M.Sc., Ph.D. (Lucknow)

Scientists Group IV (3)
Sanjay Batra, M.Sc., Ph.D. (Meerut)
Atul Goel, M.Sc., Ph.D. (Lucknow)
Gautam Panda, M.Sc. (IIT, Kharagpur), Ph.D.
(Hyderabad)
T. Narender, M.Sc., Ph.D. (Kakatiya)

Scientist Group IV (2)
K.V. Sashidhara, M.Sc. (Baroda), Ph.D. (Avadh)

Scientist Group IV (1)
Prem Prakash Yadav, M.Sc. (Allahabad), Ph.D. (Avadh)

Technical Officer Group III (7)
R.K. Asthana, M.Sc. (Agra), Ph.D. (Agra)

Technical Officers Group III (6)
S.P. Vishnoi, M.Sc., Ph.D. (Meerut)
A.K. Mandwal, M.Sc., Ph.D. (Avadh)
S.C. Tripathi, B.Sc.
Janki Prasad, AMIE, M.Tech. (BHU)
Keshav Prasad, AMIE, M.Tech. (BHU)

Technical Officers Group III (5)
Suresh Chandra, B.Sc., L.L.B.
S.P.S. Bhandari, M.Sc. Ph.D. (Avadh)
P.N. Rai, Dip. Mech. Engg.
S.K. Kakaji, B.Sc.
Vasi Ahmed, B.Sc.
Zahid Ali, B.Sc., L.L.B.
Tara Rawat, B.Sc.
Deepali Pandey, B.Sc.

Technical Officer Group III (4)
A.S. Kushwaha, B.Sc.

Technical Assistant Group III (2)
Ashok Kumar Sharma, B.Sc., D.Ch.E., A.M.I.E.

Technical Assistants Group III (1)
Atma Prakash Dwivedi
Vidisha Sharma
K.S. Anil Kumar
Tahseen Akhtar
Surya Pratap Singh

Technical Assistants Group II (4)
Preeti Rastogi, M.Sc.
Ramjeet, B.Sc., PGDC
Zaheer Ahmad (Glass Blowing)
Radha Rani Gupta, B.Sc.
Raju Arora, B.Sc.

Technical Assistants Group II (3)
V.K. Maurya
A.K. Srivastava, M.Sc.
Shashi Rastogi, M.Sc.
Mithilesh Sharma, M.Sc.
Tika Ram
Veena Mehrotra, M.Sc.
Rajesh Kumar [Expired on 31/12/2009]
Rajesh Kumar
K.M. Shukla, B.Sc.
Akhilesh Kumar Srivastava, B.Sc.
D.N. Vishwakarma
Manju, B.Sc.

Technical Assistant Group II (2)
Ram Lakhan

Technical Assistants Group II (1)
H.R. Misra, B.Sc.
N.P. Misra, B.Sc.
Krishna Kumar

Helpers Group I (4)
Ram Sanehi
M.S. Bhol
G.S. Sonkar [Expired on 22/06/2009]
J.C. Rajan

Helper Group I (2)
Satish Chandra, B.Sc.

Sr. Steno
Renuka Mushran

Sr. Steno (H)
Avadhesh Kumar

Jr. Steno
Surendra Kumar

MICROBIOLOGY

Scientist Group IV (6)
Ranjana Srivastava, M.Sc., Ph.D. (Kanpur), *In-Charge*

Scientists Group IV (4)
D.C. Kaushal, M.Sc. (Pantnagar), Ph.D. (Kanpur)
[Retired on 30/04/2009]
K.K. Srivastava, M.Sc., Ph.D. (Kanpur)

Scientist Group IV (3)
B.N. Singh, M.Sc., Ph.D. (BHU)

Scientist Group IV (2)
Sudhir Kumar Singh, M.Sc., M.Tech.
(BHU), Ph.D. (Purvanchal)

Technical Officers Group III (7)
A.P. Singh, M.Sc. (Lucknow)
[Retired on 31/07/2009]
M.N. Joshi, M.Sc., Ph.D. (Agra)

Technical Officer Group III (5)
Reeta Singh, M.Sc., Ph.D. (Kanpur)
[Retired on 31/1/2009]

Technical Assistant Group III (1)
Sandeep Kumar Sharma, M.Sc. (Barkatullah)

Technical Assistants Group II (3)
P.D. Misra
Nuzhat Kamal, B.Sc.
D.K. Tripathi, M.Sc. (Avadh)

Helpers Group I (4)
U.C. Pandey
J.C. Pant

Helpers Group I (1)
Ravi Shankar Misra
Ram Prakash
Shyam Sunder Yadav

MOLECULAR & STRUCTURAL BIOLOGY DIVISION

Scientists Group IV (5)
Vinod Bhakuni, M.Sc., Ph.D. (Lucknow), FNA, FASc,
FNASc, *In-Charge*
P.R. Maulik, M.Sc., Ph.D. (Calcutta)

Scientists Group IV (4)
Saman Habib, M.Sc. (Delhi), Ph.D. (NII, Delhi)
Ravishankar R., M.Sc., Ph.D. (IISC, Bangalore)

Scientists Group IV (3)
Ashish Arora, M.Sc. (Jaipur), Ph.D. (Chandigarh)
Jimut Kanti Ghosh, M.Sc., Ph.D. (Kalyani)
J. Venkatesh Pratap, M.Sc., Ph.D. (IISc, Bangalore)

Scientists Group IV (2)
Mohammad Imran Siddiqi, M.Sc., Ph.D. (AIIMS)
Amogh Anant Sahasrabuddhe, M.Sc. (Kanpur),
Ph.D. (JNU)
Shakil Ahmed, M.Sc. (Aligarh), Ph.D. (Punjab)
Mohammad Sohail Akhtar, M.Sc. (Calicut),
Ph.D. (JNU)

Technical Officers Group III (4)
R.K. Srivastava, B.Sc.
J.P. Srivastava, B.Sc., L.L.B.

Technical Assistants Group III (1)
Ruchir Kant, M.Sc. (Lucknow)
Anupam Jain, M.Sc. (Agra)
Sarita Tripathi, M.Sc. (Lucknow)

Technical Assistant Group II (3)
Ram Radhey Shyam

PARASITOLOGY

Scientists Group IV (6)
S.K. Puri, M.Sc., Ph.D. (Punjab), FNASc., *In-Charge*
Shailja Bhattacharya, M.Sc. (Lucknow), Ph.D. (Kanpur)
P.K. Murthy, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientists Group IV (5)
Anuradha Dube, M.Sc. (Lucknow), Ph.D. (Kanpur)
Suman Gupta, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientists Group IV (4)
N.A. Kaushal, M.Sc. (Lucknow), Ph.D. (Kanpur)
Renu Tripathi, M.Sc. (Lucknow), Ph.D. (Kanpur)

Scientists Group IV (3)
Kumkum Srivastava, M.Sc. (Lucknow), Ph.D. (Kanpur)
S. Rajakumar, M.Sc. (Madras)

Technical Officer Group III (7)
S.C. Nigam, M.Sc., Ph.D. (Kanpur) [Retired on 31/07/2009]

Technical Officers Group III (5)
A.K. Roy, M.Sc. (Kanpur)
R.N. Lal, M.Sc. (Agra)

Technical Assistants Group II (4)
V.K. Bose
R.S. Dubey
Ram Dayal
Ravi Kumar Mehra
K.K. Singh, M.Sc.

Helper Group I (4)
Saheb Prasad

Helper Group I (1)
Prem Babu

Sr. Steno (ACP)
T.S. Sashi Kumar

PHARMACEUTICS

Scientist Group IV (5)
A.K. Dwivedi, M.Sc., Ph.D. (Agra), *In-Charge*

Scientist Group IV (4)
Amit Misra, M.Pharm. (Delhi), Ph.D. (JNU)

Scientist Group IV (3)
Prabhat Ranjan Mishra, M.Pharm., Ph.D. (Sagar)

Scientist Group IV (2)
Manish Kumar Chourasia, M.Pharm., Ph.D. (Sagar)

Technical Officer Group III (6)
Madhuri Chaudhry, M.Sc. (Lucknow)

Technical Assistant Group II (3)
S.K. Bhatnagar, B.Sc.

Helper Group I (1)
Ram Kumar

Jr. Steno
Pooja Taneja

PHARMACOKINETICS AND METABOLISM

Scientist Group IV (5)
G.K. Jain, M.Sc. (Rewa), Ph.D. (Kanpur),
In-Charge

Scientists Group IV (4)
S.K. Singh, M.Sc. (Patna), Ph.D. (IIT, Kanpur)
Jawahar Lal, M.Pharm., Ph.D. (BHU)

Scientists Group IV (1)
R.S. Bhatta, M.Pharm. (Nagpur), Ph.D. (JNU)
Wahajuddin, M.S. Pharm. (NIPER)

Technical Officer Group III (6)
S.K. Pandey, M.Sc. (Kanpur)

Technical Assistant Group II (3)
Narendra Kumar

Technical Assistant Group II (1)
Akhilesh Kumar

Helper Group I (4)
Shiv Lal

Helpers Group I (1)
Ram Bhajan Shukla
Ram Sunder Lal
Chandramani

Sr. Steno
Nandita Pandey

PHARMACOLOGY

Scientists Group IV (6)
G. Palit, M.B.B.S., M.D. (Lucknow), *In-Charge*
Ram Raghubir, M.V.Sc., Ph.D. (Agra)

Scientists Group IV (5)
Madhu Dikshit, M.Sc., Ph.D. (Kanpur) *(Unit In-charge, Cardiovascular Pharmacology (Unit)*
Rakesh Shukla, M.Sc., Ph.D. (Lucknow)

Scientist Group IV (4)
Amar Nath, M.Sc. (Lucknow)

Scientist Group IV (2)
Manoj K. Barthwal, M.Sc., Ph.D. (Lucknow)

Scientist Group IV (1)
Kashif Hanif, M.Sc. (Hamdard), Ph.D. (Delhi)

Technical Officer Group III (7)
G.P. Singh, M.Sc. (Kanpur)

Technical Officers Group III (5)
S. Sengupta, B.Sc.
T.L. Seth, B.Sc.
Jharna Arun, B.Sc.
M.L. Bhatnagar, B.Sc.
V.S. Nigam, B.Sc.
C.P. Pandey, M.Sc. (Chandigarh)

Technical Assistants Group III (1)
Sultana Jawaid, B.Sc.
Sheeba Saji Samuel, M.Sc. (M.G. Univ.)
Sachi Bharti, M.Sc. (Kanpur)

Technical Assistant Group II (4)
O.P. Pandey, B.A.

Technical Assistants Group II (3)
Bharti Bhushan, B.Sc.
H.C. Verma, B.A.
Shailendra Mohan, M.Sc. (Kanpur)
Ramesh Chandra, M.Sc. (Kanpur)

Technical Assistant Group II (2)
Anil Kumar Verma, B.Sc.

Technical Assistant Group II (1)
Surendra Singh, M.Sc., Ph.D. (Kanpur)

Helpers Group I (1)
Pankaj Sengupta
Hari Joshi

Sr. Steno
Varun Kumar Pathak

TOXICOLOGY

Scientist Group IV (6)
C. Nath, M.B.B.S., M.D. (Lucknow), *In-Charge*

Scientist Group IV (5)
Neeraj Sinha, M.Sc., Ph.D., D.Sc. (Kanpur)

Scientists Group IV (4)
Sharad Sharma, M.B.B.S., M.D. (Kanpur)
S.K. Rath, M.Sc. (Utkal), Ph.D. (BHU)

Scientist Group IV (3)
R.K. Tripathi, M.Sc., Ph.D. (Kanpur)

Scientists Group IV (2)
R.K. Singh, M.Sc., Ph.D., D.Sc. (Lucknow),
Aamir Nazir, M.Sc., Ph.D. (Jamia Hamdard)

Scientists Group IV (1)
Smrati Bhadauria, M.Sc., Ph.D. (Jiwaji)
Sarika Singh, M.Sc., Ph.D. (Lucknow)
Poonam Singh, M.Sc., Ph.D. (Kanpur)

Technical Officers Group III (5)
S.M. Verma, B.Sc.
Sadan Kumar, M.Sc. (Bihar)
P.K. Agnihotri, M.Sc. (Lucknow), Ph.D. (Kanpur)

Technical Assistants Group III (1)
Neeti Sagar, M.Sc. (Lucknow)
Anurag Kumar Srivastava, B.Sc.

Technical Assistant Group II (3)
Anupma

Helpers Group I (4)
Mahabir
V.K. Samant
Shree Krishan
R.K. Sarkar

Helpers Group I (1)
Ram Kumar
Nand Lal Yadav
Ganesh Prasad

Jr. Steno
Himanshu Upadhyay

CLINICAL PHARMACOLOGY UNIT (CDRI), SETH G.S. MEDICAL COLLEGE, MUMBAI

Technical Assistant Group III (1)
N.A. Rajwade

Technical Assistant Group II (4)
P.S. Acharya

Technical Assistant Group II (2)
Vijal J. Ashar, M.Sc.

Helper Group I (4)
R.B. Pawar

TECHNICAL INFRASTRUCTURE DIVISIONS / UNITS

BIOMETRY AND STATISTICS

Scientist Group IV (5)
M. Abbas, M.Sc. (IIT, Kanpur), Ph.D. (IIT, Bombay), *In-Charge*

Technical Officer Group III (6)
Mukesh Srivastava, M.Sc. (Lucknow), Ph.D. (Kanpur)

Technical Assistant Group II (4)
M.P.S. Negi

Helper Group I (2)
Savitri Devi

DIVISION OF LABORATORY ANIMALS

Scientists Group IV (4)
D.S. Upadhyay, M.V.Sc. (Pantnagar), Ph.D. (Izatnagar), *In-Charge*
A.K. Srivastava, M.Sc., Ph.D. (Lucknow)

Scientist Group IV (2)
Dhananjoy Hansda, M.V.Sc. (IVRI)

Technical Officers Group III (5)
S.N.A. Rizvi, M.Sc. (Lucknow)
A.K. Bhargava, B.Sc.
Karunesh Rai, M.Sc. (Lucknow)

Technical Assistants Group II (4)
Baldev Singh [Retired on 30/06/2009]
A.K. Dubey

Technical Assistants Group II (3)
Ravinder Singh
Ram Avatar
S.R. Yadav
Deep Mala Misra
Ravi Kumar Shukla
Sanjeev Kumar Saxena

Technical Assistants Group II (2)
Narendra Kumar
Dinesh Kumar
Pradeep Tirkey

Technical Assistant Group II (1)
Arun Sharma, B.Sc.

Helpers Group I (4)
Ahrar [Retired on 31/12/2009]
Asharfi Lal
Singh Vikram
Wazahtullah
Gaffar Ali
Hari Lal [Voluntary Retirement on 01/09/2009]
M.D. Kushwaha
V.B.L. Srivastava
T.B. Thapa
P.B. Thapa
Shiv Pal Singh
O.P. Verma
S.K. Varma
Mohd. Saleem
G.K. Sharma
Dilip Kumar
R.P. Maurya
Singh Bhim

Helpers Group I (1)
Changa Lal
Jameel Beg
Najbullah

Jr. Steno (H)
Raj Kumar

DIVISION OF S & T MANAGEMENT

Scientist Group IV (6)
Zaka Imam, M.Sc., M.Phil., Ph.D. (AMU), *In-Charge*

Scientists Group IV (5)
A.K. Goel, M.Sc., Ph.D. (Lucknow)
Vinay Tripathi, M.Sc., M.B.A. (AMU),
P.G. Dip. in S&T (Pilani)

Scientists Group IV (4)
N.S. Rana, M.Sc. (Kumoun)
D.N. Upadhyay, M.Sc., Ph.D. (Gorakhpur)

Scientist Group IV (3)
Prem Prakash, M.Pharm. (BHU)

Scientists Group IV (1)
Anand P. Kulkarni, M.Sc. (Karnatak), Ph.D. (Mysore)
Sripathi Rao S. Kulkarni, M.Sc. (SRTMU, Nanded), Ph.D. (JNTU, Hyderabad),
P.G. Dip. in Patents Law (NALSAR, Hyderabad)

Technical Officer Group III (7)
Shri Ram, B.Sc., L.L.B.

Technical Assistant Group II (4)
Krishna Prasad, B.Sc.

Technical Assistant Group II (3)
Chandrika Singh, B.Sc., L.L.B.

Technical Assistant Group II (1)
Preeti, M.C.A.

Helpers Group I (4)
Madho Singh
Kamlesh

Sr. Steno (ACP)
Manoshi Chatterjee, B.A., B.L.I.Sc.

Sr. Steno (H)
Jitendra Patel

DRAWING AND PHOTOMICROGRAPHY

Technical Officer Group III (7)
Ali Kausar, B.F.A. (Lucknow), *In-Charge*

Technical Officer Group III (6)
G.C. Gupta, B.Sc.

Technical Officer Group III (5)
R.M. Pathak, B.F.A. (Lucknow)

Technical Officer Group III (4)
R.N.S. Londhe, GD Art (Comm.), Art Teachers Dip.

Helper Group I (3)
Basanti Mukherjee

INSTRUMENTATION

Scientist Group IV (5)
Ravinder Singh, B.E., *In-Charge*

Scientist Group IV (4)
N.K. Agarwal, M.Sc. (Calcutta)

Technical Officer Group III (7)
Usha Kapil, I.Sc., Diploma

Technical Assistant Group III (3)
Ram Karan Harijan, AMIE

Technical Assistant Group III (2)
Sanjay Kumar, Diploma

Technical Assistant Group II (4)
Kamal Singh

Technical Assistant Group II (3)
Laxmi Narain

S&T KNOWLEDGE RESOURCE CENTRE

Scientists Group IV (5)
Sheela Tandon, M.Sc., Ph.D. (Agra), B.L.I.Sc. (IGNOU), *In-Charge*
A.K. Srivastava, B.Tech. (Bangalore)
Shyamala Saxena, M.Sc. (Tirupati), B.L.Sc. (Lucknow)
S.K. Mallik, M.A. (JNU), M.L.I.Sc. (Alagappa)

Scientist Group IV (4)
N.N. Mehrotra, M.Sc. (Pantnagar), Ph.D. (AIIMS)

Technical Officer Group III (7)
Seema Mehrotra, M.Sc. (Lucknow)

Technical Officers Group III (6)
J.A. Zaidi, M.Sc. (Aligarh), M.L.I.Sc. (IGNOU)
Sanjay Kumar, M.L.I.Sc (IGNOU)
V.K. Vohra, B.Sc.

Technical Officers Group III (5)
W.F. Rahman, M.A. (Rohailkhand), M.L.I.Sc. (Alagappa)
A.K. Verma, M.A. (Kanpur), L.L.B. (Lucknow)

Technical Assistant Group III (2)
Ramesh Chandra Gupta, M.L.I.Sc. (Lucknow)

Technical Assistant Group II (4)
B.K. Sethi

Technical Assistants Group II (3)
Nazir Akbar
Y.C. Pandey

Helpers Group I (4)
Mohd Moen
Rasheed Ahmad
S. Islam

Helper Group I (1)
Deepayan

Asst. (G) Gr. I
M.K. Thapar (Retired on 31/01/2010)

SOPHISTICATED ANALYTICAL INSTRUMENT FACILITY

Scientist Group IV (6)
D.K. Dikshit, M.Sc., Ph.D. (Lucknow), *In-charge*

Scientist Group IV (4)
Brijesh Kumar, M.Sc., Ph.D. (Awadh)

Scientist Group IV (2)
Sanjeev Kanojiya, M.Sc. (Jabalpur)

Scientist Group IV (1)
Sanjeev Kumar Shukla, M.Sc., Ph.D. (Kanpur)

Technical Officer Group III (7)
Prakash Narain, M.Sc. (Lucknow) [Retired on 31/07/2009]

Technical Officers Group III (6)
H.M. Gauniyal, M.Sc. (Garhwal)
A.L. Vishwakarma, M.Sc. (Kanpur)
Rakesh Khanna, B.Sc., A.I.C. (Calcutta)
A.K. Sinha, M.Sc. (Kanpur)

Technical Officers Group III (5)
A. Vohra, B.Sc., M.A. (Lucknow)
A.K. Sircar, B.Sc., B.A.
Sunil Kumar, B.Sc.
Pramod Kumar, M.Sc. (Bundelkhand)

Technical Officer Group III (4)
R.K. Purshottam, B.Sc.

Technical Assistant Group III (1)
Binod Kumar Saw, M.Sc. (Hazaribag)

Technical Assistants Group II (4)
R.K. Varma
Ashok Pandey, B.Sc.
Sandeep Sengupta, B.Sc.

Technical Assistants Group II (3)
Abdul Haleem
Radhey Krishna, B.Sc., L.T., C.Lib.Sc.
Vashundhara Madhwar, B.A.
Madhu Chaturvedi
S.A. Singh, B.Sc., PGDCA

Asst. (G) Grade I
V.K. Kanal

Helpers Group I (1)
Mansoor Ali
J.S. Singh

ACADEMIC AFFAIRS UNIT

Scientist Group IV (5)
Alka Singh, M.Sc., Ph.D. (Rajasthan)

Scientist Group IV (4)
Sheela Ghoshal, M.Sc. (Burdwan), Ph.D. (Kanpur) [Retired on 31/10/2009]

Technical Assistant Group II (4)
A.K. Pandey

BUSINESS MANAGEMENT UNIT

Scientist Group IV (5)
Rajendra Prasad, M.Sc., Ph.D. (Lucknow), *Unit In-Charge*

Scientists Group IV (1)
Ranveer Singh, M.Tech. (IIT, Delhi)
Naseem Ahmed Siddiqui, M.B.A. (Rohilkhand)

ELECTRON MICROSCOPY UNIT

Scientist Group IV (6)
V.K. Bajpai, M.Sc., Ph.D. (Kanpur) [Retired on 30/06/2009]

Scientist Group IV (1)
Kalyan Mitra, M.Sc. (Culcutta), Ph.D. (Kolkata)

Technical Officer Group III (6)
Abha Arya, B.Sc., B.Ed. (Kumaun)

Technical Assistant Group III (2)
Kavita Singh, M.Sc. Ph.D. (Lucknow)

Technical Assistant Group III (1)
Manish Singh, M.Sc. (Allahabad)

Technical Assistant Group II (3)
Madhuli Srivastava

INFORMATION TECHNOLOGY UNIT

Scientist Group IV (4)
Kural, BE (BIT, MESRA), *Unit In-Charge*

Technical Assistant Group III (2)
Ajay Kumar Maurya, MCA (Purvanchal)

TISSUE AND CELL CULTURE UNIT

Scientist Group IV (5)
A.K. Balapure, M.Sc., Ph.D. (Lucknow), *Unit In-Charge*

Technical Officer Group III (5)
Ramesh Sharma, M.Sc., Ph.D. (Kanpur)

DIVISION OF ENGINEERING SERVICES

Senior Deputy Secretary **(**Project Monitoring, New CDRI**)**
Tariq Qutubuddin, M.Sc. (Aligarh)

Senior Superintending Engineer Group III (7)
Parvez Mahmood, B.Sc. Engineering, *In-Charge,* Engineering Services

Executive Engineers Group III (5)
Manoj Kumar, B.Sc. Engineering
Kamal Jain, B.E., MBA

Technical Officer Group III (4)
A. Dayal, Diploma

Technical Officers Group III (3)
Mohit Kumar Shukla
Jai Prakash
Sidho Hembrom

Technical Assistant Group III (2)
D.K. Vishwakarma

Technical Assistants Group II (4)
Khan Abdul Jabbar
Sayeed Mohammad
A.K. Tewari
B.P. Sunwar
S.R. Shukla
E.A. Bhatti
Om Prakash
K.K. Kaul
A.K. Sonkar
S.K. Biswas
V.K. Mishra
Radhey Lal
Mahindra Singh
Radhey Shyam

Technical Assistants Group II (3)
Ramakant Ram
M.S. Verma
S.K. Kar
Naseem Mohammad
Harish Kumar
Vijay Kumar
Pradhan Basudev
Verma Kamal Kishore
Ramesh Kunwar
G.C. Roy
Arun Kumar Srivastava
Swapan Karmi
S.S. Bhakuni
Ram Karan Ram
Rajesh Chand Dwivedi
R.C. Samanta [Retired on 30/11/2009]

Technical Assistant Group II (1)
Bhagwan Singh Pokhariya
R.A. Prajapati

Helpers Group I (4)
A.N. Rabbani
Popinder Singh
Ramanuj
Ram Anjore
Hussain Taqui
Kandhai Lal [Expired on 11/11/2009]
S.K. Bhattacharya
Munna Lal
T.P. Pathak
S.K. Yadav
A.K. Misra
Lallu
R. K. Yadav
Raju
Mahabir Prasad
N.K. Mudgal
Shiv Giri
Bishan Singh
Om Prakash [Retired on 31/07/2009]
Rama
Iftikhar Ahmad
Ganeshi Prasad
Garibe [Retired on 31/08/2009]
Ram Lal [Retired on 31/08/2009]
Shankar Roy
Tan Sen
Om Prakash
Phool Chand

Helpers Group I (3)
Z.U. Beg
Ramesh Chandra

Helpers Group I (2)
Tara Chand

Helpers Group I (1)
Dhirendra Misra
Mohd. Irfan
Ram Autar
Raju Vishwakarma
Hari Om Garg
Sandeep Roy
Ram Samujh
Darshan Lal
Suresh Kumar
Bindeswari Prasad
Pradeep Kumar

Asstt. (G) Grade I
N.K. Checker
B.K. Shukla

ADMINISTRATION

Controller of Administration
B.D. Vashisth, M.A. (Kurukshetra)

Administrative Officer
L.R. Arya

COA OFFICE

Private Secretary
G.M. Dayal

Jr. Steno
Kamla Kandpal

Helpers Group I (4)
Maiku Lal
Sohan Lal

DIRECTOR'S OFFICE

Private Secretary
Kanhaiya Lal

Sr. Steno (ACP)
Sunita Chopra

Helper Group I (1)
Nand Kishore

Helper Group D
Ramswarth Prasad Rai

ESTABLISHMENT I

Section Officer (G)
Sunil Kumar

Asstt. (G) Grade I
Sachin Mehrotra
Krishna Raj Singh

Asstt. (G) Grade II
Smriti Srivastava
Saju P. Nair
Reena Bisaria

Sr. Steno (H)
Mohd. Sufiyan

Helper Group I (4)
Vinod Kumar

Helper Gp-'C' Cdr-D
Manju Yadav

ESTABLISHMENT II

Section Officer (G)
Biranchi Sarang

Asstt. (G) Grade I
B.K. Pillai
Rashmi Srivastava
Dilip Kumr Sen

Sr. Steno
Vinod Kumar Yadav

Asstt. (G) Grade II
Gangadin Yadav
Aparna Bajpai
Lata Bhatia
Neena Raizada
Madan Chandra

Helper Group I (3)
Bhagwanti Devi

Helper Group D
Ram Kumar
Mohd. Saleem

GENERAL SECTION

Section Officer (G)
Ramesh Singh

Asstt. (G) Grade I (ACP)
Masood Sahab [Retired on 31/03/2009]

Asstt. (G) Grade I
Kailash Chandra

Sr. Steno
Seema Rani Srivastava

Asstt. (G) Grade II
Rajendra Prasad
Ajay Shukla
Rani

Asstt. (G) Grade III
Mohd. Irfan

Technical Assistants Group II (2)
K.K. Kashyap
Shakeel Ahmad Khan

Driver
Chote Lal [Retired on 31/03/2009]
Prem Chand
Daya Shankar Singh

Helper Group I (4)
Kishori Kumari
Mohd Islam

Helper Group D
Kalpanath Sharma

Helper Gp-'C' Cdr-D
Munna [Expired on 10/12/2009]

BILL SECTION

Section Officer (G)
Madhuranjan Pandey

Asstt. (G) Grade I
H.K. Jauhar
Vatlsala G. Nair
Hem Chandra
Rama Dhawan
Harsh Bahadur
Vivek Bajpai
Dilip Kumar (Cash)

Asstt. (G) Grade II
Naseem Imam

Helper Group I (2)
Vinod Kumar Sharma

Helper Group I (1)
Lalji Prasad

VIGILANCE

Asstt. (G) Grade I
C.P. Nawani
Chandra Kant Kaushik

Asstt. (G) Grade II
Tez Singh

Helper Group I (4)
Shanti Devi

Sr. Steno
P.S. Padmini

RECORDS

Asstt. (G) Grade I
Birendra Singh

Asstt. (G) Grade II
S.K. Pandey [Retired on 31/10/2009]

Helper Group I (4)
Ved Prakash Misra

HINDI SECTION

Senior Hindi Officer
V.N. Tiwari, M.A., Ph.D. (BHU)

Senior Translator (Hindi)
Mrs. Neelam Srivastava, M.A., L.L.B. (Lucknow)

Sr. Steno (Hindi)
Anil Kumar

Helper Group I (4)
Ghanshyam

SECURITY

Senior Security Officer
R.S. Deswal, B.Sc., L.L.B.

Security Guard Group D
Chakrasen Singh

FINANCE & ACCOUNTS

Controller of Finance & Accounts
Padam Singh

Finance & Accounts Officer
A.K. Dwivedi

Section Officers (F&A)
A.K. Chauhan
Ankeshwar Misra
Ram Rishi Raman
Kailash Singh

Private Secretary
V.P. Singh

Asstt. (F&A) Grade I
R.P. Tripathi
S.L. Gupta
Nitu Kumari
Viresh
Mahesh Babu
R.C. Bisht
Ajitha Nair

Asstt. (F&A) Grade II (ACP)
Sashidharan Radha
U.K. Tewari

Asstt. (F&A) Grade II
D.K. Khare
Mahendra Kumar
Sanjay Kumar
Tahseen Talat

Asstt. (F&A) Grade III
S.A. Siddiqui
Chandrashekhar

Jr. Steno
Rekha Tripathi

Helper Group I (1)
Vikramaditya
Angad Prasad

Helper Group D
Mohd. Firoz

STORES & PURCHASE

Stores & Purchase Officer
Thomas T. Kuriakose

Section Officers (Stores & Purchase)
Shekhar Sarcar
Praphul Kumar
Prasenjeet Mitra

Asstt. (S&P) Grade I
P.S. Chauhan
Arun Wadhera
A.K. Misra
A.K. Govil
H.B. Neolia

Asstt. (S&P) Grade II (ACP)
K.K. Mishra

Asstt. (S&P) Grade II
R.C. Dwivedi
M.C. Verma
Srikant Mishra

Asstt. (S&P) Grade III
Kanchan Bala
Vandana Parwani
G.P. Tripathi

Asstt. (G) Grade III
Shakuntala Singh

Sr. Steno (ACP)
K.P. Ballaney

Helpers Group I (4)
Kishan Kumar
Rama Shukla

Attendant
Hardwari

CSIR DISPENSARY

Medical Officers Group III (7)
D.K. Bhateja, M.B.B.S., M.D. *In-Charge*

Medical Officer Group III (6)
Asha Negi, M.B.B.S., M.D.

Medical Officer Group III (4)
N.K. Srivastava, M.B.B.S., M.D.

Technical Assistants Group II (5)
Nandita Dhar
H.U. Khan

Technical Assistant Group II (1)
Shraddha
Shabara

Jr. Steno
Ajay Kumar

Helper Group I (4)
S.K. Paswan

Gp-'C' Cdr-D
Sundari

CANTEEN

Manager
J.P. Satti

Asstt. Manager
R.S. Tewari

Count Clerk (ACP)
Ram Jiyawan Tewari
Y.K. Singh

Cook (ACP)
Man Bahadur

Asstt. Halwai
Uma Shanker Tewari

Bearers
Dil Bahadur
Ganga Ram Yadav
Rajender
Kripa Shanker
Sukhdev Prasad

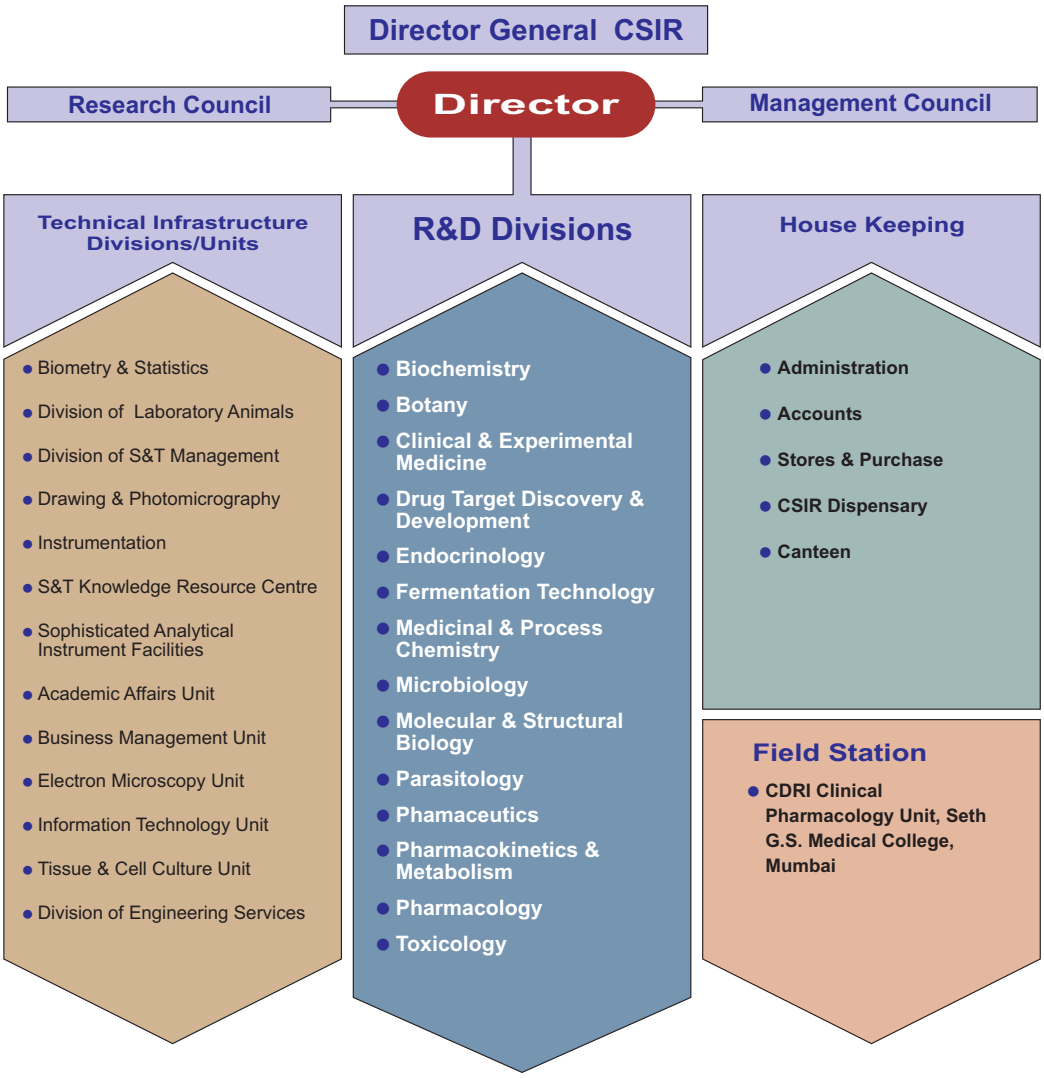
S/Man
Raj Kumar

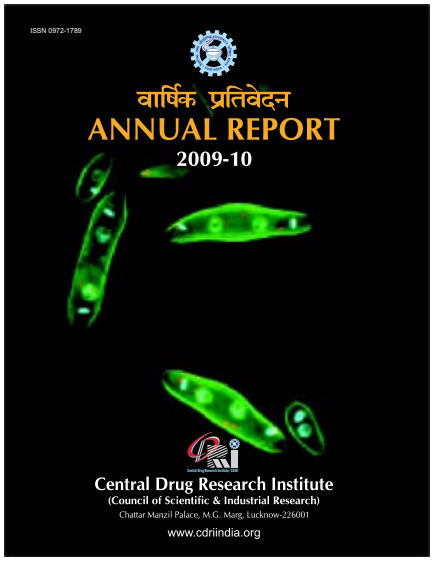
Wash Boys
Ram Murat
Dinesh Pal Singh

Notes

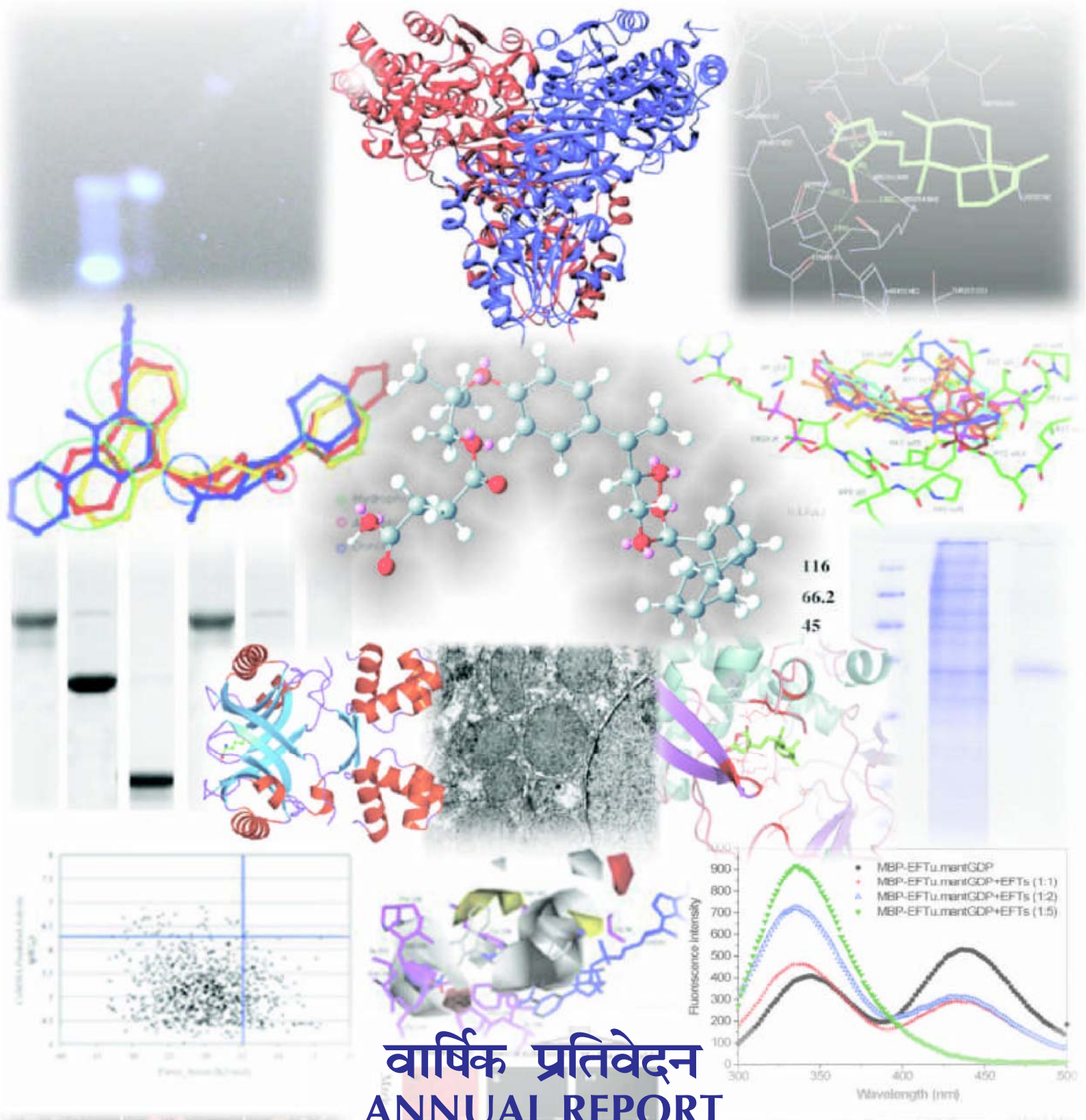
Notes

Organizational Structure





Leishmania donovani cells attain bipolar-cell morphology after reduction in CRN12 (*Leishmania*-coronin) expression levels in the heterozygous CRN12 gene knockout mutants. Bipolar morphology arises due to defects in corset-microtubule dynamics during cytokinesis (***Sahasrabuddhe et al., J. Cell Sci. 2009; 122:1691-1699***). Phase contrast (gray) and fluorescence images (Green, tubulin; red, kinesin K39; cyan, DNA (nuclei and kinetoplasts).



वार्षिक प्रतिवेदन

ANNUAL REPORT
2009-10

केन्द्रीय औषधि अनुसंधान संस्थान

(वैज्ञानिक तथा औद्योगिक अनुसंधान परिषद्)

छत्तर मंजिल पैलेस, महात्मा गांधी मार्ग, लखनऊ

Central Drug Research Institute

(Council of Scientific & Industrial Research)

Chattar Manzil Palace, Mahatma Gandhi Marg, Lucknow- 226 001(India)

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