

CSIR NEWS

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Team CSIR



NPL-India signs MoUs with NPL-UK and PTB-Germany

THE National Physical Laboratory (NPL-I), New Delhi, India, has recently signed memoranda of understanding with:

**National Physical Laboratory (NPL-UK), Teddington, UK, and
Physikalisch-Technische Bundesanstalt (PTB), Germany**

to continue the long-standing cooperation and to foster future collaborative activities in the field of Metrology. The objective of these memoranda is to strengthen relations between NPL-I and NPL-UK and NPL-I and PTB, and promote the exchange of information and technical and scientific knowledge and the augmentation of the technical capabilities of these organizations. Under the memoranda, cooperative activities will be carried out in the area of Scientific and Technical Metrology and may include, but are not limited to, such topics of mutual interest as inter-comparison of measurement standards. The other topics / activities as may be mutually agreed upon may be included. The above activities will be implemented using modes of cooperation such as:

- A) Exchange of technical and scientific information, materials and publications
- B) Exchange of personnel
- C) Implementation of collaborative projects
- D) Other modes as may be needed, upon mutual agreement.



Dr Vikram Kumar
Director, NPL, New
Delhi, India (left)
and Prof. Stephen
McQuillan,
Managing Director,
NPL-UK,
Teddington, UK
exchanging the
MoU documents





Hidden Mutations in Oculocutaneous Albinism (type 1) unmasked

OCULOCUTANEOUS albinism (OCA) is a group of developmental disorders that results from deficient synthesis of pigment in skin, eye and hair follicles. We all inherit two copies of each gene from our parents and OCA occurs owing to defect in some of these genes. Therefore, it is a genetic disease. Albinos (the affected individuals) are not only at high risk of skin cancer due to absence or reduction of melanin that protects the skin from UV light; but in most of the cases they are also legally blind. In fact, a person who inherits both the defective copies of certain gene becomes an albino (Fig. 1) whereas defect in one copy of the gene makes him/her a carrier of the disease. However, a carrier has a normal life but when the person unwittingly marries another carrier, the couple takes 25% chance of having an albino child. Thus, especially in those ethnic groups, where marriage within the same community is a common practice, occurrence of the genetic diseases including OCA is expected to be higher. On average, worldwide 1 in 30,000 individual suffers from OCA and the disease is a lot more frequent in some ethnic groups. Among 16 different genes known to cause OCA, defects in tyrosinase gene (TYR)



Fig. 1: An OCA-affected child (*right*) with his father (*left*) who is a carrier for the disease but indistinguishable from any normally pigmented individual

accounts for a major subtype – oculocutaneous albinism type 1 (OCA1).

OCA is one of the four major causes of childhood blindness in India, but very little is known about its molecular basis. During the studies conducted by M. Chaki, A. Mukhopadhyay and A. Ray of the Indian Institute of Chemical Biology (IICB), Kolkata, among various ethnic groups of eastern and southern India, the researchers have identified some defects in the tyrosinase gene causing OCA1. They noticed that the published literature world over had reported that in case of 15% of the OCA1

patients, the second TYR mutation could not be detected despite extensive mutation screening. Therefore, on the basis of the genetic markers, counseling of those families would be difficult. In the literature, there was already a report of a pseudogene (i.e. a non-functional copy of the gene) of TYR. They also observed that the way, by which the mutation screenings were conducted till date, could mask the molecular defects in one portion (3'-region) of TYR, because the pseudogene shares almost 98.55% sequence identity with that region of the gene.

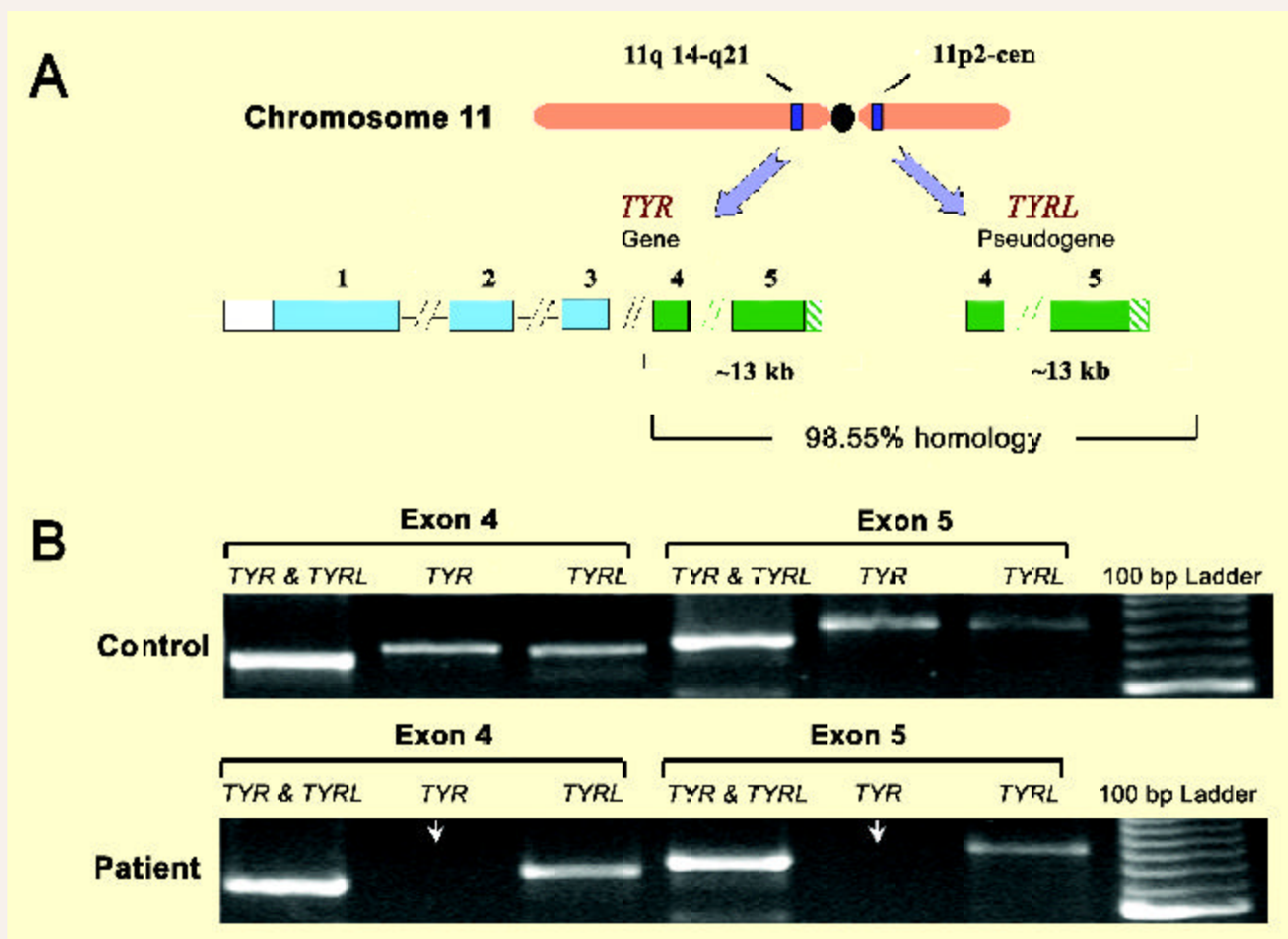


Fig. 2: Panel A shows the locations of *TYR* (gene) and *TYRL* (pseudogene) within chromosome 11 (drawing is not in scale). The homologous region (~13kb) of the gene and the pseudogene is marked in green. Panel B demonstrates the gel picture showing the results of locus-specific amplification in one of the OCA1 patients and determination of a homozygous gross deletion encompassing the 3' region of the *TYR*, as the region could be amplified with *TYRL* specific primers as well as primers common to both *TYR* and *TYRL*, but no PCR product was obtained using *TYR* specific primers

The IICB researchers' observation raised the question regarding the authenticity of the 204 single nucleotide polymorphisms (SNPs) in tyrosinase gene (*TYR*) available in dbSNP and 27 *TYR* mutations in OCA1 patients that are publicly available. They devised a PCR-based method that would unequivocally identify all the *TYR*

mutations in the 3'-region of the gene that is homologous to the pseudogene (Fig. 2). The strategy used by the researchers, i.e. employing gene-specific primers for amplification directly from genomic DNA provides much easier, cost effective as well as reliable means for identification of *TYR* mutations causing OCA1 and

could be used for revalidation of the reported mutations where appropriate.

This study entitled 'Determination of variants in the 3'-region of Tyrosinase gene requires locus specific amplification' has been published in *Human Mutation*, 26 (2005) 53-58.

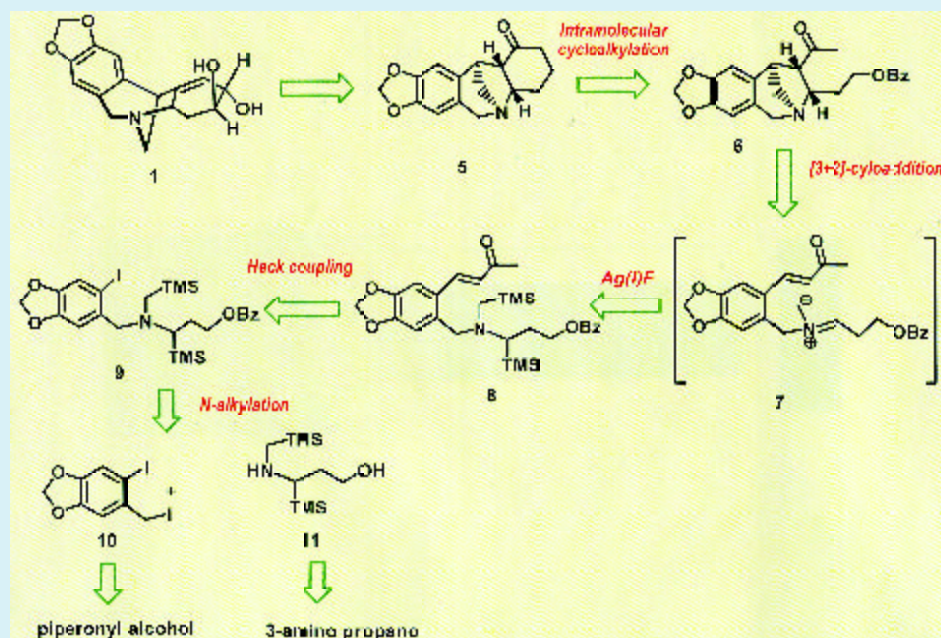
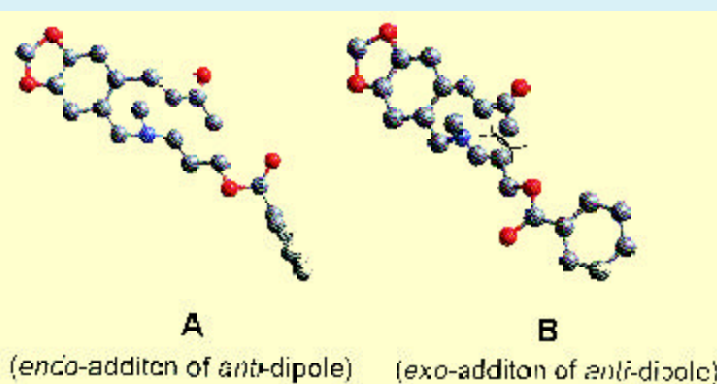
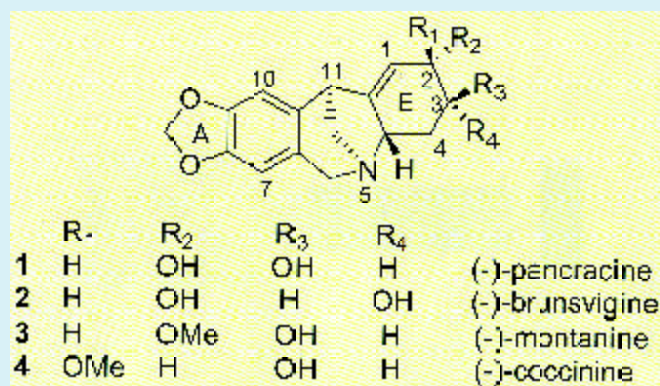


Stereospecific Route to 5, 11-Methanomorphanthridine Alkaloids via Intramolecular 1,3 Dipolar Cycloaddition of Non-stabilized Azomethine Ylide: Formal Total Synthesis of (\pm)-Pancracine

THE 5,11-methanomorphanthridine alkaloids, belonging to Amaryllidaceae subclass have a unique pentacyclic framework. Ganesh Pandey, Prabal Banerjee, Ravindra Kumar, Vedavati G. Puranik of the Division of Organic Chemistry (Synthesis) at National

Chemical Laboratory (NCL), Pune, have developed a conceptually new approach for constructing structurally complex pentacyclic 5, 11-methanomorphanthridine core structure in one step employing intramolecular cycloaddition of non-stabilized

azomethine ylide generated by sequential double desilylation of α , α' -bis (trimethylsilyl) methyl amine mediated by Ag (I)F as one electron oxidant. This strategy has been demonstrated by accomplishing the formal total synthesis of (\pm)-Pancracine.



The formation of single diastereomer in the key step of the present synthetic reaction was envisioned considering intramolecular endo-attack of the azomethine ylide to the α , β -unsaturated carbonyl moiety which would be energetically more favoured (A) over the exo-attack (B) due to steric repulsion.

The retrosynthetic design for the synthesis of (\pm)-Pancracine is given here and the detail of the synthesis is discussed in paper published in *Organic Letters*, 7 (2005), 3713-3716.



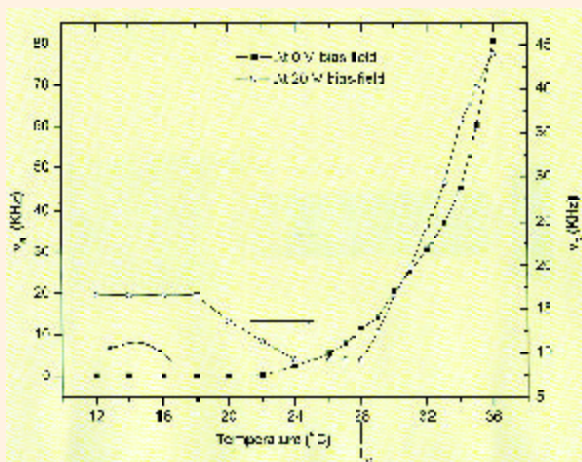
Is Curie-Weiss Law Valid in Every Ferro to Ppara Transition?

THE Curie-Weiss law describes the magnetic susceptibility of a ferromagnet above the Curie point, i.e. the temperature above which a ferromagnetic substance loses its ferromagnetism.

The law is obeyed where there is a change in the order parameter and the symmetry of the molecules at the transition temperature (T_c) of ferro-to-para phase. However, the ferroelectric transition is not strictly governed by the Curie-Weiss law. In fact, a number of solid ferroelectrics show deviation from the Curie-Weiss law. It must be emphasized that a hyperbolic dependence of the dielectric constant on temperature, such as the Curie-Weiss is by no means a necessary condition for a ferroelectric transition, as was customarily believed in the early

stages of ferroelectric research. In their research communication entitled 'Is Curie-Weiss law valid in every ferro to para transition?', published in *Applied Physics Letters*, 87 (2005), 2507, S. Kaur, A.K. Thakur, A. Choudhary, S.S. Bawa, A.M. Biradar and S. Annapoorni of National Physical Laboratory (NPL), New Delhi, have shown that the ferroelectric liquid crystals, with a wide smectic-A phase and a high electroclinic effect called de-Vries electroclinic liquid crystals, do not obey the Curie-Weiss law. Figure below shows the relaxation frequency, ν_R as a function of temperature from Smectic-C* to Smectic-A phase with and without bias. Here, there is no clear isolation of the phase fluctuation (Goldstone) mode and tilt fluctuation (soft) mode near T_c at 0 V bias. Even at 20 V

bias, the anomaly in ν_R is in such a wide temperature range that it does not obey the Curie-Weiss law. Thus, the researchers conclude that it is the de-Vries tilted wide Sm-A phase materials with no layer shrinkage and thus a negligible θ fluctuation leading to the non-observance of soft mode, which does not obey the Curie-Weiss law.



Temperature dependence of relaxation frequency (ν_R) at 0 V and 20 V bias in Sm-C* and Sm-A phases.

MERADO releases 6 tpd Oil Expeller Technology

THE Mechanical Engineering Research & Development Organisation (MERADO), Ludhiana, has recently released its 'Technology of 6 tpd Oil Expeller' to four leading Oil Expeller Manufacturers of Ludhiana and Delhi.

This technology is unique as the oil expeller will yield pungent quality of oil from mustard seeds. Production of pungent oil was otherwise not possible through oil expellers available in the market. Pungent mustard oil has a great demand in the market and is sold at higher price as compared to the nonpungent oil. It has a very good preservative in the form of iso-thiocyanate. Lately the doctors from AIIMS have been advocating the use of pungent mustard oil as one of the best vegetable oils for human consumption.

Shri R. Nigam, Scientist-in-Charge, MERADO, Ludhiana, in his address during the release function, informed that it is for the first time in the world that an oil expeller has been developed that would yield the pungent mustard oil. He also assured the licensees of this technology, viz. M/s Guru Teg Engg. Co., M/s Gobind Expeller



Co. M/s Swastic Traders of Ludhiana and M/s P. Roy Expellers of Delhi, of the MERADO support in effective implementation of this technology.

Shri S. Salman Mojiz, Scientist and Head, Business Development Group, in his address said that MERADO strictly believes in continual improvement of its services and technologies and the release of the 6 tpd oil expeller is a milestone in its journey.

Licensees of the technology opined that this technology was a dream come true for them. Speaking on the occasion, Shri J.P. Meena IAS, Joint Secretary, Ministry of Agriculture and Cooperation, Technology Mission on Oil Seeds Pulses & Maize, expressed his happiness over the release of this technology. He said that it gives him immense pleasure to note that industry is showing tremendous interest in this technology. He said that MERADO developed technology should be an example for others. He assured his Ministry's full financial support to MERADO for sponsored projects in future.

Central Drug Research Institute, Lucknow

R & D Highlights

THE Central Drug Research Institute (CDRI), Lucknow, has made great strides during 2004-2005. A few examples: (i) three major collaborative-cum-licensing agreements with industry for novel products — herbal medicament for cerebral stroke, antimalarial compound 97/78 and lipid lowering agent 80/574; (ii) collaboration with a company for development of drug toxicity prediction tools and with another, for use of DNA microarray based gene expression platform for discovery of active ingredients in herbal mixtures for diabetes and associated disorders, (iii) 164 publications and 41 patents.

Marketing surveillance studies on Consap have been initiated by the licensee firm. The other products under development (Picroliv, CT-1, CDR-134, 80/574) have progressed well. During the year, institute synthesized a record number of 1495 compounds and 13 libraries consisting of 380 compounds have been developed.

One hundred and sixty-four research papers were published in journals of international repute with much improved impact factor per paper, as compared to previous years. The year witnessed a significant increase in IPR protection as 20 Indian patents and 21 foreign patents were filed. Number of Indian/foreign patents granted were 21 and 8, respectively.

A brief account of some of the significant R & D achievements of the institute is as follows:

Clinical Studies

Post marketing surveillance studies on CONSAP (contraceptive cream) have been initiated with a target of 1000 women in six cities for the year. Clinical trials of *Arteether* (blood schizonticidal) have been initiated in four medical colleges and a total of 47 cases have been completed. Results from the treated patients, suffering from *P. falciparum*, are encouraging. Compound 80-53 (antirelapse antimalarial) was sent to Clinical Pharmacology Unit, Seth G.S. Medical College, Mumbai, for evaluation of its use as a gametocytocidal agent. Studies related to evaluation of hepatoprotective effects of Picroliv in patients with alcoholic cirrhosis, CT-1, CDR-134D123 (antidiabetic) and 80-574 (hypolipidemic) are progressing well.

Pharmacokinetic Studies

Pharmacokinetic and metabolic studies on several candidate drugs were carried out. These include 97-78, 99-357, 99-411, α/β -*Arteether* (antimalarials); interaction of Centchroman with theophylline, metronidazole and antidiabetic drugs; Bulaquine (antimalarial); 99-373 and S-001-281 (antiosteoporotic) and 85-92 (antiulcer). In addition, pharmacokinetic studies on



several herbal preparations were also carried out viz. Picroliv (hepatoprotective), CT-1 (antidiabetic); CDR-134 (antidiabetic and antidiarrhoeal); and Herbal medicament (anti-stroke).

Toxicity Studies

Toxicity testing of a wide range of candidate drugs, including a rDNA product, Lysostaphin was carried out during the year. A total of seven compounds have been tested for systemic toxicity, two for genotoxicity and one for short-term bioassay for carcinogenicity. A new model viz. PPAR-gamma mediated adipogenesis assay in 3T3 L1 cells was established.

R&D Project Areas

During the year 2004, a total of 1495 new synthetic compounds and 13 libraries consisting of 380 compounds were prepared. Nineteen New terrestrial plants and 21 marine flora/fauna samples were collected by Botany Division.

Reproductive Health Research

Twenty-one synthetic compounds and seven natural products were tested for antiresorptive activity *in vitro* and one compound was active (T/C ratio 0.48). Spermicidal screening of 70 samples did not yield any encouraging results. Thirty-six Synthetic compounds and 29 natural products were screened for anti-implantation activity in rats and materials showing 100% activity are being further evaluated. In the studies related to development of anti-STI agents, *Trichomonas vaginalis* culture has been

established and validated. Molecular mechanisms of action of centchroman (CC) indicate that 7-OH-CC is a potent antiestrogen at AP-1 enhancer site as compared to CC. Studies related to pharmacological and pharmacokinetic interaction of CC with antibiotics, antiasthmatic and antidiabetic drugs are continuing. Substituted isoxazolecarbalde-hydes have shown spermicidal and acrosin inhibitory activities suggesting those non-detergent molecules may be useful as topical and prophylactic contraceptives.

Filariasis

Thirty-nine marine and 2260 samples under CSIR coordinated project were tested for *in vitro* antifilarial efficacy while 27 synthetic compounds, 19 plant extracts and three marine extracts were tested for *in vivo* antifilarial efficacy but no appreciable activity was observed. In the immunological studies, tetracycline significantly reduced the microfilarial density at 200 mg/kg dose. A cDNA expression library of adult *B. malayi* female worms was screened and two cDNA clones, encoding immunodominant antigens were selected for identification and characterization. Studies on isolation of isoenzymic forms of filarial acetyl cholinesterase revealed 2-3 protein bands in two eluted fractions. Five clones expressing monoclonal antibodies, against filarial acetyl cholinesterase, were isolated and were found to be IgM isotype.

Malaria

A total of 630 synthetic compounds, 22 plant/microbial extracts, 47 marine extracts and over 3800 products of natural origin (under CSIR coordinated network programme) were screened against *Plasmodium falciparum in vitro* for their antimalarial potential. Promising compounds/leads are being further investigated. Libraries of active molecules have been prepared for lead optimization. A total of 69 plant extracts and 19 marine products were screened for their *in vivo* antimalarial potential but none of them yielded any significant activity.

Lead optimization studies with peroxide derivatives continued and 82 new compounds were screened against multi-drug resistant model of *P. yoelii* in Swiss mice. Three compounds were identified as promising leads for follow-up studies.

Studies with monoclonal antibodies against *P. cynomolgi* / *P. vivax* revealed five different epitopes on MSP-1 antigen of which four are conformational and one is linear. These studies will be helpful in measuring antibodies against conformational epitopes of MSP-1 antigen in sera of protected monkeys. Exploration studies on putative proteins from *P. falciparum* genome database, to search candidate drug targets, are continuing. Studies on analysis of DNA-protein interactions at multiple regions and effect of other prokaryotic translation inhibitors, on apicoplast EF-Tu expression, are in progress.



Natural Products

Collection, identification and documentation of 55 terrestrial plants and 15 marine flora/fauna were completed. Studies on evaluation of antidiabetic and antihyperglycemic activity are continuing on plant numbers 3200, 4499, 4536, 4542, 4574, 4630, 4636 and marine extract CDR-267. Bone forming activity has been observed in the plant number 1020. Chemical modifications of lupeol, solanesol, psoralin and other natural products have been carried out and the resulting compounds have been subjected to a wide range of biological screening. Three unknown compounds were isolated from marine extract CDR - 267 while promising *in vitro* antifungal activity was observed in CDR-292.

CNS/CVS and Other Disorders

Herbal Medicament, being developed for treatment/prevention of cerebral stroke, was found to be quite effective in embolic and focal ischemia and its efficacy was confirmed by MRI studies also.

A total of 102 synthetic compounds / crude extracts were tested for anti-stress, antianxiety and antiulcer activities. Those found active in preliminary screening are being followed up for confirmation of activity. Potent adaptogenic activity has been confirmed in the standardized extract of *Bacopa monniera*. Studies related to anti-ulcerogenic and ulcer healing properties of extracts demonstrated that *Ocimum sanctum* could act as a potent therapeutic agent.

Microbial Infections

Two genes of *V. cholerae*, viz. Vc0973 and Vc0974, have been cloned and sequenced. The former one has been expressed in *E. coli* and recombinant protein has been purified. A total of 2550 samples were tested for their *in vitro* and nine samples for *in vivo* antitubercular potential against *M. tuberculosis* but none of these had significant activity. Two attenuated mutants of *M. fortitum* were generated by transposon mutagenesis and sequenced for identification of virulence gene. A protein, Rv3878, was cloned from *M. tuberculosis* genome, purified and antibodies were raised. Genetic studies on expression analysis, identification of human T-cell responses against *M. tuberculosis* membrane antigens and interaction of mycobacterial Eis and hspX with macrophages are underway. In order to develop new and novel antifungal agents, 489 samples were evaluated for their *in vitro* potential. However, none of them had appreciable effect as compared to 1% clotrimazole.

Studies on fusion experiments for generating monoclonal antibodies against *C. albicans*, use of PCR for rapid diagnosis of fungal infections and passage culture of fungal strains were in progress. With regard to institute's studies on viral infections, 110 compounds were screened against reverse transcriptase activity *in vitro* and nine of them have been selected and sent to NARI, Pune, for cell-based assay and their results are awaited.

Leishmania

During the period, green fluorescent protein and luciferase

screening models were developed for *in vitro* screening. Quite a number of synthetic compounds, plant and marine samples were tested and those found active *in vitro* are being followed-up in the hamster model. Four compounds have shown moderate degree of activity in the *in vivo* system.

Identification of TH1 specific proteins for immunoprophylaxis was carried out and the F2 fraction offered good prophylactic efficacy against *L. donovani* challenge. Considerable progress has been made in biochemical and molecular mechanism studies related to drug resistance. Several enzymes/proteins have been cloned and over expressed, viz. serine hydroxymethyl transferase, pteridine reductase, trypanothione reductase and carboxy peptidases.

In the characterization of actin network, actin in *Leishmania* was forming filamentous structure in both promastigotes and amastigote forms of the parasite. Genomic microarray analysis for gene expression of proteins is underway.

Technology Development

Chemical Technology

Development of appropriate technology for process development and improvement of drug candidates was continued. Synthesis of 97-78 (antimalarial) was achieved on 100g. scale. Further optimization is in progress. Compound 80-574 (hypolipidemic) was prepared in five kg quantity for clinical trials while 2.0 kg of 80-53 (antirelapse antimalarial) were prepared for generating additional clinical data.



Amongst natural products, 13.4 kg of Picroliv (hepatoprotective) and 8.2 kg of CDR-134D123 (antidiarrhoeal and antidiabetic) were supplied for clinical trials.

Fermentation Technology

Screening of microbial cultures for antibacterial/antifungal compounds continued during the year also. A strain of *Streptomyces* sp. (C5) was studied for the production of antibacterial metabolites and active compounds are at various stages of purification and chemical characterization. In order to improve the activity profile and induce novel activities in synthetic compounds, biotransformation of 80/574 and guggulsterone was carried out and derivatives were submitted for bioactivity evaluation.

For the commercialization of microbial products of pharmaceutical interest, fermented runs of *E. coli* and *P. methanolytica*, for the production of desired proteins, were undertaken. Production of L-PAC of desired purity and optical rotation, alternative growth and nutritional conditions were standardized. Cells of *Kluyveromyces lactis* were cultivated under different nutritional conditions and hydrolysis of lactose was investigated under varying biotransformation conditions so as to optimize the process parameters.

Pharmaceutical Technology

Quality control and stability studies on several compounds and candidate drugs were carried out. These include: Herbal Medicament (for prevention/cure of cerebral stroke; 80-574 (hypolipidemic);

99-357 and 99-411 (antimalarial); CDR-134F194 and CDR-267F018 (antidiabetic and lipid lowering). Technical know-how for manufacturing the spermicidal formulation CONSAP cream, licensed to industry last year, was imparted and post-marketing surveillance studies are currently in progress. Marketing permission of Centchroman (contraceptive) for veterinary use (in dogs) has been obtained. Under NMITLI Project, inhalable microparticles, containing two anti-TB drugs, were taken up for product development and quality assurance and stability studies were conducted. As reported earlier, delivery system for testosterone 20 (for use as a stand alone male contraceptive or for hormonal replacement) was developed on a Matlab® platform. Studies on the effect of cyclodextrin on permeation of compound 97-78 and delivery system for cyclosporine were conducted during the year.

Newer Approaches in Drug Discovery and Design

Solid phase of synthesis of novel heterosystems has been carried out for the first time by introducing modification in the resin bound amine substrate with three points diversity resulting in the synthesis of compounds in high yields and greater purity. A novel intramolecular transamidation on the solid-phase under mild basic conditions has been developed. Twenty-four Compounds were synthesized and tested for HIV-RT inhibitory activity and two of them were active. Structure function studies of hemolysin E, a recently

identified toxin from a pathogenic strain of *E. coli*, are progressing well. Two analogs of melittin have been designed and synthesized after selectively replacing heptadic leucine with alanine. As part of the crystal structure elucidation effort, 10 proteins from *M. tuberculosis* have cloned, expressed and purified. Crystallization and about 3D X-ray data collection of 41 compounds of biological and structural importance were completed.

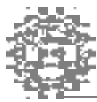
Biological Screening

The HTS laboratory has developed its own data management software 'HT Genius' in collaboration with a Lucknow based software firm. Several high throughput-screening assays are being used for screening viz. antitubercular, antileishmanial, antimalarial, inflammation, antithrombin, cytotoxicity and anticancer. Chemical libraries of CDRI, IICT and NCL have been screened in HTS laboratory. Six compounds for antitubercular and four compounds for antimalarial activity have been selected for lead optimization. Collaborative anticancer screening studies with Dabur led to selection of 45 molecules for further development through synthesis of analogues.

Business Development and Contract Research

The institute has signed various agreements with pharmaceutical industries during the financial year 2004-2005, details are as follows:

- Themis Medicare Limited, Mumbai, has entered into a



- collaborative-cum-license agreement for the development of a new Herbal Medicament for the treatment and prevention of cerebral stroke.
- Cadila Pharmaceuticals Ltd, Ahmedabad, has entered into a similar agreement for the development of CDRI compounds 80/574 as a lipid-lowering agent.
 - IPCA Laboratories Ltd, Mumbai, has executed a collaborative-cum-license agreement for the development of the compound 97/78, a promising synthetic substitute for drugs based on Artemisinin, derived from the plant *Artemisia annua*.
 - Strand Genomics Pvt. Ltd, Bangalore, has signed a collaborative agreement for the development of Drug Toxicity Prediction (DTP) tools which will help to predict potential toxicity of drug candidates.
 - Connexious Life Sciences, Bangalore, has signed an MoU with CDRI for the use of DNA microarray based gene expression platform in combination with its proprietary pathway knowledge base and computational mining tools. This would arrive at pathway level fingerprints of herbal mixtures in a more modern genomics based discovery of valuable active ingredients present in the mixtures in the area of diabetes and associated disorders.
 - CDRI has signed an MoU with Kandhari Software, Lucknow, for designing, developing and marketing of software for its use in HTS and combichem studies.

- M/s Avestha Gengraine Technologies Pvt. Ltd, Bangalore, are evaluating CDRI plants/marine products 4416, 4570, 109K022 and CDR-134F194 for the treatment and management of stress and osteoporosis under two secrecy agreements.
- Ranbaxy Laboratories Ltd, New Delhi, has shown interest in CDRI's lead molecules and data is being evaluated by the company under secrecy agreement with a view to decide further development.

Technical Services

National facilities viz. Sophisticated Analytical Instruments Facility and National Laboratory Animal Centre, continued to provide their services all over India to academia and industrial users. The Sophisticated Analytical Instruments Facility provided their services to R&D institutions, universities, academic institutions, etc. Over 8,500 external and 20,000 internal samples were analysed. There were 520 external users and 260 internal users. Collaborative work in association with several scientific organizations continued. Under the national project on 'Development of Potential Drugs from Ocean', publication of quarterly bulletin Ocean Drugs Alert continued and all the four issues were published. Special emphasis has been given on international patents in the area of marine drugs. Publication of current awareness **bulletins viz. Drugs & Pharmaceuticals – Industry Highlights and Drugs & Pharmaceuticals – R&D Highlights** continued.

Bioinformatics User sub-center rendered specialized services to scientific community. These search services include, bibliographic and full text databases, monographs/profile on plants, patent literature, chemical structure, etc.

Human Resource Development

CSIR has initiated a scheme of providing training for laboratory scientists in business development activities and under this programme one scientist has been deputed from this institute for advance training in the TNBD Division, CSIR Headquarters, New Delhi. Further, 16 other members of the staff were deputed for advance trainings in different courses.

Honours and Awards

CDRI, as an institute, was awarded Gold Medal for its contributions to World Science and International Scientific Collaborations by the Scientific Partnership Foundation, Russia. CDRI became member of the Associated Chambers of Commerce and Industry of India (ASSOCHAM), New Delhi. Besides, the institute is now a Life Member of Lucknow Management Association, Lucknow; Member of Consultancy Development Centre (CDC), New Delhi and Member of World Association of Industrial & Technology Research Organization (WAITRO), SIRIM, Berhard.

Several staff members received recognition for their scientific contributions. Dr C.M.Gupta,

Director, CDRI, was elected as the President, Society of Biological Chemists (India) for the years 2005 and 2006. Dr A.K. Saxena received the 2004 Honorary Medal from Scientific Partnership Foundation, Russia. Dr Pratima Srivastava was awarded the Prof. B.K. Bacchawat Memorial Young Scientist Award from National Academy of Sciences, Allahabad (2003-04). Shri Rit Vatsyayan, Research Fellow, received Young Scientist Award given by Indian Society for Parasitology during 3rd Global Meet on Parasitic Diseases held at Bangalore. Association of Physicians of India conferred Dr Ashim Ghatak upon the Smt. J.R. Vakil Oration for Cardio-Pulmonary Disease – 2004 award. Dr Sudhir Srivastava co-authored a WHO publication '*Hand-book of Non-clinical Safety Testing*'. Dr Ram Raghubir won the first prize in the Molecular Neuroscience Group on his paper '*HSP-70 Protein Expression in Permanent and Temporary Focal Ischemia*' at NBRC International Symposium: Building the Brain.

Bioethics Symposium at CDRI

THE Central Drug Research Institute (CDRI), Lucknow, in the recent past organized a Bioethics symposium, 'Protecting human participants in clinical research'. The symposium was sponsored by CDRI, Indian Council of Medical Research (ICMR), New Delhi, and Joint Centre for Bioethics, University of Toronto, Canada. The main objective of this symposium was to address issues related to implementation of ethical guidelines while planning, conducting and monitoring of clinical research. The symposium was attended by nearly 70 participants from King George Medical University, Sanjay Gandhi Post Graduate Institute of Medical Sciences and CDRI.

Welcoming the distinguished gathering of medical experts and scientists from the city and ICMR, Dr C.M. Gupta, Director, CDRI, said that this is for the first time that such a symposium has been organized in the institute. Dr Gupta also inaugurated the symposium and deliberated on three major issues in this context: objectives of clinical research, understanding the value of ethics review and ethics viewed as hindrance with investigations unwilling to undergo ethical review. He informed that India is becoming hub of clinical trials on drugs and vaccines mainly due to certain inherent advantages like low cost, large patient pool, fast patient recruitment and large base of qualified medical research personnel. Therefore

there is a clear need to prevent any form of exploitation of human participants.

The faculty for this symposium included experts, who have been instrumental in developing Ethical Guidelines for Biomedical Research on Human Subjects from Indian Council of Medical Research, New Delhi, King George Medical University, Lucknow and CDRI. The symposium was open to members of ethics committees of medical institutions and health care professionals participating in clinical research/clinical trials. The programme consisted of seven lectures spread over three scientific sessions.

In the first session a keynote lecture was delivered by Dr Vasantha Muthuswamy, Sr. DDG, ICMR, on 'Ethical principles and ethical guidelines'. Quoting examples from World War II, she emphasized the need of utmost care in conducting any clinical research including testing of new drugs and vaccines on human subjects.

The second session included three lectures which were: Ethical consideration in clinical evaluation of drugs (Prof S. D. Seth, Chair in Clinical Pharmacology, ICMR); Quality assurance and monitoring of clinical research (Prof S.S. Agarwal, Hon. Consultant, CDRI); and Informed consent-elements of informed consent and preparation of informed consent document (Dr Nandini Kumar, DDG, ICMR).



Prof S. D. Seth discussed various phases of clinical trials and emphasized on ethical responsibility of clinical investigators and ethics committee members. Prof S.S. Agarwal deliberated on need and methods of quality assurance in clinical research. He spoke on various measures highlighted in Good Clinical Practice (GCP) guidelines developed in India. Dr Nandini Kumar, DDG, ICMR, clearly delineated the components of informed consent highlighting voluntariness, need of adequate disclosure of information and comprehension by the human participants before including them for clinical trials.

The Third and final session also consisted of three lectures on Research ethics review-Roles and responsibilities of ethics committees (Dr Roli Mathur, ICMR); Vulnerable populations – Special issues in subject selection and recruitment (Prof Shally Awasthi, KGMU); and International research ethics-equivalent protections (Dr J.S. Srivastava, CDRI). Dr Roli Mathur from ICMR discussed the role of institutional ethics committees before undertaking any clinical research by the institutions across the country. Prof Shally Awasthi dwelled on the vulnerable populations including children, women from various age groups, mentally compromised and

elderly subjects. Dr J.S. Srivastava delivered a talk on International research ethics requiring equivalent protection for human subjects from developed as well as developing countries.

A panel discussion, moderated by Dr O. P. Asthana, Head, Clinical & Exp. Medicine, was also organized on this occasion at the end of these lectures in which many concrete suggestions were given by the clinical researchers and eminent scientists. Major suggestions included education and training of persons involved in ethical review of research proposals submitted to institutional ethics committees of medical institutions. A strong need was felt to organize continuing medical education programmes, seminars and workshops to build capacity in the country itself.

At the end of the symposium Dr Nityanand, former Director, CDRI, briefly but aptly concluded the symposium and advised to pursue a line of action in this regard which is good enough to encourage gradual but lasting acceptability in future plans for effective implementation of ethical guidelines developed by Indian Council of Medical Research, New Delhi.

The symposium ended with a Vote of Thanks by Dr O.P. Asthana.

Workshop cum Training Programme on Disaster Management

THE Central Building Research Institute (CBRI), Roorkee, in the recent past organized a 2-day workshop cum training programme on 'General Insurance and Disaster Management' for the Personnel of Housing Cooperatives jointly with NCHF and United India Insurance Company. Inaugurating the workshop, Shri Nav Prabhat, Minister for Forest, Environment and Urban Development, Government of Uttaranchal, said that human settlements are frequently affected by natural disasters, whether it may be an earthquake, floods, hurricanes, cyclones, landslides etc. He further added that the rate of such natural disasters has been increasing over the years because of human interference with nature and also global warming that threaten to increase the frequency and severity of such disasters. Therefore we have to chalk out preventive and implementable strategies to look into the mitigation factors and post disaster management.

Shri Prabhat mentioned that throughout the world, the local communities are being made aware of

Post Disaster Management. The period from 1990 to 2000 has been declared as the 'International Decade for Natural Disaster Reduction (IDNDR) by the U.N.' The aim of such efforts is to reduce disaster risk at the local level and enable the communities and individuals to reduce significantly their vulnerability to hazards.

He informed that the Government of India has set up a National Disaster Management Authority under the Chairmanship of the Hon'ble Prime Minister to deal with emergency situation arising out of natural disasters and man made disasters. It will provide necessary guidelines to deal with emergency situations and the role of the Central Government is supportive only in the term of provision of physical and financial resources. The basic responsibility for this is of the concerned State Government. The local level organizations, like Housing Cooperatives, Self-help groups, NGOs etc. can perform an important role to create awareness among the masses for proactive measures of preparedness, protection, prevention, publicity related action and also post disasters reconstruction activities. The self-help groups and the cooperatives would have to work in preparing and training their personnel and common man for disaster management and rehabilitating and reconstructing the community after disaster.

He suggested that construction of buildings should be designed and executed keeping in mind the potential disasters and cooperative housing societies should seek guidance and help of CBRI, BMTPC and other research organizations in designing and making earthquake resistant houses. He further said that insurance companies should come forward with liberal insurance policy framework beneficial to the general public and cooperatives. The insurance of buildings must be made mandatory, He added.

Earlier, in his welcome address, Shri Deep Chand Sharma, Chairman, NCHF, said that India and the world at large have faced a number of natural and man made disasters and there seems to be no fool-proof answers in sight. Hence, there is an urgent need to keep ourselves prepared for a quick response from within to provide relief measures to the affected community during disasters. Timely and immediate help can certainly save many lives and reduce the number of deaths and injuries, thus, we should respond collectively through advanced preparedness to deal with natural disasters.

Shri S.N. Sharma, MLA and Ex-Cabinet Minister, Chattisgarh state, also discussed the issues related to Disaster Management.

In his Presidential Address, Prof. K. Ganesh Babu, Director, CBRI, Roorkee, focused on the need and importance of taking effective steps

in preparing action plan so as to provide timely help to the victims of these disasters. He also explained the various R&D work being pursued at CBRI.

Dr M.L.Khurana, Managing Director, NCHF briefly outlined the objectives and details of the programme. Over 150 delegates, representing cooperative housing organisations, senior officers of Central and State Governments, CBRI, United India Insurance Company, BMTPC, NHB, HUDCO and other concerned organisations participated in the programme.

Shri Vinod Kumar, Head, HRG, CBRI, also spoke on this occasion. Shri S.C. Jain, MLA and Prof. Prem Vrat, Director, IIT and Shri N.K. Shangari, Director grade Scientist, also graced the occasion. Shri N. K. Shangari, presented the activities of the institute. Shri J. K. Prasad, Chief (BM), BMTPC delivered a talk on Initiatives of BMTPC in the Disaster Management. Shri Mangat Ram, Divisional Manager and Sardar Jassa Singh, BM, United India Insurance Company, explained the concept, terms & conditions of Fire Insurance Policy for the Cooperative Housing Societies.

While concluding Dr M. L. Khurana, Managing Director, NCHF, thanked the whole hearted contribution of Shri Vinod Kumar, Dr Atul Kumar Agarwal and Shri Rajeev for the success of training programme.

Shri B. S. Manhas, Vice-Chairman, NCHF proposed a Vote of Thanks.



NIO conducts Training for Science Teachers

THE National Institute of Oceanography (NIO), Goa, recently organized a five-day 'Faculty Motivation and Training Programme' for High School science teachers from Goa. The programme was funded by the Human Resource Development Group of CSIR. The training was aimed to upgrade the knowledge base of the participants, especially in new emerging areas of science, and also to provide opportunities for the trainees to interact with the scientific community. The programme was attended by 22 science teachers from different schools of Goa. Smt. Sujata Kaisary, Scientist, HRDG, NIO, coordinated the programme.

Dr S.R. Shetye, Director, NIO, welcomed the participants and briefly introduced the purpose of the programme. He urged that the teachers should make maximum use

of the skills acquired by them through the course, for inculcating scientific temper among the students. He also mentioned that the need is felt that students joining the science stream, do so by deriving inspiration from science. Similarly, Shri P.R. Nadkarni, Chairman, Goa Board of Secondary and Higher Secondary Education, also encouraged the teachers to use new skills of teaching through interaction with the scientists.

The training consisted of lectures on topics like oceans and climate, natural resources, understanding past climate, environmental pollution prevention and control, microbiology & biotechnology, alternative energy resources, coastal hazards and information technology. All these topics were centered around the main theme, i.e., how science relate

to our day to day life? Demos on specialized equipments such as Atomic Absorption Spectrophotometer, Electron Microscope and X-ray Diffractometer, group discussions and presentations were organized. Visits to field and to NIO's Coastal Research Vessel *Sagar Sukti*, were also included in the programme.

In the concluding session, Dr N. B. Bhosle, Deputy Director, NIO, congratulated the participants and awarded the certificates. Shri Michael D'Souza, Director (Admn.), Directorate of Education, was the guest of honour. He emphasized that the teachers must put into practice whatever knowledge they have gained from the training and inspire the students. Smt. Sujata Kaisary, Programme Coordinator, proposed the Vote of thanks.



Dr S.R. Shetye, Director, NIO, addressing the participants Inset: Participant receiving certificate at the hands of Dr N.B. Bhosle, Dy. Director

Prof. Kennedy delivers Dr Mashelkar Endowment Lecture at NCL

PROF. Joseph P. Kennedy, Distinguished Professor of Polymer Science and Chemistry, Institute of Polymer Research, The University of Akron, USA, recently delivered the second Dr R. A. Mashelkar endowment lecture at the National Chemical Laboratory (NCL), Pune. Organized by NCL Research Foundation (NCL RF), the Dr Mashelkar endowment lecture is sponsored by Dorabji Tata Trust, Mumbai.

Prof. Kennedy spoke on 'A career in polymers'. He focused his talk at delivering products suitable to market needs through fundamental research. He admired NCL's motto encrypted on the entrance wall that 'the purpose of this laboratory is to use chemical sciences for the good of people' and said that it is his philosophy too. He elaborated his experiences in polymer science as an example and said that it is exhilarating to explore, discover and understand; but it is no longer sufficient.

He started his lecture by quoting two basic points from a book 'Wealth from Knowledge' that are essential for research professionals. There are two roads of innovation that are governed by either a 'discovery-push' or a 'market-pull'. He pointed out precisely that if a fundamental research is conceived properly that

can lead to new unexpected technologies. The essence of polymer professional is to create materials that are useful to society. He briefed about the discover-push by citing contributions of his research in understanding the mechanism of cationic polymerization of isobutylene. He spoke about the ability to control molecular weight, molecular weight distribution, functionalization of chain-ends and to form block copolymers from isobutylene achieved through his research over 15 to 20 years that led to the development of new materials that were commercialized later by Konaka, Japan and BASF, Germany. These materials are telethelic liquid polyisobutylene rubber and thermoplastic elastomers that consist of di- and tri- block copolymers of polyisobutylene and styrene. In 1995, he found out that the outstanding properties of these thermoplastic elastomers also include biocompatibility. He explained how these polyisobutylene block copolymers can be used as drug eluting stents in cardiology for treatment of coronary artery disease. He said that the advantage of polymeric stents which replaced metallic stents is that it can be loaded with drug to eliminate vascular accumulation. Today, world over, millions of patients are treated with this drug loaded polyisobutylene stents in cardiology treatment. He

emphasized that this is an example that how a fundamental science can be taken into the market. In another example, he elaborated the development of amphiphilic smart co-network consisting of hydrophobic polyisobutylene and hydrophilic polyethylene oxide in his laboratory. He explained how diabetic control can be achieved by implanting such a co-network membrane embedded with cells of pig that can produce insulin. His lecture summarized the importance of basic science in placing designed functional polymeric materials in to the market place.

Earlier, Dr S. Sivaram, Director, NCL, in his welcome remarks described Prof. Kennedy as most distinguished polymer chemist. He also remembered his post-doc days with Prof. Kennedy and introduced Prof. Kennedy to the audience. NCL RF, an institution aimed at promoting excellence in science and technology, in association with Dorabji Tata Trust has instituted an Endowment Lecture Series in honour of Dr R.A. Mashelkar. The lecture honours Dr Mashelkar's dynamic leadership and multifaceted contributions to the area of polymer science and engineering research, public policies, R&D Management, creation and management of intellectual property, grass root innovation and promoting excellence in organization. The Endowment Lecture Series



Honours & Awards

has been initiated to inspire succeeding generations of scientists of NCL to emulate the qualities of Dr R. A. Mashelkar. The first lecture in the series was delivered by Prof. Morton M. Denn, Albert Einstein Professor, City College of the City University of New York, USA on 2 January 2005.

Dr Rakesh Kumar awarded the United States — Asia Environmental Partnership 'Environmental Leadership Award'

DR Rakesh Kumar, Scientist-in-Charge, the National Environmental Engineering Research Institute (NEERI's) Zonal Laboratory, Mumbai, has been awarded the United States — Asia Environmental Partnership 'Environmental Leadership Award' in recognition of outstanding contributions made through working in partnership to improve the environment and quality of life for the people of Asia.

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