

CSIR NEWS

VOL 57 NO 22 30 NOVEMBER 2007



Team CSIR



CFTRI bags National Award for Excellence in Consultancy Services

The Central Food Technological Research Institute (CFTRI), Mysore, received 'Certificate of Merit' for Excellence in Consultancy Services, instituted by the Consultancy Development Centre (Department of Scientific and Industrial Research, Government of India), New Delhi, for the successful implementation of the project, "Integrated Pilot Scale Fruit Processing Unit" promoted by M/s Rishang Keishing Foundation for Management of Tribal Areas (MATA), Imphal, Manipur. The award was received by Dr K. N. Gurudutt, In-charge Director, CFTRI, from Shri Tejendra Khanna, Chairman, Ranbaxy Laboratories Ltd, on 15 January 2007 during the inaugural session of the Ninth National Consultancy Congress on "Consultancy and Services: Global Market", in the presence of an august audience at India Habitat Centre, New Delhi.

Manipur hills are famous for diverse crops, such as pineapple, oranges, lime, lemon, papaya, banana, plum, peach, berries and passion fruits. The people of the state are mainly engaged in the cultivation of paddy and horticultural crops. The State Government, the North Eastern Development Council and the Central Government have been promoting horticulture plantation in the hill areas to improve the living standards of the local population.

In this background, an integrated fruit processing facility was established at Litan, as part of a new Food Industrial Park at Thotchanram, Ukhrul district. The unit is equipped to process 5000 MT fruits, such as pineapple, oranges and passion fruit per annum. The project will benefit about 38,000 Jhumia families and envisages income generation of Rs 11.8 crore along with other projects being implemented in the Food Park.



Dr K.N. Gurudutt, In-charge Director, CFTRI, receiving the National Award from Shri Tejendra Khanna, Chairman, Ranbaxy Laboratories Ltd. Shri P.C.S. Nambiar, Project Coordinator, CFTRI, is also seen



As per the MoU, CFTRI was entrusted with providing total turnkey solutions comprising the engineering aspects, erection of the plant and machineries, training on plant administration and production of various fruit products. The DSIR, under PATSER scheme and Ministry of Food Processing, Government of India and CSIR provided the requisite financial support.

Novelty of the process is the application of the Membrane Technology for clarification and concentration of pineapple and orange juices with the micro-filtration and reverse osmosis. The clarified juice is also suggested to be used in the canning of slices instead of sugar syrup.

The advantages of membrane processing include low energy consumption, minimal thermal damage to heat sensitive components, retention of natural flavours, improved yield, cold sterilization and lower operational cost. A compact membrane filtration unit to match the capacity has been

installed at the plant along with other processing systems, such as pasteurization, vacuum concentration, canning and bottling for extraction of pineapple, oranges and other fruits and to make various value added products. The unit is expected to create direct and indirect employment generation of around 1000 people.

The Triumph

Transportation of capital goods, materials and mobility of the project team to the site were affected time to time due to the prevailing conditions in the state. The locational disadvantage was another factor that too influenced the project execution.

The project team scaled up the membrane processing from laboratory scale to pilot level to suit the requirements. Technical personnel were trained to take up handling of raw materials and the processing of a number of products hygienically based on various technologies developed by CFTRI. The plant was successfully commissioned in April 2006.



A view of the Membrane Processing Unit at Integrated fruit juice processing plant, Litan, Imphal — the plant was set up by CFTRI for MATA Foundation

Investigation of gas hydrate along the western continental margin

Gas hydrates are ice-like non-stoichiometric crystalline entities formed under high pressure and low temperature when gas concentration exceeds the saturation limit. These are widely present in continental slope environments where a deep water column exerts enough pressure to stabilize the gas hydrate. The occurrence of gas hydrates can be inferred from the presence of Bottom-Simulating Reflectors (BSRs) on stacked reflection seismic data. A BSR is identified on seismic sections based on its distinct characteristics, i.e., (i) mimicking the sea-floor topography, (ii) an opposite polarity with respect to the seafloor, (iii) typical association with amplitude blanking in the hydrate stability zone, and (iv) cross-cutting the existing geological horizons because it represents a phase transition. Seismic studies on several active and passive margins demonstrate that a high amplitude BSR is primarily due to the presence of free gas at the base of hydrate stability zone. The occurrence of gas hydrates has been inferred from the presence of BSRs along the

western continental margin of India (WCMI). The presence of several gas escape features has also been observed in shallow seismic records on the margin. Interval velocity and Amplitude Versus Offset (AVO) analysis of the multi-channel seismic (MCS) reflection data collected along the WCMI show the existence of free gas below the BSR and suggests a hydrate/free gas mechanism for the BSR formation along the margin.

The scientists of National Institute of Oceanography (NIO), Goa, have assessed spatial and vertical distribution of gas hydrates by analyzing the interval velocities and AVO responses obtained from MCSs [Velocity and AVO analysis for the investigation of gas hydrate along a profile in the western continental margin. Dewangan, P.; Ramprasad, T. *Mar. Geophys. Res.*: 28(3); 2007; 201-211]. The hydrate cements the grains of the host sediment, thereby increasing its velocity, whereas the free gas below the base of hydrate stability zone decreases the interval velocity. Conventionally, velocities are obtained from the semblance analysis on the Common Mid-Point (CMP) gathers. Waveequation datuming was used to remove the effect of the water column before the velocity analysis. The NIO study shows that the interval velocities obtained in this fashion are more stable than those computed from the conventional semblance analysis. The initial velocity model thus obtained is updated using the tomographic velocity analysis to account for lateral heterogeneity. The resultant interval velocity model shows large lateral velocity variations in the hydrate layer and some low velocity zones associated with free gas at the location of structural traps. The reflection from the base of the gas layer is also visible in the stacked seismic data. Vertical variation in hydrate distribution is assessed by analyzing the AVO response at selected locations. AVO analysis is carried out after applying true amplitude processing. The average amplitudes of BSRs are almost constant with offset, suggesting a fluid expulsion model for hydrate formation. In such a model, the hydrate concentrations are gradational with maxima occurring at the base of hydrate stability zone.

CFTRI process for preparation of hypoglycemic foods and formulations thereof (US Patent No. 7153528)

Diet therapy plays a major role in the clinical management of diabetes. Proper dietary schedule helps in the management of diabetes besides delaying the onset of diabetes in population at risk. Dietary recommendations for the diabetics include, complex carbohydrate backed up with adequate amounts of dietary fiber, micronutrients and nutraceuticals with insulin secretagogue and sensitizing properties.

The Central Food Technological Research Institute (CFTRI), Mysore, has developed a hypoglycemic food formulation containing cereals other than rice, mixed legumes, small proportion of milk solids, vegetable fat rich in essential fatty acids, spices and condiments including fenugreek, and natural herbal ingredients with insulin secretagogue and sensitizing properties, and fortified with essential vitamins and minerals. The cereals are scoured to remove the outermost fibrous layer, whereas, the legumes are used in the form of dhal. Cereals, legumes and spices are mildly toasted to improve the sensory attributes and blended suitably with other ingredients to prepare a ready-to-cook product.

The hypoglycemic food formulation contains about 14% protein and 18% dietary fibre and exhibits moderate glycemic response. The hypoglycemic food formulation can be utilized as a dietary supplement or as a meal substitute for diabetics. The formulation and the process are covered under Indian and US Patents.



Application of Cellulases in Biofinishing of Denims

Increasing concern for the environmental issues has imposed constraints on the textile industry. The freshly dyed denim fabric is tumbled with pumice stones to give a faded appearance in conventional stonewashing process. Stonewashing has the disadvantage of waste production and its subsequent disposal. Cellulase enzyme treatment has been promoted to avoid the machine induced severe wear and loss of tensile strength during denim processing. The minimization of water contamination, clean up effort and substantial reduction in use of toxic chemicals are areas where enzymes have potential to play a significant role in decreasing the pollution. Enzymatic treatment of fabric is an eco-friendly process and allows up to 50% higher jeans load and yields the desired look and a softer finish. Cellulases are also used to improve the appearance of cellulosic fabric by removing fuzz fibre and pills from the surface, reducing pilling propensity, or delivering softening benefits. The damage caused to the machine wear is negligible and there is no clogging

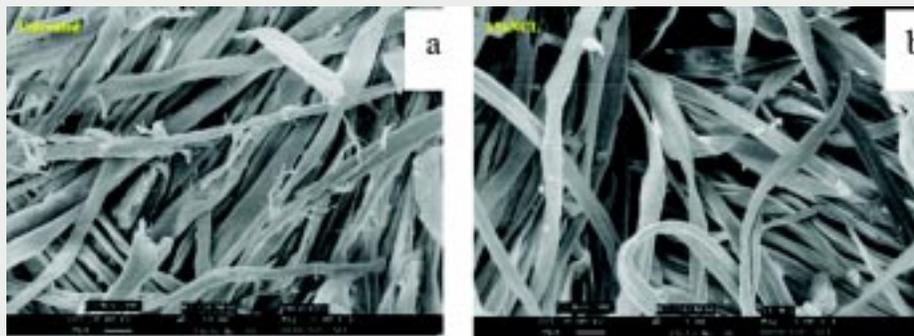
of outlet of washing machine by sand due to eroding of pumice stone in the traditional process. However, the existing enzymatic washing of denim, involving acid or neutral cellulase, causes backstaining.

Dr Mala Rao and colleagues from Biochemical Sciences Division, National Chemical Laboratory (NCL), Pune, have been working on extremophilic organisms which are not only important for biotechnological applications but also significant in understanding the basis of structure-function relationship. An alkalothermophilic organism growing optimally at pH 9.0 and temperature 50°C was identified to secrete alkali-stable cellulases and xylanases. The NCL scientists demonstrated the application of these cellulases for biofinishing of denims in collaboration with Ahmedabad Textile Industry's Research Association (ATIRA). These cellulases were effective in biofinishing of denim with respect to the removal of hairiness with marginal total weight loss, increasing softness of the fabric and abrasive activity with low

backstaining. The scanning electron micrographic (SEM) pictures showed the removal of protruding hairs from the denim fabric after treatment with this cellulase.

The molecular weights of these cellulases range from 14 to 65kDa, and the cellulases have been characterized at molecular level from the extracellular culture filtrate. A low molecular weight cellulase has been crystallized and X-ray diffracted at 2.3Å. Lichenases and xylanases from this organism have also been characterized. The research on increasing the yield of cellulase, optimizing its production in a fermentor and cloning of the cellulase in a suitable host for overexpression is in progress. Dr Mala Rao and her students have filed two patents and published about ten papers on this work, which include:

- Rao *et al.*, Indian patent application number 1299/DEL/2004.
- Rao *et al.*, Indian patent application number. 1298/DEL/2004.
- Rao *et al.*, 2007, *Bioresource Technology*, 98: 368 - 372.
- Rao *et al.*, 2007, *Biotechnology and Bioengineering*, 96: 48 - 56.
- Rao *et al.*, 2006, *Biochemical and Biophysical Research Communications*, 347: 428 - 432.
- Rao *et al.*, 2006, *Acta Crystallographica Section F*, F62: 385 - 387.
- Rao *et al.*, 2005, *Biochemical and Biophysical Research Communications*, 329: 111 - 116.



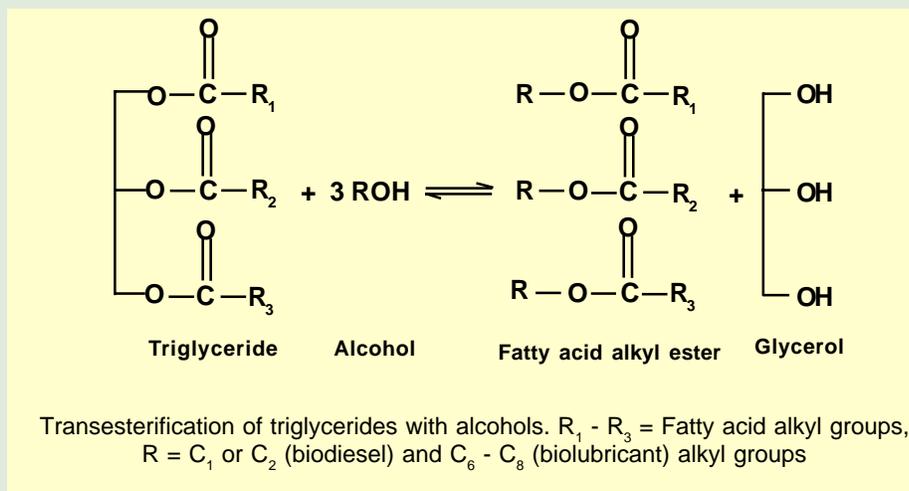
SEM of denim fabric under 1,000X magnification.
a: Untreated denim fabric; b: denim fabric treated with cellulase

Highly Efficient, Solid Catalysts for Production of Biodiesel and Biolubricants

Biodiesel is a biodegradable, cleaner burning, renewable alternative to petrodiesel. It consists of mono alkyl esters of long chain fatty acids produced from vegetable oils or animal fats by transesterification with methanol or ethanol. Biolubricants are produced when longer chain alcohols (octanol, for example) are used (as shown in the reaction). Biodiesel leads to ~25% reduction in the emission of harmful pollutants like carbon monoxide, sulfur oxides, and other particulate matter. Application of (1) heterogeneous, solid catalysts instead of homogeneous catalysts and (2) use of unrefined, non-edible oils and waste cooking oils instead of expensive refined, edible oils in biodiesel and lubricants production would make manufacture of biodiesel economically and environmentally attractive.

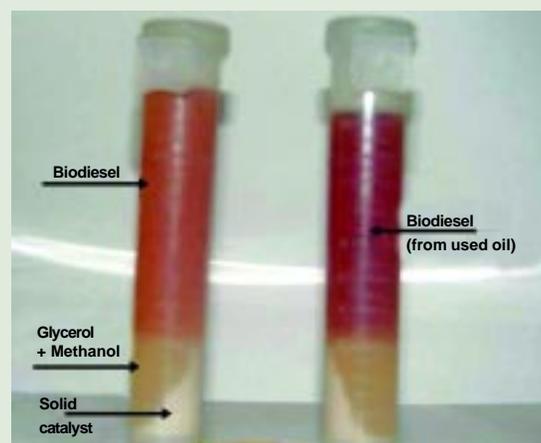
Conventionally, biodiesel is produced using mineral acid or alkali catalysts. In addition to the corrosion problems, these homogeneous catalyst-based processes involve elaborate process steps for removal of free fatty acids (FFAs) and water from the feedstock and catalyst from the products. There have been some reports on the application of solid catalysts but most of those lose their activity on recycle and/or require pretreatment of the feedstock to remove the FFAs and water.

Darbha Srinivas and his group at National Chemical Laboratory (NCL), Pune, have discovered a



Margarine oil and ethanolysis products—fatty acid ethyl ester and colourless by-product glycerol

novel, solid double metal composition (DMC) catalyst which is highly active (95-98% conversion) for the conversion of a range of oils including *Jatropha*, *Karanja* and unrefined rubber seed oil (containing up to 18% of FFAs) and used oils into biodiesel and biolubricants [P.S. Sreeprasanth, R. Srivastava, D. Srinivas and P. Ratnasamy, *Appl. Catal.*





A: General 314 (2006) 148 - 159]. Both transesterification (of the triglycerides) and esterification (of the FFAs) are accomplished by this solid catalyst in a single step. The biodiesels and biolubricants produced meet the specifications.

The solid catalysts developed at NCL are reusable and active even when significant quantities of water are present (unrefined oils). Most importantly, in the process developed by NCL scientists, the by-product glycerol obtained during the biodiesel and biolubricants manufacturing is also converted into a high cetane diesel additive and thereby increasing the yield and fuel burning characteristics of biodiesel. Lewis acidity and hydrophobicity have been found to be the possible causes for the highly efficient activity of NCL's DMC catalysts for biodiesel and biolubricants production. Four patent applications are pending covering various applications of this process.

CENTRAL DRUG RESEARCH INSTITUTE, LUCKNOW

R&D Highlights: 2006-07

With focus on modernization with the acquisition of latest research tools and techniques and dedicated research efforts which meet the requirements of pharma and drug industry, the Central Drug Research Institute (CDRI), Lucknow, continues to pursue its longstanding open door policy to encourage business cooperation with public and private industry and national and international research organizations and academia. During 2006-07, CDRI signed several secrecy agreements and shared findings with the interested companies. The industry has been particularly interested in many new leads and candidate drugs under development, which include CDR-134F194, CDR-267F018, NP-1, S-002-853, S-002-857 and compound 99-411. The year witnessed cooperation with Ranbaxy, IPCA, Indigene Pharmaceutical and Satsang Rasaishana Mandir. A large number of projects were being pursued with the support of MOH, DBT, DST, MoES, ICMR, CSIR, DRDO, ICAR, NMITLI and IFCPAR Indo-French program.

The major activities/accomplishments are highlighted below under the R&D programmes on Drug Development and Drug Discovery.

DRUG DEVELOPMENT

Clinical studies: The licensee firm Hindustan Latex conducted a product acceptability study on Consap (contraceptive cream) at Chennai and Cochin and found that the product was

acceptable and convenient to use by women volunteers. The antimalarial drug Arteether continued its multicentric efficacy studies in Dibrugarh, Rourkela, Jabalpur, Jodhpur and Guwahati completing so far 234 cases, and data compilation has since commenced. Capsules of the other antimalarial drug, compound 80/53, were sent to Thailand for safety evaluation in G6-PD deficient cases suffering from malaria. The findings reported by Thai researchers confirm efficacy and safety of the compound. Phase III multicentric clinical trials on compound 80/574 (hypolipidemic) have been initiated at SGPGI and KGMU, Lucknow; PGI, Chandigarh; and Seth G.S. Medical College, Mumbai, in addition to pharmacokinetic studies. Clinical studies to evaluate efficacy of Picroliv (hepatoprotective) in alcoholic cirrhosis and in tuberculosis patients on MDT have been carried out at three centres (Seth G.S Medical College, T.N. Medical College, and KG's Medical University). Exploratory double blind clinical trials carried out on CT-1 (anti-diabetic) in a total of 55 patients, at KGMU, Lucknow, have been concluded. The findings reveal statistically significant reduction in total serum proteins, SGOT, SGPT in CT-1 treated patients. Among other products under clinical studies, CDR-134D123 (antihyperglycemic) has completed Phase I single dose double blind studies in healthy volunteers, and protocols for Phase I studies on compound 97/78 (antimalarial), as per GCP guidelines, have been developed.

Regulatory toxicity studies:

Regulatory toxicity studies were carried out on inhouse as well as outside products, besides some basic and applied toxicity studies. CDRI products 99/411, 97/78, herbal medicament, CDR-267F018, CDR-134F194 were evaluated for generating their safety profiles. Industry sponsored products were evaluated under contract research. Experimental studies carried out included hepatotoxic effects of isoniazid with special reference to oxidative stress and apoptosis using hepatoma cell line (Hep-G2), nephrotoxic effects of cisplatin, amphotericin B and gentamycin by using renal cortical slices, primary cell cultures and renal cell lines, and teratogenicity potential of cyclophosphamide and synthetic compounds was studied by measuring biochemical changes in an *in vitro* system.

Pharmacokinetic studies:

Pharmacokinetic evaluation (PK) studies were carried out on three candidate drugs 97/78 (antimalarial), S-002-853 (antidiabetic) and 99-373 (anti-osteoporotic). Multiple dose PK studies on compound 97/78 and its metabolite in rhesus monkeys revealed insignificant plasma accumulation. Further, metabolite stability and CYP profile suggest involvement of CYP3A4 in its metabolism. Tissue distribution profile of compound 99/373 and its two major metabolites in rat liver, lung, spleen and kidney has been established. Urinary excretion studies have revealed excretion of the compound and its metabolite in conjugated form. Plasma pharmacokinetic studies of

antidiabetic compound S-002-853 are in progress. Active S-isomer of this compound showed good systemic exposure with long elimination half-life.

Technology development:

Efforts have been made to develop appropriate technologies — chemical, fermentation and pharmaceutical — for institute's candidate drugs and sponsored products, and several products have been produced in required quantities for further studies. An improved process for simvastatin with lesser number of steps, which also allows reactant recovery and recycling, has been developed at bench scale. A 5-step improved process for the synthesis of sertraline hydrochloride developed at bench scale avoids the use of hazardous titanium tetrachloride. Scaling up processes for paroxetine hydrochloride (antidepressant) is in progress. The in-house products prepared for further studies include compound 99/411 (110 g) and Picroliv (9 kg). Some cultures derived from soil samples have been characterized as *Talaromyces assiutensis* MTCC 7582 and *Streptomyces capoamus* MTCC 8123 and have shown strong antifungal activity against unicellular and filamentous fungi. Chemical characterization of the active compound produced by cultures is in progress. Studies on hydroxylation of compound 80/574 with the help of *Aspergillus ochraceus* is continuing and its derivatives are under pharmacokinetic evaluation. Experiments related to long-term preservation of microbial cultures

by freeze-drying and their maintenance are being carried out. Preserved cultures are checked at regular intervals for their purity, potency and viability. Quality control and stability studies on several candidate drugs are continued, besides using HPLC methods for proper resolution of starting materials and for separation of chiral preparations. Efforts for development of novel delivery systems have led to progress on several fronts: preparation of nanometer emulsion for albendazole, studies on new formulation of inhalable biodegradable microparticles containing antitubercular drugs, and surfactant vesicles containing cyclosporin, etc.

DRUG DISCOVERY

Drug discovery efforts comprised basic studies to find out novel targets on one hand and natural products/synthetic compounds screening, the lead optimization, and other required studies on the other. During the year, 21 new terrestrial plants and 12 new marine flora & fauna samples were collected and documented. A record number of 1749 new synthetic molecules were prepared. The compounds and extracts were evaluated for various primary and follow up biological screenings under different disease oriented research programs. A summary of significant achievements under different areas is presented below:

Biological screening: The project focus is on anti-TB and anticancer



screening using both conventional and HTS based tools, and on anti-leishmanial screening and botanical screening (CSIR-Procter & Gamble) using entirely HTS tools. Out of 338 compounds screened against *M. tuberculosis* H37Rv, two compounds were found active *in vitro* with none showing toxicity towards Vero cells or mouse bone marrow derived macrophages. On screening in mice, two compounds showed variable degree of infection clearance in spleen and lungs. The level of activity of these molecules was reconfirmed and further evaluations are underway. The mouse bone marrow model of TB has been developed and adopted in routine use. Under the project on anticancer drug, focus was on chemistry-based lead optimization. Hit molecules of four chemical classes were short listed and from hit molecules approximately 70 new analogs were synthesized and subjected to advanced screening using eight cancer cell lines. To screen out poor candidate drugs based on their rapid clearance or conversion to toxic metabolites by cytochrome P450 enzymes, a metabolic profiling assay using five Cyp enzymes (CYP3A4, CYP2D6, CYP2C9, CYP1A2 and CYP2C19) commonly involved in drug metabolism, have been developed and subsequently used for screening of 10 lead molecules.

Newer approaches in drug discovery and design: To capitalise on newer approaches now available for drug discovery, an integrated environment for informatics systems, computational chemistry and molecular modeling is in

operation at the institute to facilitate and enhance drug design and discovery in different target therapeutic areas. Structure-based investigations and computational predictive models for structure activity relationship studies including molecular docking and CoMFA and CoMSIA studies were applied on diaryloxy methano phenanthrene analogues as anti-tubercular agents, on 4-thiazolidinones as HIV-1 RT inhibitors and on human mitotic kinesin Eg5 inhibitors as anti-cancer agents. The results provided clear guidelines and reasonably good activity predictions for designing novel inhibitors. A rational evaluation of a series of R and S amino acid derived, 3-substituted 1,4-benzodiazepin-2-ones as anti-ischaemic agents has been carried out by molecular modeling and docking studies. Some of these compounds have shown promising neuronal protection activity. Interaction and assembly of the leucine zipper peptide (LZP), its single alanine substituted analog, and double alanine substituted analogs to human red blood and *E. coli* cells as a model system were studied. Fluorescence resonance energy transfer and gel electrophoresis experiments revealed the differences among the amino acids in their assembly onto the live human RBC and in their oligomeric states in zwitterionic lipid vesicles and human RBC ghost membrane. The findings have disclosed that assembly of these peptides in human RBC and *E. coli* is pivotal in determining their lytic activity against the corresponding

cells. Studies on the design and synthesis of thiazolidinone as HIV-RT inhibitors were continued and several compounds were synthesized and the biological activity evaluation was in progress. Crystallization and 3D X-ray intensity data collection of 43 compounds of biological and structural importance was completed. Structure determination and refinement of 32 compounds were completed. A significant milestone in the structure determination of the potential drug target, viz. peptidyl-tRNA hydrolase from *M. tuberculosis* H37Rv in solution by NMR spectroscopy was achieved. Significant progress was also made in characterization of CFP-10 and ESAT-6 T-cell antigens of *M. tuberculosis* H37Rv.

CNS/CVS & other disorders: Neuroprotective effect of herbal medicament (HM) was investigated with respect to cytochrome C translocation and caspase dependent death pathway leading to necrosis and/or apoptosis. HM was found to exert its neuroprotective effects by acting at multiple targets in the signaling pathways that are activated in ischaemic and neurodegenerative brain diseases. It appears to be a promising agent for the treatment of cerebral stroke. Studies on memory enhancing activity of Gugulipid have shown significant improvement in memory deficit induced by either scopolamine or streptozotocin in Morris water maze test in mice. Essential safety pharmacology studies of three candidate drugs CDR-134D123; 99-411; Lysostaphin

cream and Lysostaphin gel have been undertaken for their effect on cardiovascular, respiratory and CNS parameters in rats, rabbits and mice.

Filariasis: In immunological studies, SDS-PAGE and western blotting of Wolbachia intact and bacteria depleted *B. malayi* adult parasite were carried out with WSP serum and three antigens (66, 39, 27 kD) were recognized in intact worm antigen. Wolbachia (endo-symbiotic bacteria) were found to play an important role in development of host tissue inflammatory reaction in birds infected with *B. malayi* during prepotency. Studies related to establishment of antifilarial efficacy of DEC with antibiotic tetracycline demonstrate that prior killing of Wolbachia has beneficial effect on the efficacy of standard antifilarial drugs. The immunological characterization of recombinant myosin was carried out in Balb/c mice. Efforts are being made to produce polyclonal antibodies against purified fraction of *S. cervi* antigen that will be used for molecular characterization of filarial circulating antigen. Biochemical and molecular studies on filarial parasites included purification of two isoforms of acetyl cholinesterase and polyclonal antibodies raised against those. In order to clone the filarial AchE gene, specific primers were designed based on conserved sequences of AchE from related parasites. PCR amplification was done using cDNA library and genomic DNA. Cloning was carried out in pGEMT vector and the sequencing of the gene inserts is underway. Hexokinase gene of

B. malayi was cloned, protein expressed and purified to a single band of 72 kDa on SDS-PAGE.

Leishmania: Development of new screening models based on reporter gene is under way. Leishmania cell lines expressing green fluorescent protein without any drug pressure were constructed by integrating the GFP-containing construct downstream of promoter of 18S ribosomal RNA gene into the genome of *L. donovani* clinical isolates. *Luciferase* tagged *L. donovani* promastigotes were transformed into axenic amastigotes and their suitability for screening of antileishmanial compounds is underway. Studies related to cloning, over expression and characterizations of *L. donovani* drug targets, viz. serine hydroxymethyl transferase, squalene synthase, triose phosphate isomerase, trypanothione reductase, dipeptidyl carboxypeptidase and glycosylphosphatidylinositol transferase-1 are progressing well. Biochemical properties and structure-modeling studies of *L. donovani* pteridine reductase 1 were performed to reveal the active site features important for ligand binding and to guide inhibitor designing. Structure based drug design on homology model, based on recombinant pteridine reductase enzyme of *L. donovani*, has enabled identification of inhibitors some of which have been tested *in vitro* and found to be inhibiting the enzyme in a target based assay. Studies on actin network of *L. donovani*, through characterization of various actinbinding proteins, have revealed its involvement in various

cell biological processes. Actin depolymerizing factor (ADF/cofilin) homologue of *L. donovani* has been found to play a role in cell development, maturation and infectivity. Overexpression of this protein in *L. donovani* has increased chemotaxis significantly whereas decreased promastigote interactions with peritoneal macrophages. *L. donovani coronin* (F-actin binding protein) gene deletion has shown defects in cytokinesis during cell division cycle. Preliminary experiments with recombinant *L. donovani* actin have shown that it forms filaments and bundles *in vitro*. An actin-related protein, which is close to ARP6 of yeast localizes predominantly in the nucleus and seems to play a role in chromatin remodeling process in promastigotes. Findings so far have collectively increased the research interests and are being perceived as a potential drug target in *L. donovani*. Use of micro-array technology has enabled the identification of important biochemical pathways for use as drug targets. One target, viz. long chain fatty acyl Co-A ligase gene has been sequenced. Detection of the endogenous copy of this gene by southern blotting and transcript by northern blotting are underway.

Malaria: The curative response with synthetic compound 99/411 was established earlier in *P. yoelii*-Swiss mice model and against *P. cynomolgi* rhesus monkey model. Further studies with this compound have demonstrated efficacy in single and double dose against the rodent model and also in simian model. As a follow-up on immunoprophylaxis



studies with recombinant MSP-1 protein against simian malaria model, 29 monoclonal antibodies were characterized for their epitope specificity. These monoclonals have been categorized in six groups on the basis of their reactivities with *P. cynomolgi* and *P. vivax* conformational and linear epitopes of MSP-1 antigen. Biochemical studies primarily focussed on molecular characterization of a putative choline kinase and transketolase from *P. falciparum* to identify novel enzyme targets for antimalarial drug development. Molecular studies continued with *P. falciparum* apicoplast and replication machinery has been characterized in terms of DNA protein interaction at replication origin. Studies have also been initiated on transcriptional machinery operative within the apicoplast. Analyses of genotype data of 4 genes, correlated with malaria susceptibility from 56 Indian sub-populations infected from *P. falciparum* were carried out. The results have revealed that extensive sub-population specific variations in allele frequency of several SNPs. *P. falciparum* malaria patient samples collected from endemic and non-endemic regions of India are being analyzed for SNP association with disease severity as well as cytokine profiles.

Microbial infections: A murine infection model of latency with *M. fortuitum* has been developed to investigate virulence factors, pathogenesis and to screen mutants defective in persistence. Two mutants defective in persistence have been isolated. The tolC gene

of *Vibrio cholerae* was cloned. The ORF encoding TolC protein plays an important role in regulating tolerance to osmolarity in small intestine. The gene has been overexpressed in *E. coli* using T7 expression vector. Work related to pathogenesis and development of a knockout of tolC is in progress. The role of Rv3878, which is deleted in BCG vaccine strain, was found associated with enhanced hydrophobicity and biofilm formation. Rapid suscitation factors of *M. tuberculosis* were cloned and demonstrated to resuscitate the dormant cells in nutrient deprived condition. A recombinant *M. aurum* for screening of FASII pathway inhibitors has been constructed and being evaluated. Role of Rv2416c (Eis) in modulation of immune response was demonstrated. A few interacting partners of Erp (Rv3910) in host have been identified by Yeast Two Hybrid method. Phosphorylation of PKC isoforms appears to be induced by direct interaction of mycobacteria with macrophages rather using cytokines as mediators. The exposure of healthy volunteers from TB endemic area to *M. tuberculosis* was confirmed by elevated serum antibody levels and *in vitro* lymphocyte proliferation *M. tuberculosis* antigens.

Natural products: Twelve new plant extracts were prepared, extracted and submitted for biological screening besides continued evaluation of previously identified plants and marine extracts. Fifteen new derivatives of K009 from the plant 3247 (antihyperglycemic) were prepared and four of them had better

activity profile than the parent compound. One novel compound from 4674 (antihyperglycemic), a rare stigmaterol glycoside derivative has been isolated. The plant 4601 (antileishmanial) yielded eight berbarine alkaloids out of which two are reported to be new and have exhibited antileishmanial and immunomodulatory activities *in vitro*. Their structures have been elucidated by spectroscopic and degradation studies. Promising osteogenic activity has been reported in five pure compounds isolated from the plant 1020. From the roots of plant 4406, 10 compounds of various classes have been isolated out of which two have shown significant anti-inflammatory and analgesic activities in dose dependant manner.

Reproductive health research: Out of several substituted phenanthrene derivatives with basic amino side chains, synthesized to search for new anticancer breast agents, one has shown appreciable activity comparable to tamoxifen. Design, synthesis, characterization and evaluation of novel non-detergent spermicides has led to the discovery of two compounds which were 25 times more potent spermicides than nonoxynol-9. Stability studies on medicated condoms coated with Sapindus saponins indicated that the product was stable up to one year from the date of manufacture.

A total of 194 research papers were published in reputed national and international journals. Fifty patents were filed – 19 in India and 31 abroad. Twenty-five patents were granted – 12 in India and 13 abroad.

Environmental Conservation and Hazards of Atmospheric and Soil Pollution

The National Geophysical Research Institute (NGRI), Hyderabad, Association of British Scholars (ABS) and British Council, Chennai, jointly organized a two-day workshop on 'Environmental Conservation and the Hazards of Atmospheric and Soil Pollution' on 21-22 July 2007 for the benefit of school teachers. About 85 school teachers from various schools of Hyderabad and Secunderabad participated.

Inaugurating the workshop, Dr V.P. Dimri, Director, NGRI, outlined, the importance of environmental studies in school education and need to familiarize the younger generation in environmental aspects towards the creation of a pollution-free society. NGRI, he said, is actively involved in geophysical environmental studies in various parts of the country and recommending the remedial measures. He informed that a rain garden has been created in NGRI campus for artificial recharge. Rain gardens are constructed by excavating the natural ground and creating storage ponds with native flowering plants and landscape. These will help harvest 100% rainfall runoff.

Shri Kartar Singh from British Council, Chennai, preside over the function and stressed the importance of the event. He asked

the teaching community to spread the message of environmental conservation and the negative effects of pollution.

Dr T. Harinarayana, Scientist, NGRI and Joint Secretary, ABS, emphasized the need to maintain better environmental measures to reduce the pollution in rural areas and the need to provide pollution-free air and water in cities as well as villages.

Dr T.V.M. Murthy, Secretary, ABS, presented his views regarding the subject, and Prof. Laxman Rao, President, ABS, gave details of the two-day programme.

Emergent professors and NGRI scientists in the field of environment gave presentations. Field visits were arranged to sewerage disposal plant and biomedical waste management plants at Hyderabad.

All the teachers actively participated

and appreciated the contents of the workshop. 'Environment' has been introduced as a compulsory subject in schools by the government. Thus the workshop greatly benefitted the teachers and the students by way of enhancing knowledge in their regular curricula.



Rain gardens with Water ponding after 57 mm of rainfall for 3 h (9-12pm) on 14 July after 10 h of the rainfall at NGRI



Stream intervention with *in situ* stones leading to rain gardens after 10 h of rainfall of 57 mm in 3 h at NGRI



Workshop on Popularization of Improved *Gur Bhatti*

About 110 persons comprising *gur bhatti* owners, gram pradhans, presidents of Ganna Sahkari Samiti, Ganna Vikas Samiti and representatives of NGOs of U.P. and Uttarakhand region participated in a one-day workshop on Popularization of Improved *Gur Bhatti*, organized by Indian Institute of Petroleum Dehra Dun, in association with the Petroleum Conservation Research Association (PCRA), on 12 September 2007. One person from Maharashtra State also attended.

In traditional *gur bhattis*, the furnace/chimney is not properly designed. A lot of heat is wasted and dense smoke is generated which is generally seen coming out of the chimney. As a result, fuel (bagasse) consumption is very high. For the benefit of the rural masses engaged in the *gur* making activity, IIP, after conducting extensive experimental trials on one of the conventional *gur bhatti*, set up an improved *bhatti*.

For this work, a popular design normally found in Dehra Dun and nearby U.P./Uttarakhand state areas was taken up. The improvements were incorporated to the extent which is feasible and cost effective in the long run. The improvements are mainly in the better design of furnace and chimney leading to better combustion performance. About 10% reduction in fuel (bagasse) consumption and cleaner chimney emissions apart from increased life of the *bhatti* (8 to 10 years) were achieved. This also resulted in increased *gur* production. The cost of the improved *bhatti* is higher as compared to the conventional design *bhatti*, but the extra cost incurred can be recovered within two *gur* production seasons.

PCRA is giving subsidy for partial or full adoption of IIP's improved *gur bhatti* technology. But so far only three owners have adopted the partial and another one,

full improvement in their *gur bhattis*. IIP is making efforts to popularize the improved *gur bhatti* technology in villages.

The main objective of the present workshop was to make aware the *gur bhatti* owners about the improvement in technology and to inform them about the incentive offered by PCRA in this regard.

Welcoming the participants, Dr M. O. Garg, Director, IIP, said that the IIP scientists who visited the *gur bhattis* in the nearby villages had found a lot of scope for improvement in these *bhattis*. He said that a detailed design was prepared and based on this design a *gur bhatti* in Miyanwala was adopted by IIP. He informed that PCRA supported the project and announced incentives.

Dr A. K. Goel, Director, PCRA, said that by adopting the improved technology the *bhatti* owners would have definite economic benefits. Additionally the smoke-free



Dr A. K. Goel, Director, PCRA, delivering his address during the workshop and the participants visiting the improved *gur bhatti* using IIP technology

environment would help them in maintaining good health. He reiterated that PCRA has already announced an incentive of Rs 20,000 for those who adopt the improved technology fully including the incorporation of fire bricks in the furnace, while Rs 5,000 would be given to those who adopt this technology partially, i.e. without fire bricks. Dr Goel presented a cheque of Rs 20,000 to Shri Prakash Chand of Biharigarh for adopting the technology completely.

Dr Rajendra Dobhal, Director, Uttarakhand State Council of Science & Technology, Dehra Dun said that IIP, a world class research institute, has the mandate of developing technologies for petroleum refining and related industry. Realizing the social obligations, the scientists of IIP studied the problems of villagers. Seeing the drawbacks of the traditional *gur bhatti*, the scientists came out with improved design. He assured all possible help from Uttarakhand Government to popularize the improved *gur bhatti* in all the villages.

The coordinator of the workshop and scientist IIP Shri U. K. Jaiswal gave an account of the budget estimate required for improving the traditional *gur bhatti*. He said that the total expenditure is Rs 13,000 which includes a platform for feeding of bagasse, fire grating, improved chimney and dampers in the chimney to control flow rate. A return of Rs 16,000 per season of *gur* making (about six months) is expected on account of savings in bagasse and increase in the rate of production of *gur*.

The owners of the *bhatti* who had adopted the technology discussed their experiences on the improved technology. The other problems of the *gur bhatti* owners were also discussed.

Workshop on Setting up of Institutional Repositories using DSpace

Information Centre for Aerospace Science and Technology of the National Aerospace Laboratories, Bangalore, organized a workshop on 'Setting up of Institutional Repositories using DSpace' during 6-10 September 2007 at the ICAST Digital Laboratories. The workshop was sponsored by the CSIR's Human Resource Development Centre (HRDC). Dr Naresh Kumar, Head, RDPD/HRDC, CSIR, delivered the inaugural address. Dr J. J. Isaac, Acting Director, NAL, presided over the function.

In his welcome speech Dr I. R. N. Goudar, Head, ICAST, gave an overview of developments on 'open access initiative' in the world and mentioned about four channels of open access for research communications including subject based e-prints archives, open access journals, institutional repositories (IRs) and self-archiving on author's website. Presenting the current scenario, he said that more than 900 IRs have been set up in the world out of which India accounts for about 25. IRs give wider exposure to the research output and thereby increase the impact factor value of the concerned journal. He also mentioned the contribution of Advisory Committee on CSIR LICs, which was headed by Dr Naresh Kumar, in identifying the five target services to be implemented at the earliest, out of which IRs is one. As the first step towards implementing the decision taken in the meeting of Heads of CSIR LICs held recently at Ghaziabad this workshop had been arranged at NAL. Dr Goudar introduced the Chief Guest and the resource persons Dr A. R. D. Prasad and Smt. Devika Madalli from ISI/DRTC and their team to the gathering.

Dr Naresh Kumar in his inaugural address narrated the efforts put in over the last 8-9 years to bring out the Manual for Procedures and Practices for Managing CSIR LICs. He recalled the contributions of CSIR LIC colleagues like Dr Goudar, Dr Tapaswi, Dr Krishnan, Dr Dhawan, Shri Sadasivan, etc. for this cause. He also mentioned about the need to implement the target services identified including online public access catalogue of all the CSIR libraries. While concluding his remarks, he assured his unstinted support to CSIR LICs including financial support. Dr A. R. D. Prasad released the CD containing the presentations, DSpace Software and many useful documents on IR.

Dr J. J. Isaac in his presidential remarks expressed his happiness about the ICAST services and the latest initiatives taken to meet the ever-growing needs of the user community. Smt. Poornima Narayana, Deputy Head, ICAST, proposed a vote of thanks.

More than 25 participants from 16 CSIR laboratories participated in the workshop. Apart from lectures an intensive hands on experience was also arranged. The resource persons were drawn from ISI/DRTC, IISc, GE and the host.



National Workshop on Design of Experiments for Scientists and Engineers

The Indian Institute of Chemical Technology (IICT), Hyderabad, and CSIR Human Resource Development Centre (HRDC) jointly organized a two-day workshop on 'Design of Experiments for Scientists and Engineers' on 16-17 August 2007.

Inaugurating the workshop, Dr J.S. Yadav, Director, IICT, highlighted the importance of Design of Experiments and mentioned about the high caliber of the IICT scientists in the area, who were going to serve as faculty.

Dr C.V.S. Murty, Head, Chemical Engineering Division and Convener of the workshop, said that main objective of the workshop was to impart knowledge to the participants on the best way of doing experiments, so that this could contribute to enhancing productivity of the nation in terms of conservation of precious resources such as time, raw materials, reagents, etc.

The workshop covered: Correlation analysis and regression modeling; Optimization, basic designs and factorial designs of experiments; Toguchi approach for robust designs; Optimization of quality parameters by reduction in variation -I and variation -II, etc. Later software demonstration was also done for the benefit of the participants. About 40 participants from academic institutions, R&D organizations, industrial establishments attended the workshop.

Modern Design Practices in Aerospace and Allied Areas

Amrita Vishwa Vidyapeetham recently organized a Faculty Development Programme (FDP) with "Modern Design Practices in Aerospace and Allied Areas" as its main theme. The event at the Amrita Institute, Coimbatore, was organized in collaboration with the National Aerospace Laboratories (NAL), Bangalore, and Hindustan Aeronautics Limited (HAL). Dr S. Viswanath, former Head, Structures Division, Dr S. Sridhara Murthy, Jt. Head, Structures, Dr Manoj Nair, Scientist, CTFD Division and Dr Kidambi Rangachari, Scientist, CTFD Division, delivered a series of lectures. Dr Balakrishna, General Manager and Shri K. S. Narayana Rao, Chief Designer of HAL also delivered lectures. The lectures covered aspects of failure investigation, re-qualification of dynamic components, ceramic structures, finite element modelling, low Reynolds number flows and design optimization. The FDP is essentially aimed to highlight modern practices in the area of engineering design with a view to bridging the gap between what is being taught in classrooms and what is being practiced in industry and R & D establishments. Indeed, it is a remarkable step by Amrita.

Amrita institute is proving to be very forward looking with its intention to enter into an MoU with NAL in order to introduce a cooperative programme in training and research. The MoU will be signed soon. This will enable students from Amrita institute to avail research facilities at NAL and tap the expertise available with the scientists. In return, Amrita institute will recognize NAL as a research centre. Thus, the MoU will be mutually beneficial. The scope of the MoU is expected to include possibility for some NAL scientists to register for degree courses at Amrita and provide an opportunity for others to serve as guest faculty. NAL scientists can also play role in selection of students, avail e-learning facilities and so on.

Dr Dwijendra Singh elected FRES

Dr Dwijendra Singh Scientist F and Head, Entomology Division, Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow, has been elected a Fellow of the Royal Entomological Society, London. An M.Sc (Ag) (Entomology) from Kanpur University, (1974) and Ph.D. from Banaras Hindu University, Varanasi (1977), Dr Singh has been with CIMAP since the past 29 years. His major contributions include development of technology for pulse grain protecting tablet, organic method of pest management in medicinal and aromatic crop plants, identification of allelopathic plant to manage mustard aphids in field, and screening of a large number of botanicals



for biopesticides against various pests of economic importance, etc.

Dr Singh has published around 75 articles in national / international journals and has three Indian patents and one US patent to his credit. Other honours and awards won by him include CSIR Hindi Book Writing Puraskar (1993), CSIR Technology Award (1999), INSA COSTED Fellowship (1998), DST Travel Grant (1988 & 2000), Bioved Fellowship Award (2003) and Dr Anand Prakash Award (2005). He

has participated in around 37 conferences/seminars/workshops/symposia, including three held in United Kingdom, Republic of China and Thailand and delivered lectures. He is on the editorial board of *Wealth of India-Raw Materials* (Second Supplement series 2006-2008) published by NISCAIR (CSIR) and in past, was on the editorial board of *Current Research on Medicinal and Aromatic Plants* (now JMPS) published by CIMAP, Lucknow. He has been Principal Investigator of two sponsored projects of DBT, Government of India and evaluator of various projects for funding.

Dr Dileep Kumar elected NAS fellow

Dr M Dileep Kumar, Scientist, National Institute of Oceanography (NIO), Goa, has been elected a Fellow of the National Academy of Sciences, India. He is already a Fellow of Indian Academy of Sciences, Bangalore (1999) and the Indian National Science Academy (2005).

Dr Dileep Kumar's main area of interest has been biogeochemistry of the Northern Indian Ocean. He is a Nodal Officer for a supra-institutional project "Science for development of a forecasting system for the waters around India" at NIO. He has 65 publications in several prestigious journals and conference proceedings.

NEIST Scientists' Research Publications find place among the 'Top 25 Hottest Articles' of `ScienceDirect`

Two research publications of Dr N. C. Barua, Scientist F and his team working on the Natural Products Chemistry at North - East Institute of Science and Technology (NEIST), Jorhat, figure among the 'Top 25 Hottest Articles' in Chemistry — *Tetrahedron: Asymmetry* on global perspective as estimated by `ScienceDirect` for each of the first quarter of two consecutive years, viz. 2006 and 2007. The research publications are-

- (i) Catalytic asymmetric Henry reaction - review article, *Tetrahedron: Asymmetry*, Volume 17, issue 24, 1 December, Pages 3315-3326 authored by Bruwa J., Gogoi N., Saikia P. P. and Barua N. C.
- (ii) Stereoselective total synthesis of (+)- boronolide, *Tetrahedron*, authored by Boruwa J. and Barua N. C.



Dr A. R. Upadhyia elected as Corresponding Member of IAA

Dr A. R. Upadhyia, Director, National Aerospace Laboratories, Bangalore, has been elected a corresponding member of Section 4 (Social Science) of the International Academy of Astronautics. The diploma was handed over to Dr Upadhyia in the Academy meeting at Hyderabad on 23 September 2007 during the International Astronautical Congress.

NAL receives Best Exhibitor Award at IAC Space Expo : 2007

The National Aerospace Laboratories (NAL), Bangalore, received Best Exhibitor Award in the category “Most Informative Display” at the International Astronautical Congress (IAC) and Space exhibition held during 24-28 September 2007 at Hyderabad.

The expo provided an opportunity to NAL to showcase its

capabilities and technologies. The exhibition witnessed the participation of internationally renowned organizations from aerospace and astronautic industry. Many visitors showed keen interest in radome technologies. Student community of the aeronautical engineering were also very keen in taking up projects at NAL. The

58th session of IAC was hosted jointly by ISRO and Astronautical Society of India, at the International Convention Centre in Hyderabad. The International Space exhibition was at the HITEX complex adjacent to the Convention Center

NAL. team comprised Shri C. V. Giriraj, Shri M. Gopinath, Dr M. N. Sathyanarayana.



Printed and Published by S.K. Rastogi on behalf of National Institute of Science Communication and Information Resources (CSIR), Dr K.S. Krishnan Marg, New Delhi -110 012 and printed at NISCAIR Press, Dr K.S. Krishnan Marg, New Delhi -110 012

Editor: Dr B.C.Kashyap; Associate Editors: Meenakshi; Vineeta Singhal; Editorial Assistant: Neelima Handoo;

Design: Pradip Banerjee; Sarla Dutta; Production: Kaushal Kishore

Phone: 25846301 Fax: 25847062 E-mail: bck@niscair.res.in; meenakshi@niscair.res.in; vineeta@niscair.res.in; Website: <http://www.niscair.res.in>

For subscription: The Sales & Distribution Officer, NISCAIR; E-mail: sales@niscair.res.in Annual Subscription: Rs 300 Single Copy: Rs 15.00

Subscription Complaint No 25843359