Details for Annual Report – 2011 - 12

NIPER-AHMEDABAD

National Institute of Pharmaceutical Education and Research – AHMEDABAD
c/o B. V. Patel PERD Centre,
S.G. Highway, Thaltej, Ahmedabad-54, Gujarat, India

CONTENTS

RESEARCH ACTIVITIES

DEPARTMENT OF BIOTECHNOLOGY

Effect of Mycobacterial lipid and Freund's adjuvant on permeability of blood brain barrier (BBB)

In this study, the aim is to elucidate the effect of Mycobacterial lipids and CFA on the *in vitro* model of BBB.

Alleviating cancer chemoresistance using NF-κB inhibitors

The project involves the evaluation of the therapeutic effect of NF-κB inhibitors on cell lines which express mutant K-RAS with EGFR overexpression.

Stimulation of neuronal precursors using natural products in combination with neurotrophic factors

The aim of the project is to stimulate the neuronal precursors using some selected plant extracts in combination with neurotrophic factors.

Evaluation of interplay between STAT3 and Survivin in mediating cancer chemoresistance

The aim of present study is to establish cancer cell line models to study the effect of activated STAT3/survivin in mediating cancer chemoresistance through DNA repair pathway and membrane efflux mechanisms.

Development of recombinant *Lactococcus lactis* for delivery of antigen in to intestinal lumen against diarrhoeal diseases

In this project the aim is to use the food grade system of *Lactococcus lactis* for the development of mucosal vaccine against Infectious diarrhoea.

Use of molecular and chemical approaches for the enhancement of Therapeutic protein expression in CHO cells.

In this project two approaches are to be carried out for the enhancement of protein expression: - a) molecular approach-use of antiapoptotic gene to enhance cell viability, b) chemical approach-use of chemicals inducing cell cycle arrest to enhance protein expression.

A non viral vector based method for inducing pluripotency

The project involves the use of a 'minicircle' DNA, as a vector for the delivery of reprogramming factors to induce pluripotency in human somatic cells.

Functional Expression of Recombinant Fusion Protein against Tumor-Associated Antigen, ErbB2 in Plant System

The present project involves construction and expression of a recombinant fusion protein, anti-erbB2, scFv-Fc-IL-2 with a molecular weight between whole antibody-IL-2 and scFv-IL-2 fusion protein in plant system.

Constitutive Expression of Blood Anticoagulant, Hirudin in Plant System

The project focuses on constitutive expression of hirudin in *Nicotiana tabacum* using *Agrobacterium*-mediated transformation.

Cloning and Expression of Recombinant Fusion Protein in *Nicotiana tabacum*

The project focuses on establishing plants as an alternative expression system for production of recombinant fusion protein, anti-ebrB2, scFv-Fc-IL-2.

Dissertation: *In vitro* Comparative Assessment of Therapeutic Value of shRNA and Small Molecule Inhibitors for Cancer

The aim of the project work is to select and test the efficacy of anti-*BCL2* shRNA in various cancer cell lines, and its effect on apoptosis induction alone and with compared to small molecule inhibitor.

DEPARTMENT OF MEDICINAL CHEMISTRY

Structure based design, Synthesis and 3D QSAR studies of novel pyrido-[1,3,5] triazines as potential anticancer agents.

The main objectives of this study are to design, synthesize, characterize and *In-vitro* assessment of novel series of pyrido-triazines derivatives as anti-cancer agents, taking the compound PMCR-242 as a lead molecule, discovered by Dept. of Medicinal Chemistry, PERD centre. The possible interactions of the designed molecule with NF-κB DNA binding site will be explored by molecular docking study and the structure activity relationship of chemical structure with biological activity values will be established by 3D QSAR.

Novel triazines as potential anti-inflammatory agents & their potential implication in the management of Alzheimer's Disease

NSAID'S inhibit the generation of the super oxide anion radical and thus they are found to be potential candidates for Alzheimer's disease. Based on the structures of some NSAID's novel heterocycles like triazine have been designed. These molecules would be synthesized and assessed preclinically for their potential anti-inflammatory and antioxidant activity. The QSAR study would be done to enhance their potential activity.

Lead based drug design, synthesis, and QSAR studies of novel fused pyrimidine analogues as potential anti-mycobacterial agents

Tuberculosis, is a major health problem in developing countries. So the present work aim towards the development of novel small heterocycles based on chemical lead (pyrimidin) that can serve as potential antimycobacterial agent. Thus fused pyrimidino-triazine, and fused pyrimidino-thiazole systems were designed. They will be synthesized, characterized, and tested for their antimycobacterial potency *in vitro.* The 3D QSAR studies will be carried out to study the meaningful structure activity relationship and to establish the structural requirement for the further development.

DEPARTMENT OF NATURAL PRODUCTS

Pharmacokinetic studies

Studies are carried out for comparing the pharmacokinetics profile of formulations of *Picrorrhiza kurroa* with that of the isolated Kutkin – the chief marker compound present in the roots and rhizomes of *Picrorrhiza kurroa*, in *Sprague-Dawley* rats.

Neuroprotection and regeneration

Few plants of ISM *viz*. *Glycyrrhizia glabra*, *Nerium indicum*, *Benincasa hispida*, *Jugulans regia* are being screened for its neuroregenerative activity. It involves detailed phytochemical evaluation of the plants, observe neuritogenesis on IMR -32 cells, observe neurogenesis and differentiation of hippocampal cells, and observe their neuroprotective effect.

Stress degradation studies of natural compounds

Forced degradation studies on berberine and its pharmaceutical dosage form is being carried out. For this purpose, a selective and validated stability-indicating HPLC assay method for berberine is being developed.

Synthesis and Development of New Chemical Entities (NCE) of Natural Scaffolds as Antimycobacterium and Antiimplantaion Leads

The Department of Natural products is actively engaged in synthesis and development of New Chemical Entities(NCE) of Natural Scaffolds (Pharmacophores) in order to generate bioactive leads with enhanced activity and reduced toxicity, which can further be developed into potential drug candidates. In this context different class of compounds like triterpenoid and naphthoquinone moieties have been selected for synthesis of a series of analogues and will be screened for antimycobacterial activity on *Mycobacterial bovis* and *M. tuberculosis*, determination of cytotoxicity on mammalian cell lines.

Chemotaxanomy

In India, there is high level of morphological similarity among the species of the Genus *Phyllanthus* (Euphorbiaceae) and the Genus *Terminalia* (Combretaceae) but differ in pharmacological and therapeutic properties. Also the taxonomic controversies plaguing the group, raw drug samples often contain species admixtures. Chemoprofiling along with DNA fingerprinting can be used for the identification of species. Currently *Phyllanthus* and *Terminalia* species of Gujarat are being studied using Integrative taxonomy.

Moreover, intra-species variation in *Bacopa monnieri* : Studies are going on for developing correlation between phytochemical content of the *Bacopa monnieri* with the DNA fingerprinting profile and distinguishing the low and high yielding varieties.

Standardization of polyherbals

Avipattikar Churna one of the most reputed drugs in Ayurveda has been extensively studied for its medicinal applications. The present work aims to formulate *Avipattikar Churna* and develop methods for its standardization and quality control parameters, and compare them with the marketed formulations.

Evaluation of Phytochemical groups for the treatment of Asthma and Arthritis

Saponins are known to inhibit IL-4 and IL-13 so that production of Ig-E decrease. Flavonoids are known to inhibit cyclooxygenase and 5- lipoxygenase. Therefore the present study is to evaluate the anti-asthmatic activity of flavonoid and saponin rich extracts from plants.

Plant derived compounds such as alkaloids, glycosides and terpenoids shows anti-inflammatory as well as anti-arthritic activity. The present work aims to access the potential of these compounds towards anti-arthritic activity

DEPARTMENT OF PHARMACEUTICAL ANALYSIS

Analytical method development and validation

Students are actively pursuing analytical method development for indapamide, xipamide, as well as simultaneous determination of a combination of aspirin, clopidogrel and atarvastatin.

A project involving development of a stability-indicating method of a combination of doxofylline and terbutaline by HPLC under GLP norms is in progress.

Bioanalytical method development and validation

Currently, method development projects for determination of fenofibrate from plasma as well as a combination of hydrochlorothiazide, losartan from rat / rabbit plasma are underway.

Impurity profiling

In addition to the method development for indapamide and xipamide as stated above, an impurity profiling study would be undertaken. This method would then be compared with a gas chromatographic method, and comparisons drawn between the two.

DEPARTMENT OF PHARMACEUTICS

Department of pharmaceutics at NIPER, Ahmedabad is equipped with state of art facility for formulation development and currently the department is involved in the formulation development of various conventional dosage form and novel drug delivery systems projects to facilitate which, we have added newer instruments like high pressure homogenizer and high shear mixture granulator, DSC etc. Currently the focus is on lipid based system, with few projects going on in the area of nanostructured lipid carrier (NLC), bilayer lipids carriers and solid Self emulsifying drug delivery system. Besides this an oral platform technology for delivery of protein drug is also being worked upon. Nimodipine, a P-glycoprotein substrate, indicated for acute stroke therapy, suffers from, low aqueous solubility (2.30 µg/ml intrinsic solubility), and extensive first pass metabolism. A Microemulsion based delivery system, combined with *in situ* gelling, and mucoadhesive is under development which if successful will improve the overall bioavailability of drug. Estimation of compatibility of any formulation with excipient is major criteria which determines the rate at a which product can be launched in market. Differential scanning calorimetry is one such method which is often used for estimation of compatibility, and is considered to be reliable and early predictor of stability. Studies based on enthalpy values and its contribution in predicting compatibility and incompatibility are also ongoing. The result obtained so far are promising and few more

studies are needed to confirm the same. Other than this, students of MS pharm pharmaceutics are actively participating in international conferences like Controlled Release Society (Mumbai), IPC, Nanoschool (Mohali) etc. Students of department have received first Prize at 'MYRIAD - The Cluster of Events (Nanotechnology based Drug Designing) organized by Institute of Research and Development, Gujarat Forensic Science University. Four papers have been accepted for publication in international journals from the department. The department is actively involved in writing research grant proposal for procuring funds from different agencies like DBT, Inspire etc.

DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY

The department of pharmacology is involved with the following projects:

- Role of tri-substituted thiazole as an adenosine receptor antagonist to down regulate the levels of IL4, IL6 and TNF-α in asthma
- Role of TLR4 Antagonist *Rs*LPS focusing on down regulation of death receptor 6 (DR6) which are over expressed in neuronal injury found to be novel target for Stroke
- Intestinal absorption studies of P-glycoprotein substrate in diabetes - correlation with disease progression with HPLC method, developed and validated for analyzing the drug and P-glycoprotein inhibitor in intestinal perfusate.
- Novel NF-kB and AP-1 inhibitors for the treatment of Rheumatoid Arthritis, in *in vitro* and *in vivo with clinical assessment*
- Pharmacokinetic profile of synthesized bis-thiazole as novel anti-inflammatory agent, *in vivo*
- *In situ* gelling mucoadhesive system for brain delivery of a model p-glycoprotein substrate via nasal route
- Gastrointestinal mucoadhesive patch system - protein loaded nanoparticles in order to overcome the major hurdles in the oral protein delivery is overcome due to opening of paracellular pathways & an enhanced bioavailability of the proteins
- Bioanalytical method development and validation of Rosuvastatin and Fenofibrate - Application of method to pharmacokinetic study
- Simultaneous determination of aliskiren, valsartan, sitagliptin & Pharmacokinetic study
- Effect of alkaloids, glycosides and terpenoids on arthritis by mechanistic pathway of by using various bioassays mimicking arthritic condition
- Therapeutic potential of saponins and flavonoids from natural sources in asthma with their mechanism of action
- The attainment of significant difference in the oral bioavailability of Picroside I and Picroside II upon administration of single compound, extract and as formulations
- Anti- implantation activity of herbs and some phytoconstituents viz lupeol, gallic acid, gallicin, β-sitosterol and corosolic acid.

ACADEMIC ACTIVITIES

ADMISSION OF STUDENTS IN 2011-2012

NIPER Ahmedabad stepped into fifth academic year from July 2011. In the fifth academic year, 47 students were admitted to six streams.

Discipline	No. of Students admitted	
	(2011-12)	(2010-11)
Natural Products	09	15
Pharmaceutics	12	17
Biotechnology	10	12
Pharmaceutical Analysis	06	06
Medicinal Chemistry	05	03
Pharmacology and toxicology	05	05
Total	**47**	**58**

Teaching schedule for the Academic Year 2011-12

1st Semester

Teaching started with the orientation week on the 4th week of July 2011. Regular teaching schedule followed the week after.

Weekly, four seminars were scheduled for the First semester students.

The Mid-term exams were scheduled from 10th to 19th October 2011 and the Final Exams are scheduled in December 2011.

3rd Semester

Third Semester started form the third week of July 2011. The students submitted their Project proposals in the First week of August 2011 followed by the Project Proposal Defense. The Project Progress Evaluation is scheduled in December 2011.

NIPER-PH. D. Program

NIPER-Ph. D. program has been started at NIPER-Ahmedabad during the academic year 2011-2012. Six Ph. D. fellows were enrolled on the basis of common NIPER-Ph. D. entrance test. Three Ph. D. fellows were taken up in the Natural products stream and three Ph. D. were recruited in the Biotechnology. The fellows have been assigned their Ph.D. mentors and are pursuing their doctoral degree.

INDUSTRIAL VISIT

A visit to Vasu Health Care Pvt. Ltd., Baroda

Vasu healthcare has its inception since 1980 and has been taking consistent strides in healthcare sector to serve mankind. It is an ISO 9001:2008, GMP and HACCP Certified Company. It deals mainly with patented Ayurvedic products and takes care to conduct rigorous trials and authentication of process. Our Natural Products department has planned one day visit in Vasu Healthcare for growing up their knowledge in various departments. Students were introduced to Vasu Healthcare and Vasu Research Centre through a corporate video followed by a visit to various departments including Research & Development, Quality Control, Production area etc.

Industrial Visit to Vasu Healthcare Pvt. Ltd., Baroda

CONFERENCE/WORKSHOP'S ORGANIZED

1. 4th Indo-Australian Conference on Innovations in Biomaterials, Tissue Engineering and Drug Delivery Systems, Organized at Sardar Patel University, Vallabh Vidyanagar, Gujarat, from February 10 – February 12, 2011.
2. Mammalian Cell Culture: Hands-On Training Programme, Organized at B. V. Patel PERD Centre, from June 27 – June 2, 2011
3. Molecular Biology: A Laboratory Training Course, Organized at B. V. Patel PERD Centre, from July 11 – July 15, 2011

MAMMALIAN CELL CULTURE: HANDS ON TRAINING PROGRAMME

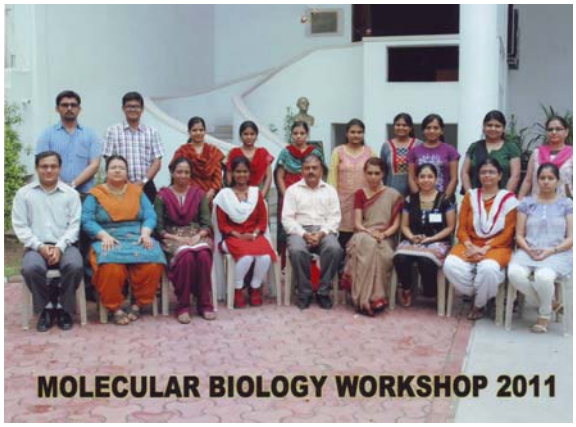
June 27 – July 2, 2011

As a part of continuing education program, PERD centre conducted a hands-on training workshop on mammalian cell culture, to provide the participants the basic theoretical and practical knowledge about the intricacies of cell culture. The training imparted during the workshop included the basic maintenance of cell lines, isolation and establishment of primary neuronal cultures, drug uptake studies using primary macrophages, transfection, cell viability assays, cytotoxicity assays, cell differentiation studies and immunocytochemistry. The theory and the practical session of the workshop were well appreciated by the participants.

Experimental Session

MOLECULAR BIOLOGY: A LABORATORY TRAINING COURSE
July 11 – July 15, 2011

Recently PERD centre, conducted its 7th annual hands-on training workshop in molecular biology techniques as a part of the Continuing Education Programme of B. V. Patel PERD Centre. The objective of this workshop is to familiarize participants with concepts pertaining to basic molecular biology principles and techniques applied in various research fields like genomics, cell biology, biotechnology, microbiology, diagnostics and therapeutics. As always the participants were allowed to perform hands on experiments so as to get practical exposure. The participants were highly satisfied with the theory and practical sessions of the workshop. Overall the workshop was well appreciated by the participants.



Participants of the workshop

PROJECTS

PROJECT ON TUBERCULOSIS

- **DOP funded project (worth 1.0 Crore)** titled 'Development and Clinical Evaluation of Novel fixed dose combination of Rifampicin and Isoniazid to improve Bioavailability of Rifampicin for the treatment of Tuberculosis' **in collaboration with AIIMS- New Delhi**.
- Clinical Trials are going on at AIIMS with **50 TB Patients**.

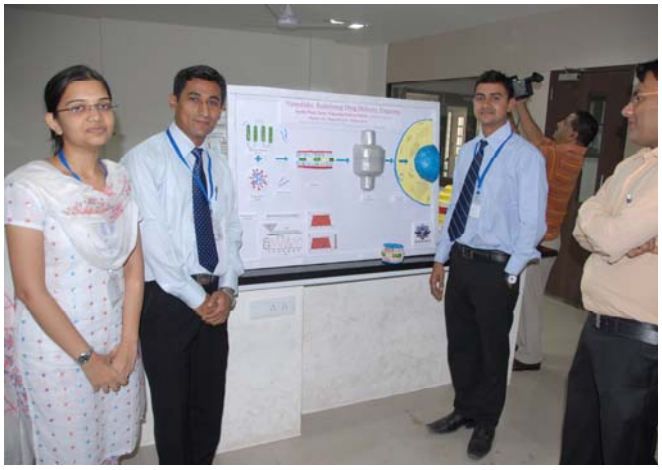
HONOURS/AWARDS

First Prize – Special Award by Royal Society of Chemistry-Process Technology Group (RSC-PTG, London) in Process Chemistry
Hitesh B. Jalani, Amit N. Pandya, Arshi B. Baraiya, Brianna Jill Williams, V. Sudarsanam, Kamala K. Vasu. Synthesis of quinazolinon-2-yl-tetrasubstituted thiophenes as modulator of NFκB and AP-1 transcription factor. Presented at 15th ISCB International Conference, Rajkot, Gujarat, 4th -7th February 2011

Best poster –
Yeolepatil P, Baraiya A, **Agarwal M**, Lakshmi S, Vasu K- Chemosensitizing effect of NF-κB inhibitors in *in vitro* model of acquired cancer chemoresistance. International Symposium on Cancer Biology, organized by National Institute of immunology, New Delhi from 14-16 November 2011.

First Prize:

Kalavadia Samir, Patel Sandip, Pathak Rudree. 'Nanodisks: Redefining drug delivery targeting'. A Model presented at 'MYRIAD – The Cluster of Events (Nanotechnology based Drug Designing). Organized by Institute of Research and Development, Gujarat Forensic Science University, Gandhinagar on 14 November 2011.



Kalavadia Samir, Patel Sandip, Pathak Rudree presenting the Model

RESEARCH PUBLICATIONS

1. Patil, S., Dash, R.P., Anandjiwala, S. and Nivsarkar, M (2011) *Biomedical Chromatography* (Accepted Manuscript).
2. Yadav, H., Mungara, P., Jivrajani, M., Nivsarkar, M and Anandjiwala S (2011) *Journal of Liquid Chromatography and Related Technologies* (Accepted Manuscript).
3. Pramod Bhise, Aliasgar Shahiwala, Manju Misra (2011). Archives of Pharmacy Practice 3(1): (Accepted Manuscript).
4. Nilesh Bagul, Aliasgar Shahiwala, Manju Misra (2011). Archives of Pharmacy Practice 3(1): (Accepted Manuscript).
5. Hitesh B. Jalani, Amit N. Pandya, Arshi B. Baraiya, Jitendra C. Kaila, Dhaivat H. Pandya, Jayesh A. Sharma, V. Sudarsanam, Kamala K. Vasu (2011) *Tetrahedron Letters 52*, 6331-6335
6. *Tejas Vyas, Ranjeet Prasad Dash, Sheetal Anandjiwala, Manish Nivsarkar* (2011). *Fitoterapia.* 82, 446–453.
7. Rathee Dharmender, Thanki Madhavi, Agrawal Reena, Sheetal Anandjiwala (2011). *Journal of Liquid Chromatography & Related Technologies*. 34:360–374.
8. Jain V, S.K. Verma, S.S. Katewa, S. Anandjiwala and B. Singh (2011). *Res. J. Med. Plant.* 5(4): 462-470.
9. Hitesh B. Jalani, Jitendra C. Kaila, Arshi B. Baraiya, Amit N. Pandya, V. Sudarsanam, Kamala K. Vasu (2010) *Tetrahedron Letters*, *51*, 5686-5689

PLACEMENT ACTIVITIES

- To provide placement to student at reputed Pharma companies, a placement Cell (including the faculty members as well as the students of NIPER-A) has been created which is responsible for publishing a placement brochure and sending it to various Pharma companies.
- Various companies have been visiting our organization for Campus Interviews.
- Our students have been placed in about 16 Pharma companies. About 80 % of the students have been placed from the third that recently passed out in June 2011.

EXTRACURRICULAR ACTIVITIES

'*Hindi Samaroh*' (14th to 17th September 2011)

14th September is celebrated as Hindi Divas because on this day Hindi was declared as official national language by Indian Constitution. To revive the interest of Hindi in the NIPERD family, *Hindi Samaroh* was organized from 14th to 17 the September 2011. Various events *viz*. *Swakavita Pathan, Antakshari, Prashna-Uttari* and *Vad-Vivad Pratiyogita* were organized. On the concluding day, the chief guest, Prof. Dr. Harish Padh distributed the prize to the winners. All in all it was a fun week where both the students and audience enjoyed a lot and realized the importance that Hindi language carries in their life.

Winners of '*Antakshari*' with Prof. Harish Padh

Celebration of Independence Day

Flag Hoisting

Lemon-spoon Race

Navratri Celebration

Ganesh Utsov

Sports activities