

## **ACHIEVEMENTS OF NIPER-AHMEDABAD**

### **RESEARCH ACTIVITIES**

#### **DEPARTMENT OF BIOTECHNOLOGY**

##### **Enhancing the expression of therapeutic proteins in mammalian cell line (CHO cell line) using different strategies**

Recombinant therapeutic proteins (RTPs) produced in mammalian cells represent a major class of biopharmaceuticals and a majority of them are produced using CHO cell lines. A major limitation of CHO cell lines being the low yield of protein and hence the higher cost, the goal of current project is to decrease the production cost by increasing the recombinant therapeutic protein yield from CHO cell lines by increasing the cell specific productivity by using cell cycle growth arrest strategy (isolating cells at G1 phase) and also by increasing the cell viability by reducing factors responsible for apoptosis of cells.

##### **In vitro and in vivo evaluation of some selected novel NF- B activators as radioprotectors**

Ionizing radiation like gamma rays is used to treat many malignant neoplasms. The aim of radiotherapy is to destroy cancer cells with little damage to the normal cells. Radioprotectants are a class of drugs that may selectively alleviate negative irradiation effects on normal tissue while allowing desirable negative effects on cancerous tissue. The main objectives for this study are:

- Evaluating *in vivo* the radioprotective effects of Novel Chemical Entities (NCEs) that have been shown to activate NF- B *in vitro*
- Testing the selective effects of different compounds (radioprotectants) including NCEs on normal cells as well as cancer cells.

We aim to contribute to the development of a novel radioprotective compound so as to overcome the side effects of radiotherapy given to cancer patients.

##### **Bioengineering *Lactococcus lactis* for the development of mucosal vaccine against *Shigella Dysentriae* Type-1**

The aim of work is to transform *Lactococcus lactis*, an innocuous bacteria used in food industry since decades, with the plasmid carrying antigenic gene sequence of *Shigella dysentriae* type-1. The resultant recombinant strain of *Lactococcus lactis* is confirmed for the heterologous protein formation at DNA, m-RNA and protein level by respectively performing PCR, RT-PCR and Western blot analysis.

##### **Strategies to enhance the protein expression level in CHO cell line**

The primary aim of the project is to analyze the correlation between transfection efficiency and expression level of the transfected gene, employing different transfection methods which includes electroporation, calcium phosphate mediated transfection, polyplex and liposome based transfection in CHO cells. As the mammalian cell line are the preferred choice of an expression system where product authenticity is primary concern. But due to its low yield, the

final costs of products are pricey. To play down it, here we need to come up with the transfection methods that can produce higher yield and thus lower the cost.

### **In vivo & In vitro Neuroprotective Effect of TLR4 Antagonist in Stroke and Stroke induced seizures**

Stroke is the leading cause of death after cardiovascular disease and cancer. It involves rapidly developing loss of neurological function due to disturbance in the blood supply to the area of brain. But the penumbra, surrounding that area remains active for some period due to the supply of blood by the collateral arteries and TLR4 antagonist will help to stop the further worsening and assist in the survival of penumbral area. This project involves the neuroprotective effect of TLR4 antagonist on “*in vivo* middle cerebral carotid artery occlusion (MCAO) model of stroke.” But there is possibility of occurrence of seizures in recovered cells due to increase in the level of glutamate in the brain. Hence to study the effect of TLR4 antagonist on seizure, it also involves “*in vitro* model of glutamate induced seizures” in the hippocampal neurons

### **Chemosensitising Effect of Novel NF- $\kappa$ B inhibitors**

NF- $\kappa$ B is recognised as an important player in mediating resistance to anti-cancer agents. Therefore it represents an attractive therapeutic target for treatment of cancer. The project involves evaluation of indigenously developed NF- $\kappa$ B inhibitor as chemosensitising agent in *in vitro* models of both acquired and innate chemoresistant cell lines. The project also includes analysis of effect of NF- $\kappa$ B inhibitor on expression of proteins such as IAPs, ABC transporters which are involved in mediating chemoresistance.

### **Gene silencing using RNAi technology**

The project conceptualizes the use of "RNA interference" (RNAi) technology to fight against Breast Cancer. Vascular endothelial growth factor isoforms A and C are found to be involved in growth and spread of the Breast Cancer through induction of angiogenesis and metastasis. Hence, simultaneous and multiple site targeted stable silencing of VEGF isoforms mRNAs can inhibit growth and metastasis of breast cancer. This can be achieved through construction of a vector which is expressing “multiple short hairpin loop RNAs (shRNAs)” against VEGF isoforms A and C, resulting in their simultaneous inhibition. As the vector is capable of being replicated in mammalian cells, the release of shRNA will be continued to the next generation, hence, providing stable inhibition of target mRNAs, resulting in long term inhibition of angiogenesis and hence metastasis in cancer cells.

### **Identification of genetic markers**

Many diseases in humans are caused by genetic variations within a gene along with other factors like environment, lifestyle, etc. Genetic factor confers susceptibility or resistance to a disease and influence the severity or progression of disease. Since we do not yet know all of the factors involved in these intricate pathways, researchers have found it difficult to develop screening tests for most diseases and disorders, such as diabetes, breast cancer many cardiovascular diseases, Alzheimer's disease, arthritis. The project aims to find such targets that can be used as a genetic marker for breast cancer and diabetes in Indian population.

## DEPARTMENT OF NATURAL PRODUCTS

### Pharmacokinetic studies –

There are lots ambiguities regarding to the dose, pharmacokinetics and safety aspects of herbal preparations. Studies are carried out for comparing the pharmacokinetics profile of Vasicine and Vasa Swaras formulated in capsule form; and formulations of *Berberis aristata* with that of the isolated berberine – the chief marker compound present in the root-bark of *B. aristata* leaves in *Sprague-Dawley* rats.

### Neuroprotection and regeneration –

Many of the plant derived products have been used in neuroprotection while some have been shown to have regeneration ability. *Tinospora cordifolia*, *Prunus amygdalus*, *Nerium indicum* are some of the plants from the Indian system of medicine that has been claimed for the neuroregeneration potential. A systematic study on these plants will lead to development of potential molecules that can be used in the treatment of neurodegenerative disorders.

### Radioprotection –

About half of all people with cancer are treated with radiation therapy, either alone or in combination with other types of cancer treatment. Development of an effective radioprotectors is of great importance. In Ayurveda, several plants have been used to treat free radical-mediated ailments and, therefore, it is logical to expect that such plants may also render some protection against radiation damage. Compounds like Ferulic acid, Berberine, Diosgenin are being evaluated for their radioprotective potential.

### Formulation development of natural products –

Lypophyllic derivatives of Berberine (isolated from the stem pieces of *Berberis aristata*) viz., dihydroberberine and tetrahydroberberine are being formulated into a topical formulation that can effectively deliver berberine into the skin. The said formulation will be effective in providing relief from skin lesions caused in Post Kala-azar Dermal Leishmaniasis.

Wounds and particularly chronic wounds are major concerns for the patient and clinician alike; chronic wounds affect a large number of patients and seriously reduce their quality of life. A Hydrogel sheet containing embelin, a wound healing agent, was developed as moist wound dressing for effective treatment of wounds with an added advantage of having anti microbial activity.

The conventional liquid ophthalmic formulation is eliminated from the precorneal area immediately upon instillation because of lacrimal secretion and nasolacrimal drainage. Ocular gels are helpful in increasing the contact time of the drug with *cul de sac* which in turn increases the absorption of the drug from the gel and thereby increasing the bioavailability of the same. Polymer based ophthalmic delivery systems of *Andrographis paniculata* extracts was developed having *in situ* gelling capabilities with sustained action to treat cataract.

### Synthesis and Development of New Chemical Entities (NCE) of Natural Scaffolds and Isolation of Bioactive 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 of the active NCEs will also be done on mammalian cell lines. Neuro-inflammation is involved in occurrence and progression of various CNS related diseases and disorders. Our research is focused on evaluation of neuroprotective effect of some specific secondary metabolites. The department has also taken up research work on screening of some Indian Medicinal Plants for anti-cancer activity employing bioassay guided isolation of the active lead and its cytotoxicity

## DEPARTMENT OF PHARMACEUTICS

The department of pharmaceuticals 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 projects based on development of novel carrier for DNA delivery, nanoparticle, solid dispersion, self-emulsifying drug delivery system, formulation of biodegradable microsphere, novel drug delivery systems etc.

The use of nanotechnology in medicine and more specifically drug delivery is set to spread rapidly. Currently many substances are under investigation for drug delivery specially to improve solubility and thereby bioavailability. Mucoadhesive nanoparticles as a novel ocular drug delivery system of moxifloxacin, a fourth generation synthetic fluoroquinolone antibacterial agent, was developed in order to extend its therapeutic action and to improve its bioavailability. Solid lipid nanoparticle of carvedilol phosphate, an antihypertensive agent was developed to improve its bioavailability.

Extended release tablets of alfuzocin hydrochloride for benign prostatic hyperplasia, rosuvastatin calcium for hyperlipidemia, tizanidine for spasticity, dipyridamole as platelet inhibitor, atenolol for hypertension were developed by various novel drug delivery techniques like controlled porosity osmotic pump, gastro retentive osmotic pump or swellable matrix system etc.

About 40% of marketed drugs are thought to be poorly water soluble and 70 to 90% of drug candidates in the pipeline are believed to have low solubility. In fact, solving solubility problems is considered to be the leading challenge in drug development. Nisoldipine, an antihypertensive agent was formulated with sustained released tablet using solid dispersion technique to improve its solubility and bioavailability. With the same object, maraviroc, an anti HIV agent was formulated as self emulsifying drug delivery system to improve its lymphatic uptake and thereby to be effective in the treatment of HIV infection.

Pulsatile systems are gaining a lot of interest as they deliver the drug at the right site of action at the right time and in the right amount, thus providing spatial and temporal delivery and increasing patient compliance. These systems are designed according to the circadian rhythm of the body. A pulsatile delivery system of valsartan, an angiotensin II receptor antagonist was designed and developed for effective treatment of high blood pressure and congestive heart failure

## ACADEMIC ACTIVITIES

### ADMISSION OF STUDENTS IN 2010-2011

NIPER Ahmedabad stepped into fourth academic year from July 2010. The institute had Masters level programme in three different disciplines till the third academic year, leading to M.S Pharm in Pharmaceutics, Natural Products and Biotechnology streams.

In the fourth academic year, three new streams have been added viz., Pharmaceutical Analysis, Medicinal Chemistry and Pharmacology.

<b>Discipline</b>	<b>No. of Students admitted (2010-11)</b>
Natural Products	15
Pharmaceutics	17
Biotechnology	15
Pharmaceutical Analysis	06
Medicinal Chemistry	05
Pharmacology and toxicology	05

### Teaching schedule for the Academic Year 2010-11

Teaching started with the orientation week on the 2<sup>nd</sup> of August 2010. Regular teaching schedule followed the week after.

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

The Mid-term exams were scheduled from 11<sup>th</sup> to 20<sup>th</sup> October 2010.

## 1<sup>st</sup> CONVOCATION

The Pioneer batch of NIPER-Ahmedabad which included 31 M.S. Pharm. Students, graduated in June 2009. They were conferred their Degree during the 1<sup>st</sup> Convocation held on June 25, 2010. The Governor of Gujarat - Dr. Shrimati Kamala Beniwal was the Chief guest and Shri Ashok Kumar, Secretary, Department of Pharmaceuticals, Ministry of Chemicals was the Guest of Honour.



Chief Guest – Dr. Shrimati Kamala Beniwal, Guest of Honour - Shri Ashok Kumar with other Guests on the Dias



First batch of NIPER-Ahmedabad students with Faculty Members and Guests

**CONFERENCE/WORKSHOP'S ORGANIZED****MAMMALIAN CELL CULTURE: HANDS ON TRAINING PROGRAMME  
June 16 – June 19, 2010**

Within a biologist's toolkit, animal cell culture has come to play a prominent role. In the pharmaceutical industry, cell culture is used to produce a significant proportion of biopharmaceuticals as well as monoclonal antibodies for diagnostic use. In addition, the use of animal cells is expanding in a wide range of other applications such as drug screening, tissue engineering, gene therapy, toxicology and traditional applications such as virology. The objective of this workshop was to provide comprehensive training in both theoretical as well as practical approaches pertaining to mammalian cell culture. The workshop aimed to provide hands on training on *Basic cell culture techniques (Culture and Maintenance of cell lines, Preparation of Culture medium, Plating etc.) Primary Cell Culture (Establishment of the culture from different tissue sources), Drug uptake studies, Transfection of cell lines, Cytotoxicity assays.*

**Experimental Session****Group discussion**

**MOLECULAR BIOLOGY: A LABORATORY TRAINING COURSE**  
**June 29 – July 3, 2010**

Molecular biology provides a foundation for work in the growing fields of genomics, cell biology, biotechnology, microbiology, diagnostics and therapeutics. The methods of molecular biology have transformed research in the biological and medical sciences. Molecular biology techniques are being used extensively in modern day drug discovery, development and diagnostics. The objective of this workshop was to familiarize participants with concepts pertaining to basic molecular biology principles and the techniques applied in various contemporary areas of research.



Participants at the workshop



Experimental Session

## 6<sup>TH</sup> INTERNATIONAL SYMPOSIUM ON INNOVATIONS IN PHARMACEUTICAL SCIENCES AND TECHNOLOGY

November 26 – November 28, 2010

The symposium focused on recent advances in wide spectrum of activities in drug discovery and development, pharmaceutical sciences, pharmaceutical industry and the profession of pharmacy. It also covered topics of relevance from emerging and active areas of science and technology, like nanoparticles, medical devices, tissue engineering, etc.



Inauguration by the Chief Minister of Gujarat – Shri Narendra Modi.



Felicitation of Prof. Harish Padh by Shri Narendra Modi



Release of the Souvenir Book



Scientific Sessions (Lecture by Dr. David Trigle)



Participants at the Symposium



Group of students with speakers

## EXTRACURRICULAR ACTIVITIES

### 'Hindi Samaroh' (27<sup>th</sup> to 29<sup>th</sup> September 2010)

14<sup>th</sup> September is celebrated as Hindi Divas because on this day Hindi was declared as official national language by Indian Constitution. However, on account of increasing importance of English language for use in educational and commercial arenas, the daily usage of Hindi is dwindling. Therefore to revive the interest of Hindi in the NIPERD family, we organized *Hindi Samaroh* from 27<sup>th</sup> to 29<sup>th</sup> September 2010. The celebration included participation of Ph.D. and M.S. Pharm students as participants in various light hearted competitions organized to assess the fluency of Hindi vocabulary and grammar in the students. An extempore competition was also carried out wherein the students were asked to express their views on the present state of affairs of Hindi language and its importance that it holds for present youth. Further a voluntary Hindi poetry recital event was also organized. 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.



Participants for '*Prashnotari*'



'*Swakavita Pathan*'

### Flag hoisting on Independence Day



## HONOURS/AWARDS

### First Prize:

**Rajan Swamy, Khushboo Patel and Ravi Suthar.** 'Nanobubble – An emerging transfection vector for Lung Diseases'. A Model presented at 'MAYRID – The Cluster of Events (Nanotechnology based Drug Designing). Organized by Institute of Research and Development, Gujarat Forensic Science University, Gandhinagar on 7<sup>th</sup> October 2010.



**Rajan Swamy, Khushboo Patel and Ravi Suthar  
presenting the Model**

### First Prize:

**Baraiya AB, Kaila JC, Pandya AN, Jalani HB, Srihasam L, Vasu KK,** Design and Synthesis of Novel 2-Aminoimidazole-2-Aminothiazole Conjugates As Inhibitors of NF- $\kappa$ B/Ap-1 Mediated Transcriptional Activation: Implication As Potential Anti-Cancer Agents. 6<sup>th</sup> International Symposium on innovations in pharmaceutical sciences and technology. Organized by B. V. Patel PERD Centre, Ahmedabad from November 26 – November 28, 2010



**Mr. Arsi Bariya receiving the award from Prof. Bhalla**