BIOINFORMATICS INFRASTRUCTURE FACILITY CENTRE (BIF)

Sponsored by

Department of Biotechnology (Govt. of India)

About the Institution

Dr. B.R. Ambedkar Center for Biomedical Research (ACBR) came into existence in March, 1991. The mandate of the Centre is high quality postgraduate education and research in Biomedical Sciences. The institute also has provision for doctoral and postdoctoral training to young scientists at the start of their research career to gain the skills and insights in frontier areas of biomedical sciences. During the last two decades the Center has grown to have strength of 220 comprising faculties, students, Ph.D scholars and supporting staff.

ACBR presents a unique amalgamation of basic and applied research in the field of human health and disease, which is first of its kind in the Indian University System. The Center possesses a unique structure having an interdisciplinary, goal oriented approach with an objective to meet the high standards of research and teaching in Biomedical Sciences. Specialised laboratories, rather than conventional departments, are the fundamental units of the ACBR. Typically headed by a senior faculty, the lab may include several other faculty and scientists from neighbouring institutes such as IGIB, INMAS, DIPAS, VPCI, ICPO, AIIMS etc. in addition to postdoctoral fellows and Ph.D. students, who share common scientific interest and teaching at the Center. This structure provides flexibility and enhances the opportunity for wide intellectual interaction and collaboration and minimizes the administrative traffic that may impede university life.

The post graduate teaching program is dedicated to educating a carefully selected group of students considered as potential leaders in their area of specialization. Students associate with a faculty/scientist-scholars, all actively engaged in research, and learn primarily through a combination of courses, discussion groups, tutorial guidance, and apprenticeship in research laboratories.

About the Bioinformatics Centre

Bioinformatics Facility was created at ACBR in the year 2003 with purchase of Molecular Modeling software Insight II, GCG, TSAR from Accelrys. Later on, since 2006 the facility is being funded and supported by Department of Biotechnology (DBT), Govt. of India. The primary objective of this facility is to promote biology teaching and understand its different aspects computationally through bioinformatics. It provides services to the host faculty and other neighbouring institutions of higher education in terms of Internet connectivity, retrieval of online and offline biological databases, bioinformatics software and tools for facilitating biological research particularly in the area of sequence and phylogenetic analysis, database development, molecular modeling and drug design, etc. We also periodically organize hands-on trainings on various aspects of application of bioinformatics tools and molecular techniques in biological research. ACBR since 2008 has consecutively organised workshops for the better understanding of different modules of drug design tools. These workshops trained number approximately 150 participants from different universities over the period of time in the field of bioinformatics and its applications in computer aided drug design.

Objectives

The primary objective of this facility is to promote biology teaching and understand its different aspects computationally through bioinformatics. It provides services to the host faculty and other neighbouring institutions of higher education in terms of retrieval of online and offline biological databases, bioinformatics software and tools for facilitating biological research particularly in the area of mining genomes and functional analysis, database development, molecular modeling and drug design and other fields of Bioinformatics.

Academic Programme at ACBR

The Master's & Ph.D. program of ACBR provides an unparalleled opportunity for highly self-motivated independent minded young scholars to acquire superb academic training, while participating as colleagues in research of fundamental importance. Prospective students should develop a commitment to a career in scientific research. Admissions to this program are granted on the basis of test conducted on all India basis, followed by interview and group discussion. Students are selected, given an opportunity to explore the research interest before selecting their field of research in specific laboratory.

Under the M.Sc.-Ph.D. Combined Program in Biomedical Sciences students usually spend the first two years in both course work and the laboratory, and the remaining years predominantly pursuing their thesis research.

- **M.Sc.-Ph.D. Combined Degree and M.Sc. Degree Program in Biomedical Sciences.**
- **Ph.D. Programme**

Achievements at a glance

Achievements of the ACBR students

M.Sc. - Ph.D. Combined Degree Program in Biomedical Sciences being an interdisciplinary course we have surveyed the background of students who qualify the admission criteria of the Centre as a reflection of the effectiveness of the selection procedures practiced at the Centre. It is observed that students with various backgrounds at the undergraduate level satisfy the selection criteria. The students of ACBR have consistently performed extremely well at the level of University and National level examinations.

The ACBR offers a unique research program in the multidisciplinary area of Biomedical Sciences. More than 126 students have completed their Ph.D. from ACBR since 1998. The Ph.D. students have done exceptionally well so far. More than 210 publications (Last five years) have ensued as a result of the research work being carried out. This work has been published in several prestigious journals such as Blood, Cancer Research, Molecular Pharmacology, Journal of Bacteriology, Journal of Biological Chemistry, New England Journal of Medicine Biochemistry, Journal of Medicinal chemistry, Nucleic Acids Research, Biochemical and Biophysical Research Communications, Phytomedicine, Journal of Chemical Information and Molecular Modeling, Sexually Transmitted Infections, Molecular and Cellular Biology, Tetrahedron, Bioorganic and Medicinal Chemistry.Almost all the students who complete their Ph.D. at ACBR pursue post-doctoral research in India or abroad. Several students have joined teaching positions at various universities and some have chosen to join pharmaceutical companies as research scientists.

Manpower trained in Bioinformatics (*In silico analysis carried out as FULL OR part of Ph.D. thesis work)*

Ph.D. ***Completed***
17

Supervisor: Dr. Madhu Chopra

1. **Nalini Yadav, Dec 2017**: Rational design and Development of anticancer compound taking lead from natural sources.
2. **Lubna Wasim**, **2017**: Epigenetic regulation of cancer through HDAC inhibitors understanding the mechanism through networks.
3. **Monika Sharma, 2016:** 3D-QSAR and virtual screening for development of novel histone deacetylase (HDAC) inhibitors
4. **Manisha Sikka, 2016**, Analysis of genes involved in pathways: Targeting Cancer through cholecystokinin antagonists and cyclooxegenase – 2 Inhibitors.

5. **Priyanka Verma, 2013:** Estimation of the level of cartilage oligomeric matrix protein (COMP) in osteoarthritis and Designing of an inhibitor to control progression of osteoarthritis, Joint Supervisor Dr.Madhu Chopra (ACBR), Supervisor Dr. Krishna Dalal (AIIMS)
6. **Ruby Gupta, 2012:** "PharmacophoreModeling, Virtual Screening and Development of novel COX-2 Selective Inhibitors. Supervisor Dr.Madhu Chopra

Supervisor Prof. Daman Saluja

7. **Divya, 2014:** Development of diagnostic assay for co-detection of *Neisseria gonorhoeae*and *Chlamydia trachomatis* and elucidating the molecular mechanism of antimicrobial resistance in *Neisseria gonorrhoeae, Supervisor Prof. Daman Saluja*
8. **Jyoti Zack, 2013**: To study the mechanism of Runx 1 and its mutants in DNA binding and altered gene expression, Supervisor Prof. Daman Saluja
9. **Divya Sachdeva, 2013**: Studies on molecular mechanism of antibiotic resistance in Neisseria and to develop easy diagnostic methods. Supervisor Prof. Daman Saluja

Supervisor: Prof. Vani Brahmachari

10. **Shweta Mehndirata,** Analysis of INO80 binding motif in the 5' and 3' flanking sequences of protein and regulatory RNA coding genes in the human genome"
11. **Shruti Jain,** "Analysis of dINO80 binding motif in the 5' flanking sequences of protein and coding genes in the Drosophila genome".
12. **Jayant Maini**: Characterization and functional analysis of cis-element involved in developmental memory in human Genome

Supervisor: Dr. P. M. Luthra

13. **Vishal Nimeysh:** Structure Prediction of Platelet Derived Epidermal Growth Factor Receptor (PDEGFR) to design novel PDEGFR antagonists for targeting tumor of brain. Supervisor Dr. P. M. Luthra.

14. **Amresh Prakash, 2012:**"In silico Approaches to Study the Role of adenosine A2A receptor (A2AR) in Parkinson's Disease for Development of Novel Therapeutics" Supervisor Dr. P. M. Luthra.

Supervisor: Dr. Manisha Tiwari

15. **Mr. Vikar Saini, 2017:** An evaluation of the anticancer activity of novel analogs of Diallyldisulfide, an active principle of garlic.
16. **Ms. Apra Manral, 2016:** Synthesis of diallylsulfideanalogs and their potential use for the treatment of Alzheimer's disease.
17. **Ms. Poonam, 2016,** Protective effects of novel aryl piperazines in a rat model of Alzheimer's disease.

M.Sc. Projects (In silico analysis carried out as a part of dissertation work) 20

Current area of research

ACBR has core faculty in the field of Chemistry and Biology, thus facilitating research and teaching in interdisciplinary areas in Biomedical Sciences. The areas of research pursued by the faculty encompasses molecular pathology of infectious diseases, Molecular Oncology, Gene Regulation, Molecular Genetics, Epigenetics, Medicinal Chemistry and Natural Product Chemistry, Drug Discovery and Drug Designing, Bioinformatics and Molecular Microbiology and Immunology.

Inter Institutional collaboration

The faculty of ACBR and other departments of University of Delhi, IGIB, INMAS, DIPAS and VPCI, ICPO, AIIMS collaborate in offering a M.Sc.-Ph.D. program of advanced study and research in advanced Biology, Chemistry and Biomedical Sciences. In addition to the didactic teaching, the ACBR arranges many research colloquia, seminars, lectures by visiting scientists under SURP (Summer Undergraduate Research Program) and other special scientific programs.

Recent publications 2012-2017

S. N.	Tilte of the Paper	Name of the Journal
1.	Jain, S., Bhattacharyya, K., Bakshi, R., Narang, A., Brahmachari, V. Distinguishing between biochemical and cellular function: Are there peptide signatures for cellular function of proteins?	2017, *Proteins.*85(4):682-693. doi: 10.1002/prot.25248.
2	Nemaysh, V., Luthra, P.M. Computational analysis revealing that K634 and T681 mutations modulate the 3D-structure of PDGFR-b and lead to sunitinib resistance.	2017, *RSC Adv.*, 7, 37612.
3	Yadav, N., Kumar, P., Chhikara, A., Chopra, M* Development of 1,3,4-oxadiazole thione based novel anticancer agents: Design, synthesis and in-vitro studies.	2017, 98, 721-730.
4	Kumari, S., Chowdhury, J., Sikka, M., Verma, P., Jha, P., Mishra, A.K., Saluja, D., Chopra, M.* Identification of potent cholecystokinin-B receptor antagonists: synthesis, molecular modeling and anti-cancer activity against pancreatic cancer cells,	*2017, MedChemComm*, 8, 1561-1574.
5	Verma, P., Dalal, K., Chopra, M. Pharmacophore development and screening for discovery of potential inhibitors of ADAMTS-4 for Osteoarthritis therapy,	2016, *Journal of Molecular Modeling,*22, 178,
6.	Arora R, Sawney S, Saluja D. Potential Therapeutic Approaches for the Treatment of Acute Myeloid Leukemia with AML1-ETO Translocation.	2016, Curr Cancer Drug Targets.16(3):215-25.
7	Jain R, Sonkar SC, Chaudhry U, Bala M, Saluja D. In-silico Hierarchical Approach for the Identification of Potential Universal Vaccine Candidates (PUVCs) from Neisseria gonorrhoeae.	2016. J Theor Biol. 2016 Dec 7;410:36-43.
8	Arora, R., Sawney, S., Saini, V., Steffi, C., Tiwari, M., &Saluja, D. Esculetin induces antiproliferative and apoptotic response in pancreatic cancer cells by directly binding to KEAP1.	2016, *Molecular cancer*, *15*(1), 64.
9.	8-(furan-2-yl)-3-phenethylthiazolo[5,4-e][1,2,4]triazolo[1,5-c]pyrimidine-2(3H)-thione as Novel, Selective and Potent Adenosine A_{2A} Receptor antagonist, Kumari, N., Mishra, C. B., Prakash, A., Kumar, N., Mongre, R.K. & Luthra, P.M.	*Neuroscience Letters*, 558 (13) 203-207. 2014
10	Functional Analysis of Hypothetical Proteins of Chlamydia Trachomatis: A Bioinformatics Based Approach for Prioritizing the Targets Prashant K Mishra, Subash C Sonkar, SreeRohit Raj, Uma	J Comput Sci SystBiol 2013, 7:1

	Chaudhry and Daman Saluja*	
11	2D-QSAR, Docking Studies, and *In Silico*ADMET Prediction of Polyphenolic Acetates as Substrates for Protein Acetyltransferase Function of Glutamine Synthetase of *Mycobacterium tuberculosis*PrijaPonnan, Shikhar Gupta, Madhu Chopra, RashmiTandon, Anil S. Baghel, Garima Gupta, Ashok K. Prasad, Ramesh C. Rastogi, Mridula Bose, and Hanumantharao G. Raj.	ISRN Structural Biology Volume 2013, Article ID 373516, http://dx.doi.org/10.1155/2013/373516
12.	Design and synthesis of (4*E*)-4-(4-substitutedbenzylideneamino)-3-substituted-2,3-dihydro-2-thioxothiazole-5-carbonitrile as novel A_{2A} receptor antagonists, Chandra Bhushan Mishra, Dimpy Sharma, Amresh Prakash, Namrata Kumari, Nitin Kumar, Pratibha Mehta Luthra	Bioorg. Med. Chem. 2013, 21, 6077
13	Identification and validation of a putative polycomb responsive element in the human genome. Hemant Bengani, Shweta Mendiratta , Jayant Maini, DasariVasanthi , Hina Sultana , Mohsen Ghasemi, Jasmine Ahluwalia, Sowmya Ramachandran, Rakesh K Mishra and Vani Brahmachari	PLoS One. 2013 Jun 21; 8(6):e67217.
14	Synthesis and evaluation of a fluorescent non-peptidic Cholecystokinin-B/Gastrin receptor specific antagonist for cancer cell imaging. SarojKumari, JoyitaChaudhury, SudhirChandana, Daman Saluja, Anil K. Mishra, Madhu Chopra*,	ChemBioChem. 2012, 13, 282-292
15	Proximity of H2A.Z containing nucleosome to the transcription start site influences gene expression levels in the mammalian liver and brain. Bargaje R, Alam P, Patowary A, Sarkar M, Ali T, Gupta S, Garg M, Singh M, Purkanti R, Scaria V, Sivasubbu S, Brahmachari V, Pillai B	Nucleic Acids Res.(2012) doi: 10.1093/nar/gks665.
16	Modeling SNP mediated differential targeting of homologous 3'UTR by MicroRNA Ahluwalia JK, Soni K, Sivasubbu S, Brahmachari V.	RNABiol.2012 Mar 1; 9(3).
17	Comparative modeling of human kappa opioid receptor and docking analysis with the peptide YFa. Mahesh C Patra, M. Krishan C Kumar, Santosh Pasha, Madhu Chopra*	Journal of Molecular Graphics and Modelling 2012, 33, 44–51
18.	In silico Study of the $A_{2A}R$-D_2R Kinetics and Interfacial Contact Surface for Heteromeriza- tion. Prakash A, Pratibha Mehta Luthra,	Amino Acids. 2012 DOI 10.1007/s00726-012-1218-x. 25

Infrastructure facilites

A. Computer & Communication facility

We have state of art computer and communication facility at the center with a number of workstations and computers. All the research labs have computers for Ph.D. students and M.Sc. Students and a well maintained computerized library and networking through Delhi University Computer Center. ACBR is equipped with two HPZ210, eight HP 4300 and 4600 workstations, one SGI silicon graphics workstation. Besides this a good number of latest computers are available in central computer room, Library and laboratories and students get hands on training on these computers which are placed in very spacious air conditioned Computer labs.

B. Scientific Software packages

ACBR BIF facility is equipped with Molecular Modelling Software from Acclerys, Sybyl X, HIPERCHEM, AMBER, discovery series (Quantity 1) for gel documentation,

Cn3D, Rasmol for Molecular visualization. The centre has Omega (GCG for sequence analysis of DNA & Proteins) and. We have number of workstations with LINUX as well as windows platform for study of Protein-protein Interaction, Ligand-protein and Ligand-DNA Interaction studies. This program can also be used to design primers from a given sequence & various sites for restriction enzymes can also be mapped on a given sequence.

Faculty membres

- **VaniBrahmachari**
  Professor
  Epigenetics lab
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1. Mining and characterisation of novel trans and cis acting elements for maintenance of developmental memory.
2. Epigenetic mechanisms of incomplete penetrance and variable expressivity: role of microRNA
3. Nucleosome organization as a part of the epigenetic architecture of the genome.
4. Mechanism of genomic imprinting: the mealybug as a model system.

The theme of work is to understand mechanisms of epigenetic regulation in development and disease. The lab combines in silico analysis and experimental validation by in vitro and in vivo studies. One of the major focus is to utilize the complete genome sequence of mouse and human to discover novel genes that could be are part of global regulation and are important for maintaining developmental memory; both trans-acting factors and cis-acting elements. Dr. Vani and her group identified the dual activity of a chromatin remodelling protein (CRM), INO80. They have reported the role of INO80 in homeotic gene regulation for the first time using transgenic Drosophila. Dr. Vani and her group have identified cis-acting element for epigenetic regulation, namely PRE/TRE (Polycomb/Trithorax Responsive Element). This element has been functionally characterized in transgenic Drosophila and human cells in culture. Further work to understand the role of these trans-factors and cis-elements in developmental memory are in progress.

This group's work on transgenic mouse models led to the identification of nucleosome organization as a modifier of repeat instability in the human genome leading to fragile X syndrome and demonstrated that repeat expansion is a post-zygotic event which is independent of parental-origin-effect in mice. In the area of incomplete penetrance and variable expressivity, they we have proposed a novel mechanism mediated by microRNA.

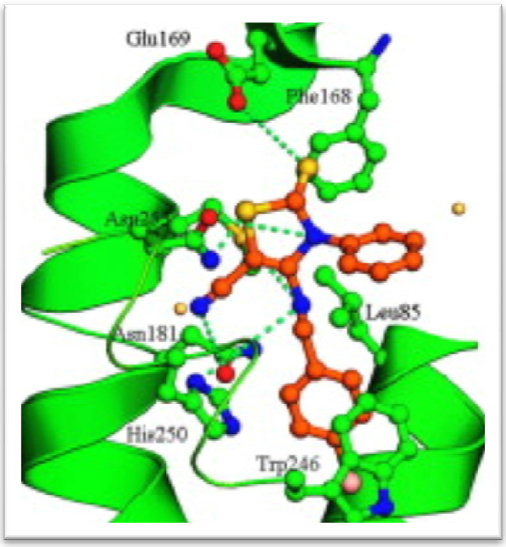
Currently, they are also sequencing the whole genome of the mealybug, a unique genetic system where genomic imprinting operates on 50% of the genome. This is being utilized as model for novel imprinting mechanisms.

- **Daman Saluja**

Professor
Medical Biotechnology
E-mail: dsalujach59@gmail.com

Prof. Saluja has been working in the area of Medical Biotechnology. Her primary contribution is in the development of beacon based Polymerase Chain Reaction (PCR) mediated diagnostic assays for sexually transmitted diseases caused by *Neisseriagonorrhoeae* and *Chlamydia trachomatis* and *Trichomonas vaginalis,* Currently her lab is working on LAMP based diagnosis of *Mycobacteriumtuberculosis.* In collaboration with Industry, Dr Saluja has also designed a low cost, hand held LAMP-PCR machine. Further work is in progress to incorporate biochips in the diagnosis of these organisms. They are also looking into mechanism of antimiccrobial resistance in Neisseria and Chlamydia and the possibility of identifying novel antigens using computational and functional genomics approach. More recently, they have developed low cost, novel method of qPCR for the detection and quantification of bcr/abl transcript for Chronic Myeloid Leukemia (CML) and for acute myeloid leukemia (AML) and are also looking into anti-leukemic activity of plant extracts. She is author of seven patent applications.

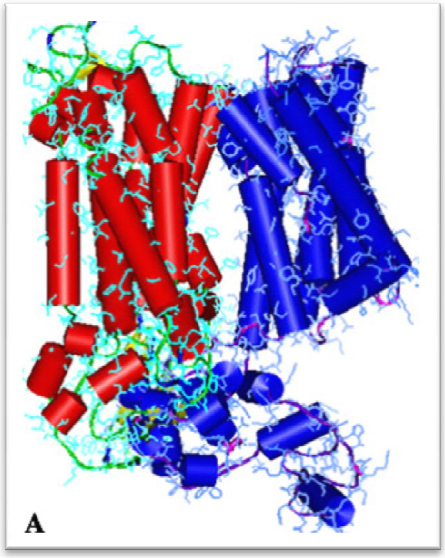
Her laboratory is also looking at regulation of gene expression in eukaryotes using sin3B as a model system. Sin3B is an important co-repressor involved in p53 mediated gene repression under genotic and non-genotoxic stress. Their recent findings suggest that Sin3 plays a pivotal role in regulating cell cycle and apoptosis under conditions of cellular stress.



- **Pratibha M. Luthra**

Associate Professor
Medicinal Chemistry Lab
E-mail: luthra_pm@delhiuniversity.com

Dr.Luthra work aspires to carry the synthesis of heterocyclic compounds and isolation of active principle from natural source for the development of potential therapeutic treatment for Parkinson's disease and brain cancer particularly GlioblastomaMultiforme using animal models, and microbial infections using in vitro assays. High Through Put Screening (In silico) is carried for defining the pharmacophore. I am also working on biochemical studies to unravel the mysteries of these diseases for novel targets.

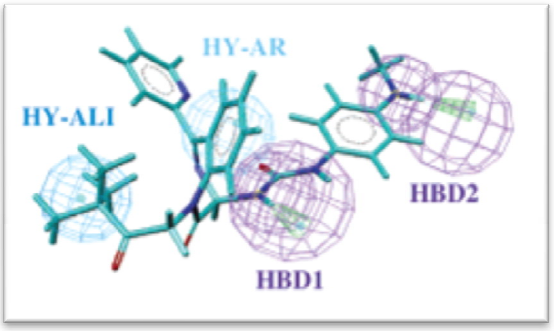


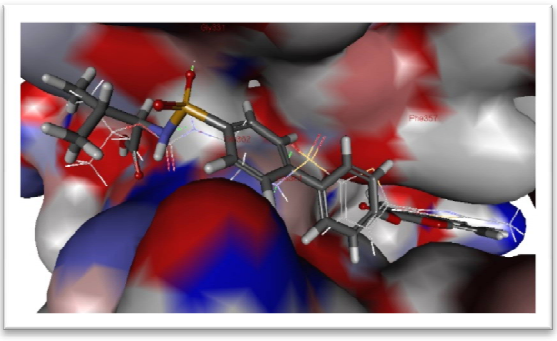
Latest Projects:

1. Synthesis of ar-turmerone and its analogues to study the mechanism of action of anti-fungal activity and Study the Molecular Mechanism of Chemopreventive and Chemoprotective Activity of Curcumin, A Natural Product From Curcuma longa **(DST-PURSE), 2009-2012.**
2. Synthesis of novel non-xanthine compounds as adenosine A2A receptor antagonists to study their anti-Parkinsonian and neuro-protecting effects (**Council of Scientific and Industrial Research**) **2010-2013**.

- Madhu Chopra
  Assistant Professor
  Molecular Modelling and Anticancer Drug Development
  E-mail : mchopradu@gmail.com,mchopra@acbr.du.ac.in

Dr.Madhu Chopra has been working on the design and synthesis of peptides and peptide-mimetics to be targeted specifically to the cancers. We have been able to design lead compounds in our lab for various medicinal purposes. E.g. CCK antagonists have been developed and checked for their in-vitro as well as in-vivo potential. The developed lead compounds would be improved for their efficacy and affinity using computational tools and will be retested in the laboratory to give novel antagonists. Other projects on development of COX-2 and HDAC inhibitors have also given several lead compounds whose structure is being refined computational which will be finally synthesized to give more potent inhibitors.

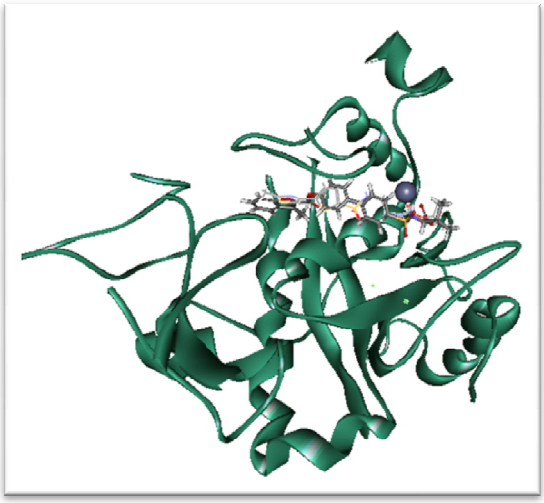




Natural products that have always been sources of wealth of drug molecules need to be explored in more scientific way. My future research interests are to exploit my ability to highest extent to screen or to isolate drugs from our natural fauna and flora for medical application, which is not available

anywhere in the world. We have initiated screening programme for evaluating the natural resources.

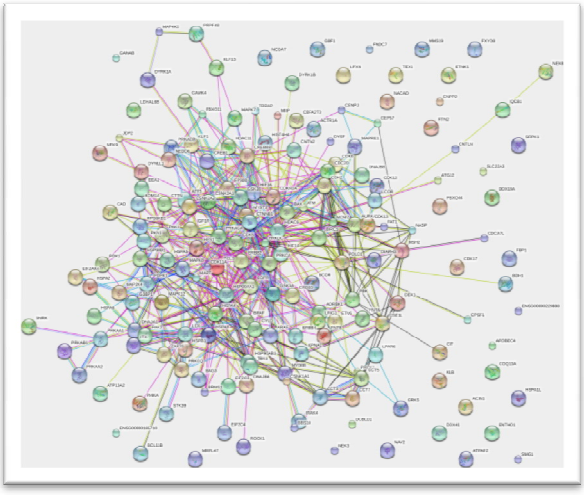
They have also been working towards developing diagnostics for tuberculosis for rapid and fast diagnosis of the disease. New methodologies are being developed in our laboratory for successful delivery of cytotoxic drug like Doxorubicin, Methotrexate etc. through nanoparticle mediated drug delivery systems.



- **Computer aided drug design**: Pharmacophore based drug design in our laboratory has resulted in development of potent compounds as cholecystokinin-B/gastrin receptor antagonists, Cyclooxygenase-2 and HDAC enzyme inhibitors and in silico screening of the designed ligands has been done for development of more potent compounds.
- **Natural Product Screening** for anticancer drug development: Three compounds have been isolated from *Boerhaviadiffusa* using activity-guided fractionation using column followed by HPLC and the compounds have been identified and one of them is a novel compound and is showing activity towards human glioma cell line. The detailed mechanism of action of all the three compounds is underway in the laboratory

- Design, **Synthesis and Evaluation of non Peptidic CCK-B receptor** Specific Antagonists for targeting CCK-B receptor expressing Tumours. 25 compounds have been synthesized and evaluated for their *in vitro* binding affinities and one of the compounds has been targeted to *in vivo* receptors in animal studies.

- **Pathway Analysis through Protein-Protein Interaction Network (PPIN) for Drug Discovery:** Pathway analysis is a rapidly developing discipline that combines software tools, database models and computational algorithms-all of which help scientists to convert molecular interaction data into a set of computational models. The models can be used to predict cell behaviour in response to a drug, nutrient, or other stimuli. We have undertaken a project wherein Interactome of various subtypes of HDACs is being studied in detail to understand their



cellular locations and specificity of their action towards acetylation status of whole interactome of HDACs. Such an analysis would provide insight into the pathways by which HDAC inhibition leads to anticancer effect and understanding their specificity towards cancer cells. Several online tools such as iRefWeb, PINA, Biogrid and STRING is being used for this work.

Contact Details

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