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MESSAGE FROM THE DESK OF THE EDITOR

‘Pharma Innovations’, the innovative e-magazine of NIET Pharmacy Institute, has covered a pretty long way of its journey of success and reached the peak of popularity amongst the students as well as the faculty members. The magazine has become a means of motivation and encouragement for the young writers and budding researchers of the Institute. The increased participation and growing interest of the students and their mentors to add quality writings to this innovative magazine have fulfilled the basic objective and purpose of this creative venture of the Institute.

I wish all the best to the members of the Editorial Board and all others associated with them for enlightening the path of progress of ‘Pharma Innovations’.

DR. R. MAZUMDER
PROFESSOR AND DEAN
NOIDA INSTITUTE OF ENGINEERING & TECHNOLOGY
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MESSAGE FROM THE DESK OF THE ASSOCIATED EDITOR

“Pharma Innovations” is a magazine coined by the Editorial Club & PharmaTech Society of Noida Institute of Engineering & Technology (Pharmacy Institute). It contains number of articles created by both student’s and teachers for the college and the number of festive memorable events and the achievements won by students and staff. This edition of magazine (2017) bring number of articles created by students to educate and improve the awareness of readers about healthcare system. The Magazine emphasizes on the newer innovations in the Pharmaceutical Industry and hospitals.

DR SANJITA DAS
PROFESSOR AND HOD (PHARMACOLOGY)
NOIDA INSTITUTE OF ENGINEERING & TECHNOLOGY
(PHARMACY INSTITUTE)
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FACULTY FORUM

PRECLINICAL EVALUATION OF NOOTROPIC AGENTS: AN OVERVIEW



SANJITA DAS

Professor and HOD (Pharmacology)

Noida Institute of Engineering and Technology (Pharmacy Institute)

Cognitive deficits have long been recognized as severe and consistent neurological disorders associated with numerous psychiatric and neurodegenerative states such as Alzheimer's disease. Dementia is one of the age-related mental problems, and a characteristic symptom of Alzheimer's disease. Alzheimer's disease (AD) is a progressive neurodegenerative disorder which affects older individuals and may progress to a totally vegetative state. Atrophy of cortical and sub-cortical areas is associated with deposition of β -amyloid protein in the form of senile plaques and formation of neurofibrillary tangles. There is marked cholinergic deficiency in the brain, though other neurotransmitter systems are also affected. Various measures to augment cholinergic transmitter in the brain have been tried. The relatively cerebroselective anti-ChEs have been approved for clinical use. Nootropic agents are clinically used in situations where there is organic disorder in learning abilities and for improving memory, mood and behavior, but the resulting side-effects associated with these agents have made their utility limited. Many experimental models are currently available for the evaluation of agents that affect learning and memory processes. In-vitro methods inhibition of acetylcholinesterase activity is measured by determining IC₅₀ with the help of Log probit analysis. In ex-vivo cholinesterase inhibition method the dose response relationship determined for drugs such as physostigmine and tacrine Agents which are H₃ receptor agonist are evaluated for [3H] Ach release activity in rat using rat brain slices. The binding affinity of potential nicotinic cholinergic agonist in brain using agonist ligand is determined by [3H]-N- methyl carbamylcholine binding nicotinic cholinergic receptors in rat frontal cortex. In In-vivo methods the inhibitory passive avoidance the test are carried on animals to test the learning and memory capacity of animal by suppressing a particular behavior. It includes step down, step through, two compartment test, up-hill avoidance, scopolamine induced test, and ischemia induced amnesia, memory impairments in basal forebrain. In active avoidance conditioned stimulus is given to the animal, which gives noxious stimulus as a result. It includes runway avoidance, shuttle box avoidance, jumping avoidance. In discrimination learning animals have no choice between the conditioned stimuli. Studies on aged monkeys provides additional advantage for neurobehavioral animal model of aging in that many of behavioral processes thought to be affected by aging.

BIOVIGILANCE AND HAEMOVIGILANCE

DR. SAUMYA DAS

Associate Professor

Noida Institute of Engineering & Technology (Pharmacy Institute)



Haemovigilance is a systematic approach to recording adverse events associated with the collection, production and administration of blood transfusions. Its objective is the early detection of new risks and quality defects; at the same time the national haemovigilance system triggers and evaluates preventive measures. Haemovigilance is the set of surveillance procedures covering the entire blood transfusion chain, from the donation and processing of blood and its components, through to their provision and transfusion to patients, and including their follow-up. It includes the monitoring, reporting, investigation and analysis of adverse events related to the donation, processing and transfusion of blood, and taking action to prevent their occurrence or recurrence. The reporting systems play a fundamental role in enhancing patient safety by learning from failures and then putting in place system changes to prevent them in future. ADR reporting made compulsory by doctors until there is no strict rules and regulations success of Pharmacovigilance program is questionable. Now a day's many of other branches like Haemovigilance, biovigilance and herbal Pharmacovigilance are comes in market to provide patient care. ADRs and Pharmacovigilance study have become prominent and one of the most important aspect of patient care. The awareness of the reporting centre is crucial due to large population of doctors were ignorant of PV centers.

STUDENTS FORUM

COMPUTER-AIDED DRUG DESIGNING LEADING PROFESSION AND PHARMACIST TOWARDS INNOVATION

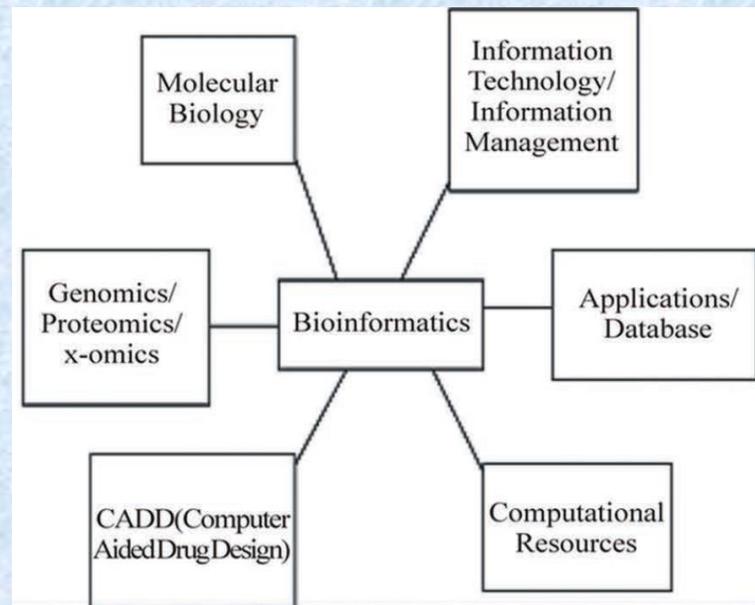
RAJNI SAWANNY

BPharm 1st year

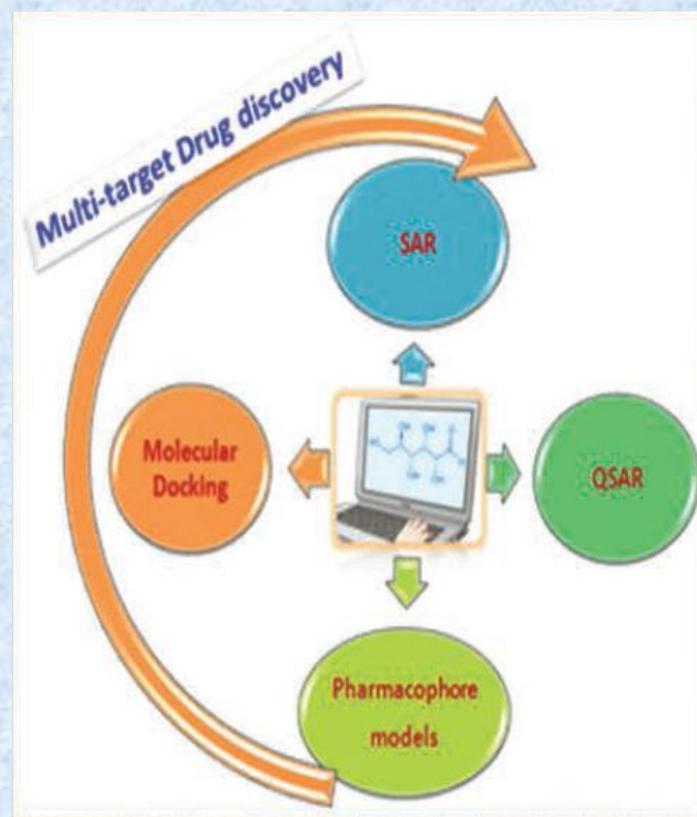
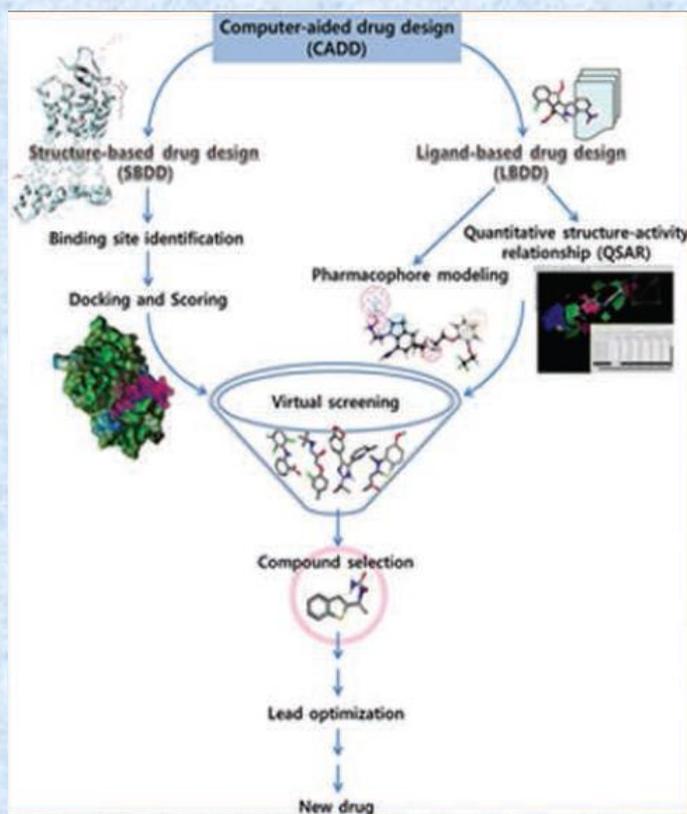
Noida Institute of Engineering and Technology (Pharmacy Institute)



CADD, computer aided drug designing has made great advances and significant contributions to the discovery and optimization of many clinically used medicines. Previously only traditional experimentation was done for therapeutic purpose, for this animal and human model were used and also other laboratory test were performed for assurance of desired pharmacological response. Two distinct approaches are possible in the area of computer aided drug design. The molecular structure of the target macromolecule is known by this technique which have achieved a high level of sophistication. It was earlier very costly and time consuming and many years are needed for the approval of a single drug. Through computational chemistry one can discover, enhance, study, and relate the biologically active molecules. When the only lead is set of known active compounds or knowledge of a biochemical transformation which is to be interrupted then the path for chemical synthesis becomes direct. Currently favored tactics include the use of neural networks including the prediction of the relative potency of different chiral forms of drugs.



The researcher and drug developers are in a new era for adopting all the computer techniques to discover, design and optimize pharmacologically active compounds. As safety, efficacy and economy are the most considered criteria during the drug discovery and remain along the time in the journey of drug discovery and remain along all the time line the journey of drug from the laboratory bench to the pharmacy shelf and at last in the hand of consumer or patient. The method of drug discovery which has been adopted based on idea of screening of synthetic and natural moiety having excellent pharmaceutical agent in past and then enhancing the activity and minimizing as much as possible the side effects by molecule optimization.



INSTANTANEOUS INTRA-AORTAL DISPERSIBLE RICE PAPER FILMS (IDF's): A NOVEL NATURE DRUG DELIVERY SYSTEM

SAMEERA ARSHAD

BPharm IIIrd Year,

Noida Institute of Engineering and Technology (Pharmacy Institute)

Now days, instantaneous intraaortal dispersible technologies as novel drug delivery system is one of the focus point of various pharmaceutical researchers. IDF's have outstanding advantages over the traditional oral & parenteral routs of drug administrations. First pass metabolism and presystemic degradation causes decrease in oral bioavailability of some essential drugs. The development of intraoral dispersible film can overcome this draw back. Experimental study is done by using natural drugs- resveratrol and curcumin having low oral bioavailability and optimization of the drug formulation is done by loading the drugs with IDF's. The formulation were evaluated for thickness, folding, endurance screening behavior among others. These factors are related to their drug release properties using pig mucosal membrane mounted on franz diffusion cell was used for evaluation of permeation. Taste panel was used for taste testing to determine acceptability. Sixteen formulations shows variation in their profiles. Formulation 16th proved optimal. The dissolution rate at steady state concentration of resveratrol was 29mg/sec and permeability coefficient was 389mg/sec cm². The dissolution rate of curcumin at steady state concentration was 0.25mg/sec and permeability efficient was 42.7mg/sec cm² resveratrol permeability rate was 0.42mg/sec and that of curcumin 0.14mg/sec. Resveratrol flux was 0.21mg/sec/cm² and curcumin flux was 0.14m/sec/cm². Drug entrapment was 80% for both molecules. The 20mg of resveratrol and curcumin dissolved in 47.6 sec and 47.4 sec respectively.

In this study after permeation a concentration of 6.73mg/ml of resveratrol and 0.061 mg/ml of curcumin was detected after 2 hours of experiment on administrating only 20mg of each of drugs. This suggest that curcumin is 100 times less permeable than resveratrol. The release profile was burst release. On contrast, curcumin oral dose of 2g/kg to rats yielded 1.35± 0.23 microgram/ml in 0.03 hrs and in humans given the same dose yielded either undetectable or extremely low. The key finding was ex-vivo release profiles of the optimized formulation revealed first order release and later zero order. Kinetics. Therefore it is evident that rice paper IDF's could efficiently deliver natural drugs into systemic circulation intraoral.

COMPUTER AIDED DRUG DESIGN: AN EMERGING TOOL FOR RESEARCH AND DRUG DEVELOPMENT

SHALINI SINGH

B.Pharm Ist Year

Noida Institute of Engineering and Technology (Pharmacy Institute)

The process of drug discovery is very complex and requires an interdisciplinary effort to design effective and commercially feasible drugs. The objective of drug design is to find a chemical compound that can fit to a specific cavity on a protein target both geometrically and chemically

- (1) It is generally recognized that drug discovery and development are very time and resources consuming processes. There is an ever growing effort to apply computational power to the combined chemical and biological space in order to streamline drug discovery, design, development and optimization. In biomedical arena, computer-aided or in silico design is being utilized to expedite and facilitate hit identification, hit-to-lead selection, optimize the absorption, distribution, metabolism, excretion and toxicity profile and avoid safety issues .
- (2) The development of any potential drug begins with years of scientific study to determine the biochemistry behind a disease, for which pharmaceutical intervention is possible. The result is the determination of specific receptors (targets). In the post genomic era, computer-aided drug design (CADD) has considerably extended its range of applications, spanning almost all stages in the drug discovery pipeline, from target identification to lead discovery, from lead optimization to preclinical or clinical trials
- (3). The rapidly expanding literature on the computational study of drug structure and activity is important both for the insights it provides into our existing drugs and for the ideas it contributes to new drug discovery.

- (4) To bring a new drug to the market is very costly, with the current price tag approximating US\$800 million, according to data reported in a recent study. Therefore, it is not surprising that pharmaceutical companies are seeking ways to optimize costs associated with R&D, with the goal of increasing profit margins. One method that was quickly adopted by industry was the use of combinatorial chemistry and HTS. In HTS, large libraries of compounds are screened against drug targets to identify lead compounds that can modulate a particular outcome. However, setting up a combinatorial chemistry program and HTS is costly and not able to address the specific needs of many biological (drug target) systems. Additionally, compounds identified in such screenings are not always amenable to further medicinal chemistry development, with poor ADME (absorption, distribution metabolism and elimination) properties. Although these methods have increased the rate at which lead compounds can be identified, there has not been a commensurate increase in the rate of introduction of new chemical entities (NCE) into the world drug market. As an attractive alternative, *in silico* methods show promise in identifying new lead compounds faster and at a fraction of the cost of combinatorial approaches and HTS. The addition of computer aided drug design technologies to the R&D approaches of a company, could lead to a reduction in the cost of drug design and development by up to 50%
- (5) CADD technologies including molecular modeling and simulation have become promising in drug discovery. Recently, CADD has even been used in designing highly selective ligands for a certain target that shares very similar structures with many proteins, which is difficult to be done by other methods. One such example is the rational design of selective inhibitors of p90 ribosomal protein S6 kinase (6) In the postgenomic era, owing to the dramatic increase of small molecule and biomacromolecule information, CADD tools have been applied in almost every stage of drug R & D, greatly changing the strategy and pipeline for drug discovery.
- (7) CADD, from its traditional application of lead discovery and optimization, has extended toward two directions: upstream for target identification and validation, and downstream for preclinical study (ADMET prediction). Target identification and validation is the first key stage in the drug discovery pipeline. However, identification and validation of druggable targets from among thousands of candidate macromolecules is still a challenging task

- (8) Numerous technologies for addressing the targets have been developed recently. Genomic and proteomic approaches are the major tools for target identification. For example, a proteomic approach for identification of binding proteins for a given small molecule involves comparison of the protein expression profiles for a given cell or tissue in the presence or absence of the given molecule. This method has not been proved very successful in target discovery because it is laborious and time-consuming.
- (9) Therefore, complementary to the experimental methods, a series of computational (insilico) tools have also been developed for target identification. They can be cataloged into sequence-based approach and structure-based approaches. Hence computational approaches to drug design fall into two general categories: those that do not assume information on the structure of the target macromolecule, and the structure-based approaches that do make use of such information
- (10) Structure based approaches are not yet applicable because the structure of the target macromolecule is unknown; in these cases, quantitative structure-activity relationship (QSAR) techniques provide the best approach to rational drug design. Traditional (two-dimensional) QSAR methods attempt to correlate biological activity with local features of atoms, whole molecular properties (e.g. charge) and substituent effects (e.g. fragment hydrophobicity indices). New developments in traditional QSAR continue to appear in the literature (e.g. the OASIS program).
- (11) Most interest in this field, however, now focuses on three-dimensional QSAR. Recent examples of molecules to which this approach has been applied include HIV-1 protease and the cholecystokinin-A receptor.

SUPERBUGS:THREATS FOR COMING DAYS

SK ASHIF JAN

B.Pharm Ist Year

Noida Institute of Engineering and Technology (Pharmacy Institute)



For nearly a century, bacteria-fighting drugs known as antibiotics, that are derivative of microbes have helped to control and destroy many of the harmful bacteria that can make human being as well as animal sick. But in recent decades, antibiotics have been losing their activity against some types of bacteria. In fact, certain bacteria are now unbeatable with today's medicines such as antibiotics. But the sad reality of today is the way we use antibiotics are creating new type of bacteria that creates antibiotics resistance. It does not cure infections with even maximum amount of drug. The newly evolved bacteria that are resistance to antibiotics are called as superbug.

The antibiotics are used usually against bacterial infection to prevent disease and kill the bacteria. But now a days the doctors or patients self treatment method by using more antibiotics drug helps to create drug-resistant bacteria. If people take more antibiotics unnecessarily, drug-resistanant can continue to thrive and spread. The mutation occurs in bacterial gene, in normal terms the bacteria contains NDM-1gene in bacterial DNA that becomes superbug. They may even share their drug-resistance traits with other bacteria by replicating and transmitting the NDM-1 gene segment. The sad story is, in India the superbugs are found in Delhi hospitals. Indian officials have admitted for the first time the presence of an superbug in Delhi hospitals. The health minister of Delhi Mr AK Walia, confirmed the presence of the NDM-1 gene, which makes bacteria resistant to almost all antibiotics, in several of the capital's leading hospitals, although he said the prevalence rate was "not alarming" and NDM-1 had not been found in the city's water and sewage lines.NDM-1 is resistance to all known antibiotics even carbapenem the last resort of modern medicine. Dr. Manish Kakkar, a microbiologist from Harvard School of Public Health who is now with Public Health Foundation of India "Since it takes 20 years and millions of molecules to develop a new antibiotic, while bacteria can replicate in 15 minutes, the specter of returning to the pre-Penicillin days of death from simple infections looms large". Antibiotic resistance, however, has a long history. "Within three years of discovering

Penicillin, drug resistance was recorded," points out Dr Sarman Singh, head of clinical microbiology at the All India Institute of Medical Sciences (AIIMS), Delhi. "Bacteria are very intelligent, in an evolutionary sense. So every antibiotic will face drug resistance in about five years." Singh, who has been with AIIMS has seen fatal multi-drug resistance (MDR) among his patients consistently.

Targeted neurotechnology restores walking in humans with spinal cord injury

Chandrabhushan Kumar

B.Pharm IIIrd Year

Noida Institute of Engineering and Technology (Pharmacy Institute)



Spinal cord injury (SCI) disrupts communication within the nervous system, leading to the loss of essential neurological functions. At present, activity based therapies are the only medical practices that can be used to enhance recovery. The volitional production of active movements during training promotes reorganization of neuronal pathways and thereby augments recovery. However, the most affected patients, who fail to produce active movements voluntarily, experience minimal benefits from these therapies.

This situation has prompted the development of multifaceted neurotechnologies, such as lower limb exoskeletons, bodyweight support systems, functional electrical stimulation of muscles, and spinal cord neuromodulation therapies, all of which share the same goal to enable patient to sustain active movements during training to enhance the reorganization of neuronal pathways. Three decades of clinical research using these neurotechnologies suggested that epidural electrical stimulation (EES) of the spinal cord may be pivotal to achieve this goal. EES not only enables the brain to exploit spared but functionally silent descending pathways in order to produce movements of paralyzed limbs, but also improves the ability of the spinal cord to translate task specific sensory information into the muscle activity that underlies standing and walking. To harness the therapeutic potential of EES, we studied its underlying mechanisms, we found that EES activates motor neurons by recruiting proprioceptive circuits within the posterior roots of the spinal cord. This understanding translated into EES protocols that targeted individual posterior roots to access the motor neuron pools located in the spinal cord segment innervated by each root. To engage motor neurons at the appropriate time, spatially selective EES trains are delivered with timing that coincides with the intended movement. Compared to empirical stimulation protocols, spatiotemporal EES enhances the potency of leg movements, which enables weight bearing locomotion in animal model of leg paralysis. When combined with overground locomotor training enabled by a gravity assist device, this stimulation promotes extensive reorganization of residual neural pathways that improves locomotion with and even without simulation.

Here, we report the development of targeted neurotechnologies for delivering spatiotemporal EES during overground locomotor training with gravity assist device in humans. Spatiotemporal EES would immediately enable voluntary locomotion despite chronic paralysis, and that the ability to sustain active movements during training would promote meaningful functional improvements with and even without simulation.

How does it work?

Spinal cord injury leads to severe locomotor deficits or even complete leg paralysis. Here we introduce targeted spinal cord stimulation neurotechnologies that enabled voluntary control of walking in individuals who had sustained a spinal cord injury more than four years ago and presented with permanent motor deficits or complete paralysis despite extensive rehabilitation. Using an implanted pulse generator with real-time triggering capabilities, we delivered trains of spatially selective stimulation to the lumbosacral spinal cord with timing that coincided with the intended movement. Within one week, this spatiotemporal stimulation had re-established adaptive control of paralyzed muscles during overground walking. Locomotor performance improved during rehabilitation. After a few months, participants regained voluntary control over previously paralyzed muscles without stimulation and could walk or cycle in ecological settings during spatiotemporal stimulation. These results establish a technological framework for improving neurological recovery and supporting the activities of daily living after spinal cord injury.

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Edition”***

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(PHARMACY INSTITUTE)**

19, Knowledge Park-II, Institutional Area, Greater Noida-201306, UP

