



APTI Women's Forum Newsletter

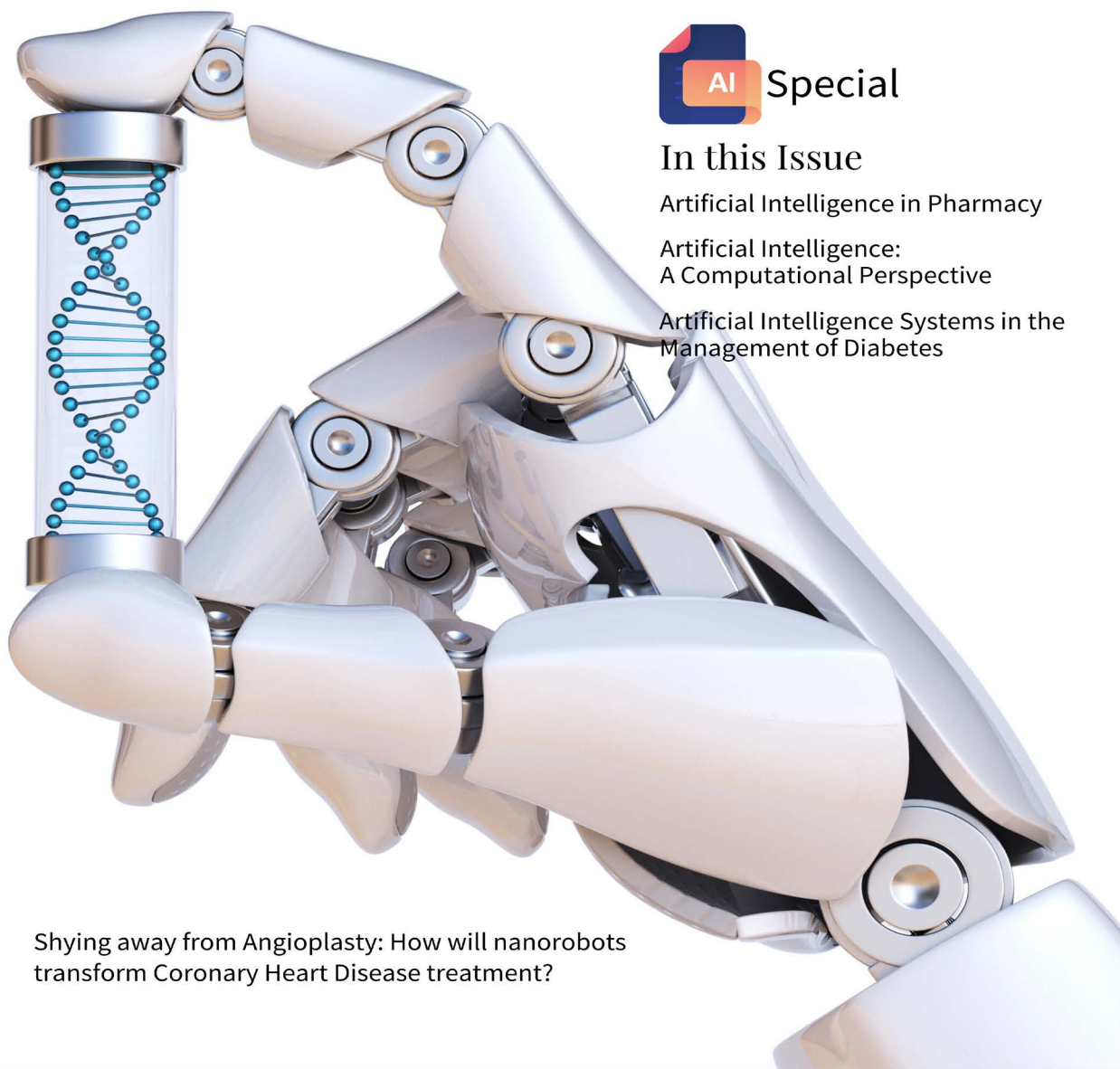


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It gives me immense pleasure to welcome you all to the present issue of APTI Women's Forum Newsletter. We aim to publish high-quality articles associated with women issues in the pharmacy profession. I am certain that the newsletter will succeed to become an invaluable source for the researchers, academicians, professionals working in hospitals, community, regulatory and industries who wish to do innovations, enhanced leadership and administrative skills and contribute to the arena of knowledge-based wisdom. I hope that the articles published in this newsletter will help the readers to achieve their professional goals and expand their knowledge base.

I am contented to know that the new format of this newsletter is solely structured and executed by India's women pharmacy community and spearheaded by the most enterprising Dr. Vandana Patravale, The Chief Editor. I also congratulate the coordination and efforts behind the team to bring out this newsletter in an excellent way. I wish them all success with this quote.

“Sabaka Sath -- Sabaka Vikas”

Dr. Swarnlata Saraf

APTI Vice President & Patron

APTI's Women Forum Newsletter

Editor's Note



Prof. Vandana B. Patravale

Chief Editor, APTI Women's Forum Newsletter

Dear Readers,

It is my huge honor and pleasure to welcome you all to this issue of APTI Women's Forum Newsletter, 2020. Our current issue focuses on the fascinating field of Artificial Intelligence and its amalgamation with Pharmaceutical Industry. Artificial intelligence (AI) has been on the forefront since its inception because of the humongous advantages of cost and time effectiveness. AI has shown the capability to bridge the gap between computational science and formulation science, enabling better planning and execution of pharmaceutical aims and objectives. The articles in this issue of APTI newsletter would enlighten and update its readers with recent trends pertaining to innovative applications of AI in pharmaceutical industry as a whole. The pole to pole section, on the other hand, aims to introduce the upcoming novel concepts which hold immense futuristic research potential. We also intend to keep the readers abreast with the imminent global news of the pharmaceutical

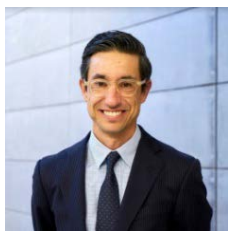
industry which have been highlighted in the industry round-up section. A summary of the approaching research grants has been compiled in a format beneficial to the readers and future researchers.

We, at the editorial board, are highly obliged to all the authors for taking time out of their busy schedule and contributing towards this newsletter to make it a captivating read. I thank the entire editorial team for their efforts in conceptualizing this newsletter. I hope and expect that you all enjoy reading this newsletter as much as we enjoyed bringing it forth to you.

Artificial Intelligence in Pharmacy

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In computer science, artificial intelligence (AI), sometimes called machine intelligence, is intelligence demonstrated by machines, in contrast to the natural intelligence displayed by humans. Leading AI textbooks define the field as the study of “intelligent agents”: any device that perceives its environment and takes actions that maximize its chance of successfully achieving its goals. Colloquially, the term “artificial intelligence” is often used to describe machines (or computers) that mimic “cognitive” functions that humans associate with the human mind, such as “learning” and “problem solving”.¹

Over the past years, our ability to store large repositories of data has surpassed the ability to effectively and efficiently develop actionable knowledge from these sources.² Large clinical databases and electronic health records are valuable data sources for clinical and translational research.³

AI is built to solve questions that include planning, reasoning, knowledge, natural language processing, perception, and the ability to move, manipulate, or omit objects. Methods used draw on statistical methods, computer science, mathematics, cognitive behavioural techniques, psychology, linguistics, and philosophy.⁴

AI has recently re-emerged into the scientific and public consciousness, as new breakthroughs and technologies

are announced from technology companies and scientists at a breakneck pace. Stripped of its science-fictional ornamentation and aspirations, AI is, at its core, a branch of computer science that attempts to both understand and build intelligent entities, often instantiated as software programs.⁵

Medicine was identified early as one of the most promising application areas for AI. Unlike the first generation of AI systems, which relied on the curation of medical knowledge by experts and on the formulation of robust decision rules, recent AI research has leveraged machine learning methods, which can account for complex interactions, to identify patterns from the data. According to the types of task that they intend to solve, basic machine-learning algorithms fall roughly into two categories: supervised and unsupervised.⁶ Supervised machine-learning methods work by collecting a large number of ‘training’ cases, which contain inputs (such as fundus photographs) and the desired output labels (such as the presence or absence of diabetic retinopathy).⁷ By analysing the patterns in all of the labelled input-output pairs, the algorithm learns to produce the correct output for a given input on new cases.⁸ Unsupervised learning algorithms are able to execute more complex processing tasks than supervised learning systems. However, unsu-

pervised learning is sometimes more unpredictable than the other model.⁴

Machine-learning methods enable the development of AI applications that facilitate the discovery of previously unrecognized patterns in the data without the need to specify decision rules for each specific task or to account for complex interactions among input features. Machine learning has thus become the preferred framework for building AI utilities.⁹ The recent renaissance in AI has to a large extent been driven by the successful application of deep learning — which involves training an artificial neural network with many layers (that is, a 'deep' neural network) on huge datasets — to large sources of labelled data. Neural networks with many layers can model complex relations between the input and output but may require more data, computation time or advanced architecture designs so as to achieve optimal performance. Modern neural networks can have tens of millions to hundreds of millions of parameters and take huge amounts of computational resources to train.⁹ Deep learning is increasingly being applied to radiomics, or the detection of clinically relevant features in imaging data beyond what can be perceived by the human eye.¹⁰

The recent confluence of large-scale annotated clinical data acquisition, advancement in machine-learning methods, open source machine-learning packages, and affordable and rapidly growing computational power and cloud storage has fuelled the recent exponential growth in AI. This promises to change the landscape of the pharmacy practice in the near term.¹¹ Since these types of findings are based on statistically-based machine learning models, they are ushering in an era of evidence- and probability-based medicine, which is generally regarded as positive but brings with it many challenges in medical ethics and patient/ clinician relationships.¹²

AI-powered text mining

Traditionally, getting information out of written papers has been manual; individuals reading, reviewing and extracting the key facts from tens or hundreds of papers by hand, in order to summarize the most up to date research in a field, or understand the landscape of information around a particular research topic. Over the past few decades AI tools, such as Natural Language Processing (NLP), have evolved that can hugely speed up and improve this data extraction. NLP solutions can enable researchers and clinicians to access information from huge volumes of scientific abstracts and literature¹³ and enables a more

efficient approach to finding key information, meaning that researchers and clinicians spend less time on search, and more time on understanding.

Inferring health status through wearable devices

Modern wearable devices record a plethora of biomedical signals, including heart rate, voice, tremor and limb movement. These biological signals could be useful for detecting diseases and inferring health conditions. By way of illustration, signs of infectious disease and inflammatory responses can be detected early by using heart rate and skin temperature data recorded by wearables.¹⁴ The inclusion of photoplethysmography sensors in wearables enables the monitoring of cardiovascular diseases, pulmonary diseases, anaemia and sleep apnoea. Wearable sensors could also detect and quantify symptoms of patients with Parkinson's disease, such as tremor and impaired hand movement, gait, posture and speech patterns.¹⁵

In a landscape filled with hundreds of health wearables, it is difficult to determine which ones meet the requirement to strategically augment a pharmaceutical care plan and provide reliable, specific, and sensitive data. With patient stratification being central to emerging concepts such as precision medicine and population health management, providers need a better understanding of the wide range of regulated and clinically vetted wearable technologies that can seamlessly capture reliable vital signs and selectively package the wearables most critical for the management of specific diseases. A Bring-Your-Own-health-Device strategy may increase the likelihood of retentive wearables use and may be the most customer-friendly way to collect health data for a pharmaceutical care plan.⁴

Clinical outcome prediction and patient monitoring

In addition to identifying biomarkers related to clinical phenotypes, the use of electronic health records (EHR) to predict clinical outcomes shows great promise. Bayesian networks can predict mortality, readmission and length of hospital stay by using EHRs from the emergency department.¹⁶ Data from health insurance claims can be used to predict mortality in elderly patients¹⁷, patient attributes in the medical notes can be employed to classify cancer

patients with different responses to chemotherapy¹⁸, and clinical predictors for the prognosis of patients receiving thoracic organ transplantation can be identified¹⁹. With deep-learning algorithms, raw patient-monitoring data could be better used to avoid information overload and alert overload while enabling more accurate clinical prediction and timely decision-making.⁶ Both providers and payers for care are also using 'population health' machine learning models to predict populations at risk of particular diseases or to predict hospital readmission.²¹ These models can be effective at prediction, although they sometimes lack all the relevant data that might add predictive capability, such as patient socio-economic status.

Combating antimicrobial resistance (AMR)

Our understanding of infectious diseases may be profoundly impacted by the advent of big data, where the internet and use of EHR enable access to datasets that were unimaginable 20 years ago. Use of machine learning for combating AMR is in its infancy but has already been applied to antimicrobial susceptibility testing (AST) genotype/phenotype prediction, rationalizing resistance definitions, improving clinical decision making and optimizing approaches to antimicrobial therapy. Due to the increasing availability of genomic datasets, the most immediate applications of machine learning to AMR are likely to be laboratory-based such as AST phenotype prediction.²²

Preventing drug shortages

Pharmaceutical companies traditionally have predicted demand for drugs based on historical data and input from sales teams. Over the past few years, they have had access to more data about drugs in their supply chain because of a new regulation that forced manufacturers in some jurisdictions to add serial numbers to medications, in part to reduce counterfeit drugs. Merck KGaA plans to use analytics and machine learning to predict and prevent drug shortages, a move that could also save it money. It will analyze in real time data from pharmacies, hospitals and wholesale distributors. This could also save drug makers hundreds of millions of dollars annually by reducing waste and avoiding costs like expedited shipments, because it can track a drug's status at every step in the

supply chain. The platform currently holds data on more than 6 billion drugs.²³

Administrative applications

Some healthcare organisations have also experimented with chatbots for patient interaction, mental health and wellness, and tele-health. These NLP-based applications may be useful for simple transactions like refilling prescriptions or making appointments. Another AI technology with relevance to claims and payment administration is machine learning, which can be used for probabilistic matching of data across different databases. Insurers have a duty to verify whether the millions of claims are correct. Reliably identifying, analysing and correcting coding issues and incorrect claims saves all stakeholders – health insurers, governments and providers alike – a great deal of time, money and effort.²⁴

Adherence

Patient engagement and adherence has long been the 'last mile' problem of healthcare – the final barrier between ineffective and good health outcomes. Several new companies are developing AI-driven technologies to facilitate patient compliance. Companies are developing platforms that use software algorithms on smart-phones to visually and automatically confirm patient identity, medication and ingestion, send ingestion/dose reminders, and adapt based on the unique patient behavioural profile. Some platforms have already been shown to increase adherence by over 50%. It is likely that hospitals and health systems will be key players in development and use of machine learning to facilitate patient compliance. A growing focus in healthcare is on effectively designing the 'choice architecture' to nudge patient behaviour in a more anticipatory way based on real-world evidence. Through information provided by provider EHR systems, biosensors, watches, smart-phones, conversational interfaces and other instrumentation, software can tailor recommendations by comparing patient data to other effective treatment pathways for similar cohorts. The recommendations can be provided to care providers, patients, call-centre agents or care delivery coordinators.²⁴ An example is the machine learning system, developed by University College London Hospital, that was trained to predict the likelihood that individual patients will arrive on time for their MRI scan appointment and was found to be very accurate.²⁵

AI triage chatbots

A chatbot is a digital application designed to simulate a digital conversation with human users through AI and that may act via auditory or textual methods. By adding clinical triage and medical content into a bot framework, the virtual personal health assistants can interact with the user on topics regarding, for instance, well-being, experienced health, questions on diseases, and information about healthcare interventions.

Due to the growing quality of interaction and the 24/7 availability of chatbots, these systems may significantly augment the day-to-day interactions with patients. Many of the frequent questions a pharmaceutical care stakeholder gets have significant commonalities and thus may be standardized and offered to patients as needed in a reliable, programmed format as a chatbot. Triage bots may prevent people from having to travel (unnecessarily) for days to reach facilities, and in the future chatbots may be augmented with drones that will provide the medication. As a result, a chatbot may provide the pharmaceutical support required for adequate drug use. The blended approach of digital support if possible and human care where needed does provide a patient's convenience, while also directing patients to the right level of care in a timely way (e.g., escalation to human care by chatbots is done in case of disturbing health signals). Additionally, providing these forms of virtual care may lower the number of calls to pharmacies, resulting in more time for pharmacists to focus on human care, where required.⁴

AI-based triage bots will be the new standard for accessing care in the near future. However, it seems that artificial intelligence can't provide the same quality of care as doctors yet. Researchers analyzed doctors' written notes on intensive care unit patients, the researchers found that the doctors' "gut feelings" about a particular patient's condition played a significant role in determining how many tests they ordered for the patient.²⁶

Pharmacists can take advantage of developments in AI to help people make the most of their drugs and keep them healthier, by detecting drug-related problems and needs, integrating improvements in healthy habits and improving adherence. Improving the efficiency of processes in community pharmacy by new technologies will allow pharmacists to provide hyper-personalized, fast, specific and valuable care to patients, being able to automate the less complicated processes and improve patient

follow-up, as patients have a better, seamless and more convenient care experience.

However, pharmacists' human abilities such as compassion, empathy, active listening and in general good communication skills will be of crucial importance for customers and patients in a world where many activities will be automatized. AI will ease to change the focus to prevention, anticipating disease and worsening in patients' health status. It can influence and change our approach from the dispensing of products to the provision of a broader range of patient care services.

Community pharmacy is an atomised industry in many countries. It is therefore essential that prominent entities or bodies facilitate the needed partnerships, investments and centralised planning to implement digital health tools in pharmacies.

It is essential that pharmacists are familiar with the opportunities, challenges, and technical and ethical issues about artificial intelligence and more broadly about digital health and digital transformation. Therefore, in Spain and some other parts of the world, pharmacy students are beginning to learn about digital health technology.

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Artificial Intelligence: a Computational Perspective”

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Artificial intelligence (AI) is simulation of human intelligence with the help of machines, especially computers.¹ AI can be categorised as strong and weak AI. Strong AI is restricted to being just a theory till date and it can be used in reasoning, puzzle solving, judgement making, learning applications, etc. Applications of weak AI are limited to a narrow sector and examples of these include Apple's Siri, Facebook's news feed, reorganizing spam texts, etc.²

Utilization of computers in pharmaceutical industry goes back to 1980s where, computers were being used in data collection, retail pharmacy management, drug storage functions, etc. Pharmaceutical companies are using AI for drug discovery, toxicity monitoring, clinical trials, clinical research, disease diagnosis, novel drug delivery system design, formulation production lines specifically for cytotoxic drugs, product optimization, data predictions, data analysis and pharmacovigilance. Fourth evolution in pharmaceutical industry is taken up by Artificial Intelligence. In spite of this, implementation rate for AI is relatively low. As pharmaceutical industry deals with the health of humans, we do not rely on computer programmes but we apply human-created algorithms. It is becoming an emerging trend as accuracy is increased and time is reduced. AI will reduce failure rate substantially and will ensure successful treatment.

Computational AI Approaches in Pharmaceutical Industry

Drug Discovery

In the field of modern drug discovery, creating molecule libraries, identifying novel drug candidates with optimal properties, predicting the biological functions of proteins, and in-depth understanding of molecules play critical roles. If drug exhibits toxic properties then it is eliminated at early stage and not used for further development, thereby saving precious screening efforts and time.³ Modification of drug moiety or finding a new lead is a time consuming process. In Computer Aided Drug Design[®] (CADD)- based software, one can simply feed in the native structure of drug moiety and modify its structure (by addition or deletion of ring or group) to study the predicted drug interactions and its allied affinity with the target receptor. It can also determine toxicity of the moiety.

Drug discovery can be hastened by using AI for rapid identification of bioactive molecules from thousands of molecules in the library, assessing parameters in chemical reaction, drug-target interactions, multidrug target discoveries, drug repurposing, biomarker identification, etc.⁴⁻⁶. This reduces cost of discovery by 5-10% surmounting to millions of dollars which will ultimately reduce cost of product development.

Prediction of Solubility

Numerous computational modules have been in use for solubility prediction using the concept of molecular dynamics. As solubility is one of the major concerns in pharmaceutical products involving poorly soluble drugs and their low bioavailability, many types of software are available for solubility predictions but there is a lack of awareness about it. Monte Carlo[®] software (product of SigmaZone) is one of them. Solubility is studied under forced field in which atoms or molecules will primarily interact with each other by Van Der Waals' forces and electrostatic interaction and then interact with covalently bonded atoms.

Solubility is determined at infinite dilution where properties of solute won't change with a change in amount of solvent. Typically transfer of solute is studied from gas to liquid phase or two liquid phases. For partition coefficient determination, **Molecular Dynamic (MD) simulations** or **Monte Carlo[®] (MC)** are used.^{6,7}

Peptide Synthesis

Peptide synthesis, screening of peptides, identifying amino acid sequence, analysis of obtained data by QSAR (Quantitative Structure Activity Relationship) models, evaluation of organ targeting of peptide, prediction of peptide binding to human cell targets, modification of peptide-based drugs to micro and nanostructures are areas where computer systems can play a role.⁸

Schrödinger[®] is one such software mainly dealing with computational chemistry, which can be used to study drug-ligand interactions, protein-peptide interactions, relative free binding energies, conformational searches, structural refinement, etc. It provides multiple methods to analyse binding of small molecules against protein targets. Protein Preparation Wizard assigns bond

orders, tautomeric and ionization states to proteins and peptides. Glide (rigid receptor docking), Induced Fit Docking (flexible receptor docking), and Piper (protein-protein docking) are tools that can be used for Docking studies. Scoring can be done by GlideScore, MM/GBSA, WaterMap, WM/MM and FEP+; they estimate Gibb's free energy. MacroModel, Desmond, and Prime are conformational search modules for molecular mechanics-based peptide conformations, solvent molecular dynamic simulations and prediction of tethered peptides, respectively. Peptide QSAR/ Canvas are statistical methods for modeling of peptide activity. Latest version 19-1 allows taking snapshots at particular time points and refinement in docking with respect to desired fragment.⁹

Cancer Diagnosis

Lack of timely detection is a major hurdle in cancer management as there are no effective techniques available. AI can get combined information from genes, metabolites, proteins, and biochemical processes with *in silico* description of cellular signalling network and onco-molecules like oncogenes and tumor suppressor genes. Simulation softwares like Parameter Optimization®, Monte Carlo®, Reverse Engineering® can be used to increase accuracy in cases involving modulation of individual tumor cells and predicting heterogeneity of tumors. Recently, an interesting technology is analysing miRNA (microRNA), which are noncoding regions on RNA, involved in gene expression of initiation and development of cancer.¹⁰

Developing Antibiotics for Resistant Superbugs

Small peptides like drosocin, pyrrolicorin, and apidaecin (Bahar & Ren, 2013) are cationic and can be used against antibiotic resistant bacteria. Cationic peptides are capable of invading anionic bacteria. Charge, hydrophobicity and amphiphilicity can have an impact on the peptide's activity. This study can be performed by using Medchem studio™ or Medchem designer™ softwares (Simulations Plus products).¹¹ They help detect required therapeutic properties of the drug and its feasibility to be formulated as a suitable dosage form. High throughput screening can also be fastened by using this software.

Predicting Effectiveness of Drug Dosing and Delivery Methods

In vivo prediction of every dose is not possible while devising the treatment strategy. Patients, on the other hand, don't adhere to prescription fearing the side effects and the resultant discontinuation of therapy enables resistant bacteria to grow, so selection of optimum dose is necessary. Example: For validating scalability, minimum human supervision, and adaptivity, metronidazole drug was studied for its effect on *Giardia lamblia*- protozoa, with the aim of predicting the effects via *in silico* analysis. Concentration of drug and cell population was categorized with help of Fuzzy C- Mean clustering algorithm. Drug- pathogen interaction was established after validation which helped in further development of the product.¹²

Dissolution Studies

Formulation selection greatly influences drug release, absorption, and metabolism, altering the drug's pharmacokinetic profile and its pharmacodynamic response. Hence, it can be inferred that the formulation can alter *in vivo* performance of drug product. Drug dissolution testing is used both in the early and the late stages of drug development for many dosage forms, including tablets and capsules. In the early drug development stage, dissolution test helps researchers to find the best formulation to tailor the *in vitro* behaviour to the desired profile. Later, dissolution profiles can be used to establish an *in vitro/in vivo* correlation (IVIVC). An *in vitro/in vivo* correlation (IVIVC) has been defined by FDA as "a predictive mathematical model describing the relationship between an *in vitro* property of a dosage form and an *in vivo* response." The U.S. Pharmacopoeia (USP) defines IVIVC as establishing a rational relationship between a biological property produced by a dosage form, and a physiochemical property of the same dosage form.

Developing and optimizing a new drug formulation may involve changes in drug composition, manufacturing process, use and type of equipment, or batch size. These changes, which can occur often, trigger the need to conduct bioavailability studies to demonstrate bioequivalence. This is found to be faster and cost-effective technique; moreover it doesn't include humans or animals. In the final stages of formulation development,

dissolution testing is used to test batch to batch consistency, stability, and to detect manufacturing defects which might lead to the rejection of an entire lot. In clinical trial phases 3 and 4, bioavailability together with pharmacokinetic data is used for NDA submission which can be done by **Gastroplus**[®] and **DDDplus**[™] (**Simulations Plus product**). In case of generic products, bioequivalence studies are a mandate for submission of ANDA data. Indian market has its identity for providing branded generic products, so simulation in this component of the industry will be helpful potential and cost-effective strategy.¹³

DDDplus[™] software¹⁴ has three main tabs: formulation (drug's physicochemical parameters are used for defining key parameters for simulation), experimental setup (setup tab, the apparatus type, instrument speed, medium volume, and medium type), and simulation. For developing dissolution method, it should be based upon three major criteria *viz.* Discriminatory, Biorelevant and Stability indicating. Dissolution prediction by *in silico* method can help to predict pharmacokinetic and pharmacodynamic properties of enteric-coated, controlled release or sustained release tablets, as dissolution is a direct indication of bioavailability. Besides modified release dosage forms, this technology is used in conventional solid dosage forms as well. Inputs for system are size, shape of dosage form, dissolution time and output obtained is drug release. Like **DDDplus**[™], **IVIVC toolkit**[™] of **Phoenix**[®] is also a simulation software available for similar functions.

Computational methods were not accepted by compendial authorities in the past, making them a non-preferred mode of study, however, upon FDA acceptance, *in silico* analysis has received a huge welcome from the industry. There are already some FDA approved formulations in market of drugs like etoricoxib, amphetamine which have applied *in silico*- based studies during their research and development phase.^{15,16}

Formulation Development

For optimization of pharmaceutical products, Design of Experiments (DoE) softwares are used. Example: Nanoparticles' efficiency depends upon size and entrapment efficiency of nanoparticles. In case of lopinavir poly-ε-caprolactone (PCL)- based polymeric nanoparticles for oral delivery, surfactant concentration, polymer amount and time of homogenisation were taken as independent variables and particle size and entrapment

efficiency as response variables. Box-Behnken design (BBD) was used to optimize response variables; results obtained after optimization were- nanoparticle size as 195.3 nm and 93.9% entrapment efficiency.¹⁷

In case of inflammatory bowel syndrome, new molecules like anti-TNF α are being suggested but they show toxicity and when enemas are given they require large volume of liquids. Hence, hydrogels were prepared using AI tools like **DataForm**[®] v.3.1 software (Intelligensys Ltd., UK) to design experiments with three different polymers and concentrations. This generated primary experimental data for further formulation development. **FormRules**[®] v4.03 (Intelligensys Ltd., UK) was used to make predictions wherein, excipient concentration as input enabled prediction of parameters like syringeability, bioadhesion, and viscosity.¹⁸the development of systems able to fulfil the requirements of this administration route is not an easy task. The present work suggests the utilization of Artificial Intelligence Tools (AIT) This software can not only be used for hydrogels but for all viscous preparations.

Conclusion

AI is undoubtedly the future of pharmaceutical industry. Companies that are more flexible and adopt AI faster will likely gain a strategic advantage in the coming years. In fact, it is predicted that the implementation of AI will soon become a routine protocol for product development and validation in the industry. Application of AI has a huge potential to reduce failure rate substantially thereby ensuring successful therapeutic effect.

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Artificial Intelligence Systems in the Management of Diabetes

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Artificial intelligence (AI), is the replication of human intelligence processes by machines, especially computer systems. AI programming focuses on learning three cognitive skills by providing step by step instructions or algorithm to complete a specific task; reasoning to select the right algorithm to reach a desired outcome and self-correction algorithms to achieve most accurate results possible.¹ The main purpose of using AI in healthcare is for diagnosis and treatment of cardiovascular, Alzheimer, cancer and various other diseases. It is not only employed for basic functions like health monitoring, medication management and maintaining health records but also for robot- assisted surgeries, computer- aided drug design, precision medicine and recognition of potentially cancerous lesions in radiology. AI also has a significant application in the management of notorious disease like diabetes.

According to the World Health Organization (WHO), diabetes is a chronic disease, which is characterized by the inability of the pancreas to produce enough insulin or inability of the body to utilize insulin effectively, leading to elevated levels of blood glucose.² Insulin is the hormone produced by β cells of pancreas, which is responsible for keeping blood sugar in control. Diabetes can be broadly classified as Type 1 Diabetes (T1D) and Type 2 Diabetes (T2D). T1D also known as insulin- dependent diabetes is an autoimmune disease in which the immune system attacks the insulin- producing β cells which happens at an early stage in life and hence known as Juvenile Diabetes. T2D is caused due to insulin resistance in which the body is unable to utilize insulin effectively. Patients with diabetes need to control their blood glucose circumspcctly to avoid ketoacidosis, hypoglycaemia, and other serious complications like heart diseases and strokes. As cited by USFDA, when managing diabetes, patients must test blood glucose levels carefully to calculate insulin doses accordingly and administer doses with an insulin needle frequently 2-3 times a day depending on the severity or insulin infusion pump to lower blood glucose. This procedure is very time-consuming, dispiriting and can lead to a lower quality of life.³

The recent engineering technology to meet clinical demand of diabetes management has progressed to using insulin pump for continuous subcutaneous insulin infusion (CSII), real-time continuous glucose monitoring (CGM) and mathematical algorithms relating CGM and CSII to facilitate automated closed-loop control known as the Artificial Pancreas (AP).⁴ The closed loop insulin delivery systems make use of a control algorithm which allows

the device to continuously monitor the blood glucose level and release insulin as and when needed with little or no inputs from the patient. AP not only maintains the normal insulin level in the body but also controls the radical variations in blood glucose levels which happen during sports activities or sleep without alerting the patient.

AP consists of three basic components which function as follows:

1. A **Continuous Glucose Monitoring (CGM)** is an electroenzymatic sensor which is placed subcutaneously and measures the glucose in the interstitial fluid surrounding the cells. The sensor tip has enzyme glucose oxidase which reacts in the presence of glucose and creates signals. Initially the glucose combines with glucose oxidase and breaks down to give hydrogen peroxide. This hydrogen peroxide reaches the base metal layer of the sensor where it is oxidized to give electrons which generate a current. The current produced is directly proportional to the person's blood glucose levels.⁵ The CGM provides a continuous monitoring and information about the patient's blood sugar levels. A small transmitter sends information to a receiver.
2. The **Closed Loop Control Algorithm** is the salient feature of AP system which consists of software entrenched in a controller (external processor) which monitors blood glucose fluctuations through CGM and actions the insulin pump, computing the insulin delivery rate every minute. It performs a series of mathematical calculations to determine the insulin dose and the controller instructs the insulin infusion pump to release a particular dose of insulin. It has been scrutinized on diabetic and computer- simulated patients. Initially, proportional-derivative control and its enhanced version, proportional-integral-derivative control were used to measure the insulin dose on the basis of blood glucose values and rate in change of blood glucose, but exhibited limitation due to unavoidable time lags in subcutaneous glucose sensing thereby delay in insulin action. Considering this limitation, the new control design, known as model-predictive control (MPC), uses a mathematical model of the metabolic rate of the person to predict its glucose dynamics improving the time delays due to subcutaneous glucose sensing and insulin infusion. With this control system, insulin overdose or extreme blood glucose fluctuations can be avoided. Also, MPC is said

to have capability of learning specifics of patients *i.e.* daily diet, work routine etc. and then optimize the insulin dose delivery using this information.⁶

3. An **Insulin Infusion Device** consists of an insulin pump, an infusion set and a reservoir. The device has insulin release mechanism analogous to natural body. It releases basal insulin throughout the day and night. At mealtime, it releases an insulin bolus for controlling the rising blood glucose from the meal which is consumed. The insulin which is administered is short and rapid acting.⁷

Another type of AP system is Hybrid closed-loop system which is characterised by the synchronization of automated insulin delivery (*via* the algorithm) and patient-initiated insulin delivery, for example, providing mealtime boluses. Patients need to enter information about mealtime carbohydrates in the device to deliver bolus insulin doses.⁸ A number of hybrid closed-loop systems have received FDA approval in recent years. The world's first artificial pancreas Medtronic's MiniMed™ 670G was approved by FDA in 2016 for T1D for 14 years and older population and in 2018 received approval for use in children between 7-13 years of age.

A system designed by Ireland- based medical device giant features SmartGuard™ Technology which automatically adjusts basal insulin every five minutes based on CGM readings and helps to keep blood sugar levels in target range all day and night. It also includes Guardian™ Sensor 3, the only FDA approved sensor to control a hybrid closed loop system with a lifespan of 7 days. The system has self- learning capabilities to assess an individual's insulin needs but requires manual entry of consumed carbohydrates and further approval for recommended bolus corrections.⁹ Bigfoot Biomedical, a California-based company founded and led by people affected by diabetes, came up with Smartloop™ Automated Insulin Delivery System, a cloud connected ecosystem which

integrates wearable insulin delivery and glucose monitoring devices *via* a smartphone application.¹⁰ Defymed in collaboration with Semma Therapeutics designed bio-artificial pancreas, MailPan®, a device consisting of semipermeable biocompatible pouch containing β cells implanted in the abdomen, and delivering the insulin required to regulate the patient's blood-sugar level. The semipermeable membrane allows glucose, nutrients and oxygen to pass through and reach the cells contained in the device and impermeable to the immune system and its antibodies, thereby protecting the patient from rejection of the implanted cells.¹¹

An example of closed loop algorithm is a personalized and configurable Diabeloop's DBLG1 system which automatically optimizes meal ratios employing a handset with secure Bluetooth Low Energy (BLE) which allows patients to read and adjust dose from their phones. It determines insulin doses by taking into consideration patient's physiology, history and data entries.¹² iLet Bionic Pancreas developed by Beta Bionics utilizes two algorithms to achieve desired blood glucose level by instructing the infusion pump to deliver two different hormones: insulin, to lower the blood glucose levels and glucagon, to treat and prevent hypoglycaemic events by raising the blood glucose level. It resembles more closely to the glucose- regulating function of pancreas than insulin- only system.¹³

According to the findings of the BMJ, it was inferred that use of AP is associated with better control of blood glucose levels in patients with T1D compared to the standard treatment. The findings of Eleni Bekiari and team, at Aristotle University of Thessaloniki, Greece, demonstrated safety and effectiveness of artificial pancreas in T1D. The treatment showed almost two and a half extra hours of normal blood glucose levels (normoglycemia) over 24-hour period, while reducing time in both high (hyperglycaemia) and low (hypoglycaemia) blood glu-

| Classification | Mechanism | Example |
|---------------------|--------------------------------|---|
| Internal locomotion | Worm like mechanism | Sequential actuation and cooling of shape memory alloys by passing current enables robot to contract and elongate like worm to move forward ¹⁰ |
| | Legged/Paddle mechanism | Legs are activated by passing signal to the robot which help the robot to adhere at a particular location inside body ¹¹ |
| | Hydrodynamic based mechanism | Propellers are attached to robot to enable them to swim in gastric fluid ¹² |
| External locomotion | Vibration based mechanism | Vibratory motor inside robot enables it to produce centripetal force which propels the robot ¹³ |
| | Magnetic field-based mechanism | An external magnet or electromagnetic coil is utilised to move robot which has internal magnet inside it ¹⁴ |

close levels when compared to other types of therapy.¹⁴ An analogy between sensor-augmented pump therapy and closed loop insulin delivery system based on clinical trials concluded that the use of closed loop system resulted in improved blood glucose levels in target glycaemia range of 3.9 mmol/l to 10 mmol/l and reduced rate of hypoglycaemia at night as compared to the remotely monitored sensor-augmented pump therapy.^{4 15 16 17}

To conclude, AI in diabetes is progressively becoming more sophisticated at doing tasks efficiently, quickly and at a lower cost. AI can also previously detect the early signs of diabetes by analysing patient's heart rates and step counts. AI applications have the potential to help patients to achieve better blood glucose control, reduce hypoglycemic episodes, and reduce diabetes co-morbidities and complications enhancing their quality of life. In future, AI technologies will hold a dominance, motivating innovation in the healthcare sector.

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Shying away from Angioplasty: How will nanorobots transform Coronary Heart Disease treatment?

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When Mr. Kulkarni was rushed to the hospital, he would have hardly imagined that he could be diagnosed with Coronary Heart Disease (CHD). A fine man, in mid-forties, eating vegetarian food only and not consuming alcohol, having a heart attack at such a young age would not have crossed his wildest imagination. His family thought that Gods must have been angry on him and decided to pursue *char-dham* yatra to please the Gods. However, Mr. Kulkarni is not the only one with this tale. A rising number of young Indians are grappling with CHD with around two million people dying each year due to cardiovascular disorders¹. It is estimated that one-third of deaths in India will be due to CHD by the end of 2020. Poor lifestyle is not the only culprit here. It is presumed that South Asians are at a high risk of CHD and are likely to get it at least 8-10 years earlier than the rest of the population². CHD involves the restriction of blood flow to heart owing to the build-up of arterial plaque. Plaque generally consists of cholesterol, fats, cell byproducts and fibrin. Various medicines like anti-platelets, cholesterol-lowering drugs, beta-blockers, nitrates, etc. are used to control the progression of this disease. In dire situations, a patient is left with surgical treatment options like Coronary Angioplasty or Coronary Artery Bypass Graft (CABG)³.

What are the existing surgical treatments?

Coronary Angioplasty involves the insertion of a tiny balloon catheter which helps to widen the blocked artery and improve the blood flow⁴. Nowadays, a small mesh tube known as a stent is also inserted into the artery along with the catheter to keep the artery open and prevent it from collapsing again. These stents are coated with drugs to prevent fibrosis and thereby avoid any potential blockage of arteries⁵. A typical angioplasty procedure in corporate hospitals of tier-1 cities can cost around 2.05 lakh to 2.20 lakh rupees⁶. The surgery can last from 30 min-2 hours and generally requires an overnight hospital stay. The total cost to the patient is significant and not everyone can afford such a treatment resulting in the death of thousands of patients due to heart attack.

Coronary Artery Bypass Graft (CABG) involves removal of a blood vessel from legs, arms or chest of the same patient and using it to create a detour across the blockage for the blood to reach the heart. In a single surgery, two or more coronary arteries can be replaced with

substitute blood vessels. CABG involves open-heart surgery which lasts for 3-6 hours. The patient has to stay in the hospital for approximately one week. The patient typically has a breathing tube in the throat for around 24 hours post-surgery⁷. The surgery costs can run to around 1.5 lakh-2.25 lakh rupees plus the hospital charges⁸. Thus, the existing treatment options for CHD are expensive as well as quite cumbersome to a patient. There is a need for a treatment that is affordable as well as user-friendly. Nanorobots are poised to revolutionize CHD treatment and bring comfort to millions of patients around the globe.

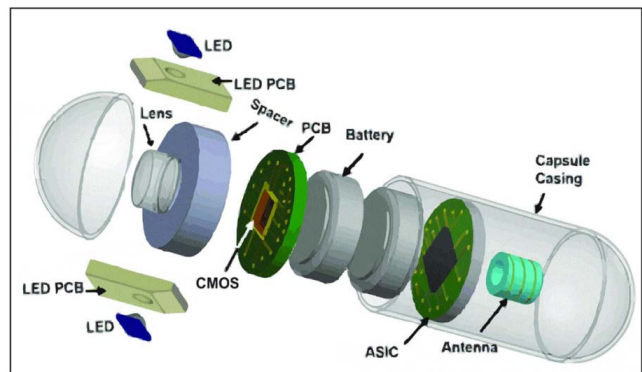


Figure 1: Description of various components in wireless capsule endoscope⁹

What are nanorobots?

The advancements in electronics, material science and nanotechnology have led to the development of different nanosized materials. The science-fiction idea of mini-submarine of medications travelling to the target organ inside the body is within the realms of reality today. One such unprecedented breakthrough is nanorobots. Nanorobots are miniature machines having dimensions ranging from few nanometers to 1000 nanometers. They are biocompatible and typically have electronic circuitry inside them which varies depending on the functionality of the nanorobot. There has been a challenge to develop nanorobots owing to their small size. Commercially available robots, also known as Medical Capsule Robots (MCRs), are a few millimeters in size. They have been launched mainly as wireless capsule endoscopes to diagnose gastrointestinal tract disorders. The break-up of typical components in a wireless capsule endoscope is depicted in Figure 1⁹.

The future of robots lies not only in diagnosing disorders but also treating them. Although no robot has been commercially launched to deliver drugs at a target site

inside body, literature has plethora of examples of robots which have been investigated to conduct targeted drug delivery. These include robots utilizing microelectromechanical systems, nonmechanical systems, biomimetic mechanisms etc. to deliver payload⁹.

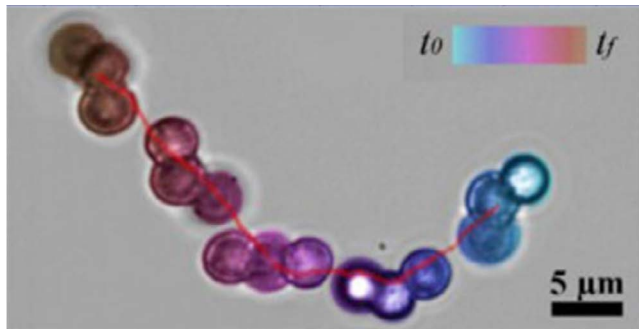


Figure 2: Nanorobot made out of magnetic nanoparticles at Drexel university^{16,17}

Researchers are exploring ways to develop nanorobots which can swim in the blood stream and travel through small diameters of blood vessels. Designing locomotion is quite difficult for such robots, since at nanoscales, the inertia present to power motion is negligible owing to low Reynolds number in blood. The two main mechanisms explored to foster locomotion in robots are internal locomotion and external locomotion. Internal locomotion involves a system wherein the actuator that propels the robot is present inside it. External locomotion involves creation of magnetic field to propel the robot⁹. **Table 1** represents various mechanisms explored under internal and external locomotion.

High cost, lack of control over drug release, inadequate power supply, limited drug storage capacity and safety issues are a few of the concerns associated with nanorobots that have precluded their commercial launch⁹.

How will nanorobots treat CHD?

It is envisaged that nanorobots will clear out arterial plague by penetrating the plague directly¹⁵. Researchers at Drexel University have developed a nanorobot that looks like a microorganism known as *Borrelia burgdorferi* as shown in Figure 2. The robot is fabricated using self-assembly of biodegradable, magnetic nanoparticles made up of Iron (II, III) Oxide (50-100 nm size). The size of the nanorobot can be tuned by carefully controlling the magnetic aggregation. An external magnetic system was utilized to steer the nanorobot in any direction in 2D. The rotating magnetic

field causes the chain of magnetic nanoparticles to rotate in a helical shape and propel in the bloodstream. The force with which the robot moves in the bloodstream can also be controlled by adjusting the intensity of the external magnetic field. The developed nanorobot was able to sustain the Brownian noise at nanoscale thereby setting a foundation for nanorobotic drug delivery in future¹⁶.

Scientists envision that doctors can inject such swimming nanorobots via catheters to the target artery inside the body. Nanorobots can then travel to the occluded area via internal or external locomotion and penetrate the plague. Using the surgical drill mounted on the top, the robot can then loosen the hardened plague present on the arterial wall and break it. Moreover, after breaking the plague, nanorobot can release an anti-coagulant to prevent accumulation of the plague particles. In this way, an occluded artery can be treated without a surgical intervention¹⁷.

Nanorobotic treatment has potential to significantly improve user-friendliness of the existing CHD treatment. Since, no significant surgical intervention is required; the cost to remove arterial plague will be considerably lower than Angioplasty or CABG. The procedure can be performed on an outpatient basis. Moreover, the existing surgical treatments are only 60% successful in treating chronic arterial total occlusion. Nanorobotic treatment can potentially help to achieve as high as 80-90% success in treating such occlusions¹⁷.

What does future look like?

New power supply, locomotion and drug payload carrier mechanisms are being developed to improve control over nanorobots. There is an ongoing effort to fabricate next-generation nanorobots at smaller sizes with advanced functionality. Moreover, safety issues are prioritized, and considerable precaution is being taken to ensure the biocompatibility of nanorobots. This increasing focus of researchers into the development of nanorobots ushers a hope that within a few years, nanorobotic treatment for CHD will be a reality. Millions of people like Mr. Kulkarni can then take a sigh of relief and not worry about living with this life-threatening condition.

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INDUSTRY ROUND UP

Sun Pharma Launches Drizalma Sprinkle in the U.S.

16th October, 2019: Sun Pharma announced its innovative product Drizalma Sprinkle™ (duloxetine delayed-release capsules) in the U.S. for oral use. Drizalma Sprinkle is a serotonin and norepinephrine reuptake inhibitor (SNRI) designed for the treatment of various neuropsychiatric and pain disorders in patients having difficulty in swallowing – affecting approximately 30-35% of the geriatric population requiring long term care. It is available in four dosage strengths (20mg, 30mg, 40mg, and 60mg). Drizalma Sprinkle is the first and only FDA-approved drug which can not only be swallowed as a whole, but also sprinkled (by emptying the contents of capsule) on one tablespoon of applesauce and swallowed or administered via nasogastric tube.

Roche launches DCGI approved Atezolizumab in India to treat extensive-stage (ES) small cell lung cancer (SCLC)

21st November 2019: Roche India announced the launch of Atezolizumab for the treatment of ES-SCLC in India. Atezolizumab is the first cancer immunotherapy to receive an approval in India as a first line treatment of ES-SCLC when given in combination with chemotherapy. Atezolizumab has been previously approved for other two types of cancers: NSCLC and urothelial carcinoma (a type of bladder and urinary tract cancer). The phase III IMpower133 study, showed that it has significantly enhanced overall survival and progression-free survival for the first time in over 20 years for patients with ES-SCLC.

FDA approves EluRyng

11th December 2019: Amneal Pharmaceuticals has launched EluRyng, a generic version of Merck's birth control medication NuvaRing®, following the US Food and Drug Administration (FDA) approval of its abbreviated

new drug application (ANDA). EluRyng is a hormonal contraceptive that involve combination of Etonogestrel and Ethinyl estradiol. NuvaRing® is a small vaginal ring made of 11.7mg etonogestrel and 2.7mg Ethinyl estradiol, indicated to prevent pregnancy. It releases 0.12mg etonogestrel and 0.015mg Ethinyl estradiol per day, on average.

US approves Merck's Ebola vaccine

23rd December 2019: Merck & Co's Ervebo has been cleared by the US regulators for the treatment of Ebola virus disease. This is the 1st vaccine which has won marketing approval in USA for the disease. The vaccine, which was developed at Canada's National Microbiology Laboratory with funding from the US government's Biomedical Advanced Research and Development Authority (BARDA), specifically protects against the Zaire ebolavirus, and can be used in individuals 18 years of age and older. Merck expects that these vaccines will start becoming available in the USA sometime in the 3rd quarter of 2020. The same vaccine was approved by the European commission in February 2019.

Dr. Reddy's launches generic hypotensive injection in US

30th December 2019: Dr. Reddy's Laboratories has launched Sodium Nitroprusside injection in USA, for immediate reduction of blood pressure in hypertensive crises. The company has launched generic Sodium Nitroprusside injection, 50 mg/2 ml (25 mg/ml) single-dose vial after getting approval from the United States Food and Drug Administration (USFDA). The product is a generic version of Hospira Inc's Nitropress injection, 50 mg/2ml.

Amgen commences strategic collaboration with BeiGene to expand oncology presence in China

6th January 2020: Amgen announced the successful completion of its transaction for a strategic collaboration with BeiGene which will allow Amgen to expand its presence in China which is the world's second largest pharmaceuticals market. Beigene is a commercial stage research based Oncology company with strong capabilities in China.

Amgen has acquired a 20.5% stake in BeiGene for approximately \$2.8 billion in cash. BeiGene will commercialize XGEVA® (denosumab), KYPROLIS® (carfilzomib) and BLINCYTO® (blinatumomab) in China, during

which time the parties will equally share profits and losses. Two of these products will revert to Amgen, one after five years and one after seven years. Following the commercialization period, BeiGene will have the right to retain one product and will be entitled to receive royalties on sales in China for an additional five years on the products returned to Amgen. XGEVA was launched in China in September 2019; New Drug Applications for KYPROLIS and BLINCYTO have been filed in China. Amgen will continue to commercialize its non-oncology product portfolio in China.

Lynparza bags FDA approval for pancreatic cancer

6th January 2020: Lynparza (olaparib) has been approved in the US as a 1st-line maintenance treatment of germline BRCA-mutated metastatic pancreatic cancer. This drug is a PARP (Poly ADP-ribose polymerase) inhibitor which was jointly developed by MSD & AstraZeneca. This makes it the first of its kind to be approved for pancreatic cancer as well as being the drug's third tumour type & fifth indication in the USA. The approval has come for adult patients with malignant or suspected malignant germline BRCA-mutated (gBRCAm) metastatic versions of the disease, for patients whose disease has shown no improvement after atleast 16 weeks of a 1st line platinum based chemotherapeutic regimen. Currently, there is no precise medical treatment to treat malignant germline BRCA-mutated metastatic pancreatic cancer. Thus, this approval comes as a ray of hope for patients.

Glenmark gets US-FDA nod for Deferasirox tablets

7th January 2020: The Indian drug manufacturer Glenmark has said that it got final approval for Deferasirox tablets for oral suspensions (125mg, 250mg, 500mg) from the US-FDA. This tablet is the generic version of Exjade tablets for oral suspension manufactured by Novartis Pharmaceuticals Corporation. Exjade is used to treat high levels of iron in the body caused by multiple drug transfusions. The estimated sales of the innovator product was about \$106.4 million.

Merck's Keytruda wins US-FDA approval for bladder cancer

9th January 2020: US-FDA approved the drug Keytruda of Merck & Co for the treatment of a reportedly "hard-to-

treat” form of bladder cancer. This marks the approval of a new treatment for bladder cancer in more than 2 decades. Keytruda is the proprietary name of pembrolizumab, a humanized antibody used in cancer immunotherapy. Keytruda is already approved for treating a number of cancers including melanoma, lung cancer, head and neck cancer and Hodgkin lymphoma. This drug was approved for the treatment in patients with a high-risk, non-muscle-invasive bladder cancer who have undergone prior treatment for whom the surgical removal of cancer is not an option. The results of this mid-stage study showed that nearly 41% of the patients showed a complete response, and about half of them showed complete response for at least 1 year.

Bayer, Exscientia to explore AI in drug discovery

10th January, 2020: A new collaboration was recently announced between Bayer & UK based Exscientia which is expected to accelerate the discovery of small molecule drugs. Artificial Intelligence will be used by the companies to take forward the development of 3 drug candidates of Bayer in cardiovascular disease & oncology.

The company will apply its Centaur Chemist AI drug discovery platform, including its “evolutionary computing” and deep learning algorithms to discover & optimise the novel drug candidates. According to the statement of Dr. Joerg Moeller (member of the executive committee) Bayer AG, AI will drive forward digital transformation in R&D as they believe that digital technologies such as AI can simplify & speed up discovery & development of new drugs for patients.

Contributors for this section: Ms. Mansi Shah, Ms. Priyanka Salunkhe and Mr. Vaibhav Ghegade, Post graduate students, Institute of Chemical Technology, Mumbai.

POLE TO POLE

Bioinspiration in Pharmaceuticals

Bioinspiration is “to tackle challenges by harnessing the power of millions of years of evolutionary patterns and understanding the principle of natural processes and recasting it.” From times immemorial, humans are deriving inspiration from nature to solve their problems, right from when the early man got inspired from rolling wood log for making wheels for transportation to design-

ing aircraft based on aerodynamics of birds. The field of pharmaceuticals is not left untouched. Bioinspiration is growing roots in areas such as drug discovery, targeted drug delivery, nano formulations, and techniques to make drug delivery systems, medical devices and lab equipments.

Bioinspired shapes and movements have proven to be advantageous in terms of avoiding phagocytosis, targeting, cell invasion, etc. over the conventional counterparts. Particles with shapes mimicking that of sperms, pollen, and particles having flagella or fimbriae for attachment as well as movements have been studied for their biomimicking properties. Another example may be pH responsive swellable or unfolding devices/dosage forms intended for increased gastric residence in low pH gastric environment which disintegrates slowly. A very innovative macroscale system something like microgrippers, for soft tissue excision for biopsies etc. which is opened and closed by the thermal stimuli has been developed.¹

The special wettability nanostructures of lotus leaf, springtail skin, rose leaf, shark skin, etc. impart them unique properties leading to their superhydrophobicity and self-cleaning ability. Harnessing these properties for the preparation of perfect spheres of micron sizes of actives, where harsh conditions are completely avoided. Here, added advantage is achievement of high yield (almost 100%) because of air as one of the interfaces and hence there is no loss of the biomaterial. The similar properties go for rose petals, where Wenzel state of a liquid droplet on a roughened surface where along with hydrophobicity, the droplet gets pinned on the surface which can be utilised as “lab on a chip.”

An excellent research developed at Wyss Institute at Harvard University to avoid biofouling and thrombus formation in cardiovascular implants like shunts and catheters etc. is by creating a slippery surface that is inspired by *Nepenthes pitcher* plant. The slipperiness is an attribute to immobilised low surface energy liquid made of proteins and sugars in nectar over the grooved microstructure. The SLIPS (Slippery liquid infused porous surfaces) technology creates anti-thrombogenic surfaces which resists the adhesion of blood components and bacteria. This is achieved by coating a tethered perfluorocarbon layer with a mobile layer of perfluorodecalin on substrates.^{2,3}

A significant and successful class of tissue adhesives are inspired from nature like mussel adhesion by mussel leg protein to sandcastle worms’ secretions, and dry

adhesives inspired from nano-structures on gecko feet. The mussel's adhesion to practically any surface like on other marine organisms, rock, ships is a feature by proteins secreted from its legs. The mussel adhesive protein (MAP) has a high percentage of DOPA which is successfully employed as a tissue sealant and can also act as a link to attach other chemical entities to the nanoparticles in order to functionalise them. Tissue adhesives for minimally invasive surgery which involves small incision either to immobilize medical devices or seal wounds etc. pose big problems like adhesion in wet settings, toxicity, non-uniform concentrations due to dilution by body fluids, improper adhesive activation at right site and desired time, viscosity etc. Getting inspired from the glue secretion mechanism of the sandcastle worm (*Phragmatopoma californica*) without clogging the secretory ducts, researchers have developed a nano encapsulated viscous glue that can easily be injected through small-bore needles for application during minimally invasive procedures. The gecko foot nanostructure enables the gecko to climb and stay stuck to any structure and employs as an alternative to sutures and tissue adhesive. The gecko-inspired structures that work based on frictional forces are strong and easy to remove adhesives. Alternate adhesion or rather gripping technique is built based on observation of attachment of the endoparasite, *Pomphorhynchus laevis*, by its proboscis to the intestine which swells and interlocks with the intestinal wall. Microneedle array that physically interlocks with the tissue by swellable microneedle tips are hence self-adhesive and can act as a substitute to staples for skin graft fixation etc.

Although limited, but the research conducted till present gives a strong evidence of the potential of bio-inspired techniques and their application in the field of pharmaceuticals as well as medical devices. In future, the amalgamation of innovative material science and a strong rationale of drug delivery systems will pave way for dynamic progress in this direction.

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Tissue glue—An emerging solution in wound care and wound management

Tissue adhesive, alternately known as surgical glue, is an upcoming technique in sealing the wounds. It is increasingly used instead of conventional modes such as sutures, staples, tapes and clips. These products are favoured over conventional invasive techniques of sealing as they overcome various limitations such as secondary tissue damage, fluid/gas leakages, post-operative infections and poor cosmetic outcomes. It is commonly administered for superficial cuts but can be further used for the treatment of severe surgical wounds as well.

The terms haemostat, sealants and bioadhesives are used alternately to address tissue glue but they differ in their functions. Haemostats are only effective in the presence of blood whereas sealants are used to prevent leakages of fluid and gases through wounds whereas, bio adhesives are used to heal wounds by holding 2 torn surfaces firmly together. Sealants and adhesives do not work properly in case of wet wounds. For optimum working of tissue glues, they should possess certain properties such as:

1. Stronger adhesion under wet conditions
2. Physiological stability and flexibility
3. Faster rate of crosslinking and settling
4. Negligible toxicity
5. Biocompatibility
6. Stronger holding capacity
7. Balanced force of adhesion and cohesion

Depending upon various polymers that have been used for the development of tissue glue, these are further classified into:

- a. **Cyanoacrylate glues** usually forming strongest interaction (Near about 68KPa) hence used for wound closure during surgeries and wound closures. The commonly utilized combination is butyl (for rapid settling) and octyl (for Flexibility) derivative of the same. Main drawbacks of these glues are cytotoxicity and lack of biodegradability. Some available marketed formulations are Dermaflex™, Dermabond™, Gluestitch™, GlueSeal™ etc.

- b. Fibrin glues** serve an additional advantage of being used for internal injuries. They show minimum adverse effects due to their biocompatibility as they are naturally present within the body. They also serve as sealants. Interactions are usually weak (Near about 13KPa) and are given as fibrinogen and prothrombin along with CaCl_2 (cross-linking agent). Drawbacks of these glues are instability, complications with pathogenic infection due to sources of fibrin extraction, complicated methods of preparations etc. Some available marketed formulations are Replixa[®], FloSeal[™], Artiss[™] etc.
- c. Polymer glue** is a vast category which covers numerous compositions of glues such as Gelatine-Resorcinol-Formaldehyde/Glutaraldehyde Glue (GRFG), Poly (ethylene glycol) (PEG)-Based Hydrogel Adhesives, Sodium Alginate, Chitosan, Oxidized dextrans, epoxy resin and protein-based glues etc. They show moderate mucoadhesive interaction ranging from (4-17KPa) depending upon the type of polymers used, and may show different forces influencing their mucoadhesive characteristics. Drawbacks of these types of glue are poor adhesive and mechanical properties and high swelling index in case of polysaccharide-based glue. Some marketed formulations available are BioGlue[®], FocalSeal[®], PeriAcryl[®], Preveleak[®].

Currently by analysing global market scenario for tissue glue, it is prominently observed that it was valued for USD 1,156.3 million in year 2015 and is estimated to grow up to USD 2,281.2 million in the year 2024 at a rate of 8.0% CAGR creating numerous opportunities in research and development of tissue glue formulations. In an expansion of this market, about 70% of the contribution is of hospitals, around 20% of the contribution from speciality clinic and about 10% by from other sources (source: Persistence market report Dec 2016, Report code PMRREP12898). Some of the key players in global tissue sealants and tissue adhesive market are Baxter International Inc., Johnson & Johnson, Exapharma, Smith & Nephew, C.R Bard and Integra LifeSciences.

Nowadays research is driven more towards the development of biomimetic tissue glues mainly to overcome major limitation of biocompatibility shown by all existing glue formulations. Many naturally available options are explored for the same purpose. **Mussel-Inspired Adhesives** (The adhesive property of mussels, specifically *Mytilus edulis* are studied as they are reversible can hold against strong water current as well giving advantages in strong wet bonding). **Gecko-Inspired Tissue**

Adhesives (Pattern of glue is designed in such a way that it mimics sticking ability of lizard to the wall. The polymer blend is used for creating nanostructure mimicking the same) **Sandcastle Worm-Inspired Tissue Adhesives** (Crosslinking pattern of glue is made similar to that of sandcastle worm). **Barnacle Mimetic Adhesives** (ring-opening polymerization pattern of monomers is designed to mimic barnacle *Balanus hameri* adhesives) and **Caddisfly-Inspired Tissue Adhesives** (in this bio mimetic system, ionic interactions were used in similar fashion to that of caddis fly which use silk thread to make cocoons).

Current market scenarios and advanced techniques open up many research opportunities in this field. Along with composition and structural advancements, chemistry aspects, as well as conformational interaction of polymer system used along with advancement with respect to therapeutic agent delivery, requires long term studies and clinical data support.

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Robotic-Assisted Percutaneous Coronary Intervention

Interventional cardiologists have witnessed an explosive growth in the cardiovascular field. A wide array of percutaneous procedures allows them to treat numerous cardiac conditions less invasively. However, the way they work has changed very little over the past decade. They continue to stand at the table for a prolonged period and are exposed to the very high risks of radiation as well as to the associated orthopedic injuries. The distance from the fluoroscopic images limits the accuracy of their procedures, and patients are at risk of operator fatigue caused by a physician standing for long hours at the table, wearing complicated radiation protection gear that is uncomfortable. Robotic-assisted coronary intervention removes the operator from the radiation field and has been shown to noticeably decrease operator exposure as well as allow for more precise positioning of balloons and stents. This technology holds great promise for making interventional procedures safer and more comfortable for the operators as well as reduce tiredness, thereby potentially improving process outcome. To enhance the accuracy and to minimize occupational hazards associated with radiation, the remote-controlled robotic system is designed.

Robotic System

The system is designed for Percutaneous Coronary Intervention (PCI) and consists of 2 major components: the interventional cockpit and a bedside unit. The interventional cockpit is a radiation-shielded, mobile workstation that is positioned in the corner of the catheterization laboratory. The interventional cardiologist sits at the cockpit and remotely performs the PCI using the touch-screen buttons. Commands from the control console are delivered as electrical signals along a communication cable that runs from the control console to the robotic drive, on which a sterile cassette is placed. The cassette, which is loaded with the interventional devices such as stent, balloon and connected to the guiding catheters, imposes axial and rotational forces on the intracoronary devices. The robotic-assisted system is compatible with all commercially available 0.014-inch guidewires, rapid-exchange coronary angioplasty balloons, and stent delivery systems. Fluoroscopic, electrocardiographic, and hemodynamic images are “slaved” to the duplicate monitors inside the cockpit, enabling visualization from a closer distance. All operators have training on the system that included either animal laboratory experience or using a high-fidelity simulator before enrolling patients in the study. After completion of diagnostic angiography, the guiding catheter is positioned at the ostium of the coronary artery and connected to the disposable cassette on the robotic drive. The guidewire is loaded into the cassette before starting the robotic-enhanced PCI. According to local site protocols, an anticoagulant is administered. Also, pre-dilation is mandatory and post-dilation is done as per operator discretion. All intracoronary devices are to be manipulated exclusively by the robotic system, with a bailout to manual conversion when needed.

Remote-controlled robotic systems are likely to reduce occupational hazards to interventional cardiologists and increase patient safety. The observation report suggested that interventional cardiologists develop posterior lens opacities and cataracts at younger age and in some cases; also develop left-sided brain tumors. Long hours of wearing a heavy lead apron during the process may adversely affect interventional cardiologists. A remote-controlled robotic system is designed to minimize the procedural challenges and occupational hazards of an operator associated with traditional percutaneous coronary intervention (PCI) in addition to increasing the degree of accuracy and control for the interventional procedure.

Future Directions of Robotics-Assisted Percutaneous Coronary Intervention

Robotic PCI technology will continue to improve with future generation devices. It would be ideal if engineers could modify active ports for advancing catheters to allow easier methods to treat complex bifurcation lesions, which are nowadays complicated to perform robotically. A further improvement would allow the use of over the wire techniques, peripheral applications, and manipulation of other coronary devices. However, it is doubtful that robotic technologies will be suitable for structural interventions. It is expected that more extensive adaptation of this new way of working in the cardiac catheterization laboratory will lead to further advances, thus making PCI procedures safer and more efficient for both the patient and the operator.

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Modeling Of Cerebral Aneurysm

Basics of Cerebral Aneurysm

Brain arterial aneurysms are common forms of arterial deformation occurring in about 5% of the adult population. The aneurysm is a bulge along the artery hanging there embedded in the surrounding tissue. This bifurcation is the part of the supplier of the brain vascular bed system so if its blow-out (rupture) causes incalculable chain reaction, there is no safe solution without any side effect to protect the patient against unpleasant consequences. It would be desirable to be able to identify those aneurysms most at risk of such an episode. This would assist clinical diagnostic procedures and avoid the potentially undesirable consequences of an unnecessary operation. It is envisaged that computational models of Intracranial Aneurysm evolution may help in achieving this aim.

Computational Advances

Advances in medical imaging, particularly CT and MRI, provide exquisite information on overall patient-specific geometries, yet limitations in spatial resolution continue to hamper estimates of wall thickness that are fundamental to computing wall stress. Applied loads arise primarily from three sources: the hemodynamic loads that act on the luminal surface, the perivascular tissue that acts on the outer surface, and an inherent pre-stretch that stresses the aorta axially. Whereas hemodynamic loads (i.e., components of the traction vector normal and tangential to the lumen) can be estimated from computational studies, perivascular effects remain difficult to assess. In vivo residual and axial pre-stresses and material properties are similarly difficult to assess on a patient-specific basis, particularly when seeking to include changes due to aging, co-morbidities, and the evolution of the lesion.

One model was based on the arterial wall. In these studies, the remodeling phenomena was modeled by changing the arterial wall thickness, the opening angle or the tissue compliance, rather than explicitly associating adaptations to the microstructural architecture evolution. In particular, a global approach was introduced by Rachev et al., 1996 in which the growth of an artery was controlled by the average wall stress, the strains at the inner and outer vessel radii, and a flow condition on the inner radius. The constrained mixture model of Humphrey and Rajagopal has been developed to capture arterial adaptation, with attention to individual constituents that turned over at different rates rather than to overall changes in the vessel. Socci et al., 2007 applied a similar approach to investigate the sites prone to aneurysm formation in U-shaped vessels resembling the curvatures of the human internal carotid artery. The results of the computational fluid dynamic (CFD) simulations, in terms of pressure and wall shear stress, were used as boundary conditions and mechanical stimuli for the structural-adaptive model. The geometry obtained after the growth-remodeling process showed an initial wall bulging and could be used for subsequent CFD simulations to assess the eventuality of aneurysm formation.

Despite tremendous advances in modeling (CFD, FSI, and FEA), we must move from computational “snapshots” during aneurysmal development (i.e., focusing on a mechanical state) to studies focusing on dynamic mechano-biological processes that encompass the time course of lesion growth and remodeling (G&R). By growth, we mean a change in mass; by remodeling, we mean a change

in structure. Because remodeling can occur via removal and replacement of material, not just reorganization, G&R are often inextricably linked and one should seek a theoretical framework that encompasses both (Humphrey and Rajagopal, 2002).

Watton et al., 2014 proposed a Fluid-Solid-Growth framework for modelling Intracranial Aneurysm evolution. This utilises a realistic constitutive model of the arterial wall and the evolving structure and composition of the tissue is explicitly linked to local haemodynamic stimuli. The model has also been integrated into physiological vasculature geometries and extended to explicitly link G&R to the local haemodynamic and cyclic deformation stimuli. Figueroa et al., 2008 developed a computational framework that considers aneurysm development belonging to the class of fluid-solid growth problems. In this case, aneurysm development was considered multi-scale both in space and in time. The biomechanical forces and biochemical stimuli are sensed at a molecular and cellular scale and cause adaptive responses from molecular (nm) to organ (cm) scales; moreover, fluid-structure phenomena act in a short time scale (s), while adaptive phenomena required longer periods (weeks-months).

Future Aspect

The development of intracranial saccular aneurysms remains an enigma: it is neither known why they form and enlarge, nor why only some of them rupture. Nonetheless, there is general agreement that mechanics play an essential role in each aspect of the natural evolution of these lesions.

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Interaction meeting on the theme “Women health and social well-being” by APTI women forum and Shakti Mahila Vigyan Bharti, Chhattisgarh

An interactive meeting on the theme “Women health and social well-being” was organized at M.L. Schroff Hall, University Institute of Pharmacy, Pt. Ravishankar Shukla University, Raipur, (C.G.) on 28th of January 2020 from 12.00 p.m onwards. This programme was organized under the aegis of APTI Women Forum and Shakti Mahila Vigyan Bharti Samiti Chhattisgarh. Programme was graced by renowned women pharmacist Dr. Archana Mudgal, Registrar, Pharmacy Council of India, New Delhi as Chief Guest and other special invited guests were Mrs. Seema Suresh renowned life motivator of society; Mrs. Alpana Chauhan social worker. Many social activists working at grass root level for women in the state of Chhattisgarh and nationwide also graced the event. Programme marked the presence of all the women faculties in the state of Chhattisgarh belonging to pharmacy and other streams like psychology, health science, economics, Medicines, Life Science, Nutrition and Sociology etc. Dr. Mudgal highlighted the importance of womens’ mental and physical health to keep the society healthy. She emphasized on importance of family in maintaining complete health. All invited guests were felicitated by APTI women representatives from state with Shawl and Sripthal. In this sequence Prof Swarnlata Saraf, Vice-president APTI central zone also stressed on the need to look after the physical, social, mental, spiritual and psychological issues of women for complete health. Dr. Manju Singh, co-convenor APTI women forum introduced the various initiatives taken to create common platform for all women pharma fraternity to discuss and sort their issues. The open interactive session was witnessed by enthusiastic participation from women teachers from various regions of Chhattisgarh.

All women faculties were motivated to interact with each other and planned to organize more events on



monthly basis where they can meet and interact for resolving various issues confronted at personnel and professional facade. The program undoubtedly motivated and encouraged the women to keep themselves healthy so as to get a healthy and cherished society.

Women Achievers



Dr. Rani Potawale, Assistant Professor at Allana College of Pharmacy, Pune, was awarded the Doctor of Philosophy degree from the Suresh Gyan Vihar University, Jaipur on 4th July, 2019.



Dr. Udichi Kataria, Associate Professor and Head of Department in Geetanjali Institute of Pharmacy, Udaipur Rajasthan, was awarded the Inspirational Associate Professor Award in DST-NSTMIS Sponsored Stakeholder Workshop at Indore, Madhya Pradesh on 28th September 2019. The title of the workshop was “A Collaborative Initiative Striving to Build A New Era of Academia-Industrial Interactions That Foster Pharmaceutical Innovations”



Mrs. Kanchan Chauhan, Assistant Professor at Allana College of Pharmacy, Pune, Maharashtra was awarded the Doctor of Philosophy degree in Pharmaceutical Chemistry under the guidance of Dr. V. P. Choudhari, Professor, MAAER'S Maharashtra Institute of Pharmacy, Pune from the Savitribai Phule Pune University on 15th November 2019.

Dr. Vandana B. Patravale, Professor of Pharmaceutics, Department of Pharmaceutical Sciences and Technology at Institute of Chemical Technology, Mumbai, and her Research Group were granted two Indian Patents

1. Indian Patent No. 323787 entitled 'Pharmaceutical Composition for Bioenhancement of Active Agents' (Date of grant: 28th October 2019)

2. Indian Patent No. 327197 entitled 'Process and Fabrication of Pharmaceutical Compositions using Supercritical Fluids' (Date of grant: 11th December 2019)

RESEARCH GRANTS

DBT-BIRAC CALL FOR DRUG DEVELOPMENT

With the aim to take India at global map in terms of R&D innovations in the area of drug development in our country, the Department of Biotechnology (DBT) has initiated a new program on "Drug Development" with a vision to develop indigenous and cost-effective new drugs against the following diseases:

- I. Communicable Diseases (Tuberculosis) &
- II. Non-Communicable Diseases Cardio-Vascular Diseases (CVD), Chronic Obstructive Pulmonary Diseases (COPD) and Cancer (oral, head and neck, cervical and breast cancer)

Purpose of the Call: The goal of this Call is to support **milestone-driven proposals focused on lead optimization and preclinical testing of candidate therapeutics for the given four diseases**. All proposed studies must be directed to regulatory submission in India and therefore this Call excludes basic research, studies of disease mechanisms or epidemiological studies.

Of the Drug Development stages as defined below, this Call is intended for research and development activi-

ties focused *ONLY* on **Lead optimization and preclinical development and Clinical therapeutic validation** to a point where there is sufficient scientific evidence to justify filing for regulatory approval.

Scope of this Call: This Call is aimed to support **collaborative proposals that combine complementary and synergistic research strengths in proposed lead candidate(s)/preclinical therapeutic lead(s)**. Proposals must have one or more identified preclinical therapeutic leads with supporting efficacy data (in animal models; supported by *ex vivo* human cells/tissues, iPSC-derived organoids, and well justified *in vitro* target/pathway engagement) for the above mentioned four diseases.

Timeline: Call for Proposal closes: **29.02.2020**

Website: www.birac.nic.in

BIOTECHNOLOGY IGNITION GRANT (BIG) SCHEME

Biotechnology Ignition Grant scheme enables technology innovators and entrepreneurs to pursue a promising technology idea, and establish and validate proof of concept (POC) for the idea.

Key features of the call

- Supports high level innovation in the Biotech sector and is not meant for basic research projects.

- Grant-in-aid up-to INR 50 lakhs for a maximum period of 18 months
- Implementation and Mentoring through BIRAC's BIG Partners

Who can apply?

- Start up age allowed for a registered company/ LLP incorporated under BIG w.e.f 1st Jan 2019: 5 years
- Scientists, Faculty, Research Scholars, Graduates in any discipline incubating/ intend to incubate at a BioIncubator

Timeline:

Call for Proposal closes: 15th February, 2020 (05:30 PM)
 Website: www.birac.nic.in

BOARD OF RESEARCH IN NUCLEAR SCIENCES (BRNS)

BRNS supports high quality research & development on advanced concepts of relevance to DAE.

Eligibility: Scientists / Engineers working in universities, academic/ research institutions of higher learning, having a regular position in government recognized universities, academic/ research institutions ONLY are eligible to apply.

Researchers associated with government recognized incubation centre and DSIR (Department of Scientific and Industrial Research) recognized R&D organizations of Private Industry can also be considered for fund-

ing. **Those working in DAE units, NGO and scientific societies should not apply.**

Applicants seeking financial assistance to carry out research projects under categories of Regular research projects (RP) should prepare their application as per the prescribe format given on the BRNS website and submit their application online. It may be noted that it is mandatory give details of the Principal Coordinator (PC) from DAE and one Co-Investigator (CI) from the same institution, at the time of applying for regular research project (RP). The CI is expected to take the responsibility of taking forward the project on technical as well as financial matters, in the absence of the PI.

Timeline: All round the year
 Website: www.brns.res.in

SCIENCE AND ENGINEERING RESEARCH BOARD (SERB)

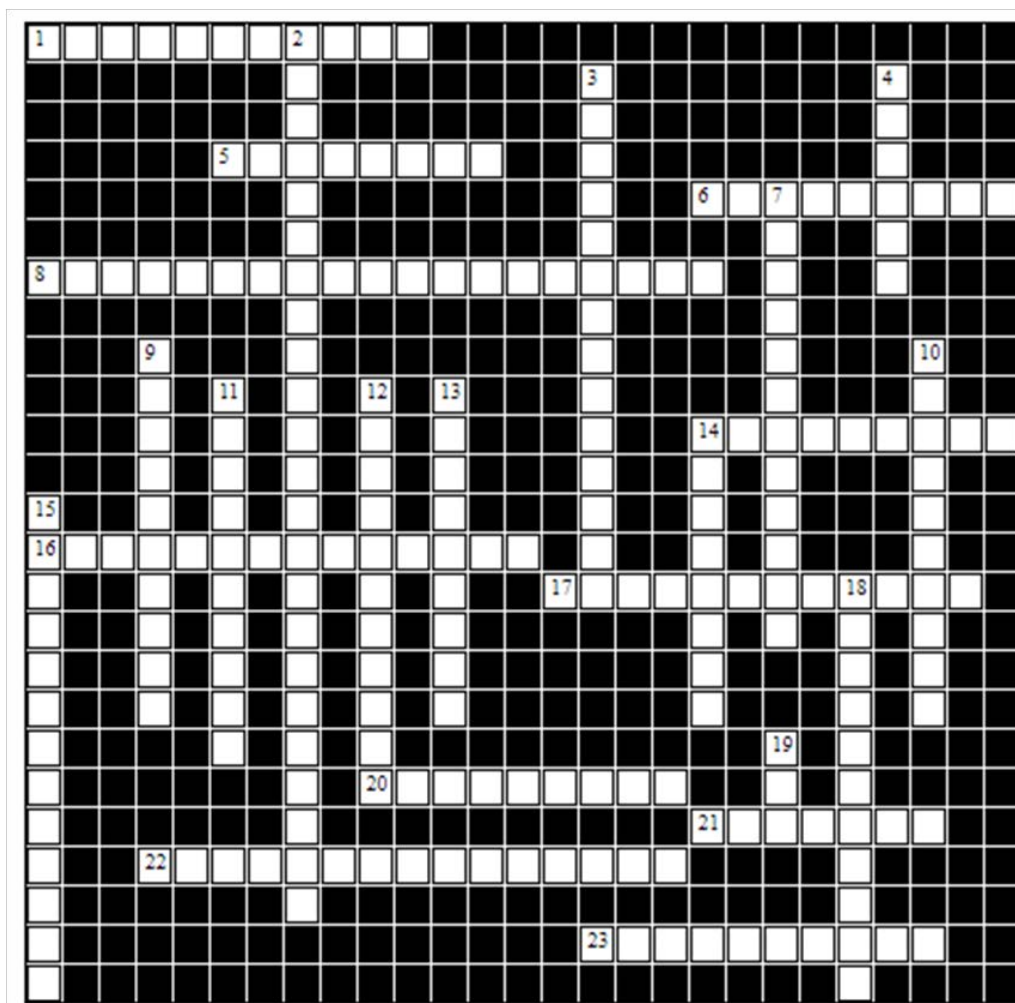
The Science and Engineering Research Board (SERB) is a statutory body established through an Act of Parliament. Supporting basic research in emerging areas of Science & Engineering are the primary and distinctive mandate of the Board. SERB supports research in frontier areas of Science and Engineering.

Following are the schedule of Call for proposals for 2020.

| Program/Scheme | Call Opening Date | Call Closing Date |
|---|-------------------|-------------------|
| Start-up Research Grant (SRG) | 1 February 2020 | 2 March 2020 |
| Core Research Grant (CRG) | 1 February 2020 | 9 March 2020 |
| Teachers Associateship for Research Excellence (TARE) | 10 February 2020 | 16 March 2020 |
| MATRICES | 24 February 2020 | 23 March 2020 |
| Scientific and Useful Profound Research Advancement (SUPRA) | 15 February 2020 | 1 April 2020 |
| Empowerment and Equity Opportunities for Excellence in Science (EMEQ) | 6 March 2020 | 6 April 2020 |
| National Postdoctoral Fellowship (NPDF) | 13 March 2020 | 13 April 2020 |
| SERB Science and Technology Award for Research (SERB STAR) | 15 June 2020 | 27 July 2020 |

Website: www.serb.gov.in

CROSSWORD PUZZLE



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| <ol style="list-style-type: none"> 1. Test for the identification of anthraquinones 5. Material of construction o Loops used for inoculation of sample on media 6. Discoverer of Morphine 8. biological indicator is used for validation of membrane filtration (2 Words) 14. Father of Indian Pharmacy (3 Words) 16. Ligand decreasing the activity of an active receptor (2 Words) 17. Unsaturated ω-6 fatty acid (2 Words) 20. Condensation product of sugar and aglycone 21. Low cost formulation alternative 22. Synthesis of glucose from fat 23. Ergot alkaloid | <ol style="list-style-type: none"> 2. Ion exchange chromatography is based on the (2 Words) 3. Indicator for complexometric titration (3 Words) 4. Molecule with 3-dimensional asymetry 7. Statin 9. Electronic list of Approved Drug Products with Therapeutic Equivalence Evaluations (2 Words) 10. Biological generic 11. Citric acid cycle (2 Words) 12. Mixing Medications 13. Cinchona alkaloid 14. Molal concentration 15. In vivo biological equivalence of two proprietary preparations of a drug 18. Reduces fever 19. IV Nutrition |
|---|--|

Unscramble:

Please unscramble the words to find the hidden pharmaceutical companies

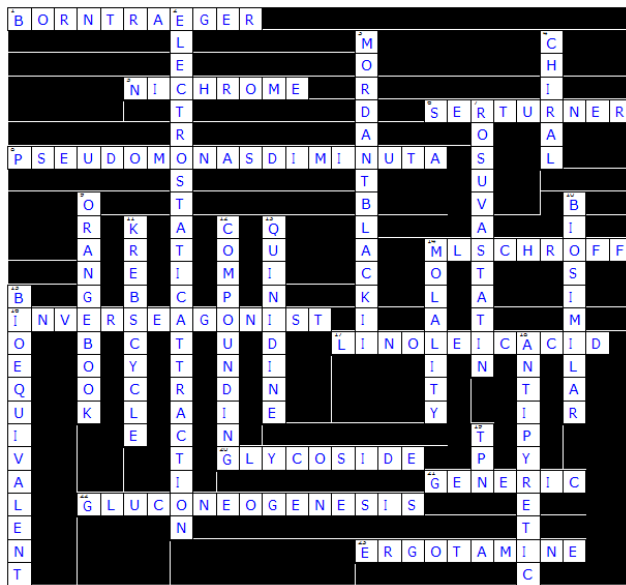
- 1. ILE IYLLL
- 2. IBVBAE
- 3. RBEAY
- 4. CRHEO
- 5. OSAIRTVN
- 6. MGNEA
- 7. RZPFIE
- 8. AKTADE
- 9. CDAHIII KSANYO
- 10. RFINGER IRPTACASELMUCAH

WORD SEARCH

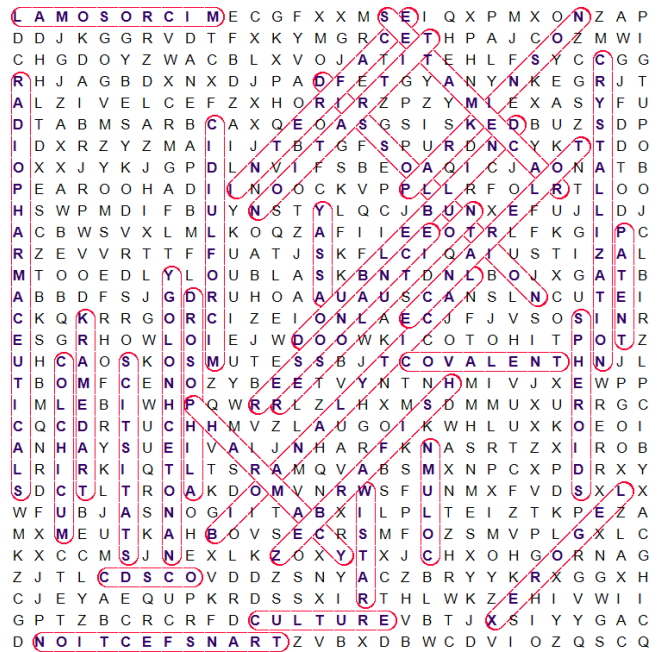
L A M O S O R C I M E C G F X X M S E I Q X P M X O N Z A P
 D D J K G G R V D T F X K Y M G R C E T H P A J C O Z M W I
 C H G D O Y Z W A C B L X V O J A T I T E H L F S Y C C G G
 R H J A G B D X N X D J P A D F E T G Y A N Y N K E G R J T
 A L Z I V E L C E F Z X H O R I R Z P Z Y M I E X A S Y F U
 D T A B M S A R B C A X Q E O A S G S I S K E D B U Z S D P
 I D X R Z Y Z M A I I J T B T G F S P U R D N C Y K T T D O
 O X X J Y K J G P D L N V I F S B E O A Q I C J A O N A T B
 P E A R O O H A D I I N O O C K V P P L L R F O L R T L O O
 H S W P M D I F B U Y N S T Y L Q C J B U N X E F U J L D J
 A C B W S V X L M L K O Q Z A F I I E E O T R L F K G I P C
 R Z E V V R T T F F U A T J S K F L C I Q A I U S T I Z A L
 M T O O E D L Y L O U B L A S K B N T D N L B O J X G A T B
 A B B D F S J G D R U H O A A U A U S C A N S L N C U T E I
 C K Q K R R G O R C I Z E I O N L A E C J F J V S O S I N R
 E S G R H O W L O I E J W D O O W K I C O T O H I T P O T Z
 U H C A O S K O S M U T E S S B J T C O V A L E N T H N J L
 T B O M F C E N O Z Y B E E T V Y N T N H M I V J X E W P P
 I M L E B I W H P Q W R R L Z L H X M S D M M U X U R R G C
 C Q C D R T U C H H M V Z L A U G O I K W H L U X K O E O I
 A N H A Y S U E I V A I J N H A R F K N A S R T Z X I R O B
 L R I R K I Q T L T S R A M Q V A B S M X N P C X P D R X Y
 S D C T L T R O A K D O M V N R W S F U N M X F V D S X L X
 W F U B J A S N O G I I T A B X I L P L T E I Z T K P E Z A
 M X M E U T K A H B O V S E C R S M F O Z S M V P L G X L C
 K X C C M S J N E X L K Z O X Y T X J C H X O H G O R N A G
 Z J T L C D S C O V D D Z S N Y A C Z B R Y Y K R X G G X H
 C J E Y A E Q U P K R D S S X I R T H L W K Z E H I V W I I
 G P T Z B C R C R F D C U L T U R E V B T J X S I Y Y G A C
 D N O I T C E F S N A R T Z V B X D B W C D V I O Z Q S C Q

| | | |
|----------------------|----------------|-------------|
| PHARMACY | CDSO | PATENT |
| TRADEMARK | COLUMN | ASSAY |
| TITRATION | PARKINSON | ZEBRAFISH |
| MICROSOMAL | COLCHICUM | DISSOLUTION |
| CRYSTALLIZATION | TOLERANCE | RACEMATES |
| XEROGEL | RESOLUTION | RESONANCE |
| WISTAR | DROSOPHILA | COVALENT |
| MICROFLUIDIC | NANOTECHNOLOGY | DOUBLEBLIND |
| INTERFACE | CULTURE | STATISTICS |
| RADIOPHARMACEUTICALS | BIOANALYTICAL | SPHEROIDS |
| TRANSFECTION | | |

Answer key for Crossword



ANSWER KEY FOR WORD SEARCH



Answer Key for scramble

1. ELI LILLY
2. ABBVIE
3. BAYER
4. ROCHE
5. NOVARTIS
6. AMGEN
7. PFIZER
8. TAKEDA
9. DAIICHI SANKYO
10. FERRING PHARMACEUTICALS

ANSWER KEY FOR WORD SEARCH

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LOTUS BACKGROUND STORY

As a lotus is able to emerge from muddy waters un-spoilt and pure it is considered to represent a wise and spiritually enlightened quality in a person; it is representative of woman who carries out their tasks with little concern for any reward and with a full liberation from attachment. Lotus-woman in the moern sense of women's qualities: she is superbly intelligent, highly educated, and totally committed to individualism. She is politically astute and works incessantly for a better and more humane society. She is exquistite in her taste for music, art and culture, abounds in social graces and performs brilliantly in communication.

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