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A REVIEW: ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY AND DEVELOPMENT

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ABSTRACT

Artificial Intelligence (AI) has recently began to gear-up its application in various sectors of the society with the pharmaceutical industry as a front runner beneficiary. This review highlights the impactful use of AI in diverse areas of the pharmaceutical sectors viz., drug discovery, development of drug , drug repurposing, improving pharmaceutical productivity, clinical trials, etc. Thus reducing the human workload as well as achieving targets in a very short period. Crosstalk on the tools and techniques utilized in enforcing AI, ongoing challenges and ways to overcome them, together with the longer term of AI within the pharmaceutical industry is additionally discussed.

Keywords *- Artificial Intelligence, Drug Discovery, New Technology, Human Intelligence*

1. INTRODUCTION

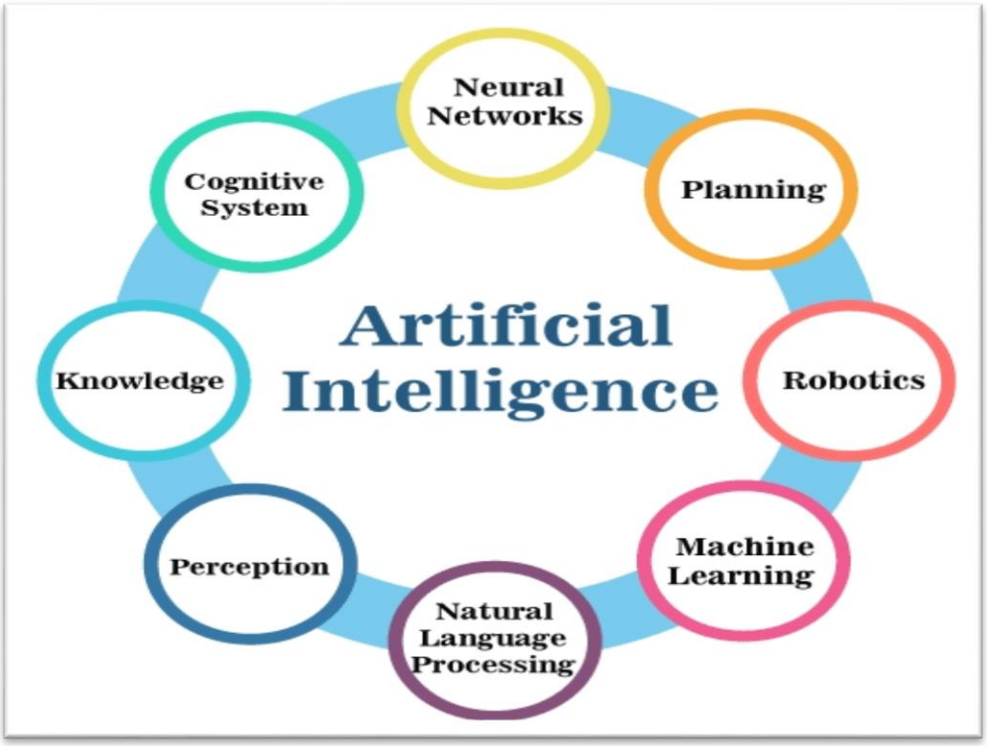
Over the past few years, there has been a drastic increase in data digitalization within the pharmaceutical sector. However, this digitalization comes with the challenge of acquiring, scrutinizing, and applying that knowledge to unravel complex clinical problems.[1] This motivates the utilization of AI, because it can handle large volumes of knowledge with enhanced automation. AI may be a technology-based system involving various advanced tools and networks that may mimic human intelligence. At the identical time, it doesn't threaten to interchange human physical presence completely. AI utilizes systems and software which will interpret and learn from the computer file to create independent decisions for accomplishing specific objectives. Its applications are continuously being extended within the pharmaceutical field, as described during this review. per the McKinsey Global Institute, the rapid advances in AI-guided automation are likely to completely change the work culture of society. [1,2,3]

2. ARTIFICIAL INTELLIGENCE

Artificial Intelligence (AI) may be a stream of science associated with intelligent machine learning, mainly intelligent computer programs, which provides leads to the similar thanks to human attention process.[4] This process generally comprises obtaining data, developing efficient systems for the uses of obtained data, illustrating definite or approximate conclusions and self corrections /adjustments. In general, AI is employed for analyzing the machine learning to imitate the cognitive tasks of people. AI technology is exercised to perform more accurate analyses in addition on attain useful interpretation. [4, 5] Artificial intelligence (AI) could be a branch of applied science that deals with the matter –solving by the help of symbolic programming . it has greatly evolved into a science of problem- solving with huge application in business, health care, engineering. the most objective of this computer science to spot useful informatics problems and provides an abstract account of the way to solve them. Such an account is termed as method and it corresponds to a theorem in mathematics. Computer science as a field that deals with the planning and application algorithms for analysis of learning from and interpreting data. AI compasses many branches of statistical and machine learning, pattern recognition, and clustering, similarity-based methods. AI may be a flourishing technology which finds application in multiple aspects of life and industry. [6,7] AI involves several method domains, like reasoning, knowledge representation, solution search, and, among them,a fundamental paradigm of machine learning (ML). ML uses algorithms which will recognize patterns within a collection of knowledge that has been further classified. A subfield of the ML is deep learning (DL), which engages artificial neural networks (ANNs). These comprise a collection of interconnected sophisticated computing elements involving 'perceptons' analogous to human biological neurons, mimicking the transmission of electrical impulses within the human brain.ANNs constitute a collection of nodes, each receiving a separate input, ultimately converting them to output, either singly or multi-linked using algorithms to resolve problems. ANNs involve various types, including multilayer perceptron (MLP) networks, recurrent neural networks (RNNs), and convolutional neural networks (CNNs), which utilize either supervised or unsupervised training procedures. [1,8]

The MLP network has applications including pattern recognition, optimization aids, process identification, and controls, are usually trained by supervised training procedures operating during a single direction only, and might be used as universal pattern classifiers. RNNs are networks with a closed-loop, having the potential to memorize and store information, like Boltzmann constants and Hopfield networks. CNNs are a series of dynamic systems with local connections, characterized by its topology, and have use in image and video processing, biological system modeling, processing complex brain functions, pattern recognition, and complex signal processing. One such tool developed using AI technology is that the International

Business Machine (IBM) Watson supercomputer (IBM, New York, USA). it had been designed to help within the analysis of a patient's medical information and its correlation with an unlimited database, leading to suggesting treatment strategies for cancer. this technique also can be used for the



rapid detection of diseases. This was demonstrated by its ability to detect carcinoma in mere 60 s. [1,2,9]

Fig. AI in various sectors

Artificial intelligence (AI) is that the simulation of the human intelligence process by computers. the method includes acquiring information, developing rules for using the data, drawing approximate or definite conclusions and self-correction. The advancement of AI is seen as a double-edged sword: many fear that it'll threaten their employment; in contrast, every advance in Al is well known thanks to the assumption that it'll vastly contribute to the betterment of society. Al is employed in various sectors from innovating educational methods to automating business processes. The sprouting idea of adopting Al within the drug development process has shifted from hype to hope. during this review, the possible applications of Al within the drug development pipeline in drug development strategies and processes, the pharmaceutical R&D efficiency and attrition, and partnerships between Al and pharmaceutical companies are discussed. [10] In Recent times the pharmaceutical industry discovers novel and innovative ways to use this powerful technology to assist solve a number of the most important problems facing pharma today. computing in Pharma refers to the utilization of automated algorithms to perform tasks which traditionally depend upon human intelligence. Over the last five years, the utilization of computing within the pharma and biotech industry has redefined how scientists develop new drugs, tackle disease, and more . [6,11]

3. ARTIFICIAL INTELLIGENCE IN PHARMA INDUSTRY

Recently, AI technology becomes a really fundamental a part of industry for the useful applications in many technical and research fields.[12]. The emergent initiative of accepting the applications of AI technology in pharmacy including drug discovery, drug delivery formulation development and other healthcare applications have already been shifted from hype to hope. [4, 12] Pharmaceutical Industry can accelerate innovation by using technological advancements. The recent technological advancement that involves mind would be AI, development of computer systems ready to perform tasks normally requiring human intelligence, like seeing, speech recognition, decision-making, and translation between languages. With humongous data available during this domain, AI are often of real help in analyzing the information and presenting results that may analysis in higher cognitive process, saving Human effort, time, money and thus help save Lives. Epidermic outbreak prediction; using machine learning /artificial intelligence one can study the history of epidermic outbreak, analyse the social media activity and predict where and when epidermic can effect with cocidarable accuracy. [6,7,11] The current drug discovery process must shift dramatically so as to satisfy needs of both society and patients within the 21st century. Pharmaceutical industry can accelerate innovation by using technological advancements. Pharmacy is one among the few top domains which might benefit the foremost from emergence of computer science, since its direct impact would be augmenting health.[13,14,15]

Artificial Intelligence (AI) focuses in producing intelligent modelling, which helps in imagining knowledge, cracking problems and higher cognitive process. Recently, AI plays a crucial role in various fields of pharmacy like drug discovery, drug delivery formulation development, polypharmacology, hospital pharmacy, etc. AI technological approaches believe like kith and kin imagining knowledge, cracking problems and higher cognitive process. As a results of the uses of AI approaches, the designing of the new hypotheses, strategies, prediction and analyses of assorted associated factors can

easily be finished the ability of less time consumption and inexpensiveness[4,16]. Artificial intelligence and machine learning are playing a critical role within the pharmaceutical industry and consumer healthcare business. From augmented intelligence applications like disease identification and diagnosis, helping identify patients for clinical trials, drug manufacturing, and predictive forecasting, these technologies have proven critical. On a recent episode of the AI Today podcast Subroto Mukherjee, who is Head of Innovation and Emerging Technology, Americas at GlaxoSmithkline Consumer Healthcare discussed how AI and ML are being applied to the pharmaceutical industry and a few unique use cases for AI and ML technology. during this follow up interview he shares his insights in additional detail.[17,18]

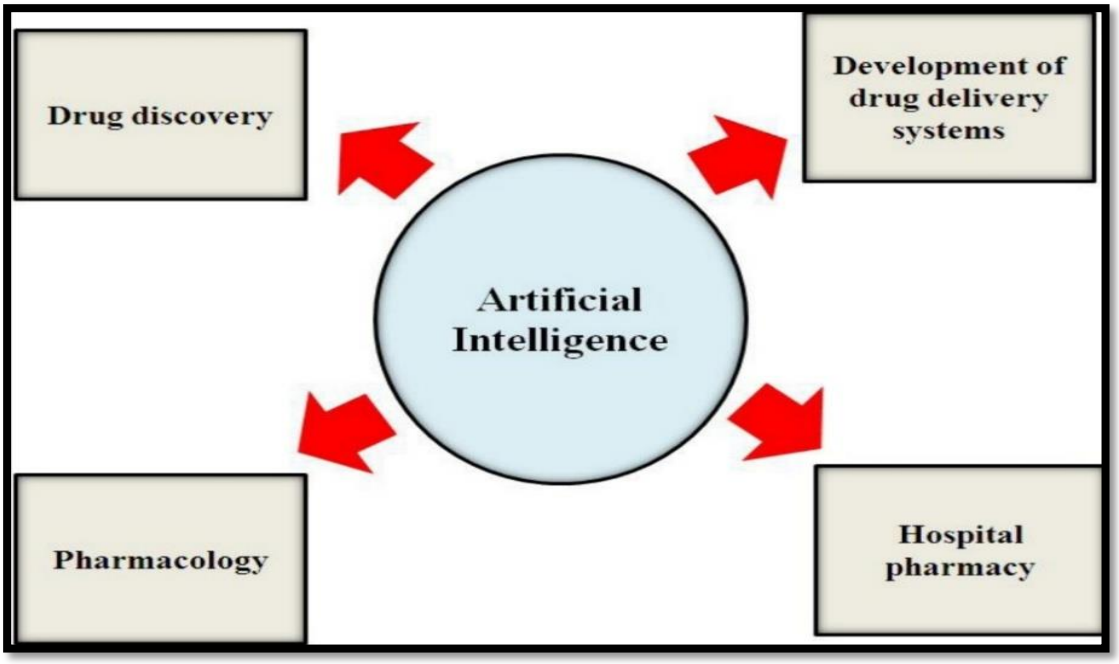


Fig. AI in pharmaceutical Industry

4. ARTIFICIAL INTELLIGENCE IN DRUG DISCOVERY

Drug discovery is well-known as a chic, time-consuming process, with low success rates. On average, developing a brand new drug costs 2.6 billion US dollars and may take over 10 years. Moreover, the success rate of launching a drug to promote from run|phase I|clinical trial|clinical test} clinical trial is daunting, but 10%. within the past decade, the practice of drug discovery has been undergoing radical transformations driven by the rapid development in computing (AI)[22]. Popular applications of AI in drug discovery include virtual screening, de novo drug design, retrosynthesis and reaction prediction, and de novo protein design, among others, which may be reduced to 2 categories, i.e., predictive and generative tasks.[20] To power these AI applications, a good range of AI techniques are involved, with model architectures evolving from traditional machine learning models to deep neural networks, like convolutional neural networks, recurrent neural networks, graph neural networks and transformers, etc. Learning paradigms also shift from supervised learning to self-supervised learning and reinforcement learning.[19, 21,23]

Drug discovery is that the initiative of the worth chain that identifies new candidate therapeutics for treating or curing human diseases.[24,25] it's the initial stage of biopharma research and development (R&D) and involves the identification and optimisation of potential new drugs and a preclinical in vivo validation through cell assays and animal models. Successful candidates that meet the regulatory requirements applied to drug discovery get in the trial phase, where they're tested for efficacy and safety in humans.[26] Our next report within the series examines the impact AI has on clinical trials (Intelligent clinical trials: Transforming through engagement). The evolution of drug discovery Historically, the invention of latest therapeutics involved the extraction of ingredients from natural products and basic research to seek out potential treatments. Progress was generally slow, frustrating and labour intensive. In some cases, discoveries occurred because of unexpected events and observations (such as penicillin). the bulk of medication discovered during the 20th century were chemically synthesised small molecules, which still conjure 90 per cent of medicine on the market today.[24,27] The advantages of small molecules include simple manufacturing and administration routes, low specificity and a stable period of time, meaning they're safe and effective for giant groups of individuals. However, low specificity may cause side effects, reducing the probabilities of success in clinical trials. Since the 1990s, scientific and technological advances have led to the invention of larger, more complex, biological therapeutics referred to as biologics. In contrast to chemically synthesised small molecules, biologics are produced or isolated from living organisms and include a large range of products like allergenic, antisense drugs, blood and blood components, recombinant therapeutic DNA and proteins, and vaccines. Biologics are highly specific to their target and have invoked high levels of media and investor interest because of their innovative techniques and potential to cure previously untreatable diseases. Only 17 of the 59 drugs approved by Food and Drug Administration (FDA) in 2018 were

biologics, largely thanks to the complex manufacturing and administration routes. As most pharma companies have integrated biologics into their pipelines, for the aim of this report we seek advice from all pharma companies as biopharma companies. [24,28]

The applications of AI in drug discovery process concerns the utilization of chemical space. In fact, the chemical space offers the phase for the identification of recent molecules since it's achievable to computationally itemise the required molecules.[29] additionally, the machine learning and related predictive tools also help for the identifications of target-specific effective molecules. the method of choosing a successful new drug molecule from lots of abundance of pharmacological active chemical entities is that the toughest a part of the entire phenomenon.[32,33]. Benevolent AI is employed for the aim of processing fewer molecules with way more surety about their activity. during this regard, de novo design necessitate the understanding of chemical science for the synthesis of in silico molecules and also the virtual screening modelling that perform because the replacements for several biochemical still as biological testing to live the efficiency yet as toxicity profiles. The aim of de novo design within the drug discovery is that the invention of newer active molecules without the uses of reference molecules. Finally, the active learning algorithms permit the invention of latest molecules with the potential actions against the target-setting of diseases or disorders. Several in silico methods for the choice of profiles like ligand-based design approaches or molecular structure-based design approaches could also be employed together with the accessible information on the little molecule modulator probes or the features of structural biology. In silico molecules is obtaining the subsequent generation AI. There are various proposals and software solutions accessible for it. This design isn't useful in drug discovery; but, it's connected to the generation of components possessing difficulty in synthesis.[4,30,31,33]

Drug discovery often takes a protracted time to check compounds against samples of diseased cells. Finding compounds that are biologically active and are worth investigating further requires even more analysis. to hurry up this screening process, Novartis research teams use images from machine learning algorithms to predict which untested compounds can be worth exploring in additional details. As computers are far quicker compared to traditional human analysis and laboratory experiments in uncovering new data sets, new and effective drugs may be made available sooner, while also reducing the operational costs related to the manual investigation of every compound [34]. this AI initiative by the highest biopharmaceutical companies include:

a) Mobile platform to enhance health outcomes –the ability to recommend patients by means of real time data collection and thus improve patient outcomes

b) Drug discovery- pharma companies in conjunction with software companies try to implement the foremost cutting –edge technologies within the costly and extensive process of drug discovery [6, 34].

5. PREDICTION OF THE PHYSICOCHEMICAL PROPERTIES

Physicochemical properties, like solubility, partition coefficient, degree of ionization, and intrinsic permeability of the drug, indirectly affect its pharmacokinetics properties and its target receptor family and, hence, must be considered when designing a brand new drug [34]. Different AI-based tools will be accustomed predict physicochemical properties. as an example, ML uses large data sets produced during compound optimization done previously to coach the program [35]. Algorithms for drug design include molecular descriptors, like SMILES strings, P.E. measurements, electron density round the molecule, and coordinates of atoms in 3D, to get feasible molecules via DNN and thereby predict its properties [36]. Zang et al. created a quantitative structure–property relationship (QSPR) workflow to work out the six physicochemical properties of environmental chemicals obtained from the Environmental Protection Agency (EPA) called the Estimation Program Interface (EPI) Suite [35]. Neural networks supported the ADMET predictor and ALGOPS program are wont to predict the lipophilicity and solubility of assorted compounds [36]. DL methods, like undirected graph recursive neural networks and graph-based convolutional neural networks (CVNN), are wont to predict the solubility of molecules[35]

Prediction of bioactivity

The efficacy of drug molecules depends on their affinity for the target protein or receptor. Drug molecules that don't show any interaction or affinity towards the targeted protein won't be ready to deliver the therapeutic response. In some instances, it'd even be possible that developed drug molecules interact with unintended proteins or receptors, resulting in toxicity. Hence, drug target binding affinity (DTBA) is significant to predict drug–target interactions. AI-based methods can measure the binding affinity of a drug by considering either the features or similarities of the drug and its target. Feature-based interactions recognize the chemical moieties of the drug which of the target to see the feature vectors. against this, in similarity-based interaction, the similarity between drug and target is taken into account, and it's assumed that similar drugs will interact with the identical targets [35,36]

Prediction of toxicity

The prediction of the toxicity of any drug molecule is significant to avoid toxic effects. Cell-based in vitro assays are often used as preliminary studies, followed by animal studies to spot the toxicity of a compound, increasing the expense of drug discovery. Several web-based tools, like LimTox, pkCSM, admetSAR, and Toxtree, are available to assist reduce the price [35]. Advanced AI-based approaches explore for similarities among compounds or project the toxicity of the compound supported input features. The Tox21 Data Challenge organized by the National Institutes of Health, Environmental Protection Agency (EPA), and US Food and Drug Administration (FDA) was an initiative to judge several computational techniques to forecast the toxicity of 12 707 environmental compounds and medicines [35]; an ML algorithm named DeepTox outperformed all methods by identifying static and dynamic features within the chemical descriptors of the molecules, like relative molecular mass (MW) and Van der Waals volume, and will efficiently predict the toxicity of a molecule supported predefined 2500 toxicophore features [37].

Prediction of the target protein structure

While developing a drug molecule, it's essential to assign the proper target for successful treatment. Numerous proteins are involved within the development of the disease and, in some cases, they're overexpressed. Hence, for selective targeting of disease, it's vital to predict the structure of the target protein to style the drug molecule. AI can assist in structure-based drug discovery by predicting the 3D protein structure because the planning is in accordance with the chemical environment of the target protein site, thus helping to predict the effect of a compound on the target together with safety considerations before their synthesis or production. The AI tool, Alpha Fold, which relies on DNNs, was wont to analyse the gap between the adjacent amino acids and therefore the corresponding angles of the peptide bonds to predict the 3D target protein structure and demonstrated excellent results by correctly predicting 25 out of 43 structures. in an exceedingly study by AlQurashi, RNN was wont to predict the protein structure. The author considered three stages (i.e., computation, geometry, and assessment) termed a recurrent geometric network (RGN). Here, the first protein sequence was encoded, and also the torsional angles for a given residue and a partially completed backbone obtained from the geometric unit upstream of this were then considered as input and provided a brand new backbone as output. the ultimate unit produced the 3D structure because the output. Assessment of the deviation of predicted and experimental structures was done using the distance-based root mean square deviation (dRMSD) metric. The parameters in RGN were optimized to stay the dRMSD low between the experimental and predicted structures [38]. AlQurashi predicted that his AI method would be quicker than Alpha Fold in terms of the time taken to predict the protein structure. However, Alpha Fold is probably going to own better accuracy in predicting protein structures with sequences like the reference structures[38,39]

Tools	Details	Website URL
DeepChem	MLP model that uses a python-based AI system to find a suitable candidate in drug discovery	https://github.com/deepchem/deepchem
DeepTox	Software that predicts the toxicity of total of 12 000 drugs	www.bioinf.jku.at/research/DeepTox
DeepNeuralNetQSAR	Python-based system driven by computational tools that aid detection of the molecular activity of compounds	https://github.com/Merck/DeepNeuralNet-QSAR
ORGANIC	A molecular generation tool that helps to create molecules with desired properties	https://github.com/aspuru-guzik-group/ORGANIC
PotentialNet	Uses NNs to predict binding affinity of ligands	https://pubs.acs.org/doi/full/10.1021/acscentsci.8b00507
Hit Dexter	ML technique to predict molecules that might respond to biochemical assays	http://hitdexter2.zbh.uni-hamburg.de
DeltaVina	A scoring function for rescoring drug–ligand binding affinity	https://github.com/chengwang88/deltavina
Neural graph fingerprint	Helps to predict properties of novel molecules	https://github.com/HIPS/neural-fingerprint
AlphaFold	Predicts 3D structures of proteins	https://deepmind.com/blog/alphafold
Chemputer	Helps to report procedure for chemical synthesis in standardized format	https://zenodo.org/record/1481731

Fig. Example of AI tools used in drug discovery

6. ARTIFICAL INTELLIGENCE IN CLINICAL TRIALS

Matching the proper trial with right patient could be a time consuming and challenging process for both the patient and clinical study team. Majority of medicine take years to come back into market, which cost billions and might even fail within the late stage of trial, having most into consideration the attempt of use of computing (A)I was advance, a concept which is important in tending this issues and which can help in a very successful drug development.Dr. Naveen Narayana, Co-founder, president and chief technology officer of biopharma company Berg, discussed his company's interrogative biology AI platform that has identified several drug targets that are in development and a minimum of 25 more are in pipeline. Berg's platform gives data on the individual patients from demographic information and environment condition to genetic mutations, so as to gather all the new treatments. He said berg's method has cut the time and money required to develop drugs quite half. "It's not only that we're reducing the time to supply the drug; the drug that's produced goes to possess more of an effect," Narain said. "That's also a metric that has to be intangibly appreciated, because you may get things done faster [using current drug development methods], but it's only visiting help 10,000 people. But if you catch on done faster [with AI] and you're helping 10 million those that are an enormous difference." [40]To recruit the proper patient into trial may be a huge investment in time and funding, better patient monitoring and methods used during ongoing test can reduce the burden and might make the top point detection more efficient. AI techniques with the mixture of wearable technology, like mobile usage, face time, and individual patient monitoring system. To act accordance with the adherence criteria, patients must keep detailed records of their medication history and other different data points which include their body functions, medication response, and daily activities. which can be overburden and sophisticated task, which may cause 40% of patients to neglect after certain days into run. So on keep and collect the record automatically of the patient data, wearable sensors and video monitoring are used. Machine learning and deep learning will be accustomed analyse the important time data for assessing, detecting and logging for the events of pertinent. this can help to collected informations for data point detection more efficiently and in an exceedingly valid way, instead of patient driven self monitoring methods, this can be called 'cognective sensing'. AI plays crucial role in image end point detection; centres where the manually reading was done started using AI. Machine earning has been recommend and is been approved, for the rapid detecting of the disease from the medical image along the algorithms that assess the pathological conditions, will help to avoid wasting time and value with image studies instead of manual processing.[24,40,41]

AI-based advanced applications

AI-based Nano robots for drug delivery Nanorobots comprise mainly integrated circuits, sensors, power supply, and secure backup of knowledge, which are maintained via computational technologies, such as AI. they're programmed to avoid the collision, target identification, detect and fasten, and at last excretion from the body. Advances in Nano/micro robots give them the flexibility to navigate to the targeted site supported physiological conditions, such as pH, thus improving the efficacy and reducing systemic adverse effects. Development of implantable Nanorobots developed for controlled delivery of medication and genes requires consideration of parameters like dose adjustment, sustained release, and control release, and also the release of the drugs requires automation controlled by AI tools, like NNs, formal logic, and integrators [42].

Microchip implants are used for programmed release furthermore on detect the placement of the implant within the body. AI together drug delivery and synergism/antagonism prediction Several combinations of medicine are approved and marketed to treat complex diseases, like TB and cancer, because they will provide a synergistic effect for quick recovery. ANNs, logistic regression, and network-based modeling can screen drug combinations and improve overall dose regimen. Rashid et al. developed a quadratic phenotype optimization platform for the detection of optimal combination therapy for the treatment of bortezomibresistant myeloma employing a collection of 114 FDA-approved drugs. This model recommended the mixture of decitabine (Dec) and mitomycin C (MitoC) because the best two-drug combination and Dec, MitoC, and mechlorethamine because the superior three-drug combination. [42,43]

Combination drug delivery may be more efficient if saved by data on the synergism or antagonism of medication administered together. The Master Regulator Inference Algorithm used 'Mater regulator genes' to efficiently predict 56% synergism. Other methods, like Network-based Laplacian regularized least square synergistic drug combination, and RF, also can be used for the identical. Li et al. developed a synergistic drug combination model using RF for the prediction of synergistic anticancer drug combinations. This model was formed supported organic phenomenon profiles and various networks, and also the authors successfully predicted 28 synergistic anticancer combinations. they need reported three such combinations, although the rest may also encourage be important.[44,42,43]

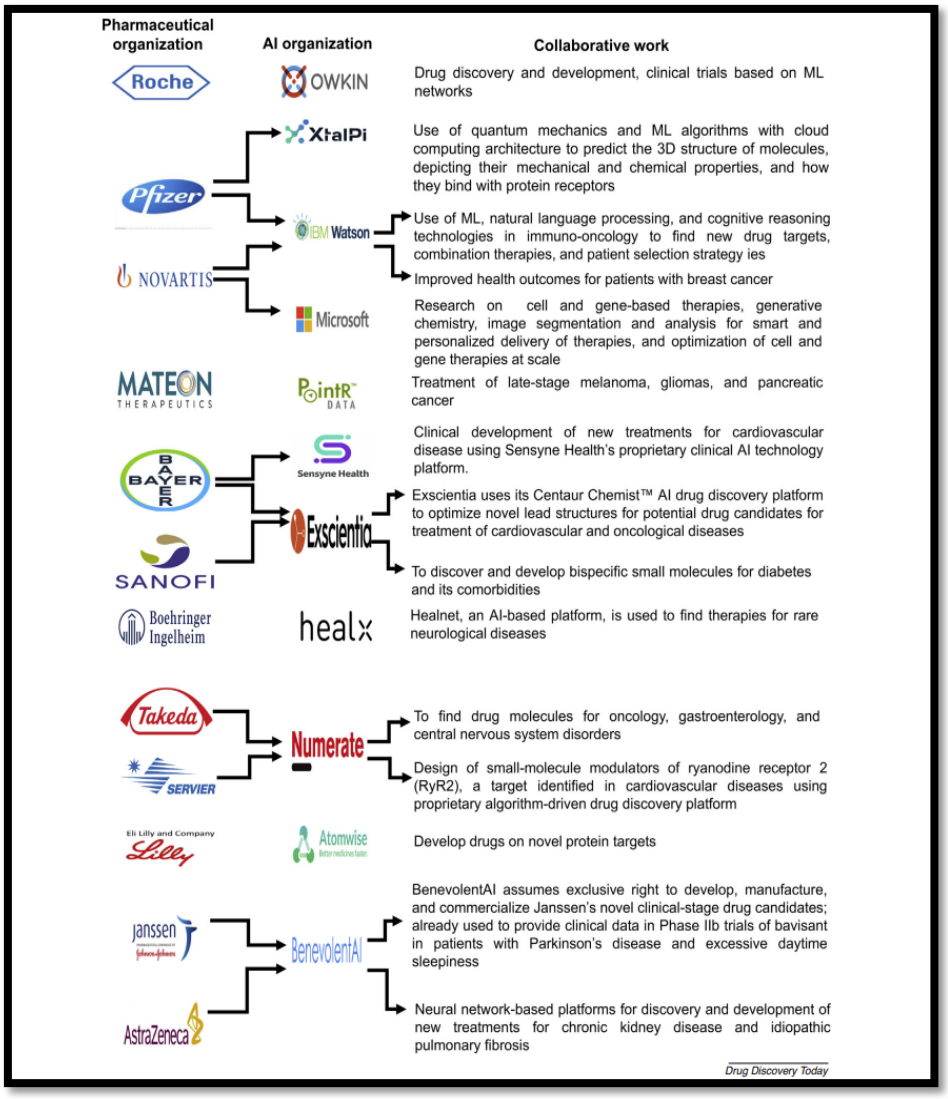


Fig. Examples of some AI based Applications

AI in pharmaceutical manufacturing

AI in pharmaceutical manufacturing with the increasing complexities of producing processes together with increasing demand for efficiency and better product quality, modern manufacturing systems are attempting to confer human knowledge to machines, continuously changing the manufacturing practice. The incorporation of AI in manufacturing can convince be a lift for the pharmaceutical industry. Tools, like CFD, uses Reynolds-Averaged NavierStokes solvers technology that studies the impact of agitation and stress levels in numerous equipment (e.g., stirred tanks), exploiting the automation of the many pharmaceutical operations. Similar systems, like direct numerical simulations and enormous eddy simulations, involve advanced approaches to unravel complicated flow problems in manufacturing. The novel Computer platform helps digital automation for the synthesis and manufacturing of molecules, incorporating various chemical codes and operating by employing a scripting language referred to as Chemical Assembly.[44] it's been successfully used for the synthesis and manufacture of sildenafil, diphenhydramine hydrochloride, and rufinamide, with the yield and purity significantly almost like manual synthesis. The estimated completion of granulation in granulators of capacities starting from 25 to 600 l are often done efficiently by AI technologies. The technology and neuro-fuzzy logic correlated critical variables to their responses. They derived a polynomial equation for the prediction of the proportion of the granulation fluid to be added, required speed, and therefore the diameter of the impeller in both geometrically similar and dissimilar granulators. DEM has been widely utilized within the pharmaceutical industry, like in studying the segregation of powders during a binary mixture, the results of varying blade speed and shape, predicting the possible path of the tablets within the coating process, together with analysis of your time spent by tablets under the spray zone. ANNs, together with fuzzy models, studied the correlation between machine settings and therefore the problem of capping to scale back tablet capping on the manufacturing line. Meta-classifier and tablet-classifier are AI tools that help to manipulate the standard standard of the ultimate product, indicating a possible error within the manufacturing of the tablet [45]. A patent has been filed, demonstrating a system capable of determining the foremost exquisite combination of drug and dosage regimen for every patient, employing a processor receiving patient information, and styles the specified skin patch accordingly. AI in internal control and quality assurance Manufacturing of the specified product from the raw materials includes a balance of varied parameters. internal control tests on the products, still as maintenance of batch-to-batch consistency, require manual interference. This won't be the simplest approach in each case, showcasing the requirement for AI implementation at this stage. The FDA amended the present Good Manufacturing Practices (cGMP) by introducing a 'Quality by Design' approach to know the critical operation and specific criteria that govern the ultimate quality of the pharmaceutical product. Gams et al. used a mix of human efforts and AI, wherein preliminary data from production batches were analysed and decision trees developed. These were further translated into rules and analyzed by the operators to guide the assembly cycle within the future. Goh et al. studied the dissolution profile, an indicator of batch-to-batch consistency of theophylline pellets with the help of ANN, which correctly predicted the dissolution of the tested formulation with a slip of that. [44,45,46] The novel computer platform helps digital automation for the synthesis and manufacturing of molecules, incorporating various chemical codes and operating by employing a scripting language called Chemical Assembly. it's been successfully used for the synthesis and manufacture of sildenafil, diphenhydramine hydrochloride, and rufinamide, with the yield and purity significantly just like manual synthesis [89]. The estimated completion of granulation in granulators of capacities starting from 25 to 600 l are often done efficiently by AI technologies. The technology and neuro-fuzzy logic correlated critical variables to their responses. 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AI in internal control and quality assurance

Manufacturing of the specified product from the raw materials includes a balance of assorted parameters. internal control tests on the products, yet as maintenance of batch-to-batch consistency, require manual interference. This won't be the most effective approach in each case, showcasing the requirement for AI implementation at this stage. The FDA amended this Good Manufacturing Practices (cGMP) by introducing a 'Quality by Design' approach to know the critical operation and specific criteria that govern the ultimate quality of the pharmaceutical product. Gams et al. used a mixture of human efforts and AI, wherein preliminary data from production batches were analyzed and decision trees developed. These were further translated into rules and analyzed by the operators to guide the assembly cycle within the future. Goh et al. studied the dissolution profile, an indicator of batch-to-batch consistency of theophylline pellets with the help of ANN, which correctly predicted the dissolution of the tested formulation with miscalculation of <8% [48]. AI may also be implemented for the regulation of in-line manufacturing processes to realize the required standard of the merchandise. ANN-based monitoring of the freeze-drying process is employed, which applies a mix of self-adaptive evolution together with local search and backpropagation algorithms. this may be wont to predict the temperature and desiccated-cake thickness at a future time point(t +Dt) for a selected set of operating conditions, eventually helping to stay a check on the ultimate product quality. an automatic data entry platform, like an Electronic Lab Notebook, together with sophisticated, intelligent techniques, can make sure the quality assurance of the merchandise. Also, data processing and various knowledge discovery techniques within the Total Quality Management expert system are often used as valuable approaches in making complex decisions, creating new technologies for intelligent internalcontrol.[44,49]

Applying deep neural networks in drug discovery

To understand how AI is being applied in practice, let's take a glance at a number of the innovative research we currently have underway. "Predictive models are central to our work," says Friedrich Rippmann, Director, Computational Chemistry & Biology at Merck. "These are statistical models that predict whether a compound idea – a not-yet-synthesized molecule – will produce a desired activity."[50]

"The technologies we're using mostly relate to machine learning. particularly, we're using various forms of deep neural networks. But we've also explored other more classical statistical techniques, with funny names like random forests and support vector machines. "Deep neural networks began to become particularly popular around 2012, when researchers from the University of Toronto won the Image Net Large Scale Visual Recognition Challenge (ILSVRC).

In recent years, this subset of machine learning techniques has revolutionized several fields like computer vision, language processing, and game playing. And now it's showing exciting promise in identifying novel compounds. "We've driving innovative research within the area of interpretable deep neural networks," continues Rippmann. "Our predictions not only tell us, 'yes, this can work' or 'no, it won't work'. Now they will also tell us why they'll or won't work, by highlighting the areas in an exceedingly molecule that are liable for a specific activity. this provides a direct indication to chemists of what to try to to to get rid of a particular unwanted activity. "Their findings are described in greater detail in a very recent, well-received article, Interpretable Deep Learning in Drug Discovery. So far, in terms of practical benefit, the research applied by Friedrich Rippmann's team and Merck's partners has made available almost 300 new models for assessing the properties of a compound, which might help predict their ability to bind to a selected disease-relevant target. "These models are already getting used by our chemists to evaluate their compound ideas before picking whether to synthesize them," adds Rippmann.[50,51]

7. COLLABORATION TO ENHANCE AI IN DRUG DISCOVERY

Advances during this field are by nature, a collaborative process. "We rarely develop novel methods entirely by ourselves," says Rippmann. "All our work is finished together with leading academic groups and start-up companies. "So far, notable collaborations include working with Professor Sepp Hochreiter at Universidad Linz in Austria – who leads one in all the highest academic groups during this research area. additionally, we're also collaborating with Cyclic in Toronto, using their predictive technology that identifies which human proteins a matter is probably going to focus on (for example, within the deconvolution of phenotypic screens).And separately, we're working with Kits, a start-up based in Paris, using their technology to automatically 'invent' novel molecules that hit predefined requirements for a drug, including binding to the drug target, lack of specific toxicities, solubility, and far more. But collaboration to reinforce AI in drug discovery is additionally happening at a bigger scale. AI analysis is barely pretty much as good because the quality of the datasets in use. For this reason, the pharmaceutical industry is increasingly seeking to collaborate by pooling data. A recent initiative to facilitate, the MELLODDY Project, involves the EU Innovative Medicines Initiative and no fewer than ten pharmaceutical companies – including Merck. It aims at improving predictive models through so-called 'federated learning', by employing a novel block chain system to store data on a secure ledger while protecting the trade secrets of individual companies.[50,52]

8. CONCLUSION

During past few years, a substantial amount of accelerating interest towards the uses of AI technology has been identified for analyzing also as interpreting some important fields of pharmacy like drug discovery, dosage form designing, polypharmacology, hospital pharmacy, etc., because the AI technological approaches believe like human beings imagining knowledge, cracking problems and deciding. The uses of automated workflows and databases for the effective analyses employing AI approaches are proved useful. As a results of the uses of AI approaches, the designing of the new hypotheses, strategies, prediction and analyses of assorted associated factors can easily be done with the power of less time consumption and inexpensiveness.

REFERENCES

[1] Ramesh, A. et al. (2004) Artificial intelligence in medicine. Annals of the Royal College of Surgeons of England 86, 334–338

[2] Miles, J. and Walker, A. (2006) The potential application of artificial intelligence in transport. In IEE Proceedings-Intelligent Transport Systems 153, 183–198

[3] Duch, W. et al. (2007) Artificial intelligence approaches for rational drug design and discovery. Current Pharmaceutical Design 13, 1497–1508

[4] Das S, Dey R, Nayak AK. Artificial Intelligence in Pharmacy. Indian J of Pharmaceutical Education and Research. 2021;55(2):304-18.

[5] Mak KK, Pichika MR. Artificial intelligence in drug development: Present status and future prospects. Drug Discov Today. 2019;24(3):773-80.

[6] Swarupa Arvapalli et.al / IJIPSR / 7 (10), 2019, 37-50 Department of Pharmaceutics ISSN (online) 2347-2154

[7] Dastha JF. Application of artificial intelligence to pharmacy and medicine. Hospital 1992;27:312-5,319-22

[8] Blasiak, A. et al. (2020) CURATE. AI: optimizing personalized medicine with artificial intelligence. SLAS Technol. 25, 95–105

[9] Baronzio, G. et al. (2015) Overview of methods for overcoming hindrance to drug delivery to tumors, with special attention to tumor interstitial fluid. Frontiers in Oncology 5, 165

[10] Kit-KayMak and MallikarjunaRao Pichika, artificial intelligence in drug development J drug discovery Today Vol.24 03.03. 2019: 773-80. https://www.academia.edu/40522235/Artificial_intelligence_in_drug_development_present_status_and_future_prospects

[11] DuchW.,SwaminathanK.,MellerJ.,ArtificialIntelligenceApproachesforRationalDrugDesignan Discovery.CurrentPharmaceuticalDesign,2007;13

[12] Russel S, Dewey D, Tegmark M. Research priorities for robust and beneficial artificial intelligence. AI Mag. 2015;36(4):105-14.

[13] Tamanna S., et al . Artificial intelligence in advance pharmacy. International Journal of Science and Research Archive, 2021, 02(01), 047–054

[14] Vamathevan, J.; Clark, D.; Czodrowski, P.; Dunham, I.; Ferran, E.; Lee, G.; Li, B.; Madabhushi, A.; Shah, P.; Spitzer, M., et al. Applications of machine learning in drug discovery and development. Nat. Rev. Drug Discov. 2019, 18, 463–477.

[15] Paul, D.; Sanap, G.; Shenoy, S.; Kalyane, D.; Kalia, K.; Tekade, R. K. Artificial intelligence in drug discovery and development. Drug Discovery Today 2021, 26, 80.

[16] Hassanzadeh P, Atyabi F, Dinarvand R. The significance of artificial intelligence in drug delivery system design. Adv Drug Deliv Rev. 2019;151:169-90.

[17] Kiran NT., et al. Artificial intelligence in pharma. Der Pharmacia Lettre, 2021, 13(5):06-14

[18] Vyas M., Thakur S., Riyaz B., et al., Asian J Pharmaceutics, 2018, 12(02):72-76.

[19] Jianyuan Deng, Zhibo Yang., et al. Artificial Intelligence in Drug Discovery:Applications and Techniques arXiv:2106.05386v4 [cs.LG] 2 Nov 2021

[20] Mullard, A. New drugs cost US $2.6 billion to develop. Nat. Rev. Drug Discov. 2014,13, 877.

[21] Dowden, H.; Munro, J. Trends in clinical success rates and therapeutic focus. Nat.Rev. Drug Discov. 2019, 18, 495–497.

[22] Schneider, G. Automating drug discovery. Nat. Rev. Drug Discov. 2018, 17, 97.

[23] Chen, H.; Engkvist, O.; Wang, Y.; Olivecrona, M.; Blaschke, T. The rise of deep learning in drug discovery. Drug Discov. Today 2018, 23, 1241–1250.

[24] A report from the Deloitte Centre for Health Solutions, Deloitte University EMEA CVBA, with registered office at B-1831 Diegem, Berkenlaan 8b www.deloitte.co.uk/centreforhealthsolutions 2019

[25] ScienceDaily,LLC,"Drugdiscovery",https://www.sciencedaily.com/terms/drug_discovery.htm, accessed 23 September 2019.

[26] Mark Steedman et al., Intelligent biopharma: Forging the links across the value chain, Deloitte Insights, September 2019, https://www2.deloitte.com/us/en/insights/industry/life-sciences/rise-of-artificial-intelligence-in-biopharma-industry.html , accessed 9 October,2019.

[27] The Technology Partnership, "New modes of drug action tackle intractable diseases", https://medium.com/@ttp_plc/new-modes-of-drug-action-tackle-intractable-diseasese7d8e2c31759, accessed 21 October 2019.

[28] Beatriz G. de la Torre and Fernando Albericio, The Pharmaceutical Industry in 2018. An Analysis of FDA Drug Approvals from the Perspective of Molecules, MDPI, 23 February 2019, https://www.mdpi.com/14203049/24/4/809/pdf, accessed 23 September 2019.

[29] Silver D, Schrittwieser J, Simonyan K. Mastering the game of Go without human knowledge. Nature. 2017;550(7676):354-9.

[30] Lakdawala AS, Okafo G, Baldoni J, Palovich M, Sikosek T, Sahni V. Adapting drug discovery to artificial intelligence. Drug Target Rev. 2018;50-2.

[31] Ferrero E, Dunham I, Sanseau P. In silico prediction of novel therapeutic targets using gene-disease association data. J Transl Med. 2017;15(1):182.

[32] Katsila T, Spyroulias GA, Patrinos GP, Matsoukas MT. Computational approaches in target identification and drug discovery. Comput Struct Biotechnol J. 2016;14:177-84.

[33] Ferrero E, Dunham I, Sanseau P. In silico prediction of novel therapeutic targets using gene-disease association data. J Transl Med. 2017;15(1):182.

[34] RÍacheBrazilThePharmaceuticalJournalDec2007

[35] Debleena Paulz, Gaurav Sanapz Snehal Shenoyz te al . Artificial intelligence Drug Discovery and development. Drug Discovery Today .Volume 26, Number 1 January 2021.

[36] Lusci, A. et al. (2013) Deep architectures and deep learning in chemoinformatics: the prediction of aqueous solubility for drug-like molecules. J. Chem. Inf. Model. 53,1563–1575

[37] Bielecki, A. and Bielecki, A. (2019) Foundations of artificial neural networks. In Models of Neurons and Perceptrons: Selected Problems and Challenges (Kacprzyk,Janusz, ed.), pp. 15–28, Springer International Publishing

[38] Al Quraishi, M. (2019) End-to-end differentiable learning of protein structure. Cell Syst. 8, 292–301

[39] Da Silva, I.N. et al. (2017) Artificial Neural Networks. Springer

[40] How Artificial Intelligence Can Make Drugs Better and Faster. By Rebecca Harrington, published on July 29, 2015, in Popular Science.

[41] Artificial Intelligence for Clinical Trial Design. Stefan Harrer, Pratik Shah, Bhavna Antony, and Jianying Hu. Trends in Pharmacological Sciences, Vol. 40, August 2019, No. 8.

[42] Fu, J. and Yan, H. (2012) Controlled drug release by a nanorobot. Nat. Biotechnol. 30, 407–408

[43] Calzolari, D. et al. (2008) Search algorithms as a framework for the optimization of drug combinations. PLoS Comput. Biol. 4, e1000249

[44] Ayesha Fatima1, C.S. Mujeebuddin ; artificial intelligence in drug discovery. Int. J. Pharm. Sci. Rev. Res., 61(1), March - April 2020; Article No. 22, Pages: 132-137

[45] Gams, M. et al. (2014) Integrating artificial and human intelligence into tablet production process. AAPS PharmSciTech 15, 1447–1453

[46] Rantanen, J. and Khinast, J. (2015) The future of pharmaceutical manufacturing sciences. J. Pharm. Sci. 104, 3612–3638

[47] Kraft, D.L. System and methods for the production of personalized drug products. US20120041778A1.

[48] Goh, W.Y. et al. (2002) Application of a recurrent neural network to prediction of drug dissolution profiles. Neural Comput. Appl. 10, 311–317

[49] Aksu, B. et al. (2013) A quality by design approach using artificial intelligence techniques to control the critical quality attributes of ramipril tablets manufactured by wet granulation. Pharm. Dev. Technol. 18, 236–245

[50] https://www.merckgroup.com/en/research/science-space/envisioning-tomorrow/precision-medicine/generativeai.html 2017

[51] **.** https://papers.nips.cc/paper/4824-imagenet-classification-with-deep-convolutional-neural-networks.pdf

[52] https://www.imi.europa.eu/projects-results/project-factsheets/melloddy