Review Article

Impact of Artificial Intelligence (AI) on Drug Discovery and Product Development

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ABSTRACT

Artificial Intelligence (AI) had transfigured different sectors in society, where the pharmaceutical sector is not an exceptional case. Pharmaceutical sectors have reached new heights with the emergence of these sophisticated technologies. The evolution of artificial intelligence in the pharmaceutical industry is in a growth phase opening the possibilities of discovering many new drugs. The diseases affecting humans are increasing tremendously whereas the drugs which are available to treat or cure are very much minimal. But this kind of scenario will not be present in the future because of the combination of artificial intelligence and the pharmaceutical industry which results in faster discovery of drugs with increased clinical outcomes. There was a shift in the paradigm of various stages in drug discovery because of the utilization of artificial intelligence. Each stage of drug discovery involves a certain timeline that can be cut down with the help of artificial intelligence. Many pharma companies are engaged with AI-based drug discovery approaches for treating various diseases like Parkinson's disease diabetes, Alzheimer's, Obsessive Compulsive Disorder, etc., AI is also being employed in product development for the fabrication of nanomedicines and nanorobots. Few AI-based drugs are already in the phase of clinical trials which indicates the growth of AI-driven drug discovery. In this review, we have highlighted the application of AI in drug discovery and product development of pharmaceuticals.

Keywords: Drug discovery, Drug delivery, Machine learning, Era of machines, Algorithm.

INTRODUCTION

The pharmaceutical industry is responsible for a variety of activities such as drug research, development, manufacturing, and distribution. Drug discovery, which involves the identification of new drug candidates, is the first step in the pharmaceutical value chain. The result of the drug discovery process is a drug candidate that is subjected to preclinical research before being transformed into clinically significant drugs, the safety, effectiveness, dosage, and tolerability of which have been proven through well-designed and conducted clinical studies.[1] If the clinical trial is deemed significant and successful, the pharmaceutical company will submit a new drug application (NDA) to the regulatory agency, which will approve the drug following a thorough review of the results. The process of drug discovery is expensive, tedious, lengthy, and unsuccessful quite often. It takes approximately 10-12 years for a molecule from the stage of discovery to market.[2] Only 10 out of 10,000 small molecules were selected for clinical research. In addition, the success rate is less than 10% for a molecule to get approved for phase-I trials. The percentage has not increased for the past ten years[3]. For the future of drug development, improving the success rate of drug discovery and clinical trials is very important. Hence, the drug discovery market is turning its attention to the use of new technologies such as artificial intelligence to improve the accuracy, predictability, and speed of drug discovery. Any computer program or system that performs the various tasks

Submission Date: 20-10-2021;
Revision Date: 08-05-2022;
Accepted Date: 14-06-2022.

DOI: 10.5530/ijper.56.3s.146

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that we consider intelligent for humans is referred to as artificial intelligence. Machine learning, deep learning, natural language processing, vision, speech recognition, supervised learning, and unsupervised learning are some of the examples of AI technologies. AI aids in the identification of hit and lead molecules, as well as faster drug target validation and drug structure optimization in drug discovery.[4-5] One of the most important step in drug discovery is determining the 3D structure of the target protein, which has become much easier thanks to machine learning tools.[6-7] One of the best example is AlphaFold, a Google DeepMind artificial intelligence tool that can predict the 3D structure of a protein-based on its amino acid sequence.[8] Creating an effective strategy for delivering the therapeutic agent is as critical as developing a new drug. Multiple physical, chemical, and histological barriers prevent drugs from entering the target site, such as the Blood-Brain Barrier (BBB), the Blood Retinal Barrier (BRB), and internal and external gastrointestinal barriers.[9] These limitations of traditional drug delivery systems can be overcome by developing a smart drug delivery system that incorporates information technology, wireless communication, and artificial neural networks (ANN).[10] Wireless communication allows for greater flexibility in controlled drug delivery systems by receiving instructions from an external source, transmitting data to the monitor, and regulating drug release.[11] Artificial intelligence can overcome nanotechnology's physical limitations by designing nanoarchitectures with greater computing power.[12] The use of artificial intelligence is not limited to the development of next-generation innovative drugs and delivery systems; it is also used in a variety of other areas of the pharmaceutical industry (Figure 1). Because of the increasing complexity of manufacturing processes and the increasing demand for efficiency and better product quality,[13] modern manufacturing systems are attempting to transfer human knowledge to machines through a continuous manufacturing process. These kinds of advancements[14] are critical in the current pandemic situation, where the discovery of SARS-CoV-2 therapy is possible due to its ability to automatically extract deep learning algorithms that can aid in more accurate models and provide more reliable results, and the generative capabilities demonstrated by the models can be used to drive more drugs to perform better prediction of epitopes, reducing the possibility of errors during the trial pipeline. Deep learning detection of SARS-CoV-2 treatment is critical for timely and accurate virus response. The patent law approaches developed for evaluating man-made inventions do not apply to artificial intelligence inventions, necessitating

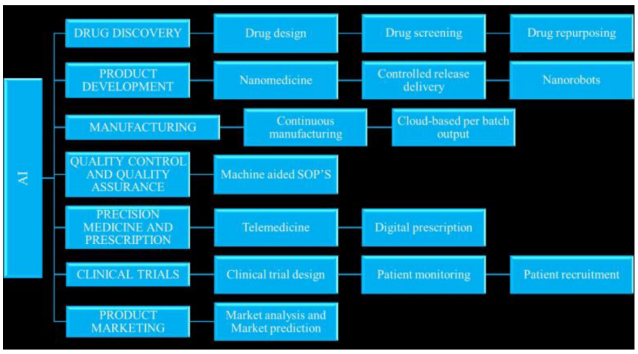

Figure 1: Applications of AI in different pharma segments.

an immediate reconsideration of the law. However, the issues of inventorship and ownership of all such scientific discoveries appear to have been widely discussed and resolved,[15-16] but the issue of obviousness remains unresolved.[17] This review focuses on the impact of AI in drug discovery and product development along with some patent perspectives.

EMPLOYING AI IN DRUG DISCOVERY

Drug discovery has evolved. During James Black's time, only a small series of hundreds of compounds were frequently synthesized, tested, and optimized in animals empirically (For Eg: Cimetidine and Propranolol).[18] When combined with new genetic insights and the increase in patient medical data over the last decade, the use of artificial intelligence in drug discovery can bring novel medications to patients more effectively and predictably than conventional methods. List of AI startups focussing on drug discovery is given in Table 1.[19]

List of AI tools employed in drug discovery

1) Neural Graph Fingerprints:[20] It is used for predicting the novel molecule. It can be utilized by accessing the URL: https://github.com/HIPS/neural-fingerprint.

Most drugs must be encoded as a fixed-size vector, known as a molecular fingerprint, to be discovered through virtual screening. The extended connectivity fingerprint (ECFP) is a popular molecular fingerprint (ECFP). These neural graph fingerprints outperform fixed fingerprints in terms of predictive performance, parsimony, and interpretability.[21]

2) DeepTOX:[22] It is used to predict toxicity. It can be utilized by accessing the URL: www.bioinf.jku.at/research/DeepTox. Deep Learning naturally supports multi-task learning, which entails learning all toxic effects in a single neural network and thus learning extremely informative chemical features. The DeepTox pipeline was created to use Deep Learning for toxicity

prediction. DeepTox begins by normalizing the chemical representations of the compounds. Then it computes a large number of chemical descriptors, which are then fed into machine learning methods. DeepTox then trains models, evaluates them, and combines the best of them to form ensembles. DeepTox[23] finally predicts the toxicity of new compounds.

3) DeepNeuralNetQSAR:[24] It is used for predicting molecular activity. It can be utilized by accessing the URL: https://github.com/ Merck/DeepNeuralNet-QSAR. In the drug discovery process, quantitative structure-activity relationship (QSAR) models are commonly used computational tools. QSAR models are regression or classification models that predict the biological activities of molecules based on molecular structure features. These models are typically used to rank a list of candidate molecules for future laboratory experiments and to assist chemists in better understanding how structural changes affect a molecule's biological activities.[25]

4) ORGANIC: It is an efficient molecular generation tool to create molecules with desired properties. It can be utilized by accessing the URL: https://github.com/aspuru-guzik-group/ORGANIC. ORGANIC is a framework based on Objective-Reinforced Generative Adversarial Networks (ORGAN) that can generate a distribution over molecular space that matches a set of desirable metrics. This methodology combines two machine learning techniques: a Generative Adversarial Network (GAN) to generate non-repetitive sensible molecular species and Reinforcement Learning (RL) to bias this generative distribution toward specific attributes.[26]

5) DeepChem:[27] It is used for various drug discovery task predictions. It can be utilized by accessing the URL: https://github.com/ deepchem/deepchem. DeepChem is written in Python and provides a feature-rich set of functionality for applying deep learning to drug discovery and cheminformatics problems. Previous deep learning frameworks, like scikit-learn, have been implemented in chemiformatics, but DeepChem is the first to utilize NVIDIA GPUs to accelerate computation.[28]

Ongoing drug discovery projects using AI

1) Exscientia and Oxford[29-30] - February 2021

The Alzheimer's Research UK Oxford Drug Discovery Institute (ARUK-ODDI) has formed a partnership with the artificial intelligence drug discovery company Exscientia to develop drug candidates for Alzheimer's disease. The NLRP3 (Nod-like receptor protein 3) inflammasome pathway, which is one of the important factors in the pathogenesis of Alzheimer's disease, is the main focus of this collaboration. The combination of Exscientia's Centaur Chemist AI-design systems and the ARUK-biology ODDI's and screening expertise will accelerate the development of ideal drug candidate molecules for Alzheimer's disease.

2) Insitro and Bristol myers squibb[31] - October 2020

Insitro, a machine-learning-driven drug discovery, and development firm has formed a five-year collaboration with Bristol Myers Squibb, an American multinational pharmaceutical company, to discover and develop novel therapies for the treatment of Amyotrophic Lateral Sclerosis (ALS) and Frontotemporal Dementia (FTD). Insitro is using its proprietary platform, the Insitro Human (ISH) platform, to develop iPSC-derived disease models for ALS and FTD.

3) Genesis therapeutics and Genentech[32] - October 2020

Genesis Therapeutics, a biotech company that uses artificial intelligence for drug discovery and development, has partnered with Genentech, a member of the Roche Group. The collaboration will use Genesis Therapeutics' graph machine learning and drug discovery expertise to identify novel drug candidates for therapeutic targets across multiple disease areas. Genentech is identifying multiple targets using Genesis' Dynamic PotentialNet AI platform and other novel neural network algorithms.

4) Recursion pharmaceuticals and bayer[33] - September 2020

Bayer, a German multinational pharmaceutical company, has joined forces with Recursion Pharmaceuticals, based in the United States. The collaboration was formed to discover and develop new therapeutic candidates for fibrotic diseases of the lung, kidney, and heart by combining Recursion Pharmaceuticals' artificial intelligence-guided drug discovery platform and small molecule compound library with Bayer's deep scientific expertise.

5) Exscientia and Bayer – January 2020[34]

Bayer has entered into a three-year collaboration with Exscientia Ltd., a UK-based Artificial Intelligence (AI)-driven drug discovery company. They had worked together to identify and optimize novel lead structures for potential drug candidates to treat cardiovascular and oncological diseases. Exscientia used its Artificial Intelligence (AI) drug discovery platform "Centaur Chemist" for this purpose. List of first of its kind AI-based drugs is given in Table 2.

EMPLOYING AI IN PRODUCT DEVELOPMENT

The goal[39] of pharmaceutical development is to create a high-quality product as well as a manufacturing process that ensures consistent production of the required high-

Table 1: List of AI startups focussing on drug discovery.[35]

Name of the Start-up	Application	Founded On
Polaris Quantum Biotech	Optimize drug candidates identified through a quantum computing-driven search of large chemical datasets.	2020
Genesis Therapeutics	Accurately predict ADMET properties.	2019
Insitro	Generate models from large, high-quality datasets and helps to address key problems in the drug discovery and development process.	2018
Bullfrog AI	Predict which patients will respond to therapies in development.	2017
Iktos	Design novel compounds that optimize for specific objective and improves the success rate of *in silico* to *in vitro* translation.	2016
Biosymetrics	Process raw phenotypic, imaging, drug, and genomic data sets.	2015
Insilico medicine	Predict pharmacological properties of drugs and supplements, and identify novel biomarkers.	2014
Benevolent AI	Ingest scientific research data sets, then form and qualify hypotheses and generate novel insights.	2013
Excientia	Learn best-practices from drug discovery data and experienced drug hunters.	2012
Innoplexus	Generate insights from billions of disparate data points from thousands of data sources.	2011
Histoindex	Analyse and quantify non-alcoholic steatohepatitis (NASH) features for treatment efficacy.	2010

Table 2: List of first of its kind AI-based drugs.

Name of the Drug and Purpose	Company	Status	Reference
DSP-1181 - treatment of obsessive-compulsive disorder (OCD).	Exscientia in collaboration with Sumitomo Dainippon Pharma	Entered phase-1 clinical trials on January 30, 2020.	30
EXS21546 - Immuno-oncology drug.	Exscientia in collaboration with Evotec	Entered phase-1 clinical trials on April 09, 2021.	31
DSP-0038 - For treatment of Alzheimer's disease psychosis.	Exscientia in collaboration with Sumitomo Dainippon Pharma	Entered First phase of clinical trials on May,13 2021.	32

quality product. AI-enabled technologies have evolved into versatile tools that can be used in a variety of stages of product development, including the design of new drugs, formulation development, drug repurposing, improving R&D efficiency, aggregating and analyzing biomedicine data, and optimizing the decision-making process to recruit study participants in clinical trials.[40-42] These potential AI applications offer the opportunity to counteract the inefficiencies and uncertainties that arise in traditional product development methods while minimizing bias and human intervention.[43] There are various types of AI algorithms used in product development.

AI algorithms employed in product development and their applications

1) General regression neural network[44,45] (GRNN) – It is used for estimation of drug behavior *in vivo* and compensation of dissimilarities in the drug release kinetics under various conditions. Stanojevi'c *et al.*[46] used two types of ANN to predict the dissolution curve of 3D printed atomoxetine tablets in their study. The effect of the inputs on atomoxetine release was visualized using a self-organizing map, and the atomoxetine release was predicted using a GRNN. The predicted dissolution profiles for the two testing formulations were found to be similar to experimental data. As a result, the GRNN developed in this study had a reasonable ability to predict the drug's dissolution behavior. In addition, GRNN is involved in a wide range of other aspects of pharmaceutical science research.

2) Recurrent neural networks[47] (RNNs) - It is used for modeling or characterizing drug release from modified-release formulations. Ibric *et al.*[48] used the multi-layered perceptron (MLP) in the design of an extended-release aspirin neural network with four inputs and one output of tablets. The NEURAL programme was used to create ten aspirin matrix tablets. Portions of MCC and GMS in the formulations, *in vitro* dissolution–time profiles at four different sampling time points, and the difference between the sampling time points, as well as coefficients n release (release order) and log k (release constant) from the one similarity factor, f as release parameters, Peppas equation[49] was estimated. The optimized GRNN model was used to determine formulation and process factors for optimized formulations that could provide the desired *in vitro* drug release profiles.

3) Artificial neural networks and Genetic algorithm[50-51] (ANN&GA) - It is used for Optimization of the formulations such as controlled released systems. Yongqiang Li *et al.*[52] used artificial neural networks with a genetic algorithm to optimize the controlled release

nanoparticle formulation of verapamil hydrochloride. Using the spherical central composite design and the ANN methodology, they successfully optimized the formulation. The resulting formulation had a high drug loading efficiency (92%) and a small mean particle size (100 nm), which is ideal for lymphatic transport via oral administration. It is found that ANN fit the experimental data better than (Response Surface Methodology) RSM, owing to ANN's ability to accommodate more complex and non-linear functional relationships.

4) Multilayer Perceptron (MLP) Network - It is used for designing controlled release formulations, predicting drug dissolution profiles, and optimizing the formulations.[53-55] Mohammad Rafienia *et al*.[56] used multilayer perceptron (MLP), radial basis function network (RBFN), and generalized regression neural network (GRNN) to predict the release profile of betamethasone (BTM) and betamethasone acetate (BTMA) as implant controlled-release system. When the release profiles calculated by ANNs are compared to the release profiles measured by HPLC, MLP is found to be more reliable and has better performance in estimating BTM and BTMA release profiles than GRNN and RBF networks.

Applications of AI in nanotechnology-based products

The approach and efficiency of experimentation in the field of nanotechnology and personalized medicine are changing dramatically. The goal of combining automation and artificial intelligence (AI) allows for the optimization of targeted therapeutic nanoparticles for specific cell types and patients. Nanomedicine and nanobots are two important nanotechnology products in which AI is widely employed (Figure 2).

1. Nanomedicine

The term "Nanomedicine" refers to the combination of nanotechnology and medicine for the diagnosis, treatment, and surveillance of disease progression, which has made a significant contribution to improving the treatment of complex and fatal diseases by delivering therapeutic agents to specific sites in the body and increasing their circulation time.[57] In recent years, there has been a tremendous amount of success in the field of clinical nanomedicine in terms of clinical studies and approval. The PLGA-Docetaxel complex, for example, has been studied for the treatment of breast cancer.[58] Clinical trials for the Spherical Nucleic Acid (SNA) platform for the treatment of glioblastoma are currently underway.[59] In addition to PEGylated liposomal doxorubicin (DOXIL), albumin-functionalized paclitaxel (Abraxane) has been approved for pancreatic cancer, lung cancer, and breast cancer.[60]

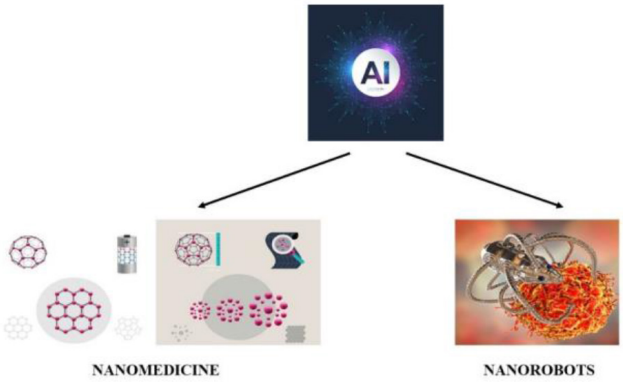

Figure 2: Applications of AI in nanotechnology-based products.

Artificial intelligence technology is widely used in the pharmaceutical industry's field of nanotechnology. Design, classification, monitoring, diagnosis, process control, programming, and planning[61] are some of the various applications of AI in the field of nanotechnology. AI applications in nanotechnology are solely focused on areas such as nanomaterials, nanophysics, and nanomedicine.[62] Artificial intelligence-based computing methods can be used to optimize the shape, size, and binding of nanoparticles, as well as drug delivery.[63] In one study, for example, artificial neural networks (ANN)[64] was used to predict the size and initial burst release rate of poly (lactic-co-glycolic acid) (PLGA) nanoparticles. The method is advantageous because the algorithm produced an error rate of less than 5% when tested against the data provided in the study; however, the main disadvantage of this computational method is that a large training set is needed to achieve higher accuracy.

Another study[65] investigated the side effects of nanoparticles using machine learning. The model predicted that 17 different metal oxide nanoparticles would be cytotoxic to *E. coli*. This method could pave the way for the development of safer nanomaterials in the future.

2. Nanorobots

Nanorobots are miniature synthetic machines[66] that can sense, move, and work on a nanometer scale while performing a variety of tasks in a continuous and controlled manner. This type of nano-scale robotic strategy for drug delivery differs from traditional drug delivery strategies in terms of targeting design, performance, detection, control, and simultaneous task execution.[67] Because of significant advances in nanotechnology, there has been a surge of interest in developing nanorobots with internal or external power supplies, sensors, and AI.[68-69]

Nanorobots have shown tremendous potential in toxic substance detection, therapeutic, and diagnostic applications.[70-73] Artificial intelligence can be used to control the behavior or movement of nanorobots.[74-75] To control the movement of nanorobots, an efficient swarm intelligence algorithm is required. Swarm Intelligence (IS) is a subfield of Artificial Intelligence (AI) that investigates algorithms based on the behavior of insects, animals, and birds. It is possible to collaborate without centralized control. Swarm Intelligence Method[76] is an algorithm designed for nanorobot artificial intelligence. The three main types of swarm intelligence[77] are ant colony optimization (ACO), artificial bee colony (ABC), and particle swarm optimization (PSO).

The particle swarm optimization (PSO) algorithm has been modified in a new way called directed particle swarm optimization (DPSO). The goal of DPSO is to deliver nanorobots to specific cancer sites. Several studies have shown that DPSO can successfully deliver nanorobots to cancer sites in a short period of time.[78-79] A study[80] looked into the capabilities of Directed Particle Swarm Optimization (DPSO). DPSO has been tested against four different algorithms, and the results show that DPSO outperforms all four algorithms in terms of reducing the time required to deploy nanorobots. As a result, it can rapidly deliver a large number of nanobots to the cancer site. The implementation of Artificial Neural Networks (ANN's) for predicting the performance of nanorobots integrated with biosensors and transducers[81-82] is one of the most promising methods for detecting tumor cells and targeted delivery.

USE OF DIFFERENT DRUG DISCOVERY TOOLS AGAINST COVID-19 – PREVENTION AND TREATMENT

1) BenevolentAI predicted using AI tools and knowledge graph,[83] a large repository of structured medical information that includes numerous machine learning connections extracted from the scientific literature. By inhibiting AP2-related protein kinase 1 (AAK1),[84] baricitinib, a drug used to treat rheumatoid arthritis, can be used as a potential treatment for COVID-19.

2) Toremifene, a first-generation selective estrogenic receptor modulator used to treat breast cancer, was identified as a potential drug candidate for testing in clinical COVID-19 research by CoV-KGE[85] (knowledge-graph (KG)-based, deep-learning methodology for drug repurposing in COVID-19) and Network Medicine Method.[86] Toremifene has also been shown *in vitro* to inhibit a variety of viral infections, including Middle East respiratory syndrome coronavirus, severe acute respiratory syndrome coronavirus,[87-88] and SARS-CoV-2.[89]

3) Exscientia[90] has demonstrated proof-of-concept for a novel class of inhibitors targeting the SARS-main CoV-2's protease enzyme, Mpro, also known as 3CLpro, the causative agent of COVID-19, using its AI platform. Mpro is also required for coronavirus replication, so giving Mpro inhibitors to patients as standalone antiviral drugs or in combination with other adjuvant therapies may be a beneficial first-line therapy. The project's goal is to identify potential coronavirus treatment options that are not only effective against COVID-19 but also against new mutations or other SARS viruses that may emerge in the future.

4) IBM used its generative AI framework to generate 3,000 new potential hit molecules for three COVID-19 target drugs.[91]

5) Gero, a Singapore-based company, utilized its AI platform (deep neural network) to identify ideal COVID-19 drug candidates. Key molecules demonstrated to be good against coronaviruses are Niclosamide, Nitazoxanide, Afatinib, Ixazomib, and Reserpine.[92-93]

6) Healx, a US-based AI company,[94] utilized its AI platform Healnet to develop drug combinations from approved drugs to find a treatment for COVID-19. Healnet integrates and examines biomedical data from various sources to predict which combination therapies will be clinically successful.

7) TCS[95-96] (Tata Consultancy Services) Innovation Laboratory in Hyderabad, India, used artificial intelligence (deep neural network-based generative and predictive models) to identify 31 molecular compounds that are likely to cure COVID-19. TCS scientists used artificial intelligence to create new compounds that help inhibit proteases, which are responsible for cleaving the virus's long polyprotein into various functional proteins required for replication in the human body.

8) A research team at the University of California's USC Viterbi School of Engineering[97] has developed a method that uses artificial intelligence[98] (AI) to speed up vaccine analysis and ensure the best possible vaccines are quickly identified. The artificial intelligence system applied to specific virus characteristics can provide candidate vaccines in seconds rather than months or years, and they can be quickly transferred to clinical trials. Researchers identified 11 of 26 potential vaccine candidates for a multi-epitope vaccine (Deepvac Pred) that can target spike proteins. Since the coronavirus has already mutated into various strains around the world, USC's artificial intelligence method will be especially

useful at this point. If currently available vaccines fail to control SARS-CoV-2, or if new vaccines are required to deal with other emerging viruses, this method can be used to quickly design other preventive mechanisms. The proposed vaccine design framework can address the three most commonly observed mutations and can be expanded to address other potentially unknown mutations.

9) Mannin Research[99] is a collaboration between Mannin GmbH, a Mannin subsidiary in Germany, and Cyclica Inc. Mannin's expertise and research capabilities will be coupled with Cyclica's proprietary AI-augmented drug discovery platform in the Mannin-Cyclica JV. The JV will concentrate on the development of novel compounds for the treatment of COVID-19. Mannin's extensive experience and research into targeting the Tie2 tyrosine kinase receptor will be integrated with Cyclica's AI-augmented Ligand Design and Ligand Express drug discovery platforms. Preliminary research has shown that minimizing vascular leakage aids in the prevention of organ failure and the treatment of acute infections. It is possible to treat vascular leakage associated with pulmonary edema by activating the Angiopoietin-Tie2 signaling pathway, thereby addressing respiratory infections caused by viruses such as COVID-19.

10) Researchers at the U.S. Department of Energy's (DOE) Argonne National Laboratory[100] have used artificial intelligence (AI) to explore a large number of small molecules in search of drug candidates against Covid-19. They recently used new computing hardware to speed up the process, reducing searches that could have taken years to mere minutes. They used the ALCF's AI testbed, which is home to some of the world's most advanced AI platforms, including the GroqChip accelerator. The researchers discovered that they could achieve 20 million predictions, or inferences, per second in tests on a large dataset of small molecules, significantly shortening the time for each search. They are still looking for the best candidates; once found, the researchers will determine which can be obtained commercially and test it on human cells at the Howard T. Ricketts Laboratory, a bioresearch facility on the Argonne campus.

PATENT PERSPECTIVES ON USING AI

Last year, the United States Patent and Trademark Office (USPTO) decided to reject the notion that "machines" with artificial intelligence can become inventors. Similarly, the United Kingdom Intellectual Property Office (UKIPO) and the European Patent Office recently rejected applications because the designated inventor is an artificial intelligence named DABUS, although they met patentability standards, and the UK Intellectual Property Office has now updated its patent practices. The guidelines expressly prohibit artificial intelligence from being referred to as an inventor. Consider the following two scenarios in the pharmaceutical industry:[101] (1) Scientists in pharmaceutical companies use artificial intelligence as a tool to discover and identify new drugs by employing artificial intelligence to perform specific tasks; (2) A pharmaceutical company purchases an artificial intelligence system from a third party (such as IBM or Exscientia), trains the system on its data set, and uses the system to develop a new drug with little or no human involvement. In the first case, determining who invented the new drug is as simple as identifying the scientists who discovered it. In the second case, the situation is more complicated: who or what invented the new drug, and who owns the intellectual property rights to the corresponding products and processes. IBM may retain all intellectual property rights in the artificial intelligence system itself but may license certain intellectual property rights in the AI system's output, such as new drug compounds, to pharmaceutical companies. Furthermore, such contracts should specify who will be held accountable for the artificial intelligence system's outcomes and actions.

Inventorship[102] currently belongs to the person who created artificial intelligence; however, with the development of artificial intelligence capabilities and minimal human supervision, this situation may become more complicated. There are no specific legal provisions addressing the concept of AI as an inventor at the moment, and most jurisdictions require the designated inventor to be a human.[103]

CONCLUSION AND FUTURE PROSPECTIVES

The introduction of artificial intelligence has resulted in tremendous growth in the pharmaceutical sector's various key areas. It had revolutionized traditional approaches to drug discovery and development by using modernized computational approaches. Many pharmaceutical behemoths have begun to implement these sophisticated technologies to develop personalized medicine. The role of artificial intelligence is critical in identifying potential treatments for chronic and life-threatening illnesses such as Parkinson's disease, diabetes, Alzheimer's, Obsessive-Compulsive Disorder, and others, which was previously difficult with existing techniques. The shift in pharmaceutical industries towards an AI-based approach is also extremely advantageous during this COVID-19 pandemic, where

faster drug discovery and development is critical. It paved the way for identifying potential therapies with the greatest therapeutic benefit and the fewest side effects, in addition to shortening the time required for discovery and development. Almost all pharmaceutical companies will undoubtedly collaborate with an AI-based company in the near future, propelling the pharmaceutical market to new heights. While new collaborations between tech leaders and pharmaceutical companies have the potential to drive significant technological progress, they also raise a new set of legal, ethical, and regulatory issues that must be resolved quickly to reap the full benefits. For decades, drug discovery and development have been time-consuming and costly. The impressive advances of AI have shifted our thinking in the direction of a new paradigm for drug design. We anticipate that the next decade of AI-based drug development will be characterized by a deep engagement of interpretable AI tools and active learning algorithms that incrementally enhance the workflow and produce interpretable ideas that scientists can monitor, evaluate, and understand at every stage of drug development.

ACKNOWLEDGEMENT

The authors would like to express their sincere thanks to Department of pharmaceutics, SRIHER, Porur, Chennai, Tamil nadu, India. for providing the support to carry out this review work.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

AI: Artificial Intelligence; **NDA:** New Drug Application; **BBB:** Blood-Brain Barrier; **BRB:** Blood Retinal Barrier; **ANN:** Artificial Neural Networks; **SARS-CoV-2:** Severe Acute Respiratory Syndrome - Coronavirus -2; **COVID-19:** Coronavirus Disease – 2019; **ARUK-ODDI:** Alzheimer's Research UK Oxford Drug Discovery Institute; **NLRP3:** Nod-like Receptor Protein 3; **ALS:** Amyotrophic Lateral Sclerosis; **FTD:** Frontotemporal Dementia the; **ISH:** Insitro Human platform; **iPSC:** induced pluripotent stem cell; **ADMET:** Absorption, Distribution, Metabolism, Excretion and Toxicity; **NASH:** Non-alcoholic steatohepatitis; **OCD:** Obsessive-Compulsive Disorder; **GRNN:** General regression neural network; **RNNs:** Recurrent neural networks; **ANN&GA:** Artificial neural networks and Genetic algorithm; **MLP:** Multilayer Perceptron Network; **PLGA:** Poly (lactic-co-glycolic acid); **SNA:** Spherical Nucleic Acid; **DOXIL:** PEGylated liposomal doxorubicin; **ACO:** Ant colony optimization; **ABC:** Artificial bee colony; **PSO:** Particles swarm optimization; **DPSO:** Directed Particle Swarm Optimization; **PSO:** Particle swarm optimization; **CFD:** Computational Fluid Dynamics; **PAT:** Process Analytical Technology; **AAK1:** AP2-related protein kinase 1; **USPTO:** United States Patent and Trademark Office; **UKIPO:** United Kingdom Intellectual Property Office.

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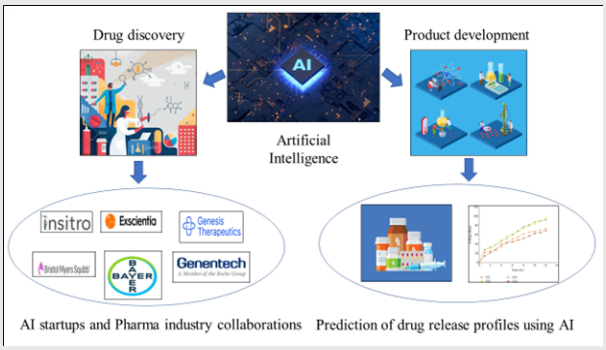
PICTORIAL ABSTRACT



SUMMARY

Artificial intelligence (AI) promises significant technological advancements that could constitute a paradigm shift in drug research and eventually clinical development. We believe that developments that currently feel revolutionary will quickly become standard practice in terms of discovery speed, novelty, and commercial potential. Many use cases have progressed to the point where their implications are fully known. The greatest future possibility is the acceleration of drug discovery and reduction of attrition rates, resulting in more novel medications reaching patients quickly.

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Cite this article: Narayanan RR, Durga N, Nagalakshmi S. Impact of Artificial Intelligence (AI) on Drug Discovery and Product Development. Indian J of Pharmaceutical Education and Research. 2022;56(3s):s387-s397.