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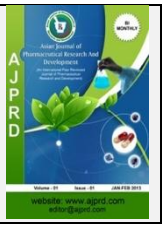

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Review Article

A Review on Artificial Intellegence in Drug Discovery & Pharmaceutical Industry

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A B S T R A C T

Introduction: The use of artificial intelligence (AI) in drug discovery and the pharma industry has been rapidly expanding in recent years. AI algorithms can analyze vast amounts of data, identify patterns, and make predictions that can accelerate drug discovery and improve patient outcomes.

Methods: AI is being used in various stages of the drug discovery process, from target identification and lead optimization to clinical trials and post-market surveillance. Machine learning algorithms, neural networks, and natural language processing are among the AI techniques used in drug discovery.

Results: AI-based drug discovery has already shown promising results, with several drugs in clinical trials or approved for use that were discovered using AI. AI is also being used to improve clinical trial design and patient selection, as well as to monitor adverse drug events and optimize drug dosing.

Conclusion: AI has the potential to transform the drug discovery and pharma industry, making drug development faster, more efficient, and more effective. However, there are still challenges that need to be addressed, such as the need for high-quality data and the potential for bias in AI algorithms. Overall, the use of AI in drug discovery and the pharma industry is an exciting and rapidly evolving field that has the potential to improve patient outcomes and revolutionize healthcare.

Key words: Artificial intelligence, Health care, Drug Discovery, Industry

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INTRODUCTION

Artificial intelligence is a branch of computer science that deals with the problem solving by the aid of symbolic programming.McCulloch and Pitts (1943) invented the first artificial neuron using simple binary threshold functions.The next important milestone came when Frank Rosenblatt, a psychologist, developed the Perceptron in 1958 as a practical model.[2]

Fuzzy expert systems Fuzzy logic is the science of reasoning, thinking and inference that recognizes and uses the real world phenomenon – that everything is a matter of degree. Instead of assuming everything is black and white (conventional logic), fuzzy logic recognizes that in reality most things would fall somewhere in between, that is varying shades of grey. It was popularized by Lofti Zadeh (1965) an engineer from the University of California. [3]

In an interview with the BBC (British Broadcasting Corporation), theoretical physicist, Professor Stephen Hawking, had said that human efforts to create machines that can think are a huge threat to the existence of human race and that the race to develop a complete artificial intelligence (AI) could mean that the human race would come to an end in the future. This warning was given by Professor Hawking after he was asked about revamping the technology that is used by him to communicate. The technology used by him involves AI of a basic nature. [4]

Tools of AI

A large number of AI tools have been created to meet the current need of the pharmaceutical industry. These tools have shown promising outcomes. Some of the AI tools that have gained huge popularity in pharmaceutical sector have been described below:

Table 1: Tools of AI discovered

TOOLS	Country	GOALS
IBM Watson for oncology	South Korea	This product information and insight to physicians and cancer patient s to help them identify personalized, evidence-based cancer care options.[5]
MEDi robot(Medicine and Engineering Designing Intelligence)	Canada	The robot first builds a rapport with the children and then tells them what to expect during a medical procedure Also to guide them during it.[6][7]
Erica robot	Japan	It has been developed with the ability to understand and answer questions with human-like facial expressions.[8][9]
TUG robots	Pittsburgh	They are designed to autonomously travel through the hospital and deliver medications, meals, specimens, materials, and haul carry heavy loads such as linen and tras[10]
Berg	Boston	It has an AI-based platform for drug discovery, which has a huge database of patients and this is used to find as well as validate the various biomarkers responsible for causing diseases and then decides therapies according to the obtained data.

Drug Development Process

The first step in drug development is the identification of novel chemical compounds with biological activity. This biological activity can arise from the interaction of the compound with a specific enzyme or with an entire organism. The first compound that shows activity against a given biological target is called a 'hit'. Hits are often found during the screening of chemical libraries, computer simulation or screening of naturally isolated materials, such as plants, bacteria and fungi. [11]

During the process of lead generation, hit molecules are systematically modified to improve their activity and selectivity towards specific biological targets, while reducing toxicity and unwanted effects. The chemically related compounds derived from a hit are called analogues and the process is referred to as hit expansion. [12]

1. Target identification: This stage involves identifying a specific biological target that plays a key role in a particular disease. Targets can be identified through a range of approaches, including genetic and genomic studies, proteomics, and metabolomics.

2. Lead generation: Once a target has been identified, potential drug candidates are identified and screened for their ability to interact with the target and modify its activity. This can involve high-throughput screening of large compound libraries, virtual screening using computer algorithms, or more targeted approaches such as structure-based drug design.[13]

3. Lead optimization: Once a promising lead compound has been identified, it undergoes further optimization to improve its efficacy, safety, and pharmacokinetic properties. This can involve modifying its chemical structure or pharmacological profile, as well as testing its activity in animal models. [14]

4. Preclinical development: In this stage, the lead compound is tested in animal models to assess its safety and efficacy, as well as its potential toxicities and side effects. This can involve a range of studies, including pharmacokinetic and pharmacodynamics studies, toxicity testing, and animal efficacy studies. [15]

5. Clinical trials: If a lead compound shows promising results in preclinical studies, it can proceed to clinical trials in humans. Clinical trials are conducted in three phases, each with increasing numbers of participants, to test the safety and efficacy of the drug in humans. [16]

6. Regulatory approval: If the drug shows safety and efficacy in clinical trials, it can be submitted for regulatory approval by the relevant authorities, such as the FDA in the United States. Approval is granted based on a range of factors, including safety, efficacy, and manufacturing quality.[17]

Tools and Technologies in the Drug Discovery Process

1. High-throughput screening (HTS): HTS is a process of rapidly testing large numbers of compounds for their ability to interact with a target of interest. This can be done using various types of assays, such as biochemical assays, cell-based assays, and whole-organism assays. HTS can help identify lead compounds that can be further optimized for drug development. [18]

2. Computational modeling: Computational modeling uses computer algorithms to predict the behavior of compounds in biological systems, allowing researchers to screen and design compounds with desired properties. This can include molecular docking, molecular dynamics simulations, and machine learning approaches. [19]

3. CRISPR/Cas9 gene editing: CRISPR/Cas9 is a genome editing tool that allows researchers to make precise changes to the DNA of cells. This can be used to create disease models for drug discovery, as well as to identify new drug targets. [20]

4. Mass spectrometry: Mass spectrometry is a powerful analytical tool that can be used to identify and quantify small molecules, peptides, and proteins. It can be used in

drug discovery to identify lead compounds, optimize their properties, and monitor their pharmacokinetics and metabolism. [21]

5. X-ray crystallography: X-ray crystallography is a technique for determining the three-dimensional structure of proteins and other biomolecules. This can be used in drug discovery to understand the interactions between small molecules and their target proteins, and to aid in the design of new compounds. [22]

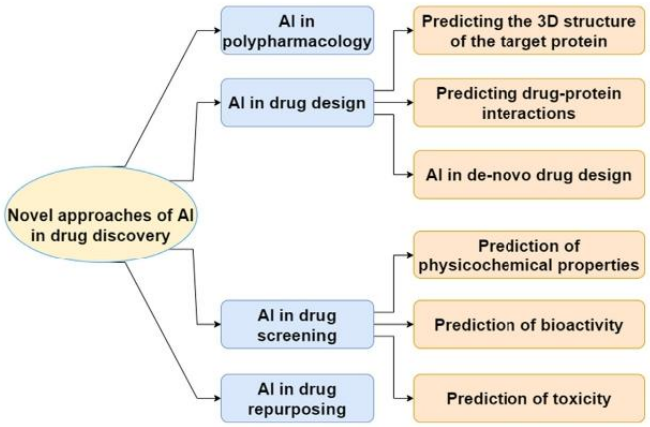


Figure 1: Application of artificial Intelligence in drug discovery [23]

AI IN DRUG DISCOVERY

Despite its advantages, AI faces some significant data challenges, such as the scale, growth, diversity, and uncertainty of the data. The data sets available for drug development in pharmaceutical companies can involve millions of compounds, and traditional ML tools might not be able to deal with these types of data. Quantitative structure-activity relationship (QSAR)-based computational model can quickly predict large numbers of compounds or simple physicochemical parameters, such as log P or log D. However, these models are some way from the predictions of complex biological properties, such as the efficacy and adverse effects of compounds. In addition, QSAR based models also face problems such as small training sets, experimental data error in training sets, and lack of experimental validations. To overcome these challenges, recently developed AI approaches, such as DL and relevant modeling studies, can be implemented for safety and efficacy evaluations of drug molecules based on big data modeling and analysis. In 2012, Merck supported a QSAR ML challenge to observe the advantages of DL in the drug discovery process in the pharmaceutical industry. DL models showed significant predctivity compared with traditional ML approaches for absorption, distribution, metabolism, excretion, and toxicity (ADMET) data sets of drug candidates. [24, 25]

One of the key areas where AI is being used in drug discovery is in the analysis of genomic and proteomic data. AI algorithms can analyze large amounts of genomic and proteomic data to identify potential drug targets and predict the efficacy of potential drugs. AI can also help to identify potential side effects and drug interactions, which can help to improve the safety of new drugs.

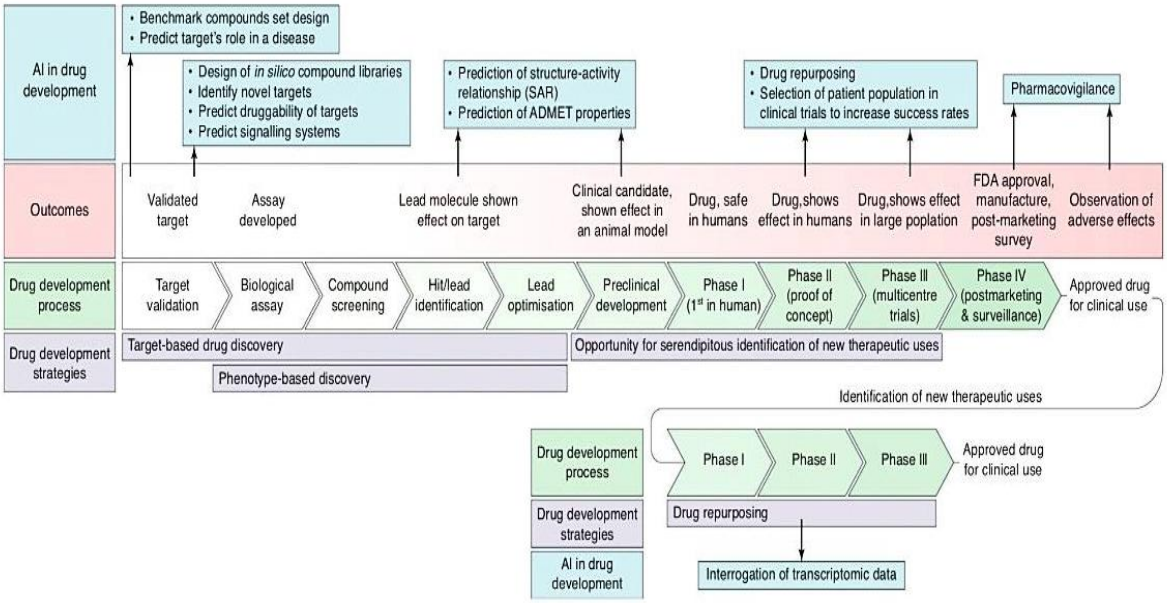
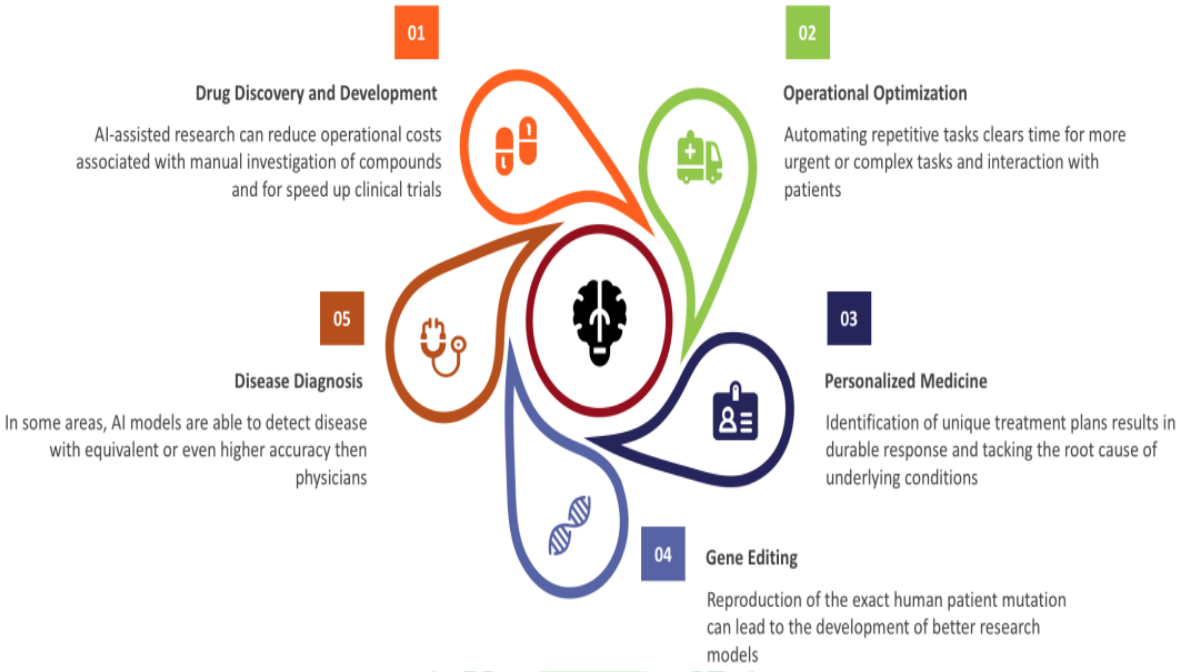


Figure 2: Utilisation of artificial intelligence (AI) in the drug development process. The outcomes and the stratifies of the various components of the drug development process are described. The application of AI at each stage of drug development is also shown.[26]

AI IN DRUG SCREENING

AI in drug screening the process of discovering and developing a drug can take over a decade and costs US$2.8 billion on average. Even then, nine out of ten therapeutic molecules fail Phase II clinical trials and regulatory approval.[27, 28]



AI IN DESIGNING DRUG MOLECULES

Prediction of the target protein structure while developing a drug molecule, it is essential to assign the correct target for successful treatment. Numerous proteins are involved in the development of the disease and, in some cases, they are overexpressed. Hence, for selective targeting of disease, it is vital to predict the structure of the target protein to design the drug molecule. AI can assist in structure-based drug discovery by predicting the 3D protein structure because the design is in accordance with the chemical environment of the target protein site, thus helping to predict the effect of a compound on the target along with safety considerations before their synthesis or production.[31]

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 keep the dRMSD low between the experimental and predicted structures. [32]

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 likely to have better accuracy in predicting protein structures with sequences similar to the reference structures. [31] A study was conducted to predict the 2D structure of a protein using MATLAB assisted by a nonlinear threelayered NN toolbox based on a feed-forward supervised learning and back propagation error algorithm. MATLAB was used to train input and output data sets, and the NNs were learning algorithms and performance evaluators. The accuracy in predicting the 2D structure was 62.72%. [33]

AI: NETWORKS AND TOOLS

AI involves several method domains, such as reasoning, knowledge representation, solution search, and, among them, a fundamental paradigm of machine learning (ML). ML uses algorithms that can recognize patterns within a set of data that has been further classified. A subfield of the ML is deep learning (DL), which engages artificial neural networks (ANNs). These comprise a set of interconnected sophisticated computing elements involving 'perceptons' analogous to human biological neurons, mimicking the transmission of electrical impulses in the human brain. [34] ANNs constitute a set of nodes, each receiving a separate input, ultimately converting them to output, either singly or multi-linked using algorithms to solve problems [33]. 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. [36, 37]

The MLP network has applications including pattern recognition, optimization aids, process identification, and controls, are usually trained by supervised training procedures operating in a single direction only, and can be used as universal pattern classifiers [37]. RNNs are networks with a closed-loop, having the capability to memorize and store information, such as Boltzmann constants and Hopfield networks [38, 39]. 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 sophisticated signal processing [39]. The more complex forms include Kohonen networks, RBF networks, LVQ networks, counter-propagation networks, and ADALINE networks [35, 38]. Examples of method domains of AI are summarized in Figure 3.

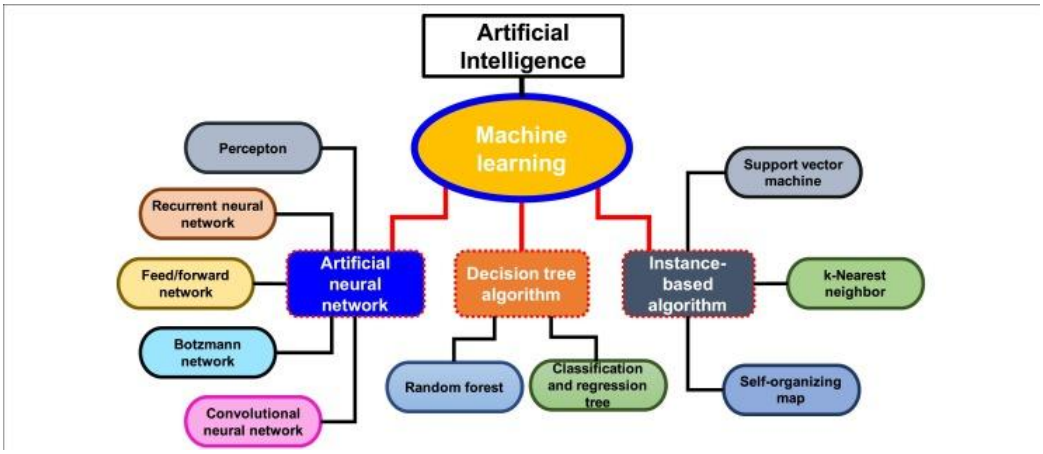


Figure3: AI networks and tools

Several tools have been developed based on the networks that form the core architecture of AI systems. One such tool developed using AI technology is the International Business Machine (IBM) Watson supercomputer (IBM, New York, USA). It was designed to assist in the analysis of a patient's medical information and its correlation with a vast database, resulting in suggesting treatment strategies for cancer. This system can also be used for the rapid detection of diseases. This was demonstrated by its ability to detect breast cancer in only 60s [41, 42]

AI-Based Advanced Applications

AI-based Nano robots for drug delivery Nano robots comprise mainly integrated circuits, sensors, power supply, and secure backup of data, which are maintained via computational technologies, such as AI [43, 44]. They are programmed to avoid the collision, target identification, detect and attach, and finally excretion from the body. Advances in Nano/micro robots give them the ability to navigate to the targeted site based on physiological conditions, such as pH, thus improving the efficacy and reducing systemic adverse effects [44]. Development of implantable Nano robots developed for controlled delivery of drugs and genes requires consideration of parameters such as dose adjustment, sustained release, and control release, and the release of the drugs requires automation controlled by AI tools, such as NNs, fuzzy logic, and integrators [45]. Microchip implants are used for programmed release as well as to detect the location of the implant in the body.

Pharmaceutical Market In AI

Nevertheless, AI has been adopted by several pharmaceutical companies, and it is expected that revenue of US$2.199 billion will be created by 2022 through AI-based solutions in the pharmaceutical sector, with an investment exceeding US$7.20 billion across 300+ deals between 2013 and 2018 by the pharmaceutical industry [46]. Pharmaceutical organizations need clarity about the potential of AI technology in finding solutions to problems once it has been implemented, along with understanding the reasonable goals that can be achieved. Skilled data scientists, software engineers with a sound knowledge of AI technology, and a clear understanding of the company business target and its R&D goal can be developed to utilize the full potential of the AI platform.

Future Prospects of AI In Pharmaceutical Market

Despite the challenges, the future prospects of AI in the pharmaceutical market are promising. The global AI in healthcare market is expected to reach $31.3 billion by 2025, driven by the increasing demand for personalized medicine, the growing need to reduce drug development costs and timelines, and the rising prevalence of chronic diseases. Pharmaceutical companies are investing heavily in AI research and development, and collaborations between industry players, academic institutions, and technology companies are expected to accelerate the adoption of AI in the pharmaceutical market. [47, 49, 53]

1. Precision Surgery: AI can help surgeons to perform more precise and accurate surgeries by analyzing medical images and identifying the exact location of tumors and other abnormalities. AI can also assist surgeons during surgery by providing real-time guidance and feedback [54]
2. Robot-Assisted Surgery: AI-powered surgical robots can perform complex surgical procedures with greater precision and accuracy, reducing the risk of complications and improving patient outcomes.[55]
3. Predictive Analytics: AI can be used to analyze patient data and predict the likelihood of surgical complications or therapy outcomes. This can help healthcare providers to develop personalized treatment plans and improve patient outcomes.[56]
4. Virtual Reality: AI-powered virtual reality technology can help to train surgeons and therapists, allowing them to practice surgical and therapeutic procedures in a virtual environment before performing them on patients.[57]
5. Real-Time Monitoring: AI can be used to monitor patient data in real-time during surgical and therapeutic

procedures, detecting changes in health status and providing alerts to healthcare providers.[58]

6. Drug Discovery: AI can help to accelerate the discovery of new therapies by analyzing vast amounts of data and identifying potential drug candidates. With the help of machine learning algorithms, AI can predict the effectiveness and safety of new drugs and reduce the cost and time required for drug development.

CONCLUSION:

AI has the potential to transform the drug discovery and pharma industry, making drug development faster, more efficient, and more effective. However, there are still challenges that need to be addressed, such as the need for high-quality data and the potential for bias in AI algorithms. Overall, the use of AI in drug discovery and the pharma industry is an exciting and rapidly evolving field that has the potential to improve patient outcomes and revolutionize healthcare.AI technologies offer tremendous opportunities for analyzing the massive amounts of multivariate data, solving the complex problems associated with designing of functional drug delivery systems, making more accurate decisions, classification and modeling of diseases, accelerated drug discovery, identifying biomarkers, drug targets, potential drug candidates and their pharmacological properties, novel indications for existing therapeutics, relationships between the formulations and processing variables, and physiological or pathophysiological pathways, optimizing dose ratio, and predicting the bioactivities and interactions of drugs, molecular behavior, disease status, cellular response, efficiency of drug combinations, and treatment outcomes

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