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Artificial Intelligence In Drug Discovery

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ABSTRACT

Traditional drug discovery process is time-consuming as well as expensive often taking over a decade and costing billions of dollars to bring a new drug to market. Out of every 5,000-10,000 compounds that go through the research and development pipeline, only one ends up being approved. the surge of Artificial intelligence can be used to hasten the drug discovery process. AI, with its advanced algorithms, computational power, explainable AI, and the integration of AI with traditional experimental methods offers a transformative approach to the traditional drug discovery process. Artificial intelligence can be simply defined as it is human intelligence in machine format where computer programs develop data-based decisions & perform tasks normally performed by humans. In this article, we simply describe in the use of various AI-based tools in the drug discovery process. Many scientists used AI-based models in their research like Deep neural network-based AlphaFold model which can predict properties of proteins, A Reinforcement learning model called ReLeaSE can be used to identify *de novo* drug design, Machine learning techniques and predictive model software also contribute to the identification of target-specific virtual molecules, long short-term memory based multi-objective lead optimization. AI can also be used in prediction like molecular properties of drug & drug-drug interaction. AI is a cost & time-efficient tool; it also has limitations like it raises concerns about the availability of suitable data, fairness & biases of results generated & losses of jobs due to automation.

Keywords: *Artificial intelligence, Drug discovery, Machine learning*

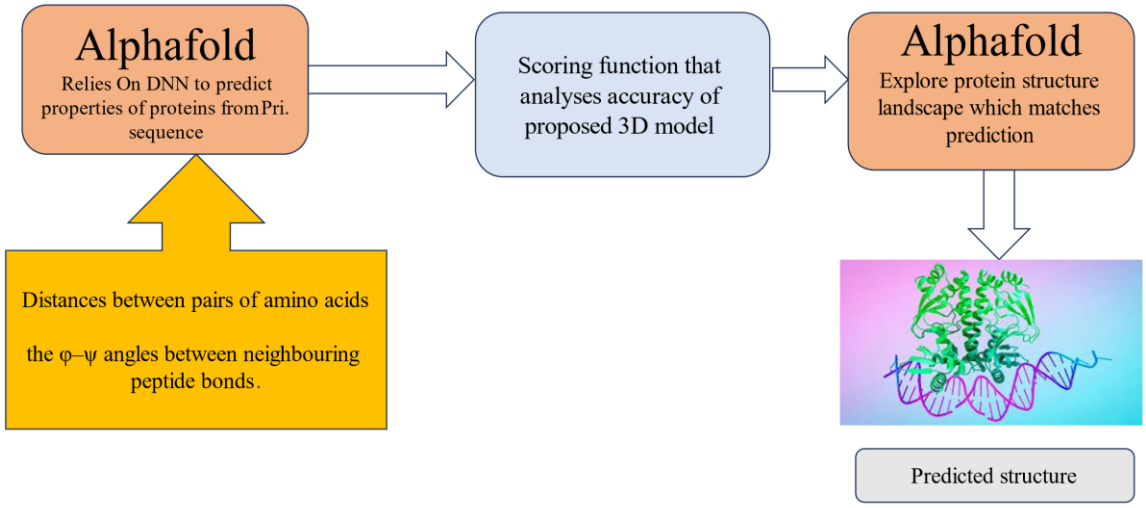
INTRODUCTION

Drug discovery is a multilayered process and it involves the identification of potential chemical drug molecule that has therapeutic effects in particular disease conditions. Drug candidates are found, synthesized, characterized, screened, and assayed for therapeutic efficacy as part of the drug discovery process. Following clinical trials, the molecule will begin the drug development process if it yields favourable findings from these studies. However, the enormous costs associated with clinical trials and research and development make the process of finding new drugs costly as well as lengthy. It takes almost 12-15 years to develop a single new drug molecule from the time it

is discovered when it is available in the market. Each successful drug will probably require an average expenditure of $900 million to $2 billion for research and development. Out of every 5,000-10,000 compounds that enter the investigation and development pipeline, only one ultimately attains approval.[i] [ii] The term "artificial intelligence" (AI) refers to the process of using a computer to mimic intelligent behaviour with the least amount of human intervention possible. An expert system in artificial intelligence comprises an information base, a user interface, and an inference engine. AI has unique qualities that provide it the ability to think and behave in the most likelihood of achieving a particular goal. AI does this by combining several algorithms that mimic even the most basic cognitive functions of human capacities. Now a days AI is gaining momentum across multiple sectors, and the pharmaceutical industry is at the forefront of this trend[iii].

Artificial intelligence in predicting the structure of target protein:

The 3D structure of the target protein is having utmost importance in the drug discovery process because according to the structure of the target protein the new drug molecules are designed and developed. Traditionally *de novo* drug design and homology modelling are used for this purpose but the new AI tool called Alphafold can be used for drug designing. In the Critical Assessment of Protein Structure Prediction contest, the AI tool AlphaFold performed very well and accurately predicted 25 out of 43 protein structures from its primary sequence. Alphafold relies on a deep neural network. It predicts the distance between pair of amino acids & neighbouring peptide bonds.[iv]



Artificial intelligence in *de novo* drug design:

De novo drug design refers to the process of creating novel druglike compounds without preexisting template[v]. While conventional structure-based and ligand-based drug design methods have improved the discovery of small-molecule drug candidates, they depend on specific knowledge about the active site of a biological target or the pharmacophore of a known active binder. This limits their

applicability to modern drug discovery.[vi]. The advancement of AI techniques has created new opportunities for *de novo* drug design and has expedited the drug discovery process. In recent years, various deep learning-based models have been proposed for *de novo* drug design, such as the reinforcement learning-based model ReLeaSE[vii], the encoder-decoder-based model ChemVAE,[viii] the GAN-based model GraphINVENT[ix], and the RNN-based model MolRNN[x].

Artificial intelligence in multi-objective optimization:

Multi-objective optimization of a chemical series is a process driven by artificial intelligence that simultaneously optimizes a molecule's affinity for the desired biological target or targets, selectivity against anti-targets, and various drug-like property measures in an effort to find compounds that simultaneously meet all the desirable characteristics of a potential preclinical drug candidate.[xi] Scientists at IKTOS and Servier described the use of deep learning for ligand-based optimization of compound. In the initial evaluation researchers start with 880 molecules and set a metric of 11 objectives to be fulfilled by molecules but none of them satisfied all of them. In the later stage they build a generator using Long Short-term memory to generate new virtual molecules. Generator creates 150 new virtual molecules from which 2 were actually synthesized[xii].

Artificial intelligence in Drug Target affinity:

Binding affinity reflects the strength of interactions between a drug and its target, and it is very important for drug discovery. While binding affinity can be determined experimentally by measuring dissociation and inhibition constants, these procedures are extremely time-consuming and expensive. A study has been carried out in Turkey using DeepDTA model which is based on a convolutional neural network (CNN). Researcher built a model to for prediction of drug target binding affinity. In DeepDTA model the drug and the target were encoded using SMILES and amino acid sequence, respectively and then they ran through CNN blocks to generate output.[xiii]

Artificial intelligence in Plasma Protein Binding:

Plasma protein binding (PPB) is an important feature of drug ADME behaviors, which can significantly influence drug efficacy and toxicity. Yuan *et al*. 2020, built a variety of ML-based QSAR model capable of predicting Plasma protein binding, testing with a set of more than 5000 compounds from open access databases such as ChEMBL and DrugBank database. Mean absolute error 0.041. The model performed very well in validation of traditional Chinese medicine, and of the new compounds identified.[xiv]

Artificial intelligence in Drug-Drug interaction:

Unexpected pharmacological effects, such as adverse drug events (ADEs), can be brought on by drug interactions, including drug-drug interactions (DDIs) and drug-food ingredient interactions (DFIs).

Creation of a Computational Structure With the names of drug-drug or drug-food constituent pairs and their structural information as inputs, DeepDDI which is based on deep neural network produces the results in the form of human-readable sentences with 86 significant DDI types. Using the DrugBank gold standard DDI dataset, DeepDDI predicts 86 DDI types with a mean accuracy of 92.4% by utilizing a deep neural network with optimal prediction performance. Using DeepDDI, one

may forecast alternative drug candidates for 62,707 drug combinations that have been found to have adverse health effects, as well as possible causal pathways for the 9,284 drug pairs that have had reported ADEs[xv].

Artificial intelligence in Toxicity:

Most of the failures in launching new drugs due to safety aspects are because of unacceptable preclinical toxicities. The most unpredictable adverse reactions to xenobiotics in humans is Drug induced liver toxicity (DILI). It is also the cause of post marketing withdrawals of approved drugs, inducing a variety of symptoms such as changes in enzyme levels, hepatotoxicity, and liver necrosis. These recurring differences between *in vitro* data and *in vivo* results in clinical trials or post marketing phases of drug development represents a potential for AI-based computational techniques.[xvi]

Xu *et al*.2015 developed DL models using four publicly available data sets, composed of annotated DILI positive or DILI negative, to predict DILI, testing on 475 drugs and predicting an external validation set of 200 drugs with an accuracy of 87%, sensitivity of 83% and specificity of 93%, outperforming previously reported DILI prediction models.[xvii] Li *et al*.2018, estimated the DILI potential of chemicals on humans based on structural properties, using five different ML methods, achieving a prediction accuracy of 80% on the test set and 83% on external validation with the SVM model.[xviii]

Challenges:

As artificial intelligence being a good tool that fastens the drug discovery process it also possesses some limitations like availability of suitable data. Artificial intelligence-based tools need a lot of information in order to be trained. The accuracy and reliability of the results can frequently be impacted by incomplete, inconsistent, or low-quality data. AI-based techniques may also raise questions regarding fairness and bias. For example, if the data used to train an ML system are biased or unrepresentative, the ensuing predictions may be incorrect or unjust. It can be overcome by applying techniques from Explainable AI (XAI). want to offer clear, comprehensible justifications for the predictions generated by machine learning algorithms. can only make predictions based on the database provided; it cannot take the place of a human researcher's knowledge and experience. However, cooperation can speed up and improve the drug development process.[xix]

CONCLUSION:

Currently, numerous pharmaceutical companies are facing obstacles in their drug development initiatives because of rising expenses and decreased effectiveness. There have been notable advancements in AI methods and tools that can potentially improve the cost-effectiveness and efficiency of these processes.

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