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Mini Review

Artificial Intelligence: Drug Discovery and Development Prospective in Medicinal Chemistry

Vinayak Walhekar[1], Pratik Birajdar[1], Chandrakant Bagul[1], Dileep Kumar[1], Amol Muthal[2] and Ravindra G Kulkarni[1]*

[1]*Department of Pharmaceutical Chemistry, BVDU'S Poona College of Pharmacy, Erandwane Pune, Maharashtra, India*

[2]*Department of Pharmacology, BVDU'S Poona College of Pharmacy, Erandwane Pune, Maharashtra, India*

***Corresponding Author:** Ravindra G Kulkarni, Department of Pharmaceutical Chemistry, BVDU'S Poona College of Pharmacy, Erandwane Pune, Maharashtra, India.

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Abstract

Artificial Intelligence is computational approach to find solution from existing data, which has wider applications in different areas like medicine, agriculture, etc. and pharmaceutical field is not out of its ambit. Artificial Intelligence plays a crucial role in drug discovery and development by minimizing the efforts of handling an enormous data generated. AI has an impeccable role in hit to lead identification by analyzing a large database of the hits and further distilling the good hits and modifying it to the lead molecule. This can be accomplished in the structure-based approach of drug design i.e. molecular docking for docking and analyzing the results. AI also has a promising role in protein modelling. Importance of AI in clinical trials is majorly observed by application of AI tools for the monitoring of the patient medication, time profile and also analyzing an enormous of statistical data.

Keywords: *Artificial Intelligence; Drug Discovery; Molecular Docking; QSAR; Clinical Trials; lead identification*

Introduction

Small molecular drug development is facing unprecedented setback in drug discovery process. Disease challenges such as cardiovascular, cancer, diabetes and infectious diseases have fueled the investment in drug discovery [1]. In the light of those efforts, new techniques have been developed to accelerate the drug discovery such as high throughput technique, combinatorial synthesis, assay procedures, target identification, protein structure and molecular modelling techniques. Despite the tremendous advancement in the small molecule drug discovery, it is facing challenges. Major bottleneck in drug discovery is the designing the molecule [2].

The molecular modelling techniques help in certain extent however, those methodologies are not enough. In this regard, artificial intelligence performs exceptionally well in prediction from the data, such predictions are performing to the expectations in self-car diving, retail customer predication, Netflix prices, business intelligence. With this Artificial Intelligence (AI) also states to open the doors of hope in drug discovery [3].

Overview of artificial intelligence

Artificial Intelligence has different application in various fields of science and nowadays AI has become a game changer in various scientific fields. Its successful applications are extended to drug discovery, development, and medicinal chemistry [4]. AI helps in analyz-

ing a large amount of data in training set and predicts test set in a very short period. Combinatorial synthesis is a type of AI in the field of organic synthesis. A large number of small drug intermediates and organic compounds are synthesized at a time using advanced instrumentation and computers.

A collection of millions and trillions of small molecules are available in the pharmaceutical and chemical market worldwide from which some of lead identification is performed using various machine-learning approaches like Quantitative Structure Activity Relationship (QSAR), Molecular docking approach and Molecular dynamic simulation. AI has eased the small molecule drug discovery process with the use of super computers and different AI based software [5].

AI tools in drug discovery

AI represents strong modelling tools that may be utilized in several phases of the drug developing process. Following methods are used for analyzing a large number of data in drug development process.

Sr. No	Tools	Sr. No	Tools
1	ORGANIC	9	SVM
2	DeepTox	10	AlphaFold
3	DeepChem	11	CAOCS
4	DeepNeuralNetQSAR	12	3N-MTCS
5	Hit Dexter	13	RNN
6	PotentialNet	14	MATLAB
7	DeltaVina	15	Neural graph fingerprint
8	Chemputer	16	R Programing

Table 1*: List of AI tools employed effectively in drug discovery.*

Above tools are used in different stages of the drug discovery process to minimize the tedious process and ease the drug discovery process [6].

Applications of AI in drug discovery process

Drug discovery and development process is a vast and consist of numerous steps like identification of disease, selection of target for the disease, collection, or designing of the ligands for the selected target protein, molecular docking of the ligands with the target protein, validation of the molecular docking studies by the use of molecular dynamic simulation study [7]. Synthesis of the best molecules from the docking and dynamics study, *in-vitro* testing of the molecules, *in-vivo* testing of the filtered molecules from the *in-vitro* studies. Clinical studies of the potent molecules selected from the pre-clinical studies. AI can be applied to various steps in the drug discovery and development process mentioned above [8].

Connoisseurs of pharmaceutical companies (Research and Development) who developed number of recent drug molecules which are effective against a selected biological target concerned in disease. This involves large numbers of experiments, prognostic models and expertise applied across many rounds of optimization, every with modifications to the simplest set of potential molecules. Long term, AI offers the hope of an efficient and automatic approach across these numerous stages. A future AI might hold among its databases the total of all data regarding biology, genes, and chemical interactions. It will be able to determine new targets and realize candidate molecules for a particular target in silico from huge libraries and develop and refine molecules to direct on the simplest ones. It will be able to specify method to synthesize the candidate molecules, gather looks at information, and refine further [9].

The task of completion of dream is a few ways off, however AI is already automated several components of the drug discovery processes. Analytics and applied mathematical models have long been applied to scale back trial and error in drug discovery. AI has the potential to get rid of abundant and residential in on higher answers much faster than is presently possible. In short term; AI might conceivably trim a year off the event of the many drugs, which might be price billions. To learn from AI, short term corporations are watching however, it will deliver across completely different components of the invention process: some during a piecemeal way, some with a read to putting together towards complete AI driven medical aid because the technology develops [10].

Pharmaceutical organizations namely Roche, Pfizer, Novartis, Mateon Therapeutics, Bayers, Sanofi, and AstraZeneca work collaboratively with the AI organizations namely OWKIN, XtalPia, IBM Watson, Microsoft, PointR Data, Sensyne Health, Exscientia, Numerate, and BenevolentAI for expedition of the drug discovery process with the reasonable capital investment [11].

There are ample of examples that portray the applications of AI and machine learning techniques in drug discovery namely ANNs (Artificial Neural Network), KNN (k-Nearest Neighbor), SVM (Support Vector Machine), DT (Decision tree), RF (Random Forest), PCA (Principal Component Analysis), and LightGMB. These techniques provide various advantages like modelling of complex non-linear relationships, easy and simple to implement with single predefined parameter, provide resistance to overfitting of models and easy to represent complex functions, handling of tedious and missing data, fast training speed, and high accuracy. These techniques are applied to predict various physical chemical properties namely solubility, permeability, stability and bioavailability of the drug or drug like molecules. There are numerous examples of research organization that work on AI for the drug discovery that are namely: towXAR, Atomwise, BERG, Cloud Pharmaceuticals, Flatiron Health, Globavir, InSilico Medicine, NuMedii, Numerate, and OptraHealth's iPhronesis [12].

AI in target protein and ligand protein interaction predictions.

Versatile protein targets are reported for different diseases in a Protein Data Bank. For the prediction of the target protein AI tools like AlphaFold which work based on DNNs that measure the distance between adjacent amino acid along the peptide bonds. RNN is another AI tool to predict the target protein. MATLAB is used to predict the 2D structure of the protein. SVM technique is used to predict the protein ligand interaction of the docked complex [13].

AI in hit to lead identification

Numerous small molecule drug intermediates are available in the chemical space for the discovery of the promising lead molecule. Synthesizing a large number of intermediates becomes a tedious job with the investment of exacerbated capital that is not an affordable approach in the drug discovery process. To overcome these difficulties, AI tools can ease the process of lead identification. AI tools namely phenotypic data and molecule network-based algorithms can be applied for the lead identification process [14].

AI in synthesizing drug like molecules

An active molecule to become drug like should follow certain rules according to the medicinal chemistry. The Lipinski rule of 5 which states that molecules must have molecular weight less than 500 Da, hydrogen bond donor atoms must be less than 5, hydrogen bond acceptor atoms must be less than 10 and Log P value also must be less than 5; so if the molecule passes all the points of the rule it can be a drug like entity. For synthesizing drug like molecules, it needs a good knowledge of organic synthesis and must synthesize the molecules in very few steps as possible that are a tedious job that can be difficult for the human being to apply the knowledge of the chemical reactions for the synthesis of the molecules. To address this issue, computers can be used to analyze the molecule and design an appropriate route of synthesis of the drug like molecule. AI tools like Computer aided organic compound synthesis (CAOCS) approach can be applied for this method. Other AI tools that are used 3N-MTCS with Monte Carlo Tree Search (MCTS) is a promising AI platform for the designing of the feasible route of synthesis of the drug like molecules that exclude the enantiomers and diasteriomeric ratio prediction in the synthetic process [14].

AI in clinical trials and medicine

A clinical trial is a crucial step in the drug development process that determines the drug like molecule can transform into a drug or it fails. Clinical trials analyze the drug like molecule i.e. the lead molecule for its safety and efficacy profile. The rate of lead molecule passing the tunnel of the clinical trials is very less, which becomes a financial question for the industry. Out of 10 molecules entering the clinical trial tunnel, only one molecule crosses the tunnel of the clinical trials that is not profitable deal for a pharmaceutical organization [14].

Enormous amount of money is invested in the enrolment of the patient for the clinical trials which if fails may hamper the success of the clinical trials. Therefore, for minimizing the capital investment and the time, AI tools can be applied to the clinical trials process. Selection of the patients for the Phase-II and III trials can be aided with AI tools like patient specific genome exposome profile analysis that can identify the drug target in the patient selected for the trials. For decreasing or managing, the outgoing patients from the clinical trials can be performed by the use of mobile software developed by the AiCure Company that monitors the dosing period of the patients that can ease the clinical trial process and subsequently decrease the investment of false capital and time [15].

Huge quantum of data is generated in the process of clinical trials, managing this high quantum of data is a havoc and may lead to the misinterpretation of results ultimately leading to several consequences. The cost of handling this data is also high hence to manage the data various AI software and machine learning techniques can be employed to ease the work.

Case study

The case study states that in the year 2015 there was an outburst of cancer patients accounting more than 1 million cases. This was a very difficult task to handle. The IBM's "Watson" i.e. an AI computational manifesto helped the doctors to manage the treatment of the cancer patients because it was arduous for the physicians to be updated about the latest treatment with advancing the scientific hub. IBM's Watson for oncology at Manipal hospitals created an easy of delivering an exceptional, efficacious, and frugal treatment for the cancer patients. The report published by Manipal hospital in 2018 stated that Watson was coherent with the panel of the cancer board for about 93% for the choice of cancer treatment. The downside of this AI was it could only help the physician's with the existing treatment and not in discovering the novel treatment for cancer [15].

Advantages and disadvantages of AI

AI is a computational tool that has spread its root deeper in the drug discovery process. There are advantages of AI which are: AI does not depend on the predetermined targets for the process of drug discovery, AI uses new advancements in the biology and the computers to develop an algorithms that can be helpful in discovering a drug or drug like molecules. AI has reduced the cost of the experimentations that had to be done in the case of conventional drug discovery process. It has a towering predictive power and reduces the possibility of occurrence of false positive results that hamper the process in future. Another important advantage is the screening process of the drugs or drug like molecules form laboratory to the virtual path like QSAR, molecular docking, and molecular dynamics technique that help to predict the biological activity virtually. AI increases the speed and effectiveness of the drug discovery process [16]. As like advantages, there are some disadvantages of the AI that are: AI runs on the algorithms so the algorithms should be accurate to get proper results. AI software runs on the super computers so the cost increases which affects the cost of the process i.e. it is not economic. The predictions that are obtained from the AI are to be scrutinized from the expert scientists i.e. we cannot totally rely on the prediction data. AI is a new system and may not be completely free from errors [17].

Challenges

In the upcoming decade, we witness to see AI getting used a lot of in drug discovery. However, some challenges ought to be self-addressed at the first site. Most country's jurisprudence deems an invention created only by AI to be the general public domain and may

not be patented. Most firms which have explored AI for drug discovery ought to bear an intense method to copyright their work to secure patent rights. Security is another challenge. There are risks using this information without the right security measures taken.

Finally, massive knowledge and huge amounts of computation required for AI to figure effectively which will mean that computation ought to be faster. The age of supercomputers will seemingly be replaced by a quantum laptop or another technology which will do the work in minutes rather than hours [18].

Conclusion

Artificial Intelligence is spreading rapidly in all areas of science and technology. AI has eased the process of handling a copious amount of data processing it and presenting a result in a very easy way. AI plays a crucial role in drug discovery and development process from head to toe i.e. from identification of molecules to the clinical trials monitoring. AI is the future of every branch in science and technology. Numerous MNC's have collaborated with AI organizations for the effective and economical drug discovery and development process.

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Conflict of Interest

Author declares no conflict of interest.

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