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Review Article

Impact of Artificial Intelligence on Pharma Industry

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Abstract

The pharma sector is undergoing a lot of advancement with the advent of artificial intelligence. Many pharmaceutical companies are adapting this technology in order to improve the drug discovery and development phase, hence this would help them undertake various research oriented projects pertaining to novel drug delivery approaches. The speed with which this system works will reduce the time lag between the development of a drug product and its commercialization. The Artificial Neural Network systems (ANN) are being developed to predict relationships within the data. Machine learning and Deep learning are also being used to study different parameters of machines and modulate them accordingly to get the desired output. Thus, the Artificial Intelligence softwares function as efficient systems in designing a drug product. They are also being used in clinical trials for generation and interpretation of data collected from patient's information. Hence, in this article we discuss the various roles of artificial intelligence in drug development, tablet manufacturing, design of antibiotic peptides and clinical research. Therefore, this gives a clear picture that artificial intelligence has an efficient impact on pharma industry.

Key words: ADME (Absorption, Distribution, Metabolism and Excretion), AI (Artificial Intelligence), AI Software, AI in Pharma industry, ANN (Artificial Neural Network), CT (Computed Tomography), DL (Deep Learning), DNN (Deep Neural Network), GAN (Generative Adversarial Networks), GP (Genetic Programming), HTS (High Throughput Screening), ML (Machine Learning), MRI (Magnetic Resonance Imaging), 3N-MCTS (Monte Carlo Tree Search), RASAR (Red Across Structural Activity Relationship)

Introduction

Artificial Intelligence (AI) has brought a prominent revolution in pharmaceutical industries. It is being majorly utilized in each and every field of healthcare. In the current scenario, many pharma companies are facing major obstacles in the discovery and development of drugs due to scarcity of resources for research and its high cost. Therefore, AI technology is a boon for efficient drug development[1].

This technology is a culmination of human intelligence and computer processing. It is an advanced version of computer aided technique that consists of collecting the information from various sources, then preparing rules accordingly to be followed for handling the required information, and drawing possible outcomes to determine appropriate results and conclusions. Various statistical tools are being employed in AI so that the computer software and processes can resemble the human behaviour. It consists of subunits such as machine learning and deep learning which provide ease in working with neural networks. Starting from the identification of hit series to the determination of lead molecule and finally, the formulation of drug molecule including clinical trials, all these involve the artificial intelligence techniques. Thus, it is of utmost importance for bringing more innovation in the pharmaceutical sector, rendering more accurate and rapid production of medicines[2].

Neural networks are a type of computational and mathematical models that derive the relationships

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of the given data amongst it without the need to generate any previous knowledge of the desired data from its user. It does not give any predictions but produce a range of outcomes that would best suit the experimental data and therefore comply with its given criteria. Further, this technique is modified to develop Artificial Neural Networks (ANN) that is worthwhile in tackling problems related to pharmaceutical research, development and formulation[3].

The optimization process can be suitably conducted with another form of artificial intelligence technology called as fuzzy logic. It simplifies the complicated concepts and involves data mining and presenting the information in an easy format so that the user can directly interpret it, and devise actions accordingly by formulating rules that would serve as guidance for conducting the progress of work efficiently and developing future prospects[1].

2. Role of artificial intelligence in drug development

Due to larger chemical space, the bridge between drug discovery and development is growing larger day by day as finding of novel drug molecules is becoming tedious and difficult. Thus, the techniques which work on the fundamentals of artificial intelligence provide great benefits in different phases of development of drug; such as identifying and validating targets of drugs, modelling of drugs and improving their druggable properties. It also plays a pivotal role in designing clinical trials for patients, hence, optimizes the strategy for making decisions[4].

One of its application called as, "Open Targets" is a new strategic program to study the relationship of drug targets with diseases and the way genes are linked to diseases. It provides a path that would guide in identifying target associated with disease or else the disease which is related to the target[4].

The drug like molecule must comply with the Lipinski's rule of five. Keeping this in consideration, a new neural network technique called as 3N-MCTS (Monte Carlo Tree Search) developed by Seglar *et al.* has an edge over the retro synthesis computer aided systems. Through this, different routes of synthesis were being devised in a short span of time with reduction in the number of steps to be followed[5].

SPIDER is an AI approach which is being used for determining the role of natural products and their utilization in drug discovery. It was constructed to mainly predict the targets for drug molecules e.g. β-Lapachone, and hence it proved that reversible and allosteric inhibition of 5-Lipoxygenase is caused by β-Lapachone. To determine the toxicity of unknown compounds, a more advanced technique such as Read Across Structure Activity Relationship (RASAR) is being used. It is an eminent tool which is being developed on the basis of creating and identifying the link between molecular structure and properties that would lead to toxicity. This is performed with the aid of database available for the chemicals[4].

The Deep Neural Network (DNN) is a system which includes the framework of neurons artificially being connected and conducting interactions with them to carry out different transformations of data. It develops the criteria for classification of drugs in their respective therapeutic class based on the pharmacological and toxicological data. Networks such as Generative Adversarial Networks (GAN's) act as base for developing new generation AI techniques[1].

Artificial Intelligence consists of an important aspect i.e. Machine Learning (ML). This field is based on the utilization of statistical attributes. Machine learning is classified into three sections:

i. Supervised learning:
   It is associated with the development of predictive approaches which are derived through the utilization of regression along with classification methods that give such predictions through the use of data obtained from input and output sources. The output data comprise of diagnostic method of disease in the classification category, the efficacy of drug and absorption, distribution, metabolism, excretion (ADME) predications are categorized in regression analysis. Thus, both these sub groups provide extensive information[6].

ii. Unsupervised learning:
This approach is entirely focused on input data. All interpretations are drawn through clustering and grouping data by employing feature finding pathways. This type of learning can provide output data regarding the category of disease in clustering sub group and the feature finding sub group would contain data regarding the origination of target for that disease[6].

iii. Re-inforcement learning:
Its major function is related to making decisions according to the environment and then execute them to obtain excellent performance. The output obtained from such type of ML consists of drug designing through *de novo* approach, that is placed in the category of decision making and the experimental drug design is placed under the category of execution. Therefore, both can be attained through the technique of modelling and by the application of quantum chemistry[6].

One more sub field of machine learning has come into picture i.e. Deep learning (DL) which is based on the area of artificial neural network that are provided with the function of adapting and learning through the use of experimental data which is widely available. Thus, for the discovery of new molecules, the data mining approach can be applied to study the data as well as algorithms could also be generated to aid in the discovery of any new entity. Thus, DL can also be employed for identification of genetic markers and many novel drug molecules. Therefore, through the application of artificial intelligence, we can counter various loop-holes pertaining to pharmaceutical product development. It will also lead to reduction in the number of drugs failing in clinical trials and thus accelerate the process of drug designing and development in a cost effective way[6].

2.1 Drug development process

The development of drugs involves a series of steps. The process is initiated by various techniques such as High Throughput Screening (HTS) and computational modelling which provide sources to generate results. There are two cycles involved in this process which is going on alternatively and they are known as inductive and deductive cycles. This series of cycles ultimately leads to determination of heat and lead compounds with the desired specifications. The errors can be minimized in this process through automation[5].

The novel compounds possessing the desired biological activity are selected and identified in the step of drug development. This biological activity can be assessed based on the results of interaction studies conducted with certain enzymes or organism. The initial compound that demonstrates the biological activity in response to a given target is referred to as "hit" molecule. Libraries of different chemical compounds are screened to identify hit molecule. Computer simulation and screening of various isolated natural products such as bacteria, plants and fungi are also being utilized to determine hit molecules. The second step involved in drug development is lead identification. The lead molecule has the desired ability of being carried forward in the development of required drug molecule for the desired disease. Cell based screening assays and animal models are being utilized to screen the generated hit series and therefore they are performed to predict the safety and efficacy of the compound. After the determination of lead compound, the structural modifications are being conducted in them and their chemical properties are also being altered to produce a compound that shows minimum toxicity and optimum therapeutic effect[5].

The lead generation step involves the modification of hit molecules in order to increase their selectivity and affinity towards the desired target, improve their biological activity and reduce side effects, and therefore develop a safe and effective molecule. Then, hit expansion is carried out to generate analogues which are chemical compounds obtained from hit molecules. The building blocks are formed, where these analogues are further combined together through a set of various reactions employed by medicinal chemists. Thus "building block" is referred to a compound which contain the essential functional group for interaction with the active site of the target[5]. The active site is an area present in the target which shows specificity towards a specific molecule and allows the binding of drug molecule through various interactions. The drug molecule binding to active site can be explained through "lock

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and key" model. Therefore, AI can be widely utilized for the following purposes:

- Identification of molecular targets and to predict the underlying mechanism of drug-target interaction.
- Determination of hit or lead compound.
- Synthesis of compounds exhibiting drug like nature.
- Repurposing of drugs.
- Selection of a population for clinical trials.
- Study and determine the mode of action of drugs.
- Design polypharmacology agents.

3. Modulation of size distribution in granules by artificial intelligence

Computational Intelligence is being utilized for developing milling procedures to produce effective particle size distribution. The dry granulation method is the most widely used method for the production of solid type of dosage form. This method consists of two steps: first is compaction of powder between two rolls rotating in opposite direction to create a ribbon and the second is milling process in which crushing of ribbons lead to the formation of granules. As particle size is an important feature in pharmaceutical drug development; in order to determine and modulate it, various artificial intelligence technologies are being developed. This approach is also being used to study various factors and properties of drug that affect the particle size and hence the crucial relations are being drawn through it, like how the properties of material, the milling parameters, and the prevailing conditions would affect the size distribution in granules[7, 8]. The change in size distribution of granules due to roller compaction can also be determined by using artificial intelligence systems that provide the relationship between the parameters of roller compaction and their influence on granule size[9].

Multiple linear regressions are a computational method being used for describing the effect of various independent factors on dependent variables. Artificial Neural Networks (ANN) method has been used for selecting the most applicable parameters for modelling granule size based on the layers criteria, as a typical ANN is composed of three types of layers i.e. first is input layer, second is hidden layer and the third one is output layer. Further, these layers also contain neurons which are connected to each other. The signals thus follow the path from input to output layer via hidden layers. In this model, a range is selected for each layer and linear scaling is being followed within the range[8].

Genetic Programming (GP) is a type of model developed on the basis of evolution theory of Darwin which states the survival of the fittest, thus by eliminating those individuals that does not fit or are not capable of surviving in the prevailing conditions. Hence, selecting and breeding those which are able to adapt themselves with the conditions and prove their fitness[7].

4. Role of artificial intelligence in clinical research

It has been observed that a large number of drugs mostly fail in clinical trials. The percentage of drugs that enter the market is declining day by day. Certain drug products pass the clinical trials but when they are introduced in the market, many problems arise. Thus, a particular digital platform has to be developed for resolving such issues. Though artificial intelligence has many applications, due to lack of scientific proofs, the use of AI in clinical research is just theoretical in nature. AI plays a significant role in clinical research as it has great impact on the following aspects[2]:

- Success or failure rate of drug product.
- Reduction in the cost of product development in terms of absolute values.
- Reduction of time taken by the drug product to enter the market.
- Decrease in the number of product recalls.

Artificial Intelligence also focuses on the following three major objectives of clinical research:

- Signals which are predictive and affect the disease pathology.
- The different steps and methods used for intervention.
- The effect of time on patient's condition and the way in which it defines the quality of life.

This field thus contains a list of references which are arranged specifically. These references, along with figures, confirm the advantage of Artificial Intelligence over other methods of medical practices. It is of great use in screening the pathological data of patients, various lab results of medical examinations and the drugs being requested based on the patient's report. This would help in distinguishing patient's condition from normal condition. The artificial neural network frameworks have been utilied to study the results of various diagnostic tests such as magnetic resonance imaging (MRI), X- ray and Computed Tomography (CT) scan. This system allows the patient undergoing a clinical trial to enter data in the mobile phone by himself and provide the required information, and thus, it develops a direct contact with the patient. The AI technology can also be used to predict allergic as well as adverse drug reactions with the help of its automated softwares that help in reporting and providing data regarding any on toward reaction[2, 10].

5. Role of artificial intelligence in the design of peptide antibiotics

The most prevalent issue regarding the use of antibiotics is the development of multiple antibiotic resistances that hinders the discovery of antibiotics. In the present era, small peptides which possess antimicrobial activity have emerged as a recent class of antibiotics. In order to design such type of broad spectrum antibiotics of small peptides, the information regarding their chemical characteristics as well as molecular biology is required. The amino acids containing the active peptides were used to create two big libraries of 9-amino-acid peptide by utilizing peptide array technology[6].

The data obtained from the above technique was collected and combined with the Artificial Neural Networks in order to design *in silico* models for antibiotic activity; these models were quantitative in nature. After their random evaluation, these models were found to be more promising in determining the activity of around one lakh peptides. The peptides demonstrating the best activity against "Superbugs" were one quartile of the total peptides. These superbugs are broad array of multidrug resistance antibiotics. Thus, such peptide antibiotics can be used for treating various superinfections. Therefore, the AI can perform enormous function in designing such novel peptides and hence assist in the determination of their efficacy and potency. Broad spectrum antimicrobials are efficiently being modulated by introducing various amino acid sequences in peptidic moiety and then re-analyzing their structure through ANN[6].

The AI incorporates a large number of databases pertaining to small molecules, peptides, amino acids etc., which can be utilized in the construction as well as design of novel drug therapeutics for treating various diseases. The drug – target interactions can be studied through this approach in order to develop effective and targeted drug delivery systems. Thus, these peptide molecules can serve a great potential to combat drug resistance and therefore can be utilized to develop effective antibiotics[1, 6].

Conclusion

Artificial Intelligence serves as an eminent platform in the advancement of pharmaceutical sector. It is widely being employed in drug discovery and development, thus paving a way for newer molecules to come into market. It is utilized in tablet manufacturing procedures such as milling, compression, dry granulation and other recent technologies that are being developed for the production of tablets. It saves time as well as provides the required set of data for analysis and quality control. The various components of AI such as ANN, deep learning, machine learning, genetic programming etc., are being used for rationale design of drug molecules as well as peptides. The AI has also influenced the area of healthcare by playing a major role in clinical research by predicting the adverse effects. The information pertaining to the patient is also being collected through this. Thus, it provides immediate results and test reports that would further aid in the determination of optimum therapy for patient. Therefore, in the upcoming era, the field of Artificial Intelligence can lead to the development of various technologies and software that would help improve the pharmaceutical product development and health management strategies.

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Conflicts of Interest

No Conflict of interests.

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