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Review Article

Pharmaceutical Applications of Artificial Intelligence

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ABSTRACT

The use of artificial intelligence in pharmaceutical technology has increased over the years, and the use of technology can save time and money while providing a better understanding of the relationships between different formulation and process parameters. Neural networks, genetic algorithms, and fuzzylogic are rapidly growing technologies that could be applied to the formulation and processing of pharmaceutical products. In this article Applications of various types of artificial intelligence are discussed.

Keywords:

Artificial intelligence, Artificial neural network, Genetic algorithms, Fuzzy logic, Controlled release tablets, Immediate release tablets.

1. INTRODUCTION

Artificial intelligence (AI) is the study of complex information which processes problems that have their rools in some aspect of biological information processing. The main aim of the subject is to identify useful information processing problems and give an abstract account of how to solve them. Such an account is called as method and it corresponds to a theorem in mathematics. Artificial Intelligence is defined as a field that deals with the design and application of algorithms for analysis of, learning from and interpreting data. Thus, broadly defined AI encompasses many branches of statistical and machine learning, pattern recognition, clustering, similarity-based methods, logics and probability theory, as well as biologically motivated approaches, such as neural networks and fuzzy modeling, collectively described as "computational

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intelligence".Pharmaceutical drug manufacturing, from formulation development to finished product, is very complex. This processincludes multivariate interactions between raw materialsand process conditions. These interactions are very importantfor the processability and quality of the finished product 1.

Artificial Neural Networks (ANNs):

In the last few years, neural networks have received recognition among scientists and engineers and they are being recommended as one of the greatest computational tools ever developed [2]. Much of this elation is due to the potential of neural networks to reproduce the brain's capability to assimilate by example. This network makes decision and draws conclusions even when presented with incomplete information. Moreover, at some primitive level, neural network imitates brain's creative process in adapting to a novel situation. [3] Artificial neural networks (ANNs) technology models the pattern recognition capabilities of the neural networks of the brain. Similarly, to a single neuron in the brain, artificial neuron unit receives inputs from many external sources, processes them, and makes decisions. Interestingly, ANN simulates the biological nervous system and draws on analogues of adaptive biological neurons.ANN is composed of numerous processing units (PE), artificial neurons. The connections among all the units vary in strength, which is defined by coefficients or weights.The ANN mimics working of human brain and potentially fulfills the cherished dream of scientists to develop machinesthat can think like human beings. ANNs simulate learning and generalization behavior of the human brain through data modeling and pattern recognition for complex multidimensional problems. A significant difference between an ANN model and a statistical model is that the ANN can generalize the relationship between independent and dependent variables without a specific mathematical function. Thus, an ANN works well for solving nonlinear problems of multivariate and multi response systems such as space analysis in quantitative structure-activity relationships in pharmacokinetic studies and structure prediction in drug development [1.]

2. GENETIC ALGORITHM

A genetic algorithm (GA) is a search heuristic that imitates the process of natural advancement in the discipline of Artificial Intelligence. This heuristic (also sometimes called a met heuristic) is regularly used to originate useful solutions to optimization and search problems. [4] Genetic algorithm is a probing technique that is used to find concurrent solutions for optimization and search problems [5]. They are stochastic optimization methods and provide a powerful means to perform directed random searches in a large problem space as encountered in chemo metrics and drug design [6]. A genetic algorithm needs two things to be defined i.e. genetic representation of solutions and fitness function [7]. To solve any problem, the first requirement is to draw the genetic representation. After the genetic representation the second requirement is to define a fitness function for the problem. The different problems have different type of fitness function. The Genetic Algorithm starts with the initialization of the population of solutions randomly and several individual solutions are randomly generated to form an initial population. The size of population relay on the nature of problem. It may consist hundreds or thousands of individual solutions. In the next, the fitness function is evaluated for each individual population. The last step is the reproduction of population. In this step the genetic operator such as selection, crossover and mutation are applied to generate the next generation of population. [8] In drugs designing, a molecule is defined as input to GA and a binary string is used to code the molecule. A large number of the solution is generated by using genetic operator. The best population is selected and further used to generate the new population until a desired solution is reached. [7]

Fuzzy Logic:

Drugs discovery & design is an intense, lengthy and consecutive process that starts with the lead & target discovery followed by lead optimization and pre-clinical in vitro & in vivo studies. [9] Earlier, computational techniques are use in the field of computer science, electrical engineering and electronics & communication engineering to solve the problems. But, now day's use of these techniques has changed the scenario in drugs discovery. & design from the last two decades. These techniques include Artificial Neural Network, Fuzzy logic, Genetic Algorithm, Genetic Programming, Evolutionary Programming, Evolutionary Strategy etc. 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. [10] Fuzzy set is differing from traditional set theory i.e. fuzzy set has un sharp boundaries. So the traditional set theory has either value 0 or 1 but in fuzzy set the value is lie in between $0 \leq \mu \geq 1$ where μ is the membership function. Most important characteristic of fuzzy logic is fuzzy inference. Fuzzy inference systems based on fuzzy set theory are considered suitable for dealing with many real world problems, characterized by complexities, uncertainties, and a lack of knowledge of the governing physical laws. The most important application of fuzzy set theory is the fuzzy rule-based models, where the relationships among system variables are modeled using linguistically interpretable rules. Fuzzy logic can be especially useful in describing target properties for optimizations. For example, the formulator might be seeking a tablet disintegration time of 200 s, i.e. any value less than 200 s has a desirability of 1 (i.e. 100%). But a tablet which disintegrates in 210 s is not entirely undesirable (as crisp logic would insist), and instead might be assigned a desirability value of 0.9 [11].

The basic steps of the fuzzy set in the process modeling described as,

- Arrange the input and output dataset.

- Clustering the output set
- Map the fuzzy inputs to the output
- Identify the significant variables
- Use the rule base in inference [11]

3. APPLICATION OF AI IN PHARMACEUTICAL RESEARCH

1. In Formulation:

Controlled release tablets:

The first work in the use of neural networks for modeling pharmaceutical formulations was performed by Hussain and coworkers at the University of Cincinnati (OH, USA). In various studies they modelled the in vitro release characteristics of a range of drugs dispersed in matrices prepared from various hydrophilic polymers. In all cases, neural networks with a single hidden layer were found to offer reasonable performance in the prediction of drug release. In general, the results were comparable with those generated through the use of statistical analysis, but when predictions outside the limits of the input data were attempted performance was poor. No attempt was made to optimize the formulations using genetic algorithms, but the results generated did lead the researchers to propose the concept of computer aided formulation design based on neural networks. [12] In a more recent study involving the formulation of diclofenac sodium from a matrix tablet prepared from cetyl alcohol, personnel from the pharmaceutical company KRKA dd (Smerjeska, Slovenia) and the University of Ljubljana (Slovenia) have used neural networks to predict the rate of drug release and to undertake optimization using two- and three-dimensional response surface analysis. Non-linear relationships were found between the release rate and the amounts of the ingredients used in the formulation, suggesting the possibility of the production of several formulations with the same release profile [9.]

Immediate release tablets:

Work in this area began only some three years ago with two studies. One by Turkoglu and coworkers from the University of Marmara (Turkey) and the University of Cincinnati11 used both neural networks and statistics to model tablet formulations of hydrochlorothiazide. The networks produced were used to prepare three-dimensional plots of massing time, compression pressure and crushing strength, or drug release, massing time and compression pressure in an attempt to maximize tablet strength or to select the best lubricant. Although trends were observed no optimal formulations were given. The trends were comparable to those generated by statistical procedures. Comparable neural network models were generated and then optimized using genetic algorithms. It was found that the optimum formulation depended on the constraints applied to ingredient levels used in the formulation and the relative importance placed on the output parameters. A high tablet strength and low friability could only be obtained at the expense of disintegration time. In all cases lactose was the preferred diluents and fluidized bed the preferred granulating technique [13.]

2. In Product Development:

The pharmaceutical product development process is a multivariate optimization problem. It involves the optimization of formulation and process variables. One of the most useful properties of artificial neural networks is their ability to generalize. These features make them suitable for solving problems in the area of optimization of formulations in pharmaceutical product development. [14] ANN models showed better fitting and predicting abilities in the development of solid dosage forms in investigations of the effects of several factors (such as formulation, compression parameters) on tablet properties (such as dissolution). ANNs provided a useful tool for the development of microemulsion-based drug-delivery systems in which experimental effort was minimized. ANNs were used to predict the phase behavior of quaternary microemulsion-forming systems consisting of oil, water and two surfactants. ANN was also used to simulate aerosol behavior, with a view to employing this type of methodology in the evaluation and design of pulmonary drug-delivery systems [15.] For controlling and decision-making, fuzzy logic is a very powerful problem-solving technique. It provides very useful rules from input data, in the form of "if… so… then". Fuzzy logic can be combined with neural networks as neuro fuzzy logic. This combination provides more flexibility and capability to the technique and provides powerful results [7.]

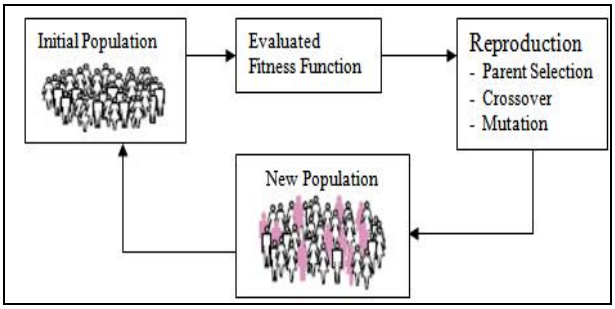

Fig 1: Working of genetic algorithm

4. CONCLUSION AND FUTURE PERSPECTIVES

Artificial Intelligence is broadly defined here as a field that deals with the design and application of algorithms for analysis of, learning from and interpretation of data. AI integrates many branches of statistical and machine learning, pattern recognition, logics and probability theory as well as biologically motivated approaches, such as neural networks, evolutionary computing or fuzzy modeling, collectively described as "computational intelligence"

The application of ANN in medical decision making has been intensely successful especially as it applies to disease diagnosis, classification and modeling. Due to their capacity

to learn, recognize patterns, and generalize, ANNs are a great tool in data analysis and modeling [14].

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