

A REVIEW ARTICLE ON ARTIFICIAL INTELLIGENCE; Change in Modern Techniques of pharmaceutical Formulation and Development.

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Abstract

Artificial intelligence the branch comes under computer science that deals with having problem solving ability by aid of symbolic programming. Health care related problems can be solving with huge applications by artificial intelligence. Development of expert system is an important and useful application of artificial intelligence. Doctors can now work accurately and trustfully, with advantage of Artificial intelligence. Under the human supervision lot of institutions are employing robots for performing certain activities. Reduction in time of drug development which results in reduction of cost and time is major advantage of the artificial intelligence. To make pharmacy profession more efficient large number of researches is being carried out. In this article we can understand Artificial intelligence application in drug development along with various tools used to do it.

Key words: Artificial intelligence, Drug discovery, ANN in F & D Tools of A.I, Applications of A.I.

1. Introduction:

Artificial intelligence can define as branch of computer science which helps us to problem solving with aid of symbolic programming. Even you are familiar or not but in the 20th century, we are all addicted by AI. At present live examples of A.I which we are using in our routine life. For example, social media like what's app, Facebook, Telegram. Search engines such as Google and yahoo. [1]Product recommendations, Email filters etc. Development of expert system is a main application of A.I. (Artificial intelligence). A.I was come into existence in year 1956. People who developed A.I are Allen Newell, Herbert A. Simon. Logic Theorist was first Artificial Intelligence system saw in 1956. In present market following are the top 10 Pharmaceutical companies which are using A.I Pfizer, Roche, Novartis, Johnson & Johnson, MSD, Sanofi, Abbvie, Glaxosmithkline, Amgen, Gilead Sciences.[2]following are some of the tools used by above industries and healthcare institutes IBM Watson for oncology , Robot pharmacy , MEDi robot , Erica robot , TUG robots , Berg . Machine learning, neural networks, Artificial intelligence (AI) and deep learning are useful in solving problems which are most critical and take lot of time to solve by humans, but same human like commitment making, deductive reasoning and conclusion by a computer is yet to be developed; link between artificial intelligence and algorithm have been grown stronger. Voice recognition, planning, learning, solving of problem are some of the artificial functions fit into the computers. [3]

2. Basics of Artificial intelligence:

Machines can only act like humans and response like humans only if that information about activity is store in that machine. Artificial intelligence has ability to judge objects, properties, categories and relations between all with the help of information coded in it. Begin common sense; logically thinking and ability of problem-solving functions in machines is a very difficult work to develop in machine. A.I. Learning involves Machine learning as a key part with not using or giving any kind of command given need a skill to recognize patterns in run or flow of inputs, and ability of learning alongside assign control includes numerical regressions and Classification. Concludes of the category is done by classification an object belongs to and regression compact alongside acquiring a set of numerical output or input examples, thereby finding of new functions allow the creation of acceptable and satisfactory outputs from the specific inputs. [4] Theoretical computer science compact alongside mathematical analysis of machine learning algorithms and their demonstration. Machine recognition deals alongside the ability to employ sensory inputs to gather the different characteristics of the world, meanwhile computer vision is the potential to analyze visual inputs along with some sub- problems such as facial, object and motion recognition. Robotics is also a crucial field connected to AI. Robots need smart intelligence and reconnaissance to navigate tasks such as object handling and navigation, along with sub-problems of mapping, localization and motion planning. Deep learning is really just a term to express definite types of neural networks and related algorithms that absorb raw input data. Data operation is done through many layers of nonlinear transformations of the input data in relation to calculate a target output. Unsupervised characteristic removal is also an zone where deep learning shine.[5] Feature extraction is when an algorithm is able to automatically derive or construct meaningful features of the data to be used for additional learning, generalization, and understanding. The load is traditionally on the data scientist or programmer to carry out the characteristic selection in most other machine learning approaches, along with characteristic selection and engineering. Characteristic selection usually involves some amount dimensionality reduction as well, which is reducing the amount of input features and data required to create meaningful results. This has many uses, which include simplification, computational and memory power reduction, and so on. Programmers would teach a neural network to observe an object or phoneme by wipe out the network with digitized versions of images comprises those objects or sound waves containing those phonemes. If the network is unable to correctly recognize a particular pattern, an algorithm would adjust the weights. The final

goal of this training was to get the network to consistently recognize the patterns in speech or sets of images that we humans know as, say, the phoneme “d” or the image of a dog. [6] This is much the same way a child learns what a dog is by noticing the details of head shape, behavior, and the like in furry, barking animals that other people call dogs. Evolution of A.I began from early man who took an effort to develop it, and the algorithmic approaches over the years included decision tree learning, inductive logic programming. [7] Clustering, reinforcement learning, and Bayesian networks among others. As we all know, none achieved the ideal goal of common AI, and even limited AI was mostly out of reach with early machine learning approaches. As it turned out, one of the very best application premises for machine learning for many years was computer vision, however it still need a great deal of hand-coding to get the job done. Individuals would go in and write hand-coded classifiers like edge detection filters so the program could point out where an object started and stopped; shape discernment to decide if it had eight sides; a classifier to acknowledge the letters “STOP.” From all those hand-coded classifiers they would promote algorithms to make sense of the image and “learn” to determine whether it was a stop sign. Good, but not mind-bendingly great. Mainly on a foggy day when the sign isn’t ideal visible or a tree obscures part of it. There’s rise in computer vision and image detection didn’t come close to match humans until very recently, it was too fragile and too prone to error. Time and the right learning algorithms made all the difference. [8]

3. Terminologies used in Artificial Intelligence.

a. Neural network

In neural network algorithms are arranged in a sequence that line up prior to acknowledge basic sequence in a set of data from an ongoing process that copy the way the human brain operates and work. Above process, neural networks work on neurons system; it can be artificial and may be natural in nature. Neural networks have ability of modifying to vary input; therefore best possible result is created by network without needing of output criteria to design again. The concept of neural networks, which has its roots in artificial intelligence, is quickly gaining favor in trading systems development. [9]

b. Basics of Neural Networks

Neural networks, in industrial evolution money/financial conditions matters, evolution help the existence of process such as algorithmic trading, time-series forecasting and classification of securities. [10] A neural network has ability works similar and smart like the neural network of human brains. Mathematical function acting is done by neuron in a neural network that gathers and also classifies information according to a particular construction. [11]

Interconnected nodes contain by a neural network in the form of layers. Each node is a perceptron, perceptron is an algorithm for supervised learning of binary classifiers and is same like to a multiple linear regression. [12], Perceptron’s are organized in interconnected layers in a multi-layered perceptron (MLP). Collection of input patterns is done by input layers. The output layer has classifications or output signals to which input patterns can map. [13] Input weightings are fine-tune by hidden layers up to the neural network’s edge of error is least. With regard to the outputs assumption is done that hidden layers gather salient features in the input data that consist of predictive power. Realization of a utility similar to statistical techniques such as principal component analysis is done by feature extraction of outline. [14]

c. Fuzzy Logic

Fuzzy logic is highly used in expert system it is a modern control systems. Fuzzy logic has ability to solve problem same like human being but much more faster than human brain and same related with decisions making. It workout by gathering of information and converting into more significant information by line up of limited truths as Fuzzy sets. In the large company business it is used for decision making support systems and personal development. It has benefit in chemicals manufacturing industry for maintaining the pH of chemicals, drying, and chemical distillation process. [15] Natural language processing and various applications in Artificial Intelligence are grabbed by fuzzy logic. Fuzzy Logic is used in company with benefit of Neural Networks as it imitates make decisions rapid and easier as compare to human brain. This is made successful by collection of data and converting that data into more meaningful data with the help of by forming partial truths as Fuzzy sets. [16]

d. NeuroFuzzy logic

Learning algorithm are used by fuzzy system and this algorithms are obtains from neural network theory to govern its parameters by data samples processing. Representation of Modern neuro-fuzzy systems are usually done as special multilayer feed forward neural networks e.g. ANFIS, GARIC, NEFCLASS etc. [17] Following is an considered example of fuzzification of neural network architecture; Self-organizing feature maps. Propagation, connection weights and activation functions vary from common neural network in neuro fuzzy networks. According to data collected different approaches found but most widely use term in neuro fuzzy system for approached which shows following different properties: Neural network theory helps fuzzy system by training it with algorithm provides by theory of neural network. Local information, procedure of learning runs on it and also makes local moderation in basic fuzzy system. A 3-layer feed forward neural network is a outlook of neurofuzzy system. Input variables represented by first layer, fuzzy rules represented by middle which is also known as hidden layer and third and last layer output variables. Encoding as (fuzzy) connection weights is done of fuzzy sets. It’s not mandatory to do representation of a fuzzy system like this to apply a learning algorithm to it. [18]

e. EVOLUTIONARY COMPUTING:

It is common term which elaborates computational process in which evolution of solutions done with help of rules of inheritance; recombination, mutation and selection. In formulation research one particular subset of this, evolutionary algorithms play an important role as its application to formulation research. [19]

f. GENETIC ALGORITHMS

John Holland in 1970 made use of Genetic algorithms. Search technique especially suited to optimization; assumption of trial population, and this evolves an iterative process is provided by genetic algorithms. Initial population of solution is generated and fitness of every member of the population is evaluated during this process.

g. MACHINE LEARNING(ML)

ML is a method which is used for doing analysis of data in which building of analytical model is done automatically using algorithms that frequently learn from data or important information. Machine learning classified into three classes that are supervised learning, unsupervised learning, reinforcement learning. And these three classes again sub classified into supervised learning into classification which result in disease diagnosis and regression which result into drug reinforcement/ADMET prediction. Unsupervised into clustering which result in disease sub type discovery and feature finding which result into disease target discovery. Reinforcement learning into decision making which result de novo drug design and excision into experiment design.

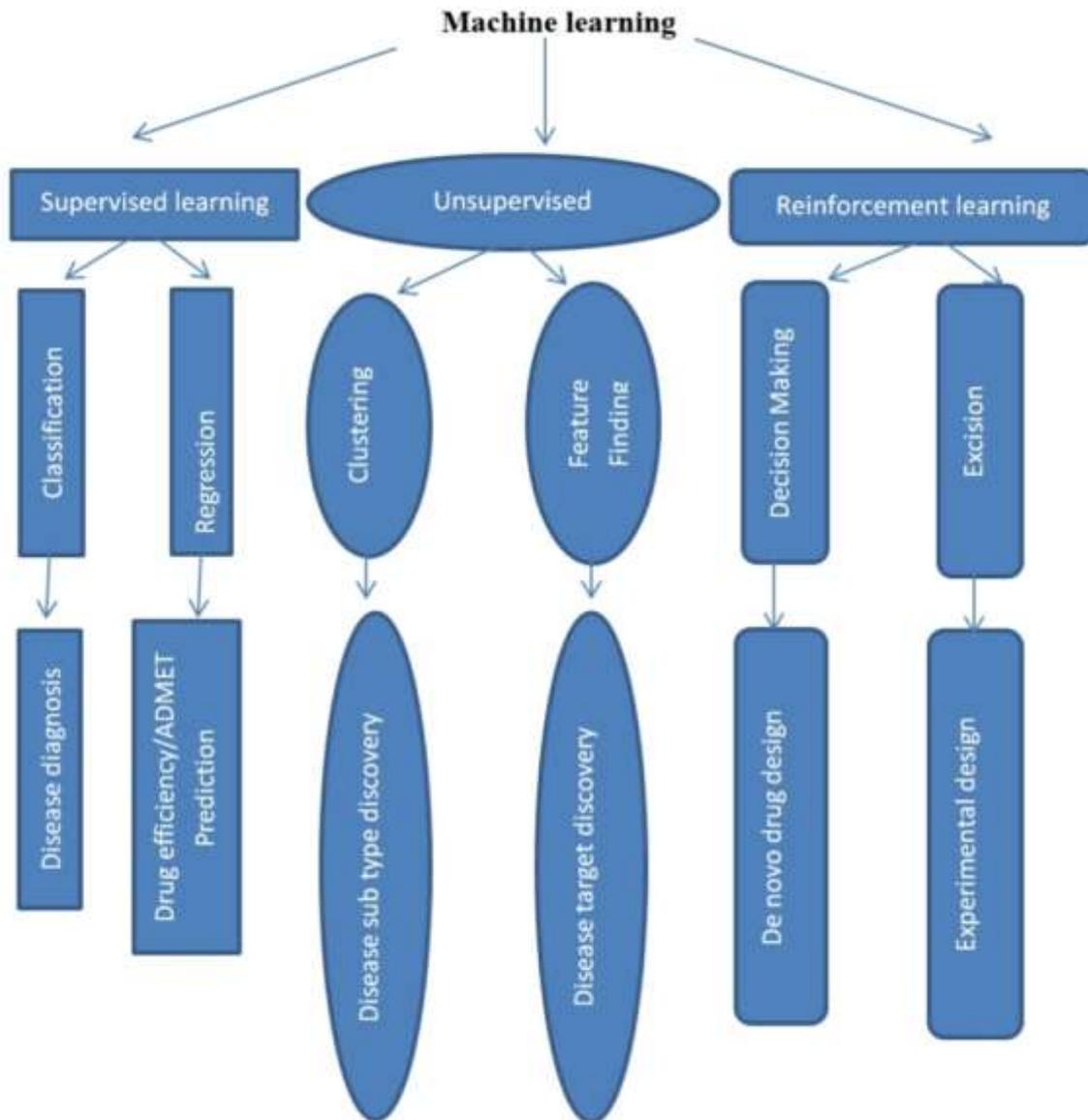


Figure 1; Machine learning Classification

4. PROGRAMING LANGUAGES USED IN A.I

SR NO	LANGUAGE	USES
1	Python	Most Effective language for A.I,Machine learning and A.I algorithms can easily implimented,
2	Prolog	Used in knowledge based and expert system,Pttern mattiching,Prebase data structuring,Automatic Tracking.Use in medical project.
3	Java	Simplified work with large scale project, good user interaction,use for making graph and interfaces.
4	Lips	Oldest and most suited for A.I,Develop by father of A.I,Capable of processing symbolic information,Create Dynamic object easily.
5	R	Statistical Programming language,analysing and manipulating data for statistical purpose,Produce methamathical symbol.

Table no 1; PROGRAMING LANGUAGES USED IN A.I

5. Introduction to Artificial neural network [ANN]:

With the help of lot of experience in algorithms learning can lead to simulation of some functions of human brain by ANN in computer programming. ANN have sensational information processing features like, parallelism, unperfected and non-success tolerance, learning, non-linearity, robustness, skill to drive imprecise and fuzzy information and their ability to discover. Optimization, pattern classification, clustering, pattern classification such real life complicated problems can be solve with help of ANN. ANN models have developed many applications.

On basis of ground root learning of algorithm, coaching of ANN model consists of supervised and non-supervised.

In supervised training data sets introduced as an input/output data sets; Then unsupervised training, introduction of input data is done individually, and identification of patterns in data is learn by model. On topology basis the connection of ANN could be feed forward or it can be feedback. The connection between the nodes never forms cycle in feed forward ANN. The model of ANN must recapitulate long time with potential before production of a response is done in some of the feedback ANN model when presentation of input is done each time. Feed forward model of ANN are easy to train as compare with feedback ANN models.

Some of types of ANN models are categories into three types are associating networks, features extracting network, non-adaptive network. For classification of data and its prediction associating networks are applied here; for organization of supervised learning need correlated output (dependent variable) and input (independent variable). For data dimension reduction feature extracting network are mostly used and to do unsupervised or competitive learning only input values are needed. [36]

a. Artificial Neuronal Network in Design of controlled release drug delivery systems

Huge advantage obtained from controlled released drug delivery system over the conventional drug delivery system.[34] However, due to the reason of present of complexity of this drug delivery system there are prominent dares to controlled release drug delivery systems development.[35] For formulation, development and evaluation of controlled release drug delivery system with help of Traditional statistic RCM(response surface methodology) is developed techniques, but there is presence of lot of limitations and restrictions.[36] Due to the restrictions of RCM, another evolutionary and advanced technique called artificial neural network (ANN) have left behind RCM and gain pick of popularity for control release drug delivery system dosage forms development.[37]

In formulation of CRDDS to develop it associating networks are applied. The nonlinear relationship is seen between drug release profiles of controlled drug release system and formulation and process factors, and also understanding is not well. Associating networks have ability to map or script the link between the formulation and process variable and response like in vitro drug release profiles training and learning process. [38] Associating networks used to generate the response such as in vitro drug release profile of newly discovered drug or formulation which is prepared with varying composition and manufacturing process. Optimization can also be done with help of associating network model in which trained and learned ANN play important role in selecting optimal formulation and process parameters. [52]

Use of ANN can be used in formulation by some of the steps which are, first of all data should be extracted from the research papers. Data can be encoded into software for formulation and development. Then data is set and training of that data is done, validation is done and testing of that data is done. Then with the help of neural network decision making is done and prediction model is get created and with help of prediction accuracy outcomes of result related to formulation and development of dosage form or product is done.

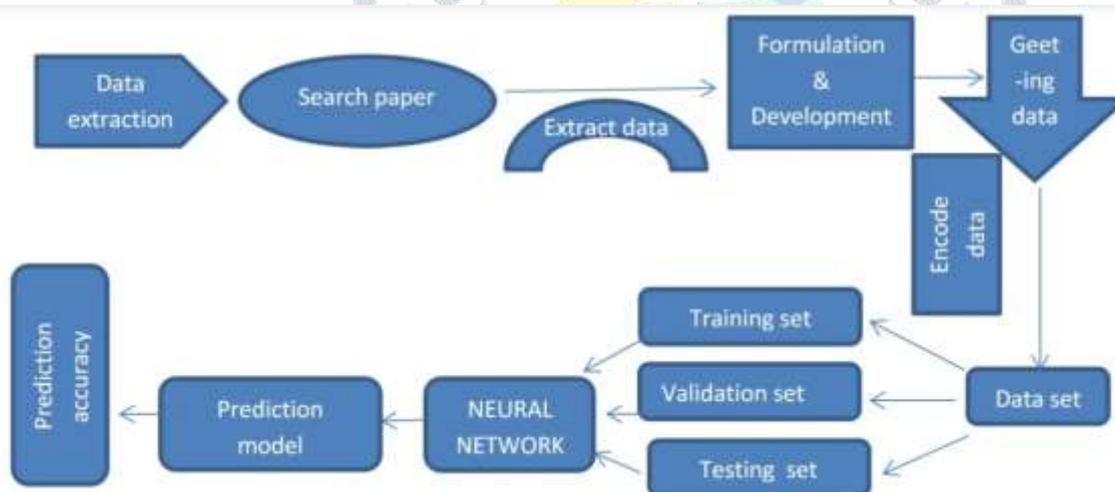


Figure 2; the flowchart of establishing model

b. ANN in Formulating Microsphere of Poly lactide co glycoside (PLGA) .

Glycolic acid and lactic acid, PLGA is a co polymer of these two polymers. Type of drug, Size of Particle, microspheres morphology, conditions of release, etc. are some of the properties on which drug release of PLGA microspheres depend. Batch of applicable properties selection for PLGA is really a challenging task for machine learning; it is more demanding because there are more than four hundred considered characteristic. For this work, we construct the selection of analytic characteristics for PLGA as a multi-objective optimization issue with the objective of reducing the mistakes of forecasting the dissolution profile while minimizing the quantity of attributes chosen.[39] For selecting the ideal property set for forecasting the dissolution profile of PLGA Four bio-inspired optimization algorithms: antlion optimization, binary version of antlion optimization, grey wolf optimization, and social spider optimization are selected. Besides these, for comparisons LASSO algorithm is also used. Choosing of important and crucible variables is carry out under the consideration that both predictability and model simplicity are of twin importance to the decider result. Input variables set are applied to search least generalization error over different predictive models and their construction during the feature selection process. The methodology assess making use of forecasting modeling for this work different tools are selected, these

tools are random forests, Cubist, artificial neural networks (monotonic MLP, deep learning MLP), multivariate adaptive regression splines, regression tree and classification, and blend systems of fuzzy logic and evolutionary computations (fugeR). The comparison of experimental result is done with the results pres by Szłęk. We get a systematic and normalized root mean square error (NRMSE) of 15.97% vs 15.4%, and the number of selected input features is very smaller, 9 versus 11. [37]

c. ANN in Modified Release Solid Dosage Forms.

Application of QbD (Quality by design) approach in pharmaceutical product development has force researchers or impels researches in the pharmaceutical industry to apply DoE that is Design of experiment as statistical tool, in development of product. RSM that is Response surface methodology is most widely used in among all DoE techniques. Pharmaceutical development is more in lead due to progress of computer science. In drug formulation machine learning tool take an important place along with implementation of statistical tool. The first paper which was describing about application of ANN in modified drug release product was found twenty years back. After that humeral work is done by researches towards application of new techniques, most preferably ANN in modeling of production, drug release and drug stability of modified released solid dosage forms. [54]

d. Drug development process

Job of searching effective and post marketing surveillance new drugs is formidable and always the toughest and lot of effortful a part of development of drug. it's origin by the massive size of what's called chemical space, it's approximate to be within the sequence of 1060 molecules. Possible uses of AI come up with the possibility to counter the disorganization and unreliability that appear within the classical drug development methods while reducing bias and human interference within the process.

The other uses of AI in drug development involve the forecasting of feasible synthetic routes for drug-like molecules , pharmacological properties , protein characteristics in addition as efficacy, drug combination and drug–target association and drug repurposing. Also, the spotting of recent pathways and targets using omics analysis becomes practicable via the creation of novel biomarkers and therapeutic targets, personalized medicine supported omics markers and discovering the connections between diseases and medicines. [20]

e. A.I and ML in Non-compartmental data analysis.

SimBiology and MATLAB are two software which plays important role in non-compartmental data analysis. There is presence of one tool in MATLAB called SimBiology which is helpful for pharmacokinetic and pharmacodynamics model. For terminal slope and linear interpolation method, parameter estimation work is done by SimBiology with the help of unweighted linear regression. SimBiology is also helpful for clinical pharmacology. Fullform of MATLAB is (Matrix Labrotary), mostly used for simulation, numerical analysis and modeling. AUC (Area Under Curve) is also find with help of SimBiology which uses linear trapezoid method to calculate it. [39].

6. Tools of Artificial Intelligence

Different types of tools have been come into exist to solve the different problems of pharmaceutical industry. Outcomes of these tools have been promising. Some of the famous tools that have achieved mind-blowing popularity are as follow.

a. IBM Watson for oncology

Supercomputers develop by IBM name as Watson.it is combination of sophisticated analytical software and A.I device design for answering question. It is design for treatment of cancer, it assist oncologist in taking better decision. It works by analyzing the medical data of a patient from a wide network of data and expertise and then allotting treatment options based on the information obtained. It is effective in analyzing meaning and context data in clinical notes and reports, May be properly structured or unstructured. It can simply gather analytical information in regard to the patient and write it in plain English which can turn out to be a very critical step in providing the correct treatment plan for the patient. It merges critical characteristics from the file of a patient with external research, clinical research, and data and then suggests or decides the most effective treatment plans that can be apply for a patient. Watson has an enormous assembling of information from literature and rationales curated by MSK, over 200 textbooks, 12 million text pages, and over 290 medical journals. [51] At present, one of the Indian software engineer, aged 39 years, was diagnosed with breast cancer of a rare form and it was developing across both her breasts very fast which was posing a threat of both breast removals. Her medical records along with her genomics data were fed into Watson by Dr. Somashekhar, an oncologist in Bengaluru, and Watson provided viable treatment options within 60 s. [44]

b. Robot pharmacy

With the Aim of increasing the safety of patients, UCSF Medical Center makes use of robotic technology for the preparation and tracking of medications. According to their report, the technology has successfully prepared 3,50, 000 medication doses with negligible error. The robot has proved to be far better than humans both in size as well as its ability to deliver accurate medications. The abilities of the robotic technology include preparation of oral as well as injectable medicines which include chemotherapy drugs that are toxic. This has given free space to the pharmacists and nurses of UCSF so that they can make use of their expertise by focusing on direct patient care and working with the physicians. [53]

Within the automated system of the pharmacy, the computers first collect medication command electronically from the physicians and pharmacists of UCSF. After this, individual doses of pills are collected, packaged, and dispensed by the robotics. This is followed by machines assembling the doses onto a bar-coded plastic ring. The thin plastic ring contains all medications that have to take by a patient within a period of 12 h. Adding to the capabilities of the automated system is their ability to prepare sterile preparations that are meant for chemotherapy along with filling of intravascular syringes with the right medications.

The automated facility also consists of an inventory management system that keeps track of every product along with a refrigerated and two non-refrigerated pharmacy warehouses for providing with storage and withdrawal of supplies and medications. All these facilities are fully automated. [53]

c. MEDi robot

MEDi is known for its medicine and engineering designing intelligence. One of the professor of Community Health Sciences at the University of Calgary in Alberta led a project for pain management robot. Idea of developing this robot she got when she saw children scream during medical procedure when she was working in a hospital. [38] The robot first builds friendly relation with the children and then tells them what to expect during a medical procedure. During the medical procedure, it instructs them on what should be done, how to breathe during the procedure, and how to cope. [55] As we know robot cannot think, plan, or make decision, it can be programmed in such way that it shows to have AI.

Aldebaran Robotics manufacture MEDi, it is consisting internally build facial recognition technology, it is having ability to speak 20 variety of languages and is highly adaptable to different situations. The retail price of the robot is \$9000, however, the cost rises to \$15000–\$30000 when the applications needed for the robot to help in medical procedures are installed. The robot was initially developed for pain management, but with time its use has expanded to comfort between procedures, physical rehabilitation, and fundraising. [33]

d. Erica robot

Hiroshi Ishiguro, a professor at Osaka University in Japan developed Erica, a new care robot. Erica was developed in collaboration with the Japan Science and Technology Agency, Kyoto University, and the Advanced Telecommunications Research Institute International (ATR). It can speak Japanese and has a combination of European and Asian facial features. [34] Like any normal human being, it likes animated films, desire to visit south-east Asia, and wants a life partner who would chat with it. The robot cannot walk independently; however, it has been developed with the ability to understand and answer questions with human-like facial expressions. Erica is the “most beautiful and intelligent” android as Ishiguro fixed up the features of 30 beautiful women and used the average for designing the robot’s nose, eyes, and so on. [35]

Optimization of formulation using ANN

Design of new network help in, making choice of the Self organizing feature maps (SOFMs) network model.[29] To forecast the output responses use of the functions like TanhAxon, SigmoidAxon, LinearTanAxon, Linear SigmoidAxon, and Axon can used.[30] Differing activations task can be presented by performance parameters like mean squared error (MSE), minimum absolute error, correlation coefficient and predicted output of the selected network models.[31]

7. Partnerships between artificial intelligence (AI) and pharmaceutical companies and areas of collaboration in drug development.[32]

SR.NO	PHARMA	AREA OF COLLEBRATION	ARTIFICIAL INTELLIGENCE
1	Astellas pharma	Drug repurposing	Biovista
2	Bayer pharma	To track real-time data via smartphones and other wearable technologies	Xbird
3	Roche	to target personalized medicine using medicine learning and large scale genome sequencing .	Bina
4	Sumitomo dainippon Pharma	To identify new tratments for psychiatric diseases	Exscientia
5	GlaxoSmithKline	To discover novel and selective small molecule	Exscientia
6	GlaxoSmithKline	To identify novel biological target and pathway	Insilico medicine
7	Abbvie	To announce the mechanism of AI based patient monitoring platform can improve adherence.	AiCure

Table no 2; Partnerships of artificial intelligence (AI) and pharmaceutical companies and areas of collaboration in drug development.

8. Conclusion:

Human being is most creative and unpredicted knowledge creative and storage machine that can be ever come into an exit. But this above line can be agreed only for few years and decades ago until A.I comes into existence. A.I 1000 times faster, error free, time saving, cost saving, efficient work ability than human beings. But take into note than A.I technology created by human beings only and let’s see in future that it becomes hell or heaven as we know words spoken by Stephen Hawking said, “This may mean the end of human race”. Everything has its two side one GOOD and another BAD. But evolution of A.I has result in decrease human load.

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