EMERGING TRENDS OF ARTIFICIAL INTELLIGENCE IN DRUG DEVELOPMENT

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Abstract

Drug discovery is an extended and challenging procedure with four primary stages: (i) target selection and validation; (ii) compound screening and lead optimization; (iii) preclinical research; and (iv) clinical trials. The combination of artificial intelligence (AI) with new experimental technologies is intended to improve the search for novel drugs faster, cheaper, and more effective. AI is the term used to describe the intelligence produced by human-made machines. It is a broad field of study that encompasses languages, cybernetics, neuro-physiology, psychology, and computer science. The drug development company is attracted to Artificial Intelligence technologies because of their robotic nature, predictive powers, and the resulting anticipated gain in productivity. Using feature-finding strategies, unsupervised machine learning can provide outcomes such as disease target and illness subtype detection. A new AI diagnostic tool is aware of when to consult a doctor. The ability of a new artificial intelligence diagnostic system to acknowledge its own limitations and seeks the aid of a carbon-based lifeform that may be able to make a more accurate judgment. The pharmaceutical and medical industries are anticipated to undergo a revolution due to artificial intelligence, according to a forecast rise of 40 percent from 2017 to 2024.Global pharmaceutical industry is working with artificial intelligence organization to build not only vital healthcare tools and drug molecules for rare disease but also for market research.

Keywords: Artificial intelligence, unsupervised machine, diagnostic tool, medical industries, rare disease

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DOI: 10.48047/ecb/2023.12.si5a.0612

Introduction

Over the last several decades, the pharmaceutical sector has greatly expanded its record digitization. With digitization arises the complexity of gathering, analyzing, and applying that knowledge to resolve complicated healthcare issues. This encourages the usage of AI since it can manage massive amounts of data with improved efficiency.AI is the term used to describe the intelligence produced by human-made machines. It is a broad field of study that encompasses languages, cybernetics, neurophysiology, psychology, and computer science. One of our era's most significant emerging technologies is thought to be artificial intelligence (AI)[1]. It includes a collection of computational algorithms that enable devices to mimic various aspects of human intelligence, including problem-solving and learning from practice. The evolution of AI can be considered as having two conflicting effects: on the one hand, several people are concerned that it will endanger their jobs, while on the other hand, every step ahead is welcomed as a positive step forward that will benefit humanity. The ability of artificial intelligence (AI) to solve problems quickly and accurately is similar to that of the human brain[2].

Considering the fact that there is no oftenly agreed definition of AI, it is widely used as a general term to refer to any technology employed in the pharmaceutical company, such as machine learning (including deep learning), natural language processing, and computer or machine vision. Deep learning, a significant part of AI, has the ability to autonomously pick features from enormous volumes of data. Deep learning can also identify information in photographs that the human eye fails to notice[3].Drug development is being changed by artificial intelligence (AI), as per research. Machine learning may have a significant impact on the health care industry (like IBM Watson Health and Google's DeepMind Health)and may create a market with yearly sales of $100 billion, as per recent analysis. In the field of health care, machine learning is being used in a wide variety of contexts. These include identifying and diagnosing diseases, creating individualized treatments, and the discovery and production of drugs. Pharmaceutical companies may be two to three years away from releasing drugs generated using artificial intelligence (AI) techniques, but in the long run, they will be crucial to existence[4].The main benefit of Artificial intelligence is its potential to process the vast quantities of biological and medical data generated every day, a task that would be impossible to accomplish without it due to its size and complexity. The danger of novel emerging diseases can be prepared and treated by mankind by carefully using this technology.

Creating a new medicine is a difficult, expensive procedure with a poor success rate is witnessed by following predictions: an average of $1.3 billion is expended on R&D for each medicine. For non-oncology drugs, the typical time to develop a new medicine is 5.9 to 7.2 years, whereas for cancer treatments, the median time to produce a new drug is 13.1, and 13.8 percent of all drug-development programmes end with approval. The drug development company is attracted to Artificial Intelligence technologies because of their robotic nature, predictive powers, and the resulting anticipated gain in productivity[5].

In order to identify computerized analysis and advances that are presently being used or are scheduled to be implemented in the coming years, the Drug Information Association (DIA) and the Tufts Center for the Study of Drug Development (CSDD) performed a study. Eight pharmaceutical and biotechnology organizations, including Amgen, Bayer, Eli Lilly, Genentech/Roche, Johnson & Johnson, Merck & Co., Novartis, and Pfizer, collaborated on the study. Regulatory, clinical operations, medical affairs, and pharmacovigilance were among the primary research and development tasks that needed to be identified, defined, and standardized [6].

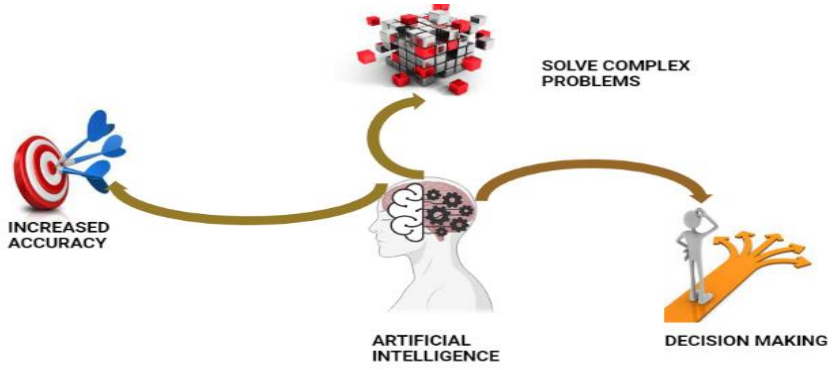

Fig 1: Basic advantages of Artificial Intelligence (AI)

Artificial Intelligence across a Whole Pharmaceutical's Product Development

Considering that AI can assist in decision-making, identify the best course of treatment for a patient, along with personalised medicines, maintain the clinical data generated, and utilise it for coming years drug development, it is acceptable to expect that it will play a role in the advancement of pharmaceutical products from the work surface to the point of care. [7]. Furthermore, Artificial Intelligence may be used in the production process by pharmaceutical companies to boost output and efficiency as well as hasten the production of life-saving drugs. AI may be useful at many stages of the manufacturing process, including quality control and preventive care. Artificial intelligence is also a helping hand for maketing executives[8]. E-VAI is a diagnostic and decision-making Artificial intelligence - based framework created by Eularis that utilises Machine learning and an intuitive user connector to generate diagnostic guidelines based on competitors, vital stakeholders, and the market share presently held to estimate key drivers in pharmaceutical sales. This aids marketing executives in distributing resources for highest market share benefit, turns around weak sales, and empowers them to predict where to invest directly[6].

Classification of Artificial Intelligence

Machine learning (ML) is a sub - discipline of AI that utilises numerical methodologies to learn either directly or indirectly. ML is classified into three categories: supervised learning, reinforcement learning, and unsupervised learning. [8].

When learning is overseen, classification and regression techniques are employed to create predictive models from input and output data. This approach has been satisfactorily utilised in image-based screens where cell phenotypic profiles alter accurately in response to treatment and can thus be categorised into distinctive groups based on the observable variation[9].The supervised machine learning algorithm (SVM) was first developed in 1990 and has since become extremely well-liked. On either linear and nonlinear challenges, they are capable of performing both classification and regression activities. In classification activities, supervised machine learning algorithm is mainly utilized to identify new blockers of a target by dividing drug classes into active and inactive groups based on molecular characteristics[10].

Approaches for identifying features and categorising data based primarily on input data are considered in unsupervised learning. Using feature-finding strategies, unsupervised machine learning can provide outcomes such as disease target and illness subtype detection[9].An unsupervised learning approach called k closest neighbour (kNN) is utilized for both classification and regression. It is the most basic nonparametric lazy learning method, and it typically works in conjunction with other statistical learners to provide the prediction. When using k-nearest neighbours, kNN counts the proportion of the class that is available in the characteristic area[10].Reinforcement learning key principles is to make decisions in a particular context and carrying those decisions out to maximise performance. De novo drug design within decision-making and experimental designs under implementation are examples of the outputs from this form of machine learning , where both can be accomplished using modelling and quantum chemistry[8].

Deep learning (DL), a subcategory of machine learning, utilises artificial neural networks (ANN) to acclimatise to and gain knowledge from vast amounts of experimental data. Big data, together with related data mining and algorithmic techniques, may enable us to find novel chemicals that could eventually lead to the development of novel medications[9].

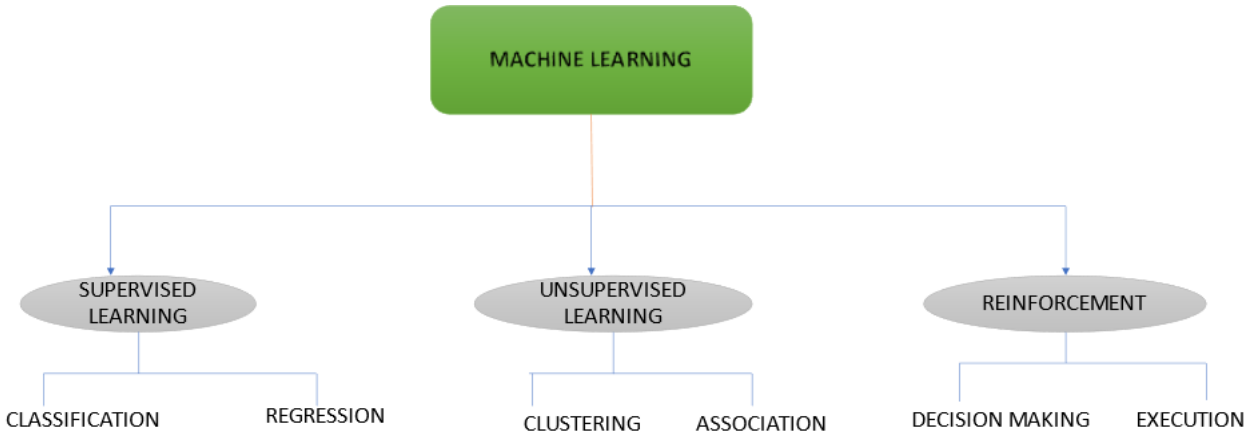

Fig 2: Classification of Machine Learning

Artificial Intelligence In Drug Discovery

The broad chemical space, which contains more than 10^{60} compounds, promotes the creation of numerous drug compounds. However, the medicine development process is hindered by an absence of advanced procedures, leaving it a time-consuming and pricey process that can be rectified by utilising artificial intelligence. AI has the ability to find hit and lead molecules, as well as intensify medicinal target validation and structural design enhancement. Despite its benefits, AI must struggle with serious data difficulties such the size, expansion, diversity, and unpredictability of the data. Huge numbers of molecules may be present in data sets accessible to drug companies for the creation of novel drugs, making typical Machine learning algorithm difficult to handle. [7]. A computational framework based on the QSAR can rapidly predict a vast amount of chemicals or basic physico - chemical properties, such as log P or log D. These models, however, are a long way from making accurate predictions about complicated biological characteristics like a compound's effectiveness and unfavourable side effects. Quantitative structure activity relationship -based models face additional challenges due to small training sets, inaccurate experimental data in training sets, and an inability of experimental validations. To resolve these concerns, massive data modelling focusing on recently accepted AI strategies, such as Deep learning and relevant modelling studies, can be used to examine the safety and potency of pharmaceutical compounds. In order to examine the benefits of DL in the drug development process in the pharmaceutical company, Merck launched a QSAR ML challenge in 2012. In correlation to conventional Ml algorithms, DL models proven relevant predictivity for 15 drug candidate absorption, distribution, metabolism, excretion, and toxicity (ADMET) data sets. [5].

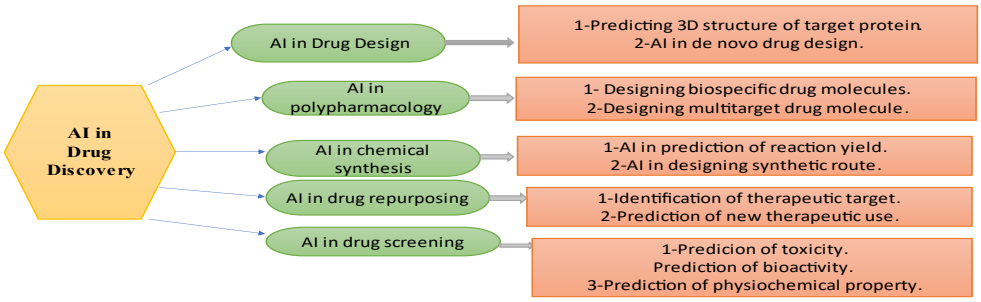

Fig 3: Artificial Intelligence's supporting role in Drug Discovery

Artificial Intelligence (Ai) In Drug Development

The emergence of a novel drug to the market is a challenging and time-consuming methodology that can take countless years and incur significant financial expenses due to an elevated turnover rates. As a result, it is vital that this methodology be enhanced using cutting-edge techniques such as artificial intelligence (AI)[1].AI-integrated innovations have evolved into adaptable tools that can be used widely in numerous phases of drug development, including the identification and validation of drug targets, the design of new drugs, drug repurposing, improving research & development effectiveness, aggregating and analysing biomedicine data, and refining the decision-making process to select patients for clinical trials. These possible applications of Artificial intelligence offer the chance to minimize bias and human interference in the procedure while resolving the difficulties and risks that result from traditional drug development procedures[11] .

1. AI in route knowledge or molecular target discovery when developing drugs-

Route or target identification techniques for treating diseases have advanced as a result of AI. The inclusion of genomic data, biochemical determinants, and target controllability made this feasible.

2. AI in finding the hit or lead –

Employing chemical space is a key aspect of applying artificial intelligence to the development of micro drug-like compounds. Because it is possible to algorithmically identify the expected organic molecules, chemical space provides an opportunity to detect novel, superior compounds. Moreover, while maximising the safety and efficacy qualities, machine learning approaches

and predictive model software help to identify target-specific virtual molecules and link them to their particular targets.AI systems can minimise turnover rate rates and research and development costs by minimising the number of molecules synthesised and evaluated in in vitro or in vivo systems. [12].

3. AI used in drug-like molecule synthesis-

Chemists frequently employ retrosynthesis for the synthesis of drug-like substances. The target compounds are systematically evaluated as the initial step in the retrosynthetic technique, after which they are successively deconstructed down into smaller fragments or accessible building components. Finding the processes that will transform these fragments into the desired chemicals is the second step. The 2nd stage is the most challenging because it is complicated for the human central nervous system to sort through the vast number of substantial organic reactions described in the literature in order to identify the most probable response. By filling in the gaps that lead to a high failure rate in predicted organic synthesis, artificial intelligence would help in forecasting the best desired reactions[5].

4. AI for clinical trial population selection-

An appropriate artificial intelligence tool for clinical trial support should be capable of detecting the disease in patients, detecting the gene targets, and predicting the effects of the targeted medicine as well as off-target affects. A unique AI platform called AiCure was developed as a mobile application to detect medication adherence in a Phase II study with schizophrenia patients. It was found that AiCure enhanced adherence by 25percent in contrast to the conventional "modified directly observed therapy". Because of the progression of artificial intelligence approaches for recognising and predicting human pathogen biomarkers, phase II and III clinical studies can now join a specific patient population. The success probability of clinical trials would enhance with the use of artificial intelligence predictive modelling in the identification of a patient population[8].

5. AI in drug repurposing-

AI makes the process of repurposing drugs more appealing and feasible. The idea of adapting a current treatment for a new illness is favourable since the new drug is eligible to move directly to Phase II trials for a new purpose without getting to go through Phase I clinical trials and toxicology testing once more. Through the use of deep learning applications, in silico techniques for drug repurposing and drug prediction using transcriptome data encompassing multiple biological systems and situations have been reported[10].

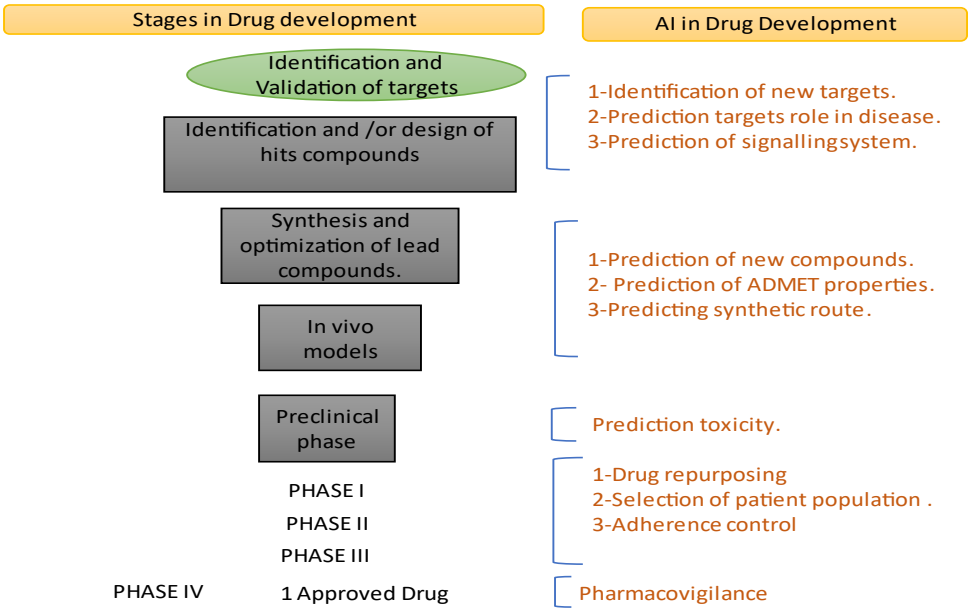

Fig 4: Role of Artificial Intelligence in drug development

Artificial Intelligence In Personalised Medicine

A drug's ability to work for some users while being less effective on others or generating negative effects in others is a constant source of surprise. Other issue is why certain individuals acquire certain diseases, like cancer, while some are unaffected. These issues may be caused by genetic make-up as well as other unique factors including age and lifestyle. Considering that each patient's condition should be treated as distinct and that treatment should be based on the biology and history of the individual. Personalized or Precision

Medicine is the term used to describe this method of treating patients[13].A branch or development of medical sciences known as personalised medicine employs clinical experience and medical judgement to provide patients with individualised healthcare. When setting up or developing personalised medicine, the application of artificial intelligence tools is crucial for the precision and accuracy of drug administration, disease diagnosis, and therapy[2].

The Use of AI Algorithms In Personalised medicine

Numerous AI and ML algorithms are employed in medicine, particularly specifically in personalised medicine. Several of these algorithms are :

1- Naïve Bayesian -The Naive Bayesian (NB) algorithm, so named in honour of Thomas Bayes (1702–1761) who first developed it, is based on a statistical model and enables the principled capture of doubt in a model by evaluating the possibility of various outcomes.

2- Artificial Neural Network (ANN) -ANNs are used in healthcare for a variety of purposes, including but not confined to diagnosing, imaging, treating back pain, memory, and analysing the aetiology and outcome of appendicitis, myocardial infarction, acute pulmonary embolism, arrhythmias, and psychiatric diseases.

3- Support Vector Machines (SVM)- Although when input data are not linearly differentiable, SVM gives appropriate classification results on a theoretical basis[14].

Artificial Intelligence (Ai) In Emerging Disease

The most promising research focuses on detecting viral mutation before a new strain ever appears. Using a rough set gene evolution approach, nucleotide substitutions in the basic ribonucleic acid sequences of the New Disease virus were predicted. Rough set concept is an information analysis concept that has proven a key tool for analysing irregular and uncertain data, primarily in AI technologies. [15]. In order to recognise the RNA sequences of future generations, an algorithm was created, and the output was matched to genuine RNA sequences. When alterations are suspected or have basically arisen, the next approach is to detect potential viral proteins from a viral sequence that can identify harmful effects for the host. Using AI techniques, a computer scientist at the UK-based DeepMind technology firm created the Alpha Fold protein structure prediction system. The software generates a neural network to analyze the distinctions among protein residues in a sequence. After employing an optimization technique, the device folds the protein into the expected configuration. Drug development is the next essential step after inferring viral structures and their functions[16].

Artificial Intelligence as a Diagnostic Tool

A new AI diagnostic tool is aware of when to consult a doctor. The ability of a new artificial intelligence diagnostic system to acknowledge its own limitations and seek the aid of a carbon-based lifeform that may be able to make a more accurate judgment. [17].

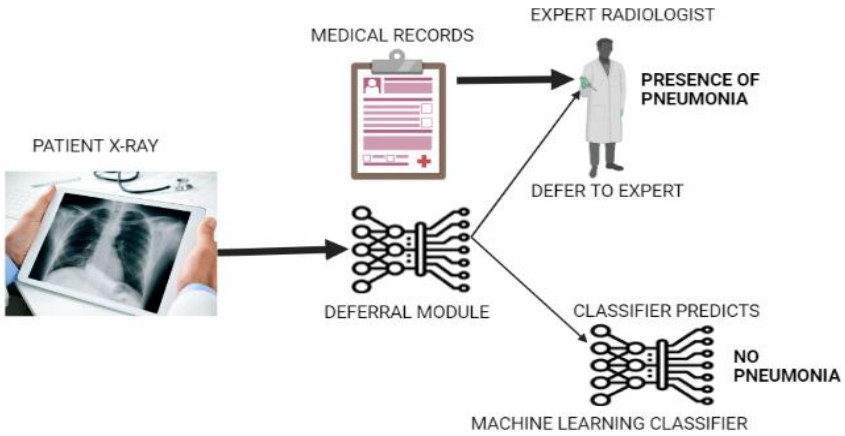

Fig 5 : Artificial Intelligence as a Diagnostic Tool

Pharmaceutical Market of Artificial Intelligence

Pharmaceutical enterprises are adopting to artificial intelligence (AI) to decrease financial expenses and failure risks. The AImarket place expanded from dollar 200 million in 2015 to dollar 700 million in 2018, and it is expected to reach dollar 5 billion by 2024[18].Multiple pharmaceutical firms have

invested in AI technologies and continue to conduct so. They have also functioned with artificial intelligence organisation to set up vital healthcare tools. As a result, major global partnerships between the pharmaceutical and artificial intelligence industries have now been established. For example, to help in the management of acute renal injury, DeepMind Technologies, a Google company, worked with Royal Free London NHS Foundation Trust .The United kingdom 100,000 Genomes Project, a global initiative with Roche, Berg, Merck, and Biogen, uses data and artificial intelligence from NHS patients with unusual diseases. [5].

Atomwise is a pioneer in medical artificial intelligence and the 1st deep learning technology for the discovery of novel tiny molecules. Working with prestigious institutions like Harvard University & Stanford University as well as pharmaceutical firms, Atomwise has aided in the development of novel potential medicines for twenty seven disease targets. Atomwise is famed for its remarkable rapidity, exactness, and variety in configurational chemistry utilizing deep learning. One of the artificial intelligence tools now employed in drug research is benevolent AI. It employs the use of text mining techniques to examine the available genomes and patents[9].

Exscientia is an artificial intelligence organization that deals in finding phenotypic drugs. Artificial intelligence significantly perform better in human investigation of highly complex datasets for high-content phenotypic medicine development[19].

Table-1:Prominent pharmaceutical organizations and their partnership with an AI organisation.

Pharmaceutical Organization	Artificial Intelligence Organization	Partnership Work
ROCHE	OWKIN	In drug discovery and drug development, clinical trial relies on Machine learning network.
Pfizer	IBM Watson	• Utilization of machine learning , natural language processing, and cognitive reasoning techniques are used in immune oncology to identify novel therapeutic targets, treatment combinations, and patient selection methods. • Improved health outcomes for breast cancer patients
SANOFI	Exscientia	To identify and create bispecific small compounds for the treatment of diabetes and associated complications.
AstraZeneca	Benevolent AI	Platforms based on neural networks for the identification and development of novel medicines for idiopathic lung illnesses and chronic kidney disease.
Lilly	Atomwise	Create new therapeutic targets and drugs.

Conclusion

Numerous AIapplications in the fields of public health, disease detection, and drug discovery have emerged in the last decade . These techniques have been employed across a number of fields to reduce cost , time and enhance procedural speed, efficiency along with precision . Deep learning and reinforcement learning are used to provide a revolutionary approach to de novo compound design that evaluates the statistical relationship between potential actions and results. The increase in the no. of start-ups based on AI and its amazing tools in pharmaceutical or healthcare sector may be explained this[20]. AI continually aimsto minimise the challenges faced by pharmaceutical companies, affecting both the drug development procedure and the whole lifecycle of the product. By incorporating AI into the pharmaceutical product production process, personalised medications with the required dose, release characteristics, and other important elements can be created in response to each patient's need[21]. The pharmaceutical and medical industries are anticipated to undergo a revolution due to artificial intelligence , according to a forecast rise of 40 percent from 2017 to 2024.Global pharmaceutical industry is working with artificial intelligence organisation to build not only vital healthcare tools and drug molecules for rare disease but also for market research[22].

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