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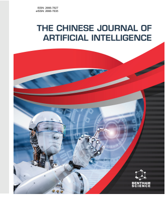
MINI-REVIEW ARTICLE



Perspectives of Artificial Intelligence (AI) in Health Care Management: Prospect and Protest

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Abstract: ***Background***: Artificial intelligence postulates that computers will eventually supervise performing tasks through various pattern recognition with less or without human interventions and assistance. It appears to mimic human cognitive functions. Resembling the human brain, it receives various forms of raw data that are stored, aligned, surveyed, interpreted, analyzed, and converted to single processed data, making it easy to conclude and understand. Recently, in the digital world, machine learning, deep learning, neural network and AI applications are expanding widely, where humans have expertise.

Methods: A detailed literature survey was performed through an online database, such as ScienceDirect, Google Scholar, Scopus, Cochrane, and PubMed. The search keywords were Machine Learning OR Deep Learning OR Neural Networks OR Applications OR Pharmaceutical Innovations OR Technology OR Artificial Intelligence AND Pharmaceutical Sectors OR Clinical Pharmacology OR Healthcare OR Medical OR Pharmacovigilance OR Clinical Trials OR Regulatory OR Challenges. The literature search was limited to studies published in English.

Results: It was found that there is an immense growth of artificial intelligence in the sector of the pharmaceutical industry applied in drug discovery and drug development, clinical trials, and the pharmacovigilance sector. It has several clinical applications of AI as a tool in health care and biomedical research besides clinical practice. It also shows several challenges faced and methods to overcome them.

Conclusion: AI has great potential and future as a valuable tool in the healthcare and pharmaceutical industry by applying a scientific approach and averting real-life challenges.

Keywords: Deep learning, machine learning, artificial intelligence, pharmacovigilance, pharmaceutical applications, health care management.

1. INTRODUCTION

Artificial intelligence (AI) is a science that has been studied for over 50 years. John McCarthy invented the term in 1956 to describe the idea that computers could someday learn to execute tasks through pattern recognition with little to no human intervention. In computer science, AI studies "intelligent agents," or systems that "perceive their environment and take actions to maximize their chances of achieving some goal." Siri on Apple's iPhone, Netflix, Alexa on Amazon Echo, and other well-known examples are all made possible by AI [1, 2]. Artificial intelligence was first coined in the 1950s as a naive concept that computers could display human intellect. In the early 1960s, the first expert system, known as 'DENDRAL,' mechanized organic chemists' decision-making and problem-solving behavior with two main programs, Heuristic Dendral and Meta Dendral. Artificial intelligence (AI) sought a place in healthcare and pharmaceuticals in the 1960s and 1970s [2].

Although progress is slow, some examples of where AI in health care include work done at UC Health in Colorado, where an AI-based scheduling tool is used to optimize surgical schedules, and many reports of incorrect medication administration or even surgery at the wrong site can be tracked down and followed up on, something that computers are particularly adapted [3]. People and scientists speculate that AI will be the herald of humanity's demise, ushering in a dystopian worldview in which robots rule the planet. On the other side, many people believe that wiser decision-making will lead to a massive boost in job prospects and economic growth [4]. In this article, we will describe both the potential and future of AI in the healthcare and pharmaceutical industry.

2. METHODS

2.1. Sources of Information and Search Strategies

A detailed literature survey was performed through an online database, such as ScienceDirect, Google Scholar,

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Scopus, Cochrane, and PubMed. The search keywords were Machine Learning OR Deep Learning OR Neural Networks OR Applications OR Pharmaceutical Innovations OR Technology OR Artificial Intelligence AND Pharmaceutical Sectors OR Clinical Pharmacology OR Healthcare OR Medical OR Pharmacovigilance OR Clinical Trials OR Regulatory OR Challenges. The literature search was limited to studies published in English.

2.2. Study Inclusion and Type of Intervention

The studies included various other studies involved with technology related to Artificial Intelligence and original articles conducted on Machine learning to assess the significance and basics of neuronal networks or technology-based interventions. Various studies on medical-based approaches and their health aspects were limited to the pharmaceutical sector.

3. MACHINE LEARNING

Artificial intelligence is a large area of study that includes a variety of technologies that function together. The following are some of the most critical technologies in healthcare: Machine learning, Neural networks, and deep learning [5]. ML is one of the most frequent types of AI. It is an analytical technique for fitting models in data or learning by training models using data, according to a 2018 Deloitte poll of 1,100 US managers whose companies were already exploring AI. It is a broad technique based on several AI approaches [5].

Traditional machine learning can be commonly utilized in precision medicine in the healthcare and pharmaceutical industries, forecasting which treatment protocols are likely to succeed on a patient based on numerous patient attributes and treatments. Most machine learning and precision medicine applications require supervised learning, which requires a training dataset with a predetermined outcome variable (*e.g.*, illness onset) [6].

3.1. Neural Networks

A neural network is a more advanced sort of machine learning that has been employed in medical research for some time. Since the 1960s, it has been widely utilized. It was employed in a classification application to identify whether a patient is at risk of contracting a specific illness based on inputs, attributes, and other criteria [7]. It examines issues regarding inputs, outputs, and changeable weights or 'features' that connect them. Although the link to brain function is not powerful, it has been compared to the signaling mechanism of neurons [8].

Synapses that connect the dendrites of a biological neuron receive several impulses and transmit a single stream of action potentials through the axon. According to early theories, each neuron performs an essential cognitive function: it reduces complexity by classifying input patterns that impact artificial neural network models, which are made up of units that aggregate several inputs and generate a single output [9] (Fig. **1**).

4. DEEP LEARNING

Deep learning is the most sophisticated kind of machine learning, which uses neural network models with multiple layers of variables to predict outcomes. The term "deep" refers to machine learning's multilayered structure. The CNNs (Convolutional neural networks) are the most promising DL technology in image recognition [10]. Deep learning in healthcare is frequently used to image potentially cancerous lesions in radiography. In the case of cancer, deep learning enables more precise imaging than prior generations of

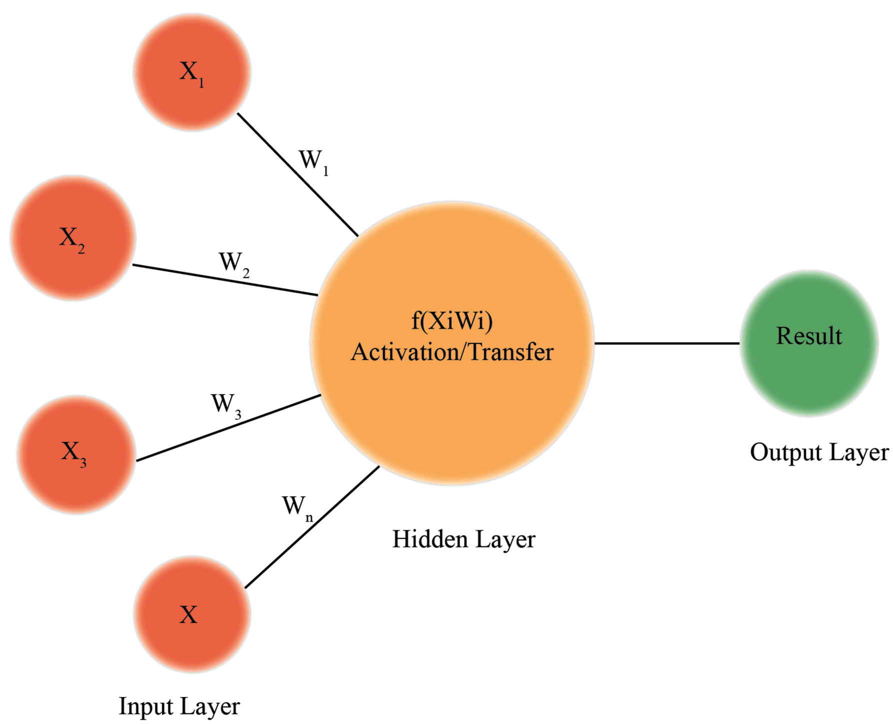

Fig. (1). Illustration of neural network. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

computer-aided detection (CAD) image analysis approaches [11]. Deep learning is gaining popularity in radionics (a branch of medicine that uses data characterization algorithms to extract a large number of quantitative information from medical images) or the discovery of clinically relevant data that the naked eye cannot discriminate. Thousands of hidden and unidentified data points may exist in such models that have yet to be identified [12] (Fig. **2**).

5. MACHINE LEARNING (ML) APPLICATIONS IN CLINICAL PHARMACOLOGY

Deep neural networks use a vast database of up to 192,284 drug-drug interactions to forecast drug-drug interactions and drug-food interactions for dietary recommendations, prescriptions, and novel compounds [13]. When it comes to individual safety, Daunhawer *et al*. employed machine learning to personalize safety in infants with hyperbilirubinemia [14]. Gaweda *et al*. also employed reinforcement learning to personalize pharmaceutical anemia therapy [15]. ML models recommend dose adjustments in real-time and could be extremely useful in customized healthcare [16].

ML has also demonstrated its value in bridging the gap between medication discovery and clinical development. For example, Hammann *et al*. used a decision tree method to predict the risk of Torsedes de Pointes from *in vitro* data, and Lancaster and Sobie used SVMs (Support Vector Machine Algorithm) to predict the risk of Torsedes de Pointes from *in vitro* data [17]. In a recent study, the ML-type control algorithm was combined with pharmacometricians' PK/PD models, resulting in a closed-loop control system [18].

6. CURRENT STATE OF AI IN THE PHARMACEUTICAL INDUSTRY

AI is gaining traction in various fields, including the pharmaceutical business. In this review, the use of AI in various pharmaceutical industry sectors is highlighted, including drug repurposing, drug discovery and development process, improving pharmaceutical productivity, and clinical trials; such implementation reduces human workload while also achieving targets in a short amount of time. AI in the pharmaceutical sector has enabled the industry to develop safe and effective treatments for previously untreatable ailments [19]. AI algorithms can drastically cut the cost and time it takes to discover and develop new drugs. AI has proven its value in pharmacovigilance by assisting in creating drug and biological toxicity databases [20]. Deep learning greatly influences science and technology in general, as well as drug development.

AI-driven technologies can be employed for drug repurposing in the case of neglected tropical diseases, which represent significant problems in terms of disease burden and death rate in underdeveloped and developing countries. These computational methods are rapid, making them excellent for screening huge libraries of available chemicals against specific molecular targets or disorders and repurposing current medications, clinical trials, and approved natural products [21]. Repurposing is advantageous since any leads discovered have already been evaluated for safety in people, allowing them to be tested in humans more rapidly and affordably than completely new medications [22].

AI has boosted the possibilities of leveraging huge data in pharmaceutical sciences, particularly machine learning technologies that allow computers to "learn" and perform jobs. The use of several computational approaches, such as molecular dynamics simulations and machine learning techniques, to forecast the water solubility of medicinal compounds has gained attention [23]. During the preformulation stage of the drug development process, the physicochemical characteristics of the drug material are assessed [24]. The stability, interaction with excipients, sol-

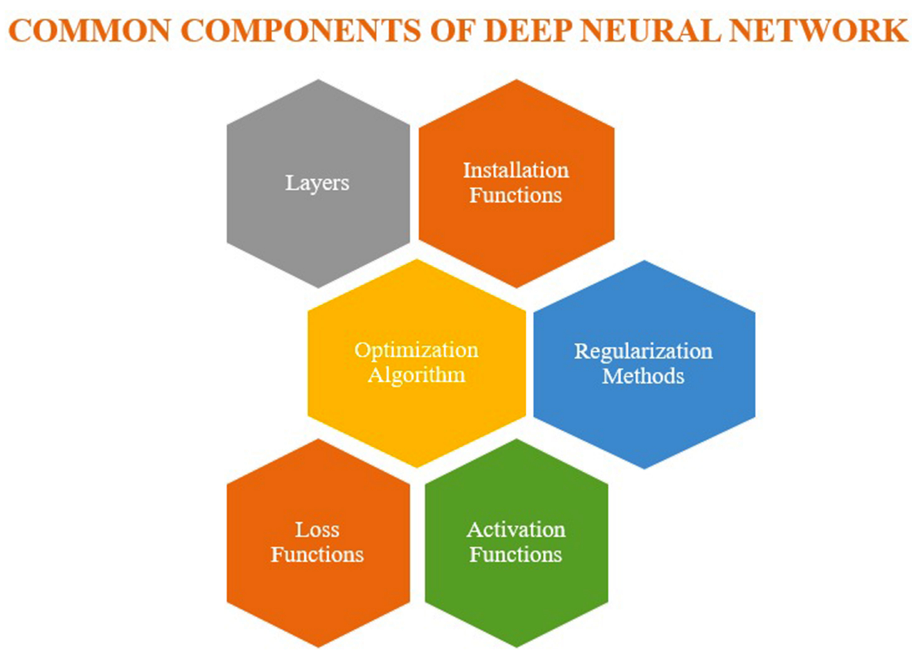

Fig. (2). Components of deep learning algorithm. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

ubility, and bioavailability of a pharmaceutical substance are all influenced by its physicochemical properties. Transfer learning has shown to be a potential machine learning approach for further investigation in pre-formulation studies [25].

Artificial intelligence applications in drug discovery and design have significantly benefited from deep learning. In the United States, the Precision Medication Initiative was established to provide access to personalized medicine for the treatment of chronic disease conditions, such as cancer and diabetes [26]. SBDD (Structure-Based Drug Design) has proven instrumental in the rapid advancement of precision medicine. Computational modeling and simulation methods have been widely employed to develop new biomarkers, forecast potential intercellular pathways, and analyze protein conformational changes and cell activity [27]. Molecular dynamics simulation is a prominent computational tool for characterizing flexible binding sites and routes, kinetics, and thermodynamics, as well as understanding macromolecular conformational changes and their biological function, which might signal potential pathogenic processes [28] (Fig. **3**).

7. PREDICTABLE FUTURE OF AI IN THE PHARMA INDUSTRY

7.1. Power of Artificial Intelligence (AI) in Healthcare, Research, and Clinical Practice

7.1.1. AI in Drug Discovery

AI can distinguish between hit and lead compounds, making it easier to validate therapeutic targets and optimize the structural design. Recently developed AI approaches, such as DL and relevant modeling studies, can be utilized to evaluate the safety and efficacy of pharmaceutical drugs based on massive data modeling and analysis [29, 30]. In 2012, Merck sponsored a QSAR ML competition to study the benefits of DL in drug discovery in the pharmaceutical industry [19]. Deep Learning models exhibited significant predictability compared to classic ML techniques for (ADMET) Absorption, Distribution, Metabolism, Excretion, and Toxicity [31]. QSAR modeling tools, such as linear discriminant analysis (LDA), have been used to identify possible drug candidates and have evolved into AI-based QSAR methodologies, support vector machines (SVMs), random forest (RF), and decision trees, which can be applied to speed up QSAR analysis [32-34] (Fig. **4**).

Transformers are a newer generation of context-based models that extract representations from sequences using attention mechanisms and self-supervision. Transformers can predict drug-target interactions, model protein sequences, and retrosynthetic reactions [23]. Due to the advances made in the natural language processing domain, the COVID-19 pandemic has cleared the way for advancements in sequence-based models, such as genomics, proteomics, and transcriptomics [35, 36]. When trained on molecules or protein sequences, recurrent neural networks (RNNs) and long short-term memory (LSTM) networks have successfully shown the ability to predict secondary structure, quantitative structure-activity relationship (QSAR) modeling, and function prediction [37].

7.1.2. AI in Drug Screening

Developing a new medicine can take a decade and cost money. Therapeutic medicines fail Phase II clinical trials and regulatory approval in most cases. Nearest-Neighbor classifiers, RF, extreme learning machines, SVMs, and deep neural networks (DNNs) are some methods used in VS to predict *in vivo* activity and toxicity [38]. Using a genetic

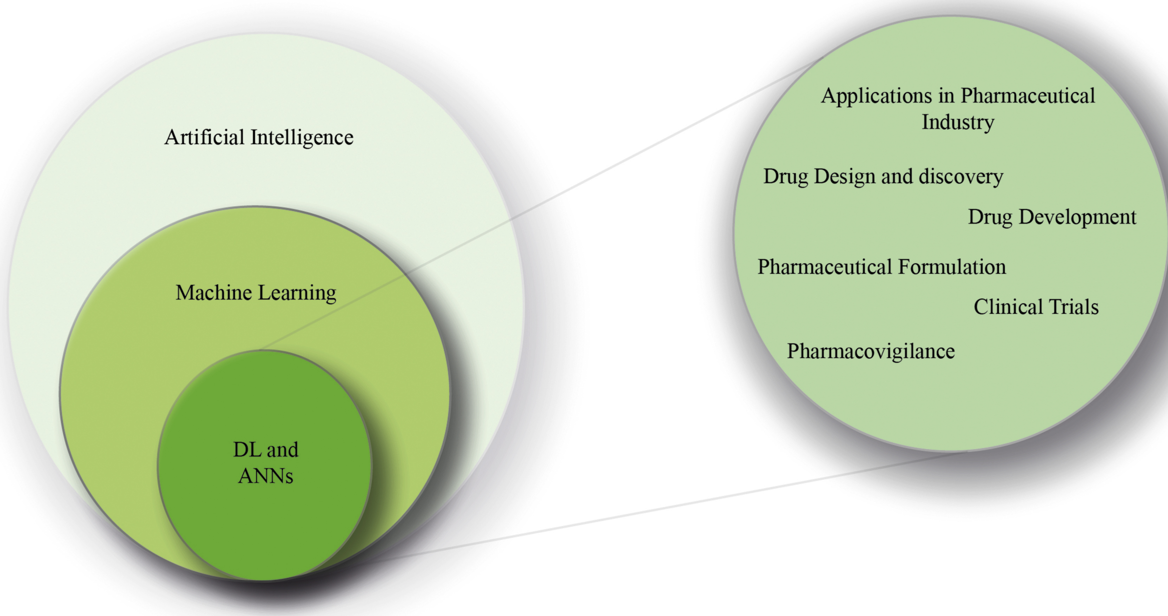

Fig. (3). Applications of AI in the pharmaceutical industry. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

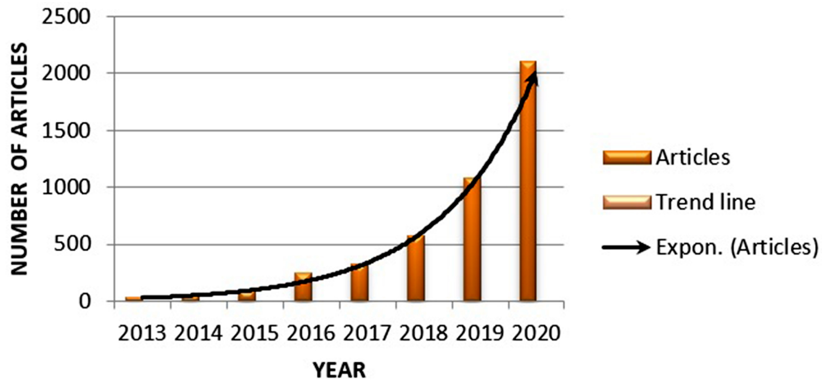

Fig. (4). Current trend logarithm for deep learning techniques. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

algorithm variable selection technique with SVMs, a study has created QSAR models for predicting vascular endothelial growth factor receptor (VEGFR) 2 inhibition by aminopyrimidine-5-carbaldehyde-oxime derivatives [39].

DNNs can frequently produce better future predictions on a group of big heterogeneous QSAR data sets, according to studies based on Merck's Drug Discovery initiative [40]. It has been noticed that great generalization capacity and powerful feature extraction ability of deep learning methods have been used in predicting chemical attributes and synthesizing the required compounds, which will further encourage the use of AI in the drug creation field [41-43].

7.1.3. Challenges in the Regulatory Environment

With the integration of AI technologies into healthcare, a slew of ethical issues arises. One such ethical challenge in clinical treatment concerns amplifying biases in existing data, regardless of individual clinical interactions. Despite the knowledge that concomitant asthma exacerbates pneumonia, AI categorized patients with pneumonia alone as high-risk but wrongly classified those with pneumonia plus asthma as low-risk [44, 45]. Health records and data are usually unreliable. Despite data purification and standardization, unforeseen loopholes will emerge, posing a threat to the quality of datasets used to train AI systems [46]. Patient data privacy is another significant issue [47]. Data is collected in real-time, and it is examined in real-time for patterns in the care process, procedures that can be improved, and other underlying patterns like different patient reactions to differential treatments [48]. Finally, these discoveries are frequently integrated into the clinical treatment process. In this setting, data leakage and data privacy concerns occur [49]. Data-driven innovations may be stifled as a result of health privacy violations [50]. As a result, politicians and regulators must collaborate with physicians, patients, and manufacturers to develop a new framework for regulation that harnesses the power of emerging technologies while ensuring appropriate security and privacy of personal data [51].

Enhanced data security standards must accompany regulations to avoid stifling progress in the industry. These range from improved data encryption per client to the adoption of federated learning, which allows models to be trained centrally despite data being spread across several clients [46, 52, 53]. The FDA has called for adopting "agile" regulatory methods for software used in medicine to accommodate the quicker rate of development and potential for innovation in software-based devices. While machine learning promises efficiency, price savings, and improved health results, regulation of this rapidly growing sector must explicitly address and call out health disparities rather than omitting how these technologies may have significant positive and negative consequences for underrepresented groups [54].

7.1.4. AI in Clinical Trials

The last five years have seen an exponential increase in digital technology penetration into clinical trials. In clinical trials, real-world data, such as electronic health records (EHRs) and clinical trial findings, varies from incorporating AI in diagnostic devices to using real-world data, such as EHRs and clinical trial outcomes [55]. EHRs are useful data sources for comparative effectiveness research and novel trial designs that can aid in resolving important clinical challenges while increasing efficiency and cutting costs. The first experience with EHRs has been positive, and as more information becomes available, the application of EHRs for clinical research will continue to evolve [56-59].

The USFDA has recently cleared the way for many biopharmaceutical companies in the USA to conduct AI-empowered virtual clinical trials. It also licensed crowd-sourced clinical trial designs and metrics that can be digitally communicated to reduce the overall expenditure [60]. Although using AI and other new digital technologies can compromise participant privacy and confidentiality, regulatory agencies and IRBs have issued guidance on using digital tools [55].

7.1.5. AI in Pharmacovigilance and Drug Safety

The purpose of pharmacovigilance is to ensure the safety of patients exposed to therapeutic medications during clinical trials and research. The most significant activities in the PV sector are the detection and reporting of ADRs, the technical coding of adverse effects, the development of safety individual reports, the assessment of severity, and the linkage with suspected pharmaceuticals [61]. All of these rely on time-consuming human interference; therefore, ADR detection needs the creation of new technology. Traditionally, pharmacovigilance is based on a clinical examination of case reports gathered by recognized organizations [62]. Data mining algorithms are created to enhance this process by allowing assessors to sift through enormous amounts of data and concentrate on topics essential to public health [63, 64].

AI and ML can make the pharmacovigilance process simpler and more effective in a variety of ways, including a) Reduced cycle times, which allows for more automatic processing, b) Improving the quality and accuracy of the data, c) Managing various types of incoming data formats, and d) Identifying ADRs [62]. Combining text mining methodologies [65] with rule-based and specific machine-learning classifiers, the US Vaccine Adverse Event Reporting System [66] highlights the feasibility of building effective medical text classifiers for spontaneous reporting systems [67].

8. AI IN CLINICAL PRACTICE AND HEALTH CARE

Possible benefits of AI are described in Table **1** [68-75].

8.1. Challenges

- Although AI can potentially transform medical practice, there are several technological challenges to solve. As machine learning relies significantly on high-quality training data, collecting data representative of the target patient population is critical [52, 76].
- When there is an unsatisfactory inter-expert agreement on a diagnostic task, consensus diagnoses have been demonstrated to significantly increase the performance of machine-learning models trained on the data. When dealing with heterogeneous data, proper data curation is required. Furthermore, attaining the gold standard of a patient's clinical status necessitates clinicians individually reviewing their clinical notes, which is prohibitively expensive on a population scale [77, 78].
- Sophisticated algorithms that can address the quirks and noises of different datasets will improve the predictability of the models and, therefore, the safety of using them in life-or-death choices [79, 80].
- Several high-performing machine-learning models produce impossible outcomes for humans to understand without assistance [81].
- Artificial intelligence (AI) could potentially replace some healthcare employees and clinicians in basic tasks, reshaping the healthcare workforce and changing the present reimbursement paradigm [82, 83].

8.2. Overcoming the Challenges

To overcome challenges, AI researchers and physicians must collaborate to prioritize and develop applications that address critical clinical requirements. Hospital administrators must assess and limit clinical workflow disturbance when adopting new AI applications [52, 84]. Companies will need to figure out the best framework for conducting prospective clinical trials to assess the efficacy of AI systems in clinical settings. Insurers should evaluate the value of medical AI systems and, if necessary, alter their payment policies to decrease healthcare costs while enhancing quality [85]. To facilitate the development and implementation of medical AI applications, multidisciplinary and multi-sector collaborations will be required [86].

9. SCIENTIFIC APPROACH

The healthcare system, like water, should adjust to changes in space and technology. It should not be stopped; instead, it should educate itself *via* its own experiences and strive to make ongoing advances in practice [87]. Today's

Table 1. Disease and possible benefits of AI.

Types of Diseases	Clinical Application of AI	Refs.
Retinal disease	We can identify, localize, and quantify pathogenic characteristics in practically every macular and retinal disease using machine learning (ML) and, in particular, deep learning (DL).	[68]
Ovarian cancer	Preoperative investigations can predict the pathology diagnosis of ovarian cancer.	[69]
Cardiovascular disease	Prediction of cardiovascular event risk.	[70]
Chronic obstructive lung diseases	The application of machine learning in the automated interpretation of pulmonary function tests for the differential diagnosis of obstructive lung disorders has been proven successful. In computed tomography, deep learning algorithms, such as convolutional neural networks, are state-of-the-art for finding obstructive patterns.	[71]
Gastrointestinal diseases	Application study in pathology, imaging, and endoscopic diagnoses for gastrointestinal illnesses using convolutional neural networks (CNNs).	[72]
Liver diseases	Clinical applications include detecting and analyzing localized liver lesions, simplifying treatment, and predicting hepatic treatment response in medical imaging of liver illnesses.	[73]
Renal diseases	Artificial intelligence is already being utilized to improve clinical care, hemodialysis prescriptions, and the prediction of increasing immunoglobulin deficiency.	[74]
Respiratory diseases	AI and machine learning are used to diagnose interstitial lung disease, and a few more papers were found on mechanical ventilation, chest X-ray interpretation, and bronchial asthma diagnosis.	[75]

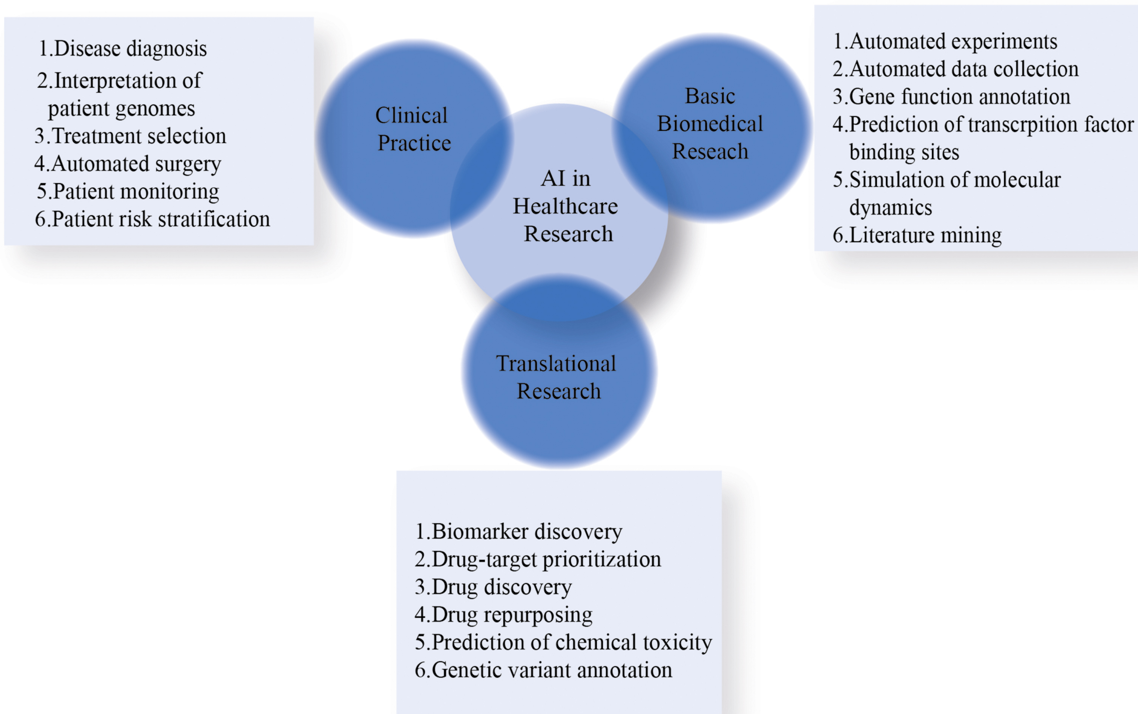

Fig. (5). Potential applications of AI in healthcare research. (*A higher resolution / colour version of this figure is available in the electronic copy of the article*).

age has progressed to the point where it is the most significant issue to alter and correct all potential flaws. Healthcare "systems thinking" considers the traditional interactions between patients and physicians and larger-scale organizations and cycles [88] (Fig. **5**).

Before using AI systems in healthcare, they must be "trained" using data generated from clinical activities, such as clinical laboratory, treatment, assignment medical notes, screening, electronic recordings from medical devices, physical examinations, diagnosis and images, *etc*., so that they can learn about similar groupings of subjects, subject-feature connections, and desired results [89, 90]. AI is successful when it contains a machine learning component for managing structured data and a natural language processing component for unstructured mining text. The implementation of AI in real life continues to face challenges. The first stumbling point is the limitations [91]. Under existing legislation, there are no standards to assess AI systems' safety and efficacy. Data exchange is a second stumbling block [92]. Apart from ethical problems, the main roadblock is that this novel feature of medical care necessitates a standardized, comparative assessment of the impact of robotic systems on health indicators, as well as assessments of changes in psychological and physical condition, side effects, and outcomes.

CONCLUSION

The pharmaceutical sector faces various complex difficulties, including increasing medication and therapy prices, and society demands considerable changes in this area. With the application of AI in pharmaceutical product manufacture, personalized medications with the requisite dosage, release characteristics, and other relevant factors may be considered according to specific patient demands. Using the maximum up-to-date AI based technology will now no longer simply shorten the time it takes for merchandise to attain the market, but it is going to additionally enhance product quality and safety of common production procedures, in addition to higher useful resource utilization and cost-effectiveness, emphasizing the significance of automation. We believe that AI has a bright future in healthcare and will favor medical practice.

AI can be useful in every step of drug development. ML and DL algorithms can bring about a shift in the paradigm of various intricacies of healthcare. AI in healthcare can potentially improve preventative care and overall quality of life. It can result in more precise treatment plans and, as a result, improved patient results. In clinical trials, AI-powered technologies may help determine the safety and efficacy of a medicinal product, as well as the best market positioning and pricing. Strict laws for the standardization of such data-driven advances are required to ensure the privacy and security of patient data. With the introduction of AI into the sector, there is a growing risk that numerous present employments may be lost. Hence, it should be implemented to reduce such losses and strain on healthcare providers. Shortly, AI is anticipated to become a valuable tool in the healthcare and pharmaceutical industries.

AUTHORS' CONTRIBUTIONS

All authors contributed to the study's conception and design. Material preparation and data collection were performed by Madhana Kumar S, Narmatha S, Lakshmi Chandran, and Ankul Singh S. The first draft of the manuscript was written by Narmatha S, and all authors commented on previous versions. The analysis of the article was performed by Ankul Singh S. All authors read and approved the final manuscript.

LIST OF ABBREVIATIONS

ADMET	=	Absorption, Distribution, Metabolism, Excretion, and Toxicity
AI	=	Artificial Intelligence
CNN's	=	Convolutional Neuronal Networks
DL	=	Deep Learning
DNNs	=	Deep Neuronal Networks
EHRs	=	Electronic Health Records
FDA/ USFDA	=	United States Food and Drug Administration
IRBs	=	Institutional Review Board
LDA	=	Linear Discriminant Analysis
LSTM	=	Long Short-term Memory
ML	=	Machine Learning
PK/PD	=	Pharmacokinetic/ Pharmacodynamic
PV	=	Pharmacovigilance
QSAR ML	=	Quantitative Structure-activity Relationship Machine Learning
RF	=	Random Forest
RNNs	=	Recurrent Neural Networks
SBDD	=	Structure-based Drug Design
SVMs	=	Support Vector Machine Algorithm
VEGFR	=	Vascular Endothelial Growth Factor Receptor

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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