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Review Article

Artificial Intelligence: An Interface in Software, Pharmaceutical and Healthcare Sector

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ABSTRACT

Low efficacy, off-target delivery, time consumption, and high cost impose a hurdle and challenges in drug design and discovery. Patient monitoring, disease diagnosis and treatment are challenging in medical sector. With the drastic enhancement of digitalization of data in the recent times, the technology of artificial intelligence (AI) has gained a storm of interest in various sectors of our daily life. The advent of AI technology finds tremendous opportunities especially in the field of pharmacy, healthcare and medicine. AI can perceive the information, comprehend, analyse the data and provide the required output. It finds its way into many facets of medical and pharmaceutical sectors like in case of drug discovery, screening, product development, identification of possible interactions between drugs and proteins, patient care, patient monitoring, disease diagnosis and treatment. This review highlights the impact of AI in all major areas of healthcare sectors and research. Crosstalk on the tools and techniques utilised in enforcing AI and collaboration of with pharmaceutical industries for product development. Though AI will be a game changer in all these domains, it yet faces significant hurdles and challenges that have to be overcome before being truly beneficial to the people are discussed in this review.

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INTRODUCTION

One of the major concerns of the pharmaceutical industry facing today is the high production cost involved in the discovery and development of a new active pharmaceutical ingredient (API). A major share of the amount spent on drug discovery goes down into drain due to the failure of the candidate even before being approved for the clinical trials. Only successful candidates that meet the requirements of the regulatory authorities move into clinical trials. In order to hasten the process of drug discovery and development, the industry should move out of the traditional trial-and-error processes which are more laborious, expensive and time consuming[1].Strategies which can facilitate the acceleration of drug development process are of enormous interest today as the world today is moving towards novel therapeutic paradigms. One such technique is Artificial intelligence (AI) which is now escalating from theoretical studies into practical applications [2].

AI is simulation of intelligence of humans in machines in order to mimic the functions of their brain. AI is a branch of engineering that deals with design and applications of algorithms for data analysis and interpretation. It makes use of the software to interpret and learn from the input data in order to take decisions independently for achieving the required objectives. The main aim of AI is to make machines responsive to environmental stimuli, by understanding their surroundings, perceive them and act accordingly. In all the domains of human life, scientists are working towards harnessing the true potential of AI and focussing on its inclusion to improve accuracy and help in better investigation of information [3].The term AI is coined by John McCarthy in the year 1956 during Dartmouth Summer Research Project. He defined it as the science and engineering of intelligent machine making. He published a paper titled "Programs with common sense" in the year 1958 and started AI lab at Stanford in 1963.

TYPES OF ARTIFICIAL INTELLIGENCE

AI can be classified as machine learning (ML), whose sub division is deep learning (DL) as shown in figure 1.In case of machine learning, machines learn from and adapt to the new data themselves, requiring no assistance from humans. Here data is fed into the machine and statistical techniques help in learning to work better at a task. While in deep learning, machines absorb large amounts of unstructured data in the form of images, videos or text. The inputs here are run through biologically inspired neural network architecture. Artificial neural networks (ANNs) are employed in case of deep learning and are similar to human neurons and mimic the transmission of electrical impulses in human brain [4].

Weak AI also known as narrow AI is where the system can carry out only one particular job and operate within a limited context i.e., it

focuses on specific tasks. Here the machine intelligence is limited to a particular area. While strong AI, also known as artificial general intelligence is where they carryout tasks that are more complicated and the machine intelligence here is equivalent to human intelligence with the ability to solve any problem.

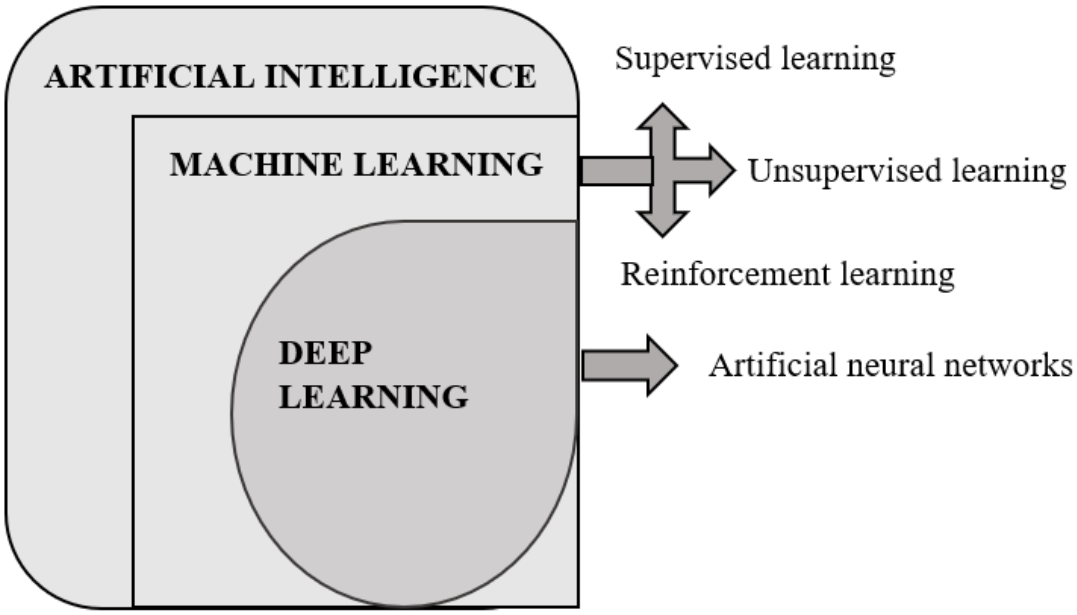

Figure 1: AI and its subdivisions

ARTIFICIAL NEURAL NETWORKS (ANN)

ANNs are the computer programs that have been inspired biologically and are designed to mimic the generalization behaviour of human brain in processing the information through data modelling and pattern recognition. They have been developed to stimulate logical thinking and reasoning of the brain for the reason of problem solving [5].They are trained through proper experience and are not programmed. As the human brain comprises of billions of neurons that are inter connected and work towards receiving and signalling the impulses, ANNs are formed from hundreds of artificial neurons that are connected together to form a neural structure [6].The use of ANNs in various domains of human needs has excited the scientists because of its ability of self-learning, highadaptability and handling complex problems. ANNs are widely used in various fields ranging from medicine, agriculture, finance, engineering, banking, insurance, management and art. ANNs are found to function similar to human brain in processing the information and coordinating the tasks to be performed [7].

ANN model significantly differs from the statistical model in the feature that the former can generalize the relationship between the independent and dependent variables without the need of any particular mathematical function. YixinCh*et al*., used ANN and near infrared spectroscopy to predict the drug

content and hardness of tablets. Experimental data obtained for drug content and tablet hardness were presented to the ANN and the possible error between the experimental data and ANN predicted output was calculated. The ANN model which provided the least value of the sum of error squared was selected [8].Tuncer D *et al*., have predicted the skin penetration of 40 substances using ANN modelling. It was observed that ANN modelling provided results which are closer to the experimental results when compared with the other previously used models. Hence, it was concluded that use of ANN model developed in this experiment, minimizes the requirement of performing penetration experiments using human skin or other model membranes [9].

AI technology offers promising advantages in the field of pharmaceutical sciences. Due to its high degree of accuracy and precision, possible errors in study design can be minimized. Pre-programming of the machines help them work continuously for stipulated time period without any breaks. When AI is employed in functional areas associated with risk, it aids in elimination of risk sources. Work load of the employees can be minimized by decreasing the steps involved in formulation development[10].

The major hurdle in the use of AI technology involves its high expense due to the requirement of skilled personnel to operate computer aided software, maintenance of machines and their repairing. It may indirectly lead to rise in unemployment and frequent software up gradation is required [11].It might lead to declined creativity among the researchers as technology cannot apply its intelligence or creativity. Suggestions are provided just based on the historical precedent [12].

APPLICATIONS OF AI

AI finds a huge range of applications especially in the field of pharmacy, medicine and health care sector (figure 2).

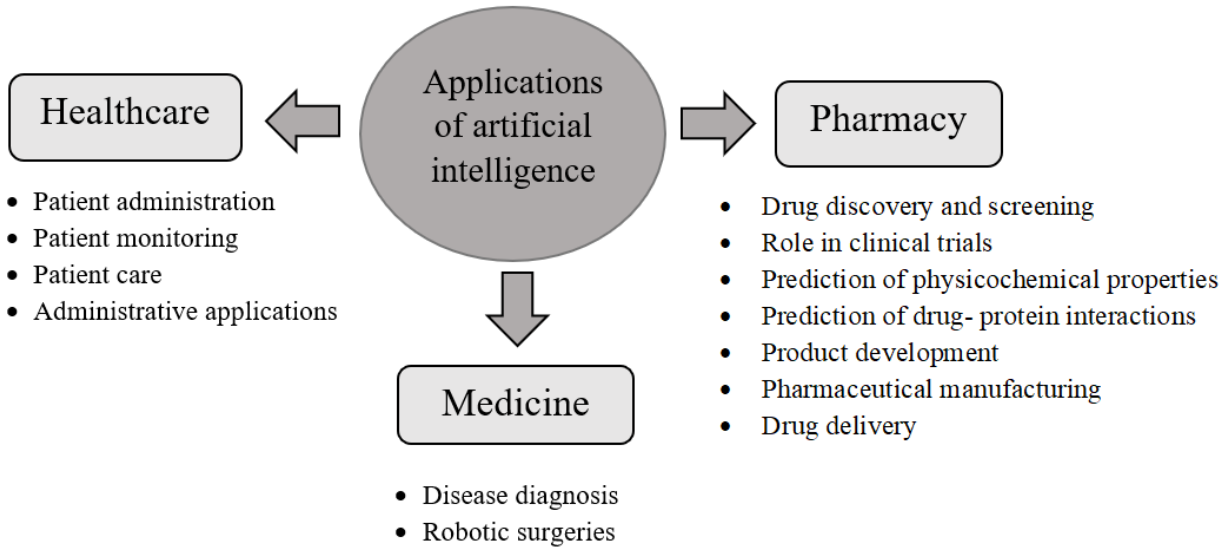

Figure 2: Applications of AI

Pharmaceutical applications

Drug discovery and screening

The process of drug screening is quite crucial due to its low success rate. Despite of the discovery of enormous number of therapeutic moieties, most of them fail during the process of clinical trials and hence do not receive the required regulatory clearance. Lower success rate, longer time required for clinical trials, stringent rules by the regulatory authorities for approval process, availability of already existing block buster drugs, make the process of drug discovery and development very tedious and expensive. Application of AI in this field can help in quicker designing of drugs, faster drug target selection, and optimization of the drug discovery process with minimal unwanted interactions.AI aids in evaluation of safety and efficacy of the drug molecule and works towards designing of new compounds that fulfil the structural criteria required to bind with the specific targets [13].

Preformulation study

Preformulation phase is a predominant phase involved in the design and development of pharmaceutical delivery systems. Here, physicochemical properties of drug and excipients are either studied alone or in combination in order to establish compatibility results. Information regarding solubility, stability, bioavailability and possible interactions between drug and excipients is studied here[14].Due to a direct relationship between aqueous solubility of the drug and its absorption from the physiological fluids, their estimation is important[15-17].Use of computational techniques for solubility prediction has made application of ML an industry feasible approach[18].A study demonstrated that solubility enhancement effect of hydrotrope molecules could be predicted using ML technique based ANNs. Physicochemical properties like melting point, log P and number of hydrogen bonds were used as descriptors for this study along with experimental data of 10 hydrotrope molecules. This ANN model was designed to predict the solubility of sixteen more potential hydrotropes utilizing an external data set. The developed model was capable of performing accurate predictions by identifying the relationship between the variables of the data set [19].Hence, this is encouraging for researchers to explore the potential of usage of models based on ANN for both prediction and enhancement of solubility of various drug substances [20].

Prediction of Pharmacokinetic parameters and their toxicity

Pharmacokinetic parameters are required to estimate the fate of a drug in body post its administration. These pharmacokinetic properties are largely dependent on their physicochemical properties like solubility, permeability, partition coefficient,

dissociation constant. From the pharmacokinetic profile of the drug, an effective formulation can be designed and developed. Transfer learning is an emerging machine learning technique which can be used effectively for this purpose in pharmaceutical industry and associated research.

In a study, an integrated transfer learning approach of machine learning was developed using the variables such as oral bioavailability, protein binding, volume of distribution and elimination half-life. The descriptors used for this study include donor and acceptor count of hydrogen bond, molecular weight, polar bond count, surface area and complexity properties. The obtained results were helpful in estimating the possible pharmacokinetic parameters of formulation [21]. Henceforth, machine learning and ANNs find potential applications in pharmaceutical product development by predicting the process related factors associated with various parameters like dissolution and release of a drug. Further the ML and AI based approach has potential to optimize the process variables such as ingredients and their concentration for best suited formulation outcomes and promising future applications in fast and efficient production. In general, for the prediction of toxicity of a compound, animal studies are performed. But with the advancement of AI, tools like DeepTox, TargeTox and PrOCTOR are being used [22].

Prediction of interactions between drug and proteins

Under *in vivo* conditions, the drugs may bind with plasma proteins resulting in alteration of effectiveness and pharmacokinetics of the drug molecules. AI helps in predicting the possible drug-target interactions by 3D visualization of their structures that aid in suggesting repurposing of the already existing drugs. It also aids in predicting the protein targets of novel compounds possessing biological activity.

Pharmaceutical manufacturing

AI serves as a platform for digital automization of the process of synthesis and manufacturing of pharmaceuticals on large industrial scale. ANN has been successfully used in designing the composition of pharmaceutical formulations, optimizing the process variables, predicting stability of the formulations, evaluating drug release from dosage forms, and helpful for correlations based on *in vitro/ in vivo* studies[23].

Product development and drug delivery

The major step involved in a pharmaceutical product development includes optimization of formulation and process variables. Exploitation of ML, ANN, Deep learning in drug product formulation and drug delivery leads to huge cuts in resource expenses. It also helps in saving time and effort involved in the wet-lab trial experiments. ANN models have shown to better predict the effects of various factors on the properties of the tablets. They have been proven to be helpful for

process of development of microemulsion based delivery systems with minimum effort of experimentation. They have also been found to simulate the behaviour of an aerosol that aids in design and evaluation of pulmonary drug delivery systems [24]. This system can be applied to the delivery of drugs for the SARS-Cov-2.Implantable robots are widely being used for controlled release delivery of several drugs. Nanorobots are integrated with sensor and AI technique, can process the information, play role in signalling, sensing, communicating, detecting toxic agents and also help in localized drug delivery. ANN technique can be used for the prediction and optimization of the performance of these nanorobots [25].Prediction of drug release from the coated nanoparticle was studied using the combination of Perturbation Theory and ML algorithm [26].

Haoshi G et al., integrated the concept of ML, molecular docking and experimental approaches to rationally design meloxicam SEDDS. They have incorporated ML algorithms in the construction of pseudo ternary phase diagrams. Random forest (RF), an optimal ML algorithm exhibited best prediction performance for accuracy, sensitivity and specificity. Hence, all the key parameters were calculated using RF [27].Blue print designs for the new antidiabetic drugs are being developed by the ML technology [28]. Limitations associated with the traditional trial and error approach were strongly shifted to beneficial approach using deep learning. Oral fast disintegrating films and oral sustained release matrix tablets were chosen as model dosage form for the comparison. Deep learning aids in splitting of data in case of algorithm and makes evaluation criteria suitable for pharmaceutical formulation [1].Another research was carried out in on deep learning models based on lipid nanoparticle drug delivery. The study could predict GFP expression in advance from the cell level microscopic imaging data from the morphology of the cell and its interactions with LNPs [29].

Role in pre-clinical testing and clinical trials

AI helps in identifying the animal models which are more accurate for a specific disease. It helps in applying predictive analytics to identify potential candidates for clinical trials and hence reducing the expenses and in overcoming the failure rate [30].

AI in healthcare system

Patient administration

AI can help in data entry of the patients and automatically review their laboratory data and imaging results. Machine learning algorithms when linked to electronic health records help the clinicians in retrieving patient information accurately [31]. They also play a pivotal role in scheduling appointments and aid in patient prioritization that further leads to reduction in waiting times. This enhances the efficient use of clinical services.

Patient monitoring

Electronic health records maintain the data relating to the patient's family medical history that helps in identifying the risk of the person to develop a hereditary disease. Use of fitness monitoring devices aids in patient monitoring and helps people in better management of their life style to stay healthy. Exploitation of AI techniques can have a monitoring of heart rate, blood pressure, tracking patient's sleep patterns. This is achieved through smart watches, smartphones, and biosensors [32].AI enabled software can also be used in intensive care units for examining and monitoring the cardiovascular and respiratory vital parameters.

Patient care

Use of robots in health care sector helps in providing assistance for the elderly and the disabled. They help in delivering medicines, meals and materials paving way for improving the quality of life. This reduces human support and also helps in regulating their day-to-day activities [33].Human-machine interfaces designed on the basis of analysing the facial expressions help disabled persons in controlling the movement of their robot assisted vehicles or even their wheel chairs, eliminating the use of sensors or joysticks previously designed to control them. Use of AI in motion analysis helps to raise an alarm in case of hazardous actions and thus prevent them.

Administrative applications

An application of AI in administrative activities helps save lots of time of the healthcare workers. Areas for utilization of AI include claim processing, management of medical records, clinical documentation and revenue cycle management [34]. It simplifies the tasks of verifying the claims, matching data across various databases, performing data audits and in payments. They can be utilized in areas like scheduling appointments and in refilling of the prescriptions.

Applications in the field of medicine

Diagnosis

In order to improve the accuracy of treatment, proper and timely diagnosis is the major requisite. AI has helped the physicians in accurate diagnosis of several diseases like acute myocardial infarction, abdominal pain and appendicitis. Biosensors and biochips are the key elements that aid in such a diagnosis. Examples include integration of glucose sensors in insulin delivery system. In the management of cancer, AI helps in distinguishing the changes caused in prostate as benign or malignant and also helps to predict the survival rates of patients suffering from colon cancer. It was also used in assessing the stage of diabetic retinopathy and stage of skin cancer [23]. ANN techniques have been used in diagnosis of acute myocardial infarction by using input data available with the physicians regarding the patients who arrived at the emergency department with acute anterior chest pain [35].

Robotic surgeries

Surgical robots help the surgeons to form minor invasive incisions and to stitch the wounds. Surgical procedures performed with the help of these robots include gynaecologic surgery, prostate surgery and surgeries related to head and neck.

PHARMACEUTICAL COMPANIES AND THEIR COLLABORATIONS FOR AI

Most of the pharmaceutical companies either acquired the technology for AI or have collaborated with tech giants for AI. This is a step up in the field of drug discovery and designing. It slices down the cost of new drugs and also permits personalization research and development process (Table S1) (Supplementary).

AI tools used in healthcare sector and other research areas

In present scenario, drug design, synthesis and development is a costly affair. Low efficacy, time consumption and off-target delivery are the hurdles and challenges. Complexity in drug discovery and development process imposed to market a new or existing drug for new indications in minimum time. AI and machine learning is the alternate for this and played a crucial role. AI is implemented in structure-based virtual screening, peptide synthesis and small molecule design, 3D structure of proteins, DNA and RNA, de novo drug design, prediction of protein folding and protein–protein interactions, structure based and ligand based virtual screening, QSAR modelling and drug repurposing, drug repositioning, prediction of physicochemical properties and bioactivity, prediction of mode of action and toxicity of compounds, toxicity study, identification of molecular pathways and polypharmacology. Many AI tools used in various areas of pharmacy and research are listed out in Table S2 (Supplementary) with applications.

CHALLENGES

Though AI proves to possess extensive potential to aid in various domains of human life, adoption of the technique is still challenging. Unfamiliarity of the technology and lack of proper infrastructure in the field of information technology prove to be the biggest hurdles in the development of AI. Limited skilled pool in data science causes delayed hiring and crunches opportunities to scale multiple AI projects. To what extent AI can be adapted into daily life still remains a query. Maintaining privacy of the patient information, guaranteed security of the data and IP issues are major hurdles to AI [36].

CONCLUSION

The shift in the technology towards the techniques combined with automation as in case of AI prove to be both challenging and also provide enormous opportunities to the research scientists. AI enabled technologies are emerging as crucial tools in driving many advances and in being able to revolutionize in the field of science and technology. This progress has triggered a wave of collaborations with software firms and led to establishment of start-ups which employ the

technology of AI in various domains of human life. Majority of the pharmaceutical companies are also exploring the utilization of AI driven solutions. They are working towards adopting this technology to integrate into drug discovery and development and also in healthcare sectors to slice down the cost of new drugs in terms of amount spent for R&D. The future will witness the advancements in AI to be able to transform many aspects of human life especially in the field of healthcare sector. AI systems to be adapted into daily life need approvals from regulatory authorities, should be standardised for uniformity of their function and need to be updated over the time.

LIST OF ABBREVIATIONS

AI: Artificial intelligence

ANNs: Artificial neural networks

API: Active pharmaceutical ingredient

DL: Deep learning

ML: Machine learning

RF: Random forest

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

REFERENCES

1. Yilong Y, Zhuyifan Y, Yan S, Qianqian Z, Xianoshan L, Defang O. Deep learning for *in vitro* prediction of pharmaceutical formulations. Acta Pharm Sin B. 2019;9(1):177-85.
2. ZhaoyiCh, Xiong L, William H, Elizabeth S, Jiang B. Applications of artificial intelligence in drug development using real-world data. Drug Discov *Today.*2021;26(5):1256-64.
3. Ade MU, Afandi S, Yuswardi, Phong TN. Role of artificial intelligence in pharma science. J Crit Rev. 2020;7(1):291-3.
4. Abhinav GVKS, Naga SS. Artificial intelligence in healthcare. J drug deliv ther. 2019;9(5):164-6.
5. Georgios M, Salvador A, Nilay S. Diagnostic tools of energy performance for supermarkets using artificial neural network algorithms. Energy Build.2013;62:304-14.
6. Agatonovic K, Beresford R. Basic concepts of artificial neural network (ANN) modeling and its application in pharmaceutical research. J Pharm Biomed Anal.2000;22:717-27.
7. Oludare IA, Aman J, Abiodun EO, Kemi VD, Nachaat AM, Humaira A. Start-of-the-art in artificial neural network applications: A Survey. Heliyon. 2018;4(11):e00938.
8. YixinCh, Shilpa ST, Reba AF, Mark SK, Ronald LR, Atul JS. Prediction of drug content and hardness of intact tablets using artificial neural network and near-infrared spectroscopy. Drug Dev Ind Pharm. 2001;27(7):623-31.
9. Tuncer D, Jonathan H, Sibel I, Yalcin O. Prediction of skin penetration using

artificial neural network modeling. J Pharm Sci. 2003;92(3):656-64.

10. Raju V, Mohd J, Ibrahim HK, Abid H. Artificial intelligence applications for COVID-19 pandemic. Diabetes MetabSyndr2020;14:337-9.
11. Sudipta D, Rimi D, Amit KN. Artificial intelligence in pharmacy. Indian J Pharm Educ Res. 2021;55(2):304-18.
12. Allan MJ. Artificial intelligence in drug design- the storm before the calm? ACS Med Chem Lett. 2018;9:1150-2.
13. Kit KM, Mallikarjuna RP. Artificial intelligence in drug development: present status and future prospects. Drug Discov*Today*. 2019;24 (3):773-80.
14. Mingkun Lu, Jiayi Yin, Qi Zhu, Gaole Lin, Minjie Mou, Fuyao Liu, Ziqi Pan. Artificial Intelligence in Pharmaceutical Sciences. Engineering. 2023. https://doi.org/10.1016/j.eng.2023.01.014.
15. Sahu A, Mishra J, Kushwaha N. Artificial Intelligence (AI) in Drugs and Pharmaceuticals. Comb Chem High Throughput Screen. 2022;25(11):1818-37.
16. Babu NJ, Nangia A. Solubility advantage of amorphous drugs and pharmaceutical cocrystals. Cryst Growth Des. 2011;11(7):2662–79.
17. Yalkowsky SH. Techniques of solubilization of drugs: PharmaMed Press; 1981.
18. Damiati SA, Martini LG, Smith NW, Lawrence MJ, Barlow DJ. Application of machine learning in prediction of hydrotropeenhanced solubilisation of indomethacin. Int J Pharm. 2017;530(1–2):99–106.
19. Chen G, Luo X, Zhang H, Fu K, Liang Z, Rongwong W, et al. Artificial neural network models for the prediction of CO2 solubility in aqueous amine solutions. Int J Greenhouse Gas Control. 2015;39:174–84.
20. Meesattham S, Charoensiritanasin P, Ongwattanakul S, Liang Z, Tontiwachwuthikul P, Sema T. Predictions of equilibrium solubility and mass transfer coefficient for CO2 absorption into aqueous solutions of 4-diethylamino-2-butanol using artificial neural networks. Petroleum 2020;6(4):385-91.
21. Ye Z, Yang Y, Li X, Cao D, Ouyang D. An integrated transfer learning and multitask learning approach for pharmacokinetic parameter prediction. Mol Pharm. 2018;16(2):533–41.
22. Debleena P, Gaurav S, Snehal S, Dnyaneshwar K, Kiran K, Rakesh KT. Artificial intelligence in drug discovery and development. Drug Discov *Today*.2021;26(1):80-93.
23. Emilija JK, Dimitrije AP, Miroslava DZ. Applications of artificial intelligence in medicine and pharmacy- ethical aspects. ActaMedicaMedianae 2019;58(3):128-37.
24. Prital S, Vineeta VK. Pharmaceutical applications of artificial intelligence. Int JPharm Res Health Sci. 2018;6(2):2342-45.
25. Parichechr H, Fatemeh A, Rassoul D. The significance of artificial intelligence in

drug delivery system and design. Adv Drug Deliv Rev.2019;151:169-90.

26. Ricardo S, Robin Z, Piedad G, Sonia A, Enrique O, Humbert G. Predicting coated-nanoparticle drug release systems with perturbation-theory machine learning (PTML) models. Nanoscale.2020;12:13471.
27. Haoshi G, Haoyue J, Jie D, Xinggang Y, Haifeng L, Defang O. Integrated *in silico* formulation design of self-emulsifying drug delivery systems. Acta Pharm Sin B. 2021.2021;11(11):3585-3594.
28. Zhao J, Xu P, Liu X, Ji X, Li M, Dev S, et al. Application of machine learning methods for the development of antidiabetic drugs. Curr Pharm Des. 2022;28(4):260-271.
29. Philip JH, Hakan W, Alan S, Johan K, Victor M, Andreas H, et al., Deep-learning models for lipid nanoparticle-based drug delivery. Nanomedicine. 2021;16(13):1097–110.
30. KrishnaveniCh, Swapna A, Sharma JVC, Divya K. Artificial intelligence in pharma industry- A review. Int J Innov Pharm Sci Res 2019;7(10);37-50.
31. Sandeep R, John F, Maulik PP. Artificial intelligence- enabled healthcare delivery. J R Soc Med. 2019;112(1):22-8.
32. Pavel H, Johanne T. Artificial intelligence in medicine. Metab. Clin. Exp.2017;69:36-40.
33. Guoguang R, Arnaldo M, Elie BA, Bo Z, Mohamad S. Artificial intelligence in healthcare: Review and prediction case studies. Engineering 2020;6:291-301.
34. Thomas D, Ravi K. The potential for artificial intelligence in healthcare. Future Healthc J. 2019;6(2):94-8.
35. William GB. Use of an artificial neural network for data analysis in clinical decision-making: The diagnosis of acute coronary occlusion. Neural Comput.1990;2:480-9.
36. Francesca L. Artificial intelligence in drug discovery: what is new, and what is next? Future DrugDiscov2019;1:2
37. Edgar R, Domrachev M, Lash AE. Gene express omnibus: NCBI gene expression and hybridization array data repository. Nucleic Acids Res. 2002;30(1):207–210.
38. Wang Z, Jensen MA, Zenklusen JC. A practical guide to The Cancer Genome Atlas (TCGA). In: Methods in Molecular Biology 2016;1418:111–41:
39. Parkinson H, Kapushesky M, Shojatalab M, Abeygunawardena N, Coulson R, Farne A, et al., ArrayExpress--a public database of microarray experiments and gene expression profiles. Nucleic Acids Res. 2007;35:D747-50.
40. vanIJzendoorn DGP, Szuhai K, Briaire-de Bruijn IH, Kostine M, Kuijjer ML, Bovée JVMG. Machine learning analysis of gene expression data reveals novel diagnostic and prognostic biomarkers and identifies therapeutic targets for soft tissue sarcomas. PLoSComput Biol. 2019;15(2):e1006826.
41. Beck T, Shorter T, Brookes AJ. GWAS Central: a comprehensive resource for the discovery and comparison of genotype and phenotype data from genome-wide

association studies. Nucleic Acids Res. 2020;48(D1):D933-40.

42. Buniello A, MacArthur JAL, Cerezo M, Harris LW, Hayhurst J, Malangone C, et al., The NHGRI-EBI GWAS Catalog of published genome-wide association studies, targeted arrays and summary statistics 2019. Nucleic Acids Res. 2019;47(D1):D1005-12.
43. Li J, Yuan X, March ME, Yao X, Sun Y, Chang X, et al., Identification of Target Genes at Juvenile Idiopathic Arthritis GWAS Loci in Human Neutrophils. Front Genet. 2019;10:181.
44. Leinonen R, Sugawara H, Shumway M. International Nucleotide Sequence Database Collaboration. The sequence read archive. Nucleic Acids Res. 2011;39:D19-21.
45. Jensen MA, Ferretti V, Grossman RL, Staudt LM. The NCI genomic data commons as an engine for precision medicine. Blood 2017;130(4):453–9.
46. Kim S, Chen J, Cheng T, Gindulyte A, He J, He S, et al., PubChem in 2021: new data content and improved web interfaces. Nucleic Acids Res. 2021;49(D1):D1388-95.
47. Mendez D, Gaulton A, Bento AP, Chambers J, De Veij M, Félix E, et al., ChEMBL: towards direct deposition of bioassay data. Nucleic Acids Res. 2019;47(D1):D930-40.
48. Wishart DS, Knox C, Guo AC, Cheng D, Shrivastava S, Tzur D, etal.,DrugBank: a knowledgebase for drugs, drug actions and drug targets. Nucleic Acids Res. 2008;36:D901-6.
49. Zhang DH, Wu KL, Zhang X, Deng SQ, Peng B. In silico screening of Chinese herbal medicines with the potential to directly inhibit 2019 novel coronavirus. J Integr Med. 2020;18(2):152-8.
50. Rose PW, Prlić A, Altunkaya A, Bi C, Bradley AR, Christie CH, et al., The RCSB protein data bank: integrative view of protein, gene and 3D structural information. Nucleic Acids Res. 2017;45(D1):D271-81.
51. Xu Z, Yang L, Zhang X, Zhang Q, Yang Z, Liu Y, et al., Discovery of Potential Flavonoid Inhibitors Against COVID-19 3CL Proteinase Based on Virtual Screening Strategy. Front MolBiosci. 2020;29;7:556481.
52. Powles J, Hodson H. Google DeepMind and healthcare in an age of algorithms. Health Technol (Berl). 2017;7(4):351-67.
53. AlQuraishi M. End-to-End differentiable learning of protein structure. Cell Syst2019;8:292-301.e3.
54. Domenico A, Nicola G, Daniela T, Fulvio C, Nicola A, Orazio N. De novo drug design of targeted chemical libraries based on artificial intelligence and pair-based multiobjective optimization. J ChemInf Model 2020;60:4582–93.
55. Yuan Y, Pei J, Lai L. LigBuilder V3: A Multi-Target *de novo* Drug Design Approach. Front Chem. 2020;28;8:142.
56. Popova M, Isayev O, Tropsha. Deep reinforcementlearning for de novo drug design. SciAdv2018;4:1–15.

57. Jang G, Lee T, Hwang S, Park C, Ahn J, Seo S, et al., PISTON: Predicting drug indications and side effects using topic modeling and natural language processing. J Biomed Inform. 2018;87:96-107.
58. Piñero J, Bravo À, Queralt-Rosinach N, Gutiérrez-Sacristán A, Deu-Pons J, Centeno E, et al., DisGeNET: a comprehensive platform integrating information on human disease-associated genes and variants. Nucleic Acids Res. 2017 Jan 4;45(D1):D833-9.
59. Szklarczyk D, Gable AL, Lyon D, Junge A, Wyder S, Huerta-Cepas J, et al., STRING v11:protein-protein association networks with increased coverage, supporting functional discovery in genome-wide experimental datasets. Nucleic Acids Res. 2019;47(D1):D607–13
60. Szklarczyk D, Santos A, von Mering C, Jensen LJ, Bork P, Kuhn M. STITCH 5: augmenting protein-chemical interaction networks with tissue and affinity data. Nucleic Acids Res. 2016;44(D1):D380-4.
61. Yan J, Bhadra P, Li A, Sethiya P, Qin L, Tai HK, et al. Deep-AmPEP30: improve short antimicrobial peptides prediction with deep learning.MolTher-Nucleic Acids 2020;20:82–894
62. Plisson F, Ramirez-Sanchez O, Martinez-Hernandez C. Machine learning-guided discovery and design of non-hemolytic peptides. Sci Rep 2020;10:1–19.
63. Kavousi K, Bagheri M, Behrouzi S, Vafadar S, Atanaki FF, Lotfabadi BT, Ariaeenejad et al. IAMPE: NMR-Assisted Computational Prediction of Antimicrobial Peptides. J ChemInf Model. 2020;60(10):4691-701.
64. Pantuck AJ, Lee D-K, Kee T, Wang P, Lakhotia S, Silverman MH, et al. Modulating BET bromodomain inhibitor ZEN-3694 and Enzalutamide combination dosing in a metastatic prostate cancer patient using CURATE.AI an artificial intelligence platform. Adv. Therap., 2018;1: 1800104.
65. Julkunen H, Cichonska A, Gautam P. Leveraging multi-way interactions for systematic prediction of pre-clinical drug combination effects. Nat Commun 2020;11,6136.
66. Sharabiani A, Bress A, Douzali E, Darabi H. Revisiting warfarin dosing using machine learning techniques. Comput Math Methods Med.2015;560108:1-9.
67. Rollinger JM, Stuppner H, Langer T. Virtual screening for the discovery of bioactive natural products. Prog Drug Res 2008;65:212–49.
68. Schuster D, Maurer EM, Laggner C, Nashev LG, Wilckens T, Lange T, et al. The discovery of new 11β-hydroxysteroid dehydrogenase type 1 inhibitors by common feature pharmacophoremodeling and virtual screening. J Med Chem 2006;49:3454–66.
69. Merget B, Turk S, Eid S, Rippmann F, Fulle S. Profiling Prediction of Kinase Inhibitors: Toward the Virtual Assay. J Med Chem. 2017;60(1):474-85.

70. Du X, Sun S, Hu C, Yao Y, Yan Y, Zhang Y. DeepPPI: Boosting Prediction of Protein-Protein Interactions with Deep Neural Networks. J ChemInf Model. 2017;57(6):1499-510.
71. Chatterjee P, Basu S, Kundu M, Nasipuri M, Plewczynski D. PPI_SVM: prediction of protein-protein interactions using machine learning, domain-domain affinities and frequency tables. Cell MolBiolLett. 2011;16(2):264-78.
72. Gupta R, Srivastava D, Sahu M, Tiwari S, Ambasta RK, Kumar P. Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Mol Divers. 2021;25(3):1315-60.
73. Wang Q, Xu J, Li Y, Huang J, Jiang Z, Wang Y, et al., Identification of a novel protein arginine methyltransferase 5 inhibitor in non-small cell lung cancer by structure-based virtual screening. Front Pharmacol. 2018;9:173.
74. Wang Y, Dou X, Jiang L, Jin H, Zhang L, Zhang L, et al. Discovery of novel glycogen synthase kinase-3α inhibitors: Structure-based virtual screening, preliminary SAR and biological evaluation for treatment of acute myeloid leukemia. Eur J Med Chem. 2019;171:221-34.
75. Yousuf Z, Iman K, Iftikhar N, Mirza MU. Structure-based virtual screening and molecular docking for the identification of potential multi-targeted inhibitors against breast cancer. Breast Cancer (Dove Med Press). 2017;9:447-59.
76. Vu BT, Vassilev L. Small-molecule inhibitors of the p53-MDM2 interaction. Curr. Top MicrobiolImmunol. 2011;348:151-72.
77. Kong Y, Bender A, Yan A. Identification of Novel Aurora Kinase A (AURKA) Inhibitors via Hierarchical Ligand-Based Virtual Screening. J ChemInf Model. 2018;58(1):36-47.
78. Yu M, Gu Q, Xu J. Discovering new PI3Kα inhibitors with a strategy of combining ligand-based and structure-based virtual screening. J Comput Aided Mol Des. 2018;32(2):347-61.
79. Halim SA, Khan S, Khan A, Wadood A, Mabood F, Hussain J, Al-Harrasi A. Targeting Dengue Virus NS-3 Helicase by Ligand based PharmacophoreModeling and Structure based Virtual Screening. Front Chem. 2017;5:88.
80. Fu Y, Sun YN, Yi KH, Li MQ, Cao HF, Li JZ, Ye F. 3D Pharmacophore-Based Virtual Screening and Docking Approaches toward the Discovery of Novel HPPD Inhibitors. Molecules. 2017;22(6):959.
81. Amin SA, Ghosh K, Gayen S, Jha T. Chemical-informatics approach to COVID-19 drug discovery: Monte Carlo based QSAR, virtual screening and molecular docking study of some *in-house* molecules as papain-like protease (PLpro) inhibitors. J BiomolStructDyn. 2021;39(13):4764-73.
82. Ferraz WR, Gomes RA, S Novaes AL, GoulartTrossini GH. Ligand and structure-based virtual screening applied

to the SARS-CoV-2 main protease: an *in silico* repurposing study. Future Med Chem. 2020;12(20):1815-28.

83. Choudhary S, Malik YS, Tomar S. Identification of SARS-CoV-2 Cell Entry Inhibitors by Drug Repurposing Using *in silico* Structure-Based Virtual Screening Approach. Front Immunol. 2020;11:1664.
84. Halder AK, Cordeiro MNDS. Development of Multi-Target Chemometric Models for the Inhibition of Class I PI3K Enzyme Isoforms: A Case Study Using QSAR-Co Tool. Int J Mol Sci. 2019;20(17):4191.
85. Wang YL, Wang F, Shi XX, Jia CY, Wu FX, Hao GF, Yang GF. Cloud 3D-QSAR: a web tool for the development of quantitative structure-activity relationship models in drug discovery. Brief Bioinform. 2021;22(4):bbaa276.
86. Martínez V, Navarro C, Cano C, Fajardo W, Blanco A. DrugNet: network-based drug-disease prioritization by integrating heterogeneous data. Artif. Intell. Med. 2015;63(1):41-9.
87. Zhang W, Xu H, Li X, Gao Q, Wang L. DRIMC: an improved drug repositioning approach using Bayesian inductive matrix completion. Bioinformatics. 2020;36(9):2839-47.
88. Fahimian G, Zahiri J, Arab SS, Sajedi RH. RepCOOL: computational drug repositioning via integrating heterogeneous biological networks. J Transl Med. 2020;18(1):375.
89. Gallo K, Goede A, Eckert A, Moahamed B, Preissner R, Gohlke BO. PROMISCUOUS 2.0: a resource for drug-repositioning. Nucleic Acids Res. 2021;49(D1):D1373-80.
90. Zeng X, Zhu S, Liu X, Zhou Y, Nussinov R, Cheng F. deepDR: a network-based deep learning approach to in silico drug repositioning. Bioinformatics. 2019;35(24):5191-8.
91. Beck BR, Shin B, Choi Y, Park S, Kang K. Predicting commercially available antiviral drugs that may act on the novel coronavirus (SARS-CoV-2) through a drug-target interaction deep learning model. ComputStructBiotechnol J. 2020;18:784-90.
92. Rashid M. Design, synthesis and ADMET prediction of bis-benzimidazole as anticancer agent. Bioorg Chem. 2020;96:103576.
93. Jiang M, Li Z, Bian Y, Wei Z. A novel protein descriptor for the prediction of drug binding sites. BMC Bioinformatics. 2019;20:478.
94. Bhattamisra SK, Banerjee P, Gupta P, Mayuren J, Patra S, Candasamy M. Artificial Intelligence in Pharmaceutical and Healthcare Research. Big Data Cogn. Comput. 2023; 7(1):10.
95. Cañada A, Capella-Gutierrez S, Rabal O, Oyarzabal J, Valencia A, Krallinger M. LimTox: a web tool for applied text mining of adverse event and toxicity associations of compounds, drugs and genes. Nucleic Acids Res. 2017;45(W1):W484-9.
96. Pires DE, Blundell TL, Ascher DB. pkCSM: Predicting Small-Molecule

Pharmacokinetic and Toxicity Properties Using Graph-Based Signatures. J Med Chem. 2015;58(9):4066-72.

97. Cheng F, Li W, Zhou Y, Shen J, Wu Z, Liu G et al (2012) AdmetSAR: A comprehensive source and free tool for assessment of chemical ADMET properties. J ChemInf Model. **2012** *52* (11), 3099-105.
98. Uygun MT, Amudi K, Turaçlı İD, Menges N. A new synthetic approach for pyrazolo[1,5-a]pyrazine-4(5H)-one derivatives and their antiproliferative effects on lung adenocarcinoma cell line. Mol Divers. 2022;26(1):113-24.
99. Srivastava A, Siddiqui S, Ahmad R, Mehrotra S, Ahmad B, Srivastava AN. Exploring nature's bounty: identification of *Withaniasomnifera* as a promising source of therapeutic agents against COVID-19 by virtual screening and *in silico* evaluation. J BiomolStructDyn. 2020:1-51.
100. Mayr A, Klambauer G, Unterthiner T, Hochreiter S. Deep- Tox: toxicity prediction using deep learning. Front. Environ. Sci. 2016;3:80.
101. Gayvert KM, Madhukar NS, Elemento O. A Data-Driven Approach to Predicting Successes and Failures of Clinical Trials. Cell Chem Biol. 2016;23(10):1294-301.
102. Pu L, Naderi M, Liu T, Wu HC, Mukhopadhyay S, Brylinski M. eToxPred: a machine learning-based approach to estimate the toxicity of drug candidates. BMC PharmacolToxicol. 2019;20(1):2.
103. Robledo-Cadena DX, Gallardo-Pérez JC, Dávila-Borja V, Pacheco-Velázquez SC, Belmont-Díaz JA, Ralph SJ, et al.. Non-Steroidal Anti-Inflammatory Drugs Increase Cisplatin, Paclitaxel, and Doxorubicin Efficacy against Human Cervix Cancer Cells. Pharmaceuticals (Basel). 2020;13(12):463.
104. Wang J, Luo C, Shan C, You Q, Lu J, Elf S, et al. Inhibition of human copper trafficking by a small molecule significantly attenuates cancer cell proliferation. Nat Chem. 2015;7,968–79.
105. Fang J, Li Y, Liu R, Pang X, Li C, Yang R, et al. Discovery of multitarget-directed ligands against Alzheimer's disease through systematic prediction of chemical-protein interactions. J ChemInf Model. 2015; 55(1):149–64.
106. Gao L, Wang KX, Zhou YZ, Fang J, Qin X, Du G. Uncovering the anticancer mechanism of compound Kushen Injection against HCC by integrating quantitative analysis, network analysis and experimental validation. Sci Rep.2018;8,624.