International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

Relationship between Artificial Intelligence and Pharmacy Practice in the aspect of Drug Discovery and Drug Development Process

Sanjeev Kumar
Research Scholar, IEC University, Baddi, Solan, Himachal Pradesh

Date of Submission: 20-07-2024 Date of Acceptance: 30-07-2024

ABSTRACT
The need for innovative drug discovery processes has been highlighted by the COVID-19 pandemic. However, the path from developing a drug's initial concept to its final application in clinical settings is protracted, costly, and fraught with numerous possible failure spots. The exponential expansion of medical information over the past ten years has been accompanied by improvements in computer technology (cloud computing, GPUs, and TPUs), as well as the emergence of deep learning. Artificial Intelligence (AI) techniques might be used to analyze medical data derived from extensive molecular screening profiles, individual health or pathology records, and public health organizations to expedite and avoid drug discovery pipeline failures.We discuss the use of AI at several phases of the drug discovery process, including de novo design and the prediction of a drug's expected features, both of which are fundamentally computational methods. The discussion of open-source databases and AI-based software tools that aid in drug design also covers the issues with molecular representation, data collecting, complexity, labeling, and label discrepancies that are related to these issues.It is also investigated how modern AI techniques, such as graph neural networks, reinforcement learning, and generated models, in addition to structure-based approaches (such as molecular dynamics simulations and molecular docking), might aid in the study of drug reactions. Finally, this article discusses recent advancements and investments in AI-based start-up firms for biotechnology and medication creation, as well as their current state, future prospects, and advancements.

Keywords: Artificial intelligence, Biotechnology, Graph neural networks, Molecule representation

I. INTRODUCTION

Healthcare costs six to seven percent of the world's GDP (8.5 to 9 trillion US dollars) per year [1], and developing a new drug can take up to 14 years and cost well over $1 billion [2]. Across all therapeutic categories globally, drug development success (defined as phase I clinical trials through medication licensure) is quite low [3]. For instance, 97% of cancer treatments fail during clinical trials [4]. Investments become riskier as a result, and the price of approved treatments increases to make up for all the failures [5].Clinical trials, precision medicine, drug development, and health policy will all gain from data-driven approaches as a result of the digitization of medical information. Such breakthrough analytical techniques and computational developments have significantly changed drug discovery during the past ten years [6] [7] [8] [9] [10]. The use of artificial intelligence (AI) technologies to enhance many phases of the drug discovery pipeline, including de novo molecular design and optimization, structure-based drug design, and pre-clinical and clinical development, is gaining significant interest as a result of recent advancements [11]. To coordinate the tools required to find beneficial medications and their therapeutic uses, biomedical information, such as genetic profiles, imaging data, and chemical and drug databases, can be combined with analytical approaches, particularly deep learning models [12].On the use of AI in drug development, there are a lot of reviews accessible. For instance, [13] discusses the role of GPU computing and deep learning models for drug discovery; [14] discusses the application of deep learning to precision medicine; [15] discusses generative models for computing the electronic properties of materials; and [8] discusses the advancements brought about by the completion of the human genome project. [16] presents the function of machine learning and its implications for understanding biological interactions in drug development. Methods employing dynamics modeling and 3D structure-based drug discovery are presented in [17], while applications of machine learning at different phases of drug design are covered in [12].In addition to

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

presenting the function of graphs in articulating therapeutic issues as machine learning tasks, [18] also highlights the limitations and uses of AI in drug development. The development of conventional machine learning techniques for protein-ligand docking scoring functions is discussed in [22], and a scoring function based on machine learning for structure-based virtual screening is discussed in [23].Deep learning techniques have made significant advancements in the previous two years as a tool for drug development. There are several open-source tools [24], benchmark datasets [25] that are AI-ready, and deep learning platforms [26] that have been built specifically for drug creation. We provide thorough analysis and current information on these subjects.In target-based discovery, the first stage is to find new targets from a vast collection of proteins (an organism's proteome) that have evidence of relationship with illness [12]. High throughput screening of compound libraries against these targets identifies compounds that may interact. In the best case scenario, compounds will be examined in pre-clinical and clinical studies, optimized for advantageous therapeutic characteristics, and granted FDA clearance. Artificial intelligence (AI) has the potential to be useful at every stage of the drug discovery process [11], including generative models for the creation of novel synthetic molecules [30], reinforcement learning (RL) to improve the properties of molecules in a specific direction [31], and GNNs to forecast drug-disease associations, drug repurposing, and the response to a drug [32].By mining the scientific literature, natural language processing (NLP) might be utilized to locate medications and automate FDA clearance procedures. [33], [34]The atom is the essential building block of these structures and may be thought of as a "machine learning datatype" since drug discovery applications concentrate on the three-dimensional structures of molecules (proteins, DNA, RNA, and drugs/medicines) and their interactions. [35, 36] Higher-level patterns that are inadequately characterized in molecular systems can be deduced from their data. In the design of data-driven systems, features of biological data that are interrelated might be represented as graphs. In order to simulate increasingly intricate links between pharmaceuticals and disease, protein-protein interactions, side effects of drugs, and drug re-purposing, graph machine learning enables modeling of unstructured multimodal information [37].Graph machine learning may be used to find drug binding sites [38], highly communicative residues/atoms, and to produce more understandable models [39] when combined with an attention mechanism.In order to develop novel chemical entities with certain desirable traits, experimental high-throughput screening, combinatorial chemistry, and other technical procedures have traditionally been the go-to options [40]. However, AI applications now have the potential to be superior than a human expert [41 , 42].

Application and use various of data science in the process of drug discovery

The rise of pandemics and epidemics like COVID-19 and influenza [43], as well as the persistence of serious illnesses like cancer and heart disease, show the continued need for medication discovery. Target validation, high throughput screening, animal research, safety and efficacy procedures, clinical trials, and regulatory approval are often required throughout the multi-stage process [12]. On average, it takes 14.6 years and costs US$ 2.6 billion to develop a new medicine [2]. The following steps in the process might make use of AI-based methods: discovering new targets [44], analyzing drug-target interactions [45], [46], looking into disease processes [12], and enhancing small molecule compound design and optimization [47]. These techniques may also be used to find and create predictive biomarkers, as well as to research therapeutic effectiveness, responsiveness and resistance mechanisms [132].

Target specificity and identification methods in drug discovery process

When developing new drugs, target identification looks for molecules, often proteins, whose activity could change a disease state. In order to find possible targets that are probably implicated in disease pathways, machine learning algorithms may scan a variety of data sources, including gene expression profiles, protein-protein interaction networks, and genomic and proteomic data [48]. Only a little more than 3,000 of the roughly 20,000 proteins in the human proteome have been identified as possible therapeutic targets [49]. Our understanding of which proteins potentially be therapeutic targets may be expanded in the future.Establishing a causal link between the target and the illness is the first stage in target identification [50]. Graphs, GNNs, or tree-based techniques can be used to find the causal connections between genes and illnesses. To identify genes linked with morbidity that are also

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

druggable, a decision tree-based meta-classifier was suggested in [51] and trained on a network topology comprising protein-protein, metabolic, and transcriptional interactions, as well as tissue expression and sub-cellular localization of proteins.Key characteristics from the decision tree were regulation by several transcription factors (TFs), centrality in metabolic pathways, and extracellular placement. Based on characteristics including protein-protein interaction, gene expression, DNA copy number, and the presence of mutations, machine learning-based algorithms identified proteins as pharmacological targets or non-targets for certain illnesses, such as lung, pancreatic, and ovarian cancer [44]. The literature is the main source of knowledge on target association with illness. The development of databases for target identification and the identification of pertinent target-disease combinations from literature may also be accomplished using text mining and Natural Language Processing (NLP) techniques [52]. You may utilize deep learning-based tools like BeFree [53], PKDE4J [54], and others to mine articles for connections between drugs and diseases, genes and diseases, and targets and drugs [55]. Without specifically addressing the target identification of those reference ligands, drug-target interactions may also be inferred in the same cell based on descriptor similarity to reference ligands. Using a method inspired by neural networks, a software tool (SPiDER) [56] discretizes the input feature similarity vector onto a so-called feature map.

Virtual screening and optimization of compounds

Artificial intelligence (AI) may be used to digitally screen and improve substances, determine their bioactivities, and foretell protein-drug interactions [57]. The creation of prediction models that can spot substances with a high likelihood of binding to a target protein is one method AI may aid with virtual screening. These models may be trained utilizing a variety of data types, including structural details, molecular descriptors, and known protein-ligand complexes. When developing a new medicine, it is important to take into account the physico-chemical characteristics of the compound, including solubility, partition coefficient (logP), degree of ionization, and intrinsic permeability, since these may indirectly affect how the compound interacts with a target receptor family [58].

Pre-clinical and clinical development

A crucial phase in the pipeline of drug creation is predicting potential reactions to a medicine. The effectiveness of a drug-target interaction can be predicted by binding affinity or free energy of binding using similarity- or feature-based machine learning techniques. While feature-based approaches identify specific qualities of medications and targets and provide the drug-target feature vector to the classifier, similarity methods make the assumption that comparable pharmaceuticals operate on similar targets [59]. Convolution and attention mechanisms are used in deep learning-based systems like DeepConv-DTI [45] and DeepAffinity [38] to learn how to integrate medications and targets.By locating pertinent human illness biomarkers, anticipating probable hazardous or needless side effects, and filtering a high dimensional collection of clinical factors to choose a cohort of individuals, AI-based algorithms can help in the selection of suitable patients for pre-clinical studies [60]. In order to reduce the possibility of any negative effects on patients, AI can also assist in forecasting clinical trial results far in advance of the actual study [61].

FDA approval and post-market analysis

Natural Language Processing (NLP) can be used to mine scientific literature to report negative effects, such as toxicity, of a drug or resistance to it, and prepare automated evaluations for regulatory (FDA) approval or a patent application [62]. NLP-based sentiment analysis methods can be used to recommend drugs [63]. Machine learning-based systems that predict likely sales of a product could help pharmaceutical companies optimize their business resources [64].

Databases and tools for drug development

Chemical and biological databases

PubChem -There are about 111 million compounds, 279 million substances, 295 million bio-activities, and 34 million articles in PubChem [27], the biggest free library of chemical information, which is divided into three interconnected online data pages: substance, compound, and bio-assay [79]. The bio-assay database contains information about bio-assays as well as their test results. It is possible to find chemicals for a certain target or protein using data mining techniques.

ChEMBL -The European Molecular Biology Laboratory (EMBL) created the open-access drug discovery database ChEMBL [65]. From full-text articles in high-impact journals, information on

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

approved and potential drugs is acquired. This information is then integrated with information on tiny molecules and their biological activities. The bio-activity data is shared with another database, such as PubChem Bioassay and BindingDB [68]. The ChEMBL database has been applied to a variety of tasks, including the identification of chemical tools for a target of interest, the prediction of drug-target interactions, the repurposing of drugs, the assessment of target tractability, and integration with already in use drug discovery tools [29].

DrugBank - DrugBank offers clinical data, medication interactions, adverse effects, and drug repurposing in addition to molecular-level information. It is frequently used for machine learning-based drug discovery, in silico drug design, and repurposing.

UniProt database -A public database of protein sequences annotated with taxonomic information and details on biological activities is called UniProt [28]. UniProt Knowledgebase (UniProtKB), UniProt Reference Clusters (UniRef), UniProt Archive (UniParc), and UniProt Metagenomic and Environmental Sequences (UniMES) are its four constituent parts. Over 189 million records are available in Uniprot, of which more than half were selected by human specialists.

AI-based software tools used for drug development process

AlphaFold2 - It is an extremely difficult and complex challenge to predict the three-dimensional (3D) structures of proteins given their amino acid sequence. AlphaFold2, created by DeepMind, is freely accessible through Google Colab and has attained a breakthrough level of accuracy [35].

Deep Chem - A Tensorflow wrapper called DeepChem [80] simplifies and comprehends the analysis of chemical datasets. It has been applied to tasks like modeling BACE-1 inhibitors and algorithmic research on one-shot deep learning algorithms for drug development [80], [90]. DeepChem may be used to count the number of cells in a microscopic picture, estimate the solubility of small molecule medications and their binding affinity to targets, and study protein structures. The DeepChem package includes MoleculeNet [78], which covers the characteristics of 700,000 molecules.

Deeper Bind - A lengthy short-term recurrent convolutional network called DeeperBind [81] can describe the interaction between transcription factors (TF) and their corresponding (DNA/RNA) binding sites by predicting protein binding specificity in respect to DNA probes. The dynamics of probe sequences may be successfully predicted using DeeperBind. Additionally, datasets with sequences of different lengths can be used for training and testing.

II. CONCLUSION

In the health care sector, AI-based techniques are being utilized in areas including medication creation, assistance for clinical decision making, diagnosis, prevention, and providing clinical recommendations. These techniques are low-cost, clever, and versatile. It was formerly believed that experimental high-throughput screening, combinatorial chemistry, and other technological advances were superior than applications of artificial intelligence (AI). It was challenging to build brand-new chemical entities from scratch using computer algorithms, with the needed properties, maybe even better than a human specialist. By using data science techniques for target discovery, De novo molecular design, medication repurposing, retrosynthesis, and reactivity and bioactivity prediction, FDA approval, and post-market analysis, the lengthy and expensive process of drug design can be hastened. Some pharmaceutical companies have already used AI, and by 2022, it is predicted that the pharmaceutical industry would generate US $2.199 billion from AI-based solutions.

REFERENCES

[1]. Organization W.H. World Health Organization; 2017. New perspectives on global health spending for universal health coverage. Tech. Rep. [Google Scholar]

[2]. Wouters O.J., McKee M., Luyten J. Estimated research and development investment needed to bring a new medicine to market, 2009-2018. JAMA. 2020;323(9):844–853. [PMC free article] [PubMed] [Google Scholar]

[3]. Khanna I. Drug discovery in pharmaceutical industry: productivity challenges and trends. Drug Discov. Today. 2012;17(19–20):1088–1102. [PubMed] [Google Scholar]

[4]. Lin A., Giuliano C.J., Palladino A., John K.M., Abramowicz C., Yuan M.L., Sausville E.L., Lukow D.A., Liu L., Chait A.R., et al. Off-target toxicity is a common mechanism of action of cancer drugs undergoing clinical trials. Sci.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

Transl. Med. 2019;11(509) [PMC free article] [PubMed] [Google Scholar]
[5]. Freedman D.H., et al. Hunting for new drugs with ai. Nature. 2019;576(7787):S49–S53. [PubMed] [Google Scholar]
[6]. Davenport T., Kalakota R. The potential for artificial intelligence in healthcare. Future Healthc. J. 2019;6(2):94. [PMC free article] [PubMed] [Google Scholar]
[7]. Yu K.-H., Beam A.L., Kohane I.S. Artificial intelligence in healthcare. Nat. Biomed. Eng. 2018;2(10):719–731. [PubMed] [Google Scholar]
[8]. Pandey M., Fernandez M., Gentile F., Isayev O., Tropsha A., Stern A.C., Cherkasov A. The transformational role of gpu computing and deep learning in drug discovery. Nat. Mach. Intell. 2022;4(3):211–221. [Google Scholar]
[9]. Sierra-Sosa D., Garcia-Zapirain B., Castillo C., Oleagordia I., Nuño-Solinis R., Urtaran-Laresgoiti M., Elmaghraby A. Scalable healthcare assessment for diabetic patients using deep learning on multiple gpus. IEEE Trans. Ind. Inform. 2019;15(10):5682–5689. [Google Scholar]
[10]. Powles J., Hodson H. Google deepmind and healthcare in an age of algorithms. Health Technol. 2017;7(4):351–367. [PMC free article] [PubMed] [Google Scholar]
[11]. Chen H., Engkvist O., Wang Y., Olivecrona M., Blaschke T. The rise of deep learning in drug discovery. Drug Discov. Today. 2018;23(6):1241–1250. [PubMed] [Google Scholar]
[12]. Vamathevan J., Clark D., Czodrowski P., Dunham I., Ferran E., Lee G., Li B., Madabhushi A., Shah P., Spitzer M., et al. Applications of machine learning in drug discovery and development. Nat. Rev. Drug Discov. 2019;18(6):463–477. [PMC free article] [PubMed] [Google Scholar]
[13]. Zhang S., Bamakan S.M.H., Qu Q., Li S. Learning for personalized medicine: a comprehensive review from a deep learning perspective. IEEE Rev. Biomed. Eng. 2018;12:194–208. [PubMed] [Google Scholar]
[14]. Gibbs R.A. The human genome project changed everything. Nat. Rev. Genet. 2020;21(10):575–576. [PMC free article] [PubMed] [Google Scholar]
[15]. Sanchez-Lengeling B., Aspuru-Guzik A. Inverse molecular design using machine learning: generative models for matter engineering. Science. 2018;361(6400):360–365. [PubMed] [Google Scholar]
[16]. Singh M., Sharma D., Garg M., Kumar A., Baliyan A., Rani R., Kumar V. Current understanding of biological interactions and processing of dna origami nanostructures: role of machine learning and implications in drug delivery. Biotechnol. Adv. 2022 [PubMed] [Google Scholar]
[17]. Ganesan A., Coote M.L., Barakat K. Molecular dynamics-driven drug discovery: leaping forward with confidence. Drug Discov. Today. 2017;22(2):249–269. [PubMed] [Google Scholar]
[18]. Gaudelet T., Day B., Jamasb A.R., Soman J., Regep C., Liu G., Hayter J.B., Vickers R., Roberts C., Tang J., et al. Utilizing graph machine learning within drug discovery and development. Brief. Bioinform. 2021;22(6) [PMC free article] [PubMed] [Google Scholar]
[19]. Waring J., Lindvall C., Umeton R. Automated machine learning: review of the state-of-the-art and opportunities for healthcare. Artif. Intell. Med. 2020;104 [PubMed] [Google Scholar]
[20]. Deng J., Yang Z., Ojima I., Samaras D., Wang F. Artificial intelligence in drug discovery: applications and techniques. Brief. Bioinform. 2022;23(1) [PubMed] [Google Scholar]
[21]. Dara S., Dhamercherla S., Jadav S.S., Babu C., Ahsan M.J. Machine learning in drug discovery: a review. Artif. Intell. Rev. 2021:1–53. [PMC free article] [PubMed] [Google Scholar]
[22]. Shen C., Ding J., Wang Z., Cao D., Ding X., Hou T. From machine learning to deep learning: advances in scoring functions for protein–ligand docking. Wiley Interdiscip. Rev. Comput. Mol. Sci. 2020;10(1) [Google Scholar]
[23]. Li H., Sze K.-H., Lu G., Ballester P.J. Machine-learning scoring functions for structure-based virtual screening. Wiley Interdiscip. Rev. Comput. Mol.

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

Sci. 2021;11(1) [PMC free article] [PubMed] [Google Scholar]

[24]. Huang K., Fu T., Glass L.M., Zitnik M., Xiao C., Sun J. Deeppurpose: a deep learning library for drug–target interaction prediction. Bioinformatics. 2020;36(22–23):5545–5547. [PMC free article] [PubMed] [Google Scholar]

[25]. K. Huang, T. Fu, W. Gao, Y. Zhao, Y. Roohani, J. Leskovec, C.W. Coley, C. Xiao, J. Sun, M. Zitnik, Therapeutics data commons: machine learning datasets and tasks for therapeutics, arXiv e-prints, 2021.

[26]. Zhu Z., Shi C., Zhang Z., Liu S., Xu M., Yuan X., Zhang Y., Chen J., Cai H., Lu J., et al. Torchdrug: a powerful and flexible machine learning platform for drug discovery.
2022. arXiv:2202.08320 preprint.

[27]. Kim S., Thiessen P.A., Bolton E.E., Chen J., Fu G., Gindulyte A., Han L., He J., He S., Shoemaker B.A., et al. Pubchem substance and compound databases. Nucleic Acids Res. 2016;44(D1):D1202–D1213. [PMC free article] [PubMed] [Google Scholar]

[28]. Consortium U. Uniprot: a hub for protein information. Nucleic Acids Res. 2015;43(D1):D204–D212. [PMC free article] [PubMed] [Google Scholar]

[29]. Mendez D., Gaulton A., Bento A.P., Chambers J., De Veij M., Félix E., Magariños M.P., Mosquera J.F., Mutowo P., Nowotka M., et al. Chembl: towards direct deposition of bioassay data. Nucleic Acids Res. 2019;47(D1):D930–D940. [PMC free article] [PubMed] [Google Scholar]

[30]. Kadurin A., Nikolenko S., Khrabrov K., Aliper A., Zhavoronkov A. drugan: an advanced generative adversarial autoencoder model for de novo generation of new molecules with desired molecular properties in silico. Mol. Pharm. 2017;14(9):3098–3104. [PubMed] [Google Scholar]

[31]. Khemchandani Y., O'Hagan S., Samanta S., Swainston N., Roberts T.J., Bollegala D., Kell D.B. Deepgraphmolgen, a multi-objective, computational strategy for generating molecules with desirable properties: a graph convolution and reinforcement learning approach. J. Cheminform. 2020;12(1):1–17. [PMC free article] [PubMed] [Google Scholar]

[32]. Li Y., Zhang L., Liu Z. Multi-objective de novo drug design with conditional graph generative model. J. Cheminform. 2018;10(1):1–24. [PMC free article] [PubMed] [Google Scholar]

[33]. Moingeon P., Kuenemann M., Guedj M. Artificial intelligence-enhanced drug design and development: toward a computational precision medicine. Drug Discov. Today. 2021 [PubMed] [Google Scholar]

[34]. Basit S.A., Qureshi R., Musleh S., Guler R., Rahman M.S., Biswas K.H., Alam T. COVID-19base v3: update of the knowledgebase for drugs and biomedical entities linked to Covid-19. Front. Public Health. 2023;11 [PMC free article] [PubMed] [Google Scholar]

[35]. Jumper J., Evans R., Pritzel A., Green T., Figurnov M., Ronneberger O., Tunyasuvunakool K., Bates R., Žídek A., Potapenko A., et al. Highly accurate protein structure prediction with alphafold. Nature. 2021;596(7873):583–589. [PMC free article] [PubMed] [Google Scholar]

[36]. Moult J., Fidelis K., Kryshtafovych A., Schwede T., Tramontano A. Critical assessment of methods of protein structure prediction (casp)—round x. Proteins, Struct. Funct. Bioinform. 2014;82:1–6. [PMC free article] [PubMed] [Google Scholar]

[37]. Baltrušaitis T., Ahuja C., Morency L.-P. Multimodal machine learning: a survey and taxonomy. IEEE Trans. Pattern Anal. Mach. Intell. 2018;41(2):423–443. [PubMed] [Google Scholar]

[38]. Karimi M., Wu D., Wang Z., Shen Y. Deepaffinity: interpretable deep learning of compound–protein affinity through unified recurrent and convolutional neural networks. Bioinformatics. 2019;35(18):3329–3338. [PMC free article] [PubMed] [Google Scholar]

[39]. Angermueller C., Pärnamaa T., Parts L., Stegle O. Deep learning for computational biology. Mol. Syst. Biol. 2016;12(7):878. [PMC free article] [PubMed] [Google Scholar]

[40]. Geromichalos G.D., Alifieris C.E., Geromichalou E.G., Trafalis D.T. Overview on the current status of virtual

high-throughput screening and combinatorial chemistry approaches in multi-target anticancer drug discovery; part I. J. Buon. 2016;21(4):764–779. [PubMed] [Google Scholar]

[41]. Schneider G. An insight into artificial intelligence in drug discovery: an interview with professor gisbert Schneider. Expert Opin. Drug Discov. 2021;16(9):933–935. [PubMed] [Google Scholar]

[42]. Wang Y., Ribeiro J.M.L., Tiwary P. Machine learning approaches for analyzing and enhancing molecular dynamics simulations. Curr. Opin. Struct. Biol. 2020;61:139–145. [PubMed] [Google Scholar]

[43]. Zheng Y., Ma Y., Zhang J., Xie X. 2020. Covid-19 and the cardiovascular system, nature reviews cardiology. [PMC free article] [PubMed] [Google Scholar]

[44]. Jeon J., Nim S., Teyra J., Datti A., Wrana J.L., Sidhu S.S., Moffat J., Kim P.M. A systematic approach to identify novel cancer drug targets using machine learning, inhibitor design and high-throughput screening. Gen. Med. 2014;6(7):1–18. [PMC free article] [PubMed] [Google Scholar]

[45]. Lee I., Keum J., Nam H. Deepconv-dti: prediction of drug-target interactions via deep learning with convolution on protein sequences. PLoS Comput. Biol. 2019;15(6) [PMC free article] [PubMed] [Google Scholar]

[46]. Katsila T., Spyroulias G.A., Patrinos G.P., Matsoukas M.-T. Computational approaches in target identification and drug discovery. Comput. Struct. Biotechnol. J. 2016;14:177–184. [PMC free article] [PubMed] [Google Scholar]

[47]. Nicolaou C.A., Brown N. Multi-objective optimization methods in drug design. Drug Discovery Today. Technologies. 2013;10(3):e427–e435. [PubMed] [Google Scholar]

[48]. Sliwoski G., Kothiwale S., Meiler J., Lowe E.W. Computational methods in drug discovery. Pharmacol. Rev. 2014;66(1):334–395. [PMC free article] [PubMed] [Google Scholar]

[49]. Bakheet T.M., Doig A.J. Properties and identification of human protein drug targets. Bioinformatics. 2009;25(4):451–457. [PubMed] [Google Scholar]

[50]. Lv B.-M., Quan Y., Zhang H.-Y. Causal inference in microbiome medicine: principles and applications. Trends Microbiol. 2021;29(8):736–746. [PubMed] [Google Scholar]

[51]. Costa P.R., Acencio M.L., Lemke N. BMC Genomics. vol. 11. Springer; 2010. A machine learning approach for genome-wide prediction of morbid and druggable human genes based on systems-level data; pp. 1–15. [PMC free article] [PubMed] [Google Scholar]

[52]. Khan J.Y., Khondaker M.T.I., Hoque I.T., Al-Absi H.R., Rahman M.S., Guler R., Alam T., Rahman M.S. Toward preparing a knowledge base to explore potential drugs and biomedical entities related to Covid-19: automated computational approach. JMIR Med. Inform. 2020;8(11) [PMC free article] [PubMed] [Google Scholar]

[53]. Bravo À., Piñero J., Queralt-Rosinach N., Rautschka M., Furlong L.I. Extraction of relations between genes and diseases from text and large-scale data analysis: implications for translational research. BMC Bioinform. 2015;16(1):1–17. [PMC free article] [PubMed] [Google Scholar]

[54]. Song M., Kim M., Kang K., Kim Y.H., Jeon S. Application of public knowledge discovery tool (pkde4j) to represent biomedical scientific knowledge. Front. Res. Metr. Anal. 2018;3:7. [Google Scholar]

[55]. Alam T., Schmeier S. Multiple Perspectives on Artificial Intelligence in Healthcare. Springer; 2021. Deep learning in biomedical text mining: contributions and challenges; pp. 169–184. [Google Scholar]

[56]. Reker D., Rodrigues T., Schneider P., Schneider G. Identifying the macromolecular targets of de novo-designed chemical entities through self-organizing map consensus. Proc. Natl. Acad. Sci. 2014;111(11):4067–4072. [PMC free article] [PubMed] [Google Scholar]

[57]. Álvarez-Machancoses Ó., Fernández-Martínez J.L. Using artificial intelligence methods to speed up drug discovery. Expert Opin. Drug Discov. 2019;14(8):769–777. [PubMed] [Google Scholar]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 620-628 www.ijprajournal.com ISSN: 2456-4494

[58]. Zang Q., Mansouri K., Williams A.J., Judson R.S., Allen D.G., Casey W.M., Kleinstreuer N.C. In silico prediction of physicochemical properties of environmental chemicals using molecular fingerprints and machine learning. J. Chem. Inf. Model. 2017;57(1):36–49. [PMC free article] [PubMed] [Google Scholar]

[59]. Sachdev K., Gupta M.K. A comprehensive review of feature based methods for drug target interaction prediction. J. Biomed. Inform. 2019;93 [PubMed] [Google Scholar]

[60]. Woo M. An ai boost for clinical trials. Nature. 2019;573(7775) [PubMed] [Google Scholar]

[61]. Harrer S., Shah P., Antony B., Hu J. Artificial intelligence for clinical trial design. Trends Pharmacol. Sci. 2019;40(8):577–591. [PubMed] [Google Scholar]

[62]. Shi Y., Ren P., Zhang Y., Gong X., Hu M., Liang H. Information extraction from fda drug labeling to enhance product-specific guidance assessment using natural language processing. Front. Res. Metr. Anal. 2021;6 [PMC free article] [PubMed] [Google Scholar]

[63]. Garg S. 2021 11th International Conference on Cloud Computing, Data Science & Engineering (Confluence) IEEE; 2021. Drug recommendation system based on sentiment analysis of drug reviews using machine learning; pp. 175–181. [Google Scholar]

[64]. Khalil Zadeh N., Sepehri M.M., Farvaresh H. Intelligent sales prediction for pharmaceutical distribution companies: a data mining based approach. Math. Probl. Eng. 2014;2014 [Google Scholar]

[65]. Gaulton A., Bellis L.J., Bento A.P., Chambers J., Davies M., Hersey A., Light Y., McGlinchey S., Michalovich D., Al-Lazikani B., et al. Chembl: a large-scale bioactivity database for drug discovery. Nucleic Acids Res. 2012;40(D1):D1100–D1107. [PMC free article] [PubMed] [Google Scholar]

[66]. Wishart D.S., Knox C., Guo A.C., Cheng D., Shrivastava S., Tzur D., Gautam B., Hassanali M. Drugbank: a knowledgebase for drugs, drug actions and drug targets. Nucleic Acids Res. 2008;36(suppl_1):D901–D906. [PMC free article] [PubMed] [Google Scholar]

[67]. Irwin J.J., Shoichet B.K. Zinc- a free database of commercially available compounds for virtual screening. J. Chem. Inf. Model. 2005;45(1):177–182. [PMC free article] [PubMed] [Google Scholar]

[68]. Gilson M.K., Liu T., Baitaluk M., Nicola G., Hwang L., Chong J. Bindingdb in 2015: a public database for medicinal chemistry, computational chemistry and systems pharmacology. Nucleic Acids Res. 2016;44(D1):D1045–D1053. [PMC free article] [PubMed] [Google Scholar]

[69]. Di L., Kerns E. Academic Press; 2015. Drug-Like Properties: Concepts, Structure Design and Methods from ADME to Toxicity Optimization. [Google Scholar]

[70]. Szklarczyk D., Santos A., Von Mering C., Jensen L.J., Bork P., Kuhn M. Stitch 5: augmenting protein–chemical interaction networks with tissue and affinity data. Nucleic Acids Res. 2016;44(D1):D380–D384. [PMC free article] [PubMed] [Google Scholar]

[71]. Kuhn M., Letunic I., Jensen L.J., Bork P. The sider database of drugs and side effects. Nucleic Acids Res. 2016;44(D1):D1075–D1079. [PMC free article] [PubMed] [Google Scholar]

[72]. Yang W., Soares J., Greninger P., Edelman E.J., Lightfoot H., Forbes S., Bindal N., Beare D., Smith J.A., Thompson I.R., et al. Genomics of drug sensitivity in cancer (gdsc): a resource for therapeutic biomarker discovery in cancer cells. Nucleic Acids Res. 2012;41(D1):D955–D961. [PMC free article] [PubMed] [Google Scholar]

[73]. Wang R., Fang X., Lu Y., Yang C.-Y., Wang S. The pdbbind database: methodologies and updates. J. Med. Chem. 2005;48(12):4111–4119. [PubMed] [Google Scholar]

[74]. Coker E.A., Mitsopoulos C., Tym J.E., Komianou A., Kannas C., Di Micco P., Villasclaras Fernandez E., Ozer B., Antolin A.A., Workman P., et al. cansar: update to the cancer translational research and drug discovery knowledgebase. Nucleic Acids Res. 2019;47(D1):D917–D922. [PMC free article] [PubMed] [Google Scholar]

[75]. Berman H.M., Westbrook J., Feng Z., Gilliland G., Bhat T.N., Weissig H., Shindyalov I.N., Bourne P.E. The protein data bank. Nucleic Acids Res. 2000;28(1):235–242. [PMC free article] [PubMed] [Google Scholar]
[76]. Townshend R.J., Vögele M., Suriana P., Derry A., Powers A., Laloudakis Y., Balachandar S., Jing B., Anderson B., Eismann S., et al. Atom3d: tasks on molecules in three dimensions. 2020. arXiv:2012.04035 preprint.
[77]. Chen X., Ji Z.L., Chen Y.Z. Ttd: therapeutic target database. Nucleic Acids Res. 2002;30(1):412–415. [PMC free article] [PubMed] [Google Scholar]
[78]. Wu Z., Ramsundar B., Feinberg E.N., Gomes J., Geniesse C., Pappu A.S., Leswing K., Pande V. Moleculenet: a benchmark for molecular machine learning. Chem. Sci. 2018;9(2):513–530. [PMC free article] [PubMed] [Google Scholar]
[79]. Wang Y., Bryant S.H., Cheng T., Wang J., Gindulyte A., Shoemaker B.A., Thiessen P.A., He S., Zhang J. Pubchem bioassay: 2017 update. Nucleic Acids Res. 2017;45(D1):D955–D963. [PMC free article] [PubMed] [Google Scholar]
[80]. Ramsundar B. Stanford University; 2018. Molecular machine learning with DeepChem. PhD thesis. [Google Scholar]