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Artificial intelligence (AI) is paving the way for a critical role in drug discovery, drug design, and studying drug–drug interactions – correspondence

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Dear Editor,

In the pharmaceutical sector, there has been a sudden acceleration in the digitalization of data over the past few years. This digitalization has come with challenges to acquire, scrutinize, and apply such particular knowledge for reaching solutions to complex clinical problems, which has ultimately motivated applications of artificial intelligence (AI) as it is able to handle huge volumes of data with augmentation of automation. AI is a system based on technology involving several modern tools and networks that mimic the intelligence of humans. Side by side, there is no threat of the physical presence of humans being completely replaced by AI. Potential applications of AI are being extended continuously in the field of pharmaceuticals, and developing pharmaceutical products from the bench to the side of the bed is imaginably provided[1]. AI can help in designing drugs rationally, assist in decision-making, help in the determination of the correct therapeutic management of patients, and be wisely exploited for developing drugs in the future. Eularis has developed an AI platform for analysis and making decisions known as E-VAI (Eularis Virtual Analytics Interface) that uses machine learning (ML) algorithms along with an easily usable user interface for creating analytical roadmaps. This helps executives in marketing allocate resources for maximum share gain in the market and reverse poor sales[2].

Various case studies have identified the potential use of AI in the discovery of drugs. AI is being successfully used for the identification of novel compounds for treating cancer. Researchers have trained a deep learning (DL) algorithm upon a huge dataset of known compounds related to cancer and their corresponding biological activity. Novel compounds with greater potential for the treatment of cancer have been obtained as an output. This demonstrates the capability of the method for discovering new candidates for therapy. Recently, the utility of ML for the identification of small molecule inhibitors of the mitogen-activated protein kinase/ERK kinase (MEK) 22 has been described. MEK is also a target for treating cancer, but developing efficacious inhibitors is a challenge for scientists. In this context, the identification of novel inhibitors of this protein by the ML algorithm has great clinical significance. Another example is the use of an ML algorithm to identify novel inhibitors of beta-secretase (BACE1), a protein found in relation to the development of Alzheimer's disease. AI has also been successfully used for the discovery of new antibiotics; a powerful ML-based approach has identified powerful antibiotics from a vast pool of 10 crore molecules and more, including one that acts against several bacteria. For example, the drug halicin can destroy *Mycobacterium tuberculosis* and carbapenem-resistant strains of the family *Enterobacteriaceae*[3–8]. The discovery of drug molecules like DSP-1181 and ISM001-055 have entered phase 1 clinical trials for treating patients with obsessive-compulsive disorder (OCD) and idiopathic pulmonary fibrosis (IPF), respectively, in humans reveals the promise that AI holds for the future discovery of many more drug molecules[9,10].

Now let us deeply analyze the role of AI in the drug discovery process. For the prediction of the desired chemical structure of a compound, several parameters, viz., predictive models, molecular similarity, the process of generation of molecules, and the utilization of approaches in silico, can be used. A new system known as DeepVS has been presented for docking several receptors and ligands and has shown excellent performance. Another approach has used a multiobjective replacement algorithm (automated) for optimizing the potency profile of an inhibitor of cyclin-dependent kinase-2 by assessing its similarity in shape, biochemical action, and physiochemical features[11,12]. Quantitative structure–activity relationship (QSAR) modeling tools are used to identify potential candidate drugs and have gradually developed into QSAR (AI-based) approaches. Such approaches include linear discriminant analysis (LDA), support vector machines (SVMs), random forests

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(RF), and decision trees. All these can be used to speed up QSAR analysis[2]. For predicting the three-dimensional (3D) pharmacophore features, implementation of ML technology has been done by HS-Pharm, Pharm-IF, and DeepSite. Two models have been built by Coveney's group for binding affinities with accuracy and reproducibility and have been implemented in ML. The models are thermodynamic integration with enhanced sampling (TIES) and enhanced sampling of molecular dynamics with approximation of continuum solvent (ESMACS). For the prediction of binding affinities after the step of molecular docking, eSimDock is another tool. Improvement of the accuracy of ligand ranking is done by integrating scoring functions by the use of ML (nonlinear). The insensitivity of eSimDock to deformations or distortions in the target structure makes it a tool with flexibility that can be used irrespective of the protein structure's quality[13].

Proposals have been put forward for several neural network algorithms for designing drugs. Such algorithms include simple ones like multilayer perceptron (MLP) on the basis of McCulloch–Pitts neurons or more complex ones like logistic, naïve Bayes, ridge, lasso, shallow neural networks, or SVMs. Satisfactory results have been shown by tree-based models among the techniques applied for designing drugs. There are wide uses of decision trees in problems that concern prediction as well as the classification of concepts and ideas. There is involvement in the construction of multiple decision trees in a random forest. Random forests are actually ML algorithms commonly used that combine the output of more than one decision tree to reach to only one result. The most complex DL network models include generative adversarial networks (GANs), convolutional neural networks (CNNs), and capsule networks (CapsNets)[14]. The GANs play a crucial role in generating helical protein (novel) backbone topologies, which is important from the perspective of designing proteins de novo. Moreover, the GAN framework can be implemented for producing new peptides for drug targets[15]. Drug–drug interaction (DDI) can be studied by applying learning-based methods like CNN-DDI[16]. For the development of classification models of hERG blockers and non-blockers, CapsNets has been adopted in a study by Wang *et al*.[17], wherein the excellent performance of CapsNets has proven their potential applications in studies related to drug discovery.

A hierarchical DL framework is RPITER, which includes CNN and stacked autoencoders. Prediction of the interactions of the protein with ribonucleic acid (RNA) (non-coding) can be done with a fair degree of accuracy by using RPITER. Further employment of probabilistic matrix factorization has been done to predict the interaction between the drug and target. This method is suitable to be applied to a large volume of data, as for predictions to be made accurately, the method requires a plethora of data inputs. The development of pairwise input neural networks (multichannel) has also been done for predicting compound–protein interactions, benefiting from the limited amount of data available in the literature[13,18,19].

In conclusion, AI has a great role to play in revolutionizing the process of drug discovery and can offer better accuracy and efficiency. AI can also accelerate the process of drug development and has the ability to develop more efficacious and personalized medicines and therapies. But it should not be forgotten that the success of AI in the discovery of high-quality drugs is dependent on the availability of data. Moreover, ethical concerns need to be addressed appropriately. Recent developments in the field of AI technology, viz, augmentation of data, explainable AI, and integration of experimental methods available traditionally with AI hold promise to overcome the limitations as well as challenges of AI in the process of drug discovery. The ever-growing attention and interest of researchers and scientists, pharmaceutical companies, and regulatory agencies, in combination with the benefits of AI, potentially make it an attractive research area that holds great promise. Ultimately, it can be said that AI has the potential to transform the process of drug discovery in modern times.

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Consent

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