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Emerging AI Techniques in ligand-Centric Drug Design: Opportunities and Constrains a Review of Current Methods and Future Prospects

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Abstract: The emergence of artificial intelligence in the modern medicinal approach represents a revolutionary approach towards solving the shortcomings of conventional techniques employed in drug design and discovery. The application of ligand-based drug design (LBDD) relies on information obtained from already existing biologically active compounds to predict potential candidate molecules that possess required properties. Emerging trends in machine learning (ML), deep learning (DL), and computational chemistry have provided new ways of improving LBDD by making precise predictions about molecular parameters like their bioactivity, toxicity, and pharmacokinetics. QSAR modeling, molecular fingerprinting, virtual screening, molecular docking, and pharmacophore modeling have become essential elements of AI-based drug design techniques. In addition to this, there is an increased focus on using generative AI to develop new molecules through de novo design and lead optimization strategies. The current paper provides an overview of the most recent achievements in AI-assisted LBDD, including relevant computational methods, applications, advantages, and challenges.

Keywords: *Artificial Intelligence; Ligand-Based Drug Design; Machine Learning ;Deep Learning; QSAR; Virtual Screening; Molecular Docking; Generative AI.*

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I. INTRODUCTION

The methodology of discovering drugs is really complicated and expensive. It takes a lot of time to find and develop compounds that're safe and work well. The traditional way of doing things can take years. It costs a lot of money and there is a big chance that it will not work out in the end (Bhat et al., 2025; Yang et al., 2021). So people are looking for ways to use computers to make drug discovery cheaper. Artificial Intelligence is a technology that is changing the way we do pharmaceutical research. Artificial Intelligence uses machine learning and deep learning to look at sets of biological and chemical data. This helps us find new drugs quickly.(Siddiqui et al., 2025) Artificial Intelligence has been really successful in finding target screening for drugs, making lead compounds better predicting toxicity and finding uses for old drugs. One way that computers can help us design new drugs is called ligand-based drug design. This method looks at what we know about molecules that already work and uses that information to predict if a new compound will be effective. We do not need to know everything about the protein we are targeting which's different from other methods. Instead we use things like descriptors and pharmacophore models to find new compounds that might work.(Chen & Harrison, 2008; Kaur & Singh, 2021)New developments in machine learning and deep learning have made ligand-based drug design better. Now we can represent molecules in a way predict how they will work and screen them more effectively. We use things like structure-activity relationship modeling, molecular fingerprint analysis and generative Artificial Intelligence to discover new drugs (Ivanenkov et al., 2019; Zhavoronkov et al., 2021). This review is going to talk about how Artificial Intelligence's helping us with ligand-based drug design. We will discuss the computer methods, machine learning techniques and strategies for screening and modeling. We will also talk about what's new, in generative Artificial Intelligence. Additionally we will look at the challenges we are facing now and what we think will happen in the future with Artificial Intelligence and drug discovery.

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II. ARTIFICIAL INTELLIGENCE FOR MODERN IN DRUG DISCOVERY

Artificial Intelligence has become an important technology in the field of drug discovery and pharmaceutical research. The old way of discovering drugs used to take a lot of time and money. Artificial Intelligence has made this process much faster and more efficient. It can quickly look at a lot of chemical and clinical data(Yang et al., 2021; Siddiqui et al., 2025).Machine learning and deep learning are useful tools for finding new drugs. They help us find the targets for drugs, predict how molecules will behave and make lead compounds better(Pathan, 2024). These approaches can find patterns in data that we might not see otherwise. So Artificial Intelligence helps researchers make decisions when they are developing new drugs.

Many studies have shown how important Artificial Intelligence is in computer-aided drug design. Artificial Intelligence techniques have been used for screening, predicting molecular properties, checking for toxicity and optimizing lead compounds(Siddiqui et al., 2025; Bhat et al., 2025). Deep learning models like neural networks have made it possible to design molecules more accurately. Recently generative Artificial Intelligence has made it possible to design molecules from scratch. This means researchers can create compounds with the properties they want.(Zhavoronkov et al., 2021)

This has made Artificial Intelligence a part of pharmaceutical research and has helped us find new drugs faster. Overall Artificial Intelligence has changed the way we discover drugs. It has made the process cheaper, faster and more successful. As Machine learning and deep learning get better Artificial Intelligence will play a bigger role in discovering new drugs(Yang et al., 2021). Artificial Intelligence is really helping us find better drugs and that is a good thing for Artificial Intelligence in drug discovery and for people who need new medicines.

III. LIGAND-BASED DRUG DESIGN AND VIRTUAL SCREENING

Ligand-based drug design is a used computer strategy. It helps. Improve potential medicines using information from known active compounds. Unlike structure-based design it does not need information about the target protein. Instead it uses the characteristics of identified active molecules. The main idea is that molecules with structures often have similar effects(Chen & Harrison, 2008).Virtual screening is an application of ligand-based design. It quickly checks libraries of chemicals to find compounds likely to work against a specific target. Traditional methods use similarity, descriptors and fingerprints to find promising candidates. Recent studies show that machine learning improves screening by recognizing complex relationships between molecular features and effects(Ballester & Mitchell, 2019).

Pharmacophore modeling is another part of ligand-based design. A pharmacophore is the arrangement of features needed for activity, such as hydrogen bond donors and acceptors. Pharmacophore-based screening finds compounds with common characteristics expanding the chemical space for drug discovery.(Kaur & Singh, 2021)

Molecular fingerprints are also widely used. They convert structures into representations that machines can process. Fingerprint-based methods help with similarity analysis, classification and bioactivity prediction. They are tools in modern drug discovery. Recent advances in machine learning have improved screening. Algorithms like Bayesian classifiers, neural networks and Random Forest models help identify active compounds while reducing costs and efforts (Ballester & Mitchell, 2019). Ligand-based design, pharmacophore modeling, molecular fingerprints and machine learning together form a strategy for accelerating the discovery of new medicines.

IV. MACHINE LEARNING APPROACHES IN LIGAND-BASED DRUG DESIGN

Machine learning (ML) has become a fundamental component of modern ligand-based drug design due to its ability to identify complex relationships between molecular structures and biological activities. By learning patterns from experimental datasets, machine learning algorithms can predict the properties and bioactivity of novel compounds with high efficiency. This capability has significantly accelerated drug discovery by reducing the need for extensive laboratory screening and experimental testing.

One of the most widely used applications of machine learning in ligand-based drug design is Quantitative Structure–Activity Relationship (QSAR) modeling. QSAR models establish mathematical relationships between molecular descriptors and biological activity, enabling researchers to predict the therapeutic potential of new compounds. The integration of machine learning algorithms with QSAR has improved prediction accuracy and expanded the applicability of computational drug discovery methods(Siddiqui et al., 2025).

Molecular fingerprints serve as important inputs for machine learning models. These fingerprints transform chemical structures into numerical vectors that capture the presence or absence of specific molecular features. Algorithms can then utilize these representations to classify compounds, predict bioactivity, and identify structurally similar molecules. Molecular fingerprinting has therefore become a key technique in ligand-based virtual screening and molecular property prediction.(Chen & Harrison, 2008)

Several machine learning algorithms have been successfully applied in drug discovery. Random Forest models are widely used because of their robustness, ability to handle high-dimensional datasets, and resistance to overfitting. Naive Bayesian classifiers have demonstrated effectiveness in virtual screening applications, while artificial neural networks are capable of modeling complex nonlinear relationships between molecular descriptors and biological activity. Gaussian mixture models and support vector machines have also shown promising results in molecular classification and activity prediction tasks(Ballester & Mitchell, 2019).

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Recent studies have demonstrated that machine learning approaches improve the efficiency of virtual screening, lead identification, toxicity prediction, and pharmacokinetic analysis. The combination of machine learning algorithms with molecular fingerprints, QSAR models, and large chemical databases has significantly enhanced the ability of researchers to identify promising drug candidates. As computational resources and biological datasets continue to expand, machine learning is expected to play an increasingly important role in the future of ligand-based drug design(Pathan, 2024; Zhang et al., 2022).

V. DEEP LEARNING AND GENERATIVE AI IN DRUG DISCOVERY

Deep learning is a part of intelligence that has really changed the way we discover new drugs. It is different from machine learning because it can find complex patterns in big sets of biological and chemical data without needing a lot of human help. This means researchers can make predictions about how molecules will behave, find new drugs and make sure they are safe (Ivanenkov et al., 2019).There are types of deep learning that work well for designing new drugs. Artificial Neural Networks, Convolutional Neural Networks and Recurrent Neural Networks are really good at predicting how molecules will act and finding drugs. These models can look at lots of information about molecules. Find the important parts that affect how they work. Recently generative artificial intelligence has become a deal in drug discovery. Models like Variational Autoencoders, Generative Adversarial Networks, Adversarial Autoencoders and Long Short-Term Memory networks can create molecular structures that have the properties we want (Zhavoronkov et al., 2021).

This helps us design drugs that do not exist yet but still have the characteristics of a good drug. Generative AI is especially useful for making drugs. It can change structures to make them work better, be more specific and safer. By looking at a lot of molecules generative models can find promising ones that we might not have found otherwise. We can also use reinforcement learning to guide the design of molecules towards goals(Pathan, 2024; Zhavoronkov et al., 2021).Deep learning and generative AI have some challenges, like getting data, understanding how the models work, needing a lot of computer power and making sure the new molecules can actually be made. As the algorithms computers and databases get better this field is moving really fast. So deep learning and generative AI will likely play a bigger role, in discovering new drugs and making medicine more precise.

VI. COMPUTATIONAL BIOLOGY, BIG DATA AND OMICS APPROACHES IN DRUG DISCOVERY

The field of drug discovery has changed a lot because of the amount of biological data that is now available. New technologies like genomics and proteomics have given us a lot of information about biology. This information can be used to help us find drugs. Computational biology is very important for understanding this data and using it to develop new treatments(Katsila et al., 2016).Using data is now a crucial part of finding new targets for drugs and understanding how diseases work. We can look at a lot of types of data like information from biological databases, chemical repositories and clinical datasets. This helps us understand biological systems. Computers can process this amount of data quickly and find patterns that we might not see otherwise. The use of omics technologies like genomics and proteomics is a way to find new targets for drugs. These technologies help us understand which genes and proteins are involved in diseases. We can also use metabolomics to understand the pathways that are involved in diseases. By combining omics technologies with intelligence and machine learning we can find targets more accurately and develop personalized medicine approaches.(Paananen & Fortino, 2020)

Computational platforms and systems for discovering drug targets have made it easier to analyze data from different sources. These platforms bring together data from omics studies, biomedical databases and experimental investigations. This helps us make decisions during the process of discovering drugs. Machine learning algorithms can identify biomarkers and predict how drugs will interact with targets(Zhang et al., 2022). They can also help us choose the promising candidates for further study.

Some recent studies have shown that using biology, big data analytics and artificial intelligence can make the process of discovering new drugs more efficient. These approaches help us find targets quickly, reduce the cost of experiments and understand complex biological mechanisms better.

As we get more biological data, computational biology and omics-driven methodologies will become even more important for developing new treatments and precision medicine. Drug discovery will benefit from biology and omics approaches. Biology and omics approaches will continue to play a big role in drug discovery.(Katsila et al., 2016; Paananen & Fortino, 2020)

VII. CHALLENGES AND LIMITATIONS OF AI-ASSISTED LIGAND-BASED DRUG DESIGN

The use of intelligence in drug discovery has made a lot of progress but there are still some big problems that need to be solved. One of the issues is that we need good quality biological and chemical data. Machine learning and deep learning models require a lot of diverse data to work properly(Pathan, 2024).If the data is incomplete, biased or inconsistent it can affect how well the models work and lead to predictions. Another big challenge is understanding how AI models work. Some of these models are like boxes so it is hard to figure out how they make predictions(Bhat et al., 2025). This lack of transparency can make it hard to trust the results especially when it comes to decisions like choosing a drug candidate or making decisions about patient care.

AI-based drug discovery also has a problem with overfitting. This means that models can work well with the data they were trained on but they do not work as well with new data. This can make it harder to use these models in real-

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world situations. Can lead to wrong predictions. The way we represent structures is also a challenge.. So the accuracy of our predictions can depend on how we represent the molecules and what machine learning approach we use. Generative AI models have their set of problems. They can create molecular structures but not all of these structures can be made in a lab or have the desired properties (Zhavoronkov et al., 2021). So we need to test these molecules further using methods like molecular docking and laboratory experiments.

We also need to think about the power required to run these models. Training deep learning models and processing large biological datasets requires a lot of computational resources, like high-performance computers and special hardware(Pathan, 2024). This can be a problem for research institutions and labs in developing countries. Finally we need to consider the ethical implications of using AI in drug discovery.

We need to have ways to validate the results and make sure they are reliable and safe. Although these are challenges people are working on solving them. We are making progress in AI, data integration, computational infrastructure and model validation. This should make AI-assisted ligand-based drug design more effective and reliable, in the future. AI-assisted ligand-based drug design will get better as we solve these challenges.(Bhat et al., 2025; Pathan, 2024)

VIII. FUTURE PERSPECTIVES

Artificial intelligence will play a role in the future of drug discovery and designing drugs based on ligands. New advancements in machine learning and biology computers are creating chances for faster, more accurate and cheaper ways to discover drugs. As biology and chemistry data keep growing AI models will get information making them better at predicting and more reliable. One exciting development is combining AI that generates things with drug design. Advanced AI models will help create molecules with the right properties(Paananen & Fortino, 2020; Zhang et al., 2022). This could speed up finding and improving drug leads. It could also help explore chemical options. Artificial intelligence combined with technologies like genomics, proteomics, transcriptomics and metabolomics will also speed up finding targets and precision medicine. AI can help analyze data to find biomarkers for diseases and create treatments for patients.

Another area that's coming up is using AI in drug discovery. This type of AI aims to make models more transparent and understandable(Yang et al., 2021). It will help researchers trust AI results more. This could make it easier for AI-based methods to be accepted in the pharmaceutical industry. Technologies like cloud computing, high-performance computing and quantum computing will also improve drug discovery using computers. They will provide the power needed to analyze data, simulate complex interactions and train advanced AI models. Also combining AI with docking molecular dynamics simulations, virtual screening and automated lab platforms could enable efficient drug discovery pipelines. Such systems could reduce research costs, speed up development and improve the success rate of candidate molecules entering clinical trials.

The future of AI-assisted ligand-based drug design looks very promising. More advancements in methods, data and collaboration are expected to change pharmaceutical research. They will help create more effective and personalized treatments. Artificial intelligence and drug discovery will work together to make better medicines. The use of AI, in drug discovery and ligand-based drug design will continue to grow. Artificial intelligence will improve the process of finding drugs. It will help make medicines(Pathan, 2024).

IX. CONCLUSION

Artificial intelligence is changing the way we do things in drug discovery. It is making the process of designing drugs much more efficient and effective. By using machine learning and other tools researchers can look at lots of chemical data, predict what molecules can do, find good candidates for new drugs and make these candidates even better(Siddiqui et al., 2025).The way we design drugs based on ligands has improved a lot with the help of intelligence. We can now use methods like molecular fingerprint analysis and virtual screening to find drug candidates. New advances in learning and artificial intelligence are also helping us design new molecules and make the process of finding new drugs faster.

We now have a lot of data and powerful computers that can help us use intelligence to find new drugs. However we still have some problems to solve such as making sure our data is good, understanding how our models work and dealing with computations. With these problems artificial intelligence is getting better and better. New developments in intelligence will help us design drugs more easily and quickly. As artificial intelligence keeps improving it will play a role in helping us find new treatments, reducing costs and making sure the drugs we take are safe and work well.

Overall, using intelligence to design drugs based on ligands is a promising area of research that can change the way we do pharmaceutical research and precision medicine. Artificial intelligence and drug discovery will keep working to make new and better drugs(Ivanenkov et al., 2019; Zhavoronkov et al., 2021). Intelligence and ligand-based drug design are the future of drug discovery(Yang et al., 2021; Bhat et al., 2025).

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