WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL RESEARCH

Review Article

2025
Volume: 02
Issue: 12
Page: 81-98

COMPUTER-AIDED DRUG DESIGN (CADD)

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Received: 10 November 2025 **Revised: 20 November 2025** **Accepted: 10 December 2025**

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❖ ABSTRACT

Computer-aided drug design, or CADD, employs mathematical equations to predict the features and architecture of molecules, whether they're established, novel, or still in the realm of the unknown. A variety of techniques are utilized by these programs, encompassing things like quantum mechanics, hybrid QM/MM, molecular bonding, and modeling, as well as molecular mechanics and QSAR, to delve into the intricacies of molecular interactions. Typically, the full arc of drug discovery, beginning with the identification of a prospective drug and culminating in clinical trials, spans roughly a year. When CADD is integrated into a company's research and development workflow, it holds the promise of significantly reducing the expenses associated with drug design and development, perhaps by as much as half. Computational methods provide a boost to the drug development timeline by facilitating data analysis and offering direction for trials. CADD essentially takes two main forms: ligandbased drug design (LBDD) and structure-based drug design (SBDD). SBDD leverages threedimensional structural information from targets such as proteins or RNA to pinpoint crucial sites and interactions that are essential for their biological roles. Computer-Aided Drug Design (CADD) is a revolutionary force that bridges the fields of biology and technology in the ever-changing field of drug discovery. The historical development of CADDs and their classification into structure-based and ligand-based approaches are reviewed in this paper. methods, and how important it is for rationalizing and accelerating drug discovery. As CADD develops, protecting data privacy and integrating a variety of biological data become critical. There are still issues that call for strong ethical frameworks and algorithm optimization. CADD's predictive power is increased by combining machine

learning and artificial intelligence, but scalability issues and ethical issues still exist. Platforms such as Open-Source Malaria serve as examples of global initiatives and collaborative efforts that highlight the democratization of drug discovery.

❖ INTRODUCTION

• DEFINATION OF DRUG DESIGN

Drug Design is the creative process of developing novel drugs using biological target knowledge.

It entails creating molecules that will bind to the biomolecular target because of their complementary shapes and charges.

• DEFINATION OF COMPUTER AIDED DRUG DESIGN (CADD)

Computer-Aided Design (CAD), also known as Computer-Aided Design and Drafting (CADD), is the process of digitally creating two-dimensional (2D) and three-dimensional (3D) models or real-world objects using computer software.

Computer-Aided Facility Management (CAFM) software frequently includes CAD, which enables businesses to visualize their spaces and layouts for occupation planning, wayfinding, maintenance management, and other management-related tasks.

Fig No.1 :- Mechanical Computer-Aided Drug Design

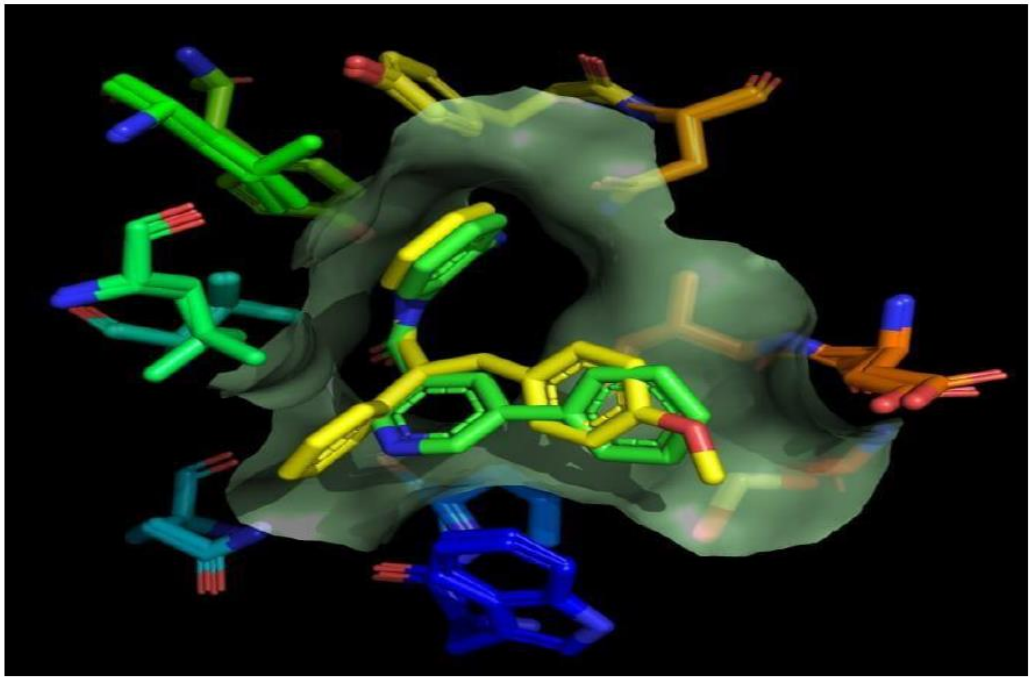


Fig No. 2 :- Computer- Aided Drug Design

❖ OBJECTIVE

1. Screening for illness assays at random.
2. Specific screening for disease assays.
3. Natural versus synthetic chemicals.
4. Development and testing of rational medicine.
5. Quicken the screening procedure.
6. Make the screening process more effective.
7. Create a new design.
8. Including testing in the design phase.
9. Rapidly stop taking medications.

- **TYPES OF CADD**

1. Structure-based Drug Design (SBDD)

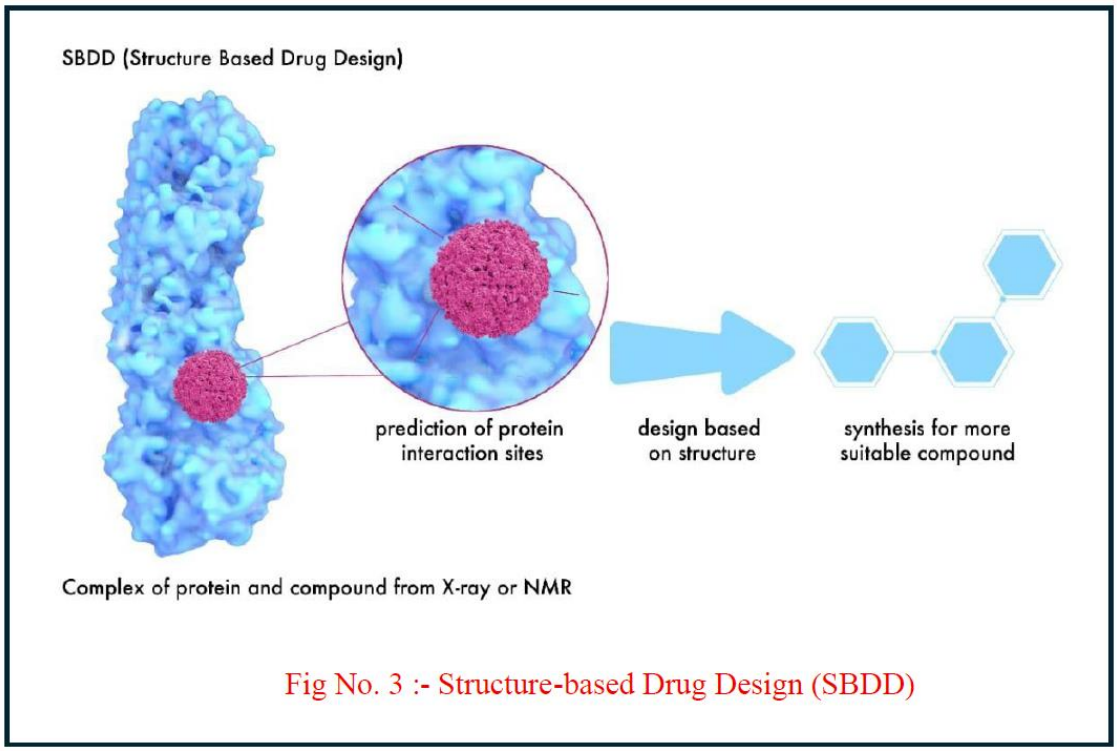


Fig No. 3 :- Structure-based Drug Design (SBDD)

2. Ligand-based drug design (LBDD)

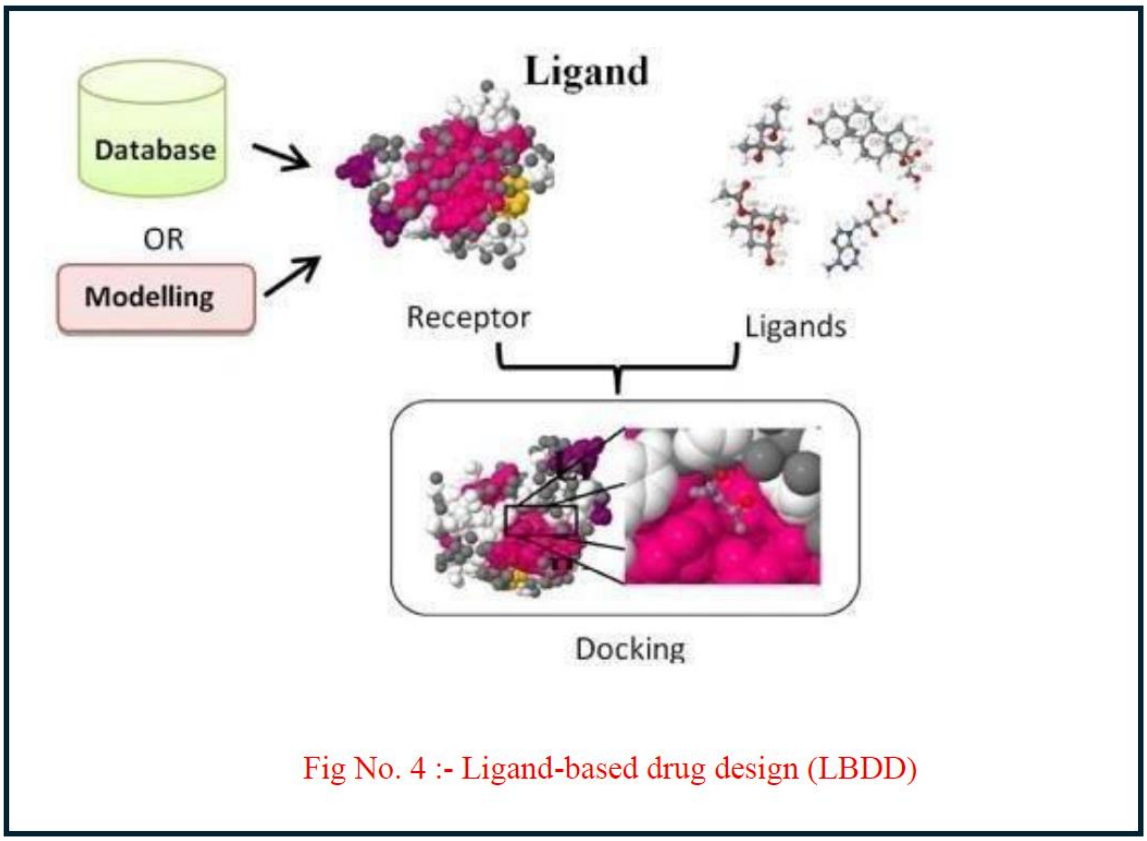


Fig No. 4 :- Ligand-based drug design (LBDD)

TARGET IDENTIFICTION OF CADD

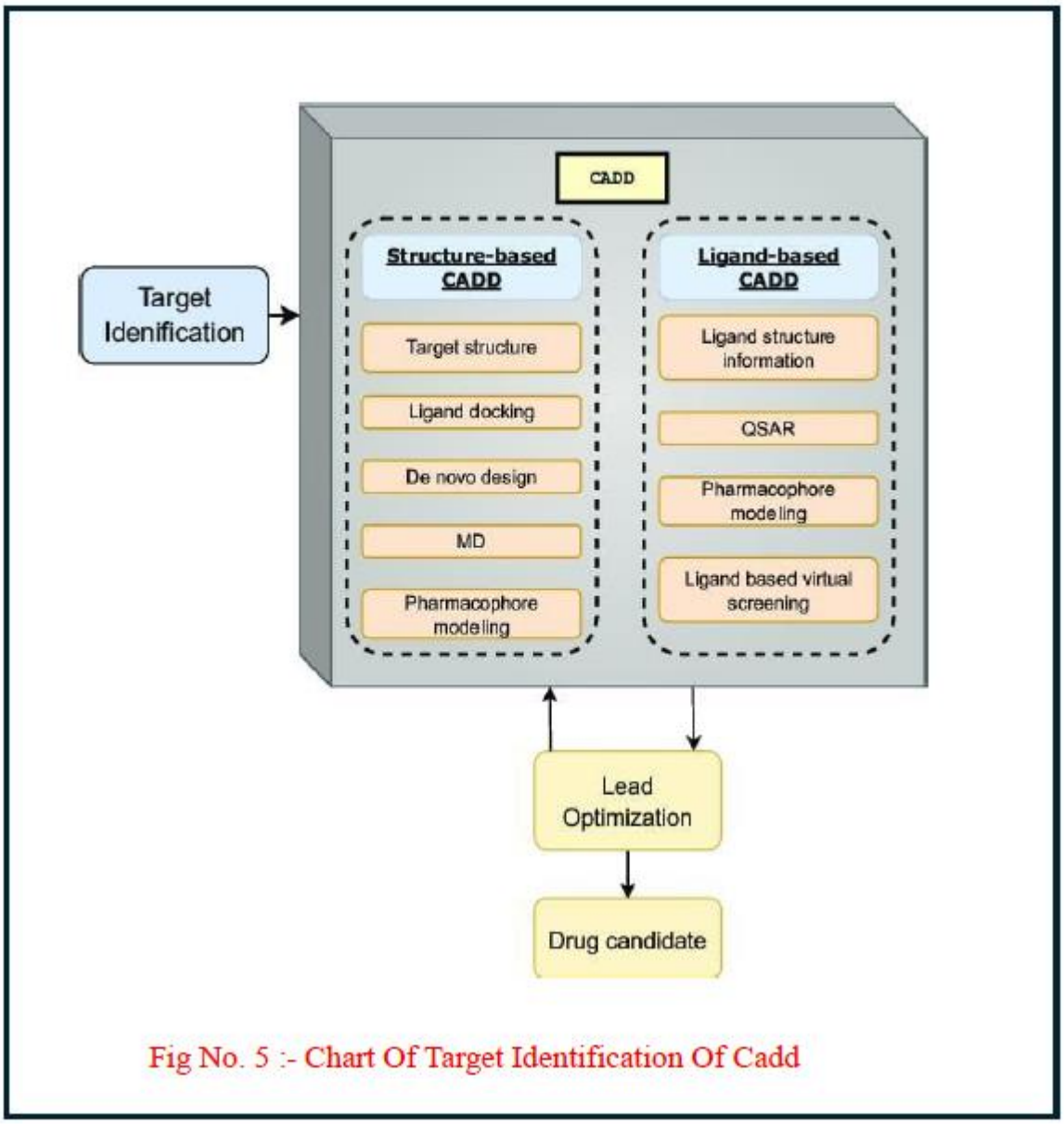


Fig No. 5 :- Chart Of Target Identification Of Cadd

- **INTRODACTION OF CADD**

Computer-aided drug design, or CADD, offers a range of techniques and resources that can be beneficial throughout the drug development journey. By employing these methods, the process of bringing new medications to market can be expedited, and expenses can be curtailed. The creation of new pharmaceuticals is, to put it mildly, an extended, expensive, and unpredictable undertaking, setting it apart from other business ventures. To accelerate this process, the pharmaceutical sector frequently turns to computer-aided drug design. Computational approaches prove particularly valuable in optimizing lead compounds, offering noteworthy financial advantages.

Research labs in the pharmaceutical industry allocate considerable funds to various phases of drug discovery. This includes pinpointing therapeutic targets, identifying possible drug candidates, and evaluating the safety and efficacy of novel medications. They also work to refine existing drugs through preliminary investigations and comprehensive clinical trials. Major pharmaceutical firms have made significant investments in ultra-high throughput screening (uHTS) to assess a vast array of drug-like substances.

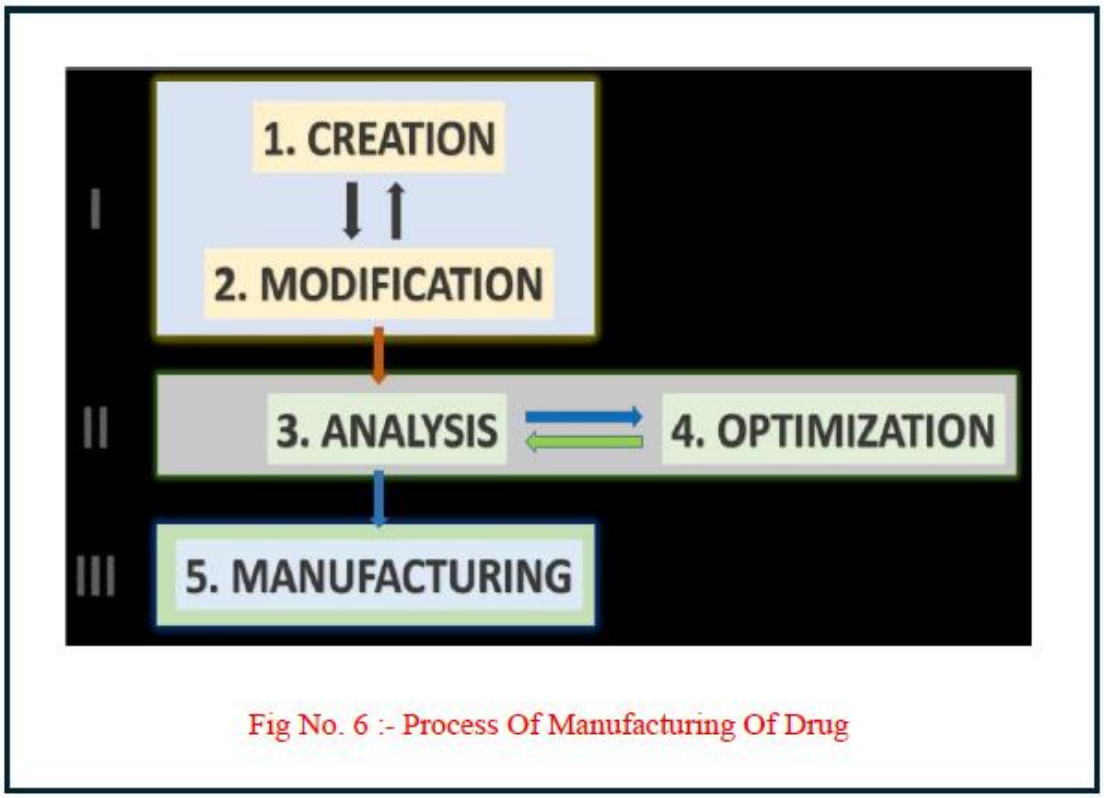


Fig No. 6 :- Process Of Manufacturing Of Drug

- **CADD in the Drug Discovery Process**

In the quest for novel therapeutics, computational approaches to drug discovery (CADD) offer a potent synergy with conventional laboratory techniques, potentially expediting and clarifying the process of identifying new medications, including vital antibiotics. This integrated methodology proves beneficial, irrespective of whether the therapeutic target is well-established or remains unidentified. Furthermore, CADD enhances the precision of drug design, thereby yielding substantial savings in both time and financial resources.

❖ METHODOLOGY OF CADD

1. Structure-Based Drug Design (SBDD)

Creates molecules that fit into the active site by using the three-dimensional structure of a target protein as determined by X-ray crystallography or NMR.

2. Ligand-Based Drug Design (LBDD)

Determines structural characteristics necessary for activity by using knowledge of known active molecules.

3. Online screening

The first approach involves finding new ligands for a particular receptor by using quick approximate docking programs to search through huge databases of small molecule 3D structures to find those that fit the receptor's binding pocket.

4. Designing new ligands from scratch

This technique involves assembling tiny pieces one at a time to build up ligand molecules inside the binding pocket's limitations.

These fragments may be single atoms or pieces of molecules. The main benefit of this approach is that new structures can be proposed.

5. By assessing suggested analogs inside the binding cavity, known ligands are optimized.

Fig No. 7 :- Computational Tools For Drug Desining

❖ COMPUTATIONAL TOOLS FOR DRUG DESNING

Categories of Software

1. Databases & Draw Tools
2. Molecular Modeling & Homology Modeling
3. Binding site prediction & Docking
4. Ligand design Screening-QSAR

5. Binding free energy estimation
6. ADME Toxicity

Draw Tools

1. Chemdraw

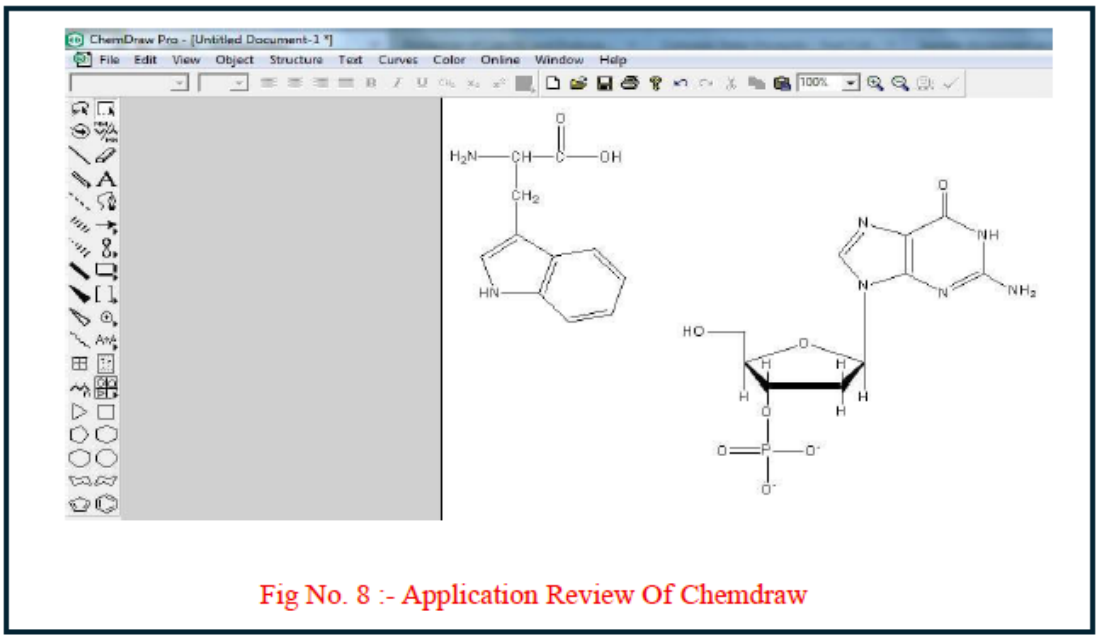


Fig No. 8 :- Application Review Of Chemdraw

2. Marvinsketch

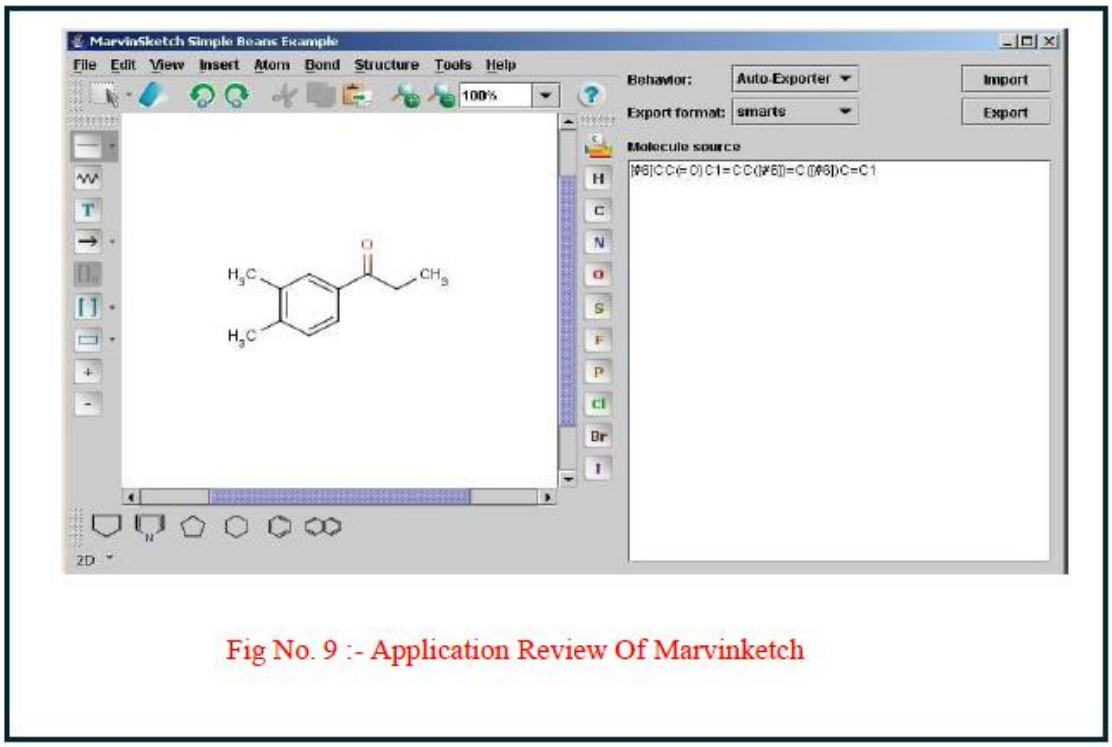


Fig No. 9 :- Application Review Of Marvinketch

3. UCSF Chimera

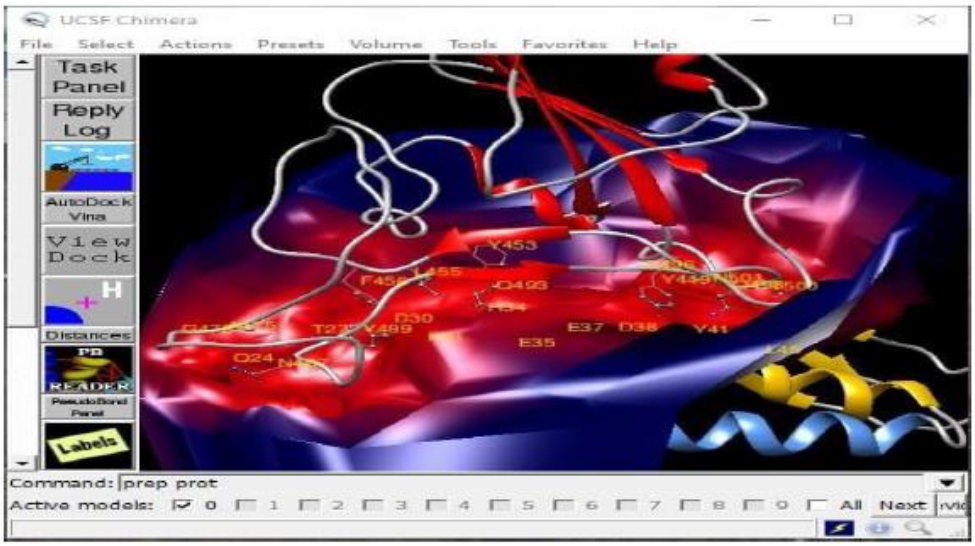


Fig No. 10 :- Application Review Of UCSFChimera

4. Kingdraw

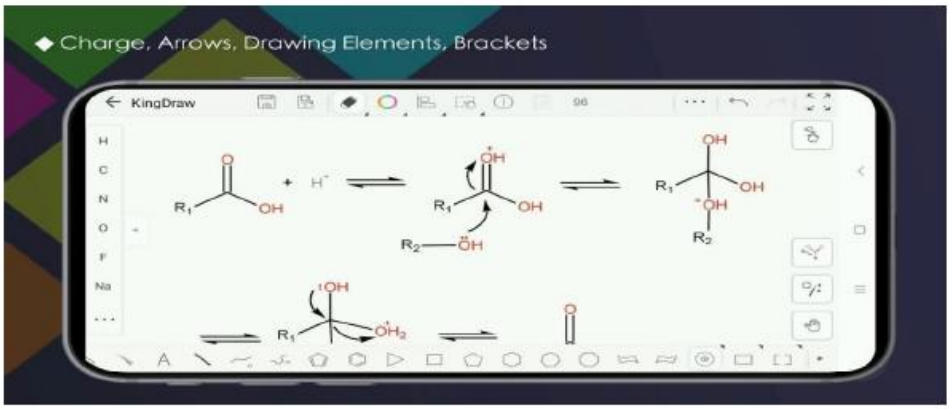


Fig No. 11 :- Application Review Of Kingdraw

❖ APPLICATIONS OF CADD

A contemporary computational method utilized in the drug discovery process is computeraided drug design, or CADD. Computational chemistry, molecular modeling, molecular design, and rational drug design are all included in CADD. In the pharmaceutical and academic sectors, CADD techniques are becoming more and more well-liked. With increased speed and precision, it has transformed the drug discovery process.

Virtual Screening

Look through sizable molecule databases to find possible therapeutic candidates. Find promising compounds for additional research quickly and effectively.

CD Using a virtual screening protocol, Computa Bio can find hits or leads by screening a small molecule library against the target.

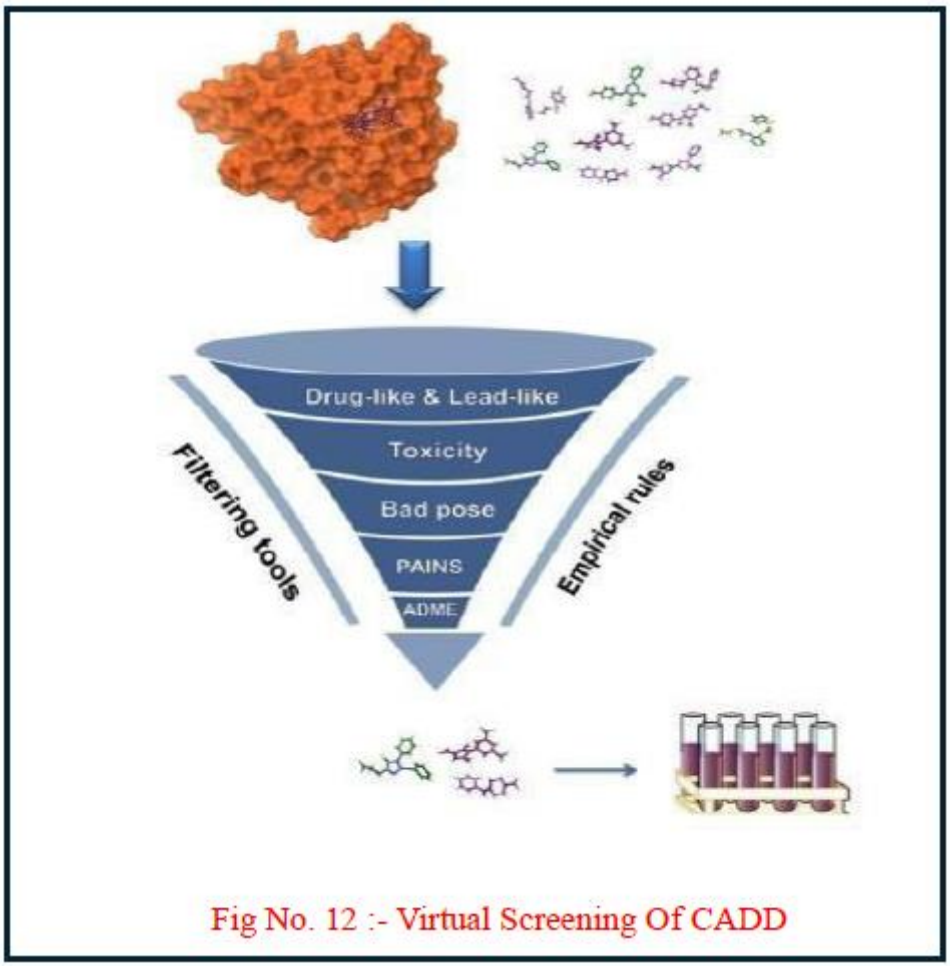
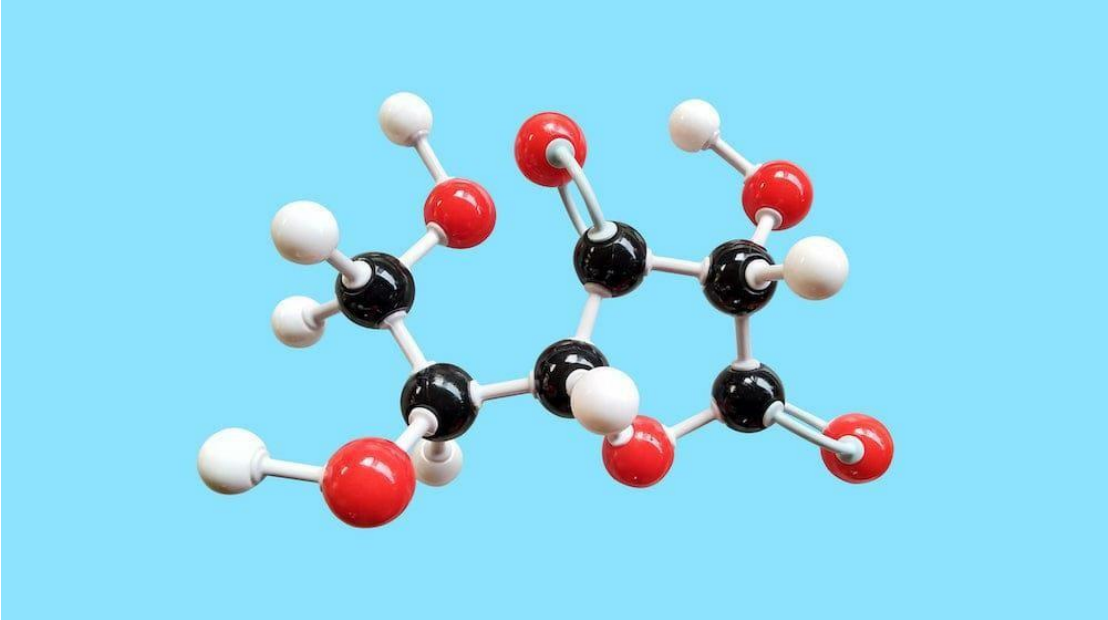


Fig No. 12 :- Virtual Screening Of CADD

Molecular Modeling

Create three-dimensional models of drug molecules to forecast their toxicity, solubility, and binding affinity.

Optimize drug candidates to increase their likelihood of success.



Docking studies

Docking Studies are used to forecast the interactions between a drug molecule and its target protein. Create more potent medications that have a high affinity for the target protein.

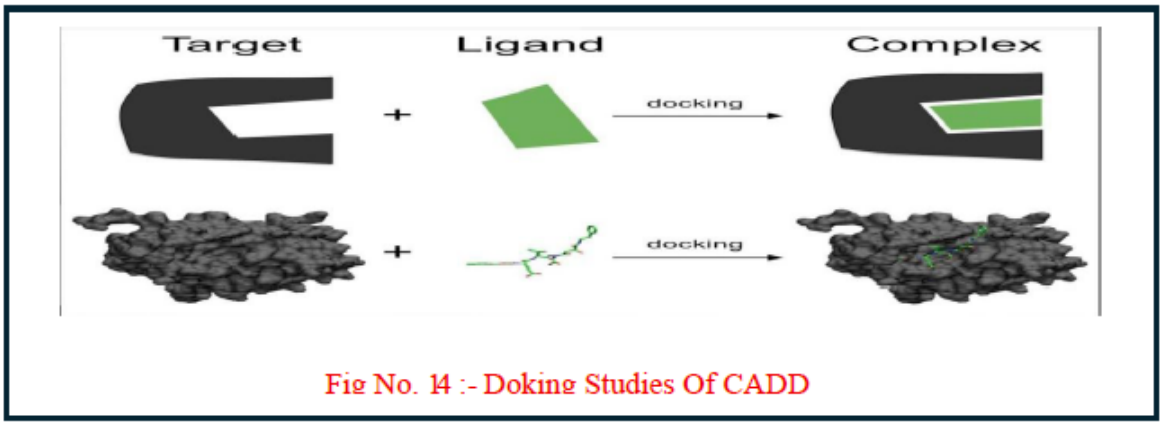


Fig No. 14 :- Doking Studies Of CADD

Lead Optimization

Create better molecules for synthesis and testing in order to maximize the leads.

Make changes to current drug molecules to enhance their potency, decrease toxicity, or boost selectivity for a specific target protein.

Using in silico methods, forecast a drug molecule's absorption, distribution, metabolism, and excretion (ADME) characteristics as well as possible toxicity.

Create medications that are safer and more efficient.

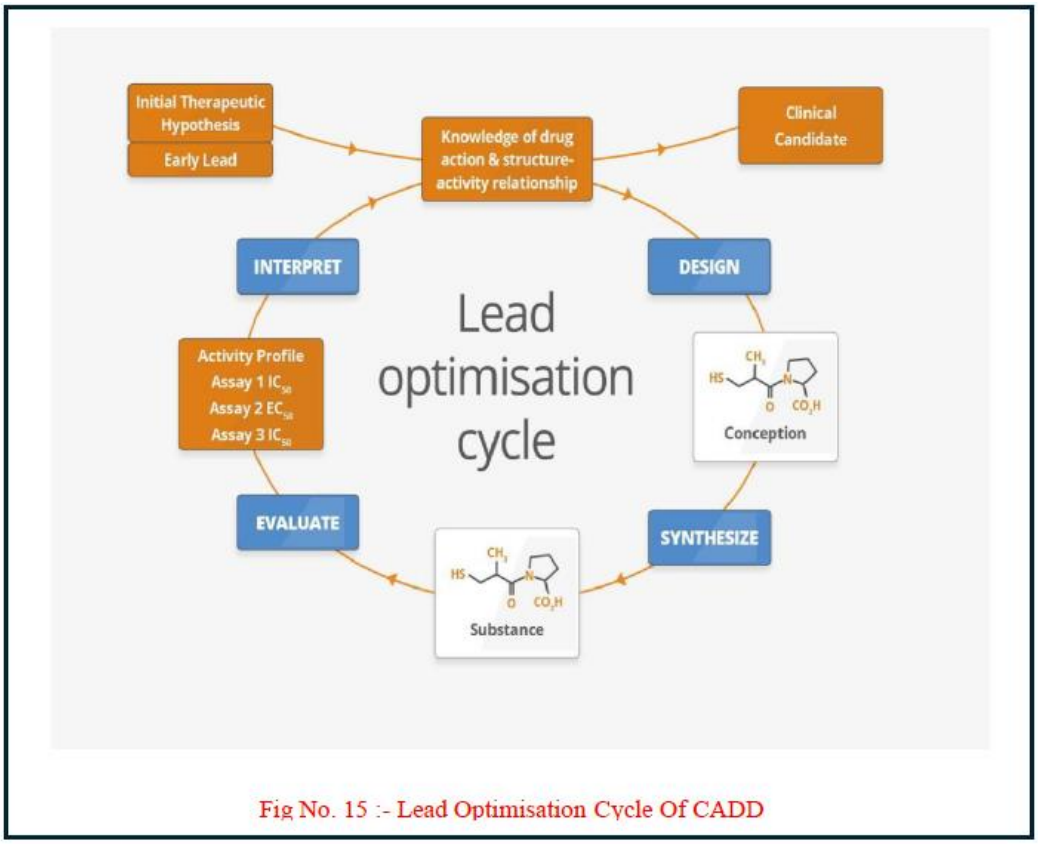


Fig No. 15 :- Lead Optimisation Cycle Of CADD

Software Packages Available

One of the most popular CADD software packages is Schrödinger Suite. It provides a number of tools for lead optimization, virtual screening, and molecular modeling. Maestro, Glide, LigPrep, and Prime are a few of its well-liked modules.

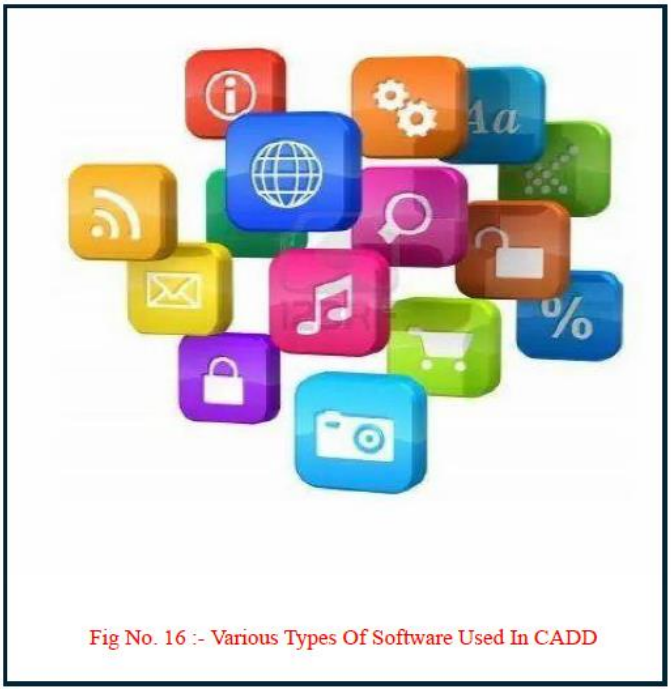


Fig No. 16 :- Various Types Of Software Used In CADD

❖ ADVANTAGES

- Duration
- The price
- Precision
- details regarding the illness
- There is less screening
- Screening of databases
- There is a need for less labor.
- Aids in the investigation of drug-target interactions.
- Pre-screening compounds in silico reduces the need for animal testing.

❖ DISADVANTAGES

- Might not be as precise for intricate systems.
- Can be costly and necessitates a license.
- Needs the Schrodinger suite, which can be costly.
- May not be as quick as other tools.
- For complex systems, it might not be as accurate.
- For complex systems, it might not be as accurate.

❖ LIMITATIONS & CHALLENGES

- Recognizing the Challenges: The Barriers in Computer-Aided Drug Development

- Although CADD provides unmatched benefits for accelerating and improving drug discovery, it is important to understand its inherent drawbacks. One significant barrier is the lack of specialists.

- Competent in CADD's AI/ML. Programs like targeted recruitment and specialized training are essential; companies like in-silico Medicine are leading the charge to close this gap and develop a workforce with the expertise to use cutting-edge computational methods for drug discovery. Resolving these issues can result in improved tactics and open the door to more efficient drug discovery processes

- Accuracy of Predictive Models: In CADD, a major challenge lies in ensuring the accuracy of computational models, given that molecular dynamics simulations, docking scores, and machine learning predictions all rely on theoretical models. These models may not fully

capture the intricate nuances of biological systems. To enhance accuracy, it is essential to delve into the intricacies of scoring algorithms.

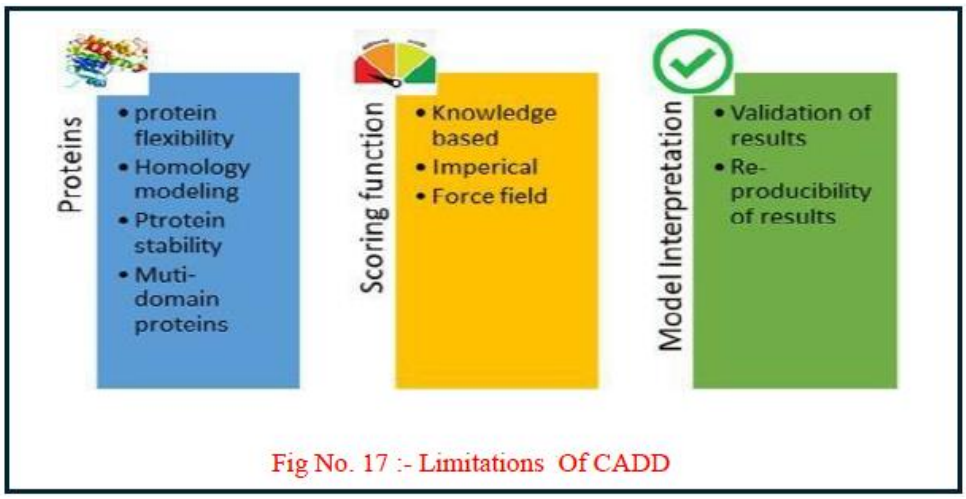


Fig No. 17 :- Limitations Of CADD

- Scoring algorithms in drug discovery are pivotal for predicting the binding affinity between molecules and their targets. To ensure their accuracy, it is imperative to actively mitigate the risk of false positives and negatives. This involves meticulous calibration of scoring parameters, the incorporation of diverse molecular descriptors, and continuous validation against experimental data. For instance, refining docking scores through rigorous validation against known binding affinities can enhance the reliability of predictions. By optimizing the balance between sensitivity and specificity, researchers can bolster confidence in scoring algorithms, reducing the likelihood of inaccuracies in drug discovery predictions.

- Data Quality and Quantity: The predictions made by CADD tools are only as good as the data they are trained on. The predictions are likely inaccurate if the underlying data are of poor quality or insufficient. The lack of curated, high-quality datasets, espe- cially in the context of machine learning in drug discovery, is a recurring challenge.

- Removing outliers and ensuring consistent data formatting can refine molecular interaction datasets, minimizing inaccuracies and bolstering the reliability of computational models. Additionally, implementing standardized experimental protocols, such as consistent assay conditions and endpoint measurements, further contributes to improved data quality in CADD, ensuring robust and dependable results. Over-reliance on Computational Predictions: While CADD is a powerful tool, over- reliance on its predictions without subsequent experimental validation can lead to mis- guided efforts. Balancing computational predictions with experimental evidence is essential for a successful drug discovery.

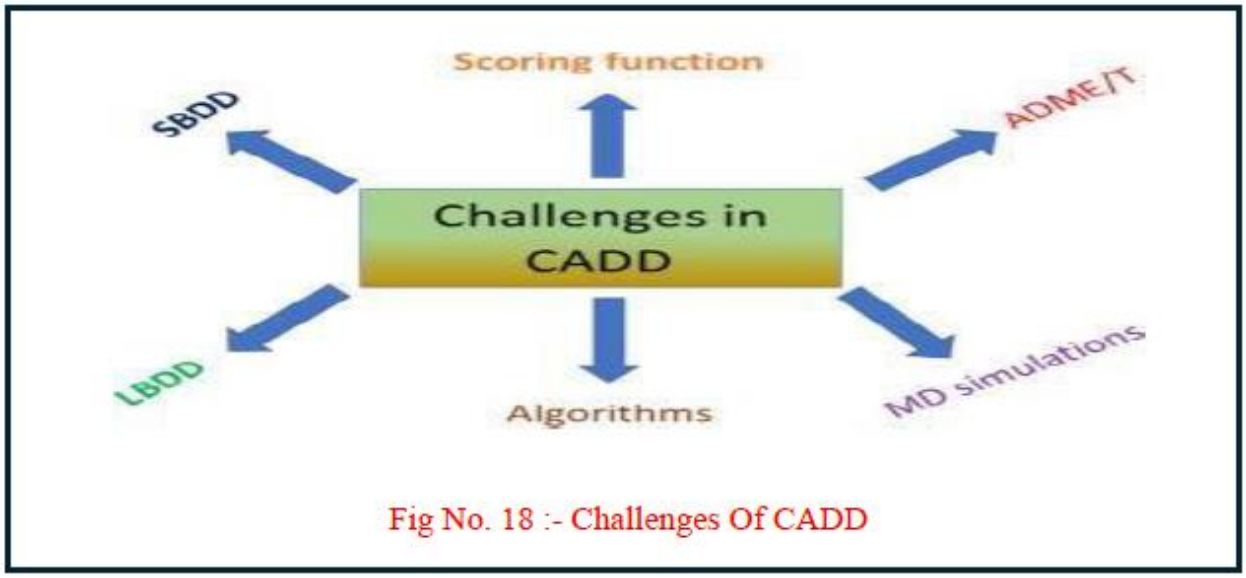


Fig No. 18 :- Challenges Of CADD

- Time and Computational Cost: Some advanced CADD techniques, especially those involving extensive molecular dynamics simulations or intricate machine learning models, require vast computational resources. The associated costs, both in terms of time and infrastructure, can be prohibitive for some research groups.

❖ CONCLUSION

Structure-based and ligand-based drug design form two branches of the computer-aided drug discovery process which plays a significant role in the design and identification of drug molecules in reduced time and cost.

The increase in the number of positive cases and deaths from COVID-19 and the lack of approved drugs and vaccines continue to be a matter of global health concern which necessitates the urgent discovery of drugs for the prevention and cure of the disease. The structural elucidation of pharmacological targets of SARS-CoV-2 has helped the researchers in the structure- based virtual identification of inhibitors, and the discovery of few lead molecules against COVID-19 has led to the use of scaffolds that can be optimized through ligand-based drug design.

Realizing the possible mutability of this RNA virus and the emergence of drug resistance problems, it is, there- fore, necessary to take a step further and consider targeting multiple drug targets that will be more effective and might help in overcoming drug resistance barriers.

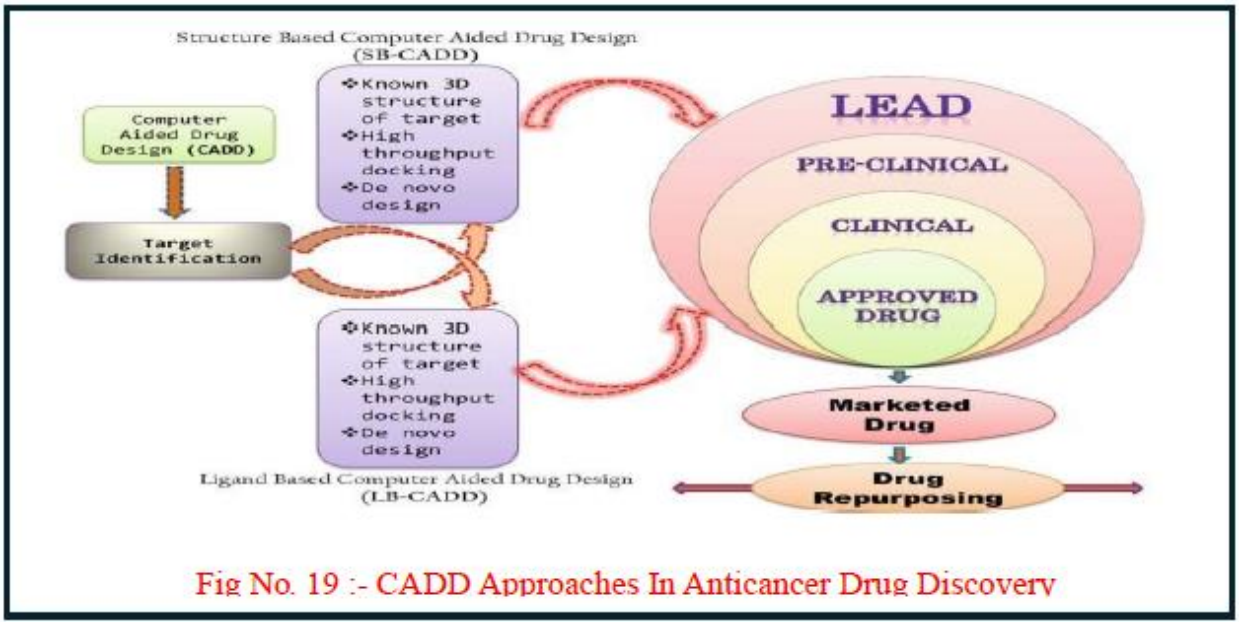


Fig No. 19 :- CADD Approaches In Anticancer Drug Discovery

CASE STUDY EXAMPLE

One of the successful applications of CADD is the creation of HIV protease inhibitors. Structure-based modeling was used to develop compounds that effectively inhibit the HIV protease enzyme and halt viral replication. Remdesivir analogs and other COVID19 antiviral medications were designed using similar techniques.

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