CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.6539501

Available online at: http://www.iajps.com *Review Article*

# REVIEW ON COMPUTER AIDED DRUG DESIGN

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**Article Received:** March 2022 **Accepted:** April 2022 **Published:** May 2022

**Abstract:**

*Computer-aided drug design (CADD) is a growing scientific field with various facets. The development of large quantities of compounds and the requirement to study these massive libraries in short periods of time characterise modern drug research. Computer-aided drug design was born out of the necessity to store, organise, and evaluate these constantly expanding resources (CADD). CADD stands for computational approaches and resources that aid in the development and discovery of novel therapeutics. The two types of methods commonly in use are structure-based drug design and ligand-based drug design.*

***Key words-*** *CADD, Modern drug discovery,* ***Bioinformatics****, Databases, Techniques, Ligand based, Structure based.*

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*Please cite this article in press* ***Arya Mudgal*** *et al,* ***Review On Computer Aided Drug Design.,*** *Indo Am. J. P. Sci, 2022; 09(5).*

## INTRODUCTION:

All computer-assisted procedures used to find, design, and optimise biologically active molecules are referred to as computer aided drug design (CADD). Modern patterns in chemical characterization in drug development have been credited to computer-aided drug design (CADD). The process of discovering and developing a new medicine is widely seen as a lengthy and expensive endeavour[1]. As a result, computer-aided drug design methods are now frequently employed to improve the efficiency of the drug discovery and development process. With the huge demand for medications on one hand and the complexity of numerous biological systems on the other, the process of drug discovery and development is long, laborious, and difficult[2].

The trial-and-error process for developing novel drugs is inefficient since it necessitates a variety of predictions, such as pharmacokinetic, pharmacodynamic, and hazardous qualities, prior to the production of a chemical compound. Finally, following these, it is discovered that only one, two, or even none of the thousands of chemicals created and tested clicks. Today's focus is not only on discovering new ways to treat human disease, but also on enhancing overall quality of life[2].

Computer-based drug design strategies offer the potential to achieve each of these objectives while also improving the process' efficiency. The emergence of two fields, rational design based on structural knowledge and powerful computational approaches to reveal the structural prerequisites for binding to a specific target, are currently dominating the drug discovery and lead optimization process. The way potential novel medications are identified has altered thanks to rational drug design procedures. Rather than a random screening procedure, the rational drug design process begins with an awareness of the disease or target's core physiological and biochemical features. The application of both knowledge of the mechanistic basis of a target disease and molecular properties of the compounds to have an influence on disease state is one technique to bring about cost effectiveness in the drug design process. This method of medicinal development is known as rational drug design[2].

CADD is a specific discipline of computer science that includes computational methods of calculation and graphical approaches for determining drug-receptor interactions. Bioinformatics applications and databases are intimately tied to CADD technologies[2].

**Merits of CADD**

- Eliminating unwanted compounds properties like poor pharmacokinetics parameters (ADMET), poor efficacy through is sites filters
- For experimental testing a list of compounds libraries[3].
- Animals and humans models can be replaced by CADD which was traditionally used and saved both time and cost.
- CADD also reduced the chances of drug resistance which lead to production of lead compounds that target the causative factor.
- It also store the high quality database and libraries for optimized use for high molecular diversity as similarity[4].

**Demerits of cadd**

- System failures may lead to the loss of all the data and designs.
- The data and design shall always be vulnerable to viruses if not controlled with appropriate software.
- It takes time to be technologically acknowledged / equipped.
- Software may be costly, and upgrading it after purchase can be costly as well.
- The operator should have proper training before operating the software.
- System and software updates can be costly and difficult to do on a regular basis.[5]

**Recent advancements in cadd**

Researchers are pouring their knowledge into publicly accessible databases, which are then accessed by laboratories all around the world for analysis and additional exploration. Rapid advances in high-performance computing resources, as well as the advent of several novel in silico methods, have drastically decreased the amount of time and money necessary.[11] The recent breakthroughs in CADD are significantly enriched with several sets of computational approaches, allowing for the integration of numerous tools/techniques to overcome individual tool/technique limitations. For drug discovery and optimization, CADD techniques can be used with molecular docking and virtual screening. De novo drug design, receptor-based ab initio pharmacophore modelling, water pharmacophores from the dynamic trajectory, free energy perturbation calculation, polypharmacology, big data, development of many protocols involving machine learning (ML)/deep learning methodologies, and application of artificial intelligence are some of the

most recent advancements in CADD approaches. [11] Cross-disciplinary research is popular these days, and studies involving experts from other domains are highly promising and profitable.[9]

**Materials**

The fundamental tools for CADD commonly used in laboratories:

Commonly used MD stimulation codes includes CHARMM (Chemistry at Harvard Macromolecular Mechanics), AMBER, NAMD, GROMACS, open MM. For SBDD, the 3D structure of the protein, RNA or other macromolecule may be obtained from Protein Data Bank (PDP). Alternatively, 3D structure may be constructed using homology modeling methods with a program such as MODELLE or one line web server such as SWISS MODEL. Visual screening are used to screen large in silico compound databases. Docking software available are DOCK and Auto Dock.

Commercially available CADD software packages include Discovery studio, Open Eye, Schrodinger and MOE. [10]

**Methods**

Computer-aided drug discovery (CADD) programmes can operate as a virtual shortcut, speeding up this lengthy process and perhaps lowering research and development costs. Structure-based and ligand-based approaches are the two types of methodologies used. Structure-based approaches are comparable to high-throughput screening in that they need knowledge of both the target and the ligand structure. Ligand docking, pharmacophore, and ligand design procedures are examples of structure-based methodologies. Only ligand information is used in ligand-based approaches to predict activity based on its similarity or dissimilarity to previously known active ligands. Molecular descriptors, ligand-based pharmacophores, and quantitative structure-activity relationships are examples of ligand-based approaches.[6]

**Researches**

Iktos generative modelling technology will be implemented and deployed to multiple Teijin Pharma small molecule drug discovery projects to speed up the identification of prospective pre-clinical candidates under the terms of the agreement. Iktos and Teijin Pharma will collaborate on the development of new AI technology aimed at improving and speeding up the medication development process.[7]

Researchers from the Chinese Academy of Sciences' Shenzhen Institutes of Advanced Technology (SIAT) looked at many aspects of the CADD process, with an emphasis on anticancer drugs. According to the study, computational drug design has aided in the identification of several new anticancer medications, marking a watershed moment in this field. The authorised medications Gefitinib, Erlotinib, Sorafenib, Lapatinib, Abiraterone, and Crizotinib were all found using computational drug techniques.[12]

**Researches in the context of COVID 19**

Selvaraj et al. (2020) used the homology modelling method to solve the three-dimensional structure of SARS-CoV-2 guanine-N7 methyltransferase (nsp14), and based on molecular docking and simulation studies, proposed five TCM database compounds—TCM 57025, TCM 3495, TCM 5376, TCM 20111, and TCM 31007—as potential antiviral phytochemicals. Gao et al. (2021) used mass spectrometry and flow cytometry to describe the SARS-CoV-2 nucleocapsid protein's physicochemical properties, subcellular distribution, and homology model, as well as further investigate its biological function. Beck et al. (2020) used a pretrained deep learning-based drug-target interaction model called molecule transformer drug to identify a few FDA-approved antiviral drugs with inhibitory potential against SARS-CoV-2 3C-like proteinase, including atazanavir, remdesivir, efavirenz, ritonavir, and dolutegravir. Because the SARS-CoV-2 genome's inherent mutability can make illness prevention and treatment more difficult, CADD can be used to predict the consequences of mutations on medication binding to molecular receptors. As a result, CADD can significantly aid in the drug development and discovery process. Umesh et al. (2021) used a computational approach (molecular docking and molecular dynamic simulation) to screen chemical species from Indian spices and found carnosol, arjunglucoside-I, and rosmanol to be strong inhibitors of the new coronavirus major protease (SARS-CoV-2 Mpro) . Abdelli et al. (2021) investigated an essential oil derived from the antiviral and antimicrobial plant Ammoides verticillata (Desf.) Briq. that inhibits SARS-CoV-2 function.[ 8]

**Future aspects of CADD**

Drug development is a time-consuming and costly procedure. In the present era of drug discovery, the application of CADD counts up the most accountability and provides computational tools and algorithm that save time costs and reduce the risk of detecting non-viable developmental leads making it

more rational and successful in future. Discovery of new drug using CADD requires a systemic understanding of molecular and pathological conditions induced by diseases.CADD currently doesn't include any information aboutnoncoding RNA species besides predicted miRNA binding sites and neurodegenerative disorders still remains a challenge for researchers and clinicians.However, CADD can assist them studying interaction between drug and receptor.The pharmacoinformaticapproach is being applied to modern drug discovery and is providing basic knowledge regarding the drug receptor interaction. [13]

Novel technologies and computational algorithms are required to design a high quality database for drug designing that should contain information about the mechanism of a specific disease, genomic and proteomic data , potential drug targets, natural leads , physiochemical properties , pharmacophore , QSAR, ADMET models , previous efforts made in drug discovery , failures and successes , clinical trial data , efficacy and side effects , as these developments are likely to lead to tools for disease identification and screening of potential lead compounds. [14]

The extensive use of computational approaches with higher accuracy could reduce the overall cost and failure of drug designing and aid drug discovery of many more curatives in future.

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