Application, principle, advantages and new advanced technique used in CADD

Saurabh Nevarekar[1]*, Shantanu Chavan[2], Sanket Shinde[3], Mudassar Mulla[4], Tohid Nadaf[5], Sushant Khot[6], Anuja Patil[7], Nilesh Chougule[8]
Students[1-6], Ashokrao Mane institute of Pharmacy, Ambap
Assistant Professor [7,8], Ashokrao Mane Institute of Pharmacy, Ambap

Abstract: CADD is known as computer aided drug design. It has emerged as an efficient means of developing candidates' drug for treatment of much disease type. Application of CADD approach to drug discovery and progressing day by day. Computer-aided Drug Design (CADD) in the 1980s revolutionized drug discovery by predicting pharmaceutical compound numbers from a large library. This process involves disease selection, target selection, lead compound identification, optimization, and validation. CADD is revolutionizing drug discovery and development, reducing costs by 50% compared to manual methods. It offers significant cost advantages in lead optimization. This paper explores CADD's application in chemo informatics. The CADD reduce the problems of medication and reduces the toxicity of drug. A various advanced technique is developed in CADD for the Drug design. It helps in removing the compound having no any pharmacological property. It changes the perception about the old research in drug design and direct the people to develop new drug knowingly. In CADD there are many software are used for visualization, molecular docking and QSAR are the technique used in drug design which can be aided by high quality computer graphics system. Bioinformatics works in computer and information technology to give better design process and knowledge and information to lead information. In this CADD helps future development in validating viable target with Support Vector Machine (SVM).

Keywords: QSAR, Molecular Docking, Support Vector Machine (SVM), Virtual Screening, Chemoinformatics, Bioinformatics

INTRODUCTION

CADD is a computational technology used for finding, producing, and evaluating pharmaceuticals and biologically active chemicals. It c, analyzes, and models compounds based on molecular interactions with targets like proteins and nucleic acids. CADD streamlines manufacturing processes and addresses challenges in drug discovery due to costs, competition, and competition. CADD approaches are widely used in the pharmaceutical industry to accelerate drug development by using a more targeted search method, aiming to describe therapeutic mechanisms and predict potential derivatives to enhance activity. [1,2]
The process of developing new pharmaceuticals has been a costly and time-consuming process since the use of herbal remedies. In the 1980s, computers were used to play a more significant role in drug discovery, known as Computer-added Drug Design (CADD). The most popular strategy is to predict the number of pharmaceutical compounds from a large library, allowing for high throughput screening at a lower cost and time without sacrificing lead discovery effectiveness. High ligand adherence interactions, hydrophobic, electrostatic, and hydrogen-bonded to the receptor are crucial for this process. The first seven types of drug discovery include disease selection, targets selection, lead compound identification, lead optimization, and lead validation. Peptides test are conducted for preclinical trials, clinical trials, and optimizing pharmacogenomics. In the future, finding novel ligands for new targets will be the weakest link in pharmacology. The field of drug discovery involves computer, bioinformatics, and other experimental methods, known as "rational" design of drugs. This includes experimental and computer-added drug design techniques (CADD) for assisted medication development. [3]

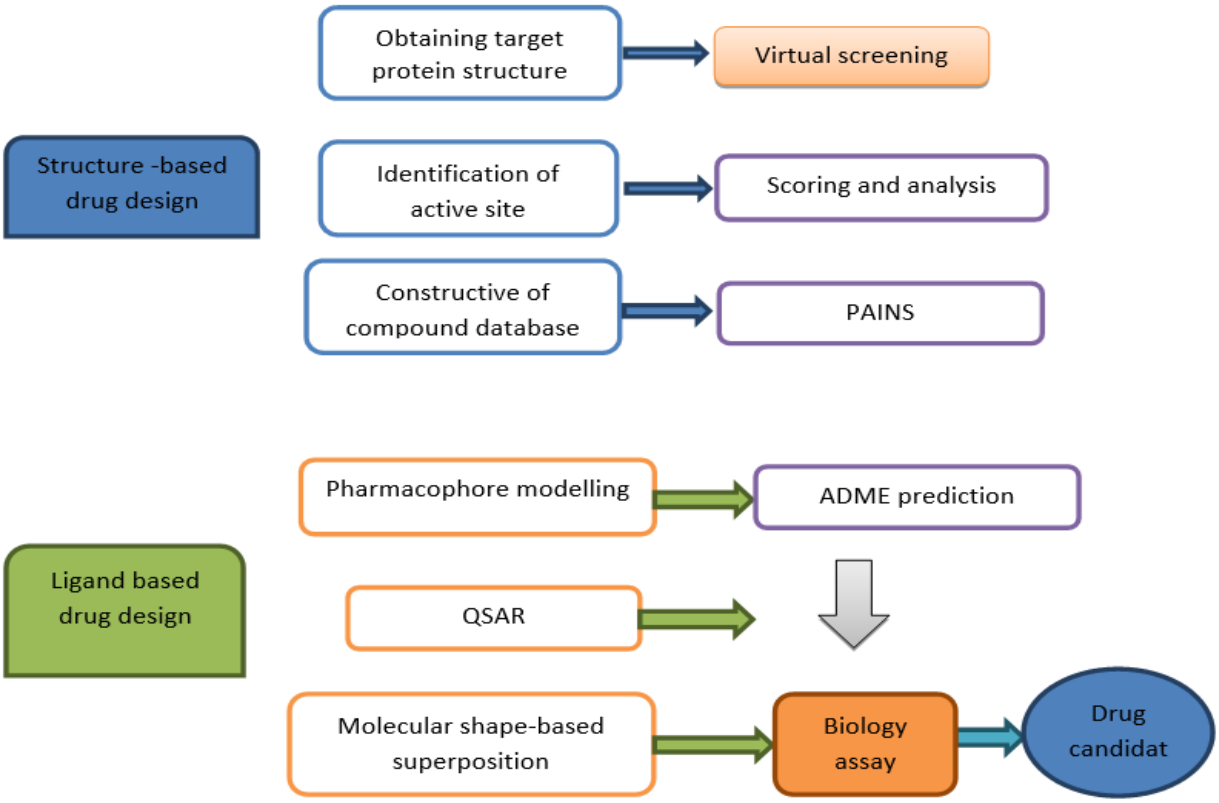
DATABASE SEARCHING

1) STRUCTURE BASED DRUG DESIGN:

Direct approach, is also known as Molecular Docking, aims to create a novel therapeutic molecule that effectively interact with the target protein without knowing ligands. [4,5].

2) LIGAND BASED DRUG DESIGN:

An indirect technique involves identifying receptors but knowing ligands for creating a pharmacophore model with required structural characteristics, assuming similar substance share biological effects and interaction with the target protein. [6,7]



What is CADD?

Full form of CADD is computer aided drug design. To enhance the discovery and design of CADD stand for computational methodologies and resource innovative treatment option.

1. Virtual screening of hit identification {structure and ligand-based design}
2. Hit-to-lead optimization for affinity and selectivity {based on structure, QSAR and design,
3. Optimizing other pharmacological characterstics while retaining is known as lead optimization. [8]

ADVANTAGES:

- Smaller number of chemicals is chosen from extensive compound libraries for experimental testing.
- The optimization of lead compound increases the metabolism and pharmacokinetics [ADME] feature such as absorption.
- Reduce possibility of medication resistance, which would be encouraging the development of lead compound that would specially address the underlying cause.
- Details regarding to illness
- There is less screening.
- It takes less labour. [9]

Principle:

A software program helps design, dock, assess, and estimate the activity of a structure, lead compound, or target, ultimately determining the drug candidate based on its drug-like properties. [10]

Drug design can be divided into two types: Ligand-based drug design (LBDD) and Structure-based drug design (SBDD). Ligand-based drug design relies on the knowledge of molecules that bind to the biological target of interest, without the need for 3D receptor information. Tools like 3D quantitative structure activity relationships (3D QSAR) and pharmacophore modeling are widely used in LBDD, providing predictive models for lead identification and optimization. [11]

Ligand-based drug design involves identifying molecules that bind to the desired target site, which can be used to derive a Pharmacophore model. A pharmacophore model is a molecule with the necessary structural abilities to bind to a desired target site. Once identified, it is determined if it is suitable for the receptor or if it needs further modification to create a potential drug.[10]Structure-based drug design (SBDD) is a highly efficient and alternative approach to drug discovery and development. It involves virtual screening and de novo drug design, using methods like Structure-based virtual scanning, molecular docking, and molecular dynamics. SBDD is more specific, efficient, and rapid for lead discovery and optimization, focusing on the 3D structure of target proteins. [12]

APPLICATION:

CADD can avoid a certain degree of blindness in the previous research process and enable intuitive design to guide people to develop new drugs purposefully

2. It gives the most promising drug candidate by eliminating the compounds with undesirable properties through in silico filters.
3. It reduces the synthetic & biological testing efforts.
4. It is cost effective, time saving, rapid and automatic
5. It knows the drug receptor interaction pattern.
6. The approaches minimize the chances of failures in the final phase.
7. It gives compounds with high hit rates through searching huge libraries of compounds in silico in comparison to traditional high throughput screening. [13,14]

Computer Assisted Drug Development (CADD) is a computer modeling technique used in drug development, potentially reducing costs by up to 50%. It involves homology modeling, molecular docking, virtual screening, QSAR, and 3D pharmacophore mapping. Molecular docking is crucial for understanding drug interactions and speeding up the search process in virtual screening. [15,16,17]

ADVANCEMENT IN CADD:

Drug receptors are target protein molecules, classified into enzymes, receptors, ion channels, and transporters. Most drugs are therapeutically used as membrane-bound proteins or enzymes. The detailed 3D structures of many membrane-bound proteins are still unknown. Homology modeling is an alternative for determining protein molecule structure. Future software and hardware programs will enable comprehensive studies of target structure and dynamics of new potential target molecules. However, these approaches present new challenges in validation and calibration of biosimulation methods. The discovery of new methods and drugs involves identifying and validating viable targets, with Support Vector Machine (SVM) and In-silico method integrated approaches continuously exploring new targets. [18]

STATISTICAL METHOD AND QSAR:

Quantitative Structural Activity Relationship (QSAR) is a mathematical method developed by Hansch and Fujita to better understand the chemistry and biological effects of a series of compounds. It assumes that the biological activities of a series of cogeneric molecules with a common mechanism of action are correlated with variations in their structural, physical, and chemical properties. QSAR uses mathematical relationships between biological activity and physico-chemical properties like hydrophobicity, electronic, and steric factors. Comparative Molecular Field Analysis (CoMFA) is a powerful 3D QSAR method that correlates molecular properties to biological activity by calculating steric and electrostatic fields for each molecule. It performs statistical analysis using the partial least square in the data set. In contrast, other statistical methods like neural networks and Support Vector Machines have been widely explored. [19,20,21]

DATA SOURCES:

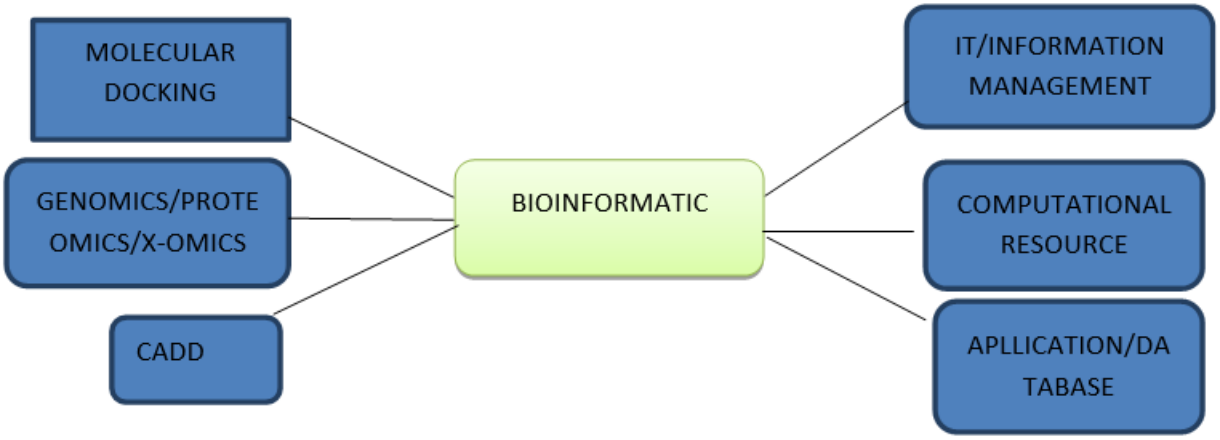
Scientific literature contains extensive information on organic molecules, amino acid sequences, and biological sequences, which is organized and stored in various databases, with the most important databases reviewed in this section.

SMALL MOLECULE DATABASE:

Mall molecule databases are crucial for modern discovery, providing valuable information about chemical compounds, carbohydrates, enzymes, reactions, and reactants. They house a vast number of FDA-approved compounds, enhancing the compilation of data.

BIOLOGICAL DATABASE:

The sequencing of human and model organism genomes has produced a vast amount of data for studying human diseases. Databases like PIR, Swiss-Prot, PDB, and EMBL provide expertly annotated protein sequences, nucleotide sequences, and structural data of biological macromolecules. Other databases have also been developed to provide a broader range of knowledge on human diseases. [22]



Chemoinformatic and Bioinformatics in CADD:
Chemoinformatic is a rapidly growing field that uses computer and informatics technology to transform data into information and knowledge for lead identification and better design processes. It has been widely used in chemical problem-solving, chemical structure representation, molecule search, design and synthesis, QSAR, structure elucidation and calculation algorithm, database retrieval, and lead identification. CARDD is a specialized discipline heavily dependent on bioinformatics tools, software application, information technology, databases, and computational resources. Bioinformatics methods are widely used in molecular biology, proteomics, genomics, and emerging areas like biological and gene ontologies and metabolomics. [23,24,25]

VIRTUAL SCREENING

Virtual Screening is a computer-aided technique used to identify the most probable compounds binding to a target molecule. It can be categorized into Ligand-based and Structure-based methods. Ligand-based methods use pharmacophore modeling and QSAR, while Structure-based methods include docking. Screening eliminates undesirable compounds through a "garbage filter" and uses the Lipinski rule to select five candidate molecules. These molecules must meet certain parameters, such as log P value, molecular weight, hydrogen bond donor and acceptor, to be considered.

DOCKING

Molecular docking is a method used to study the interaction between a ligand and a receptor, identifying active binding sites. It provides the most energetically stable geometry of the complex, with functions like dock score, potential of mean force score, and steric and electrostatic score representing the minimum energy of interaction. This helps predict the binding affinity of a ligand towards the receptor, enabling the screening of compounds for lead identification. [26]

CONCLUSION

Computer-added drug design (CADD) is a complex field that uses advanced techniques to speed up the search for novel chemicals with biological activity, requiring fundamental data. CADD is a valuable tool in drug discovery, providing valuable information about target molecules, lead compounds, screening, and optimization, and can be used to develop new therapeutic agents. Computer-aided approaches, including structure-based, ligand-based pharmacophore modeling, molecular mechanics, and virtual screening, are revolutionizing drug discovery and development in the digital era.

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