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Review Article

Review on Computer-Aided Drug Designing for Targeted Drug Delivery Systems

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Abstract

The article provides an overview of computer-aided drug design (CADD) and its applications in designing targeted drug delivery systems (TDDS). CADD is a process that uses computational tools and techniques to design drugs and predict their biological activity, pharmacological properties, and toxicity. TDDS is designed to deliver drugs specifically to the affected site, reducing the side effects associated with traditional drug delivery methods. The article also covers the history of CADD, the software and aids used in CADD, and the parameters involved in CADD for TDDS. The overview steps involved in CADD are also discussed, including target identification, virtual screening, drug optimization, validation, and regulatory approval. As well as The article provides an overview of computer-aided drug design (CADD) for targeted drug delivery systems (TDDS). CADD is a process of designing drugs using computational tools and techniques to predict the biological activity, pharmacological properties, and toxicity of potential drug compounds. TDDS is designed to deliver drugs specifically to the affected site, reducing the side effects associated with traditional drug delivery methods. Different types of drug delivery vehicles, such as polymeric micelles, liposomes, lipoprotein-based drug carriers, nano-particle drug carriers, dendrimers, etc., are used in TDDS. The article also covers the history, software, and aids used in CADD, and the overview steps involved in CADD for TDDS. Parameters for CADD for TDDS include target identification, drug release kinetics, biocompatibility, pharmacokinetics, targeting efficiency, and drug toxicity.

Keywords: Computer-aided drug design; Targeted drug delivery systems; Lipoprotein-based drug carriers; Nano-particle drug carriers; Dendrimers; Virtual screening; Molecular dynamics simulations; Pharmacogenomics; Force fields.

Introduction

Computer-aided drug design (CADD) is a process of designing drugs using computational tools and techniques. It involves the use of computer software to predict biological activity, pharmacological properties, and toxicity of potential drug compounds. One of the applications of CADD is in the design of targeted drug delivery systems [1,2].

Targeted drug delivery systems are designed to deliver drugs specifically to the affected site, reducing the side effects associated with traditional drug delivery methods. The use of CADD in targeted drug delivery allows for the development of drugs with improved efficacy and reduced toxicity [3].

Different types of drug delivery vehicles, such as polymeric micelles, liposomes, lipoprotein-based drug carriers, nano-particle drug carriers, dendrimers, etc. are being used in TDDS [3,4].

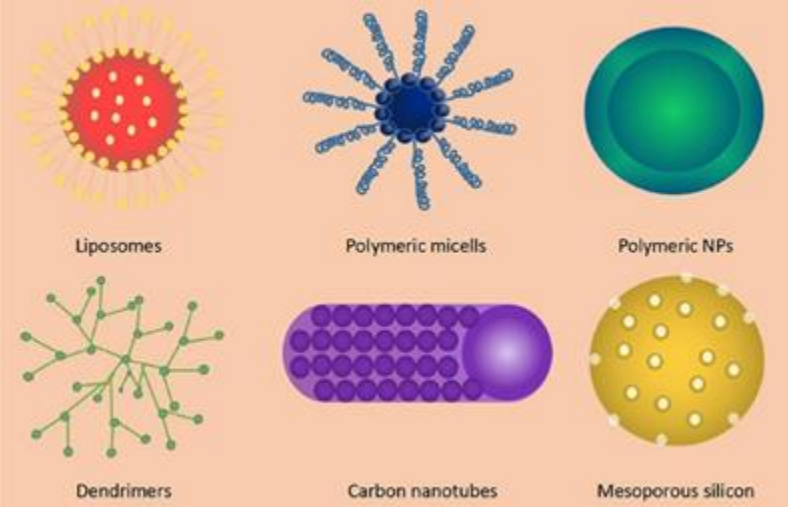

Figure 1: Vehicles used in Target Drug Delivery System.

Discovery

In the 1950s and 2000s, the development of faster computers and more sophisticated software tools led to a rapid expansion of CADD research. This included the development of new methods for virtual screening, molecular dynamics simulations, and other applications [3].

Today, CADD is a rapidly evolving field that encompasses a broad range of research areas, including drug discovery, structural biology, and bioinformatics. CADD has become an essential tool for drug discovery and development, as it allows researchers to design and optimize drug candidates more efficiently and effectively than traditional experimental methods [1,4].

History of computer-aided drug design

- The 1960s Review the target-drug interaction
- 1980s Automation: High-throughput target/drug selection

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- 1980s Databases (information technology): Combinatorial libraries
- 1980s Fast Computers: Docking
- 1990s Fast computers: Genome assembly,genomic-based target selection
- 2000s Vast information handling:Pharmacogenomics [1].

Software and aids

The subset of software packages described below represents examples of fundamental tools for CADD (Computer-Aided Drug Design) that are commonly used in our laboratory. CADD methods are mathematical tools used to manipulate and quantify the properties of potential drug candidates, and they are implemented in a number of programs, both publicly and commercially available [5,6].

Commonly used MD simulation codes include CHARMM, AMBER, NAMD, GROMACS, Open MM, etc. These programs run on many computer architectures and are optimized for parallel processing and more recently graphics processing on multi-core processing units (CPUs). unit (GPU), video as it is often used in games.

For SBDD, the 3D structure of a protein, RNA, or other macromolecule can be obtained from the Protein Data Bank (PDB) if it has been solved experimentally by X-ray crystallography or nuclear magnetic resonance (NMR). Alternatively, 3D models can be created using homology models using programs such as MODELLER or online web servers such as SWISS-MODEL [2,6].

To perform MD simulations, homology modeling, data analysis, or other CADD methods, a dynamic force is required for the molecule of interest. For example, related software uses these forces to estimate the forces and energies associated with protein-drug complexes.

Force fields such as the CHARMM or AMBER families are used to describe the internal and external forces of molecular systems during energy minimization or MD simulations. If there is no limitation in the force field, which is good for small objects such as medicine, the force field can be made using the CGenFF program, or the function parameters use automation, such as Antechamber. Virtual database scanning (VS) techniques are often used in large screen in silico combinatorial databases to identify potential binding sites for research purposes. Examples of embedding tools used for this purpose are DOCK and AutoDock and AutoDock Vina, both of which are free. Another example is the Pharmer application, which uses 3D pharmacophores for database validation [1,3].

A CADD computer database of drugs such as VS drugs is an essential part of ligand identification. The common compound for VS is ZINC, which currently has about 90 million compounds and can be purchased from many suppliers. Internal databases can be created for specific VS needs, and pharmacology sites such as ChemBridge and ChemDiv provide chemical catalogs in SDF format for download. However, this can be difficult to translate into 3D structures, and keys in the data require physically valid protonation and tautomeric states. CADD products include Discovery Studio, OpenEye,

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Schrödinger, and MOE. These services are generally available to academic users at a reasonable cost and include many of the features required for CADD, including SBDD and LBDD methods [7].

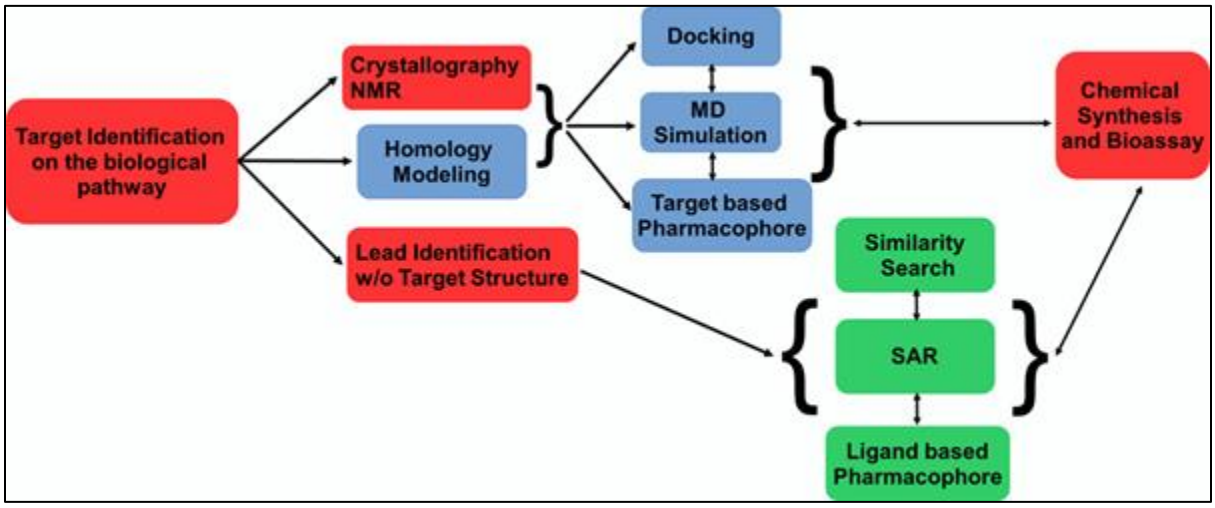

Figure 2: Basic CADD workflow in drug discovery. The wet process, SBDD, and LBDD CADD processes are described with solid, dashed, or dotted lines, respectively. The two arrowheads indicate that the two methods can be used interchangeably in different ligand designs.

Overview steps involve in CADD

1. Identification of the target molecule or biomolecule involved in the disease or condition of interest.
2. Preparation of a 3D model of the target molecule using molecular modeling software.
3. Virtual screening of large chemical libraries to identify potential drug candidates that can bind to the target molecule.
4. Optimization of the drug candidates using computational techniques such as molecular docking and molecular dynamics simulations to improve the efficacy and safety of the drug.
5. Selection of the most promising drug candidates for further validation using in vitro and in vivo experiments.
6. Validation of the selected drug candidates through clinical trials and regulatory approval before the drug can be marketed and used for treatment [3,4].

Parameters in CADD for TDDS

- Target identification
- Drug release kinetics
- Biocompatibility
- Pharmacokinetics
- Targeting efficiency
- Drug stability etc. [8]

Ligand-based drug design

Ligand-based drug design is another method commonly used in computer-assisted drug design and is used when a three-dimensional model of the target receptor is not available. Data from a panel of compounds against a

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given target can be used to identify electronic components and structures responsible for biological activity, respectively, such as the fact that similar social structures correspond to similar biological functions [9]. Some of the methods used in ligand-based virtual screening include pharmacophore modeling, quality-relationship analysis (QSAR), and artificial intelligence (AI) [2,9].

QSAR (Quantitative Structure-Activity Relationship)

In target drug design, QSAR (Quantitative Structure-Activity Relationship) is a useful tool for predicting the biological activity of new compounds before they are synthesized or tested in vitro. QSAR can help researchers identify which structural features of a compound are important for its activity against a specific target (e.g., receptor, enzyme, or protein). By analyzing the relationship between a compound's chemical structure and its biological activity, QSAR can help guide the design of new compounds that are more potent, selective, and less toxic than existing drugs [1,3,5].

QSAR can be used in various stages of target drug design, from lead identification to optimization. During lead identification, QSAR can be used to screen large chemical libraries and identify potential hits based on their predicted activity against a target of interest. QSAR can also be used to prioritize compounds for further development based on their predicted potency, selectivity, and ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) properties [1,3]. During lead optimization, QSAR can help guide chemical modifications to improve a compound's activity or selectivity while minimizing its toxicity or unwanted side effects. QSAR can also be used to predict the activity of analogs or derivatives of a lead compound, which can help identify potential backup compounds or optimize the lead further [1,2,4,9].

Overall, QSAR is a powerful tool in target drug design, as it allows researchers to make informed decisions about which compounds to synthesize, and test based on their predicted biological activity and properties.

Conclusion

Computer-Aided Drug Design (CADD) has become an essential tool for drug discovery and development. It involves the use of computer software to predict biological activity, pharmacological properties, and toxicity of potential drug compounds. Targeted drug delivery systems (TDDS) are designed to deliver drugs specifically to the affected site, reducing the side effects associated with traditional drug delivery methods. The use of CADD in TDDS allows for the development of drugs with improved efficacy and reduced toxicity. Different types of drug delivery vehicles such as polymeric micelles, liposomes, lipoprotein-based drug carriers, nanoparticle drug carriers, dendrimers, etc. are being used in TDDS. The history of CADD dates to the 1960s, with the development of faster computers and more sophisticated software tools leading to a rapid expansion of CADD research in the 1950s and 2000s. CADD methods are mathematical tools used to manipulate and quantify the properties of potential drug candidates, and they are implemented in a number of programs, both publicly and commercially available. Ligand-based drug design is one of

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the most used CADD techniques, which involves the design of drugs based on the properties of known ligands that bind to a specific target. The key parameters involved in CADD for TDDS include target identification, drug release kinetics, biocompatibility, pharmacokinetics, targeting efficiency, and drug stability.

In conclusion, computer-aided drug design (CADD) has emerged as a critical tool for drug discovery and development, with the ability to design and optimize drug candidates more efficiently and effectively than traditional experimental methods. Targeted drug delivery systems designed using CADD tools deliver drugs specifically to the affected site, reducing the side effects associated with traditional drug delivery methods. CADD is a rapidly evolving field that encompasses a broad range of research areas, including drug discovery, structural biology, and bioinformatics. The development of faster computers and more sophisticated software tools has led to a rapid expansion of CADD research. The common software packages used in CADD include CHARMM, AMBER, NAMD, GROMACS, Open MM, and others. The process of CADD involves the identification of the target molecule or biomolecule involved in the disease or condition of interest, preparation of a 3D model of the target molecule, virtual screening of large chemical libraries to identify potential drug candidates, optimization of drug candidates using computational techniques such as molecular docking and molecular dynamics simulations, selection of the most promising drug candidates for further validation using in vitro and in vivo experiments, and validation of the selected drug candidates through clinical trials and regulatory approval before the drug can be marketed and used for treatment. The parameters in CADD for targeted drug delivery systems include target identification, drug release kinetics, biocompatibility, pharmacokinetics, targeting efficiency, drug stability, and others.

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