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Role Of Computer Aided Drug Design In Drug Discovery & Development .

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ABSTRACT
Drug discovery is a process which aims at identifying a compound therapeutically useful in curing and treating disease. This process involves the identification of candidates, synthesis, characterization, validation, optimization, screening and assays for therapeutic efficacy.
Over the last Few years, computer aided drug design (CADD) also known as in silico Screening has become a powerful technique because of its utility in Various phases of drug discovery and development through various advanced features.
Computer-aided drug design (CADD) is the use of computers (or workstations) to aid in the creation, modification, analysis, or optimization of a design.[1] This software is used to increase the productivity of the designer, improve the quality of design, improve communications through documentation, and to create a database for manufacturing.
This review Focuses on computational chemistry and computer aided drug discovery Which are aimed to cover a wide range of computational approaches Including new methodologies as well as practical aspects in this area.
Basic concepts about computational techniques such as Molecular Modeling, QSAR, Docking, Pharmacophore Mapping, Virtual Screening and Deno Drug Design.
KEYWORDS: *Drug discovery, CADD, virtual screening, Drug design, pharmacophore, QSAR.*

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I. INTRODUCTION

Drug discovery is a process which is intended to identify a small synthetic molecule or a large biomolecule for comprehensive evaluation as a potential drug candidate. … Drug development process can be segregated into preclinical and clinical development stages .

Drug discovery is a lengthy process that takes around 10-15 years [1] and costs up to 2.558 billion USD for a drug to reach the market [2]. It is a multistep process that begins with the identification of suitable drug target, validation of drug target, hit to lead discovery, optimization of lead molecules, and preclinical and clinical studies.

The use of computer-aided drug discovery (CADD) techniques in preliminary studies by leading pharmaceutical companies and research groups has helped to expedite the drug discovery and development process minimizing the costs and failures in the final stage .

The application of rational drug design as an integral part of CADD provides useful insights into the understanding of the binding affinity and molecular interaction between target protein and ligand.

Different methods employed in the identification of new inhibitors from chemical databases include pharmacophore modeling, quantitative structure-activity relationship (QSAR), molecular docking, quantum mechanics, and statistical learning methods.

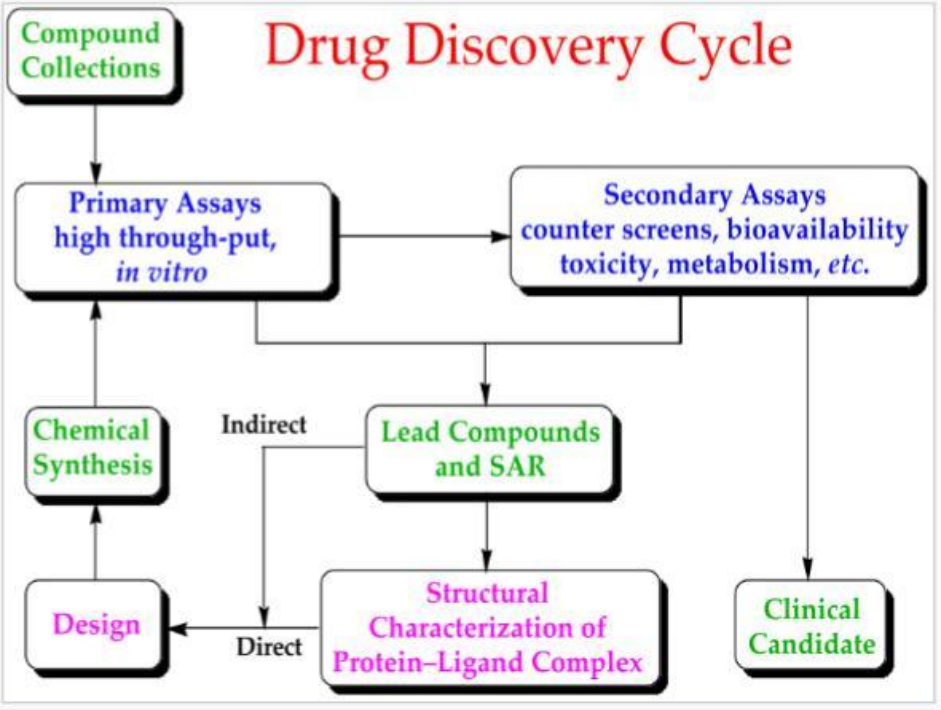
CADD can be broadly divided into structure-based and ligand-based drug design approaches, both have been widely used in the drug discovery process in the identification of suitable lead molecules.

Information from the CADD methods is then used to design compounds that are subjected to chemical synthesis and biological assay, with the information from those experiments used to further develop the SAR, yielding further improvements in the compounds with respect to activity as well as absorption, disposition, metabolism and excretion (ADME) considerations.

Application of CADD in the field of pharmaceutical Industries like numerous of approved drugs that Credited their discovery in large part to the tools of CADD were reported, such as: angiotensin converting enzyme (ACE) inhibitor captopril for The treatment of hypertension 9, 10, Carbonic Anhydrase inhibitor dorzolamide for the treatment Of cystoid macular edema 11, 12, renin inhibitor Aliskiren, which is used for

essential hypertension 13, 14, 15, Human immunodeficiency virus (HIV) Protease inhibitors saquinavir, ritonavir and indinavir For the treatment of HIV.

The flow chart of drug discovery and development.



Significance of CADD in Drug Discovery and development.

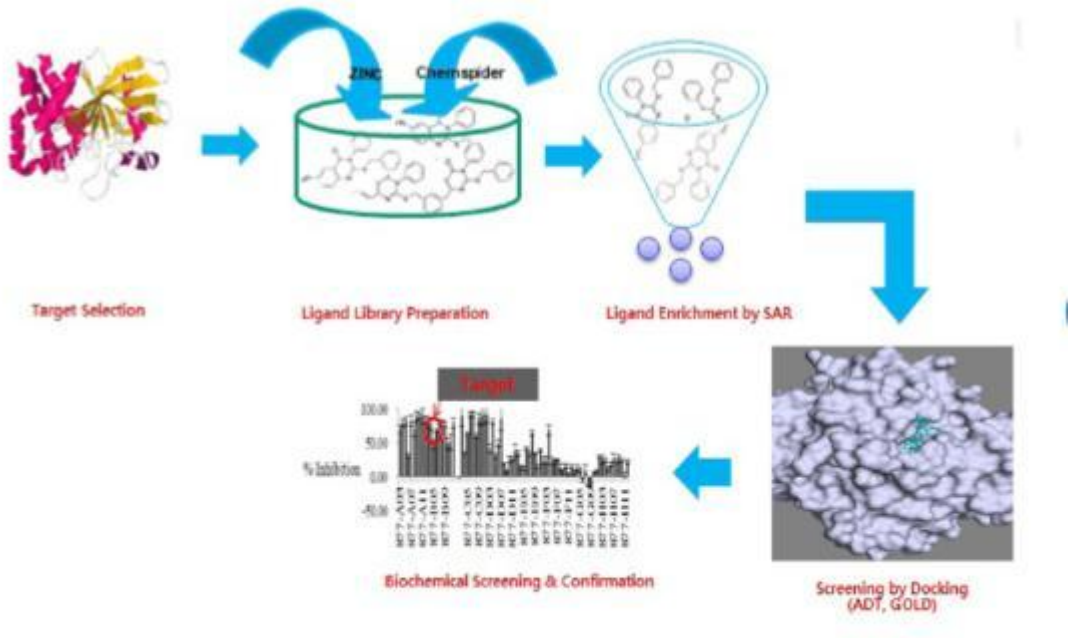
- Filtration of large compound libraries into Smaller compounds sets of predicted activity Those could be further tested experimentally.
- Gives information about optimization of lead Compounds, whether to increase bio affinity And pharmacokinetic properties like absorption, Distribution, metabolism, excretion (ADME) as Well as toxicity knowledge
- Designing of novel compounds containing one Functional group in a chemical compound or new Chemo types by Joining different Fragments.

Techniques of CADD

- ***Pharmacophore modeling***
- ***Virtual screening***
- ***Molecular modelling***
- ***QSAR***
- ***De novo drug design***
- ***Molecular docking .***

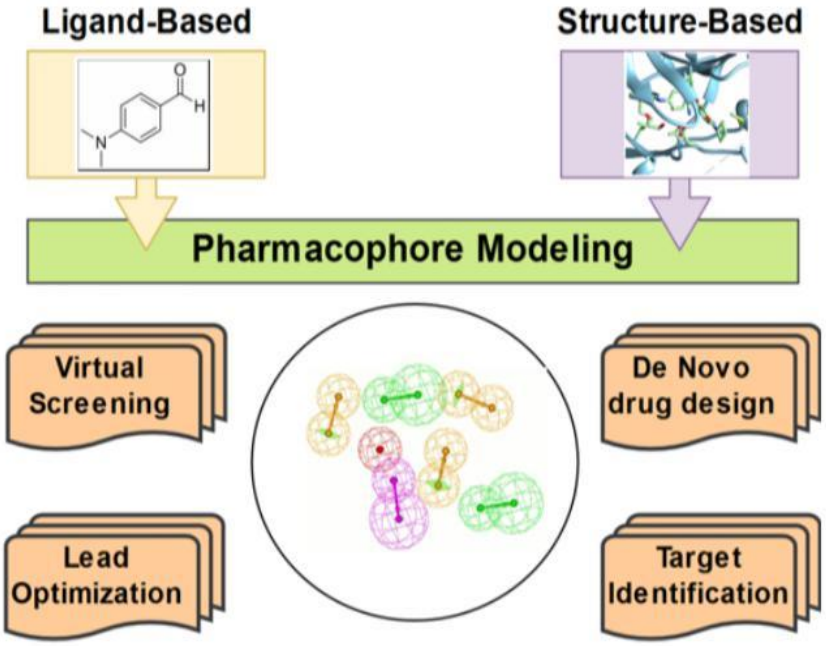
1.Virtual screening(VS)

- Virtual screening (VS) is a computational technique used in drug discovery to search libraries of small molecules in order to identify those structures which are most likely to bind to a drug target, typically a protein receptor or enzyme.
- VS be divided into two distinct categories ligand-based VS and structure-based VS.



2. Pharmacophore modeling

- Pharmacophore approaches are successful subfields of computer-aided drug design (CADD) which have become one of the major tools in hit identification, lead optimization, and rational design of novel drugs
- A pharmacophore model is the ensemble of common steric and electronic features that are necessary to ensure the optimal molecular interactions with a specific biological target and to trigger (or block) its biological response.



- Pharmacophores can be used to represent and identify molecules on a 2D or 3D level by schematically depicting the key elements of molecular recognition.

3.Molecular modelling

- Molecular modelling encompasses all methods theoretical and computational, used to model or mimic the Behavior of molecules.
- The methods are used in the fields of computational chemistry, drug design, computational biology and materials science to study molecular systems ranging from small chemical systems to large biological molecules and material assemblies.
- Is one aspect of molecular modelling, as it involves the use of classical mechanics (Newtonian mechanics) to describe the physical basis behind the models.

4. **QSAR**

Quantitative structure–activity relationship models (QSAR models) are regression or classification models used in the chemical and biological sciences and engineering.

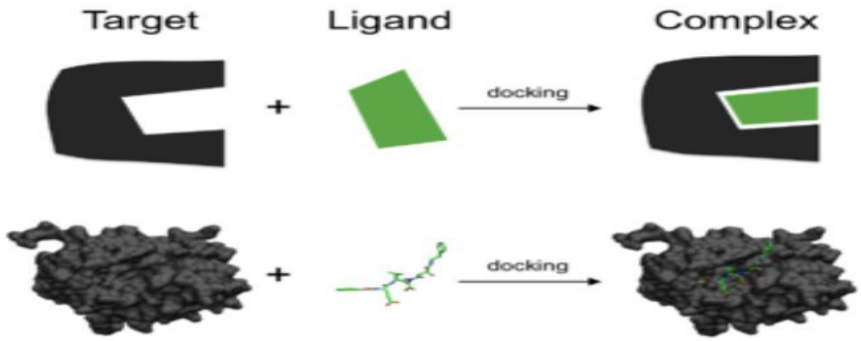
In QSAR modeling, the predictors consist of physico-chemical properties or theoretical molecular descriptors[1][2] of chemicals; the QSAR response-variable could be a biological activity of the chemicals.

Different properties or behaviors of chemical molecules have been investigated in the field of QSPR. Some examples are quantitative structure–reactivity relationships (QSRRs), quantitative structure–chromatography relationships (QSCRs) and, quantitative structure–toxicity relationships (QSTRs), quantitative structure–electrochemistry relationships (QSERs).

5. Molecular docking.

In the field of molecular modeling, docking is a method which predicts the preferred orientation of one molecule to a second when a ligand a target are bound to each other to form a stable complex.

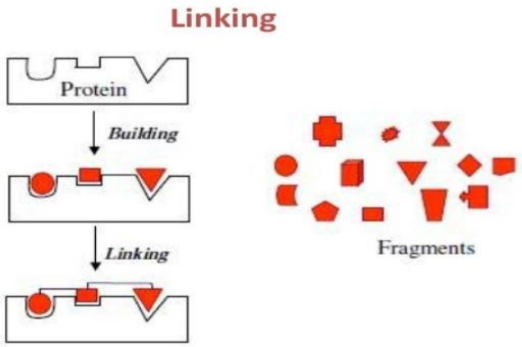
Molecular docking is one of the most frequently used methods in structure-based drug design, due to its ability to predict the binding-conformation of small molecule ligands to the appropriate target binding site.



Schematic illustration of docking a small molecule ligand (green) to a protein target (black) producing a stable complex.

6. **De novo drug design.**

De novo drug design is an iterative process in which the three-dimensional structure of the receptor is used to design newer molecules. It involves structure determination of the lead target complexes and the design of lead modifications using molecular modeling tools.



II. CONCLUSION

Gives valuable information about target molecules, Lead compounds, screening and optimization. The Latest advancements like QSAR, combinatorial Chemistry, different databases and available new Software tools provide a basis for designing of Ligands and inhibitors that require specificity. Different approaches, stages of designing, docking, Pharmacophore modelling, homology modelling Are the backbone of the CADD process.

CADD can assist researchers studying interactions between drugs and receptors. We believe this review will be helpful for better understanding of CADD and its applications towards the discovery of new drug candidates against various fatal NDs.

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REFERENCES

[1]. MartiRenom MA, Stuart AC, Fiser A, Sanchez R, Melo F And Sali A: Comparative protein structure modelling of Genes and genomes. Annual Review of Biophysics and Bio Molecular Structure 2000; 29(1): 291-325.
[2]. Pfisterer JH, Liang Y, Schneider O and Bandarenka AS: Direct instrumental identification of catalytically active Surface sites. Nature. 2017; 549(7670): 74-77.
[3]. Boissel JP, Lee WR, Presnell SR, Cohen FE and Bunn HF: Erythropoietin structure-function relationships. Mutant Proteins that test a model of tertiary structure. Journal Of biological chemistry, 2013; 268(21):15983-15993.
[4]. Neema Bisht and B. K. Singh, ROLE OF COMPUTER AIDED DRUG DESIGN IN DRUG DEVELOPMENT AND DRUG and development, IJPSR, 2018; Vol. 9(4): 1405-1415.
[5]. actus.nci.nih.gov/download/NCI.
[6]. shabana Bibi and katsumi sakata,
[7]. Dharampreet singh, Ramanjeet Kaur , Dr.R.K.Patil, Dr.H.C.Patil, A review on : Computer Aided Drug Design", International Journal of Emerging Technologies and Innovative Research ; ISSN:2349-5162, Vol.7, Issue 3, page no.1165-1176, March-2020.
[8]. Kapetanovic I.M. Computer-aided drug discovery and development (CADDD): in silico-chemicobiological approach. Chem. Biol. Interact. 2008;171(2):165–176. [http://dx.doi.org/ 10.1016/j.cbi.2006.12.006]. [PMID: 17229415]
[9]. R.A.Hodo, B.A. Kidd, K. Shameer, B.P. Reudhead, J.T. Dudley in silico method for drug repurposing and Pharmacology computational approaches to drug repurposing and pharmacology WIRREs syst. Biol. Med. 186 ,2016.
[10]. Injamul Hoque, Arkendu Chatterjee, Somenath Bhattacharya, Raj Biswas, An Approach of Computer-Aided Drug Design (CADD) Tools For In Silico Pharmaceutical Drug Design and Development; International Journal of Advanced Research in Biological Sciences; ISSN: 2348-8069; Volume 4, Issue 2 – 2017.
[11]. Veselovsk AV, Ivanov AS; Strategy of computer- aided drug design; Russian academy of medical Science; 2003; 3(1); 33-40.
[12]. Vyas VK, Ukawala RD, Ghate M, Chintha C;Homology modeling a fast tool for drug ,Discovery: current perspectives; Indian journal of Pharmaceutical sciences; 2012; 74(1); 1–17.
[13]. Lipinski CA; Lead- and drug-like compounds: the Rule-of-five revolution; Drug discovery today Technologies; 2004; 1(4); 337–341.
[14]. Anderson AC. The process of structure-based drug design. Chemistry & biology. 2003; 10(9):787-97.
[15]. Hopfinger AJ. Computer-assisted drug design. Journal of medicinal chemistry. 1985; 28(9):1133-9
[16]. Daina A, Blatter MC, Baillie Gerritsen V, Palagi PM, Marek D, Xenarios I, et al. Drug Design Workshop: A Web-Based Educational Tool To Introduce Computer-Aided Drug Design to the General Public. Journal of Chemical Education. 2017; 94(3):335-44.
[17]. Zhang S. Computer-aided drug discovery and development. In Drug Design and Discovery. 2011; 716:23-38.
[18]. Shekhar C. In silico pharmacology: computer-aided methods could transform drug development. Chemistry & biology. 2008; 15(5):413-4.