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A UNIFIED FRAMEWORK FOR COMPUTER-AIDED DRUG DESIGN: INTEGRATION MOLECULAR DOCKING, AND ADMET PREDICTION

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ABSTRACT

This review explores the integration of molecular docking, and also ADMET prediction in computer-aided drug design (CADD). It highlights how these computational methods enhance the drug discovery process, providing efficient and cost-effective strategies to predict drug behaviour, optimize pharmacokinetic properties, and identify promising drug candidates. Despite addressing several challenges, including the quality of datasets, the integration of these tools offers a synergistic framework that can significantly streamline drug design and development.

KEYWORDS: CADD, Molecular docking, ADMET, Virtual screening.

INTRODUCTION

In the rapidly evolving landscape of pharmaceutical research and the integration of computational methods has become a cornerstone in drug discovery and development efforts. Computer-aided drug design (CADD) offers a more efficient and cost-effective approach, complementing traditional experimental techniques. By leveraging computational tools such as molecular modelling, structure–

activity relationships, and virtual screening, researchers can predict the behaviour of drug candidates, assess their interactions with biological targets, and optimize their pharmacokinetic properties before synthesis and experimental validation.[1-3]

CADD and Drug Discovery aim to showcase some of the latest advancements in this interdisciplinary field, highlighting the applications of computational approaches in accelerating the identification and optimization of therapeutic agents.[4] The drug discovery has been significantly transformed by the advent of CADD, which integrates computational tools with traditional pharmacological methods to streamline the discovery and development of novel therapeutic agents.[5] In its most common form, drug discovery and design involve the identification and modification (molecular optimization) of an active scaffold, or linking known active scaffolds.[5]

Despite the rapid evolution of CADD and its integration into modern drug discovery, several key limitations and challenges remain unaddressed. One is the biggest challenges in CADD are the availability and quality of biological and chemical datasets. In Many datasets used for training AI models in drug discovery are proprietary, incomplete, or biased toward well-studied compounds, leading to reduced predictive accuracy.[6]

It can perform a wide range of tasks, from identifying potential drug leads to optimizing their physicochemical and biological properties, thus contributing to a substantial reduction in both the financial cost and time required for drug discovery.[7] The main origin of virtual screening is the structure-based compound screening or docking and the chemical-similarity searching based on small molecules.[8] This approach is more cost effective to drug discovery since it applies high-performance computing to analyze chemical databases, selecting more promising compounds for experimental assays.[9]

The virtual screening (VS) is an automatic evaluation of virtual libraries of chemical compounds, using bioinformatics tools. There are two approaches for VS methods; the first one, named target-based virtual screening (TBVS) or receptor-based, exploits the molecular recognition between the ligand and a target protein when structural information about the target is available, and selects chemical that has high affinity for the target's active site.[10]

VS techniques can be grouped into two major categories, depending on the available structural information. The term structure-based virtual screening (SBVS), often denoted as

target-based VS, encompasses methods that exploit the three-dimensional (3D) structure of the target. These are most widely used SBVS technique is molecular docking, which uses the structural and chemical complementarity resulting from the interaction between a fragment-like or drug-like compound and its target receptor, predicting the preferred pose of ligands in the binding site through the use of scoring functions, often supplemented with pharmacophoric constraints[11] Molecular docking is a central method in structure-based ligand design and is used both to screen for ligands in chemical libraries and to model protein-ligand interactions in lead optimization. Based on a protein structure, molecular docking algorithms aim to predict both the binding mode of a ligand and the affinity of complex.[12]

the absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of chemicals are play vital roles in every stage of drug discovery and development.[13] This review is strongly focused on molecular docking of drug design, ADMET & specifically in virtual screening drug design for gives pharmacokinetic and safety profiles of molecules.

OVERVIEW OF CADD

Computer-aided drug discovery and design (CADDD) involve the use of information technologies to assist in the identification and/or development of novel chemical scaffolds with the desired alignment of relevant physicochemical and biological properties.[14] It has been seen that by use of CADD approaches we can reduce the cost of drug discovery and development up to 50%. CADD consist use of any software program-based process for establishing a standard to relate activity to structure.

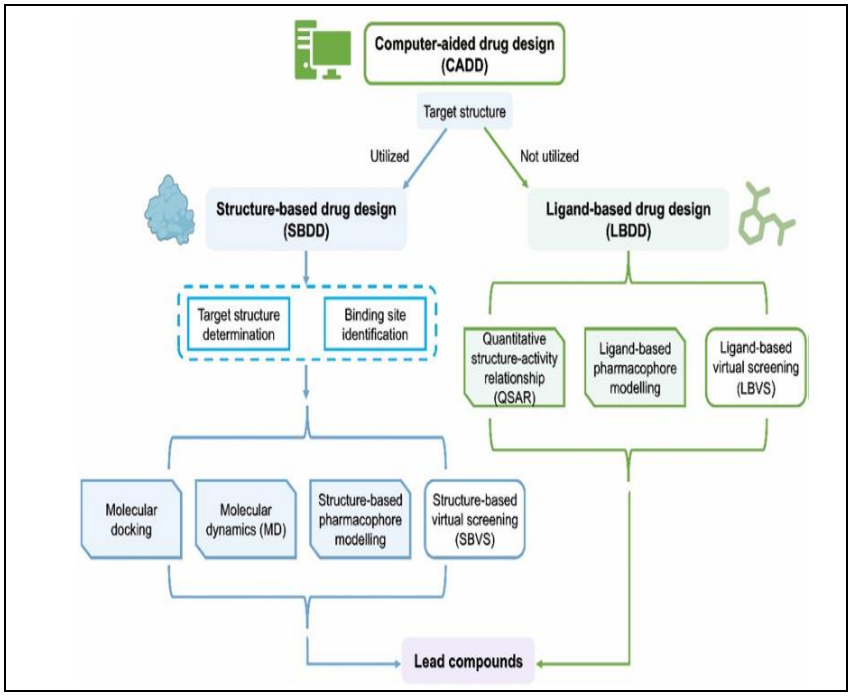

Fig. 1: **It can be classified into two primary categories including SBDD and LBDD, depending on whether the structure of the target is employed.[15]**

1. STRUCTURE-BASED DRUG DESIGN

In SBDD, structure of the target protein is known and interaction or bio-affinity for all tested compounds calculate after the process of docking; to design a new drug molecule, which shows better interaction with target protein.[16]

Overview of the process involved in SBDD

It runs through multiple cycles before the optimized lead reached into clinical trials. The first cycle comprises isolation, purification and structure determination of the target protein by one of three key methods: like X-ray crystallography, homology modelling also NMR. Using compounds comes through virtual screening of different databases are placed into a selected region (active site) of the protein. These compounds are scored and ranked on the bases of steric, hydrophobic, electrostatic interaction of these molecules with the active site of target protein.[17]

2. Ligand-Based drug design

In LBDD, 3D structure of the target protein is not known but knowledge of ligands which binds to the desired target site is known. These ligands can be used to develop a pharmacophore model or molecule which possesses all necessary structural features for bind to a target active site.[18,19]

MOLECULAR DOCKING

The process of molecules interacting with receptors is known as molecular docking. As cells connect to form a stable complex, a natural process takes place in a matter of seconds. They entail predicting how tiny compounds would interact with their biological targets using computational methods. Docking assists in identifying compounds that expected to exhibit favourable binding energies, making them viable candidates for additional development, by estimating the binding affinities and poses [binding conformations] of that ligand within the target protein's active sites.

The following are the fundamental prerequisites for molecular docking:

1. Ligand Representation

By adding or removing hydrogens, the most likely dominant structure is typically further altered, providing an estimate of the pKa values. It is important to ensure accurate atom typing occurs.

2. Receptor Representation

The superiority of the receptor structure employed has a major impact on the effectiveness of docking calculations. This implies that higher resolutions of the employed crystal structure will yield better docking results. A new assessment of protein–ligand complex structure's accuracy, limitations, and possible risks.

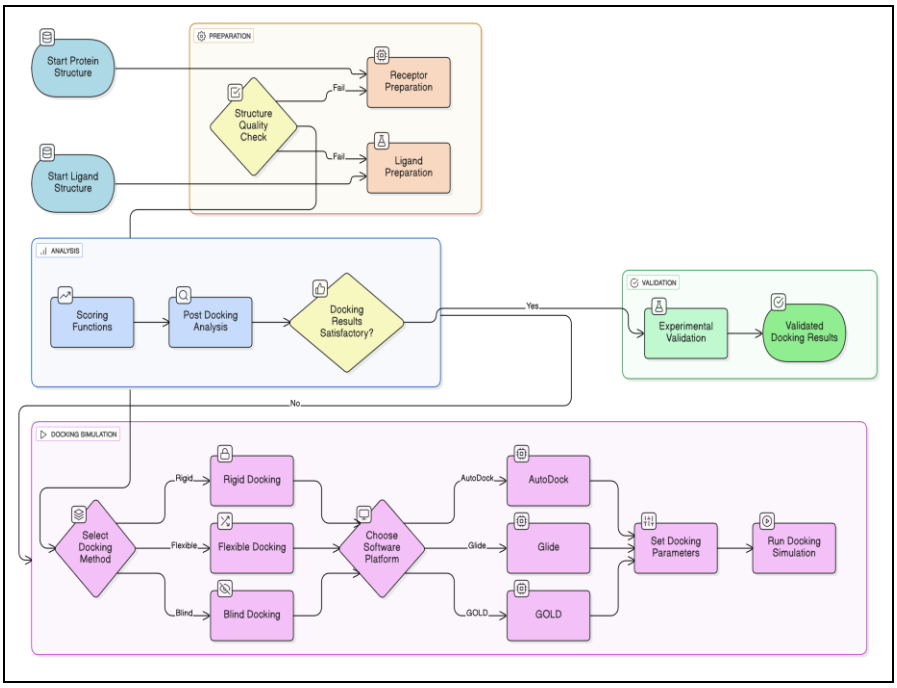

Fig. 2: Diagrammatic presentation of molecular docking.

MECHANISMS STEP OF MOLECULAR DOCKING

Setting up the attention protein is the first stage in creating a docking screen. To preserve the structure, X-ray crystallography or less frequently, NMR spectroscopy has been applied as biophysical approach. A docking method uses this protein arrangement as an input along with a folder holding ligands.

The following steps are involved in carrying out the molecular docking:

1. Preparation of protein

The three-dimensional structure of the protein must be obtained from the PDB and pre-processed. Under the conditions, this should result in side chains, stabilize the charges, allow water molecules to be amputated in the hollow, and substantially fill in the missing residue.

Estimating the active website the protein's active site needs to be predicted following protein synthesis. Although there are multiple active sites on the receptor, just the one that is of concern should be selected. Heteroatoms and water molecules are rarely important when they are present.

2. Creating the ligand

Ligands can be found in a variety of databases, including ZINC and PubChem, or they can be shown using the ChemSketch and ChemDraw tools. Lipinski's rule of five is the greatest guideline to follow when choosing a ligand. They stands for computer-aided drug design and detection. Because medications that satisfy two or more of the following criteria are comparable, it provides a substantial amount of opportunity for success or failure.

3. Docking

The interactions are examined once the protein and ligand have been docked.

4. Visualization

We can assess docking outcomes in two ways. Finding the score function that the software employs is the first step. For some score functions, smaller values indicate better interactions, whereas larger values indicate better interactions. Additionally, look for the decomposition of the score.

And ligand-protein interaction is show in visualization software such as Discovery studio visualizer and Chimera.

APPLICATIONS AND IMPORTANCES OF MOLECULAR DOCKING STUDIES

1. The lowest free energy forms of the receptor–ligand combination were identified.
2. Calculating the differential binding of a ligand to two separate macromolecular receptors
3. Analysis of geometry of a particular ligand-receptor complex.
4. Searching databases, sorting hits, generating leads, and optimizing future drug candidates.
5. To promote altering lead compounds to enhance their potency or other properties.
6. Designing libraries and creating data banks.
7. A potential drug's specificity against homologous proteins can also tested via docking.
8. It is feasible to screen for adverse effects that could arise from interactions with proteins, including proteases and cytochrome P450.
9. Docking is another popular method for predicting protein–protein interactions.
10. Understanding the many pathways taking place in the live system can be aided by understanding the molecular interaction through docking.
11. To draw attention to the potential drug targets.
12. Docking-based virtual HTS is less costly than of normal HTS and the faster than traditional screening.

ADMET PREDICTION IN DRUG DISCOVERY

ADMET stands for absorption, distribution, metabolism, excretion, and toxicity. These characteristics are crucial at every step of the drug development process. For users, ADMET Lab offers a practical and user-friendly interface. To support single molecule and the batch evaluation, two services—screening and evaluation—are built. The input parameters and also output data for each will be explained. The majority of issues that arise throughout the drug discovery process include unfavourable ADMET properties, which have been identified as a primary reason why promising molecules fail in the drug development pipeline and contribute to significant time, financial, and human resource expenditures.

In order to improve the likelihood that a molecule will make it to later phases of drug development, ADMET has raised interest in the early-stage prediction of ADMET features of therapeutic candidates. The efficacy of the compound with enhanced ADMET characteristics is then assessed further using appropriate animal models. Through a four-step procedure known as the clinical trials, the improved chemical is tested on human subjects to validate and confirm its potency, therapeutic efficacy, ADMET, and potential adverse drug reaction.

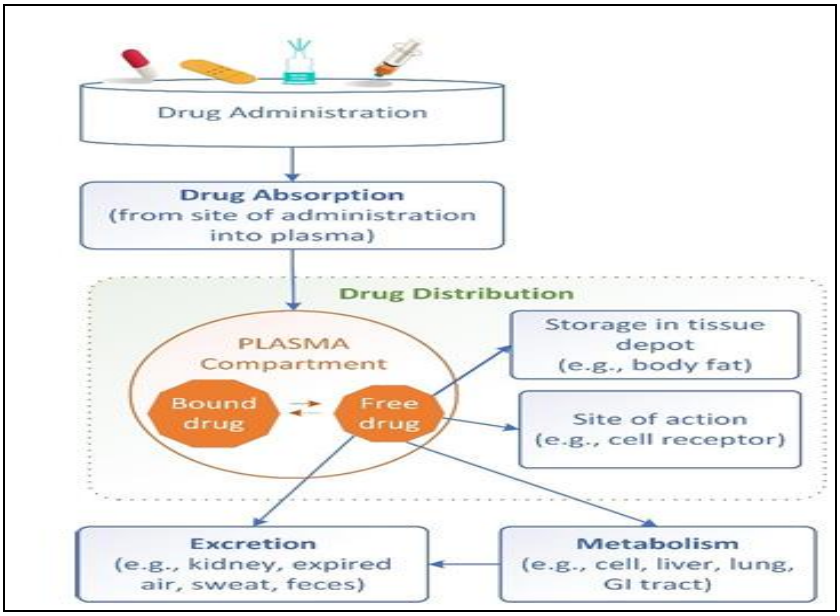

Fig. 3: Processing of ADMET.

Predicting toxicity (T) and absorption, distribution, metabolism, and excretion (ADME) characteristics aids in the selection of suitable drug candidates and promotes drug-likeness throughout the drug development process. Numerous AI-based techniques have been used in recent research to forecast ADMET features in an effort to lower preclinical failure rates in the drug discovery sector. With the help of the ADMET attributes, which are constructed using SVM or Bayesian techniques, the SwissADME web tool predicts physicochemical characteristics, descriptors, and drug-likeness. Large amounts of high-quality data are necessary to produce reliable prediction results since the quality of the prediction model is dependent on the input data. Drug discovery will be able to anticipate ADMET features more accurately with the help of multiple attempts to create extensive databases and benchmarks as well as algorithmic development.

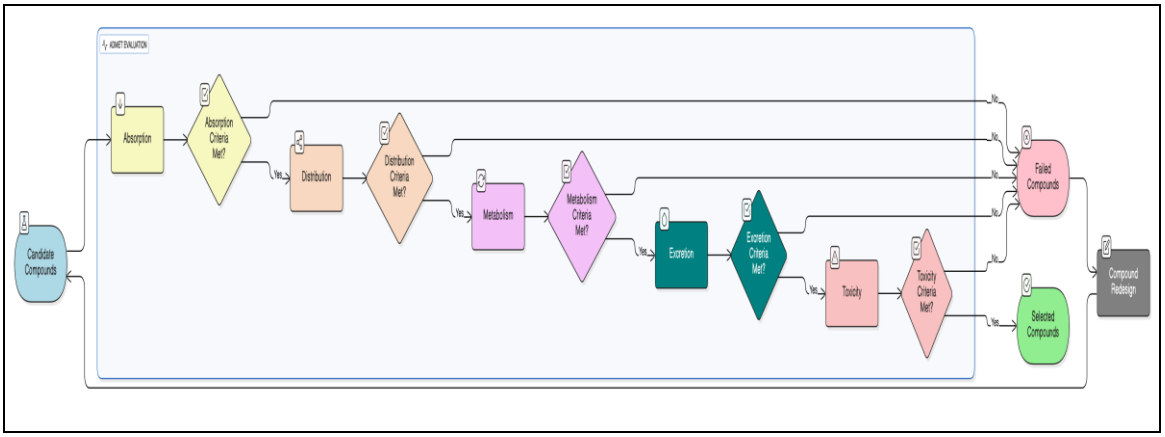

Fig. 4: Steps of ADMET.

INTEGRATION OF DOCKING AND ADMET

A complete pipeline for lead optimization is produced by combining molecular docking and ADMET prediction. In order to remove compounds with poor pharmacokinetics or toxicity, molecules found through docking are usually filtered using Lipinski's Rule of Five and then subjected to in silico ADMET screening.

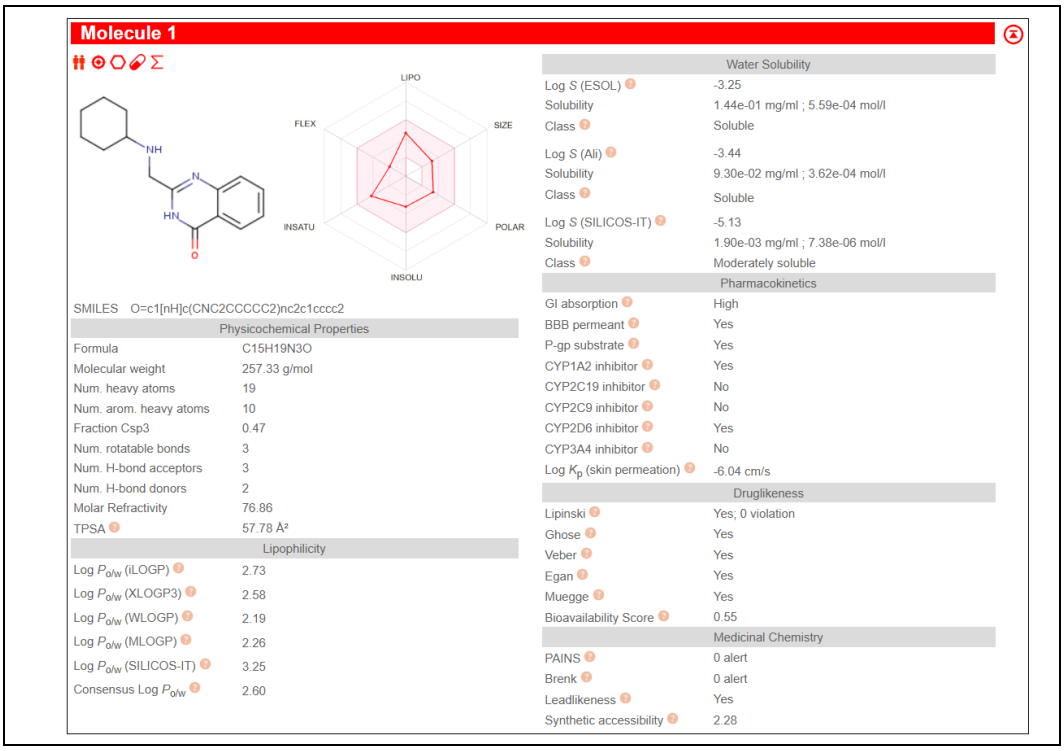

Fig. 5: SwissADME software molecules.

CHALLENGES AND FUTURE PERSPECTIVES

Virtual screening has drawbacks despite its achievements, such as protein flexibility, imprecise scoring, and inflated ADMET predictions. AI and machine learning will be used in the future to improve predictive ADMET modelling and docking accuracy using massive datasets.

High-quality data is a crucial component of research, as evidenced by the recent development and applications of big data and AI techniques to create statistical and computational models to address a variety of drug discovery issues. We have covered the many aspects of AI modelling techniques, large data pre-processing, and AI-based drug design applications, such as predicting SBVS and ADMET properties also identifying target protein binding sites.

CONCLUSION

Virtual screening, molecular docking, and ADMET prediction form a synergistic framework for rational drug design. Their integration allows faster, cost-effective, and more reliable identification of promising drug candidates. With continued improvements in algorithms and data integration, these computational approaches will transform drug discovery.

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REFERENCES

1. Ye, F.; Lin, M.; Jin, J.; Broussy, S. Editorial: Computer-Aided Drug Design: Drug Discovery, Computational Modelling, and Artificial Intelligence. Front. Chem. 2022; 10: 968687.
2. Anwar, T.; Kumar, P.; Khan, A.U. Modern Tools and Techniques in Computer-Aided Drug Design. In Molecular Docking for Computer-Aided Drug Design: Fundamentals, Techniques, Resources, and Applications; Elsevier: Amsterdam, The Netherlands, 2021; 1–30.
3. Oli, B. Revolutionizing Drug Discovery: A Comprehensive Review of Computer-Aided Drug Design Approaches. Int. J. Res. Appl. Sci. Eng. Technol, 2024; 12: 308–317.
4. Dorahy, G.; Chen, J.Z.; Balle, T. Computer-Aided Drug Design towards New Psychotropic and Neurological Drugs. Molecules, 2023; 28: 1324.
5. Medina-Franco, J.L. Grand Challenges of Computer-Aided Drug Design: The Road Ahead. Front. Drug Discov., 2021L; 1: 728551
6. Dorahy, G.; Chen, J.Z.; Balle, T. Computer-Aided Drug Design towards New Psychotropic and Neurological Drugs. Molecules, 2023; 28: 1324.

7. Bassani D, Moro S. Correction: Bassani, D.; Moro, S. Past, Present, and Future Perspectives on Computer-Aided Drug Design Methodologies. *Molecules* 2023, *28*, 3906. *Molecules*, 2023; 28(13): 5223. Published 2023 Jul 5.
8. Waszkowycz B. Structure-based approaches to drug design and virtual screening. *Curr Opin Drug Discov Devel*., 2002; 5(3): 407-413.
9. Ghosh S, Nie A, An J, Huang Z. Structure-based virtual screening of chemical libraries for drug discovery. *Curr Opin Chem Biol*., 2006; 10(3): 194-202.
10. Tudor I Oprea, Hans Matter, Integrating virtual screening in lead discovery, Current Opinion in Chemical Biology, 2004; 8(4): 349-358, ISSN 1367-5931, https://doi.org/10.1016/j.cbpa.2004.06.008
11. Pagadala, N.S.; Syed, K.; Tuszynski, J. Software for molecular docking: A review. Biophys. Rev., 2017; 9: 91–102.
12. Kitchen DB, Decornez H, Furr JR, and Bajorath J (2004) Docking and scoring in virtual screening for drug discovery: methods and applications. Nat Rev Drug Discov, 3: 935–949.
13. Guan L, Yang H, Cai Y, et al. ADMET-score - a comprehensive scoring function for evaluation of chemical drug-likeness. *Medchemcomm*, 2018; 10(1): 148-157. Published 2018 Nov 30.
14. Xiang M, Cao Y, Fan W, Chen L, Mo Y. Computer-aided drug design: lead discovery and optimization. Combinatorial chemistry & high throughput screening, 2012; 15(4): 328-37.
15. Hopfinger AJ. Computer-assisted drug design. Journal of medicinal chemistry, 1985; 28(9): 1133-9
16. Imam SS, Gilani SJ. Computer Aided Drug Design: A Novel Loom to Drug Discovery. Org. Med. Chem., 2017; 1(4): 1-6
17. Anderson AC. The process of structure-based drug design. Chemistry & biology, 2003; 10(9): 787-97
18. Hoque I, Chatterjee A, Bhattacharya S, Biswas R. An Approach of Computer-Aided Drug Design (CADD) Tools for In Silico Pharmaceutical Drug Design and Development. Int. J. Adv. Res. Biol. Sci., 2017; 4(2): 60-71.
19. Vázquez J, López M, Gibert E, Herrero E, Luque FJ. Merging Ligand-Based and Structure-Based Methods in Drug Discovery: An Overview of Combined Virtual Screening Approaches. *Molecules*., 2020; 25(20): 4723. Published 2020 Oct 15.