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Review article

Computational transformation in drug discovery: A comprehensive study on molecular docking and quantitative structure activity relationship (QSAR)

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ABSTRACT

The procedure for learning and creating a new medicine is widely seen as a drawn-out and costly endeavor. Different rational strategies are considered, depending on their requirements, as potential ways; nevertheless, techniques to designing drugs based on structure and ligands are well acknowledged as very practical and potent tactics in drug discovery. Computational approaches help decrease the need for Medicinal research with animals, helping to develop fresh, safe therapeutic concepts via rational design and positioning of existing products and supporting pharmaceutical scientists and medicinal chemists during the medication development process. Computer-aided drug discovery (CADD) methods are useful for reducing the time and cost of drug discovery and development and understanding the molecular mechanisms of drug action and toxicity. Molecular docking is a technique that predicts a ligand's binding mode and affinity to a target protein. At the same time, QSAR is a technique that establishes mathematical relationships between the structural features and biological activities of a series of compounds. This study reviews the current state and applications of CADD methods, focusing on molecular docking and quantitative structure–activity relationship (QSAR) techniques. This study reviews the principles, advantages, limitations, and challenges of these methods, as well as some recent advances and examples of their applications in drug discovery for various diseases. The study also discusses the future prospects and directions of CADD methods in the era of big data and artificial intelligence.

1. Introduction

In the 21st century, people are dependent on drugs because of many different lifestyles and diseases. Many medical fields like homeopathy, Ayurveda, and allopathy are popular globally. People, according to their views, rely on these medical professions. Medicine is a probabilistic science, not a pure science. Advances in medicine are primarily concerned with the science of healing and the advancement of science in the medical realm. Its history ranges from prehistoric times to the present. Medicine is the science of cures, including illness treatment and prevention, diagnostic practice, and health promotion. It also mentions plant ingredients, medications, and medicines used to treat various disorders and enhance health. The dictionary defines medicine as “the art of illness prevention."

Modern medicine has contributed significantly to healing in infectious diseases and emergencies. In most other areas, the primary purpose is control, which is also known as relief. Pharmacology, including psychopharmacology, is also primarily aimed at such management and remedies. Both clinical and research momentum must now be resolutely directed towards prevention and treatment. Longevity with happiness is another major challenge in modern medicine. The progress of vaccines for hypertension, diabetes, cancer, etc. is noteworthy. It also plays a role in meditation, yoga, spirituality, etc., preventing illness at various levels. The study of longevity, lifestyle changes, and healthy people over 100

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deserves special scrutiny to find something that supports longevity and well-being. Complementary and alternative medicine needs to be scrutinized to identify the appropriate model they may have.[1]

A drug development program begins when there is a sickness or clinical condition for which no viable pharmaceutical products exist, and the project's underlying driving force is this unmet clinical need. The first investigation, common in academia, gathers evidence to back up a hypothesis that blocking or activating a protein or pathway will have a therapeutic effect in a disease state. It takes 12–15 years to develop a novel pharmaceutical, and it costs more than $1 billion from the initial concept to the launch of the final product. Academic, clinical, and commercial research can all contribute to the development of a target. It may take numerous years to accumulate supporting evidence before deciding on a target for an expensive drug discovery program. After deciding on a target, a few academic institutions and the pharmaceutical industry have optimized many early steps for identifying compounds with desirable properties for use as medications. Starting with identifying a target, this review will focus on important preclinical stages of the drug development process.[2]

The reason why natural drug discovery is the program's goal is to supply one or more clinical candidate molecules, each with full evidence of biological activities for the relevant objectives for illnesses, as well as enough safety and drug properties. To be entered into the test house. This, we plan to discover and develop entirely new drugs with a different action method for a clinical sign that is not treated with approved drugs. The best drugs are repeated improvements to current drugs that are useful because they can provide existing drug benefits in energy, security, tolerance, or convenience but are often unrelated to manipulating goals. Biology differs from people who are directly affected by existing drugs.[3]

Drug research and development is a resource- and time-intensive process. More attempts are being made to use computer power in biological and chemical space combinations to speed up the discovery and development of drugs. Computational or *in silico* design is utilized in biomedicine to maximize absorption, hit-to-read selection, toxicity profiles, metabolism, hit identification, excretion, distribution, metabolism, and safety concerns to avoid existing. Quantitative structure, structure-related drug design, ligand-based drug design, and pharmacophore-based drug design are common computational approaches used in drug design (drug target docking). This involves a quantitative relationship between structure and activity and activity correlation.[4]

Traditional medicinal chemistry strategies are frequently combined with modern ligand-based drug design (LBDD) and structure-based drug design (SBDD) approaches to explore the extensive biological and chemical space as a critical component in the lead optimization, hit-to-lead generation and new chemical entity development processes.[5] A range of information technologies and the drug discovery process have evolved over the last 25 years to the point at which they are now inseparable parts of a pipeline that starts with fundamental research and ends with disease-specific medications. The intertwining of information technology (it) and the drug development process dates back to the mid-to late-1970s in academic research laboratories. The introduction of air-cooled, floor-standing 'minicomputers' was a crucial enabler (Fig. 1). Enzyme and chemical kinetics, x-ray crystallography, various types of spectroscopy, simple ligand binding assays, and early statistical techniques for protein structure prediction were among the applications.[6] Until now, drug discovery was essentially a linear process based on biology and chemistry's sequential methodologies. As a result, scientific disciplines have been divided into 'functional silos,' with little debate during the process of drug discovery. Screening large, randomised chemical libraries against a handful of pharmacologically relevant, and in a few cases poorly defined, biological targets is the principal method in developing the drug process. Despite this strategy having some favorable outcomes, the effect of hts, high-speed combinatorial chemistry technologies, and ultra-hts has been less than the 'multi-fold' boost in drug development productivity that was originally predicted.[7]

In preliminary investigations, leading pharmaceutical companies and

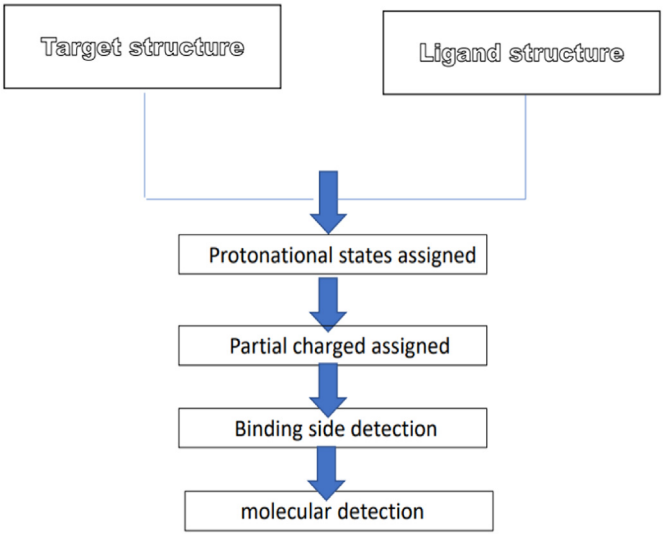

Fig. 1. Flow process of computer drug delivery.

research organizations have adopted computer-aided drug discovery (CADD) methodologies to help speed up drug discovery and development while lowering the cost and failures occurring in the final stage. Some of the methods used to uncover novel inhibitors in chemical databases include quantitative structure–activity relationship (QSAR), pharmacophore modelling, molecular docking, statistical learning approaches, and quantum mechanics.[8] Wet-lab techniques can be combined with computer-aided drug design (CADD) to understand drug resistance mechanisms better, find new antibiotic targets, and develop novel antibiotics for known and unexplored targets. CADD is a valuable tool for searching new molecular entities. These are areas of current focus, including creating predictive tools to spot potential adme/tox liabilities, improved data source design and management, computer programs to create sizable libraries of pharmacologically interesting compounds, and new algorithms to assess the selectivity and potency of lead candidates. We look at some of the most important tools and services created to help seek novel drug candidates.[9]

The use of computer technology in medication research has made significant progress. Increase your understanding of structural, chemical, and biological facts. These methods are beneficial. To analyse large amounts of data from empirical and clinical investigations. In recent years, pharmaceutical corporations and university researchers have utilized calculation approaches for drug discovery, such as pharmacophore modelling and virtual screening, analysis of QSAR, and molecular docking to create pharmacologically active drugs.[10]

Through a range of sophisticated characteristics, computer-aided drug development (CADD), which is also known as '*in silico* screening', is now a potent approach due to its utility at many stages of drug discovery and development. *In silico* screening also lays the way for manufacturing and testing molecules chosen for improved therapy. This review mainly concentrates on computational chemistry and drug development, and it tries to cover a broad spectrum of computational methodologies, which include novel methods and practical elements of the subject. CADD generated clinically approved pharmaceuticals; it is also crucial for *in silico* drug design, such as homology modelling, docking, pharmacophore creation, multi-target search and design, quantitative structure–activity connection, and conformation generation.

Computational technology is quickly gaining acceptance, adoption, and reputation in drug research and development procedures. Computational drug design, computer-aided drug development (CADD), computational molecule design (CAMD), computational molecule modelling (CAMM), insilco drug design, rational drug design, computer-assisted rational drug design, and so on are all subfields of this topic. The

term CADD stands for computer-aided drug discovery and development, which encompasses the complete process in this domain overall. Computational and laboratory approaches are both significant in drug discovery and development.[11] This paper aims to show how molecular docking can be a game changer for the medical field and provide much use for people in the medical field.

This study examines the present status and uses of computer-aided drug discovery (CADD) technologies, specifically focusing on molecular docking and quantitative structure–activity relationship (QSAR) tools. This study's primary goals are to conduct an in-depth analysis on the use of computational techniques, specifically molecular docking and QSAR, in the drug discovery and development field. Examine the fundamentals, benefits, difficulties, and latest developments of molecular docking and QSAR methods for creating new inhibitors and enhancing lead compounds. To show the application of molecular docking and QSAR techniques using specific instances of drug targets and therapeutic candidates for diseases including chikungunya virus, cancer, and complex disorders and discuss the future possibilities and directions of computer-aided drug design and its integration with disciplines like systems biology, artificial intelligence, and machine learning.

2. Classification of computer-aided methods for drug discovery

Different methods involved in computer aided drug discovery are as follows.

2.1. Quantitative structure activity relationship (QSAR)

In computational drug design, QSAR is a vital chemometric instrument. QSAR research relates structural characteristics and physical and chemical qualities of closely structured compounds to their therapeutic activity. It tries to find a link connecting a series of compounds' experimental activity and molecular descriptors to define structure information. The response of biologically active chemicals to their structural, physical, and chemical features are represented by QSAR/QSPR models, which are mathematical equations.[12]

2.2. Docking

The ligand-target molecule interaction is determined using the molecular docking approach. It calculates the ligand's binding affinity to form a stable complex with the protein by determining the preferred direction of the minimal free binding energy. Ionic bonds, hydrogen bonds, hydrophobic contacts, and van der Waals interactions are Non-covalent interactions involved in this. Molecular docking research between protein and protein, ligand and protein, and protein and nucleotide is conceivable. The molecular docking approach involves the preparation of ligands, production of three-dimensional structures of proteins, determination of binding energy in a protein ligand complex, and interpretation of data.[13]

2.3. Lead optimization

In a drug metabolic environment, lead optimization is a complicated process. It usually entails using a variety of *in vivo* and *in vitro* screens in order to evaluate the drug metabolism and pharmacokinetic (DMPK) features of many compounds and to give an early check on safety issues that can be analyzed in a higher throughput manner. The goal is to develop a molecule with the requisite DMPK characteristics, biological activity, and a safety profile suitable for the therapeutic indication.[14]

2.4. ADME estimation

The typical method for studying pharmacokinetics, or what happens to a drug molecule in the body, is categorizing the various factors affecting target access into separate parameters. These ADME (Absorption, Distribution, Metabolism, and Excretion) factors can be assessed individually using specialized methodologies. Early ADME estimation in the discovery phase has significantly minimized the percentage of pharmacokinetics-related failure in the clinical phases1. Computer models have been promoted as an effective substitute for experimental approaches for ADME prediction, particularly in the early stages when there are few chemical structures but few compounds.[15]

2.5. Homology modelling

The similarity of environmental residues in reference proteins at topologically analogous locations is represented by homology modelling. Due to the absence of experimental data, the only reliable way to obtain structural information is to develop a model based on a known 3D structure of homologous protein. Protein 3D structures give crucial insights into the molecular basis of their actions. Recent developments in homology modelling, notably in finding and to arrange template structures linearly with sequences, distant homologues, modelling the side chains and loops, and identifying faults in a model, have helped for a consistent prediction of protein structure that was previously impossible. This review concentrated on the characteristics and importance of homology.[16]

2.6. Structure based drug discovery

SBDD is currently essential for the effective creation of medicinal medicines and the comprehension of metabolic processes. SBDD is more effective than traditional drug discovery methods because SBDD tries to comprehend the molecular structure of disease and uses information on the biological target's 3D structure in the process. It is possible to discover the underlying molecular interactions used in ligand-protein binding and interpret experimental data in atomic-level detail by applying computational approaches and 3D structural information of the protein target. Using computers in drug development has the added benefit of producing novel medication candidates more swiftly and cheaply.[17]

2.7. Molecular dynamics

Molecular dynamics (MD) is a useful computational method for determining the physical foundation of structure, the function of biological macromolecules, and the dynamic development of a system. Bovine pancreatic trypsin inhibitor (BPTI) was the foremost MD simulation of biological molecules published fourteen years later. Although the X-ray structure of BPTI was precise at that time, its physiological function remained unclear.

The Research Collaboratory for Structural Bioinformatics (RCSB) is a key resource for MD simulations since it makes three-dimensional empirically established biological macromolecular structural data available. The RCSB Protein Data Bank (PDB) is a global depository for the processing and sharing 3D structural data of macromolecules like nucleic acids and proteins and is a vital resource for researchers.[18]

3. Docking method in drug discovery

Jain (2017)[19] talked about the use of computer-aided techniques in drug discovery. It is a method for predicting the location of tiny molecules or ligands within their target protein's active region (receptor). The basic goals of molecular docking methods are a prediction of ligand orientation concerning the receptor, strength by which ligand and receptor bind, and virtual screening, all of which are interrelated. It provides a compound with a high hit rate, and the chances of failure in the final stage are very low. We can get knowledge about drug interaction relationships. This method can remove the drug having low efficacy and poor ADMET property.

Tripathi and Misra (2017)[13] convey the structure-based approach to drug design called Molecular docking. The intermolecular interaction of

therapeutic targets, such as nucleic acids, proteins, lipids, and ligands, is the subject of molecular docking and simulation research. The docking methodology can be categorised in Induced fit docking: ligands and receptors can bind easily by arranging themselves in particular shapes and sizes. Rigid body docking: In this, both ligand and receptor are rigid and give tight bonding. They have restricted motion, so they cannot easily change conformation. Ensemble docking: Several protein structures were used as an ensemble for docking with ligands. Molecular docking helps drug discovery by identifying targets, evaluating drugs against disease, getting ideas about active sites, and preparing chemical compounds in less time.

Torres et al. (2019)[20] discussed various things involved in the docking method of drug discovery. Molecular docking is widely used in educational institutes and industries. We highlighted contemporary tendencies in the literature for advancing and applying the process for effective drug design, as well as critical features of the methodology. Benchmarking sets and the many metrics available are essential for validating performance advances. New docking software can help, yet it must be carefully picked because no one can be considered perfect. Using numerous SFs for consensus posing and scoring can be accomplished.

de Ruyck et al. (2016)[21] discussed the use of mechanics and other techniques in molecular docking. A thorough understanding of enzymes at the molecular level is critical in biological research. This can be done with the help of quantum mechanics of molecules. Researchers employed mixed techniques, in which the system is calculated using a molecular mechanics (MM) force field as a whole, then treat the spot with an ab initio (QM) treatment of curiosity. Secondly, they explain the interaction between ligands and drug molecules, which plays a significant role in drug discovery. Lastly, they discussed the protein–protein interaction as well as its structure. Furthermore, molecular docking techniques are being employed for other objectives, such as clarifying noncanonical quaternary representation or enzymatic processes of biological protein complexes structure.

Forli et al (2016)[22] discussed the role of computational docking in protein-ligand interaction in drug discovery. It starts with knowing the structure of the enzyme of our interest. Docking is then used to know the conformation and binding energy of drug molecules that bind to the target. There are various software and other methods that are useful in docking. In circumstances where the limits of requiring a speedy approach for energy evaluation are too restricted, advanced docking methods may be employed to improve outcomes. Auto Dock Vina will give you coordinates for one or more optimal ligand postures. With Raccoon2, tens of thousands of molecules can be docked and ranked against a macromolecular target. Auto Ligand examines atomic affinity maps to determine the best sites for substrate binding. This, along with many more advanced methods, was invented and is useful in docking.

Kitchen et al (2004)[23] discussed the scoring and docking method in drug discovery. The docking manner predicts the ligand configuration and orientation in one Targeted binding site. By this method, we have two major findings: First, we know the structure of the model, and second, the drug molecule's activity. It's crucial to consider how the ligand and protein are represented when comparing docking approaches. The receptor can be represented in three ways: Atomic, surface, and grid are used interchangeably. Virtual screening approaches, like ligand-based virtual screening, allow the de novo identification of active compounds without bias toward previous leads or hits. Even though docking and scoring are based on several approximations, their use in lead optimization, typically in conjunction with other computational methods, already goes beyond more conventional approaches to structure-based design.

Nguyen, Yu, and Keller (2018)[24] discussed the study of the chikungunya virus's binding sites and inhibitors. Because of their critical functions in virus attachment and entry, the chikungunya virus (CHIKV) contains envelope glycoproteins, regarded as vital prospective targets for anti-CHIKV medication development. Virtual screenings based on focused and blind dockings were carried out in this investigation using two obtainable crystal structures of mature and immature envelope glycoproteins to discover potential hit compounds and binding pockets for the virus. The docking data were used to understand further how the envelope glycoprotein complexes interact. For two envelope glycoprotein complexes, promising hit compounds have been found. 3N42 consists of two novel binding pockets, Pockets 2 and 3, since Pockets 1 and 4 had been described previously. These associations of hits from docking studies with the protein activities of these glycoproteins presented a viable drug discovery and design method to target these proteins and inhibit virus entry and attachment.

Mendie and Hemalatha (2022)[25] using a silico manner, this research looked at bioactive chemicals that can target GFRs. Growth factor receptors (GFRs) are proteins that are activated by interacting with their respective ligands (proliferation factors) and play essential roles in tumor cell growth, angiogenesis, metastasis, cell survival, cell migration, cell death, differentiation, chemoresistance, neovascularization, and organogenesis. The binding energy determines the binding affinity between receptors and ligands; the lower the energy, the stronger the binding affinity. The binding energy (kcal/mol), inhibitory constant (M/nM), and the number of hydrogen bonds and amino acids implicated in hydrogen bonding were all recorded after docking. This indicates that bioactive substances could bind to GFRs, inhibiting growth factors and, consequently, cancer cell proliferation.

Sharma, Sharma, and Kumar (2016)[26] discussed that docking studies have proven to be an important parameter for harnessing the structural dissimilarity in natural source products in an organized manner. This gives information regarding pyrido acridines containing Glide (Schrodinger). Anticancer pigments were docked using Investigations to identify whether potential molecules target these pigments. Docking was performed on various cancer macromolecules involved in various cell cycle pathways. Docking studies of selected macromolecule PCNP ligands and KIs.

Table 1 explores the diverse studies on docking method in the context of drug discovery.

4. QSAR for drug discovery

Factor (2010)[27] discussed the role of QSAR method in drug discovery. Complex illnesses, which entail single DNA variations (SNPs) in DNA, post-translational polypeptide alterations, as well as globally, climatic factors have a significant role in disability and mortality. Drugs, peptides, nucleotides, metabolic activity, illnesses, and communities are all examples of real dynamic structures that can all be statistically described

Table 1
Comprehensive review of docking method for drug discovery.

Software	Posing	Scoring	Availability
Vina	Iterated Local Search + BFGS Local Optimiser	Empirical/ Knowledge-Based	Free (Apache License)
Glide	Optimization (XP mode also uses anchor-and-grow)	Empirical	Commercial
Surflex	Fragmentation and alignment to idealised molecule (Protomol) BFGS optimisation	Empirical	Commercial
Plants	Ant colony optimisation	Empirical	Commercial
ICM	Biased probability + monte carlo + local optimization	Empirical	Commercial
Gold	Genetic algorithm	Empirical	Commercial
Gemdock	Geneticevolutionary algorithm	Phyisics based	Commercial
Flexx	Pattern recognition + incremental growth	Empirical	Commercial
Fred	Conformer generation + systematic rigid body	Emperical	Commercial

and compared depending on the characteristics of the relationships between their constituent parts. Quantitative Protein (or Proteome)-Disease Relationships (QPDRs) and QSAR are frequently used for predicting pharmacological effects and diseases, respectively. In 3 domains, cardiology and oncology—the study examined the most pertinent QSAR results in medication planning and application for complex illnesses. Categorizations of parts based on molecule characteristics and complicated network/graph theory are used in the quick QSAR approaches to produce mathematical models as tools for innovative drug creation against critical disorders.

Winkler (2002)[28] discussed the importance of QSAR in biomolecular discovery. By the QSAR method, we can find the molecule's three-dimensional structure. QSAR method involves obtaining a descriptor from molecular structure, identifying the best descriptor, mapping molecular structure, and finalizing the best descriptor. Various methods are available to generate descriptors. Selecting a descriptor is one of the most essential steps, but using poor descriptors leads to various problems in discovery. For mapping, the majority are regression techniques, the earliest of which is multiple linear regression. And lastly, it is necessary to know how predictive the finalized structure is. Improved based on chemical entities, a better knowledge of which molecular properties are most essential for a certain feature being simulated, and increased usage of genetic and artificial intelligence technologies will elevate QSAR's utility even higher than it is now.

Abdel-Ilah et al. (2017)[29] discussed the applications of QSAR in drug discovery. QSAR is one of the best techniques as it is also less expensive than others. QSAR/QSPR research may be used to develop and find novel inhibitors from scratch and improve the toxicity, ingestion, dispersion, metabolic activity, and elimination profiles of identified compounds from various sources. Various steps involved in this technique include identifying the molecule, calculating various descriptors, choosing the best descriptor, and checking and proving the descriptor. Validating the model's performance is critical in determining whether or not the findings meet the researcher's expectations. Two statistical metrics are utilized for this purpose: R square and Q square. However, QSAR predictability and robustness levels cannot be determined just by R2 and Q2 values; additional factors must be considered to reach a firm conclusion. The best-correlating descriptors in this study provide information on crucial functional groups in the structures of the chemicals studied. Although QSAR should not be used to substitute experimental values, it is a valuable forecasting tool that might be used without data.

Neves et al. (2018)[30] QSAR is an effective method for developing mathematical models that use regression and classification techniques to establish a continuously categorical or binary (active, dormant, dangerous, innocuous, etc.) biological or toxicology feature and chemical construction that is statistically significant. A QSAR model should also have the following characteristics: (I) a specific endpoint; (ii) an explicit approach; (iii) a specified area of application; (iv) sufficient measures of gawd, durability, and which get; and (v) a physiological understanding, if it is feasible. QSAR is still commonly utilised in research sans justification or an additional perspective since it remains regarded as a complement to clinical assessment and synthesis research. The industry researched a handful of VS executions, most of which resulted in identifying potential hits and leading candidates. The uses of Appropriately VS for attack optimization and finding new hits are shown in the instances below.

Rudrapal and Chetia (2020)[12] the Quantitative Structure–Activity Relationship approach may be developed to construct quantitative correlations connecting a structure with its biological activity (QSAR). The main principle of QSAR is to make certain compound modifications to improve its activity and form new compounds. Creating a data set, optimizing the structure, computing and selecting molecular descriptors, and ultimately, model assessment and evaluation are all processes in QSAR analysis. These days, two types of QSAR are used 2D and 3D QSAR. A QSAR model must follow clear algorithm methods and satisfy several tests, including model fitness, robustness, and predictability. It functions as a tool for studying mechanisms of biological responses using extraction. Notably, in descriptors, there are patterns. It is associated with the observed biological activity.

Designing drugs based on their structures (SBDD) and ligands (LBDD) a vital basis in rational design. Virtual or *in silico* screening supplements drug discovery using large-scale screening (HTS) programs to recognize biomolecules. Docking serves two important functions: Searching for the ligand's conformation and configuration, there is a binding site, which ranks assessing the strength of the connection between agonist as well as the receptor when posing a specific small molecule on a specific docking, which rates several ligands based on their relative affinity for a specific target.

Kleandrova et al. (2021)[31] presented the first model with several targets (mt-QSAR-MLP) to realistically build based on quantitative structure–activity correlations and a multilayer perceptron neural network and extremely adaptable enzymes that affect different dangerous worms' ability to survive and/or attack hosts. The facts on the antagonistic strength, or even the level necessary to produce 50% interference (IC50) in any of the five-parasite proteins indicated above, were retrieved from physiochemical data.

Wang et al. (2015)[32] Experimenting with blood–brain barrier drug molecule permeability models is high in cost and lengthy. As alternatives, several conventional (QSAR) models have indeed been created in the past. A five-fold bridge was utilized to verify the produced models, and the high-quality design was used to validate forecast set chemicals externally. Moreover, we generated transporter profiles for important target chemicals using previously published membrane transporter models.

Kwon et al. (2019)[33] use a computational modelling technique called the quantitative structure–activity relationship (QSAR) to identify correlations between the structural characteristics of chemical compounds and their biological functions. Drug development depends on QSAR simulation. It suggested a thorough evolutionary algorithm for developing cross-verified models and fusing them using second-level meta-learning. Additionally, we describe a reduced single-molecule effective in monitoring (SMILES)-based end-to-end machine-learning individual encoder that can automatically generate sequential characteristics.)

Zhang et al. (2006)[34] the modelling strategy that was developed utilizing the principle of passive training. A least squares statistical method and the bioactivities of the substances in the test dataset, which are most chemically identical to the test compound, are used to forecast the action of the test substance. An innovative Autonomous Lazy Leaning Quantification Structure–Activity Association (ALL-QSAR) modelling technique has been created based on the lazy learning theory.

Table 2 explores the diverse studies on QSAR in the context of drug discovery.

5. Future aspects

Molecular Docking offers compounds with high success rates. These methods reduce the likelihood of failures in the final phase. It teaches us about the structure of polypharmacy.[19] Docking can be used to anticipate where a ligand will bind to a protein and in what relative orientation. This knowledge could be used to create more potent and selective analogs.[13] Docking is increasingly frequently used to help with a range of drug discovery activities, such as identifying innovative chemical frameworks from vast substance databases, *in silico* target scanning and screening for medication repurposing, polypharmacology, and adverse effect estimation, among others.[35] QSPR/QSAR models that predict the properties or behaviors of organic compounds may be made using several techniques. Thanks to the adjectives employed in model construction, you may be able to concentrate on particular characteristics that explain a compound's desired feature or activity. Even though experimental data shouldn't replace QSAR,it is a valuable forecasting tool that might be used without data.[28] QSAR modelling will be particularly valuable in the

Table 2
Systematic study on QSAR for drug discovery.

Source	Ta	Posing b	Consensus strategy	Analysis
DUD-E/PDB	102/3	4	STANDARD DEVIATION CONSENSUS(SDC)	RANK/SCORE CURVES
PDBBIND DUD	228/1	VINA/AUTODOCK	COMPOUND REJECTION IF POSE RMSD<2.0	SUCCESS RATE
MTOR INHIBITORS	1	GLIDE	LINEAR COMBINATION	BEI CORRELATION
PDB	100	AUTODOCK	SUPERVISED LEARNING	AVERAGE RMSD SUCCESS RATE
PDBBIND CSAR	421	GLIDE	SUPPORT VECTOR	TOP POSE/TOP RANK

future since it is a time-, labor-, and cost-effective technique for discovering hit compounds and leading candidates in the early phases of drug development.[30] Improved QSAR technologies, higher microchips, and monetary support to produce safer, more effective drugs more affordably should help these developments continue. Computer-based toxicity guesses based solely on chemical properties will become increasingly prevalent in the future, even though the usage of QSAR in toxicity, particularly in regulated contexts, may delay behind the corporate companies.[36]

6. Conclusion

This study examines the present status and uses of computer-aided drug discovery (CADD) technologies, specifically focusing on molecular docking and quantitative structure–activity relationship (QSAR) tools. Computer-aided drug design is a useful tool in developing and discovering new medications. We can use it to find the most promising drug candidate quickly and cost-effectively. However, these are preliminary and undoubtedly require experimental validation; these will be carried out shortly via molecular biology investigations. It always gives optimism for progress in the field of drug research. Many outstanding research studies have been accomplished in recent years thanks to computer-aided drug design, and it may remain crucial in the foreseeable future. Recently, the use of *in silico* predicting methods has shown rapid success. This is expected to be an ongoing focus in drug design applications and predictive toxicology. QSAR has been noted in the field of drug development for facilitating the creation of safe and effective drug prospects. QSAR models can be used to determine the pharmacodynamic & pharmacokinetic characteristics of compounds during drug discovery & development. These *in silico* assessments involve predicting several qualities (such as physicochemical, ADME) and activities to help optimize and prioritize medication prospects. We have presented an overview of various Quantitative Structure–Activity Relationship (QSAR) methodologies and current advancements in fragment-based strategies, using specific studies as examples. Researchers should select suitable QSAR approaches based on the available information about the objective & ligand, considering the strengths and weaknesses of each method.

Availability of data and material

All relevant data and material are presented in the main paper.

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Manan Shah: Writing – original draft. **Maanit Patel:** Validation. **Monit Shah:** Writing – original draft. **Monali Patel:** Writing – review & editing. **Mitul Prajapati:** Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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