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Review of bioinformatic tools used in Computer Aided Drug Design (CADD)

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Abstract

Drug discovery is a time consuming process of finding out a new drug molecule. The process takes many years to complete and needs human resource. These is difficulties have been overcome by introducing computer programmes in drug discovery (CADD) which includes target identification, hit identification, and molecular modification of a lead compound to optimize desired effects and minimize side effects, based on the knowledge of their biological targets. Molecular modelling is the process of designing a molecule with a computer-based collection of programmes (in-silico design) for deriving, representing, and manipulating the structures and reactions of molecules. Numerous Software tools, online data bases and computer programmes are used in the field of CADD in which some relevant, user friendly and precise ones are reviewed in this article. Software is available for personal use and for commercial purposes. All these tools are highly useful in the field of drug design and discovery. The article will be helpful for selecting a tool for computer aided drug design.

Keywords: CADD; Drug Discovery; Software; Autodock

1. Introduction

Drug discovery is a lengthy process of finding out a new drug molecule by complex synthetic and analytical procedures. The process takes many years to complete and is difficult if we follow the conventional methods. These difficulties have been overcome by introducing computer programmes in drug discovery. The main advantage of Computer-Aided Drug Design (CADD) is the reduction of the time and human resources needed for the process of drug discovery. CADD helps us design a molecule by modifying a pre-existing drug molecule or by newly inventing a molecule to predict its possible biological activities. It includes target identification, hit identification, and molecular modification of a lead compound to optimize desired effects and minimize side effects, based on the knowledge of their biological targets.

CADD can increase the hit rate of novel drug compounds in the drug design as it uses a more targeted search than traditional High Throughput Screening (HTS) and combinatorial chemistry. It aims to explain a drug's molecular basis and therapeutic activity and to predict possible derivatives that would improve the biological activity by minimizing the undesired effects. A lead compound is a molecule having a particular biological activity obtained either from a natural or synthetic source [1].

Structure-based computer-aided drug design relies upon the ability to determine and analyze three dimensional (3D) structures of biological target molecules. The core hypothesis of this approach is that a molecule's ability to interact with a specific target protein and exert a desired biological effect depends on its ability to favorably interact with a particular binding site on that target. Molecules that share those favorable interactions will also exert similar biologic effects [25].

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Ligand-based drug design trusts the awareness of new ligand molecules that bind with the target protein molecule. These differently designed molecules are used to develop a new strategy that explains each element responsible for the interaction between ligand and target molecule. Ligand-based drug design depends on small molecules that bind to the active binding site of the biological target with their interest [2]. These molecules are used to extract a suitable model that provides the important structural properties of a lead molecule, which helps in the binding process with the target molecule. It is otherwise called indirect drug design.

Molecular modelling is the process of designing a molecule with a computer-based collection of programmes (in-silico design) for deriving, representing, and manipulating the structures and reactions of molecules. The properties of these molecules are dependent on their three-dimensional structures. Several computer-based programmes suitable for in-silico drug design have been developed during these years in which the most reliable ones have been reviewed here in this article [13].

Ideally the computational method should be able to predict affinity before a compound is synthesized and hence in theory only one compound needs to be synthesized. The reality however is that present computational methods are imperfect and provide at best only qualitatively accurate estimates of affinity. Therefore, in practice, it still takes several iterations of design, synthesis, and testing before an optimal molecule is discovered. On the other hand, computational methods have accelerated discovery by reducing the number of iterations required and in addition have often provided more novel small molecule structures [3,8].

1.1. Docking

Docking means a computational simulation of a candidate ligand binding to a receptor. In molecular modelling, docking is used to predict how a target protein will interact with a small molecule. The flexibility of molecules plays a crucial role in docking analysis.

1.2. Rigid Docking and Flexible Docking

Rigid docking means there is no modification in the bond angles, bond lengths and torsion angles of the components at any stage of complex generation, whereas in flexible docking, we can modify all these, which permits conformational change and results in the best-docked pose.[12].

2. Material and methods

2.1. Molecular Editors and Visualization Tools

Molecular editors are the commonly used tools to draw and manipulate chemical structures. These tools also provide several facilities such as geometry optimisation, structure visualisation, energy minimisation and three-dimensional image creations.

Many tools are used in computer-aided drug design for different purposes like creating 3D structures of chemical entities, creating SMILES notations, 3D molecular visualisation tools, prediction of pharmacological activities, toxicity predictions, and docking studies. These tools help design a new chemical entity to produce a desired pharmacological effect [4,19]. Here we discuss some newly introduced software that can be used as the best tools for in-silico drug design studies.

2.2. Graphical User Interface

Several computer programmes can be utilised as drug design and development tools, providing all the basic functionalities related to the drug design. Some important ones are reviewed below.

2.3. Molecular viewers and Editors

Molecular viewers and editors are used to view the 3-dimensional structure of both small molecules and biological macromolecules such as proteins.

2.3.1. Molecular Operating Environment (MOE)

MOE is one of the computer-based software tools designed to support Cheminformatics and drug design. MOE is good with its wide-ranging, flexible, and high-quality modelling tools ranging from protein modelling applications to cheminformatics and statistical data analysis tools. It provides a wide variety of operations such as three-dimensional

molecular visualisation, structure-based drug design, molecular simulations, peptide modelling, QSAR, structural bioinformatics, Structure-Activity Relationship (SAR) Explorer, Ligand Based Drug design, Protein, DNA/RNA modelling, Virtual screening, and antibody design [17,29].

2.3.2. SYBYL-X

It is a comprehensive molecular modelling and simulation suite developed to accelerate the process of drug design and other molecular discovery projects, from high throughput screening to late lead optimisation. Its latest version, SYBYL-X 2.1, features a new Job Control System which provides a consistent interface across the entire tool suite. This feature enables users to submit their jobs remotely from Windows, Linux, or Mac to any Linux system where SYBYL-X is installed. It also provides improved multi-processor support for key applications such as Surflex-Sim, Surflex-Dock, Topomer Search, and UNITY. A Python toolkit for 3D-QSAR makes QSAR functionality accessible outside of SYBYL-X as standalone Python scripts have also been incorporated [5,6].

2.3.3. Accelrys Discovery Studio

Accelrys Discovery Studio is a software suite from Biovia for simulating small molecule and macromolecule systems, including silico techniques such as molecular mechanics, free energy calculations, and biotherapeutics developments. It is an apt tool to explore biological and physicochemical processes down to the atomic level [16,19]. A researcher must optimise both biochemical potency and, at the same time, optimise other characteristics such as ADME and toxicity. It is an advanced tool for protein chemistry and discovering small and large molecule therapeutics from target identification to lead optimisation [32,43]. It is a key aspect of the analysis and designing of a molecule. It also includes a graphical visualisation tool for viewing, sharing, and analysing protein and modelling data.

2.3.4. ICM Pro

ICM-Pro helps a biologist or chemist by providing a high-quality protein structure analysis, modelling, and docking desktop software environment. There will be direct access to sequence and structural databases, which allows for all the jobs related to drug design and development. Its key features include Protein Structure Analysis, Pocket Finder, 3D Interactive Editor, Small Molecule Docking, Protein-Protein Docking, Protein Structure Prediction, Predict Effect of Mutation, Bioinformatics Tools, Electrostatics, and molecular graphical tools [5,6 27].

2.3.5. PyMOL

PyMOL is a molecular visualisation system on an open-source foundation, maintained and distributed by Schrodinger. It supports all the operating systems like Windows, iOS, and Linux. PyMOL 2.5 is the latest version for this.

2.3.6. Chem3D

Chem 3D is a tool to produce colourful three-dimensional chemical structures useful in presentations, posters, and drug designing. It can be used to convert a two-dimensional structure to a three-dimensional structure. It can convert an image in CIF format to a PDB file. It is also useful to visualise, manipulate, calculate bond lengths and angles, perform molecular modelling calculations, and perform molecular dynamics calculations [22,91].

2.3.7. Chimera

UCSF ChimeraX (or simply ChimeraX) is the next-generation molecular visualisation program from the Resource for Biocomputing, Visualization, and Informatics (RBVI), following UCSF Chimera. UCSF Chimera is a program for the interactive visualisation and analysis of molecular structures and related data, including density maps, trajectories, and sequence alignments. It is available in both free (non-commercial) and commercial forms [7,9].

2.3.8. Jmol

It is a free and open-source three-dimensional chemical structure writing tool used in drug design. It is cross-platform, running on Windows, iOS, and Linux/Unix systems. The Jmol Viewer is a development tool kit that can be integrated into other Java applications. It supports all major web browsers: Firefox, Safari, Chrome, Opera, and Edge. High-performance 3D rendering with no hardware requirements is the advantage [10,18].

2.4. Chemical drawing and visualization software

2.4.1. PubChem sketcher

It is a network-based tool for molecular sketching which is incorporated with PubChem. It is a web-based information pool for chemical and bioactivity. It is a Web-bas0ed drawing tool for interactive sketching of chemical structures. It is a complete platform for independent and verified work on all major Web browsers, including older ones without support for Web2.0 JavaScript objects [11,15].

2.4.2. ChemSketch

ChemSketch is a drawing package that allows drawing chemical structures, including organics, organometallics, polymers, and Markush structures. It also includes calculation of molecular properties like molecular weight, density, molar refractivity, 2D and 3D structure cleaning and viewing, functionality for naming structures (fewer than fifty atoms and three rings), and prediction of logP. The freeware version of ChemSketch does not include all of the functionality of the commercial version. Visit ACD/ChemSketch to learn more about the commercial version [14,28].

2.4.3. Chemdraw

KingDraw is a free chemical drawing editor that allows users to sketch molecules, reactions, and organic chemistry objects and pathways. Users can also use it to analyse compound property, convert chemical structures to IUPAC names and view 3D models. KingDraw will provide strong software support for chemical research, including more chemical-related functions and new structure drawing modes to connect Android & iOS devices and PC, realising rapid transforming from KingDraw to Office, ChemDraw and picture. It has many powerful functions, like AI image identification, intelligent gesture drawing, clean up structure, get 3D model, conversion between name and structure, structural formula searching, chemical property analysis, built-in group and free sharing [16,20,].

2.4.4. Chemdoodle

XDrawChem is a two-dimensional molecule drawing program for Unix operating systems. It is similar to other molecule drawing programs such as ChemDraw (TM, CambridgeSoft). It can read and write MDL Molfiles and read ChemDraw text and binary files to allow sharing between XDrawChem and other chemistry applications, and it can create images in popular formats like PNG and EPS. XDrawChem has been tested on Linux, SGI IRIX 6.5, Sun Solaris, Mac OS X, and Windows [21,23].

2.4.5. Marvin Suite

Marvin suite is a chemically intelligent desktop toolkit that helps draw, edit, publish, render, import and export chemical structures and allows conversion between various chemical and graphical file formats. It is free for individual, academic and non-commercial use. MarvinSketch features extensive functionalities to enable the fast and accurate drawing of chemical compounds, reactions, Markush structures, and query molecules. MarvinView is an advanced chemical viewer for single and multiple 2D/3D chemical structures, queries, reactions, and associated data. It also supports the widest selection of industrially acknowledged standard chemical file formats [24,26].

2.4.6. BKChem

It is a free chemical drawing program. It was conceived and written by Beda Kosata and is currently maintained by Reinis Danne. BKChem is written in Python, an interpreted and excellent programming language, implying some of the program features:

- Platform independence – It runs on any platform that Python does.
- Performance - as Python is interpreted language, one should not expect the performance of a native code compiled application (in present days, a cheap trade-off for platform independence). It is developed on GNU/Linux. It was, however, successfully used under Windows XP and MacOS X.

2.4.7. MedChem Designer

It is a tool that combines innovative molecule drawing features with fast and accurate ADMET property predictions from our top ranked ADMET Predictor. Chemists who design new compounds for pharmaceutical, cosmetic, industrial chemical, herbicide, pesticide, and food applications will enjoy the highly intuitive interface with several convenience features and capabilities not available in other molecule drawing software [27].

2.4.8. Activity Miner

The Activity Miner component of Flare™ enables rapid navigation of complex SAR while highlighting key activity changes. Dedicated interfaces enable detailed investigation of activity cliffs and near neighbours to enhance understanding. It can compare selected molecules for changes in electrostatics, shape, protein interactions or clusters using 3D or 2D relationships. Activity Miner explains the reasons behind an activity change. It offers multiple data views to help find key molecule pairs in SAR. For each pair, Activity Miner shows how the electrostatic and shape properties differ, building an understanding of designing better compounds with better properties. The different views enable the user to focus on various aspects of SAR [32,39].

2.4.9. Flare

Flare Viewer is a free version of Flare ligand-based and structure-based drug design solution enabling research chemists to discover novel small molecules more efficiently and effectively in a single platform. It is used for the design and Optimisations of ligand binding [44,64].

2.4.10. Ligand Scout

Ligand Scout is software used for creating three-dimensional (3D) pharmacophore models from structural data of macromolecule–ligand complexes. It incorporates the 3D chemical features such as hydrogen bond donors, acceptors, lipophilic areas, positively and negatively ionisable chemical groups that describe the interaction of a bound small organic molecule (ligand) and the surrounding binding site of the macromolecule. These pharmacophores can be overlaid and superimposed using a pattern-matching based alignment algorithm based solely on pharmacophoric feature points instead of chemical structure. The software has successfully predicted new lead structures in drug design [40,87].

2.4.11. ChemBioDraw

ChemDraw, available from CambridgeSoft, has long been the preferred package for drawing chemical structures for publication-quality graphics. It also has been used as the drawing package for database queries and electronic notebooks. The package has developed enhancements such as NMR spectra prediction, TLC plate tools, molecular and physicochemical property calculations, and structure naming. With the latest version (Version 11), perhaps the first surprise is the name change to reflect the increased emphasis on the biological drawing features of BioDraw [30,31].

2.4.12. ChemAxon

It provides several desktop tools such as the drawing tool Marvin and plugins to calculate various physicochemical properties. A tool to calculate pKa and the resulting LogD, the essential physicochemical property in medicinal chemistry. There are command-line versions of these calculations that are invaluable for dealing with huge datasets, and these were used in a script to analyse fragment collections [81,83].

2.4.13. ForgeV10

ForgeV10 allows the scientist to use Cresset's proprietary electrostatic and physicochemical fields to align, score and compare diverse molecules. It allows the user to build field-based pharmacophores to understand structure-activity and then use the template to undertake a virtual screen to identify novel scaffolds [57,34].

2.4.14. Vortex

Vortex is a chemically aware data analysis and spreadsheet tool from Dotmatics. It can import files from a SQL database and do substructure or structural similarity searches. Calculate many physicochemical properties and perform data analysis and display. It is an interactive data visualisation and analysis solution for scientific decision support. Building on and extending the spreadsheet paradigm, it provides the data manipulation, statistical analysis and sophisticated plotting capabilities required to explore and understand any complexity and size of data. Vortex is also scientifically aware, providing native cheminformatics and bioinformatics analysis and visualisations [80,93,].

2.4.15. Molinspiration

Molinspiration offers a broad range of cheminformatics server tools supporting molecule manipulation and processing, including SMILES and SD file conversion, normalisation of molecules, generation of tautomer's, molecule fragmentation, calculation of various molecular properties needed in QSAR, molecular modelling and drug design, high-quality molecule depiction, molecular database tools supporting substructure and similarity searches. Our products also

support fragment-based virtual screening, bioactivity prediction and data visualisation. Molinspiration tools are written in Java and can be used on any computer platform [50,63].

2.4.16. Accord for Excel

Accord for Excel is a valuable tool used by all the synthetic chemists at Biovitrum. We first acquired Accord with the combinatorial chemistry add-in to provide an easy-to-use method for chemists (both medicinal and combinatorial) to enumerate libraries and combine structural and analytical data, often exported from instruments in Excel format. It provides us with a convenient method of moving chemical structures and data between systems and performing simple calculations on those structures [47,54].

2.4.17. Docking tools

Some docking applications will generate a 3D structure and multiple conformations of the proposed ligand, and many also include a variety of scoring functions to rank the proposed poses.

2.4.18. SeeSAR

It is a virtual drug design platform. Quick and informative calculations can be used to dock, design, and analyse a new chemical entity in a flash. It evaluates ligand-target interactions by intuitive colour codes and gorgeous visualisation. Drag and Drop facilities for both ligands and targets are available. If we choose the structure-based drug design, there may be facilities to edit the target protein virtually. The most exciting part of the platform is its Inspirator mode which gives new ideas to discover new scaffolds, explore and grow into free cavities, or link molecules using fragment libraries for elegant solutions [59,60,82].

2.4.19. AutoDock

Autodock is a suite of automated docking tools. It is designed to predict how small molecules, such as substrates or drug candidates bind to a known 3D structure receptor. It has been modified and improved to add new functionalities, and multiple engines have been developed. Now two major generations are there: AutoDock 4 and AutoDock Vina. AutoDock-GPU is an accelerated version of AutoDock4 that is hundreds of times faster than the original single-CPU docking code. It can also help to guide organic synthetic chemists to design better binders [68,69].

2.4.20. Autodock Vina

Autodock is one of the docking engines of the AutoDock Suite, an open-source program for molecular docking. It is more accurate than Autodock. It is more compatible and easier to use.

2.4.21. Swiss dock

It is an online docking web service that provides services to dock and predict molecular interactions between a biological target molecule and a ligand drug molecule. It consists of a database, namely S3DB, which manually curates target and ligand structures inspired by the Ligand-Protein Database. It can generate a complex to perform subsequent calculations. It works on its own server for docking, giving an accurate docked score compared to others. The time taken for docking may vary. Large molecules cannot be used on this service [70,79].

2.4.22. InfiniSee

InfiniSee is a virtual screening platform. It finds molecules of interest in chemical spaces of (almost) infinite size based on similarity. Given a template or query molecule, infiniSee returns similar molecules from these chemical spaces or screening libraries [75].

2.4.23. Zdock

Zdock performs a full rigid-body search of docking orientations between two proteins. The current version, 3.0.2, includes performance optimisation and a novel pairwise statistical energy potential. M-ZDOCK: A modification of ZDOCK to predict symmetric assemblies using a subunit structure. ZRANK: A docking refinement program developed to provide fast and accurate rescoring of models from initial-stage docking (e.g., from ZDOCK), as well as refined docking models (e.g., from Rosetta Dock). ZDOCK Server: a protein docking server permitting users to run the latest versions of ZDOCK [73,89].

2.4.24. GOLD

It is the validated, configurable protein-ligand docking software for expert drug discovery from virtual screening to lead optimisation. The extensively validated scoring functions in GOLD can be trusted. It has the features of pose prediction, multiple scoring functions, flexible docking, virtual screening, water handling and covalent docking.

2.4.25. Glide

Glide offers the full range of speed vs accuracy options, from high-throughput virtual screening mode for efficiently enriching million compound libraries to the standard precision mode for reliably docking tens to hundreds of thousands of ligands with high accuracy, to the XP (extra precision) mode where further elimination of false positives is accomplished by more extensive sampling and advanced scoring, resulting in even higher enrichment [86,62].

2.4.26. FlexAID

It is a molecular docking software that can use small molecules and peptides as ligands and proteins and nucleic acids as docking targets. As the name suggests, FlexAID supports complete ligand flexibility and side-chain flexibility of the target. It does use a soft scoring function based on the complementarity of the two surfaces [58,76].

2.4.27. GEMDOCK

The generic evolutionary method of docking is named GEMDOCK. It is a program for computing a ligand conformation and orientation relative to the target protein's active site. It may run as either a purely flexible or hybrid docking approach. It automatically generates all docking variables, such as atom formal charge, atom type, and the ligand-binding site of a protein. It is now accompanied by many add-on programmes, making it truly convenient and less time-consuming [71,72].

2.4.28. MS-Dock

MS-DOCK is an efficient multiple conformation rigid-body docking approach based on DOCK. It can be easily used for the generation of multi-conformer libraries and for shape-based filtering within a multi-step structure-based screening protocol to shorten computation time [42,53].

2.4.29. Ligand Fit

Ligand Fit is a shape-based method for accurately docking the ligands into a protein's active binding site. The method employs a cavity detection algorithm for detecting invaginations in the protein as candidate active site regions. Candidate poses are minimised in the context of the active site using a grid-based method for evaluating protein-ligand interaction energies [35,36].

2.4.30. UCSF Dock

UCSF dock is another docking software in which DOCK6 is the latest version written in C++ and is functionally separated into independent components allowing a high degree of flexibility. It needs about 100 MB of disk space. The new features added include additional scoring options for energy minimisation, Delphi electrostatics, ligand conformational entropy corrections, ligand desolvation, receptor desolvation, receptor flexibility, conjugate grading minimization [55,56].

2.4.31. GalaxyPepDock

GalaxyPepDock is a web server-based protein-protein docking interface. It performs similarity-based docking by finding templates from the database of experimentally determined structures and building models using energy-based optimisation that allows for structural flexibility [52, 41].

2.4.32. Stardrop

It is one of the best in-silico technological tools used in Cheminformatics, model building and analysis of chemical entities in drug design and development. It brings about the latest data of drug molecules and targets, which is extremely helpful in predicting biological activity and molecular modelling. It is the best tool to rely on for decision-making while researching drug design. Both the free version and commercial versions are available for this [66,49].

2.4.33. rDock

rDock is a fast and versatile open-source program for docking ligands to proteins and nucleic acids, primarily designed for high-throughput virtual screening and prediction of binding mode [38, 67].

2.5. Biological Activity Prediction Tools

2.5.1. Way2Drug

Way2Drug portal has been developed and supported by the multidisciplinary team of researchers working in bioinformatics, cheminformatics, and computer-aided drug discovery for about thirty years. It provides a local correspondence concept, according to which biological activity of drugs-like organic compounds are based on the molecular recognition between the particular atoms of the ligand and the target. Using this concept, we have developed a consistent system of atom-centred neighbourhoods of atoms descriptors, including MNA (Filimonov et al., 1999), QNA (Filimonov et al., 2009), and LMNA (Rudik et al., 2014), and have implemented them in several SAR/QSAR/QSPR modelling approaches [45,46].

2.5.2. PASS

The concept of the biological activity spectrum was introduced to describe the properties of biologically active substances. The PASS (prediction of activity spectra for substances) software product, which predicts more than three hundred pharmacological effects and biochemical mechanisms based on the structural formula of a substance, maybe efficiently be used to find new targets (mechanisms) for some ligands and, conversely, to reveal new ligands for some biological targets. We have developed a WWW interface for the PASS software. A WWW server for the online prediction of the biological activity spectra of substances has been constructed [48,85].

2.5.3. GUSAR

GUSAR software was developed to create QSAR/QSPR models based on the appropriate training sets represented as SD files containing data about chemical structures and endpoint in quantitative terms. GUSAR has been developed according to OECD (Organisation for Economic. Co-operation and Development) principles and includes the last achievements in QSAR modelling: consensus prediction, applicability domain assessment, internal and external models' validation, and precise interpretations of obtaining results [61,84].

2.5.4. BRENDA

It is the most comprehensive information repository on enzymes and enzyme ligand data. The BRENDA enzyme information system has developed into an elaborate system of enzyme and enzyme-ligand information obtained from various sources, combined with flexible query systems and evaluation tools [51,90].

2.5.5. Pharma Expert Software

PharmaExpert determines the existing relationships between pharmacological effects and biochemical mechanisms. The current version of PharmaExpert covers 1587 mechanisms of action, 418 pharmaco-therapeutical effects and 2664 types of relationships between them. Each biologically active compound reveals various biological actions in biological systems (human organisms, animals, in vivo and in vitro assays). It is impossible to study each compound in all tests currently available. Therefore, the ability to select compounds with required types of biological activity and without unwanted adverse effects and toxicity is very desirable [77,78].

2.5.6. Chemical Checker

It is a resource of chemical and biological small molecule similarities. Molecules are compared from multiple viewpoints relevant to the drug discovery pipeline, from the chemical properties to the clinical outcomes [37, 65].

2.5.7. Toxtree

Toxtree is a fully featured and flexible, user-friendly open-source application that can estimate toxic hazards using a decision tree approach. Toxtree could be applied to datasets from various compatible file types. User-defined molecular structures are also supported – they could be entered by SMILES or the built-in 2D structure diagram editor [74,92].

2.6. Open-Source Cheminformatics toolkits

Open-Source Cheminformatics toolkits are software development kits that allow the development of unique computer applications for virtual screening and bioinformatics. The toolkits include ADMET predictor, MedChem studio, MedChem designer and OpenBabel [88].

Strategy to follow is to use keywords from your title in first few sentences

3. Results and discussion

This from the data reviewed from various authentified journal publications, we found that several bioinformatics tools are being used for drug design through docking studies. All these software is based on computer simulations and large databases. By reviewing one by one, it has been noticed that some of them are incredibly useful and precise compared to others. The consolidated report on these is given as follows:

Table 1 Consolidated report of features of docking software

Software	Release Year	Open Access	Operating System	Docking score accuracy	Ligand edited	Auto binding site detection	ADMET properties	3D visualisation	Rating
SeeSAR	2019	No	Windows	8	Yes	Yes	Yes	Yes	7
Autodock	1990	Yes	Windows	9	Yes	Yes	Yes	Yes	9
Autodock Vina Extended	2018	Yes	Windows	9	Yes	Yes	Yes	Yes	9
Swiss Dock	2011	Yes	Windows	7	No	No	Yes	Yes	8
InfiniSee	2019	No	Windows	8	Yes	Yes	Yes	Yes	8
Zdock	2010	Yes	Windows	6	No	No	Yes	Yes	6
GOLD	1995	No	Windows	6	No	No	Yes	Yes	6
Glide	2004	No	Windows	7	Yes	No	Yes	Yes	6
FlexAID	2015	Yes	Windows	6	No	No	Yes	Yes	5
GEMDOCK	2004	Yes	Windows	7	Yes	No	Yes	Yes	7
SeeSAR	2019	No	Windows	8	Yes	Yes	Yes	Yes	7
MS-Dock	2008	No	Windows	5	No	No	Yes	Yes	5
LigandFit	2003	No	Windows	6	Yes	No	Yes	Yes	6
UCSF Dock	1982	Yes	Windows	8	Yes	Yes	Yes	Yes	8
GalaxyPepDock	2018	No	Windows	5	Yes	No	Yes	Yes	5
Stardrop	2016	No	Windows	7	Yes	Yes	Yes	Yes	7
rDock	1998	Yes	Windows	5	No	No	Yes	Yes	6
Way2Drug	2016	Yes	Windows	7	No	No	Yes	Yes	9
Blaster	2009	Yes	Windows	7	No	No	Yes	Yes	5
Haddock	2003	Yes	Windows	6	No	No	Yes	Yes	5

4. Conclusion

The present review has shown that several bioinformatics tools are used for drug design through docking studies. For docking, it has been noticed that a few reliable and high-profile software are available only as commercial versions. To access these, we need to invest a considerable amount of money annually since they do not provide lifetime access to any of these paid versions. Apart from all these, only a precise docking result will give perfect biological activity prediction depending on the flexibility of both the ligand and the target. This can be obtained by dealing with a broad database and perfect computer simulations. Both these features are found only in a minimal amount of software. Since it is meant to be used commercially and costs high, it is not familiar among academicians, research scholars, and students. Therefore, many people are ignorant about the usefulness of these software.

Autodock still has the upper hand among all the bioinformatic tools because of its accuracy and free availability. Its latest version available is Autodock Vina extended. Several Graphical User Interfaces (GUIs) are available for Autodock

Vina, making it functional and significantly less time-consuming for the docking process. This programme's advantage is that it does not need any language commands now, as in their older versions. It also supports both Windows and Mac operating systems. The only disadvantage is needing a bit larger disk space to run the programme. Apart from Autodock, SeeSAR and infiniSee are also high-profile software from BiosolveIT. Next comes UCSF Chimera and PASS because of their reliability of results. The use of activity prediction and other QSAR studies, the software used are strictly based on the reliability of its results.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest.

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