Computation in Chemistry: Representative Software and Resources

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ABSTRACT

The use of modern computer software in the teaching of chemistry creates the basis for the increased interest of students and researchers in chemistry and the transfer and consolidation of knowledge. A chemical computer program is a program used to draw simple and complex chemical compounds as well as perform calculations of complex chemical equations and processes, making it possible to biologically interpret complex systems. This review covers common and mostly free applications that can be used to learn chemistry and to serve as a reference or tool for searching, identifying, and displaying the parameters of various materials. In addition, structured interpretation approaches and programs designed to aid in the description of unknown compounds are analyzed and discussed in this work.

Keywords: *Drawing programs, ACD software, Gaussian, Virtual screening, Auto Duck*

INTRODUCTION

Since there are many *in silico* applications of chemistry available to students, chemical professionals, and instructors, harnessing digital technology for education by helping researchers gain knowledge through interactive learning is a crucial step for researchers and graduate students[1]. Chemical computer programs are a type of software that calculates complex chemical equations and processes. The vast majority of these applications are functional in nature, allowing for the drawing of basic and complex chemical formulas, the processing of spectrum data by nuclear magnetic resonance or mass spectrometry, and the possible interpretation of the biology of complex systems as well as other chemical processes also, chemical chemists can use chemical informatics technologies to help them acquire, analyze, and manage data and information about chemical substances and their attributes.

A wide range of programs are utilized in many drug development research projects, with a particular focus on data management. Information sharing across multiple programs normally necessitates some effort[2,3]. Table 1 reports the various types of chemical programs and their properties.

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Table 1. A list of freeware that is useful Computers in Chemistry

Topic	**Required software Assuming you want to use it with Microsoft Windows, or on Android or iOS**
Chemical structure drawing Software	ChemDraw (Microsoft Windows) ACD/ChemSketch (Microsoft Windows or on Android and iOS) Chirys Draw (Android and iOS) KingDraw (Android and iOS).
Explore structures in 3D.	ACD/ChemSketch, Hyperchem, Chemdraw
Structure optimization based on non-electronic structure methods: Molecular Mechanics Methods of Electronic Structure Molecular Dynamics	HyperChem (for Microsoft Windows or on Android and iOS)
The software's for Theoretical Chemistry	Gaussian (Microsoft Windows) HyperChem (Microsoft Windows)
Predicting programs for possible chemical hazards	Chemical Reactivity Worksheet Chemical Safety data sheet
Predict binding mode and approximate binding energy of a compound to a target	Auto Dock (website)
Identify active compounds for a specific target from a chemical library based on docking techniques and on pharmacophore modeling techniques	Virtual Screening
Computational software for the drug discovery in a resource-limited environment	Swiss drug design (website)

LIST OF DRAWING PROGRAMS IN CHEMISTRY

Creating chemical structures with traditional drawing software applications will be very laborious and practically impossible. With the prism in mind, aesthetics and quality come to the fore, ensuring compact moldings, bound bonds of fixed lengths and angles, etc. Direct 3D editing is usually not possible-3D molecule profiles can only be visualized using a proven/hashed bond drawing methodology. The accessibility of various means (palette of lines, arrows, lines, curves, arcs, and other shapes or elementary drawings) is also of great importance. If an accurate 3D representation of the molecule is needed, importing the molecule from a modeling program or 3D database is the best practical approach, although recent drawing packages typically hold a simple 2D–3D unit converter or add-on tool[4].

The graphic software applications are offered to run on Windows, Macintosh, Android, and iOS platforms. Under "Windows, most of the tasks (printing, screen, printer fonts, resolution, or any other system-level parameter) are maintained by Windows itself, and its setting is the deciding factor". Another important point is the ease of use of the program. This means that the program's user interface, which allows for two-way interactive communication between the user and the device, should be straightforward and effective.

Sharing information with other programs, database applications must also be multifaceted. Chemical drawing software gives researchers an easy, fast, and convenient way to create chemical structures and drawings. So, download any or all of the above chemical drawing programs, which can be easily looped for the overall task. If the user is a student, teacher, scientist, or researcher, this software can greatly help with all kinds of chemical projects[5]. The most popular publishing-quality chemical graphic software applications will be reviewed on the Microsoft Windows Platform, and a number of them are mentioned as follows:

ChemDraw

This program (ChemDraw) is considered a powerful and parallel technology. Hundreds of thousands of scientists use chemical drawing to quickly and accurately draw molecules and reactions for use in papers and electronic laboratory observations, to search databases, to derive precise names of structures, and to predict properties and spectra. The evolution of this journey began as a drawing tool, and has evolved into a highly effective chemical application over time. As a result, high-quality articles worthy of publication can be produced quickly[6]. Particles of ever-increasing complexity are drawn. Its powers have now grown far beyond those of a simple drawing tool. ChemOffice+Cloud, a new version of the program, has been released. This is a powerful all-in-one solution, created with the aim of making things easier for you. and boost the rate of chemical bonding and transformation. Chemical drawings contain chemical information that can be shared. There are now four different versions of the ChemDraw software program[7]:

1. "ChemDraw Prime" is a full-featured entry-level structure drawing application that includes everything a researcher needs to create chemically intelligent, "publication-ready chemical" structures and reactions, laboratory notes, and experiment write-ups quickly and efficiently. In addition to a rich set of chemical structure essentials, ChemDraw Prime includes the following facilities: property calculators, chemical and lab equipment templates, as well as handy TLC and "Gel Electrophoresis Plate design tools".

2. "ChemDraw Professional" has all of the features of "ChemDraw Prime", as well as ChemDraw Cloud, Bio Draw, NMR prediction, better name to structure, increased retro synthesis tools, and even integration with chemical databases, such as SciFinder. ChemDraw Professional also works with ChemDraw for Excel, Chem Finder Standard, Chem Script, and ChemDraw 3D to organize and process structural data.

3. Chem Office Professional is the world's most comprehensive and scientifically intelligent research productivity package. It expands on the foundations of ChemDraw Prime and Professional by giving chemists and biologists alike access to strong features that help them keep track of their work, visualize their findings, and get a better understanding of their findings. The following programs are included in Chem Office:

A. ChemDraw for "Excel adds chemical intelligence" to "Microsoft Excel spreadsheets", allowing scientists to utilize Excel's analytical, sorting, and organizing features to further edit and enhance sets of compounds and data, as well as study structure-activity connections.

B. Chem3D builds three-dimensional models so that scientists may examine the form and characteristics of their molecules in order to maximize activity or specificity.

C. ChemDraw and Chem3D both provide tools for forecasting NMR and IR spectra.

D. "ChemFinder" is a "chemically intelligent personal database system", which scientists use to organize their compounds, search for structures, and connect structures with biological attributes.

4. "ChemDraw Direct" may be integrated into web browsers as well as "internal applications" that require chemicalization. "ChemDraw Direct" has the main functionality of the ChemDraw series, including the favorite drawing features, sophisticated name-to-structure, structure-to-name, hotkeys/shortcuts, structure templates, and structure query tools, all packaged in a lightweight package[8].

ACD/ChemSketch

It (ACD/ChemSketch) is a powerful structural editor with a wide range of tools and features for communicating scientific and chemical data. Create molecular structures by drawing them, generating them from InChI or SMILES strings, or copying and pasting from ChemDraw. Incorporate well-known compounds fast and easily. They include pre-drawn templates for amino acids, aromatics, steroids, sugars, and other compounds. Search through over 170,000 systematic and commercial names in the dictionary and draw reactions and complicated chemical schemas quickly (including biotransformation maps). Liquid parameters, including molar refractivity, molar volume, index of refraction, surface tension, density, and dielectric constant, may all be calculated using ChemSketch [5,9,10,11]. These computations are done using topological and group additive approaches[12]. Chem sketch can be downloaded freely for academic purposes.

Chirys Draw

It (Chirys Draw) is an innovative way to draw complex molecular structures and reaction plans with the fingertips. Even intricate multi-loop loops are simple and enjoyable to design with a simple circle gesture. Adding several double connections or workgroups at the same time is simple. Chirys Sketch improves the speed with which scientists draw and communicate. Drawing reactions and interaction diagrams with reaction conditions, creating multi-line text annotations with lines and colors, complex fused and spiro looping systems, single pairs, transferring photos to a camera album, as well as resonance and balance, users may compute characteristics and utilize the "glowing molecule" display to highlight certain attributes once you've sketched the structure. All properties are computed using Amazon Web Services' Asteris cloud server, and core properties, such as LogP, molecular weight, TPSA, and HBD/A, are available in an endless number of combinations (Figure 1). The StarDrop ADME characteristics have some limitations. However, users can compute the properties of up to 20 compounds for free each month. An in-app purchase allows users to do more computations.

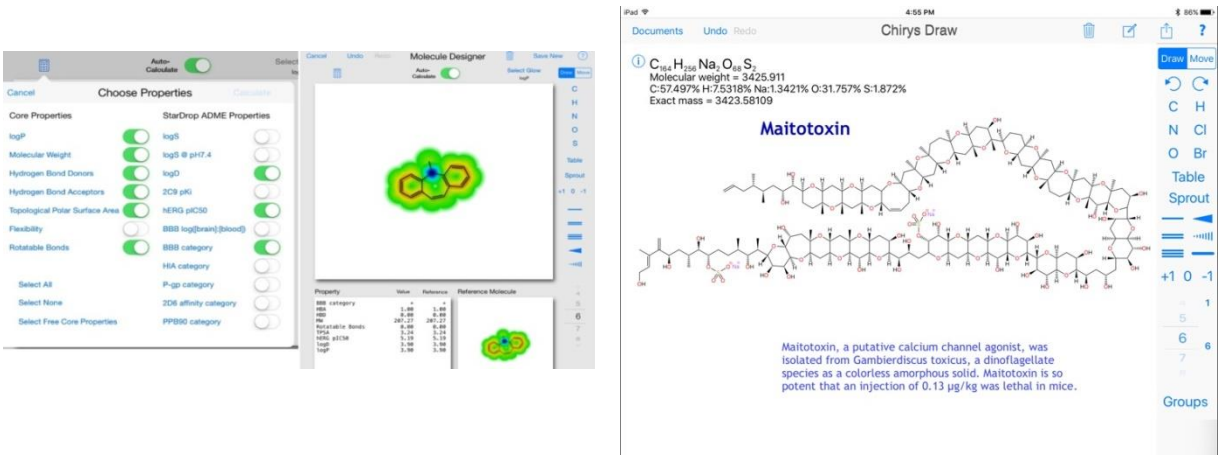

Figure 1. Screenshots of the Chirys Draw graphical user interface

KingDraw

It (KingDraw) is a professional chemical structural formula editor for iOS and Android that was created specifically for chemists, academics, and students. The current version supports intelligent gesture drawing, clearing up, 3D modeling, inter-conversion between name and structure, structure searching, chemical properties analysis, and built-in groups to meet the requirements of drawing structures quickly; To meet the requirements of drawing in various situations, it supports multi-terminal synchronization on the cell phone, pad, and PC with one ID and one-click sync.

KingDraw works with ChemDraw and other important chemical structure drawing applications to convert file formats. It can save files in a variety of formats (mol, cdx, SMILES) and supports ACS 1996 and many other drawing standards. The chemical properties include decimals, formulas, exact mass, m/z, molecular weight, and elemental analyses. All the features in the phone, tablet, and PC versions are always free. Simply spray KingDraw to capture all of the ideas. Finally, using the KingDraw cloud account, users will create an all-platform chemical structure system.

Predicting Programs for Possible Chemical Hazards

Chemical Reactivity Worksheet (CRW)

The CRW database's chemical data sheets (CRW) provide information on each chemical's inherent risks as well as whether they react with air, water, or other materials. They also provide case studies with references to specific chemical accidents. The data collected in worksheets provide structural properties of the intrinsic reactivity of each compound, such as flammability, peroxidized ability, polymerizability, explosively, strong oxidizer or reducer capability, water or air reactivity, pyrophoricity, known catalytic activity, instability, and radioactivity, which can result in hazards such as heat generation or toxic gas byproducts. Users can also build their own bespoke chemical datasheets if the entity produces a proprietary chemical that isn't included in the CRW database. It also contains a "reactivity prediction worksheet" that users may use to visually "mix" chemicals to model unintended chemical mixes and learn about the hazards that may result.

If a process is projected to create gases, the CRW could spot potential gaseous products as well as literature citations to back up the estimate. Two further CRW packages are especially helpful to the chemical industry. One of them discusses known incompatibility between certain compounds and commonly used absorbent materials in spill cleanup. The other new application in CRW 4 includes information on known incompatible between specific chemicals and materials utilized in the construction of containers, pipelines, and valuing systems on industrial chemical sites[13-15].

Users may also search the CRW database for chemicals, see a preview of the information on "chemical datasheets", and construct a simulated combination of chemicals on the Mixture Manager website. Users may access all additional software elements from this screen, including a compatibility diagram and danger summary for each composition they make, reference information for the reactive kits used in CRW, and information about absorption mismatch with particular compounds, as illustrated in Figure 2. The suitability chart displays the "predicted hazards of mixing the chemicals" in a combination in an "easy-to-use graphical manner". The reactivity predictions are color-coded, and users may learn more about particular predicted responses by clicking on the boxes on the graph. The bottom of the figure shows general danger statements, projected gas products, and literature documentation for the selected pair of chemicals[13-15].

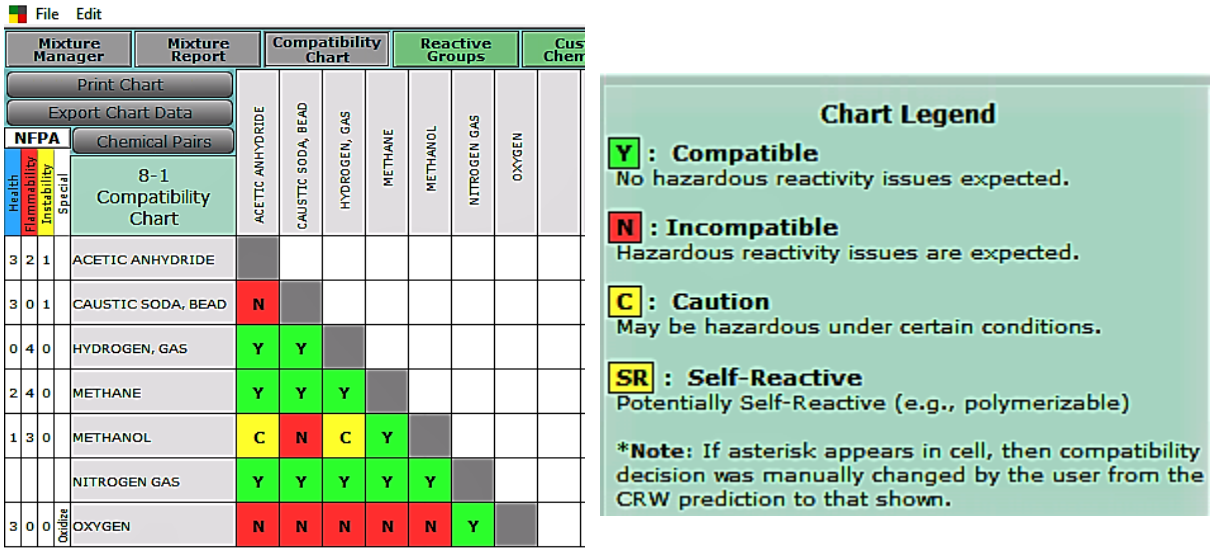

Figure 2. The Compatibility Chart shows the predicted hazards of mixing the chemicals in a mixture in an easy-to-use graphical interface. The reactivity predictions are color coded, and the cells on the chart can be clicked to find more information about specific predicted reactions. General hazard statements, predicted gas products, and literature documentation for the selected pair of chemicals are shown at the bottom of the chart

Chemical Safety Data Sheet

This application Chemical Safety Data Sheet, displays the "International Chemical Safety Cards (ICSC)" created by the "United Nations Environment Program (UNEP), the International Labor Organization (ILO), and the World Health Organization (WHO)". The chemicals in ICSCs are summarized for use on the "shop floor" by employees and employers in industries such as agriculture, construction, and other workplaces. The ICSC can be compared to the Material Safety Data Sheet (MSDS), which is a manufacturer's standard reference document for chemical information to be stored anywhere employees may be exposed to these chemicals for safety reasons. On the other hand, ICSCs present peer-reviewed information regarding the material in a more compact, standard, and straightforward manner in one- or two-page documents that always follow the same structure. When working with applicable chemicals, use the information in this application to supplement Occupational Health and Safety as an adjunct to the MSDS. The feature of this application is a fully indexed and searchable chemical list by name, CAS number, "RTECS (Registry of Toxic Effects of Chemical Substances) number", and an archived history of previously viewed chemicals.

Theoretical Chemistry/Computational Chemistry Software

Computational chemistry is a hot topic in the chemical sciences that is quickly gaining traction as a valuable tool for providing insights and predictions on experimental systems. To enhance accuracy and computing efficiency, new computational approaches are being developed. These advancements, when combined with breakthroughs in the computer capacity of current processors, make computational modeling of realistic chemical processes more beneficial and widespread. For example, molecular dynamics (MD) has several applications in the modeling of massive organic systems such as proteins and polymers. Numerical simulations are used in chemistry, physics, and biology to better understand real-life experiments and to test the predictions of theoretical models.

If a paradigm accurately describes the essential processes that are critical for following statements, then simulation results based on that paradigm should mimic the primary elements of the relevant physical investigation. For systems that are tiny (usually up to 200 atoms) yet exceedingly varied, quantum mechanical (QM) computations are utilized. Creating an approximation of the wave function. Calculating the estimated wave function or electron density provides access to a wealth of basic ideas. Fundamental and mechanistic research is keenly interested in structural, electrical, and energetic aspects. Furthermore, these computations can produce NMR shifts, absorption spectra, EPR (Electron paramagnetic resonance) spectra, and Mössbauer isomer shifts. As a result, chemical modeling can assist a vast number of researchers[16-19].

Gaussian

It (Gaussian) is a collection of computational chemistry programs used by "chemists, chemical engineers, biochemists, physicists, and other researchers". Gaussian offers semiempirical quantum chemistry techniques and also chemical mechanics to predict values, molecule structures, "spectroscopic data (NMR, IR, UV, and so on)", and often more. It was released in 1970 by "John Pople and his research group at Carnegie-Mellon University as Gaussian 70 (G70)". It has been continuously updated since then. As shown in Figure 3, Gaussian 90 (G90) provides state-of-the-art capabilities for electronic structure modeling. Here is a short list of the most useful types of jobs. "Layout design, single-point energy, frequencies, and thermochemistry reliability, molecular orbitals and population analysis, UV/Vis and electronic transitions, potential energy surface, and solvation impact". Other molecular properties may include polarizability forces on nuclei, molecular volume, NMR analysis, electrostatic potential, and electron density[12,20].

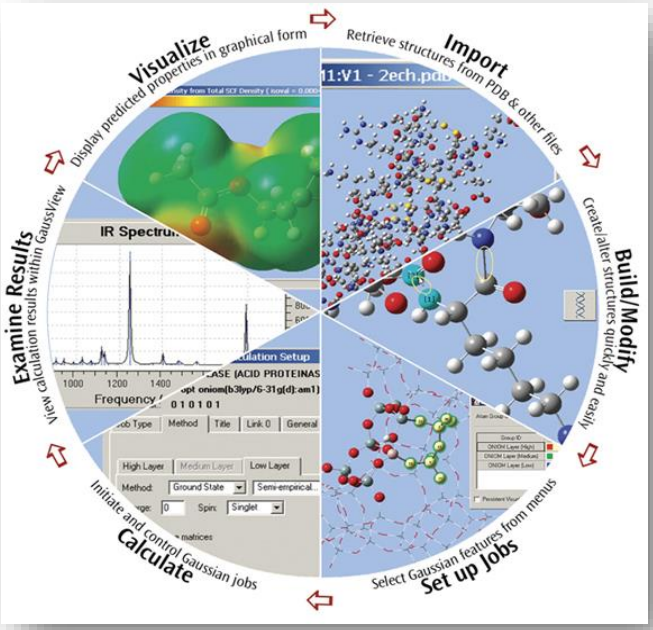

Figure 3. The various capabilities of the Gaussian software

(https://www.slideshare.net/mojdehy/gaussian-presentation**)**

HyperChem

It (HyperChem) is a high-end "molecular modeling environment" with a reputation for reliability, versatility, and ease of use. HyperChem delivers more molecular modeling capabilities at your fingertips than any other Windows application by "combining 3D visualization and animation with quantum chemistry computations", "molecular mechanics, and dynamics". "HyperChem Release 8.0" is a fully functional 32-bit software for Windows XP, Vista, and 7. As shown in Figure 4, this software includes more advanced computational chemistry capabilities than ever before, as well as support for a wide range of third-party applications. Many computational approaches are supported, including interaction configuration and improved metal and inorganic compound support. More stereochemistry, floating element checkbox, vis-UV, and vibration settings are available. Analytics is more thorough when it comes to orbital analysis. HyperChem is quick, accurate, and generally simple to use. Reviewers suggest this application as an educational and research tool.

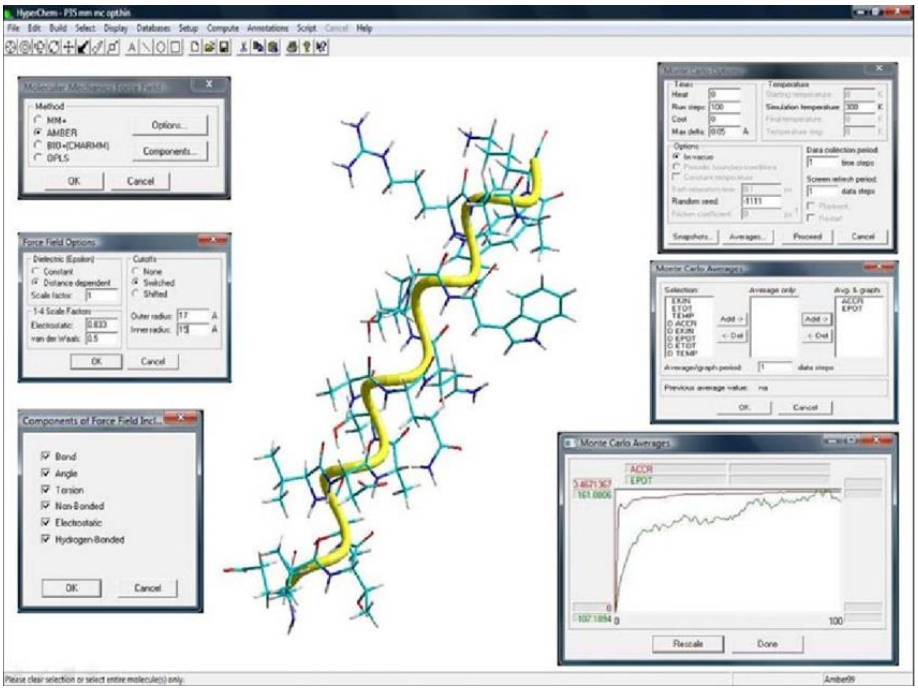

Figure 4. Screenshots of HyperChem graphical user interface[21]

Computational Software for the Drug Discovery in a Resource-Limited Environment

Drug discovery is an important and visible field in the chemical and biological sciences. Bonding/receptor interactions and fragment modification are fundamental principles, so drug development today relies heavily on predictive modeling and informatics. Computational tools can have an influence. Data mining and analysis techniques can assist in better informing and speeding up the target evaluation process.

Virtual screening (VS) is a well-known computer approach for locating hits on specific protein targets. Medicinal chemistry programs use docking, QSAR analysis, Swiss target prediction, and matched molecular pairs (MMP) to convert hits into leads. Big data analysis and artificial intelligence approaches are two new contributions to the computational toolbox (usually in the form of deep neural networks).

Computational approaches have all played a part in the development of various drug candidates and licensed medications. Academic drug development institutes and smaller biotech businesses frequently lack the skills of major pharmaceutical corporations, limiting the tools and data that may be accessible. Computational approaches that are available to everyone, on the other hand, can speed up and lower the cost of drug development in a variety of ways[22].

Virtual Screening

VS is a computational approach for searching catalogues of small molecules for structures that are most likely to attach to a therapeutic target. Because of its unique benefits over "experimental HTS" (High-Throughput Screening) "drug target-relevant", competitive pricing, and efficiency, this has become a vital step in premature drug development[23]. The VS methods are mainly divided into two types:

I. Structure-Based Virtual Screening (SBVS)

As illustrated in Figure 5, the overall scheme of this (SBVS) technique focuses on the analysis of three-dimensional target protein structures of the pharmaceutical specific protein (obtained either experimental data or difficult to perform through sequence alignment), followed by the docking of small molecules to specified binding sites. Among many other factors, the clasped molecules are ranked based on their expected "binding affinity or complementarity to the binding site". Only a handful of the top-ranking compounds are usually chosen as candidates for further testing. VS is made easier with our quick and precise ligand docking and scoring algorithms[24].

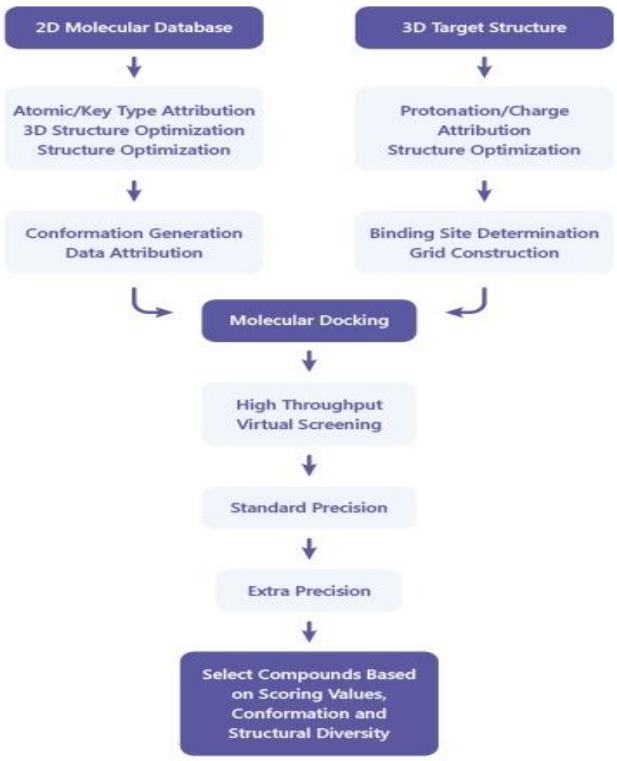

Figure 5. The SBVS protocol

https://www.medchemexpress.com/virtual-screening.html

II. Ligand-Based Virtual Screening (LBVS)

This approach (LBVS) is a popular tool for drug discovery and lead optimization in the lack of "3D structures" of probable pharmaceutical targets. Biological data is evaluated in order to identify known active or inactive molecules that may be used to identify alternative, potent molecules scaffolds for evaluation. LBVS techniques include homology and structural searches, "quantitative structure-activity relationships (QSAR), pharmacophore mapping, and machine learning"[25].

The benefits of this program are that it sorts by ligand and structure and is the default setting. A high-performance computer vehicle database with over 4 million chemicals is available for purchase. The approach used is determined by the quantity of data available about the ailment under investigation. By creating a three-dimensional pharmaceutical model, as shown in Figures 6-7, LBVS techniques include taking into account the impacts of water, using a solution, and using machine learning[26].

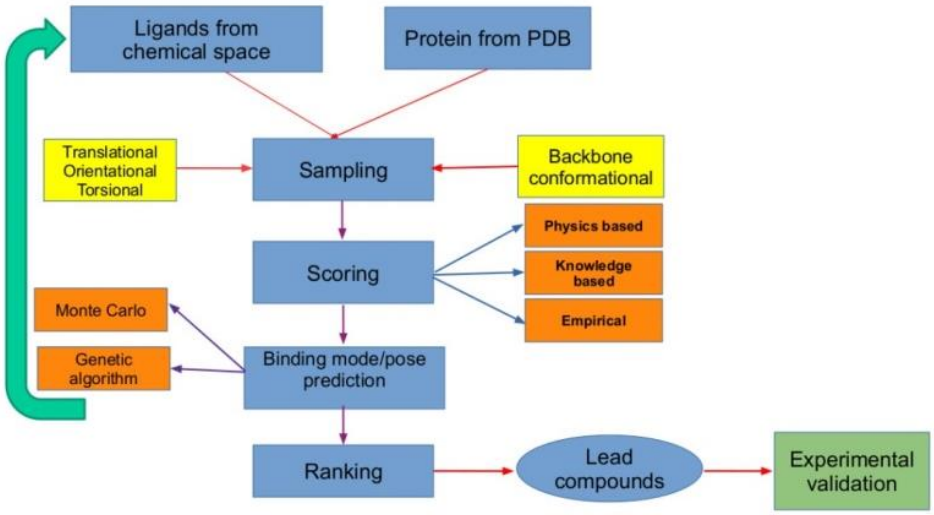

Figure 6. Workflow for computer-aided drug discovery where the lead compounds are identified using virtual screening

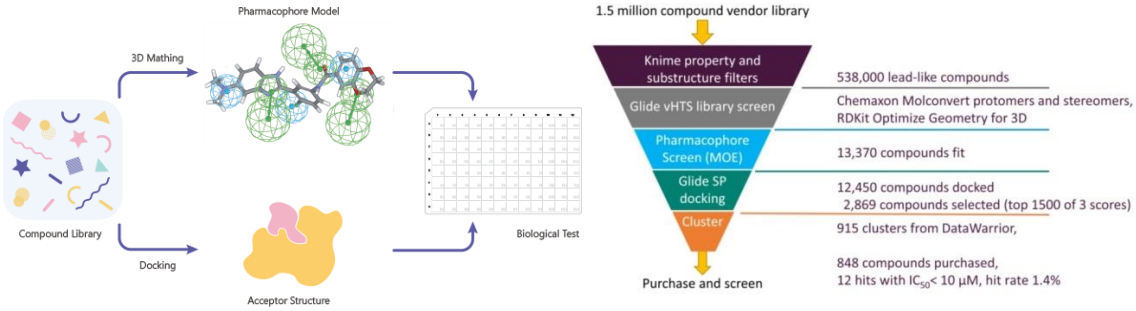

Figure 7. Example of a VS funnel successfully used in-house. The tools used at the various steps are also indicated. (https://www.medchemexpress.com/virtual-screening.html)

Auto Duck

It (Auto Duck) is a collection of docking software that may be used to automate the process. Its goal is to anticipate how tiny compounds, such as substrates or therapeutic candidates, bind to a "3D-structured receptor"[27]. Application programming interfaces (APIs) have been documented for years using Autoduck. Programmers can communicate knowledge about a growing codebase by including API documentation in source files. Auto Duck can create online help files with complete hypertext code, as well as links and keyword lists. An "Auto Duck" is usually connected to the build process so that a fresh help database may be created automatically after each build. It is simpler to keep documentation current when it's integrated with code. Developers can update the comment blocks at the same time as they make changes to APIs. When APIs are released for use by outside customers, user education personnel can edit the comment blocks, add example code, and generate final "RTF (Rich Text Format)" files for inclusion in the printed or online documentation[28]. Current distributions of "AutoDock" consist of two generations of software:

I. AutoDock 4

It (AutoDock 4) is made up of two primary applications. The first autogrid docks the ligand to a set of grids that describe the target protein, while the second autogrid precalculates these grids. The atomic attraction grids can be shown in addition to being used for docking. This can assist organic synthesis chemists, for example, create better binders[29] (Figure 8)

II. AutoDock Vina

It (AutoDock Vina) is one of the commonest and fastest open-source docking engines. A fundamental scoring function and a quick gradient-optimization conformational search provide the foundation of a comprehensive computational docking program. It was developed and implemented by "Dr. Oleg Trott of the Molecular Graphics Lab". Others are actively using it. This website is maintained and developed by "the Scripps Research Institute's Forli Lab"[30]. AutoDock 4 (and previous versions) and "AutoDock Vina" were designed by the Scripps Research Institute's Molecular Graphics Lab. Vina borrows some AutoDock 4 ideas and perspectives, such as treating docking as a stochastic global optimization of the scoring function, precalculating grid maps (which Vina does internally), and other implementation tricks, such as precalculating the interplay between every atom type couple throughout each location.

For optimum interoperability with auxiliary applications, it also employs the same structural format named "PDBQT (Protein Data Bank, Partial Charge, and Atom Type)". Because the source code, scoring functionality, and actual algorithms employed are all entirely new, AutoDock Vina should be considered a new generation of AutoDock rather than a version. The user does not need to learn about Vina's implementation details, play with obscure search terms, parameters, or cluster discoveries, or have a solid understanding of advanced algebra (quaternions)[31]. Only the molecular structures to be docked, as well as the search space specification, which contains the binding site, are required. There is no requirement to compute "grid maps or assign atom charges (when using Vina or Vinardo forcefields)". As shown in Figure 8, the speed and accuracy of "AutoDock Vina" were compared, and "AutoDock Vina" performed much better on average. However, for any given aim, any software may be superior, but "AutoDock Vina" is more likely to do so[32].

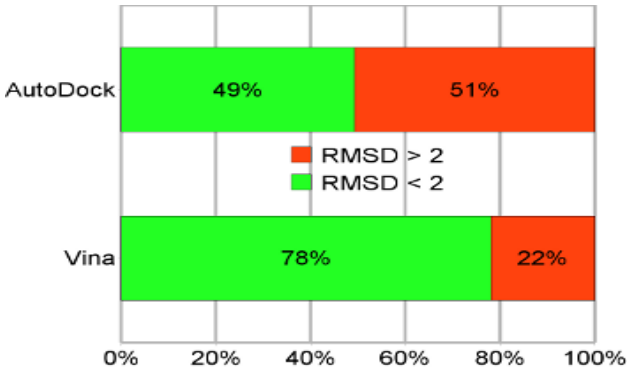

Figure 8. Binding mode prediction accuracy on the test set. AutoDock refers to AutoDock 4, and Vina to AutoDock Vina

SwissDrugDesign

The "SwissDrugDesign project (SwissDrugDesign)" brings together a collection of online tools that are connected in theory or by real-life ties. The project itself does not have a website, but each component tool has its own URL or may be accessed via interoperability features, as shown in Figure 9. SwissDrugDesign began in 2010 with the creation of the "SwissDock web-based docking engine". Since then, a number of additional options have been made accessible to the scientific community as free websites. Notably, all tools are free for non-profit study and education and may be used without registering[33].

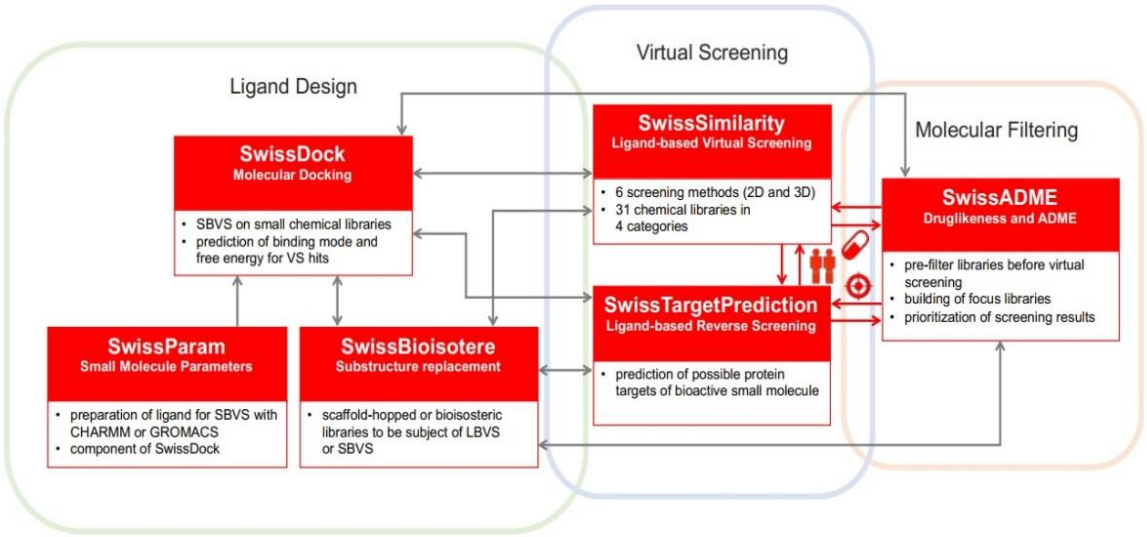

Figure 9. VS applications of the different on-line tools of the SwissDrugDesign project[34,35]

Virtual screening applications of the different on-line tools of the SwissDrugDesign project (boxed in red). Grey arrows represent “soft” relationships, for which the output of one tool can be the input of another tool by means of some user manipulation (e.g., copy/paste of SMILES). Red arrows represent actual interoperability capacities. In this way, submission of the result of one tool is simply achieved by “one-click” on the icon corresponding to the desired tool: “twins” for SwissSimilarity, “target” for SwissTargetPrediction and “pill” for SwissADME

The SwissDrugDesign project includes many areas, which can be briefly dissected as follows:

I. Swiss Similarity

It is a user-friendly online tool (SwissSimilarity) for ligand-based virtual screening of chemical libraries in order to locate compounds that are similar to a query molecule. SwissSimilarity has a number of chemical libraries available for screening, including licensed pharmaceuticals, recognized bioactive molecules, commercially available, and synthetically accessible compounds, as shown in Figure 10.

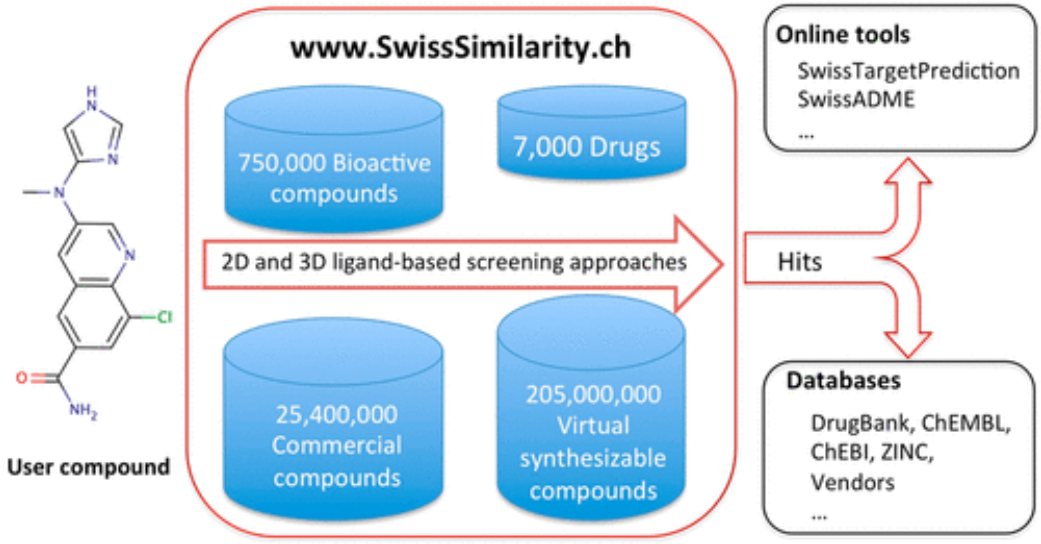

Figure 10. The SwissSimilarity workflow steps[36]

SwissSimilarity presents multiple 2D and 3D molecular fingerprints to determine molecular similarity, which encodes molecules in various digital forms and may be used to assess chemical similarity. In light of the concept of similarity, as shown in Figure 11, the list of SwissSimilarity's output compounds should be enhanced with molecules with similar bioactivity to the query substance. As a result, the method may be used to locate novel, potentially "bioactive compounds (hit finding)", comparable compounds with chemically distinct "core structures (scaffold hopping)", and compounds that are conveniently accessible for first structure-activity connection research.

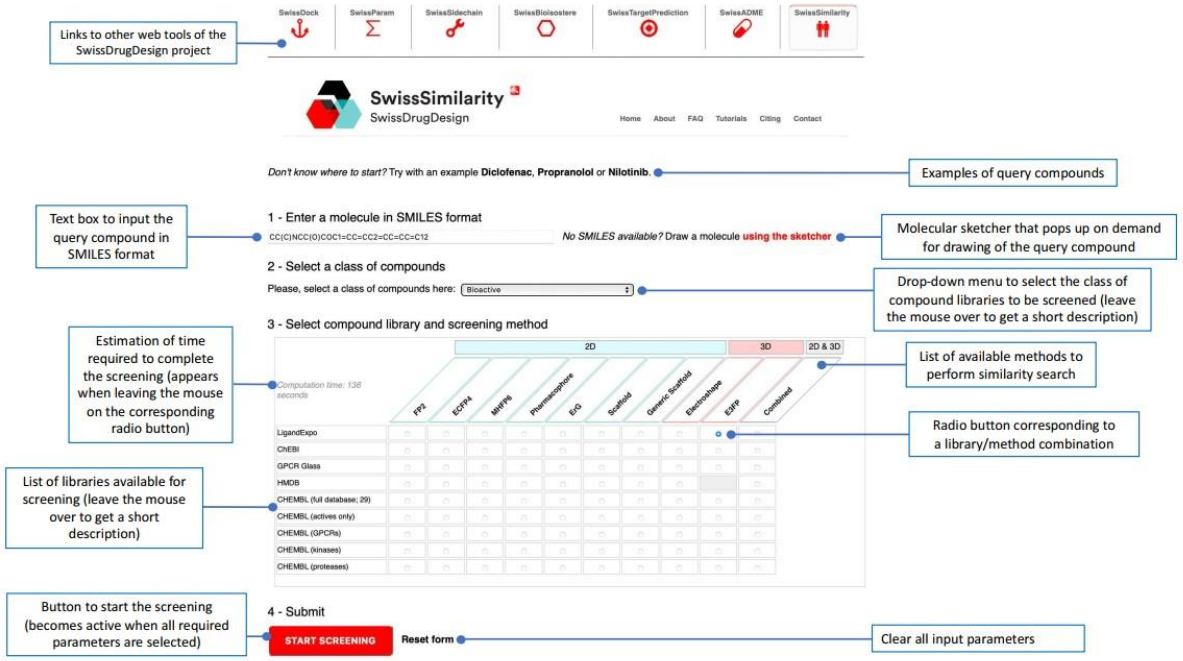

Figure 11. Submission page to set up, parameterize, and launch SwissSimilarity project[37].

As shown in Figure 12, SwissSimilarity may also be used to find comparable compounds in marketed medications or clinical drug prospects (e.g., to aid drug repurposing) or among those whose experimental structures have been discovered in association with their protein targets "(e.g. to support molecular docking studies)". It can also be used to confirm de novo developed compounds' chemical uniqueness[34].

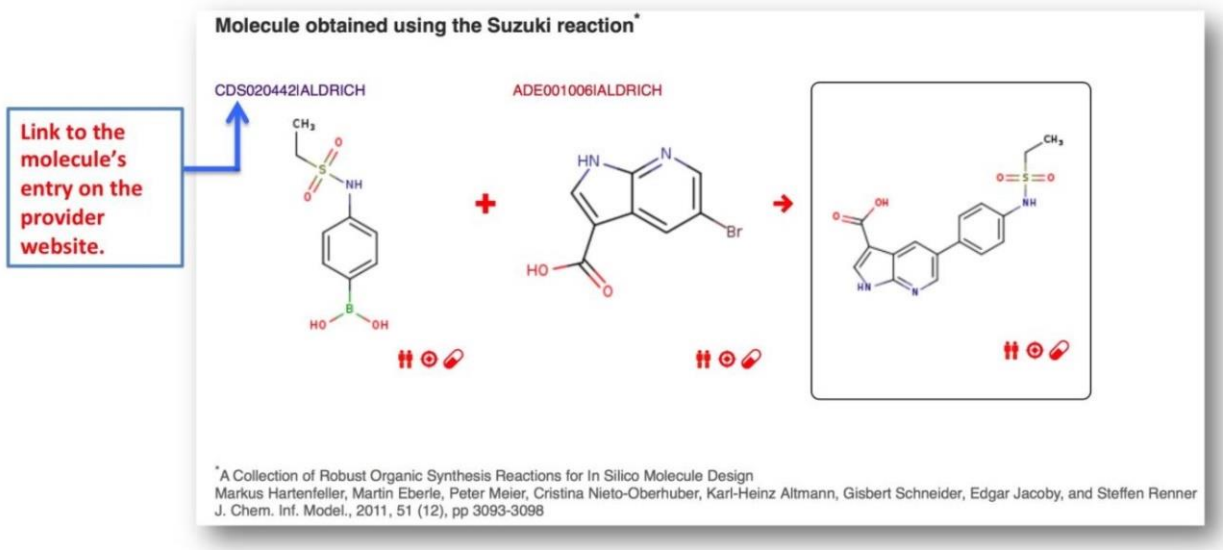

Figure 12. Example of a possible synthesis proposed by SwissSimilarity for a virtual hit compound[33].

II. SwissTargetPrediction

It is a web-based application (SwissTargetPrediction) that predicts the most likely protein targets for bioactive small compounds. Such predictions are valuable for understanding the molecular mechanisms underlying a certain phenotype, rationalizing hypothetical positive or negative side effects, predicting off-targets of known compounds, and laying a reasonable framework for therapeutic repurposing, as shown in Figures 13 and 14.

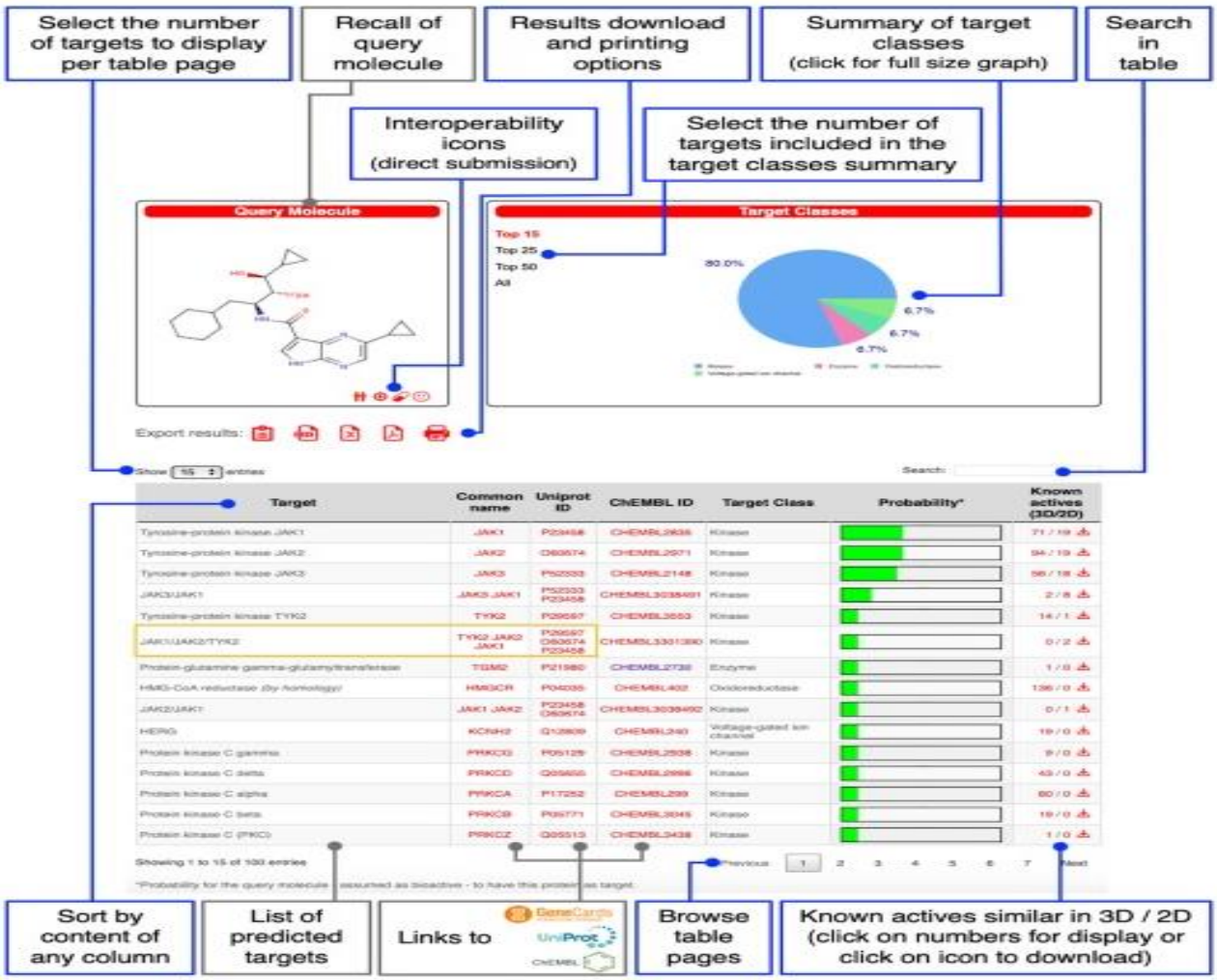

Figure 13. Submission page of the SwissTargetPrediction[34].

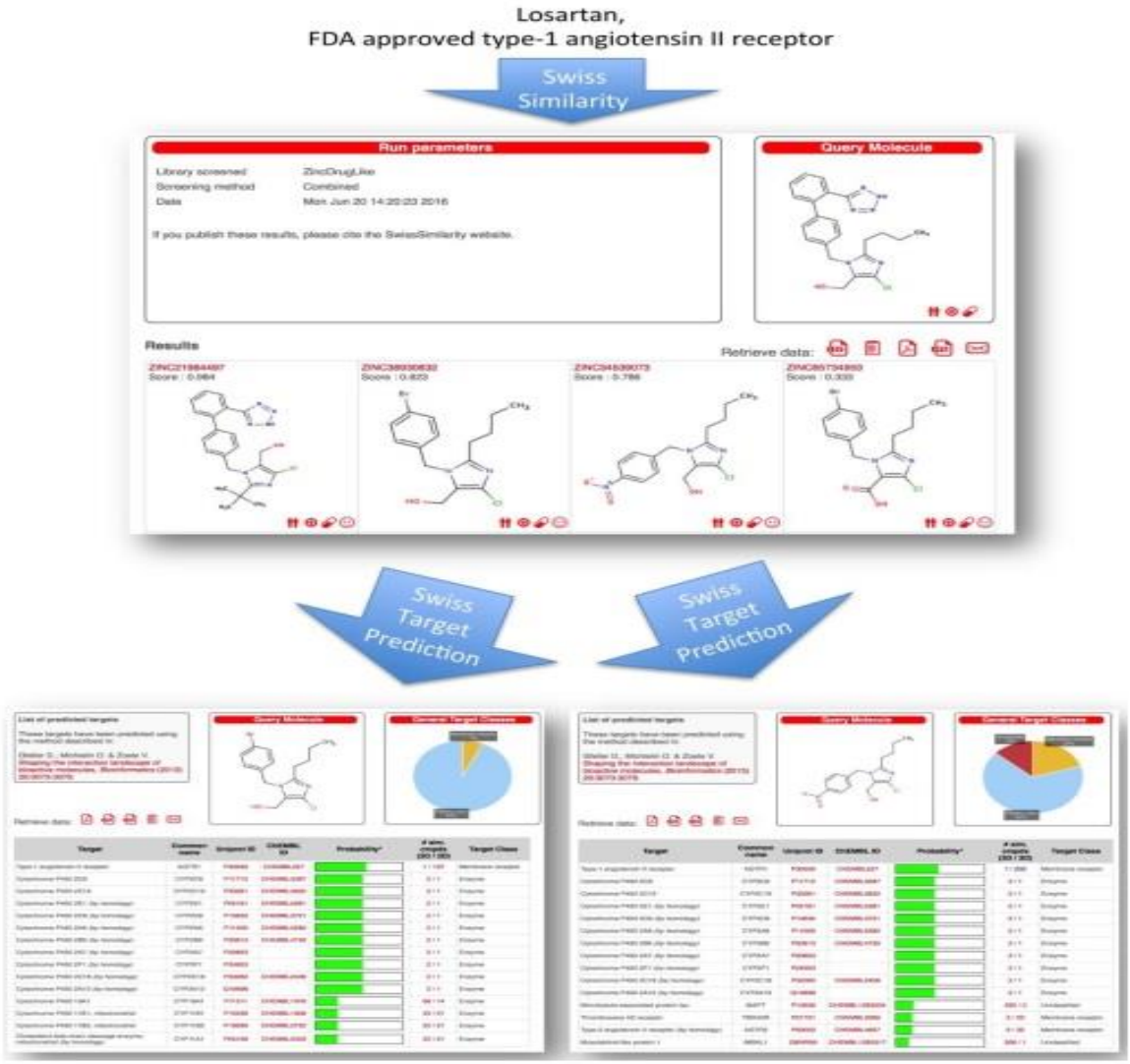

Figure 14. Example of a successful use case in the context of ligand-based virtual screening[33].

Example of a successful use case in the context of ligand based virtual screening. The ZINC drug-like library was screened against Losartan, a FDA approved ligand of the type-1 angiotensin II receptor, using the combined score. Compounds ranked 2 and 3 were submitted to SwissTargetPrediction.ch by clicking on the “target” icon. Both were predicted to be also ligands of the type-1 angiotensin II receptor[33].

"SwissTargetPrediction" is a reverse LBVS approach for target fishing that uses a dual-scoring logistic regression to combine 2D and 3D similarity measurements. Using a viewer web - based interface for proteins from multiple species, users may easily map estimates depending on target homology throughout source organisms. In its most latest versions, "SwissTargetPrediction" makes predictions based on reverse screening of a library of 376,342 major compounds to be experimentally active on a set of 3068 macromolecular targets. The approach also calculates the likelihood that a query molecule, which is considered to be bioactive, would bind each anticipated protein in a sorted list. It also contains the structures of the most comparable active compounds (in 2D and 3D), which were used to make the prediction. The latter feature is a valuable advantage when it comes to medication design[38].

III. SwissADME

It is a web-based program (SwissADME) that provides users with free access to a library of fast but accurate prediction models for "physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry friendliness". SwissADME has access to innovative methodologies developed in-house, such as iLOGP (a physics-based lipophilicity model) and the BOILED-Egg (an intuitive graphical classification model for gastrointestinal absorption and brain access)[35]. This application is the first web interface that allows batch computations for hundreds of distinct compounds, making pharmacokinetic optimization and chemical library analysis more efficient[39]. The latter capability is particularly useful for prefiltering complex collections before VS. This may be used to examine just drug-like, non-toxic, stable, and soluble molecules while omitting pain and other problematic moieties. As shown in Figure 15, other project-specific features pertaining to absorption, distribution, metabolism, excretion, or pharmacokinetics, such as parameter ranges to optimal brain access, can also be examined[40].

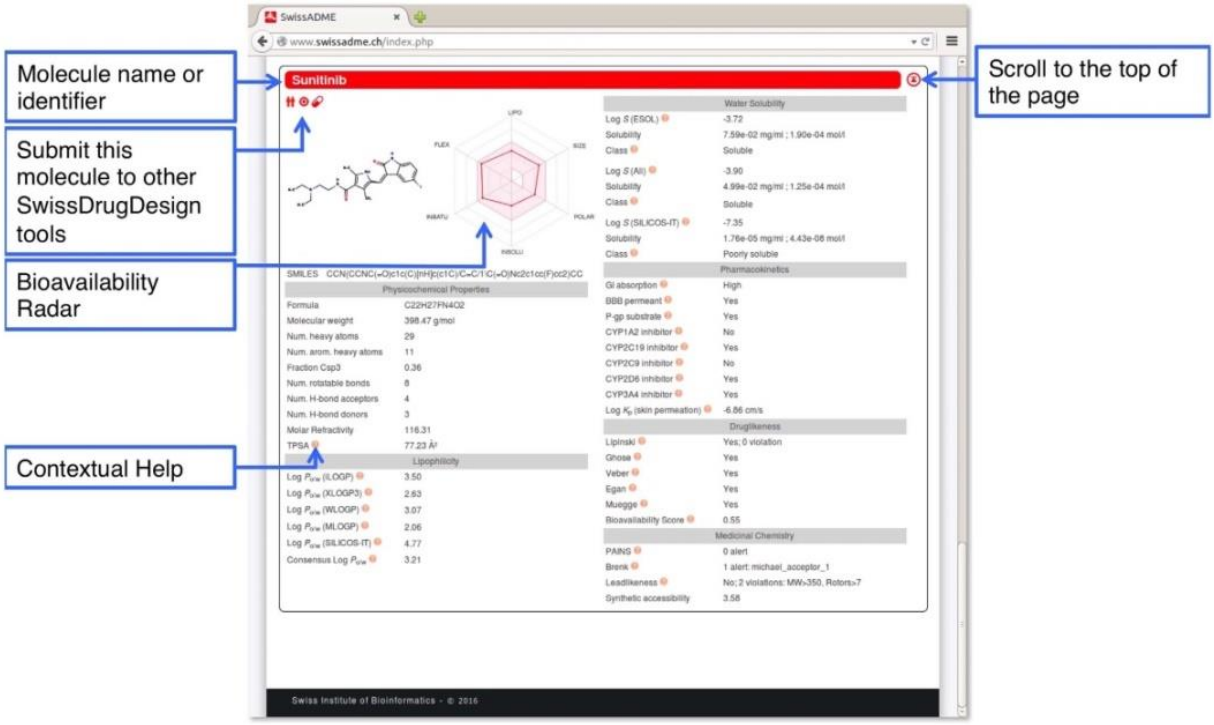

Figure 15. Computed parameter values are grouped in the different sections of the one-panel-par-molecule output (physicochemical properties, lipophilicity, pharmacokinetics, drug-likeness and medicinal chemistry)[39]

IV. SwissBioisostere

It (SwissBioisostere) was the first systematic and publically accessible dataset comprising over 4.5 million molecular sub-structural substitutions obtained from the literature, as well as statistics on how commonly such modifications were utilized and their impact on measured bioactivity[41]. This information, as shown in Figure 16, is particularly useful for changing small compounds in order to boost affinity or avoid a pharmacodynamic, pharmacokinetic, or intellectual property problem. Scaffold-hopping, as shown in Figure 17, can benefit from the replacement of central cores with "fragment replacements", while lead optimization can benefit from the alteration of peripheral groups. Experts can use SwissBioisostere's output to create small "chemical libraries" of putative bioisosteric or related structures that can subsequently be subjected to VS[42].

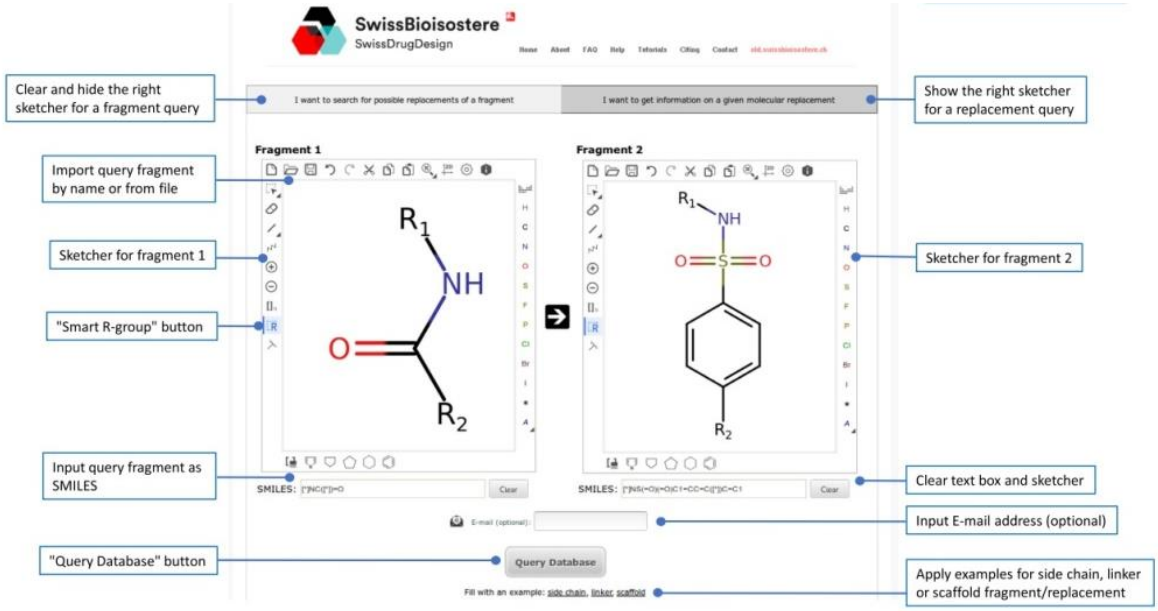

Figure 16: SwissBioisostere input page

Figure 17. Retrieval of details for a particular molecular replacement. The user enters the replacement as chemical substructures in sketcher 1 and 2 (1), or follows a link from the result page presented in Figure 3. The query results in a detailed overview page that presents the underlying data for this particular replacement: (2) general statistics, (3) bioactivity difference distribution plot, (4) bioactivity difference distributions by attachment point context, (5)

filter for assay and compound properties, (6) results table, (7) sorts columns, (8) column filter for assays, targets, target classes, (9)detail view for particular data record and (10) data export[40].

V. SwissParam

It (SwissParam) is an online service that provides topologies and characteristics for tiny organic molecules. SBVS, like other "structure-based drug discovery techniques", is often based on "ligand-protein docking" and estimations of rapid binding energy. This needs force field modelling for all drug options. SwissParam is a rapid force field generation tool that uses the Merck Molecular Force Field to build topologies and variables for any small tridimensional molecular structure in the MOL2 (tripos molecular structure) format. The topologies and parameters are presented in a functional format that is compatible with the CHARMM force field. The output files can be used directly in "CHARMM or GROMACS". SwissDock makes heavy use of SwissParam findings to parameterize ligands[43].

VI. SwissDock

It is based on the "EADock DSS program", which uses the most proficient components of the EADock2 method, which is "physics-based" since it follows to the CHARMM force field description in its entirety. The present version is fast quite enough online use and "serial docking of small chemical libraries in SBVS". As shown in Figure 18, when using the "LPDB benchmark set of protein-ligand complexes, EADock DSS had a 55% success rate in reproducing molecular interactions between proteins and drug-like molecules when using only the top-ranked solution over the entire protein surface (i.e., blind docking)" and a 64% success rate when using all five "top-ranked solutions". Docking an LPDB complex requires the server an average of 24 minutes.

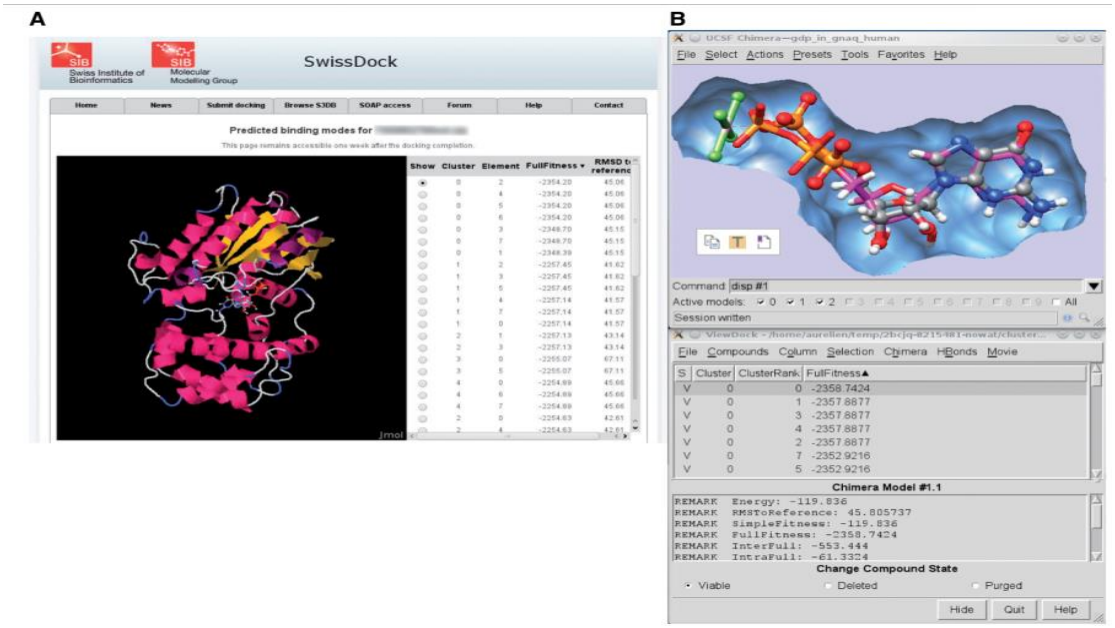

Figure 18. This figure shows a typical output of SwissDock for the docking of the Guanine nucleotide-binding protein G(q) subunit alpha, a target involved in uveal melanoma (35). (A) Screenshot of the Jmol applet which renders predicted BMs within the web browser. (B) Visual investigation using the ViewDock plugin of UCSF Chimera. The predicted BM of the guanosine diphosphate (magenta sticks) is superimposed to the X-ray BM (ball and sticks). As it can be seen in the lower part of the figure, this particular predicted BM has the most favorable energy[43]

Conclusion

Exploring bioactive chemical scaffolds by traditional synthetic and testing approaches still suffers from several limitations. Some of these limitations are time-consuming, high processing costs, heavy attempts for optimization, and a lot of resources. Computation in chemistry may offer a window of hope to treat these obstacles by developing and creating many software programs. Also, these programs can facilitate home-working specifically under special circumstances like the COVID-19 pandemic. Accordingly, the chemical-aid development programs have attracted a great deal of attention and are now involved in a significant number of scientific papers. To summarize, developing a reliable, expandable, and long-term molecular simulation tool necessitates a cross-team of domain scientists, computer programmers and software developers, and applied mathematicians. Chemical-aid development programs could serve as a residence and objectivity for interconnection and interoperability between various modeling communities in order to tackle new levels of science championship series troubles that are presently beyond the scope of further customized societies.

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