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# A Review on Computational Software Tools for Drug Design and Discovery

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**ABSTRACT:** In the current era of modern drug design & development via computer-aided drug design, the potential role of computational software tools is widely enlarged in use. Computer-based drug design is revolutionary in the new drug discovery process because these processes are fast, time, and cost-saving with more efficient pharmacological activity. Computer-Based drug design is mainly applied for the drug-design and gets many successes in new drug research. There is plenty of software available in drug design; however; still, many issues are rising during its use. To clarify these issues, an attempt has been provided here in this article about the information about worldwide used 189 computation tools along with citation of software tools, download links, computer operative system and application of tools for available software such as Molecular modeling, docking, proteins conformation, pharmacophore mapping, ADMET, Docking pose visualization, force field calculation, homology modeling, 3D structure generator, Computational Crystallography, protein Database, and calculation software. This vital information enlightens all the software right from old to a recent one. Review article important for choice and application of wide-reaching used Drug Design software. 

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## INTRODUCTION

The process of drug discovery and development is very convenient with the invention of various computational software and tools. Drug design and discovery are usually made by using computer software for virtual screening by structure or ligand-based design and lead optimization. There is also some computer software available for structural affinity by selective structure-based design and lead optimization of some physicochemical properties for the improvement of drugs. Drug design and discovery approaches include combinatorial chemistry, biology, high-throughput screening, and drug metabolism (ADME) groups, which are link together [1, 2]. A lot of computational software or tools are available worldwide for drug design with different uses, accuracy, and precise techniques. The invention of computational tools used for novel drugs design and discovery is one of the fast-developing recent achievement for Molecular modeling, docking, proteins conformation pharmacophore mapping, ADMET Docking poses visualization, force field calculation, homology modeling, 3D structure generator, Computational Crystallography, Pharmacophore search, protein Database, and calculation software molecular biology. Computational tools are essential for lead optimization, lead discovery, and pre-clinical in vitro examination criteria for initiating clinical development (**Figure 1**). [3, 4, 5].

Computational tools are essential for Computer-aided drug design because these processes are a cost-effective, reliable, and time-saving technique. The novel drug discovery and design it is widely used different technique such as rational

drug design and structure-based drug design. Structure-based drug design means that we use three-dimensional structures (protein, enzymes, and receptor) to design drug/new drugs (ligand) and rational drug design is the creative process of finding new medications based on the data of a biological target. Both techniques work with the help of computers and software by checking receptor- drug binding affinity. In the history where random synthesis gave a little bit of success while in today's modern drug design era use of computational software is but evident for fast and feasible research. For accurate prediction of biological activity of designed small molecule and protein target, the computation software can play an essential role in rational drug design [3, 6, 7]. Computational tools are helpful for new drug candidates; therefore, it is beneficial to apply computational tools in the drug design and discovery process [8, 9]. The main complication of computational software tools for CADD (computer-aided drug discovery) are elucidation issues for protein-ligand(drug), Issue of excluding Computational tools, Issue of superiority Datasets, Issue of inconsistency software, Issue of precise Scoring Functions by software, protein-ligand complex Model overlapping, multi-domain proteins issue and protein-drug (ligand) false binding pocket [1-9].

## METHODS FOR INFORMATION AND APPLICATION OF COMPUTATIONAL TOOLS

A total of 189 computational tools used for drug design and discovery have been shown in Table 1(Appendix). Table 1 provides the details on different computation software tools like software name, year of availability, organization name, country name, web facility/ weblink/details for software. Also, in **Table 1**, the information about the best Google citation, Publication citation review/ research/ conformance/ meeting, and patent citation application of computational tools, availability, and operating system is provided.

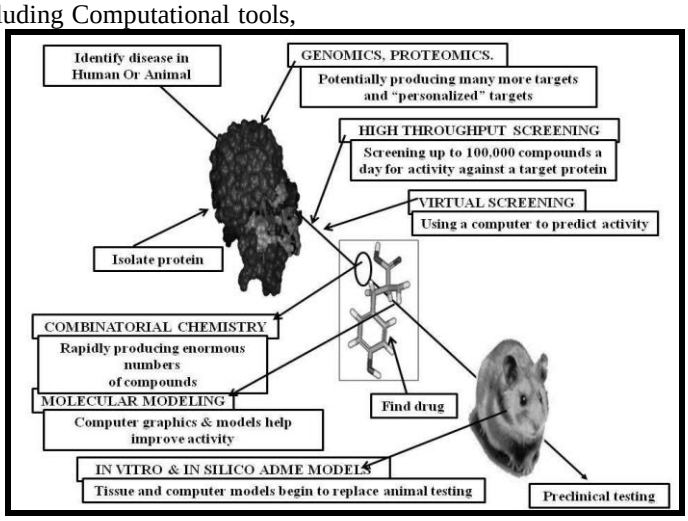


**Figure: 1 Computational tools impact in drug design and discovery process**

**Table 1: List of computational software and their details for drug design and discovery.**

| Sr No. | Software Name | Year of availability | Organization name | Country name | Web facility/ web link/Details for software | Availability of Software (free or commercial licenses) | Operative system |
|---|---|---|---|---|---|---|---|
| 1. | DOCK | 1982 | UCSF (University of California, San Francisco) | USA | http://dock.compbio.ucsf.edu/ Accessed September the 10th2019 | Freeware | Linux, mac OS, Windows |
| 2. | Abalone | 1985 | Nuclear Engineering Department and Materials Science and Technology Division | USA | http://www.biomolecular-modeling.com/Abalone/abalone-ii.html/ Accessed September the 10th2019 | Commercial | Windows XP, 7 |
| 3. | ChemOffice/ ChemDraw | 1985 | PerkinElmer | US | http://www.perkinelmer.com/product/chemdraw-professional-chemdrawpro/ Accessed September the 10th2019 | Commercial | MacOS, Microsoft Windows |
| 4. | Winmostar software packages | 1989 | X-Ability Co., Ltd. | Japan | https://winmostar.com/en/ and https://x-ability.co.jp/en/index.php/ Accessed September the 10th2019 | Commercial | Windows Vista, 7, 8, 10 |
| 5. | AutoDock | 1990 | Scripps Research | USA | http://autodock.scripps.edu/ Accessed September the 10th2019 | Open source | Linux, Mac OS X, SGI IRIX and Microsoft Windows |

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|---|---|---|---|---|---|---|---|
| 6. | FANTOM | 1990 | Eidgenössische Technische Hochschule-Höngge rberg | Switzerla nd | http://bose.utmb.edu/fantom/ Accessed September the 10th2019 | Free software package for academic users | Commands to run |
| 7. | SOFT Docking | 1991 | University of California | USA | https://www.sciencedirect.com/scie nce/article/pii/0022283691908595/ Accessed September the 10th2019 | Academic | Docking Server |
| 8. | hint!® | 1991 | Medical College of Virginia/ Virginia Commonwealth University | USA | http://www.edusoft-lc.com/hint/ Accessed September the 10th2019 | Commercial | Windows |
| 9. | DockVision | 1992 | University of Alberta | Canada | http://dockvision.sness.net/ Accessed September the 10th2019 | Commercial | Graphical User Interface |
| 10. | IMMD Inc. | 1992 | Institute of Medicinal Molecular Design, Inc | JAPAN | http://www.immd.co.jp/en/product_ 2.html/ Accessed September the 10th2019 | Commercial | Graphical User Interface |
| 11. | ADAPT | 1992 | The Pennsylvania State University | USA | http://research.chem.psu.edu/pcjgro up/ Accessed September the 10th2019 | Commercial | Unix operating system |
| 12. | PROCHECK | 1993 | Department of Biochemistry and Molecular Biology, University College | UK | https://www.ebi.ac.uk/thornton-srv/software/PROCHECK/ Accessed September the 10th2019 | Free | Unix/Linux |
| 13. | Naccess | 1993 | Department of Biochemistry and Molecular Biology, University College | United Kingdom | http://www.bioinf.manchester.ac.uk /naccess/ Accessed September the 10th2019 | Academic or non-commercial use | Unix/Linux |
| 14. | ICM-Dock | 1994 | Molsoft L.L.C. | USA | http://www.molsoft.com/gui/start-dock.html/ Accessed September the 10th2019 | Commercial | Graphical User Interface |
| 15. | ADAM | 1994 | University of Tokyo | Japan | http://www.immd.co.jp/en/product_ 2.html/ Accessed September the 10th2019 | Commercial | Graphical User Interface |
| 16. | FLOG | 1994 | Merck Research Laboratories | USA | https://link.springer.com/article/10. 1007%2FBF00123666/ Accessed September the 10th2019 | Commercial | Linux |
| 17. | Corina | 1994 | Molecular Networks GmbH – Computer chemie and Altamira LLC | Germany and USA | https://www.mn-am.com/products/corina/ Accessed September the 10th2019 | Commercial | Microsoft Windows 7/8/10, Server 2008, Server 2012, 86 Linux RHEL5/6 |
| 18. | DIVALI | 1995 | University of California-San Francisco | USA | https://onlinelibrary.wiley.com/doi/ abs/10.1002/jcc.540161004/ Accessed September the 10th 2019 | Free | - |
| 19. | GOLD | 1995 | University of Sheffield | UK | https://www.ch.cam.ac.uk/computin g/software/gold-suite / Accessed September the 10th 2019 | Commercial | DOS, Microsoft Windows |
| 20. | Shape-it™ | 1995 | Silicos-it | Belgium | http://silicos-it.be.s3-website-eu-west-1.amazonaws.com/software/shape-it/1.0.1/shape-it.html/ Accessed September the 10th 2019 | Open source software tools | OS X 10.7 and OS X 10.8 |
| 21. | RasMol | 1995 | Glaxo Wellcome Medicines Research Centre | UK | http://www.rasmol.org/ Accessed September the 10th 2019 | Open Source | Mac (PPC), Windows, Unix, and Linux systems |
| 22. | Gromacs | 1995 | The University of Groningen | Netherlan ds | http://www.gromacs.org/ Accessed September the 10th 2019 | Free | Linux, mac OS, Windows, |
| 23. | Hammerhead | 1996 | Arris Pharmaceutical Corporation | USA | https://www.ncbi.nlm.nih.gov/pubm ed/8807875/ Accessed September the 10th2019 | Academic | Graphical User Interface |
| 24. | LIGIN | 1996 | Weizmann Institute of Science | Israel | https://swift.cmbi.umcn.nl/gv/servic e/ligin/ Accessed September the 10th2019 | Commercial | DOS |

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|---|---|---|---|---|---|---|---|
| 25. | GASP | 1996 | National Human Genome Research Institute | Maryland | https://research.nhgri.nih.gov/software/GASP/index.shtml Accessed September the 10th 2019 | Academic | Red Hat Enterprise Linux 6.8/ x86_64 hardware |
| 26. | VMD | 1996 | University of Illinois | USA | http://www.ks.uiuc.edu/Research/vmd/allversions/what_is_vmd.html/ Accessed September the 10th2019 | Open Source License | Mac OS X, Unix, or Windows |
| 27. | PROMOTIF | 1996 | Department of Biochemistry and Molecular Biology, University College | UK | http://www.img.bio.uni-goettingen.de/ms-www/internal/manuals/promotif/promotif.html/ Accessed September the 10th 2019 | Academic | DOS |
| 28. | DSSP | 1996 | Dutch Tech center for Life Sciences | Netherlands | https://swift.cmbi.umcn.nl/gv/dssp/ Accessed September the 10th2019 AND https://github.com/cmbi/xssp/releases | Free | UNIX/Linux |
| 29. | Open Eye Scientific Software tools | 1997 | Open Eye Scientific | USA | www.eyesopen.com/ Accessed September the 10th 2019 | Free to academic | OS X, Red Hat, SuSE, Ubuntu, Windows |
| 30. | FTDOCK | 1997 | Biomolecular Modelling Laboratory | UK | http://www.sbg.bio.ic.ac.uk/docking/download.html/ Accessed September the 10th 2019 | Free to both academic and commercial users | Unix/Linux |
| 31. | QXP | 1997 | Novartis Pharmaceuticals Corporation | Switzerland | https://link.springer.com/article/10.1023%2FA%3A1007907728892/ Accessed September the 10th2019 | Academic | DOS |
| 32. | SANDOCK | 1998 | The University of Edinburgh | UK | No web service available | Academic | window |
| 33. | GETAREA | 1998 | UTMB (University of Texas Medical Branch) | USA | http://curie.utmb.edu/getarea.html/ Accessed September the 10th 2019 | Free | PyMOL |
| 34. | Quasi | 1998 | Biographics Laboratory | Switzerland | http://www.cse.scitech.ac.uk/ccg/collaboration/quasi/ Accessed September the 10th 2019 | Free | GUI, DOS |
| 35. | BOSS | 1998 | Yale University Department of Chemistry | USA | http://zarbi.chem.yale.edu/software.html/ Accessed September the 10th 2019 | Commercial | Unix, Linux, Windows |
| 36. | MCDOCK | 1999 | Georgetown University Medical Center | USA | https://github.com/andersx/mcdock/ Accessed September the 10th2019 | Academic | DOS |
| 37. | PRODOCK | 1999 | Cornell University | USA | No web information Available | Academic | Windows 10, 8.1, 8, 7 |
| 38. | LPC/CSU | 1999 | Weizmann Institute of Science | Israel | https://webhome.weizmann.ac.il/home/edg/Proteomic_Web_pages_data.html/ Accessed September the 10th2019 And http://oca.weizmann.ac.il/oca-bin/lpccsu/ Accessed September the 10th2019 | Free | Online |
| 39. | CATS | 1999 | F. Hoffmann-La Roche Ltd | Switzerland | http://www.cadd.ethz.ch/software/catslight2.html/ Accessed September the 10th 2019 | Free Online | Online |
| 40. | FlexX | 2000 | BioSolvIT | Germany | https://www.biosolveit.de/FlexX/ Accessed September the 10th 2019 | Commercial | Linux x86 64 bit, Microsoft windows 64 bit, apple mac os x |
| 41. | Combinatorial library design | 2000 | CombiChem, Inc. | USA | http://chemoinfo.ipmc.cnrs.fr/eDESIGN/reagent.html/Accessed September the 10th 2019 | Free and open to non-commercial users | Online web |
| 42. | DARwin | 2000 | The Wistar Institute | USA | http://darwin.cirad.fr/ Accessed September the 10th 2019 | Free for use in research and education | all current Microsoft Windows operating |

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| | | | | | | | systems, Microsoft Windows Visual Basic Studio.Net targeted on Microsoft .Net Framework 4.0., MacOS or Linux |
| 43. | MPACK | 2000 | University of Texas Medical Branch | USA | http://curie.utmb.edu/mpack/ Accessed September the 10th 2019 | Commercial | Linux, IRIX |
| 44. | Filter-it™ | 2000 | Cheminformatics, Novartis Pharma AG | Switzerland | http://silicos-it.be.s3-website-eu-west-1.amazonaws.com/software/filter-it/1.0.2/filter-it.html#ertl/ Accessed September the 10th 2019 | Open source software tools | Mac Book Pro, OS X Lion 10.7.3, 10.8. |
| 45. | FTrees | 2000 | BioSolvIT | Germany | https://www.biosolveit.de/FTrees-FS/ Accessed September the 10th 2019 | Commercial | Linux x86 64 bit, Microsoft windows 64 bit, apple mac os x |
| 46. | Ascalaph | 2000 | University of Stockholm | Sweden | http://www.biomolecular-modeling.com/Products.html | Free | Linux using Wine, Windows XP, 7 |
| 47. | MOLARIS-XG | 2000 | University of Southern California | USA | https://laetro.usc.edu/software.html/ Accessed September the 10th 2019 | Commercial | GNU/Linux |
| 48. | SEED | 2001 | University of Zürich | Switzerland | http://www.biochem-caflisch.uzh.ch/download and https://gitlab.com/CaflischLab/SEED/ Accessed September the 10th 2019 | Open source | DOS |
| 49. | FFLD | 2001 | University of Zürich | Switzerland | http://www.biochem-caflisch.uzh.ch/ Accessed September the 10th2019 | Free open source | Window |
| 50. | EUDOC | 2001 | Mayo Clinic Cancer Center | USA | https://mayoclinic.pure.elsevier.com/en/searchAll/index/?search=EUDOC%3A+a+computer+program+for+identification+of+drug+interaction+sites+in+macromolecules+and+drug+leads+from+chemical+databases&pageSize=25&showAdvanced=false&allConcepts=true&inferConcepts=true&searchBy=PartOfNameOrTitle/ Accessed September the 10th 2019 | Academic | Window |
| 51. | PocketMol | 2001 | Wright State University | USA | http://knoesis.org/search/node/PocketMol And http://www.mybiosoftware.com/pocketmol-1-0-molecular-visualization-program-pocket-pc.html/ Accessed September the 10th 2019 | Freeware | Command line Window Based |
| 52. | QMOL | 2001 | Cornell University | USA | https://www.dnastar.com/ Accessed September the 10th 2019 | Freeware | Windows |
| 53. | YASARA | 2002 | Center for Molecular and Biomolecular Informatics | Netherlands | http://www.yasara.org/ Accessed September the 10th 2019 | Free | Windows, Linux and Mac OS X |
| 54. | Pymol | 2002 | Schrodinger | USA | https://pymol.org/ Accessed September the 10th 2019 | Free and open-source | Windows, Mac OSX, Unix, and Linux |
| 55. | SDAP | 2002 | UTMB (University of Texas | USA | http://fermi.utmb.edu/SDAP/ Accessed September the 10th 2019 | Free | Online Database |

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| | | | Medical Branch) | | | | |
| 56. | FDS | 2003 | University of Southampton | UK | https://www.southampton.ac.uk/chemistry/about/staff/jwe1.page#publications/ Accessed September the 10th 2019 | Academic | Online Server |
| 57. | HADDOCK | 2003 | Utrecht University | Netherlands | http://milou.science.uu.nl/services/HADDOCK2.2/haddock.php/ Accessed September the 10th 2019 | Freeware | DOS |
| 58. | LigandFit BioVia | 2003 | BIOVIA | USA | http://www.3dsbiovia.com/services/training/life-science/StructureBasedDesignDescription.html/ Accessed September the 10th 2019 | Commercial | Command-line and graphical user interface |
| 59. | Surflex-Dock | 2003 | BioPharmics LLC | USA | http://www.biopharmics.com/downloads.html/ Accessed September the 10th 2019 | Academic or non-profit | Windows, Linux, and Mac platforms |
| 60. | Tuplets | 2003 | Dick Cramer | USA | http://www.tri-ibiotech.com/upload/file/sybyl-x/6-Tuplets.pdf/ Accessed September the 10th 2019 | Free | Windows |
| 61. | CDK | 2003 | Max-Planck-Institute of Chemical Ecology | Germany | https://cdk.github.io/ Accessed September the 10th 2019 | Open-source | Java based |
| 62. | SageMD | 2003 | Sarov Open Computing Center, | Russia | http://sagemd.com/ Accessed September the 10th 2019 | Free | Linux, FreeBSD, SGI IRIX, HP-UX, IBM AIX, SUN Solaris, DEC/Compaq Tru64 UNIX, and MS-Windows |
| 63. | GEMDOCK | 2004 | NCTU (National Chiao Tung University) | Taiwan | http://gemdock.life.nctu.edu.tw/dock/igemdock.php/ Accessed September the 10th 2019 | Freeware | windows XP/ Vista/ 7, CentOS 5, Suse Linux 9, Ubuntu Linux |
| 64. | Glide Schrödinger | 2004 | Schrodinger | USA | https://www.schrodinger.com/science-articles/docking-and-scoring/ Accessed September the 10th 2019 | Commercial | Linux, Windows, Mac, GPGPU |
| 65. | ArgusLab | 2004 | Pacific Northwest National Laboratory | USA | http://www.arguslab.com/arguslab.com/ArgusLab.html/ Accessed September the 10th 2019 | Freeware | Mac, Window, Linux |
| 66. | JOELib | 2004 | University of Tübingen | Germany | http://www.ra.cs.uni-tuebingen.de/software/joelib/introduction.html/ Accessed September the 10th 2019 | Open source | Java based software |
| 67. | VEGA On-line | 2004 | University of Milan | Italy | http://www.ddl.unimi.it/ Accessed September the 10th 2019 | Open Online | Online command-line |
| 68. | UCSF Chimera | 2004 | University of California | USA | http://www.cgl.ucsf.edu/chimera/index.html/ Accessed September the 10th 2019 | Free to academic | Windows, Linux, Mac OS X, IRIX, and Tru64 Unix |
| 69. | SuperPose | 2004 | University of Alberta | Canada | http://wishart.biology.ualberta.ca/SuperPose/ Accessed September the 10th 2019 | Open source | web online server |
| 70. | SRS 3D | 2004 | LION bioscience AG | Germany | http://srs3d.org/ Accessed September the 10th 2019 | Open source | Online |
| 71. | MEDock | 2005 | National Taiwan University | Taiwan | http://medock.ee.ncku.edu.tw/documentation.html#medock/ Accessed September the 10th 2019 | Web server | Online |
| 72. | PatchDock | 2005 | Tel Aviv University | Israel | https://bioinfo3d.cs.tau.ac.il/PatchD | Web server | Online |

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| | | | | | ock/ Accessed September the 10th 2019 | | |
| 73. | LigandScout | 2005 | Inte:Ligand GmbH | Austria | http://www.inteligand.com/ligandscout/ Accessed September the 10th 2019 | Proprietary commercial software | Windows, Mac OS X, Linux |
| 74. | e-LEA3D/ Drug design or Screen | 2005 | Faculté de Pharmacie, Université Montpellier I | France | http://chemoinfo.ipmc.cnrs.fr/ Accessed September the 10th 2019 | Free for an academic | Linux |
| 75. | FoldX | 2005 | Universiteit Brussel | Belgium | http://foldxsuite.crg.eu/ Accessed September the 10th 2019 | Academic and commercial licenses | command line |
| 76. | Visualizer DS | 2005 | BIOVIA | USA | http://accelrys.com/products/collaborative-science/biovia-discovery-studio/visualization.html/ Accessed September the 10th 2019 | commercial | Windows 7 SP1, Windows 10, Red Hat Enterprise Linux v6.3+, Linux v7, SUSE® Linux Enterprise Server 11.4, CentOS 7, (All version 64Bit) |
| 77. | AURAmol | 2005 | The University of York | UK (England ) | https://www.cs.york.ac.uk/auramol/index.html/ Accessed September the 10th 2019 | Free | C++ library and runs on Linux, Windows and UNIX |
| 78. | PowerMV | 2005 | National Institute of Statistical Sciences | USA | https://www.niss.org/research/software/powermv/ Accessed September the 10th 2019 | Free | Windows XP/7 |
| 79. | PLANTS | 2006 | University of Konstanz | Germany | https://www.mnf.uni-tuebingen.de/fachbereiche/pharmazie-und-biochemie/pharmazie/pharmazeutische-chemie/pd-dr-t-exner/research/plants.html/ Accessed September the 10th 2019 | Free for academic use | Linux, Win32, and OSX |
| 80. | PSI-DOCK | 2006 | Peking University | China | http://cqb.pku.edu.cn/en/ Accessed September the 10th 2019 | Academic | Windows, Linux, Mac |
| 81. | DAIM | 2006 | University of Zürich | Switzerland | http://www.biochem-caflisch.uzh.ch/ Accessed September the 10th 2019 | Commercial | command lines |
| 82. | kinDOCK/@TOME | 2006 | Atelier de Bio- et Chimie-Informatique Structurale | France | http://abcis.cbs.cnrs.fr/kindock/ And http://atome.cbs.cnrs.fr/AT23/index.html/ Accessed September the 10th 2019 | Free and open | Web server |
| 83. | CoLiBRI | 2006 | BioSolvIT | USA | https://www.biosolveit.de/CoLibri/ Accessed September the 10th 2019 | Commercial | Windows, Linux |
| 84. | Molegro Virtual Docker | 2006 | Molegro ApS | Denmark | https://molegrovirtualdocker.weebly.com/ Accessed September the 10th 2019 | Academic | Graphical user interface and Unix/Linux, Mac OS, Windows |
| 85. | BDT | 2006 | Universitat Rovira i Virgili | Spain | http://www.quimica.urv.cat/~pujadas/BDT/ Accessed September the 10th 2019 | Free | Unix/Linux, Mac OS, Windows |
| 86. | InterProSurf | 2006 | UTMB (University of Texas Medical Branch) | USA | http://curie.utmb.edu/prosurf.html/ Accessed September the 10th2019 | Open | Web server |
| 87. | GFscore | 2006 | IBSM (Institute for Structural Biology and Microbiology) | France | http://gfscore.cnrs-mrs.fr/index.htm/ Accessed September the 10th2019 | Open | Web server |
| 88. | SiMMap | 2006 | University of | Denmark | http://simmap.life.nctu.edu.tw/ | Open | Mac OS X, |

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| | | | Copenhagen | | Accessed September the 10th2019 | | Linux, Windows |
| 89. | Dragon | 2006 | University of Milano-Bicocca | Italy | http://www.talete.mi.it/products/dragon_description.htm/ Accessed September the 10th2019 | Commercial | Linux Fedora Core 13, Ubuntu 10.04, kernel 2.6, Windows XP/Vista/7 |
| 90. | AFGen | 2006 | University of Minnesota | USA | http://glaros.dtc.umn.edu/gkhome/afgen/overview/ Accessed September the 10th2019 | Free | Linux (i686/x86_64) |
| 91. | AQUASOL | 2006 | Unité de Dynamique Structurale des Macromolécules | France | http://lorentz.dynstr.pasteur.fr/suny/index.php?id0=aquasol#welcome/ Accessed September the 10th 2019 | Open | --- |
| 92. | MODELLER | 2006 | Biovia | California | https://salilab.org/modeller// Accessed September the 10th 2019 | Free of charge to academic | Unix/Linux, Windows, Mac. |
| 93. | ParDOCK | 2007 | Indian Institute of Technology | India | http://www.scfbio-iitd.res.in/dock/pardock.jsp#1/ Accessed September the 10th 2019 | Freeware | Web server |
| 94. | EADock | 2007 | Swiss Institute of Bioinformatics | Switzerland | http://www.swissdock.ch/ Accessed September the 10th 2019 | Freeware | Web server |
| 95. | FLIPDock | 2007 | The Scripps Research Institute | United States | http://flipdock.scripps.edu/ Accessed September the 10th 2019 | Free for academic use | Linux |
| 96. | Fitted | 2007 | Molecular Forecaster Inc. | Canada | http://molecularforecaster.com/fitted.html/ Accessed September the 10th 2019 | Free for academic use | Linux, Windows, Mac. |
| 97. | PSO@AUTODOCK | 2007 | Leipzig University | Germany | http://pacosy.informatik.uni-leipzig.de/7-1-Software.html/ Accessed September the 10th 2019 | Academic | Ubuntu |
| 98. | SODOCK | 2007 | Feng Chia University | Taiwan | http://www.iecs.fcu.edu.tw/wSite/ct?xItem=T80036&ctNode=14823&mp=370201/ Accessed September the 10th 2019 | Academic | Ubuntu |
| 99. | eHiTS | 2007 | SymBioSys Inc | Canada | https://www.simbiosys.ca/ Accessed September the 10th 2019 | Commercial | Linux |
| 100. | Glam Dock | 2007 | Ludwig-Maximilians-University | Germany | http://www.chil2.de/Glamdock.html/ Accessed September the 10th 2019 | Freely available | ---- |
| 101. | Fleksy | 2007 | Radboud University | Netherlands | http://www.cmbi.ru.nl/software/fleksy/index.spy?site=fleksy&action=Introduction/ Accessed September the 10th 2019 | Commercial | Linux, Windows, Mac. |
| 102. | pyDock/ pyDockSER | 2007 | University of Cambridge | United Kingdom | https://life.bsc.es/pid/pydock/details.html/ Accessed September the 10th 2019 | Academic | Web user interface |
| 103. | WinDock | 2007 | Howard University College of Medicine | USA | http://www.ivanyu.ca/#/windock/ Accessed September the 10th 2019 | Free | Microsoft Windows 32/64-bit |
| 104. | Spartan | 2007 | Wavefunction, Inc. | USA | https://www.wavefun.com/ Accessed September the 10th 2019 | Commercial | Mac, Linux, Windows |
| 105. | HyperChem | 2007 | Institute of Molecular Function | Japan | http://www.hyper.com/ Accessed September the 10th 2019 | Commercial | Windows 98, Windows XP |
| 106. | Bioclipse | 2007 | Uppsala University | Sweden | https://sourceforge.net/projects/bioclipse/files/bioclipse/ Accessed September the 10th 2019 | Free and open source | Java-based, |
| 107. | GMA | 2007 | Ludwig-Maximilians-University | Germany | http://www.chil2.de/Gma.html/ Accessed September the 10th 2019 | Freely available | --- |
| 108. | Balloon | 2007 | Åbo Akademi University | Finland | http://users.abo.fi/mivainio/balloon/ Accessed September the 10th 2019 | Free | Linux, Mac OS X, Microsoft Windows |
| 109. | Epik | 2007 | Schrödinger, LLC | USA | https://www.schrodinger.com/epik/ Accessed September the 10th 2019 | Commercial | Linux, Windows |
| 110. | FDS | 2008 | Indian Institute of Technology | Indian | http://www.scfbio-iitd.res.in/dock/fds.jsp/ Accessed | Academic | Web server online |

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| 111. | Rosetta Dock | 2008 | Johns Hopkins University | USA | https://www.rosettacommons.org/manuals/archive/rosetta3.4_user_guide/index.html/ Accessed September the 10th 2019 | Commercial | Linux v3 or greater, x86, 32-bit, GCC 4.0, Enterprise Linux v3 or greater, x86, 32-bit, Intel C++ 9.1, Microsoft Windows XP, 32-bit, GCC 3.4 |
| 112. | Lead finder | 2008 | Mol Tech | Canada | http://moltech.ru/ Accessed September the 10th 2019 | Commercial | Windows 32-bit and Linux 32/64-bit |
| 113. | MS-DOCK | 2008 | INSERM, University Paris Descartes | France | http://dock.compbio.ucsf.edu/ Accessed September the 10th 2019 and http://dock.compbio.ucsf.edu/Contributed_Code/multiconfdock.htm/ Accessed September the 10th 2019 | Academic | Linux / MAC OS X |
| 114. | HomDock | 2008 | Chil² - Molecular Design for Science and Technology | Germany | http://www.chil2.de/HomDock.html / Accessed September the 10th 2019 | Freely available | --- |
| 115. | ISE-Dock | 2008 | Hebrew University of Jerusalem | Israel | http://www.academia.edu/35901164/Iterative_Stochastic_Elimination_for_Solving_Complex_Combinatorial_Problems_in_Drug_Discovery/ Accessed September the 10th 2019 | Not available | --- |
| 116. | ASEDock | 2008 | MOLSIS Inc. | Japan | https://www.molsis.co.jp/wp-content/themes/molsis/images/ccg/support/svl/2016.08/asedock/asedock.html/ Accessed September the 10th 2019 | Not available | --- |
| 117. | OSDD | 2008 | CSIR | India | http://crdd.osdd.net/osddlinux1/chemoresource.php/ Accessed September the 10th2019 | Open Source | Web server online |
| 118. | PEPSI-Dock/ NANO-D | 2008 | NANO-D – INRIA Grenoble – Rhône-Alpes | France | http://www.samson-connect.net/ and https://team.inria.fr/nano-d/ Accessed September the 10th 2019 | Free | Linux, Windows, Mac. |
| 119. | Q-Dock | 2008 | Georgia Institute of Technology | USA | http://cssb.biology.gatech.edu/skolnick/files/Q-Dock/index.html/ Accessed September the 10th 2019 | Freeware | DOS |
| 120. | PharmaGist | 2008 | Tel Aviv University | Israel | http://bioinfo3d.cs.tau.ac.il/PharmaGist/ Accessed September the 10th 2019 | Freely | Online web server |
| 121. | DOVIS | 2008 | Biotechnology High Performance Computing Software Applications Institute (BHSAI) | USA | http://bhsai.org/software/ Accessed September the 10th 2019 | Freely | Linux |
| 122. | Align-it™ | 2008 | Silicos NV | Belgium | http://silicos-it.be.s3-website-eu-west-1.amazonaws.com/software/align-it/1.0.4/align-it.html/ Accessed September the 10th 2019 | Free | Command-line |
| 123. | DOCK Blaster | 2009 | University of California San Francisco | USA | http://blaster.docking.org/ Accessed September the 10th 2019 | Free | web online server |
| 124. | Docking Server | 2009 | Virtua Drug Ltd | Hungary | https://www.dockingserver.com/web/ Accessed September the 10th 2019 | Commercial | web online server |
| 125. | Catalyst | 2009 | BIOVIA | USA | http://accelrys.com/products/collaborative-science/biovia-discovery-studio/pharmacophore-and-ligand-based-design.html/ Accessed September the 10th 2019 | Commercial | web online server |
| 126. | FINDSITE-LHM | 2009 | Stanford University | USA | http://www.mybiosoftware.com/fin | Free | Linux |

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| | | | | | dsite-lhm-1-0-homology-modeling-approach-flexible-ligand-docking.html/ Accessed September the 10th 2019 | | |
| 127. | PLATINUM | 2009 | Russian Academy of Sciences | Russia | https://model.nmr.ru/platinum/ Accessed September the 10th 2019 | Freeware | Web online server |
| 128. | VSDMIP | 2009 | (CBMSO) Centro De Biología Molecular Severo Ochoa | Spain | https://ub.cbm.uam.es/software/vsdmip/ Accessed September the 10th 2019 | Free | Debian 6.0, Windows (32 bits), Scientific Linux 6.0 |
| 129. | wwLigCSRre | 2009 | Université Paris Diderot - Paris 7 | France | http://bioserv.rpbs.univ-paris-diderot.fr/services/wwLigCSRre/ Accessed September the 10th 2019 | Free | Web online server |
| 130. | ShaEP | 2009 | Abo Akademi University | Finland | http://users.abo.fi/mivainio/shaep/ Accessed September the 10th 2019 | Free | Linux, Windows, Mac. |
| 131. | fpocket | 2009 | University of Orléans | France | http://fpocket.sourceforge.net/ Accessed September the 10th2019 | Free | Online server tools |
| 132. | AutoDock Vina | 2010 | Scripps Research | United States | http://vina.scripps.edu/download.html/ Accessed September the 10th 2019 | Open source | Unix/Linux, Mac OS, Windows |
| 133. | VLifeMDS | 2010 | VLife Sciences Technologies Pvt. Ltd. | India | http://www.vlifesciences.com/products/Functional_products/VLifeDock.php/ Accessed September the 10th 2019 | Commercial | Linux and Windows |
| 134. | ParaDockS | 2010 | Martin-Luther-University Halle-Wittenberg | Germany | http://bioinfo3d.cs.tau.ac.il/ParaDock/ Accessed September the 10th 2019 | Open source | Web server online |
| 135. | GriDock | 2010 | Universita degli Studi di Milano | Italy | http://nova.disfarm.unimi.it/cms/index.php?Software_projects:GriDock/ Accessed September the 10th 2019 | Open source | Windows 32/64 bit, Linux 32/64 bit |
| 136. | DockoMatic | 2010 | Boise State University | USA | https://dockomatic.soft112.com/ Accessed September the 10th 2019 | Free | Window XP/Vista, Window7 x64, Window7 x32 |
| 137. | BioDrugScreen | 2010 | Indiana University School of Medicin | USA | http://www.biodrugscreen.org/ Accessed September the 10th 2019 | Commercial | Database |
| 138. | PharmMapper | 2010 | Chinese Academy of Sciences | China | http://lilab.ecust.edu.cn/pharmmapper/ Accessed September the 10th 2019 | Academic | web-based tool |
| 139. | Phenix | 2010 | Lawrence Berkeley Laboratory | USA | https://www.phenix-online.org/ Accessed September the 10th 2019 | Commercial | Linux, Mac |
| 140. | MOLA | 2010 | CIMO-ESA | Portugal | http://esa.ipb.pt/biochemcore/index.php/ds/m/ Accessed September the 10th 2019 | Free | Linux, Mac |
| 141. | NNScore | 2010 | University of California San Diego | USA | http://rocce-vm0.ucsd.edu/data/sw/hosted/nnscore/ Accessed September the 10th 2019 | Free | Ubuntu 10.04.1 LTS, Mac OS X 10.6.8, Windows XP Professional |
| 142. | Mol Sign | 2010 | VLife Sciences Technologies Pvt. Ltd. | India | http://www.vlifesciences.com/products/Functional_products/Molsign.php/ Accessed September the 10th 2019 | Commercial | Linux and Windows |
| 143. | ISIDA | 2010 | Université de Strasbourg-CNRS | France | http://infochim.u-strasbg.fr/ Accessed September the 10th 2019 | Freely available | Linux 64 bits, Windows 64 bits, MacOSX 64 bits |
| 144. | AADS | 2011 | Indian Institute of Technology | India | http://www.scfbio-iitd.res.in/dock/ActiveSite_new.jsp/ Accessed September the 10th 2019 | Free | Web server online |

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| 145. | BetaDock | 2011 | Voronoi Diagram Research Center, Hanyang University | South Korea | http://voronoi.hanyang.ac.kr/software.htm#BetaDock/ Accessed September the 10th 2019 | Freeware | Linux 64bit |
| 146. | iScreen | 2011 | China Medical University | Taiwan | http://iscreen.cmu.edu.tw/intro.php/ Accessed September the 10th 2019 | Freeware | Web-server |
| 147. | LigDockCSA | 2011 | Seoul National University | South Korea | https://chem.snu.ac.kr/eng/about/overview.asp/ Accessed September the 10th 2019 | Academic | Linux, MAC OS X |
| 148. | PythDock | 2011 | Hanyang University | South Korea | http://jhah.hanyang.ac.kr/front/publications?lang=us/ Accessed September the 10th 2019 | Academic | Windows, Linux/Unix, Mac OS X |
| 149. | SwissDock | 2011 | Swiss Institute of Bioinformatics | Switzerland | http://www.swissdock.ch/ Accessed September the 10th 2019 | Free for academic use | Online web Server |
| 150. | VoteDock | 2011 | University of Warsaw | Poland | http://business2science.com/sysbio/Systems_Biology/Welcome.html/ Accessed September the 10th 2019 | Academic | Mac OS X |
| 151. | Rosetta FlexPepDock | 2011 | The Hebrew University | Israel | http://flexpepdock.furmanlab.cs.huji.ac.il/ Accessed September the 10th 2019 | Free | Web server online |
| 152. | Pose & Rank | 2011 | University of California | USA | https://modbase.compbio.ucsf.edu/poseandrank/ Accessed September the 10th 2019 | Free | Web server online |
| 153. | Pharmer/ ZINC Pharmer | 2011 | University of Pittsburgh | USA | http://smoothdock.ccbb.pitt.edu/pharmer/ And https://sourceforge.net/projects/pharmer/ Accessed September the 10th 2019 | Free | Web server online |
| 154. | SHAFTS | 2011 | ECUST (East China University of Science and Technology) | China | http://lilab.ecust.edu.cn/chemmapper/help.html/ Accessed September the 10th 2019 | Open resource | Web Server |
| 155. | Open Babel | 2011 | University of Pittsburgh | USA | https://sourceforge.net/projects/openbabel/files/openbabel/2.4.1/OpenBabel-2.4.1-x86.exe/download/ Accessed September the 10th 2019 | Free and open source software | Windows, macOS, Linux, Android |
| 156. | Open3DALIGN | 2011 | University of Turin | Italy | http://open3dalign.sourceforge.net/?Home/ Accessed September the 10th 2019 | Open source software | Windows, Linux, Intel Mac OS X,Solaris x86, FreeBSD |
| 157. | pep:MMs:MIMIC | 2011 | CRS4-Bioinformatics Laboratory | Italy | http://mms.dsfarm.unipd.it/pepMMsMIMIC/index.php/ Accessed September the 10th 2019 | Free | online web server |
| 158. | PaDEL-Descriptor | 2011 | National University of Singapore | Singapore | http://www.yapcwsoft.com/dd/padeldescriptor/ Accessed September the 10th 2019 | Free | Windows Vista /7 |
| 159. | AquaSAXS | 2011 | Institut Pasteur | France | http://lorentz.dynstr.pasteur.fr/suny/index.php?id0=aquasaxs#welcome/ Accessed September the 10th 2019 | Open | ---- |
| 160. | MDpocket | 2011 | Universitat de Barcelona | Spain | http://bioserv.rpbs.univ-paris-diderot.fr/services/fpocket/mdpocket_online.html AND https://omictools.com/mdpocket-tool/ Accessed September the 10th 2019 | Free and open source | Command Line |
| 161. | GPCR automodel | 2012 | INRA | France | http://genome.jouy.inra.fr/GPCRautomdl/cgi-bin/welcome.pl/ Accessed September the 10th 2019 | Free for academic use | web server online |
| 162. | FINDSITEX | 2012 | Center For The Study of Systems Biology | USA | http://pwp.gatech.edu/cssb/new-human-gpcr-modeling-and-virtual-screening-database/ Accessed September the 10th 2019 | Freely available to academic users | Web service |
| 163. | GalaxyDock | 2012 | Seoul National University | South Korea | http://galaxy.seoklab.org/ Accessed September the 10th 2019 | Freely | Linux, MAC OS X |
| 164. | idTarget | 2012 | National Taiwan University | Taiwan | http://idtarget.rcas.sinica.edu.tw/ Accessed September the 10th 2019 | Freeware | Web server online |
| 165. | 1-Click Docking Mcule | 2012 | Mcule, Inc. | United States | https://mcule.com/apps/1-click-docking/ Accessed September the 10th 2019 | Free | Online services |

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| 166. | SCIGRESS | 2012 | Fujitsu Limited | Poland | http://www.fqs.pl/en/chemistry/products/scigress | Free and commercial | Windows - 7, 8 and 10 - 64 bit, Linux - Ubuntu, Red Hat, Centos - 64 bit, Mac OS - OS X 10.9, OpenGL accelerated graphics hardware. |
| 167. | COPICAT | 2012 | Keio University | Japan | https://www.dna.bio.keio.ac.jp/ Accessed September the 10th 2019 | Freely | web service |
| 168. | DecoyFinder | 2012 | Universitat Rovira i Virgili | Spain | http://urvnutrigenomica-ctns.github.io/DecoyFinder/ And https://github.com/URVnutrigenomica-CTNS/DecoyFinder/ Accessed September the 10th 2019 | Free | Windows, Ubuntu 12.04, Linux |
| 169. | Auto ClickChem | 2012 | University of California San Diego | USA | http://nbcr-222.ucsd.edu/autoclickchem/download.php/ Accessed September the 10th 2019 | Free | Online web service |
| 170. | Anchor Query | 2012 | University of Pittsburgh, Pittsburgh | USA | http://anchorquery.ccbb.pitt.edu/ Accessed September the 10th 2019 | Free | Online web service |
| 171. | Vina MPI | 2013 | University of Tennessee | USA | http://www.virtualdocking.com/ Accessed September the 10th 2019 | Free | Common Language Infrastructure, Java, MATLAB, OCaml, Python, R based |
| 172. | FINDSITEcomb | 2013 | Center for the Study of Systems Biology, School of Biology, Georgia Institute of Technology | USA | http://pwp.gatech.edu/cssb/findsite-comb/ Accessed September the 10th 2019 | Freely | Online web server |
| 173. | Sirius | 2013 | Friedrich-Schiller-Universität Jena | Germany | http://www.sdsc.edu/ Accessed September the 10th 2019 | Freeware | Windows, Linux, mac OS |
| 174. | rDock | 2014 | Vernalis Research and University of York | UK | http://rdock.sourceforge.net/ Accessed September the 10th 2019 | Open source | All Linux |
| 175. | MAPS | 2014 | Scienomics SARL | France | http://www.scienomics.com/ Accessed September the 10th 2019 | Commercial | Graphical User Interfaces |
| 176. | Q-Chem | 2014 | University of South Carolina | USA | http://www.q-chem.com/ Accessed September the 10th 2019 | Free open source | Mac OS X, Windows, Linux. |
| 177. | CABS-dock | 2015 | University of Warsaw | Poland | http://biocomp.chem.uw.edu.pl/CABSdock/ Accessed September the 10th 2019 | Freeware for academic use | Online web service |
| 178. | FlexAID | 2015 | University of Sherbrooke | Canada | http://biophys.umontreal.ca/nrg/NRG/FlexAID.html | Open source | Unix/Linux, Mac OS, Windows |
| 179. | DOLINA | 2015 | University of Basel | Switzerland | https://modeling.unibas.ch/ Accessed September the 10th 2019 | Academic | --- |
| 180. | PyRx | 2015 | The Scripps Research Institute | USA | https://pyrx.sourceforge.io/ Accessed September the 10th 2019 | Commercial | Windows, Linux and Mac OS X. |
| 181. | Aggregator Advisor | 2015 | University of California | USA | http://advisor.bkslab.org/search/ Accessed September the 10th 2019 | Free | Online web server |
| 182. | MOLS 2.0 | 2016 | University of Madras | India | https://mole.upol.cz/ Accessed September the 10th 2019 | Open Source | Online web server |
| 183. | ADMET Predictor | 2016 | Simulations Plus, Inc. | USA | https://www.simulations-plus.com/software/admetpredictor/ Accessed September the 10th 2019 | Commercial | Unix/Linux Mac OS, , |

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| 184. | MOLGEN | 2016 | University of Bayreuth, Bayreuth, | Germany | http://molgen.de/online.html/ Accessed September the 10th 2019 | Free | Windows 7+ and online web server |
| 185. | MOE | 2018 | Chemical Computing Group | Canada | https://www.chemcomp.com/MOE-Molecular_Operating_Environment.htm/ Accessed September the 10th 2019 | Commercial | Windows, Linux and Mac |
| 186. | Tinker | 2018 | Washington University | USA | https://dasher.wustl.edu/tinker/ Accessed September the 10th 2019 | Freeware | Windows, MAC OS X, Linux, Unix |
| 187. | LigPrep | 2018 | Schrödinger, LLC | USA | https://www.schrodinger.com/ligprep/ Accessed September the 10th 2019 | Commercial | Unix/Linux, Mac OS, Windows |
| 188. | Pse-in-One | 2015 | Liu Lab, Harbin Institute Of Technology | China | http://bioinformatics.hitsz.edu.cn/Pse-in-One/ Accessed September the 10th 2019 | Freeware | Windows, Linux, Unix, Mac OS |
| 189. | ChemAxon | 1998 | Chem Axon | USA | https://chemaxon.com/ Accessed September the 10th 2019 | Freeware for academic use | Windows, Linux, Mac OS |

DOCK software tools can be used for scoring functions like screening, docking, algorithms process determined by Incremental extension, and force field technique. DOCK software tools are used for many features like binding modes prediction protein complexes, search databases of ligands, search databases of bind protein-ligands, check protein-protein, and protein-DNA complexes [10]. AMBER program is used for molecular graphics with protein-ligand complexes in a force field calculation. This program can also be used for other calculations like Molecular model building, Force Fields, Geometry optimization, Molecular dynamics, Hybrid Monte Carlo [11]. Chem Office package is developed by PerkinElmer used for Chemical structure draw, Chemical IUPAC name to structure exchange, NMR spectrum replication, Mass spectrum replication, Structure tidying, an extensive collection of templates, 2-D to 3-D Structure conversion, many international journal style template draw the chemical structure [12]. Winmostar is different software packages tools used for visualization, systematic skill calculation, GPGPU (General-purpose computing on graphics processing units) conversion, data analysis, simulation, machine learning. It is different tools used for the Solubility parameter calculation module used for the Hansen solubility parameter can be calculated and QM-MD calculation method [13]. AutoDock is a beneficial docking software where the docking score of known 3D structure with target protein can be obtained in terms of affinity. This docking score gives facts regarding how the fixing of a new molecule is attaching with an active site of the target. This can give the predictive activity of a molecule before actual synthesis, so time, cost, and recourses can be easily saved. The AutoDock has engrossed its application in X-ray crystallography, structure-based drug design, lead optimization, virtual screening (HTS), combinatorial library design, protein-protein docking, chemical mechanism studies [14]. Another online web program named FANTOM (Fast Newton-Raphson Torsion Angle Minimizer) is utilized for molecular modeling to calculate low-energy conformations of polypeptides and proteins, distance and dihedral angle constraints which are based on energy minimizations, Protein-solvent interaction and Monte Carlo simulations of an empirical energy function. Protein-solvent interaction is calculated by the GETAREA technique and the GETAREA technique accessed by a stand-alone program [15]. "Soft docking" is a new technique for molecular identification for docking. "Soft docking" includes minor conformational changes like charge-charge interaction, hydrogen bonding, van der Waals' interaction, size, and shape of surfaces these all phenomena used and represent surface cubes technique. The cubes technique is used for easily protein-ligand interaction detection [16]. Hint software tools are used for de novo drug design, molecular modelling and nucleic acid or else protein structural analysis. The hint software tools are other important features of protein-ligand calculation like partition coefficient, 3D QSAR calculation, hydrophobicity, and 3D hydropathy fields calculate estimates LogP for modelled molecules or statistics files. Graphically and numerically evaluates, evaluates mutagenesis on protein structure stability [17]. DockVision software tool searches scoring functions screening docking algorithms process determine by simulated annealing genetic algorithm and force field technique. DockVision software tool includes mother features like easy-to-use, flow-chart based Graphical User Interface, RSDB (ReSearch DataBase) docking algorithm, cluster analysis, automated molecular parameter assignment, automated topology and ligand conformer generation, Real-Time analysis tools, DockCam 3D viewer tools [18]. IMMD (Institute of Medicinal Molecular Design) is a rational drug discovery method using a proprietary software system for rational drug design. IMMD`s software program like KeyRecep, ADAM, Bluto, LEGEND, Key3D, Pdbfil, ProSide [19]. ADAPT software is used to calculate molecular descriptor for chemical structure. These molecular descriptors are used for structure-activity relationships [20]. PROCHECK software is used for protein structure for checking the stereochemical quality. The PROCHECK software programs give a complete check on the stereochemistry of a protein structure by NMR spectroscopy [21]. Naccess program is used for calculations of atomic macromolecule the Van der Waal's surface and diagrams of protein-ligand interactions. Two

programs are available for the Biomolecular Structure and Modelling Units like HBPLUS and LIGPLOT. HBPLUS is used to calculate hydrogen bonds, hydrogen atom positions and can suggest optimal conformations for asparagine, Glycine and Histidine side chains. LIGPLOT used for schematic diagrams of protein-ligand interactions [22]. The ICM Suite of Software tools is used for many features like protein-ligand analysis, visualization, sequences of protein, binding sites analysis, molecular modelling, flexible protein-ligand docking, virtual ligand screening, chemical similarity searching, chemical clustering. ICM-Dock program search methods and scoring functions determined by simulated annealing and force field technique [23]. ADAM software tools search methods and scoring functions determined by Incremental extension and Empirical technique. ADAM docking process is based on high-throughput virtual screening method and also working on QSAR study and analysis of protein-ligand interaction which plays an important role in discovery and design for new drug [24]. FLOG (flexible ligand oriented on a grid) software tool searches methods and scoring functions determined by Incremental extension and Empirical technique. FLOG is used for Rigid-body docking software using databases [25, 204]. Corina (Centre for Molecular and Biomolecular Informatics) is software tool used for a 3D structure generator for small to medium-sized, typically drug-like molecules, robustness, comprehensiveness, speed and performance structure clean-up, Three-Dimensional Model Builders Using 639 X-ray Structures, convert 2D into 3D chemical structure, and standardization methods, large chemical datasets [26]. DIVALI (Docking with evolutionary algorithms) software is a flexible and rigid ligand-receptor binding mode search. This software is working based on AMBER and GA (genetic algorithm) technique [27]. The GOLD Suite software tools used for Hermes for 3D visualisation pre- and post-docking, interactive docking setup, protein-ligand docking, GoldMine for post-processing of docking results [28]. Shape-it™ is a program that aligns a reference molecule against a set of database molecules using best scoring molecules for drug design. Shape-it™ is a program based on Gaussian volumes as a descriptor for molecular shape [29]. RasMol is a molecular graphics program used for the visualisation display, teaching and high-quality images of proteins, nucleic acids ligand. Operating systems are working in a program like Microsoft Windows, Apple Macintosh, UNIX and VMS systems. It should be ‘RasMol represents depth-cued wireframes, 'Dreading' sticks, space-filling (CPK) spheres, ball and stick, solid and protein strand ribbons, atom labels, and surfaces [30]. GROMACS (Groningen Machine for Chemical Simulations) program is used to perform molecular bonded interactions at calculating the non bonded interactions for proteins, lipids, and nucleic acids [31]. The hammerhead software tool is used for fast fragment-based drug design for flexible protein-ligands binding site scoring function [32]. Molecular shape and chemical nature of the atoms of the interacting molecules identify by ligin docking tool [33]. GASP (genetic algorithm similarity program) is a software tool used for genetic model analysis by statistical parameter [34]. VMD is a graphical front end for an external molecular dynamics program designed for modelling displaying, animating, visualization, and analysis of proteins, nucleic acids, lipid bilayer and molecular dynamics (MD) simulation [35]. PROMOTIF is software programs used for proteins structure analysis like Secondary structure, Disulphide bridges, Beta turns, Gamma turns, helical geometry, Helical interactions, Main-chain hydrogen bonding patterns [36]. The DSSP program is used to standardize protein secondary structure. It does not predict the secondary structure [37]. OpenEye Scientific Software tools are used for lead discovery, lead optimization, customization, cheminformatics and molecular modelling. Similar to OpenEye Scientific Software tools are available such as AFITT (Automatic Ligand Fitting to Crystallographic Density), BROOD (Fragment Replacement and Molecular Design), EON (Electrostatic Similarity for Lead-hopping), FILTER (Compound Property Calculation & Removal of Undesirables), OEDocking (Molecular Docking Tools and Workflows for Protein-ligand Interaction), OMEGA (Conformer Ensembles Containing Bioactive Conformations), pKa Prospector (Providing Protonation Insights for Novel Molecules), QUACPAC (Tautomer/Protomer Enumeration & Charge Assignment), ROCS (Shape Similarity for Virtual Screening & Lead Hopping), SZMAP/GamePlan (Water…Where it Matters, When it Matters), SZYBKI/FreeForm (Molecular Structure Optimization in situ with MMFF94), VIDA (Visualization & Communication of Modelling Results)[38]. FTDock docking programmes search methods and scoring functions determined by force field and rigid-body docking technique. FTDock(Fourier Transform Dock ) is a Katchalski-Katzir algorithm based on working software. Katchalski-Katzir is an electrostatics function amenable to the Fourier correlation that was developed in this laboratory. FTDock yield multiple calculations that can be monitor using biochemical information [39]. QXP programmes search methods and scoring functions determined by Monte Carlo perturbation, simulated annealing and force field techniques, some other techniques like for docking template appropriate and construction pseudo-receptors [40]. SANDOCK is three-dimensional database docking programme. SANDOCK docking program is working on the force field and rigid-body docking way [41]. GETAREA is an online software its calculation solvent accessible surface area. This value used in the FANTOM program [42]. The QUASI software tools extend and implement techniques for combined QM/MM (quantum mechanics/molecular mechanics) simulations on a variety of High-Performance Computing (HPC) platforms. These techniques help for QSAR based on receptor modelling [43]. Molecular modelling program The BOSS software is based on molecular mechanics (MM) calculations, Metropolis MC (Monte Carlo) statistical mechanics simulations, and semi-empirical (like AM1, PM3, and PDDG/PM3) QM (quantum mechanics) calculations. The Monte Carlo techniques are used for pure liquids, solutions, clusters, or gas-phase systems, free energies of solvation. [44]. MCDOCK (Monte Carlo dock) software is used for protein-ligand binding site Prediction, or flexibility protein-ligand molecular docking calculations. MCDOCK software is automatically working on a non-conventional MC (Monte Carlo) replication technique [45,205]. PRODOCK is a flexible

protein-ligand docking and protein medalling software. In protein Modelling this software is based on an atom with the AMBER IV or elseECEPP/3 geometry and force field calculation, depending on whether the ligand is a peptidic molecule or not. PRODOCK is an optimization of the energy function Monte Carlo method plus energy minimization and this method used for the docking process. PRODOCK is a new grid-based energy evaluation technique using Bezier splines [46]. LPC/CSU (Ligand-Protein Contacts/Contacts of Structural Units) software Tools are used for protein-ligand interaction calculation. LPC software tool is based on an analysis of interatomic contacts and interface complementarities. Such calculation like calculating the solvent-accessible surface of every atom, determining the contacting residues like hydrophobic-hydrophobic, aromatic-aromatic interaction, indicating all putative hydrogen bonds [47]. CATS (The Chemically Advanced Template Search) software is used for determining the distance between the pharmacophore fingerprints and the "topological pharmacophore" searching technique [48]. FlexX is a virtual screening and docking binding mode prediction application. FlexX sets new records in vHTS screening compounds advantage of a novel pharmacophore-based combinatorial docking. FlexX software is in key features such as pharmacophore constraints for guided docking, fast docking of combinatorial libraries, flexible protein docking [49]. Combinatorial library design is an online web server to make a combinatorial library of molecules. Combinatorial library design working based on fragments as user R-groups to connect a user-defined scaffold [50]. DARwin(Dissimilarity Analysis and Representation) is docking calculations with proteins- ligand interaction. DARWIN program is working based on the Genetic Algorithm for optimization of the molecule's conformation and orientation, which is under the selective pressure of minimizing the potential energy of the complex and a new based on CHARMM mechanics [51]. MPACK software tools are used for homology modeling new modeling methods those ab initio (to build three-dimensional protein models) modeling procedures. Homology modeling packages MPACK is working similar to PCPmer to identify conserved regions, EXDIS to extract angle and distance constraints, DIAMOD to generate protein models from geometric constraints. [52]. Filter-it™ is a program for filtering of molecules with unwanted properties and rapid calculation of molecular properties and Physicochemical parameters, such as logP, topological polar surface area criteria, number of hydrogen bond acceptors and donors, and Lipinski's rule-of-five, Graph-based properties, including ring-based parameters and rotatable bond criteria, Selection criteria through smarts patterns, Similarity criteria, Three-dimensional distances between user-definable fragments [53]. FTrees-FS is software used for combinatorial fragment space extension module, lead finding, HTS analysis, general virtual screening applications. FTrees-FS is the fragment assembling use of the search/comparison/screening of combinatorial libraries or any fragment-generating procedure [54]. Ascalaph is a computer program used for molecular modelling based on quantum mechanics calculations, molecular dynamics and mechanics simulations in the gas or solid stage molecules [55]. MOLARIS-XG is software program packages used for proteins simulating and other functions like catalytic power, folding energy, redox properties, drug binding, pKa's, conformational transition, ion transfer, and optical properties, as well as QM/MM capacity. The software working is based on the protein-ligand complex to using the Empirical Valence Bond and the Free Energy Perturbation) method [56]. Moreover, A library-based molecular docking software SEED (Solvation Energy for Exhaustive Docking) is working on the solvation energy evaluation base using determination by optimal positions and orientations of small-to-medium-sized molecular fragments in the binding site of a rigid protein and protein-ligand binding energy levels [57-58]. FFLD (Fragment-Based Flexible Ligand Docking) software is a used for solvation term in scoring function, coulombic term in scoring function, flexible protein binding site residues, typing flexSwarm docking, monte Carlo based optimization [59]. The evaluation of the EUDOC program was from the standpoints of the force field and sampling issues using 154 experimentally determined ligand-receptor complexes and four "real-life" applications. This EUDOC program's key principle is based on structural water molecules in the active site and different atomic charge models on docking results [60]. PocketMol is used for molecular visualization programs and manipulates molecular structures [61]. Qmol is a Windows-based molecular visualization program designed for viewing, simulations, theoretical calculations of peptides and small molecules [62].YASARA View/Model/Dynamics uses Autodock and Fleksy. YASARA software features are like molecular graphics, modelling and analysis, plus advanced molecular modelling, Dynamics, prediction validation and docking molecular structure, NMR module for structure [63]. PyMOL is a free software used for molecular graphics packages system. PyMOL is based on computer language C or Fortran [64]. SDAP (Structural Database of Allergenic Proteins) is a Web server that integrates a database of allergenic proteins with various computational tools used for a study about the sequence and structural determinants of allergenicity, allergens motifs, and database mining for the identification of potential allergens [65]. FDS software can be used for flexible ligand and receptor docking with a continuum solvent model and soft-core energy function [66]. HADDOCK (High Ambiguity Driven dock) software is used for molecular modelling and docking approach of protein-protein, protein-nucleic acids and protein-ligand complexes. HADDOCK software works on ab-initio docking methods and AIRs (ambiguous interaction restraints). Ab-initio docking methods is used for encoding and predicting the information of protein interfaces and AIRs method used for the docking process [67]. LigandFit software is used for Structure-Based Design. LigandFit software is working based on ligand conformations generated by Monte-Carlo method and docking based on active shape and size of molecules. These are active shape and site on working other technique like CHARMm minimization. CHARMm is a molecular dynamics technique [68]. Surflex software is for computational drug design. Surflex software is features of molecular docking, molecular similarity, off-target prediction, and binding affinity prediction. Surflex software is working based on a couple of

physical realism in modelling, protein-ligand interactions with algorithms for rapid optimization of conformation and alignment of ligand [69]. Tuplets are a program used for searching pharmacophore, lead hopping capabilities, virtual combinatorial libraries [70]. CDK (Chemistry Development Kit) java-based open-source software is used to calculations molecular descriptor for chemical structure. These molecular descriptors are used for structure-activity relationships and QSAR descriptor calculations [71]. SageMD is a computer program used for the molecular dynamics simulation, molecular visualization tool, graphs and tools and GUI (Graphical User Interface). SageMD is used for some calculation like to study the behaviour of the crystal lattice, calculate RDF (Radial Distribution Function), modelling the properties of materials with covalent chemical bonds, quantum chemical programs such as GAUSSIAN and ABINIT [72]. GEMDOCK software tool is a generic evolutionary method and scoring function used for molecular docking. GEMDOCK software tool works based on an empirical scoring function like AMBER-based energy function and generic evolutionary method based on a new rotamer-based mutation operator to reduce the search space of ligand structure conformations [73]. Virtual screening by highly successful Glide Schrödinger software, it is work on structure drug discovery and lead optimization. Docking software Glide Schrödinger does the docking process by a great library of compounds into one or more high-resolution structures of the target receptor and predicts lead optimization past identifying small molecules likely to bind well to a protein target and docking process such as polypeptide and macrocycle pose prediction, predicting protein-ligand complex geometries, and preparing congeneric series for binding affinity prediction with methods based on Free Energy Perturbation or MM-GBSA. Glide Schrödinger software tools are OPLS34 (Glide SP & XP) or OPLS2005 (GLIDE HTVS) with a distance-dependent dielectric model. PDM (post-docking minimization) technique used for small poses identification of flexibility receptor-ligand interaction [74]. ArgusLab is a molecular modelling, molecular graphics, and drug design software. ArgusLab docking software is freely licensed [75]. JOELib is an open-source Java-based software library used for Cheminformatics, molecular modelling [76]. VEGA online program is for the development of using a multipurpose graphical environment for molecular docking calculation and graphical image. VEGA online tools are like VEGA WE, MolEdit, ProBuilder Virtual logP, Score, PropKa, Picture gallery. Hear VEGA WE used for File translation tool, properties and surface calculation. MolEdit used for 2D molecular editor & structure optimization. ProBuilder used for Protein/peptide builder from 1D to 3D. Virtual logP used for Bernard Testa's calculator for Scoring, and that score can be used for molecular docking. Prop Ka used for Protein pKa calculation. Picture gallery used for VEGA graphical images [77].UCSF Chimera is a software free of charge for academic, government, non-profit, and personal use for interactive visualization and analysis of molecular structures, including density maps, supramolecular assemblies, sequence alignments, docking results, trajectories, and conformational ensembles, High-quality images and animations. Chimera includes documentation and several tutorials and can be downloaded. Chimera is developed by the Resource for Biocomputing, RBVI (Visualization, and Informatics) , supported in part by the National Institutes of Health (P41-GM103311) [78]. SuperPose is a web online server for protein superpositions which uses a modified approach of two or more structures, structure alignments, sequence alignments, RMSD statistics, PDB coordinates, Difference Distance Plots, and interactive images of proteins [79]. SRS 3D is a software tool used for integrating structures, sequences and features [80]. MEDock a Maximum-Entropy based docking web online server. MEDock is used for drug design and discovery. MEDock is working on a genetic algorithm and given a threshold for several energy evaluations in the docking imitation [81]. PatchDock is a web online server docking process. Patchdock is working based on three algorithms like Molecular Shape Representation, Surface Patch Matching, Filtering and Scoring. Molecular Shape Representation means the surface of the molecule apply a segmentation algorithm for detection of geometric patches (concave, convex and flat surface pieces). The isolated patches with 'hot spot' residues are retained. Surface Patch Matching means a hybrid of the Geometric Hashing and Pose-Clustering matching techniques, Concave patches are matched with convex and flat patches with any type of patches. Filtering and Scoring means the candidate complexes are a geometric shape complementarily scores. SymmDock is an Algorithm for guass of Complexes with Cn Symmetry [82]. LigandScout software tools are used for designing, 3D pharmacophore modelling, virtual screening and filtering. LigandScout is available in three different tools like LigandScout Essential, LigandScout Advanced, and LigandScout by Inte: Ligand LigandScout Knime [83]. e-LEA3D is an online web server used for computer-aided drug design based on molecular fragments by docking scoring function [84-85]. The FoldX is an online web server used force field for protein-ligand interaction. The FoldX new features available like LoopX (loop reconstruction) and PepX (peptide docking) [86]. Visualizer DS software tools help in viewing, sharing, sequencing and analyzing protein 3D molecular structures. Also with predicting other features of molecular surface properties like H-bonds, Charge, Ionizability, Lipophilicity, Aromaticity and Solvent Accessibility addition and removal [87]. AURAmol is a web online server used for 2D or 3D molecular shape, search for similarly shaped molecules in large databases. These databases are working on the server to supercomputers [88-89]. PowerMV is software used for an environment for statistical analysis, molecular viewing, descriptor generation and calculation of molecular structure [90]. PLANTS software is used for docking study which is working on lead optimization and virtual screening and the latest version of this software is ant colony optimization (ACO). PLANTS software has other features like ACO-based search engine, two scoring functions (PLANTSCHEMPLP and PLANTSPLP), flexible protein side-chains, rigid-body docking of multi conformer libraries into rigid and flexible receptors, constraint system, docking with selected explicit, displaceable water molecules, fully automatic ligand setup, virtual screening, rescoring capability [91]. PSI (Pose-Sensitive Inclined) DOCK is an improved method for flexible

ligand docking score by SCORE function method. SCORE technique is working based on binding free energy evaluation, ligand binding pose exploration. An updated PSI method is a tabu-enhanced genetic algorithm with a rapid shape-complementary scoring function [92]. DAIM (Decomposition and Identification of Molecule) is a library-based molecular docking software. DAIM is capable of identifying the molecule fragments and filtering fragment-based drug designing. These are databases working on rotatable bond counts, donors/acceptors [93]. kinDOCK/@TOME (@utomatic Threading Optimization Modeling and Evaluation) is an online webserver to molecular docking and drug design program. @TOME program contains features like fold recognition, protein-ligand modelling and comparative docking or virtual screening, template selection, structural alignment editing, structure comparisons, 3D-model construction and evaluation [94]. CoLiBRI (Complimentary Ligands Based on Receptor Information) software tool is used for the structure-based drug design approach. CoLiBRI works on receptor and drug binding sites of special chemical descriptors interaction means of a geometry technique known as Delaunay tessellation by X-ray characterized from ligand-receptor complexes [95].Molegro Virtual Docker software tools are protein-ligand interactions scoring function based on a hybrid search algorithm with a force-field. MolDock software tools are working on the assignation of charges and protonation states, protein-ligand interactions cavities. Molegro Virtual Docker software tools indicate the features like 3D molecular graphics, Interactive model building, Quantum chemistry for small molecules, Force Field development, Biomicro molecular dynamic simulations, Free energy estimation [96].BDT Fortran computer language software tool is available free to use for a graphic front-end. This program helps to make grids, combine grids, make docks and analyze, and which is controlled by AutoGrid and AutoDock runs [97]. InterProSurf is an online web server used for Protein Data Bank search, to find interface residues in protein complexes of your interest, Predict interacting residues on a monomeric protein surface using patch analysis and cluster analysis [98]. GFscore is Tripos Inc. online web server based on the methodology of High Throughput Screening (HTS) by using the score in a Non-Linear Neural Network manner [99]. SiMMap is an online web server used for a site-moiety map represents in protein- drug docking process. SiMMap calculates specific physicochemical properties by binding pocket with conserved interacting residues, moiety preferences of the pocket, Pocket-moiety interaction type all seen by online [100].Dragon software is used to calculate molecular descriptor for chemical structure. These molecular descriptors are used for structure-activity relationships [101]. AFGen is a computer-based program used for Fragment-based Descriptors for Chemical Compounds. This tool calculates the graph-based properties of chemicals, paths (PF), acyclic subgraphs (AF), arbitrary topology subgraphs (GF) graph properties [102]. AquaSol program is used for calculating solvent density map into electrostatic interactions between the solute charges, the solvent charges and the solvent itself, treated as an assembly of orientable dipoles (Langevin dipoles) [103]. MODELLER is a free downloaded computer program used for Comparative protein structure modelling. MODELLER program is used for de novo modelling of loops in protein structures, searching databases, flexibility, clustering, sequence and comparison of protein structures [104]. ParDOCK is online services for calculating all-atom energy based Monte Carlo, rigid protein-ligand docking, the binding mode of the ligand in receptor target [105]. EADock is a new efficient DSS (dihedral space sampling) technique which forms new programEADock2. EADock2 is fast protein and drug-like ligands docking scoring function. DSS technique gives the best and most potent binding pose based on within 2 Å RMSD to the crystal structure [106]. FLIPDock is working on flexible forms of ligand and receptor for a molecular docking and scoring program. FLIPDock program is working on Python language. This program works on two bases like FlexTree data structures and a protein-ligand complex. The FlexTree technique is transformation matrices and regenerates the new conformations. Other features of FLIPDock uses a searching engine, such as a genetic algorithm, to optimize the motion variables and minimize the given scoring function based drug design [107].FITTED is docking software working on a genetic algorithm (GA) and it is fast. FITTED software is automated docking software which checks the presence of bridge "displaceable" water molecules in flexible forms of ligand and receptor, more so having new features of better accuracy with zinc metalloenzymes, displaceable water molecules, explicit water or particle water molecules, Side-chain protein flexibility, Highly predictive scoring function, Covalent inhibitor docking, Hybrid Matching algorithm / Genetic algorithm, Pharmacophore oriented docking, virtual screening for valid docking pose [108]. pso@autodock (Particle Swarm Optimization @autodock) software tool is used for quick flexible molecular docking. Particle Swarm Optimization new algorithms technology are suited for fast flexible molecular docking. pso@autodock software tool gives the smallest number of RMSD. So pso@autodock software tool is speedy flexible protein-peptide docking and virtual screening program [109]. SODOCK (swarm optimization dock) software tool is an optimization algorithm based on particle swarm optimization (PSO) for fast flexible molecular docking. SODOCK is improved and robust program than particle swarm optimization (PSO) [110]. eHiTS software is a fragment-based flexible docking. This software is validated by X-ray structures with high precision RMSD and VHTS (virtual high throughput scarring) techniques. eHiTS software gives precise docking score by using molecule torsional angles if steric constraints. This software helps in pocket detection on the protein surface and Automatic assignment of partial charges to atoms hydrogen protonation states considering all alternatives in a single docking [111]. Glam Dock is a fast virtual screening, high-quality docking and a de novo molecular design software tools. Glam Dock is working based on a Monte-Carlo minimization method and also searches hybrid interaction matching / internal coordinate search space [112]. Fleksy software is used for flexibility receptor-ligand molecule docking. Fleksy software is based on a backbone-dependent rotamer library and scoring functions determined by force field energies [113]. pyDock program is used for

protein-protein docking algorithm. pyDock is a working based on electrostatics force, desolvation energy, van der Waals calculations given a best rigid-body docking poses [114]. WinDock window base C++ computer language software is used for 3D libraries, homology modelling tools, and ligand-protein docking programs [115]. Spartan'18 is used for docking and simulation applications. Spartan Software's working is based on flexible molecules and to NMR spectra [116]. The HyperChem software tool is important for descriptor value calculation. HyperChem software tool does the unique molecular drawing system such as drawing structures, automatic 3D function of molecular formula, automatic protonation function, automatic force field parameter setting function, amino acid, nucleic acid, sugar, polymer, and crystal edit functions, RMS fitting and molecular overlay functions, conformation search function [117]. The Bioclipse is a Java-based software tool which is a free and open-source project, visual platform for chemo- and bioinformatics based on the Eclipse Rich Client Platform (RCP) for the life sciences and drug discovery [118]. GMA (Graph-based molecular alignment) is a method used for a combined 2D/3D approach for flexible chemical structures, which is based on a gradient-based torsion space optimization algorithm, which is helpful in computational technique [119]. A balloon is software used to create 3D atomic coordinates from molecular connectivity via distance geometry and conformer ensembles using a genetic algorithm. The software has been run by to Linux, Mac OS X, and Microsoft Windows platforms [120]. Epik is a Schrödinger software tool used for calculates structure or pKa value, Hammett, and Taft methods in conjunction with ionization and tautomerization tools [121]. The FDS (flexible Docking and Scoring) is online services for all-atom energy based Monte Carlo, flexible protein-ligand docking, parallel processing mode, which can predict the binding mode of the ligand in receptor target site [122]. Rosetta is a computational library for predicting and designing protein structures, protein folding mechanisms, and protein-protein interactions process with the tools like Atom, Residue type, Residue, Conformation, Pose, Score Function, Score Type. These components provide data and services. Rosetta contains source code for free applications [123]. Lead-Finder software is used for calculating protein-ligand interaction binding affinity. The main features of Lead-Finder software are automatic processing of protein structures, accuracy protein-ligand docking result, the free energy of ligand binding. This software is working on a virtual screening method and a docking algorithm. Others feature of Lead-Finder software are like drug discovery, toxicity calculation based on ADMET properties in silico, and use of rational drug design [124]. MS-DOCK software is based on a search for ligand flexibility as apply to DOCK5. This software is working on an RMSD (root-mean-square deviation) technical judgment with an external conformation [125]. HomDock software tool is used for protein-ligand docking process modified technology compares with the Glam Dock software tool. HomDock software is works based on a combination of the ligand-based GMA (Graph-based molecular alignment) molecular alignment tool [126]. ISE-dock program is used for Docking based on the iterative stochastic elimination (ISE) algorithm. ISE algorithm is useful for optimizing the docking poses [127]. ASEDock tool is used for Pharmacophore Docking. AS Dock tool is based on ligand at the alpha site; the alpha site is present at receptor pocket shape [128]. OSDD (Open Source Drug Discovery) is Linux software used for designing, discovering and simulating new drugs. There is different OSDD software available like Protein structure and function prediction packages, Designing epitope-based vaccine, Molecular Interactions and modifications, Drug Designing, Therapeutic Peptides designing [129]. The NANO-D develops SAMSON is a software tool used for molecular modeling, Docking, and simulating nanosystems. PEPSI-Dock is a docking tool for protein-protein Docking develops by SAMSON. PEPSI-Dock is working on Polynomial Expansion of Protein Structures and Interactions for Docking [130]. Q-Dock software is a protein-ligand interaction parameter calculation. Q-Dock software does some parameter calculation like flexible protein-ligand docking by the generic force field combined with the pocket-specific chains, docking energy calculation, generating low-resolution docking image, rebuild the all-atom model from the low-resolution image [131]. PharmaGist is an online freely available web server used for Pharmacophore finding by virtual screening isolate on a commonly used data set of G-Protein Coupled Receptor alpha1A [132]. DOVIS software tool is useful for virtual screening of the docking process. DOVIS upgraded tool is used for more accurate docking process helping in Auto Dock 4.0 software [133]. Align-it™ is a software program to align molecules according to their pharmacophores. Drug-receptor interactions by using Align-it tools for hydrogen bonding, charge transfer, electrostatic and hydrophobic interactions checking in docking molecules [134]. DOCK Blaster is an open access online web server for structure-based ligand discovery. Its provide ZINC database for molecules and dock3.6 software calculates protein-ligand interaction scoring result [135]. Docking Server is a web online server for molecular docking study of protein-ligand interaction. This software is easy to use and give a docking score. Software is working on a high throughput screening method used for a library to proteins target. This software calculates parameters like accurate ligand geometry optimization, energy minimization, charge calculation, docking calculation and protein-ligand complex illustration [136]. Catalyst® software is used for pharmacophore mapping and redesign and it performs better than parallel computing tools [137]. FINDSITE-LHM software is used for homology modelling in the flexible ligand docking process. Flexible ligand docking is working on referring similarity-based ligand binding pose prediction and give scoring function [138]. PLATINUM (Protein-Ligand Attractions Investigation Numerically) is a web application for Protein-Ligand interaction analysis docking poses and visualization of hydrophobic/hydrophilic properties of three-dimensional molecules. PLATINUM software calculates hydrophobic/hydrophilic interaction based on MHP (empirical molecular hydrophobicity potential) techniques [139]. VSDMIP (Virtual Screening Data Management on an Integrated Platform) software tool is used for virtual screening vs. chemical libraries (MySQL) relational database [140]. WwLigCSRre is used for searching banks for

compounds detect a query, based on both coordinates and physicochemical properties of atoms [141]. ShaEP is software used for 3D QSAR modelling and the virtual screening of libraries of chemical structures [142]. Fpocket is a C programming language software used for detection protein pocket cavity algorithm. fpocket software can be combined with other tools like dpocket & tpocket, which extract pocket descriptors and scoring functions [143]. AutoDock Vina is an open-source freeware molecular docking program. The invariance of the covalent bond lengths is automatically verified in the output structures. Vina avoids imposing artificial restrictions, such as the number of atoms in the input, the number of torsions, the size of the search space, the exhaustiveness of the search, etc. AutoDock 4 and Vina program combined and it used for choosing receptor Flexible side chains while performing docking [144]. VLifeMDS software is used for molecular docking process. VLifeMDS software is used for scoring functions determined by Grid-based Docking, genetic algorithm, and VLife's GRIP docking (a unique rapid screening docking). VLifeDock provides an array of scoring functions such as PLP score, XCscore and Steric positive Electrostatic score for evaluation of docked poses [145]. ParaDockS is an online open-source web server for rigid protein - Flexible DNA complementarity docking process. ParaDock online tools are working based on a novel ab initio protein - DNA docking algorithm [146]. GriDock is used for molecular Docking of ligands stored in single database software of C++ computer language. GriDock is working on MPICH2 technology. MPICH2 is a balancing technology for computational processor between docking grid nodes [147]. DockoMatic is Java Net beans program used for virtual peptide ligand creation, molecular docking job setup, reporting results, and analysis for Docking. DockoMatic is working based on Inverse Virtual Screening (IVS) experiments, build and confirm homology models [148]. BioDrugScreen is a computational drug design and discovery program for molecular Docking to the human proteome. Docked Proteome Interaction Network (DOPIN) database are used to pre-docking and give docking scoring function [149]. PharmMapper is a freely available online web server used for pharmacophore mapping with a statistical process for molecular Docking based on high throughput scanning [150]. The PHENIX (Python-based Hierarchical Environment for Integrated Xtallography) software tools are used for SOLVE/RESOLVE, Phaser, Mol Probity, and the Computational Crystallography [151]. MOLA software tool is used for Virtual Screening using docking software like AutoDock4/Vina in a computer cluster using non-dedicated multi-platform computers [152]. NNScore (A Neural-Network-Based Scoring Function) is a software tool used for Protein-Ligand Complexes docking calculation. NNScore is working based on Virtual screening method [153]. MolSign software tool is used for pharmacophore modelling and identification where pharmacophoric features such as H-bond donor, H-bond acceptor, positive charge, negative charge and hydrophobe can be also obtained. MolSign is helpful tool for other program like VLifeMDS, VLifeQSAR, ChemDBS, LeadGrow [154]. ISIDA is a software program used for Property-Labelled Fragment Descriptors from Structure-Data File (SDF) and also to calculate substructural molecular fragment [155]. AADS software is an online web server for active site prediction and it will predict the protein cavity points with active ligand molecules at the top ten cavity points [156]. Beta Dock is a Molecular docking software based on the Beta-complex theory [157]. The first iScreen web-server docking software is working on virtual screening and the de novo drug design process for traditional Chinese medicine (TCM). This web-server TCM database performs Docking and screening, and the de novo TCM drug design. The PLANTs docking corresponds with its TCM database for the virtual screening based on known protein-ligand conformation, and results can be viewed and downloaded [158]. LigDockCSA software is a docking process. This software is developed by two techniques like lig dock (conformational space annealing (CSA)) and AutoDock energy (piecewise linear potential (PLP)) torsion energy. LigDockCSA provides a highly accurate, docking result. LigDockCSA finds a precise scoring pose contained by the RMSD technique [159]. PythDock is a structure-based drug design and docking scoring program. PythDock program uses Python language. PythDock scoring result is based on electrostatic and dispersion/repulsion and particle swarm optimization algorithm conditions. PythDock provides easier and precise poses than other programs like AutoDock and DOCK [160]. SwissDock is a web server services program for protein-ligand (small molecules) docking interaction. SwissDock performs different features like posing a binding mode for a ligand, Create figures for protein-ligand interaction; produce a complex to do subsequent calculations, Design inhibitors for the aim of your selection [161]. VoteDock is a web server online protein-ligand docking program. This software cannot be given under academic license agreement, only can be given to standard users [162]. Rosetta FlexPepDock is a web server online, a high-resolution protein-peptide docking program, also shows a near-native model of the interaction [163-164]. Pose & Rank is an online free server used for protein-ligand docking calculation scoring function. PoseScore is a working based on native binding geometries of ligands from other poses, and RankScore is an individual ligand from nonbinding molecules. PoseScore and RankScore are based on a set of 8,885 crystallographic structures of protein-ligand complexes [165]. Pharmer (ZINCPharmer) online program is searching for a pharmacophore from the ZINC database library [166-167]. SHAFTS software is used for 3D molecular similarity calculation. SHAFTS software is another collaboration software Server like ChemMapper [168]. Open Babel is a software used as a chemical toolbox. This toolbox is the language of chemical data for molecular modeling, cheminformatics, Organic chemistry, inorganic chemistry, solid-state materials, nuclear chemistry, solid-state materials, and biochemistry [169]. Open3DALIGN is software tools used in a command-line tool that is operated by a view of some structure file. Open3DALIGN is software tools important for PyMOL's viewport [170]. pep:MMs:MIMIC is an online web server used for a three-dimensional peptide structure, can automate a multi conformers 3-D similarity search [171]. PaDEL-Descriptor software is used to calculate molecular descriptors for chemical structure. These molecular

descriptors are used for structure-activity relationships [172]. AquaSAXS is a new and better program than AquaSol, which uses a dipolar solvent model. AquaSAXS is working based on a hydration map around the macromolecule, as a solvent density map on a 3D grid [173]. MDpocket is free, and an open-source tool is used for detection of protein pocket cavity for tracking small molecule binding sites and gas migration pathways on molecular dynamics (MDs) trajectories or other conformational ensembles [174]. GPCRs (G-protein-coupled receptors) auto model are docking online process. G-protein-coupled receptors are a significant class of proteins. This online software's main feature is searching for low-resolution protein conformation. Other features of this software are friendly users working on high-throughput screening techniques and homology modeling of mammalian [175]. New Human GPCR modeling and virtual screening are constructing by FINDSITEX online database. FINDSITEX identifies human GPCR approximately 998 or more. Primary, TASSERVMT-lite gives an update of all human GPCR structures before modeled in its laboratory. The function of this software is the detection of an algorithm to screen all human GPCRs aligned with the ZINC8 non-redundant ligand set joint with ligands since the GLIDA database. Other features of this database have off-target predictions and search using text input, FASTA formatted sequence input. This database is available free only for an academic purpose [176]. GalaxyDock is an online web server computational study software. This web server provides different services like Protein structure prediction from a sequence by template-based modeling, Protein-peptide docking based on interaction similarity and Symmetric, asymmetric protein-protein Docking, and Flexible GPCR-ligand docking [177]. IdTarget web server online processes for small molecules with drug conquer docking scoring function. IdTarget works majorly on the oldest remedy in used natural product effects, docking scoring function based on regression analysis and quantum chemical charge models [178]. Mcule is online services for new drug discovery and design. Its features of molecular modeling tools, the highest quality compound database, IT infrastructure, and compound procurement service, run virtual screens to identify new drugs applications to get better their affinity [179]. SCIGRESS is a software tool used for visualization tools, molecular design, and modeling QSAR/QSPR analysis. SCIGRESS software tools have other features like Determination of total energy (DFT), the heat of formation (semi-empirical methods) or strain energy (MM), Reaction mechanism determination via transition state searching and evaluation and visualization of intrinsic reaction coordinates, Determination of low energy conformations, vibrational analysis including visualization of IR spectra, Interactions with radiation including visualization of UV-visible spectra, and identification of molecular orbitals, electron densities, and electrostatic surfaces, Molecular dynamics study and analysis of phase transitions, expansion, defects, compressibility, tensile strength, adsorption, absorption, and thermal conductivity, Protein-ligand docking, Quantum chemistry of full proteins [180]. COPICAT software is used to calculate protein-drug interaction from drug bank thorough SVM (statistical learning method) [181]. DecoyFinder software is a graphical tool which used for finding decoy molecules for a set of active molecules. This software is used for searching molecules physically similar yet chemically different from the active ligand [182]. AutoClickChem is a software tool used in the python program for combinatorial libraries of compounds that are used for virtual screens, drug optimization, and rational drug design [183]. AnchorQuery™ is a software used for interactive virtual screening of searching pharmacophore [184]. VinaMPI is a massively parallel Message Passing Interface (MPI) program that is based on a multithreaded virtual docking program AutodockVina. This method is important in distributing tasks, while multithreading is used to accelerate individual docking tasks [185]. FINDSITEcomb is an online web server freely available, which is used for docking programs against the DUD (Directory of Useful Decoys). This software is working on virtual screening and screens ten million compounds within 2 days on a single computer node [186]. Sirius software program is molecular modeling and analysis for protein and small molecules system. Sirius program is used for structure building, 3D graphics, visualizing molecular dynamics, and primary protein sequences [187]. rDock is Open Source proteins and nucleic acids versus drug molecules docking program. This software is working on the HTVS method (High Throughput Virtual Screening). This software is made by computer languages like C++, Perl, or python. rDock has features of Docking, binding score, Binding Mode Prediction, High Throughput Virtual Screening [188]. MAPS software tools are used for calculation likes molecular dynamics simulations and Monte Carlo simulations, PC-SAFT for thermodynamics modeling, and Structure QSAR/QSPR [189]. Q-Chem is an ab initio quantum chemistry correlation methods such as integrated graphics interface including molecular builder, input generator, contextual help and visualization toolkit, Dispersion-corrected and double hybrid DFT functional, Faster algorithms for DFT, HF, and coupled-cluster calculations, Structures and vibrations of excited states with TD-DFT, Efficient valence space models for strong correlation, Methods for mapping complicated potential energy surfaces, More choices for excited states, solvation, and charge-transfer, Effective Fragment Potential and QM/MM for large systems [190]. The CABS-dock web server is working on molecular modeling, protein-peptide interactions using a flexible docking and peptides –proteins docking. Other features of the CABS-dock server do not require such pre-defined localization of the binding site [191-192]. FlexAID computational software used for drug design and developments for protein and drug flexible docking processes. FlexAID works on less than 2Å RMSD (root-mean-square deviation) conformations method and over successive rounds of Monte Carlo optimization method [193]. Dolina computational software is available free to excess for academic purposes. This software used for receptor and synthetic ligands (drug) pharmacophore mapping. Dolina, which is not working on flexibility criteria but a pool of low-energy conformers and identifies binding-pose for the receptor (crystal structure) with synthetic ligands (co-crystallized), docked [194]. Pyrx software tool is used for virtual screening and powerful visualization engine of drug discovery to screen

libraries of compounds against potential drug [195]. Aggregator Advisor online tools used for biochemical assays. Aggregator Advisor is working based on chemical similarity to identified aggregators and physical properties [196]. MOLS 2.0 software working on two mathematical calculation like Computation of the Delaunay triangulation (in terms of mathematics and computational geometry, a Delaunay triangulation), Voronoi diagram (in terms of mathematics, a Voronoi diagram is a partitioning of a plane into regions based on the distance to points in a specific subset of the plane) of the atomic centers. MOLS 2.0 computational software is working on protein-ligand docking feature like the construction of the molecular surface, identification of cavities, identification of possible channel start and endpoints, localization of channels using, and filtering of the localized channels [197]. ADMET software is used to calculate molecular descriptors for chemical structure. These molecular descriptors are used for structure-activity relationships, QSAR/QSPR, and easily manipulate and visualize data [198]. The MOLGEN is an online web server used for molecular structure elucidation, QSAR, generating all chemical structures by providing molecular formula [199]. Molecular Operating Environment (MOE) software's used for Structure-Based Design. Feature of MOE is Ligand-Receptor Docking, Active Site Detection, Multi-Fragment Search, Automated Structure Preparation for Ligand Optimization [200]. The Tinker is molecular modeling software for molecular mechanics and dynamics. which is having algorithms search like flexible implementation of atomic multi pole-based electrostatics with explicit dipole polarizability, various continuum solvation treatments including several generalized Born (GB/SA) models, generalized Kirkwood implicit solvation for AMOEBA, an interface to APBS for Poisson-Boltzmann calculations, efficient truncated Newton (TNCG) local optimization, free energy calculations via the Bennett Acceptance Ratio (BAR) method, surface areas and volumes with derivatives, free energy calculations via the Bennett Acceptance Ratio (BAR) method, normal mode vibrational analysis, torsional or rigid body space, minimization in Cartesian, symplectic RESPA multiple time-step integration for molecular dynamics, velocity verlet stochastic dynamics, pairwise neighbour lists and splinted spherical energy cut-off methods, particle mesh Ewald (PME) summation for partial charges and polarisable multipoles, a novel reaction field treatment of long-range electrostatics, fast distance geometry metrization with better sampling than standard methods, Elber's reaction path algorithm, potential smoothing and search (PSS) methods for global optimization, Monte Carlo Minimization (MCM) for efficient potential surface scanning [201]. LigPrep is a Schrödinger software tool used for minimization of structures which applies sophisticated rules to correct Lewis structures and to eliminate mistakes in ligands to reduce computational errors [202]. Pse-in-One: a web server used for determining different modes of pseudo components of RNA, DNA, and protein sequences. ChemAxon software package used for different tools like Marvin Suite used to a chemical structure can draw & view, JChem tools used for chemical structures search from database, JChem interface tools used for and predictions cluster, screen, fragment form virtual screening [206].

# RESULTS AND DISCUSSION

**Comparison of internationally used computational software tools**

In **Table 2**, most cited software for drug design and discovery are compared in terms of publication citation/review/research and patent citation. In this review, 25 software tools among a total of 189 computational software tools are differentiated, which are cited nearly a thousand times and globally used and are shown by graphical representations in **figure-2** and **3**.

**Table: 2 Most cited Computational software Programs:**

| Sr No. | Software Name | Publication citation review/ research/ conformance/ meeting* | Patent citation* |
|---|---|---|---|
| 1 | VMD | 27086 | 100 |
| 2 | PROCHECK | 23800 | 100 |
| 3 | UCSF Chimera | 18300 | 100 |
| 4 | Phenix | 11900 | 100 |
| 5 | AutoDock Vina | 7250 | 30 |
| 6 | Gromacs | 5810 | 10 |
| 7 | ChemOffice/ ChemDraw | 4640 | 220 |
| 8 | Glide Schrödinger | 4480 | 20 |
| 9 | MODELLER | 4320 | 20 |
| 10 | RasMol | 2950 | 30 |
| 11 | DOCK | 2280 | 120 |
| 12 | Open Babel | 2194 | - |
| 13 | HADDOCK | 1990 | 10 |
| 14 | Filter-it™ | 1870 | 10 |
| 15 | GOLD | 1530 | 20 |
| 16 | ICM-Dock | 1420 | 20 |
| 17 | PatchDock | 1390 | 10 |
| 18 | Molegro Virtual Docker | 1310 | - |
| 19 | AutoDock | 1220 | 90 |
| 20 | PROMOTIF | 1120 | 10 |
| 21 | LigandScout | 1041 | - |
| 22 | Surflex-Dock | 1030 | 10 |
| 23 | FoldX | 1010 | 10 |
| 24 | YASARA | 1006 | 4 |
| 25 | OSDD | 975 | 6 |

***Indicate that citation till up to December-2018**

VMD is a most-cited 3-D graphics, a molecular visualization program for analyzing, display and animate docking tools supported MacOS X, Unix, or Windows-based computer program [35]. PROCHECK and PROCHECK-NMR software tools are used for protein structures, stereochemical quality, analysis, and ensembles [21]. UCSF Chimera is the most cited docking and drug design with the help of protein-ligand visualization and analysis, assemblies, sequence alignments, docking results, trajectories, and conformational ensembles [78]. PHENIX is the most cited and used for protein X-ray crystallography structure producer [151]. AutoDock Vina program is the most cited and used for docking, discovery, and

virtual screening for new drug design and discovering [144]. GROMACS is free, open-source tools of structure used for dynamical, simulations of biomolecules & chemical structure, calculations free-energy [31].

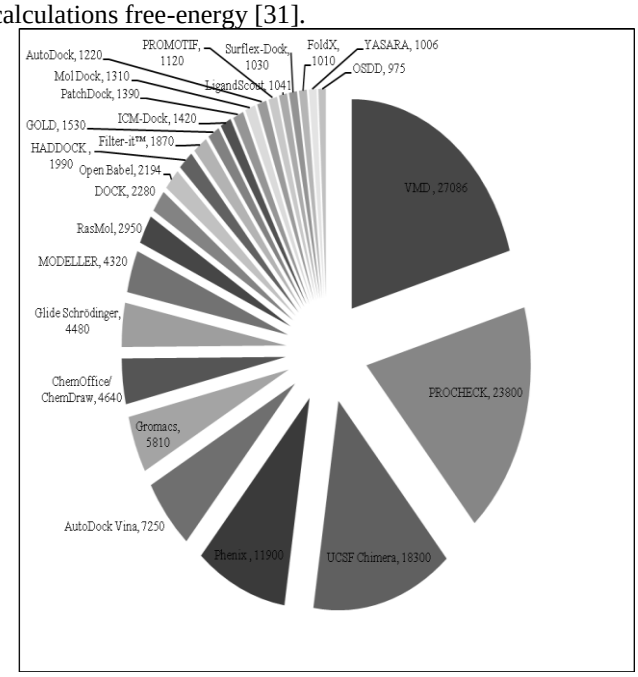


**Figure: 2 Shown in most cited software versus publication citation review/ research/ conformance/ meeting***

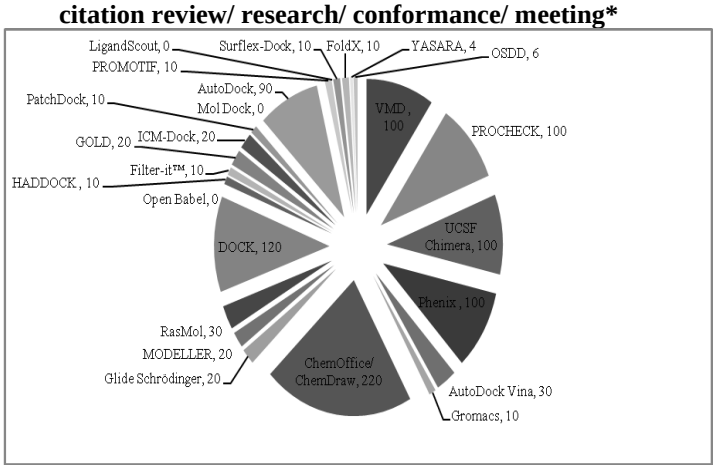


**Figure: 3 Shown in most cited software versus patent citation***

ChemOffice/ ChemDraw Professional is most cited used by rapidly and successfully draw molecules, chemical structural property, Chemical structure to name conversion, Chemical name to structure conversion, NMR spectrum simulation (1H and 13C), Mass spectrum simulation, Structure cleanup, an extensive collection of templates, including style chemical structure templates [12]. Schrödinger's non-commercial paid software computer program is the most cited tool for small molecule modeling and simulations, macromolecular modeling and simulations, lead discovery, lead optimization, and visualization and automation [74,121,202]. MODELLER is the most cited software used for homology modeling and automatically calculates all non-hydrogen atoms [104]. RasMol is the oldest third most cited used for molecular graphics, visualization, and look at biological macromolecule structures those found by a Protein Data Bank [30]. DOCK is a third most cited and first invented geometric algorithm based working [10]. ChemOffice/ ChemDraw than after most cited freely available for Windows, Unix, Linux, macOS, and Android software of Open Babel is a chemical expert structure interconvert chemical file formats [179]. HADDOCK is the fourth most cited modeling problem [67]. Filter-it™ is the most cited program for filtering out molecules with unwanted properties [53]. GOLD is used for virtual screening, lead optimization, and identifying the correct binding mode program [28]. The ICM-Dock is used for docking solutions, binding site analysis, visualization of grid potentials, adjustment of potential grid areas, and configurable preferences for ligand size and score thresholds [23]. PatchDock program is used for docking in three ways like Molecular Shape Representation, Surface Patch Matching - Geometric Hashing and Pose-Clustering to match the patches, and Filtering and Scoring methods [82]. Molegro Virtual Docker tools are used molecules docking after a novel optimization technique for drug design [96]. AutoDock is an automat docking tool for small 3D molecules structure bind to a receptor site given a binding pose [14]. PROMOTIF program is used for drug structures with an ensemble of NMR protein structures [36]. LigandScout is a tool used for pharmacophores mapping software for drug structure with protein [83]. Surflex-Dock tool is used for searching pockets and optimize them and generate the pose of a protein-ligand complex [69]. FoldX is used for getting better protein stability for efficient genetic engineering and docking process [86].YASARA is a Virtual molecular modeling and simulations and molecular-graphics program operated by Windows, Linux, macOS, and Android systems [63]. OSDD (Open Source Drug Discovery) is Linux computer-based web services, libraries, open-source program use for drug discovery [129].

# CONCLUSION

Computational software tools are now used routinely to investigate the structure, dynamics, surface properties, and thermodynamics of inorganic, biological, and polymeric systems. Computational software tools are a vital part of the guide for drug discovery. It is widely used in rational drug design and structure-based drug design process. Structure-based drug design means that we use three-dimensional structures (protein, receptor, enzymes) to design new drugs (ligand) with the help of software by checking receptor- drug binding affinity. This review article helps select computational tools for drug design and discovery. The process of drug design and discovery is essential in the invention of a new chemical entity. For this process, plenty of computational tools are available globally, those computational software tools are fast, free, open online excess, paid but which one is most potent and efficient computational tools. In this review article, the study on total 189 worldwide computational software tools predicted most cited, more used software tools which are of the download link, use, application of software, limitation, availability, operating system used all given in the

brief introduction and which is presented in a graphical and tabulated form.

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## CONFLICT OF INTEREST

The authors confirm no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Not declared.

## ETHICS STATEMENT

The authors have taken all the necessary permissions as per ethical guidelines wherever applicable. The authors will be responsible for all the technical content mentioned in the manuscript. Journal and Publisher will not be responsible for any copyright infringement and plagiarism issue.

## AUTHOR CONTRIBUTIONS

The entire study was conceptualized, designed and conducted the study with the help of other authors, wrote the first draft of the manuscript, and other authors contributed significantly to the revision of the manuscript. All Authors read and approved the final manuscript.

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