**Chapter 13: Real-world application of Molecular Docking in Drug Discovery**

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**Supplementary Files**

Supplementary Table 1: Comparison of Docking Tools and Their Features

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Docking Tool** | **Search Algorithms** | **Scoring Functions** | **Auxiliary Tools** | **Partial Charges** | **Evaluation Methods** | **Type of Docking** | **Supported Platforms** | **License** | **References (PMID)** |
| **AutoDock** | Genetic Algorithm, Local Search | Free Energy of Binding, Empirical Force Field | AutoGrid, AutoDockTools | Gasteiger | RMSD, Binding Affinity | Rigid and flexible ligand | Windows, macOS, Linux | Open-source (GPL) | [27077332](https://pubmed.ncbi.nlm.nih.gov/27077332) |
| **AutoDock Vina** | Iterated Local Search Global Optimizer | Empirical Scoring Function | AutoDockTools, OpenBabel | Gasteiger, AutoDock Charges | RMSD, Binding Affinity | Rigid and flexible ligand | Windows, macOS, Linux | Open-source (Apache) | [19499576](https://pubmed.ncbi.nlm.nih.gov/19499576) |
| **DOCK** | Anchor-and-Grow, Hierarchical Search | Grid-based Energy Scoring | Chimera, UCSF DOCK Suite | AMBER | RMSD, Energy Scores | Flexible ligand, rigid protein | Windows, macOS, Linux | Open-source (GPL) | [25914306](https://pubmed.ncbi.nlm.nih.gov/25914306) |
| **FlexX** | Fragment-based Incremental Construction | Empirical, Forcefield-based | SYBYL, BioSolveIT | Gasteiger | Energy Scores, Visual Inspection | Rigid and flexible ligand | Windows, Linux | Commercial | [17886339](http://www.ncbi.nlm.nih.gov/pubmed/17886339) |
| **RosettaDock** | Monte Carlo, Low-Resolution Search | Rosetta Energy Function | PyMOL, RosettaScripts | AMBER, CHARMM | Interface RMSD (iRMSD), Energy Scores | Protein-protein docking | Linux | Open-source | [18442991](https://pubmed.ncbi.nlm.nih.gov/18442991) |
| **ICM** | Biased Probability Monte Carlo (BPMC) | Empirical, Docking Score, Free Energy | ICM Browser, PyMOL | Gasteiger | RMSD, Binding Affinity | Flexible ligand, receptor flexibility | Windows, Linux | Commercial | <https://doi.org/10.1002/jcc.540150503> |
| **GOLD** | Genetic Algorithm | ChemScore, Piecewise Linear Potential (PLP) | Hermes Visualizer, PyMOL | Gasteiger,MMFF94 | RMSD, Binding Affinity | Flexible ligand, protein flexibility | Windows, Linux | Commercial | 12910460 |
| **Prescience In-Silico** | Custom Algorithms | Proprietary Scoring Function | Prescience Suite | AMBER, MMFF94 | Binding Affinity, Energy Scores | Flexible ligand, custom protocols | Windows, macOS, Linux | Commercial | <https://www.prescience.in/prins> |
| **MOE** | Simulated Annealing, Genetic Algorithm | Forcefield-based, Free Energy, Empirical | PyMOL, MOE Visualizer | AMBER | RMSD, Binding Affinity | Rigid and flexible ligand | Windows, macOS, Linux | Commercial | 19075767 |
| **Schrödinger Glide** | Systematic Search, Monte Carlo | GlideScore (empirical), ChemScore, Emodel | Maestro, PyMOL | OPLS, MMFF94 | RMSD, Energy Scores | Flexible ligand | Windows, Linux | Commercial | <https://www.schrodinger.com/> |
| **LeDock** | Systematic Search | Empirical Scoring | PyMOL, LePro | AMBER | Binding Affinity, Visual Inspection | Rigid and flexible ligand | Windows, macOS, Linux | Free for academic use | 10.1088/1755-1315/218/1/012143 |

Supplementary Table2: Interaction profile of top leading phytochemical drug candidates for spike protein of SARS-COV2 variant.

|  |  |  |
| --- | --- | --- |
| **Compound** | **Docking score (Kcal/mole)** | **Hydrogen bonds (bond distance in Å)** |
| Rosmarinic-Acid | -6.716 | ARG398(2.96), ASN412(2.84), GLY491(3.11), HIS500(2.82) |
| Taxifolin | -6.233 | ARG398(2.67), TYR448(1.87), SER489(1.74), HIS500(1.95) |
| Indigotin | -5.637 | GLN488(3.65), PHE492(3.94), TYR496(3.09), HIS500(3.85) |
| Castanospermine | -5.275 | ARG398(2.83), GLU401(2.71), GLN404(3.11), ASN412(2.84) |
| Morin | -5.263 | ARG398(2.12), ASN412(1.97), TYR448(2.35), GLY491(1.86), HIS500(2.15) |
| Baphicacanthin A | -5.232 | ARG398(3.48), TYR448(2.12), GLY491(2.13) |
| Diosmetin | -5.096 | ARG398(2.78), TYR448(3.39), GLY491(2.07), PHE492(3.48), HIS500(2.09) |
| Anhydropodophyllol | -4.762 | ARG398(2.02), GLU401(2.41), TYR448(1.82), SER489(1.84), GLY491(2.00) |
| Citric Acid (PG) | -4.704 | GLU401(2.50), GLN404(2.11), ASN412(1.72) |
| 2-O-Caffeoylhydroxycitric Acid | -4.365 | GLU401(2.09), GLN404(2.19), ASN412(2.92), ILE413(3.26), TYR448(1.99), SER489(3.00), GLY491(1.74) |
| Pectin (PG) | -4.358 | ARG398(3.18), GLU401(3.39), GLN404(1.91), ASN412(2.19) |
| Isoliquiritigenin | -4.339 | ARG398(3.34), ASN412(2.15), GLY491(1.94), HIS500(1.58) |
| Isoliquiritigenin | -4.205 | GLY491(2.06) |
| Gallic-Acid | -486 | ARG398(2.15), GLU401(1.66), GLN404(2.07), ASN412(3.01), ILE413(3.08) |
| Dihydrofisetin | -3.996 | TYR448(2.98), SER489(1.91), HIS500(1.94) |
| Genistein | -3.993 | GLY491(2.02), HIS500(1.90) |
| 4-Hydroxy-3,5-Dimethylacetophenone (Hf) | -3.952 | ARG398(2.85), GLY491(1.96), PHE492(3.41) |
| Malic Acid (PG) | -3.896 | GLU401(2.36), GLN404(2.07), ASN412(1.74), ILE413(3.36) |

Supplementary Table 3: ADME Profile of the top-scored phytochemicals

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Molecules** | **Lipophilicity** | **Solubility** | **Pharmacokinetics** | **Druglikeness** | | **Medicinal Chemistry** | |
|  | iLOGP | LogS (ESOL) | GI absorption | Lipinski | Bioavailability Score | PAINS | Lead likeness |
| Rosmarinic-Acid | 1.17 | -3.44 | Low | Yes; 0 violation | 0.56 | 1 alert: catechol\_A | No; 1 violation: MW>350 |
| Taxifolin | 1.30 | -2.66 | High | Yes; 0 violation | 0.55 | 1 alert: catechol\_A | Yes |
| Indigotin | 2.19 | -3.67 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Castanospermine | 0.94 | 0.40 | Low | Yes; 0 violation | 0.55 | 0 alert | No; 1 violation: MW<250 |
| Morin | 1.47 | -3.16 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Baphicacanthin A | 2.43 | -3.01 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Diosmetin | 2.47 | -4.06 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Anhydropodophyllol | 3.62 | -3.90 | High | Yes; 0 violation | 0.55 | 0 alert | No; 1 violation: MW>350 |
| Citric Acid (PG) | -1.49 | 0.38 | Low | Yes; 0 violation | 0.56 | 0 alert | No; 1 violation: MW<250 |
| 2-O-Caffeoylhydroxycitric Acid | -0.07 | -1.32 | Low | No; 2 violations: NorO>10, NHorOH>5 | 0.11 | 1 alert: catechol\_A | No; 2 violations: MW>350, Rotors>7 |
| Pectin (PG) | 0.10 | 0.95 | Low | Yes; 0 violation | 0.55 | 0 alert | No; 1 violation: MW<250 |
| Isoliquiritigenin | 2.02 | -3.70 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Isoliquiritigenin | 2.02 | -3.70 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| Gallic-Acid | 0.21 | -1.64 | High | Yes; 0 violation | 0.56 | 1 alert: catechol\_A | No; 1 violation: MW<250 |
| Dihydrofisetin | 1.47 | -2.53 | High | Yes; 0 violation | 0.55 | 1 alert: catechol\_A | Yes |
| Genistein | 1.91 | -3.72 | High | Yes; 0 violation | 0.55 | 0 alert | Yes |
| 4-Hydroxy-3,5-Dimethylacetophenone (Hf) | 1.95 | -1.82 | High | Yes; 0 violation | 0.55 | 0 alert | No; 1 violation: MW<250 |
| Malic Acid (PG) | -0.01 | 0.32 | High | Yes; 0 violation | 0.56 | 0 alert | No; 1 violation: MW<250 |

|  |  |
| --- | --- |
| **Molecules** | **Hepatotoxicity** |
| Rosmarinic-Acid | Inactive |
| Taxifolin | Inactive |
| Indigotin | Active |
| Castanospermine | Inactive |
| Morin | Inactive |
| Baphicacanthin A | Inactive |
| Diosmetin | Inactive |
| Anhydropodophyllol | Inactive |
| Citric Acid (PG) | Inactive |
| 2-O-Caffeoylhydroxycitric Acid | Inactive |
| Pectin (PG) | Active |
| Isoliquiritigenin | Inactive |
| Isoliquiritigenin | Inactive |
| Gallic-Acid | Inactive |
| Dihydrofisetin | Inactive |
| Genistein | Inactive |
| 4-Hydroxy-3,5-Dimethylacetophenone (Hf) | Inactive |
| Malic Acid (PG) | Inactive |

Supplementary Table 4: Selected molecules and their respective Hepatotoxicity