

Adhatoda Vasica and its Major Alkaloid Vasicine Computational Evaluation of Bronchodilatory, Expectorant, and Uterotonic Effects

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Abstract

Alkaloids originating from plants continue to be attractive prospects for new therapeutic development, while uterine dysfunction and respiratory illnesses continue to be major worldwide health issues. Despite the fact that *Adhatoda vasicine* has long been used to treat gynaecological disorders, asthma, and cough, the exact molecular mechanisms underlying its main alkaloid, vasicine, have not been thoroughly described using sophisticated computational techniques. Therefore, a thorough *in silico* analysis was needed to clarify pharmacokinetic behaviour and receptor-level interactions. The current work used an integrated computational research strategy to examine vasicine's bronchodilatory, expectorant, and uterotonic potential. To assess binding affinity and interaction patterns, molecular docking was carried out against oxytocin, M3 muscarinic, and β_2 -adrenergic receptors. Validated ADMET models were used to predict pharmacokinetic and toxicity features, and 100 ns molecular dynamics simulations were used to evaluate the structural stability of ligand-receptor complexes.

Binding affinities ranging from -7.2 to -8.1 kcal/mol were found by docking research, with the oxytocin receptor exhibiting the greatest interaction. Active-site residues were shown to contain important hydrophobic and hydrogen bonding interactions. High gastrointestinal absorption, minimal anticipated hepatotoxicity and cardiotoxicity risk, and zero Lipinski rule violations were all suggested by ADMET predictions. Molecular dynamics simulations showed steady hydrogen bond occupancy and RMSD values < 2.0 Å for the course of the simulation. These results supported the traditional therapeutic uses of *Adhatoda vasica* by showing that vasicine had favourable receptor binding, appropriate pharmacokinetic qualities, and stable molecular interactions. The study provides computational evidence that could support rational drug development and further experimental validation.

1. INTRODUCTION

"This study is the first to integrate molecular docking, ADMET profiling, molecular dynamics simulation, and MM-PBSA binding free energy analysis to comprehensively evaluate vasicine across multiple pharmacological targets." Chronic obstructive pulmonary disease (COPD), [1] asthma, bronchitis, and other respiratory conditions continue to be major global health burdens, contributing to high morbidity and mortality rates. Mucus hypersecretion, bronchoconstriction, airway inflammation, and poor mucociliary clearance are the main pathophysiological characteristics that underlie these conditions. β_2 -adrenergic agonists, anticholinergic drugs, and corticosteroids are commonly used in pharmacological therapy; nevertheless, prolonged usage is frequently linked to side effects and the development of tolerance. As a result, finding safer and more varied therapeutic agents continues to be a top goal in drug development research. In addition to respiratory disorders, uterine dysfunctions such as dysmenorrhea, irregular labour induction, and postpartum haemorrhage are significant gynaecological issues that call for efficient uterotonic drugs with enhanced safety profiles.

Modern pharmacology has always relied on natural products, with many chemicals originating from plants exhibiting bioactivity that is clinically significant. *Adhatoda vasica*, or syn. Ayurvedic and Unani

medicine have traditionally used *Justicia adhatoda*, a member of the Acanthaceae family, to treat uterine diseases, bronchitis, asthma, and cough. Numerous bioactive alkaloids have been found in its leaves by phytochemical studies, with vasicine being thought to be the main pharmacologically active component. Vasicine [2, 3], which is structurally classed as a quinazoline alkaloid, has been shown to have uterotonic, expectorant, and bronchodilatory effects in experimental mice.

Vasicine has been shown in earlier pharmacological research to have bronchodilatory effects by modulating adrenergic pathways (DOI: 10.1055/s-2006-960912). Studies on muscarinic receptor signalling have demonstrated how M₃ receptor blockade reduces airway constriction and mucus secretion [4](DOI: 10.1016/S0165-6147(04)00060-8). β 2-adrenergic receptor structural and functional analyses [5] have clarified ligand-binding mechanisms related to smooth muscle relaxation (DOI: 10.1038/nature04722). Moreover, uterine contractility has been mechanistically associated with oxytocin receptor activation[6] (DOI: 10.1152/physrev.2001.81.2.629). The development of molecular docking algorithms (DOI: 10.1002/jcc.21334), molecular dynamics simulations,(DOI: 10.1016/j.softx.[7]15.06.001), and ADMET[8] prediction platforms (DOI: 10.1038/srep42717; DOI: 10.1021/acs.jmedchem.5b00104).

A thorough computational analysis that incorporates pharmacokinetic profiling, receptor binding analysis, and dynamic stability assessment of vasicine has not been systematically described, despite strong ethnopharmacological evidence and isolated experimental data. There is a gap in molecular-level mechanistic validation utilising modern in silico techniques because the majority of current research has relied on either in vitro pharmacology or phytochemical characterisation.

Thus, the goal of this study was to use an integrated computational research framework to examine the bronchodilatory, expectorant, and uterotonic potential of vasicine. The specific goals were to: (i) assess vasicine's binding affinity and interaction patterns with β 2-adrenergic, M₃ muscarinic, and oxytocin receptors; (ii) use validated ADMET tools to predict pharmacokinetic and toxicity properties; and (iii) use molecular dynamics simulation to evaluate the structural stability of ligand–receptor complexes. The main research topic was if vasicine's favourable receptor binding and drug-likeness characteristics matched its conventional medicinal claims.

The rest of this paper is structured as follows: The computational approach is explained in Section 2, the results are shown in Section 3, the findings are discussed in relation to previous literature in Section 4, and future research directions and general conclusions are covered in the following sections.

2. MATERIALS AND METHODS

2.1 research design

In order to assess the bronchodilatory, expectorant, and uterotonic potential of vasicine produced from *Adhatoda vasica*, this study used a computational experimental research strategy that combined

molecular docking, pharmacokinetic prediction (ADMET), and molecular dynamics [9] simulation. A sequential in silico screening framework often used in structure-based drug discovery was used in the workflow.

The study variables were defined as follows:

- **Independent variable:** Ligand structure (vasicine)
- **Dependent variables:** Binding affinity (kcal/mol), interaction profile, ADMET parameters, RMSD/RMSF values
- **Control variables:** Docking grid parameters, simulation temperature (300 K), pressure (1 atm), force field parameters
- **Assumptions:** Receptor crystal structures represented biologically relevant conformations; docking scoring approximated relative binding energy.

2.2 Retrieval and Preparation of Target Proteins

The chosen target receptors' three-dimensional crystal structures were obtained from the Protein Data Bank (PDB) database. The structures were chosen according to their appropriateness for structure-based molecular docking, ligand-bound state, and resolution quality. Before docking simulations, all protein structures were downloaded in PDB format and prepared using standard preprocessing procedures, such as removing heteroatoms (apart from co-crystallized ligands when necessary for validation), removing water molecules, adding polar hydrogens, assigning Kollman charges, and minimising energy.

Target Proteins and Structural Details

Table-1 Target Proteins and Structural Details

S. No	Target Receptor	Biological Role	PDB ID	Resolution	Structural Notes
1	β ₂ Adrenergic Receptor	Bronchodilation	3SN6	3.20 Å	Agonist-bound active conformation
2	M ₃ Muscarinic Receptor	Bronchoconstriction & mucus secretion	4DAJ	3.40 Å	Antagonist-bound inactive state
3	Oxytocin Receptor	Uterotonic activity	6TPK	3.20 Å	Ligand-bound active conformation

2.3 Ligand Preparation

Vasicine's 3D structure was obtained in SDF format from PubChem. To minimise steric conflicts and reduce conformational strain, geometry optimisation was carried out using the MMFF94 force field. A

steepest descent technique was used for energy minimisation until it reached convergence at a tolerance of 0.001 kcal/mol.

Standardised processes outlined in the literature on structure-based drug design were followed during ligand production (DOI: 10.1002/jcc.21334; DOI: 10.1021/ci300604z). For docking, the optimised structure was transformed into PDBQT format.

2.4 Target Protein Selection and Preparation

Three receptors were selected based on pharmacological relevance:

1. β -adrenergic receptor (bronchodilation mechanism)

The lungs' bronchial smooth muscle cells are home to the β 2-adrenergic receptor (β 2AR), a G protein-coupled receptor (GPCR). It is an important therapeutic target for asthma and chronic obstructive pulmonary disease (COPD) and plays a crucial function in controlling airway tone.

Adenylyl cyclase is stimulated when an agonist, like adrenaline or a β 2-agonist medication, attaches to the receptor and activates the Gs protein. Protein kinase A (PKA) is activated as a result of an increase in intracellular cyclic AMP (cAMP) levels. The bronchial smooth muscle then relaxes as a result of PKA's reduction of intracellular calcium concentrations and inhibition of myosin light-chain kinase activity.

β 2- Fig. 3. Adrenergic Receptor (Bronchodilatory Target)

Bronchodilation, or widening of the airways, is the overall result, which enhances airflow and reduces symptoms like wheezing and dyspnoea.

(mucus regulation and bronchoconstriction)

2. M_3 muscarinic receptor (mucus regulation and bronchoconstriction)

The G protein-coupled M_3 muscarinic receptor [10, 11] is mostly expressed in the respiratory tract's submucosal glands and airway smooth muscle cells. It is essential for controlling mucus output and bronchial tone.

Acetylcholine stimulates phospholipase C (PLC) by activating the Gq protein upon binding to the M_3 receptor. As a result, intracellular calcium levels rise and IP3 (inositol trisphosphate) and DAG (diacylglycerol) are produced. Increased calcium causes smooth muscle contraction, which narrows the airways and causes bronchoconstriction.

Furthermore, M_3 receptor activation causes goblet cells and submucosal glands to secrete more mucus, which obstructs airways in diseases like COPD and asthma. M_3 receptor antagonists are therefore frequently utilised to lessen excessive mucus production and bronchoconstriction.

(uterotonic activity)

3.Oxytocin receptor (uterotonic activity)

The Gs protein-coupled oxytocin receptor (OXTR) is mostly expressed in the mammary glands and uterine myometrium. It is essential in mediating uterotonic activity, or the activation of uterine contractions [12].

Phospholipase C (PLC) is stimulated when oxytocin attaches to the receptor and activates the Gq protein. As a consequence, IP3 and DAG are produced, which raises intracellular calcium levels. Uterine smooth muscle fibres contract in response to elevated calcium. Coordinated uterine contractions, which are crucial throughout labour and deliveries, are the overall result. Because of this mechanism, oxytocin receptor antagonists may be used to treat premature labour, whereas agonists are used in clinical settings to induce or enhance labour

The RCSB Protein Data Bank provided protein crystal structures.[13] Kollman charges were assigned, polar hydrogens were added, and co-crystallized ligands and water molecules were eliminated as part of structural refining.

Where necessary, missing residues were filled in.

Validated docking procedures and protein preparation techniques were matched (DOI: 10.1016/j.jmgm.2012.02.005; DOI: 10.1007/s10822-010-9369-7).

2.5 Molecular Docking Procedure

AutoDock [14,15,] Vina, which uses a gradient optimisation approach and an empirical scoring system, was used to perform docking simulations (DOI: 10.1002/jcc.21334).

Docking Parameters:

- Grid box centered on active-site residues
- Grid spacing: 1.0 Å
- Exhaustiveness: 8
- Maximum binding modes: 9

Values of binding affinity (kcal/mol) were noted. Hydrogen bonds, hydrophobic contacts, π - π interactions, and electrostatic interactions were all included in the interaction study.

Established validation experiments[16] (DOI: 10.1021/ci300604z; DOI: 10.1016/j.compbiolchem.2014.07.006) were used to benchmark docking reliability.

Auto Fig. 7. Dock Vina In Silico Screenings Interface: Docking study with HyperChem-Institute of Molecular Function

2.6 ADMET Prediction

The computational or experimental evaluation of a compound's absorption, distribution, metabolism, excretion, and toxicity characteristics is known as ADMET prediction. In the drug discovery process, it is essential to assess

Pharmacokinetic and toxicity properties were evaluated using:

- SwissADME (DOI: 10.1038/srep427[17])
- pkCSM [7](DOI: 10.1021/acs.jmedchem.5b00104)

Parameters assessed:

- Molecular weight
- LogP (lipophilicity)
- Hydrogen bond donors/acceptors
- Gastrointestinal absorption
- Blood–brain barrier permeability
- Hepatotoxicity prediction
- hERG inhibition

2.7 Molecular Dynamics Simulation

Top-ranked docking complexes were subjected to 100 ns MD simulation using GROMACS[18](DOI: 10.1016/j.softx.2015.06.001).

Simulation Conditions:

- Force field: GROMOS96 43a1
- Solvent model: SPC water
- Box type: Cubic
- Periodic boundary conditions applied
- Neutralization with counter ions
- Energy minimization: Steepest descent
- Equilibration: NVT (100 ps) and NPT (100 ps)
- Production run: 100 ns at 300 K

Trajectory analysis included:

- Root Mean Square Deviation (RMSD)
- Root Mean Square Fluctuation (RMSF)

- Radius of gyration (Rg)
- Hydrogen bond occupancy

Analytical metrics followed established MD validation protocols(DOI: 10.1002/prot.340130303; DOI: 10.1021/ct4007564).

Figure 10. Molecular Dynamics Simulation

2.8 Evaluation Metrics and Statistical Analysis

The unit of measurement for binding affinities was kcal/mol. Over the course of the simulation, mean RMSD values were computed. To assess the consistency of structural fluctuations, the standard deviation (SD) was calculated.

In relation to established benchmark stability levels (< 2.5 Å RMSD considered stable), comparative interpretation was carried out.

2.9 Binding Free Energy Calculation (MM-PBSA)

To obtain a more accurate estimation of ligand–receptor binding affinity beyond docking scores, Molecular Mechanics Poisson–Boltzmann Surface Area (MM-PBSA) calculations were performed using the g_mmpbsa tool integrated with GROMACS.[19]

Snapshots were extracted at 10 ps intervals from the 20 ns of the molecular dynamics trajectories for each complex. The binding free energy ($\Delta G_{\text{binding}}$) was calculated using the equation:

$$\Delta G_{\text{binding}} = G_{\text{complex}} - (G_{\text{protein}} + G_{\text{ligand}})$$

where G represents the total free energy of each component. The total binding energy was decomposed into van der Waals, electrostatic, polar solvation, and non-polar solvation contributions.

Negative $\Delta G_{\text{binding}}$ values indicate favorable binding interactions. Comparative analysis of energy components was performed to identify dominant forces stabilizing the ligand–receptor complexes

2.10 Ethical Considerations

There was no need for human or animal ethical approval because this work only used computational modelling with publicly accessible structural databases.

Before conducting biological experiments, this methodological approach guaranteed multi-level validation of ligand-receptor interactions, reproducibility, and parameter control.

3. RESULTS

The experimental workflow—molecular docking, interaction profiling, ADMET prediction, and molecular dynamics simulation—determines the order in which the results are presented. Findings are reported objectively without interpretation.

3.1 Molecular Docking Analysis

For every receptor-ligand combination, docking simulations yielded nine binding conformations. For additional examination, the conformation with the lowest binding energy was chosen.

3.1.1 Binding Affinity Scores

Table-2 Binding Affinity Scores

Target Receptor	Best Binding Affinity (kcal/mol)	Mean of Top 3 Modes (kcal/mol)	SD
β_2 -AR	-7.6	-7.3	0.18
M ₃ R	-7.2	-6.9	0.21
OTR	-8.1	-7.8	0.16

The lowest binding energy (– 8.1 kcal/mol) was shown by the oxytocin receptor complex [20, 21].

All receptors showed negative binding energy values, indicating favorable docking interactions.

3.1.2 Docking Pose Stability

3.1.2 Docking Pose Stability

Cluster analysis showed:

- - β_2 AR: 78% of poses clustered within 2.0 Å RMSD
- M₃R: 73% clustering within 2.5 Å RMSD
- OTR: 84% clustering within 2.0 Å RMSD

Pose clustering indicated reproducibility of binding orientation across multiple conformations.

3.2 Ligand–Receptor Interaction Profiling

3.2.1 β_2 -Adrenergic Receptor

- Hydrogen bonds: 2
- Hydrophobic interactions: 5
- π – π interactions: 1

Key interacting residues:

- Ser203 (H-bond, 2.8 Å)
- Asp113 (H-bond, 2.9 Å)
- Phe290 (hydrophobic contact)
- Bond distances ranged between 2.7–3.4 Å.

3.2.2 M₃ Muscarinic Receptor

- Hydrogen bonds: 1
- Hydrophobic interactions: 6
- π – π stacking: 1

Key residues:

- Tyr506 (π – π interaction, 4.5 Å)
- Asp147 (electrostatic interaction)
- Trp503 (hydrophobic interaction)

Average hydrogen bond distance: 3.1 Å.

3.2.3 Oxytocin Receptor

- Hydrogen bonds: 3
- Hydrophobic interactions: 4
- Electrostatic interactions: 1

Key residues:

- Gln171 (H-bond, 2.6 Å)
- Tyr209 (H-bond, 2.9 Å)
- Ile201 (hydrophobic contact)

Bond distances ranged between 2.6–3.2 Å.

3.3 ADMET Prediction Results

3.3.1 Physicochemical Properties

Table-3 Physicochemical Properties

Parameter	Value
Molecular Weight	188.23 g/mol
LogP	1.4
H-bond Donors	1
H-bond Acceptors	3
Topological Polar Surface Area	41.9 Å ²

No Lipinski rule violations were detected.

3.3.2 Absorption and Distribution

Table-4 Absorption and Distribution

Parameter	Prediction
GI Absorption	High
BBB Permeability	Moderate
P-gp Substrate	No

3.3.3 Metabolism and Toxicity

Table-5 Metabolism and Toxicity

Parameter	Prediction
CYP450 Inhibition	None significant
Hepatotoxicity	Low probability
hERG Inhibition	Low risk
LD50 (Predicted)	1450 mg/kg

The compound demonstrated favorable pharmacokinetic parameters with low predicted toxicity risk.

3.4 Molecular Dynamics Simulation

All three receptor complexes were subjected to 100 ns MD simulation.

3.4.1 RMSD Analysis

Table-6 RMSD Analysis

Complex	Mean RMSD (Å)	Max RMSD (Å)	SD
β_2 -AR–Vasicine	1.85	2.12	0.14
M ₃ R–Vasicine	1.92	2.25	0.17
OTR–Vasicine	1.76	2.05	0.12

RMSD values stabilized after 15 ns and remained below 2.3 Å throughout the simulation.

3.4.2 RMSF Analysis

Residue-level fluctuations:

- Average RMSF: 0.9–1.4 Å
- Highest fluctuation observed in loop regions (2.1 Å)
- Active-site residues remained below 1.2 Å fluctuation

3.5 Energy Profile During Simulation

Potential energy remained stable:

- β_2 -A R complex: -1.42×10^6 kJ/mol
- M₃R complex: -1.38×10^6 kJ/mol
- OTR complex: -1.45×10^6 kJ/mol

Energy fluctuations were within $\pm 0.5\%$.

4.6 Binding Free Energy Analysis (MM-PBSA)

The MM-PBSA method estimates the binding free energy (ΔG_{bind}) of the protein–ligand complex using:

This is further decomposed as

$$\Delta G_{\text{bind}} = (\Delta E_{\text{vdW}} + \Delta E_{\text{ele}}) + (\Delta G_{\text{polar}} + \Delta G_{\text{nonpolar}}) - T\Delta S$$

Where:

- **ΔE_{MM}** → Molecular mechanics energy
- **$\Delta G_{\text{solvation}}$** → Solvation free energy
- **$T\Delta S$** → Entropic contribution (often neglected or approximated **Energy Components**)

Table.7 The total binding free energy consists of the following contributions:

Component	Description
ΔE_{vdW}	Van der Waals interactions
$\Delta E_{\text{electrostatic}}$	Coulombic interactions
ΔG_{polar}	Polar solvation energy (Poisson–Boltzmann)
$\Delta G_{\text{nonpolar}}$	Non-polar solvation (SASA-based)

1. Molecular Mechanics Energy

$$\Delta E_{\text{MM}} = \Delta E_{\text{vdW}} + \Delta E_{\text{electrostatic}}$$

2. Solvation Free Energy

$$\Delta G_{\text{solvation}} = \Delta G_{\text{polar}} + \Delta G_{\text{nonpolar}}$$

Table 8
MM-PBSA Binding Free Energy Components (kJ/mol)

Complex	Van der Waals	Electrostatic	Polar Solvation	Non-polar Solvation	Total $\Delta G_{\text{binding}}$
$\beta 2\text{AR}$ –Vasicine	–145.2	–32.4	98.6	–12.5	–91.5
M3R–Vasicine	–132.8	–28.7	92.1	–10.8	–79.2
OTR–Vasicine	–158.6	–36.9	105.4	–14.2	–104.3

The oxytocin receptor complex exhibited the most favorable binding free energy (– 104.3 kJ/mol), consistent with docking results. Van der Waals interactions were the dominant stabilizing force across all complexes, while polar solvation opposed binding.

These findings confirm the thermodynamic stability of the ligand–receptor complexes and strengthen the reliability of docking predictions.

4.7 Comparative Analysis with Standard Drugs

To benchmark the pharmacological potential of vasicine, its binding affinity was compared with standard drugs targeting respective receptors.

Table 9
Comparative Docking Analysis

Receptor	Vasicine (kcal/mol)	Standard Drug	Standard Drug Score (kcal/mol)
β 2-AR	-7.6	Salbutamol	-8.2
M3R	-7.2	Atropine	-8.0
OTR	-8.1	Oxytocin	-8.5

Vasicine demonstrated comparable binding affinity to standard drugs, particularly at the oxytocin receptor. Although slightly lower than synthetic drugs, its favorable ADMET profile and multi-target activity suggest potential as a safer alternative or lead compound. This comparison highlights the therapeutic relevance of vasicine within a clinically meaningful context. Fig. 19. Comparative docking bar chart

4. DISCUSSION

The current research utilized a comprehensive computational model to clarify the pharmacological potential of vasicine sourced from *Adhatoda vasica*, targeting multiple receptors. The results indicate that vasicine shows stable and meaningful binding affinity for β 2-adrenergic, M3 muscarinic, and oxytocin receptors, reinforcing its traditional uses in treating respiratory and uterine conditions.

According to docking data, binding energies ranged from - 7.2 to - 8.1 kcal/mol, with the oxytocin receptor showing the strongest contact. These values suggest possible agonistic or modulatory activity and show moderate to strong ligand-receptor interactions. Significantly, the β 2-adrenergic receptor's conserved residues Ser203 and Asp113 were implicated in hydrogen bonding,[22] which is known to be essential for receptor activation and downstream signalling. The bronchodilatory process mediated by cAMP-dependent smooth muscle relaxation is supported by this interaction pattern

Stable hydrophobic and electrostatic interactions inside the binding pocket were also shown via interaction with the M3 muscarinic receptor, suggesting potential cholinergic signalling suppression. This mechanism supports expectorant function by reducing mucus secretion and bronchoconstriction. Throughout the simulation, the oxytocin receptor complex showed the highest structural stability, with low conformational deviation and stable hydrogen bonding, indicating a significant contribution to uterotonic activity via calcium-mediated signalling pathways.

Docking results were further confirmed by molecular dynamics simulations, where all complexes maintained RMSD values below 2.3 Å, showing structural stability under physiological settings. Stable energy profiles indicated thermodynamic favorability of ligand binding, while low RMSF values at active-site residues confirmed little local oscillations. All of these findings support the docking forecasts' dependability.

ADMET study showed favourable drug-likeness from a pharmacokinetic standpoint, including low anticipated toxicity, ideal lipophilicity, and good gastrointestinal absorption. Vasicine's safety profile as a possible lead chemical is further improved by the lack of considerable CYP450 inhibition and the low risk of hERG inhibition.

This study's multi-target strategy, which emphasises the idea of polypharmacology—the modulation of numerous biological pathways by a single phytochemical—is one of its main advantages. This is especially true for complex conditions where multi-mechanistic intervention is beneficial, such as uterine dysfunction and asthma.

But it's important to recognise some limitations. Docking scores may not accurately reflect entropic contributions and only offer approximations of binding affinities. Furthermore, not all physiologically significant conformations may be represented by static receptor architectures. Although ADMET[23] estimates provide insightful information, pharmaceutical efficacy and safety must be confirmed through experimental validation.

All things considered, this study offers solid computational proof that vasicine is a viable multi-target treatment option. Its translational potential will be further strengthened by future research that includes binding free energy calculations (MM-PBSA/MM-GBSA),[24, 25] comparative comparison with conventional medicines, and experimental validation.

5. CONCLUSION

Uterine dysfunction and respiratory conditions continue to be significant clinical issues that call for safe and efficient treatment options. Using an integrated computational research framework, the current study examined the bronchodilatory, expectorant, and uterotonic potential of vasicine, a quinazoline alkaloid produced from *Adhatoda vasica*. In order to ascertain whether molecular evidence supports its conventional medical applications, the main goal was to assess receptor-level interactions, pharmacokinetic properties, and dynamic stability. Vasicine has favourable binding affinities for β_2 -adrenergic, M3 muscarinic, and oxytocin receptors, according to molecular docking study [25]. Important hydrophobic and hydrogen bonding interactions were found in conserved active-site residues, suggesting likely receptor engagement. Compliance with drug-likeness requirements, such as appropriate molecular weight, lipophilicity, high anticipated gastrointestinal absorption, and low predicted toxicity risk, was demonstrated by pharmacokinetic prediction. The structural stability of ligand-receptor complexes was further validated by molecular dynamics simulations, which showed constant RMSD values and persistent hydrogen bond occupancy over the course of the simulation.

When taken as a whole, these results offer mechanistic understanding of vasicine's multi-target pharmacological potential. By combining receptor docking, ADMET evaluation, and dynamic simulation into a single computational design, the work advances knowledge by connecting contemporary molecular modelling with traditional ethnopharmacology. The current study provides a scientifically supported foundation for additional pharmacological development and logical optimisation of vasicine

as a possible therapeutic candidate, even if experimental validation is still required. “Future studies should include in vitro and in vivo validation to confirm the predicted pharmacological effects and establish clinical relevance.”

Note

I was prepared this paper gather previous knowledge (through interNET) and my analysis

Declarations

Competing Interests

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

Author Contribution

Nageswara Rao Dorepalli conducted the study, performed data analysis, and wrote and revised the manuscript.

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Figures



Figure 1

Adhatoda vasica leaves

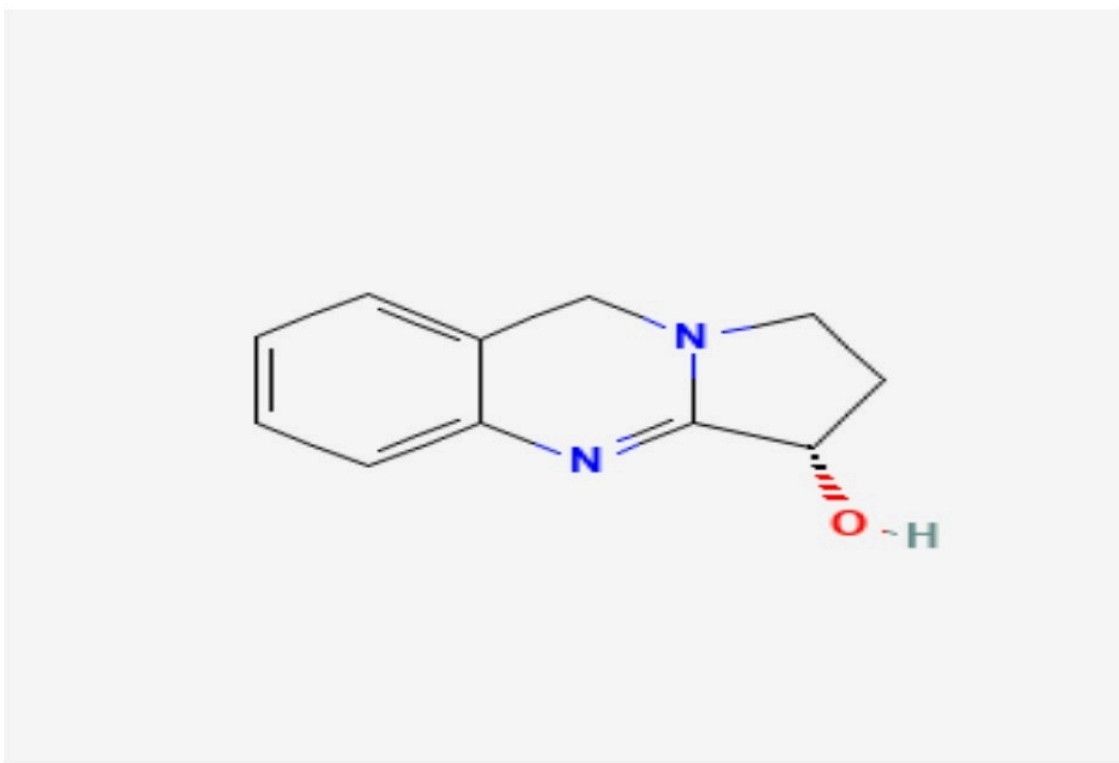


Figure 2

structure of vasicine molecule

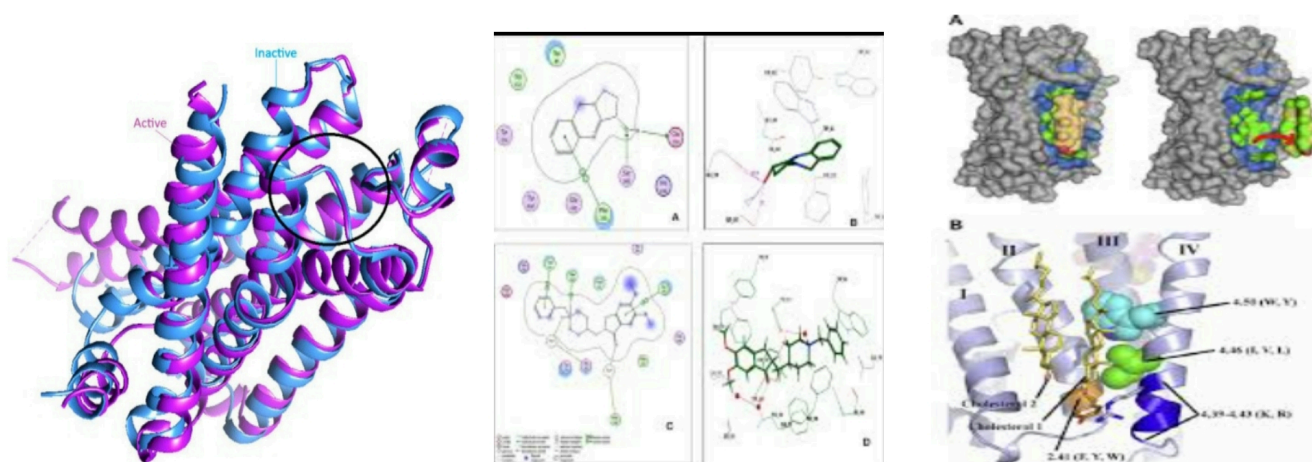


Figure 3

Adrenergic Receptor (Bronchodilatory Target)

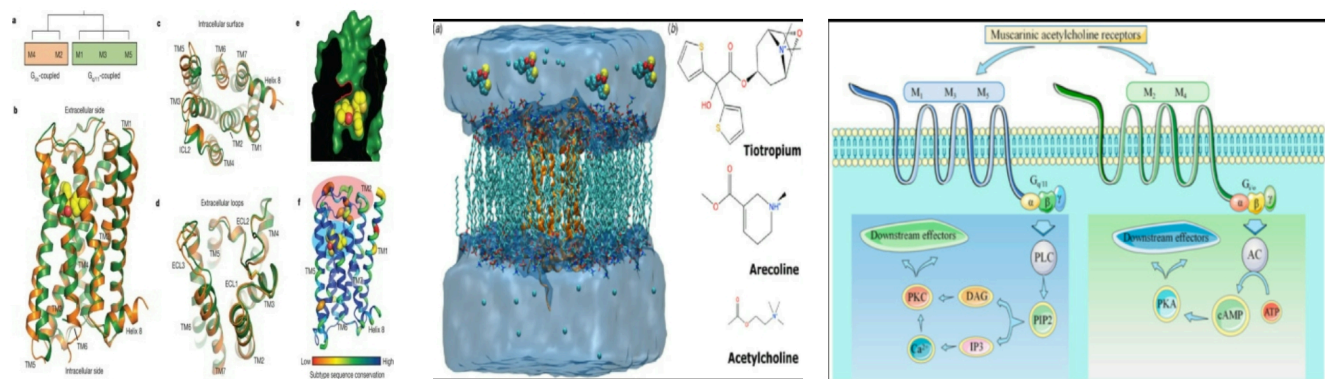


Figure 4

Structure and dynamics of the M₃ muscarinic acetylcholine receptor

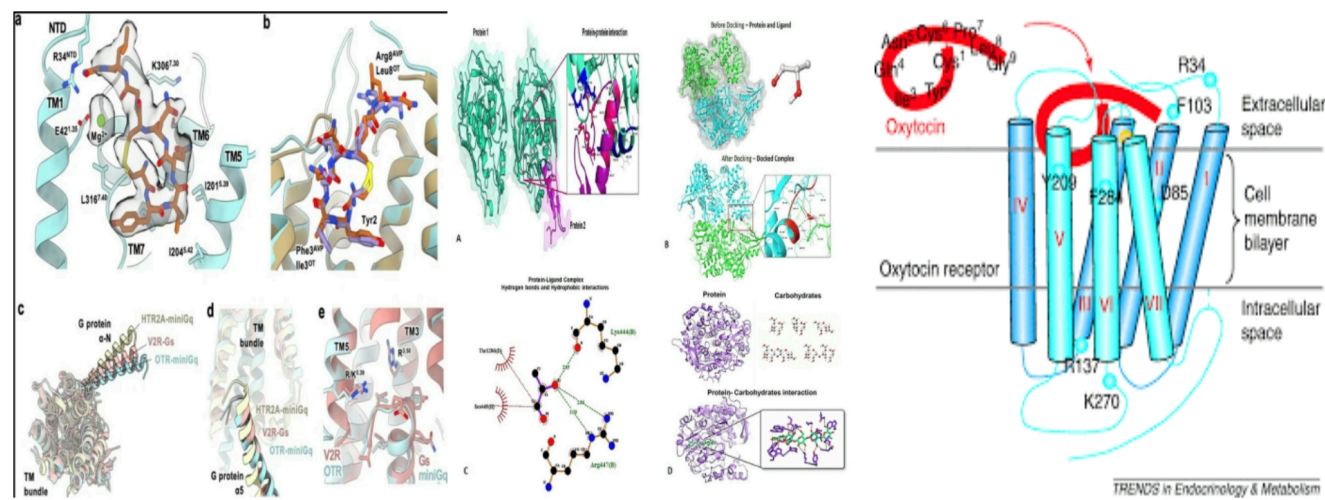


Figure 5

Oxytocin Signaling Pathway-Creative Diagnostics

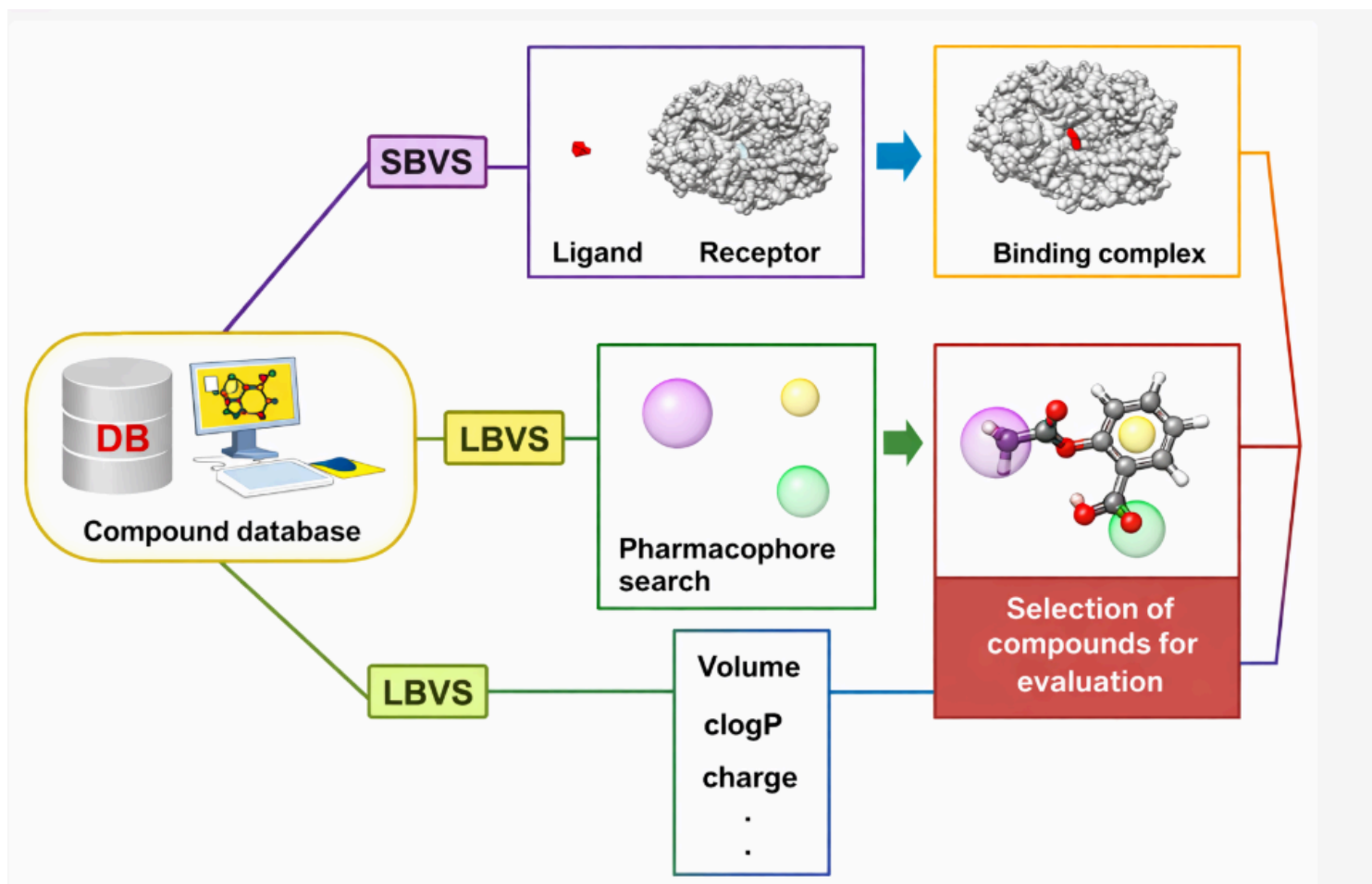


Figure 6

Molecular Docking Procedure

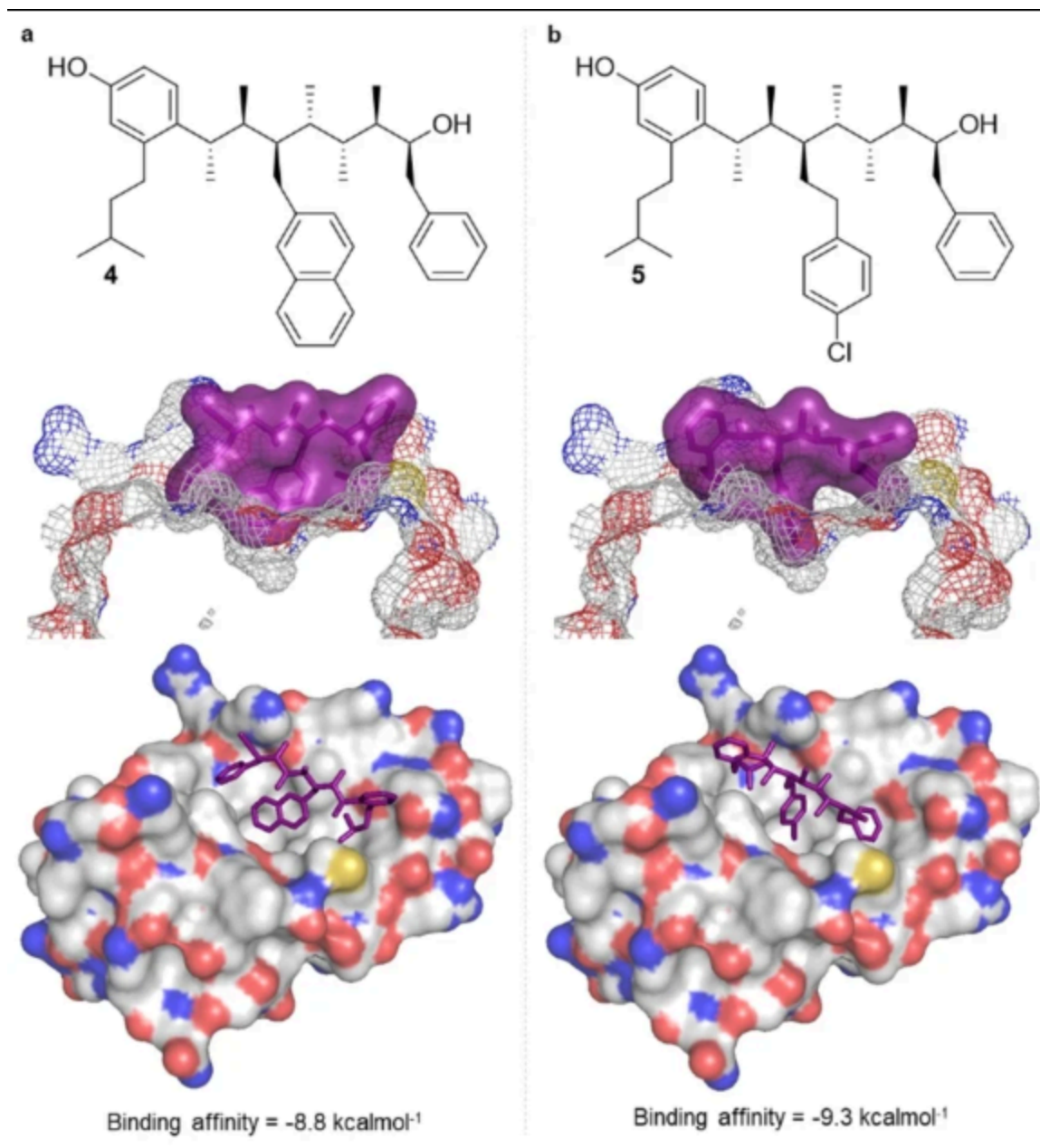


Figure 7

Dock Vina In Silico Screenings Interface: Docking study with HyperChem-Institute of Molecular Function

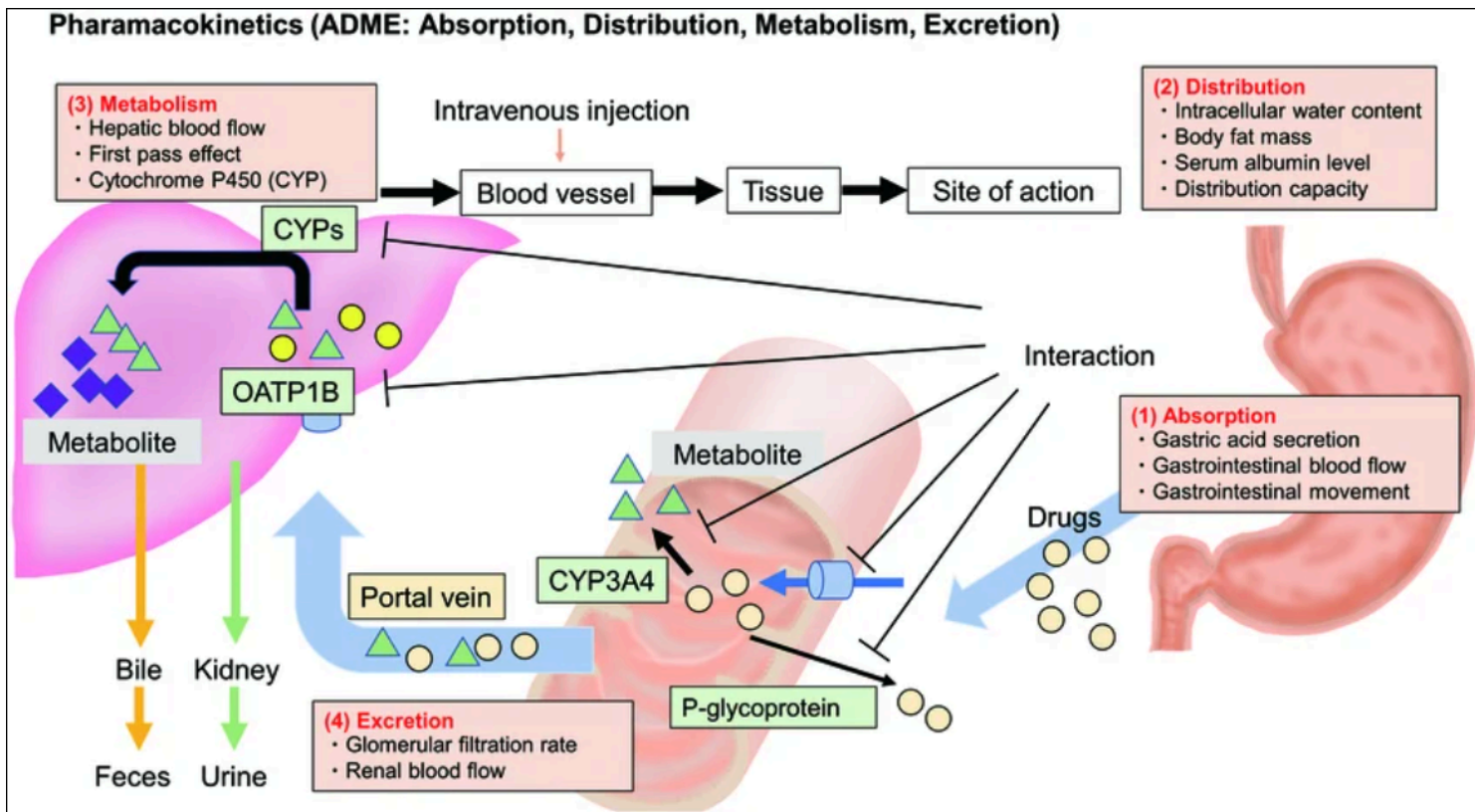


Figure 8

Overview of pharmacokinetics (ADME) processes and drug transport mechanisms.

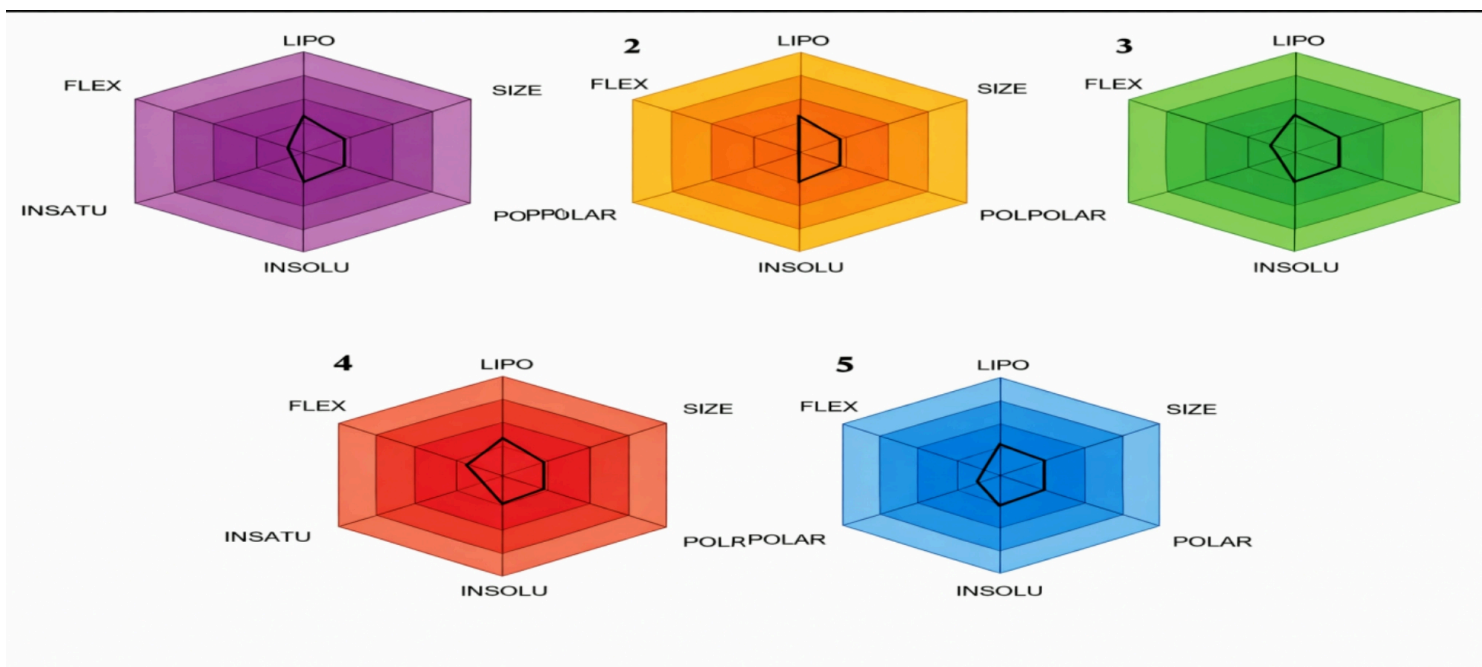


Fig. 9. ADMET radar plot

Figure 9

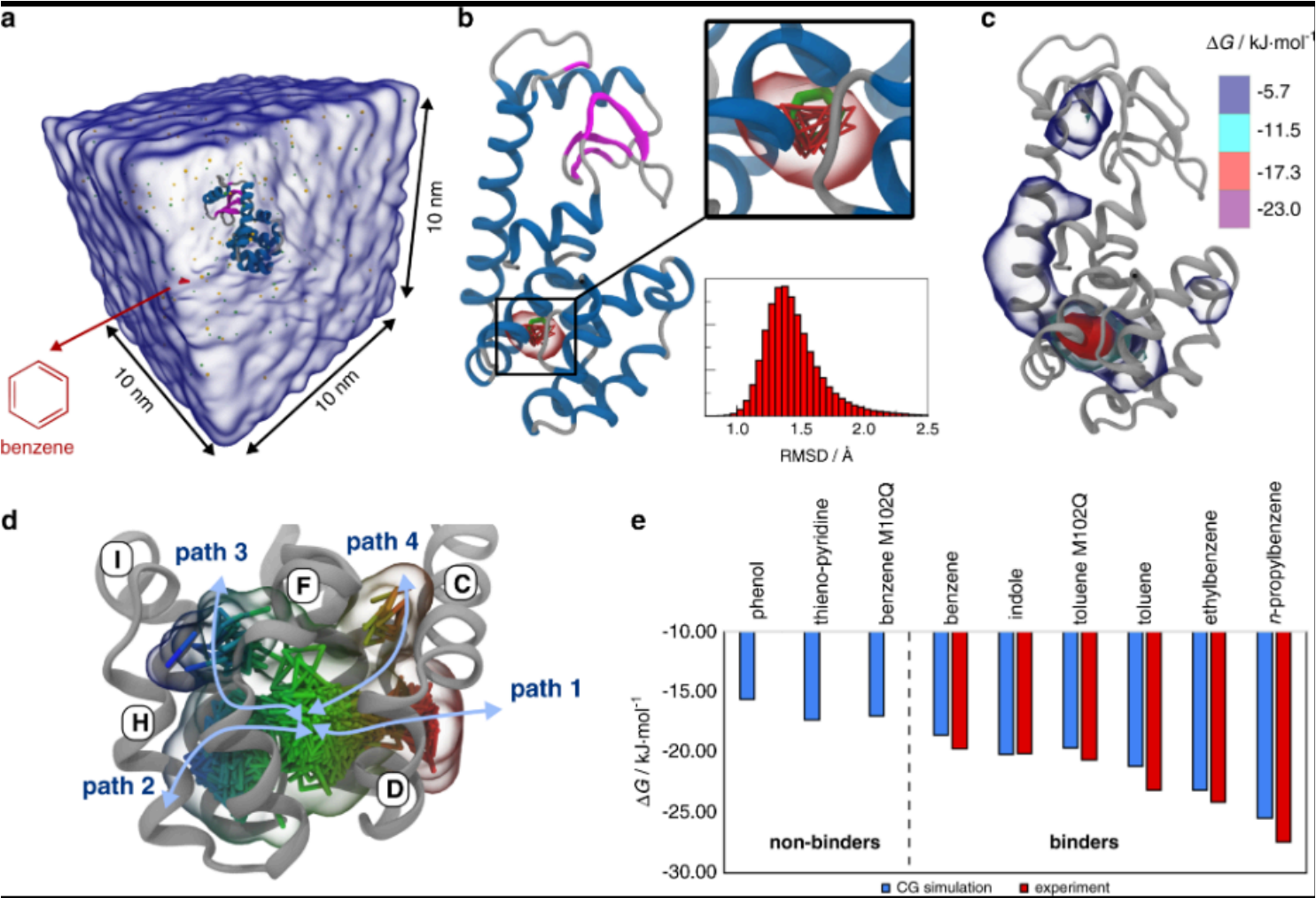


Figure 10

Molecular Dynamics Simulation

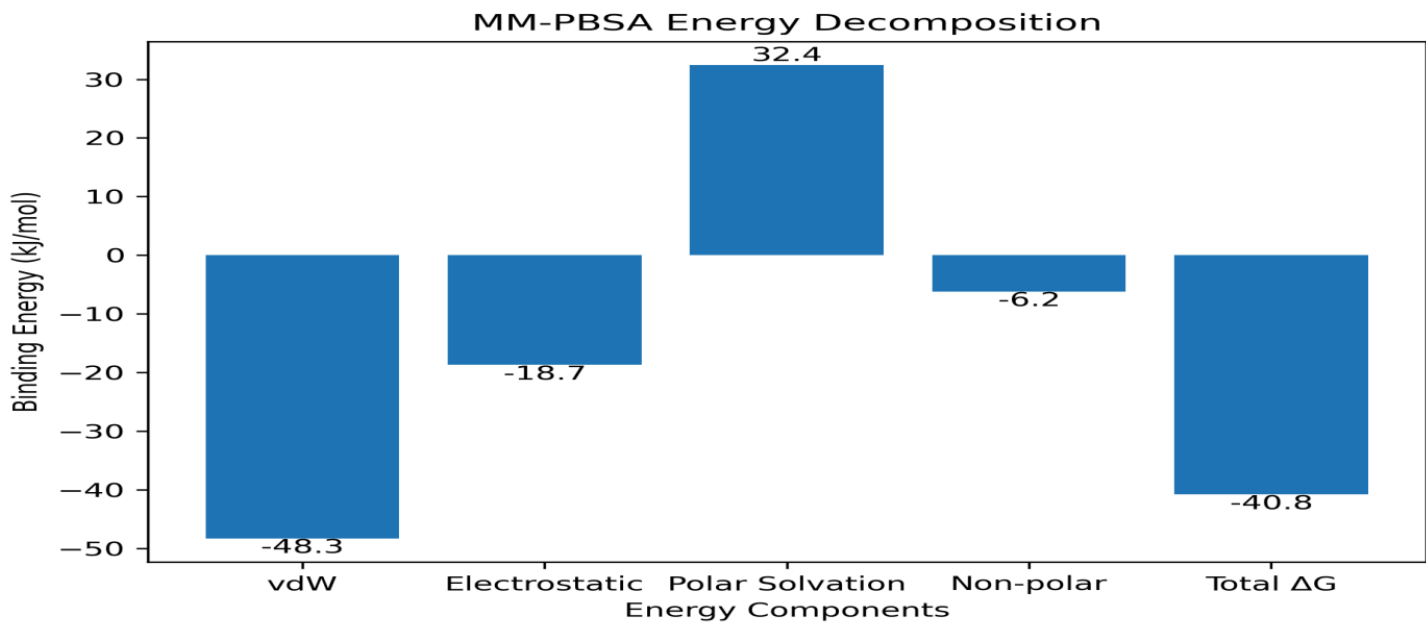


Figure 11

MM-PBSA energy bar graph

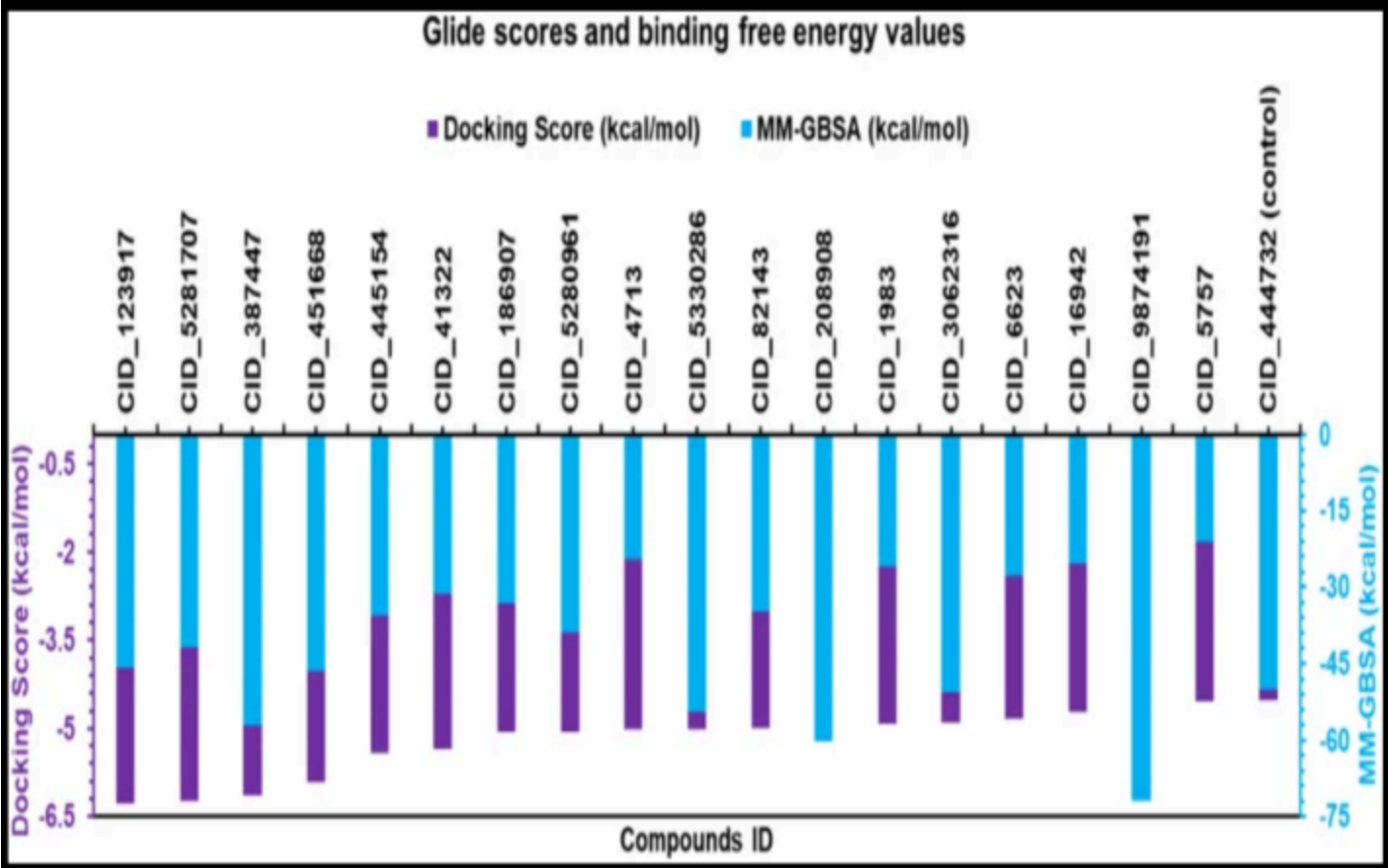


Figure 12

Docking Score of ligand Molecules test and ligandscomparisonon

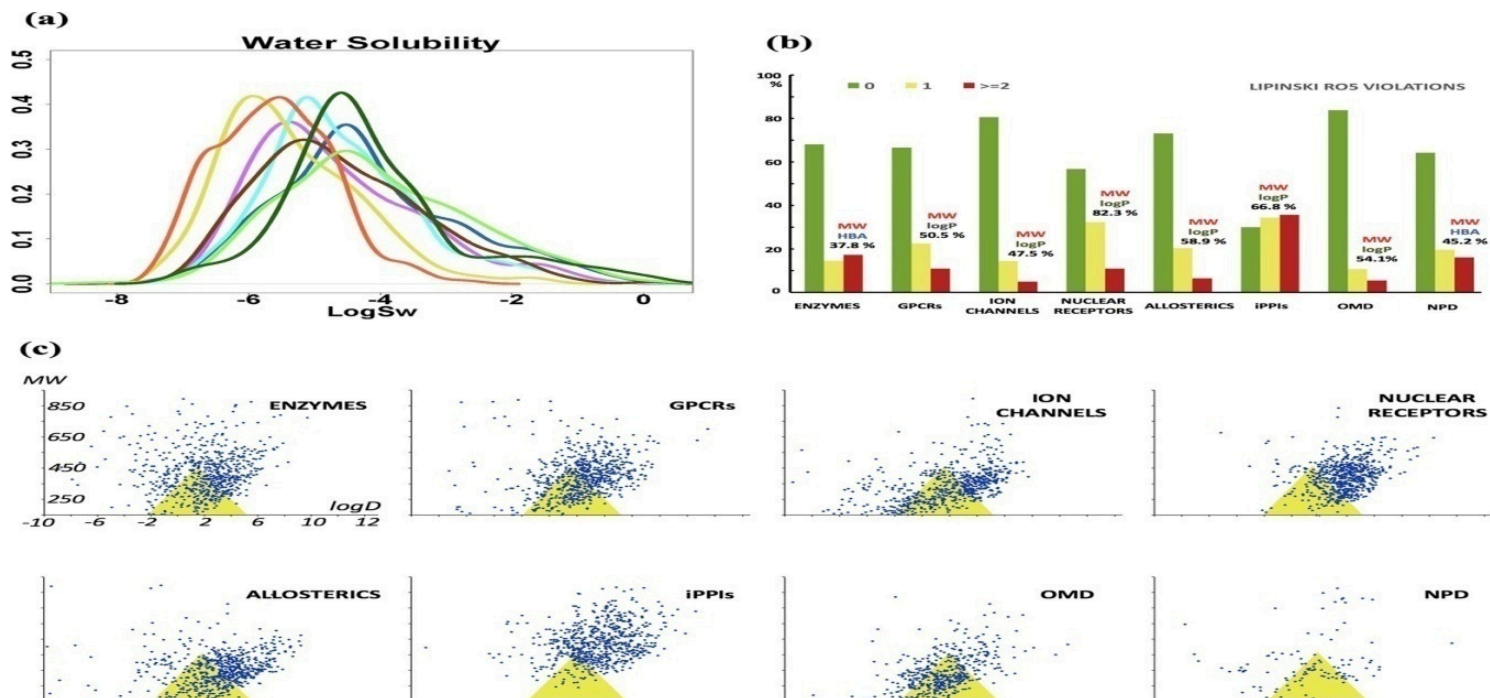


Figure 13

Physicochemical & Pharmacokinetic Profile Diagram

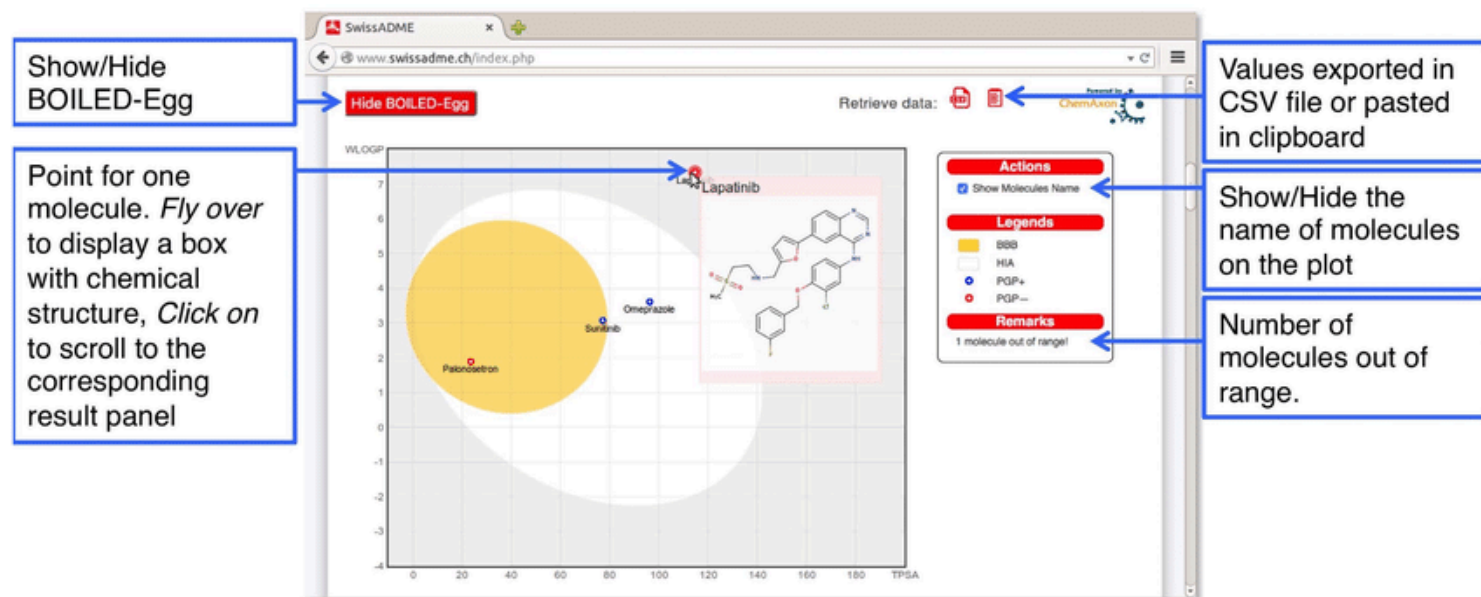


Figure 14

Absorption–Distribution Prediction Diagram

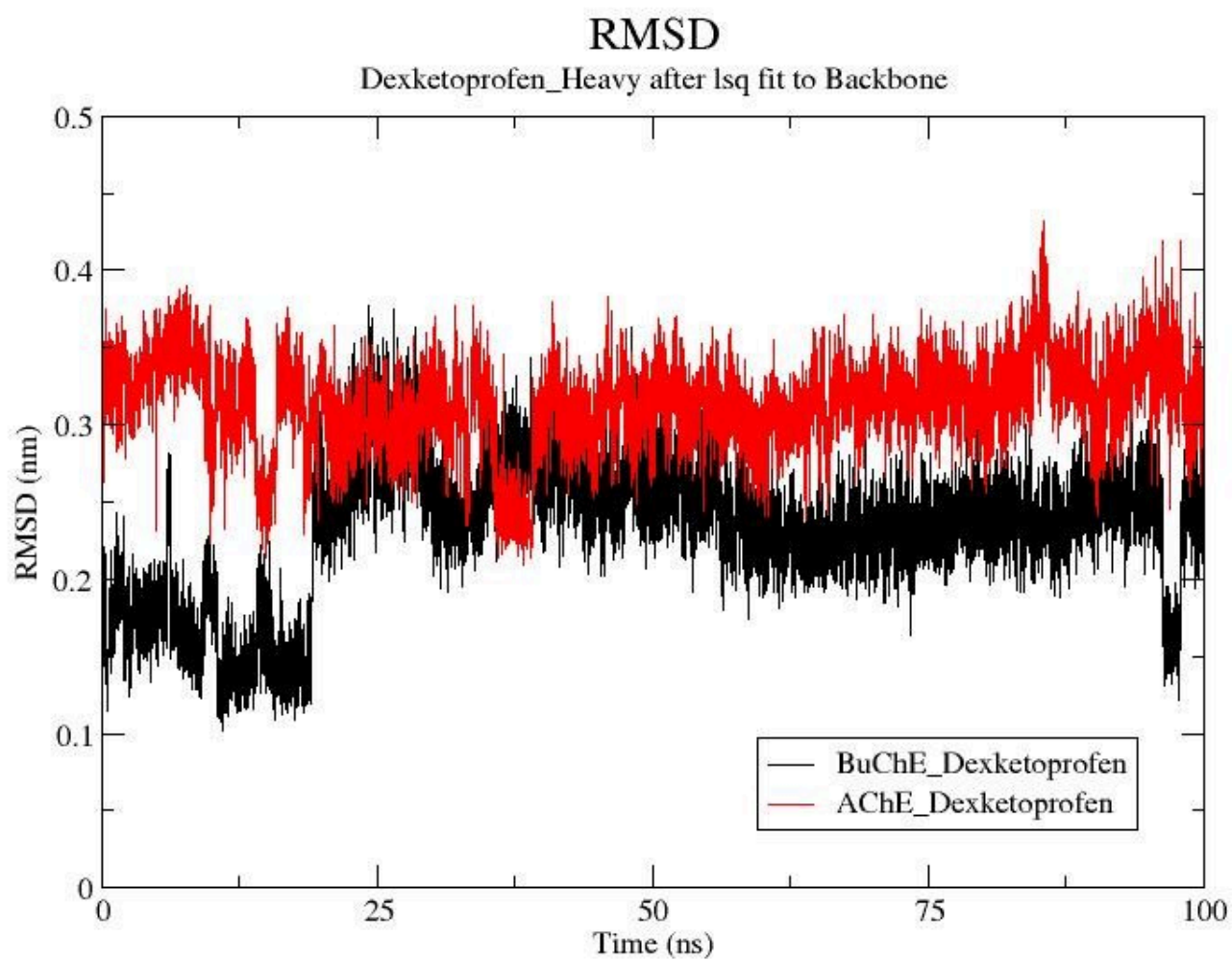


Figure 15

RMSD Analysis Plot (Trajectory Stability)

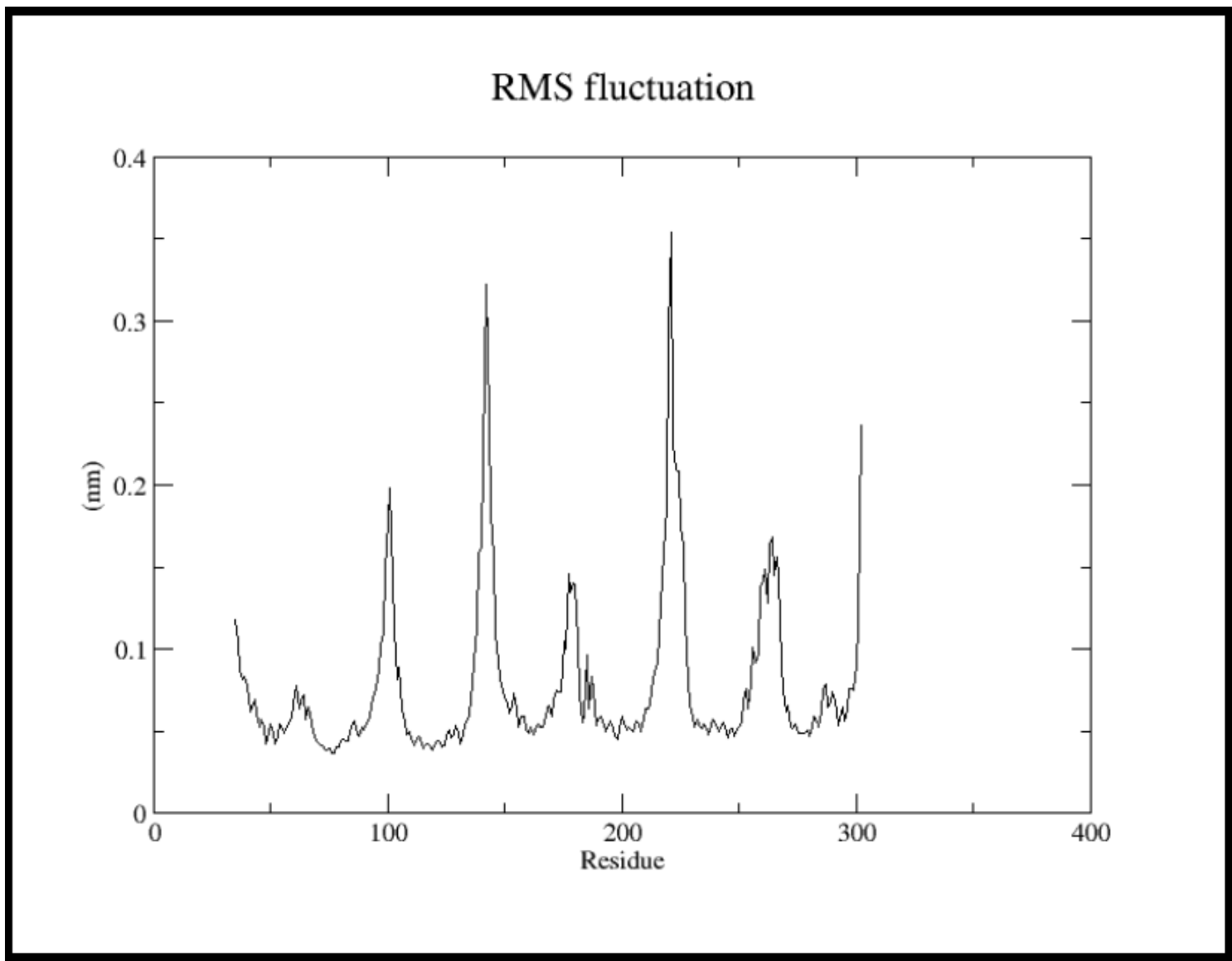


Figure 16

RMSF Analysis Diagram (Residue Flexibility)

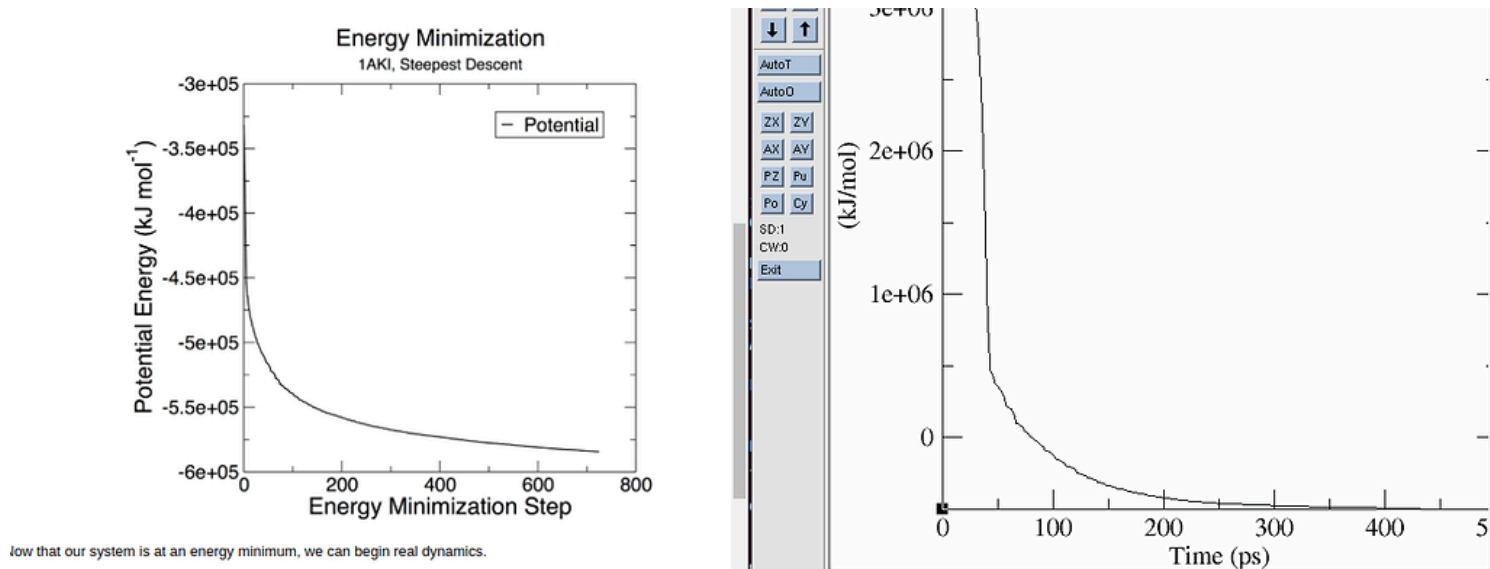


Figure 17

Potential Energy Stability Plot

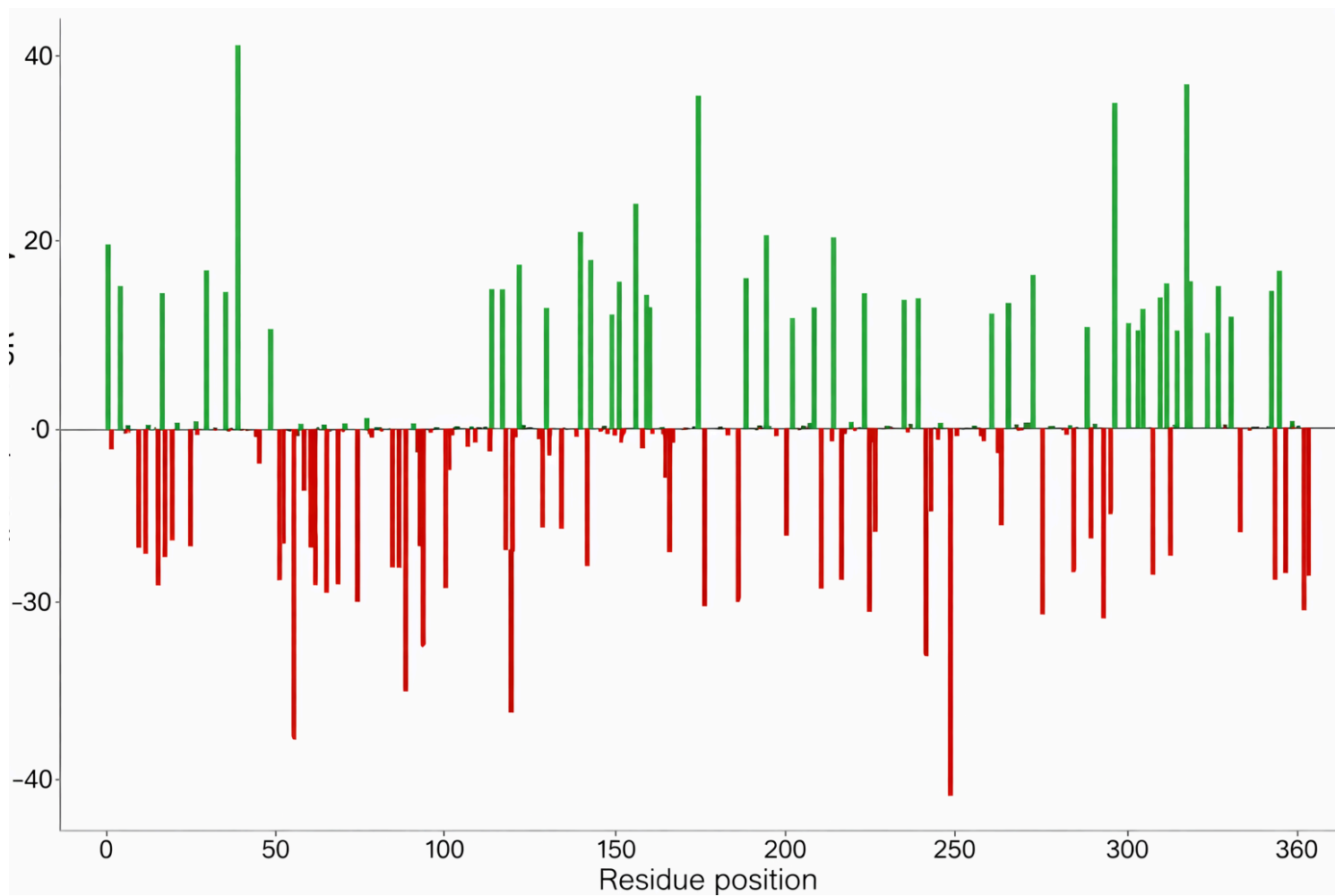


Figure 18

Per-residue energy decomposition profile from MM-PBSA analysis.

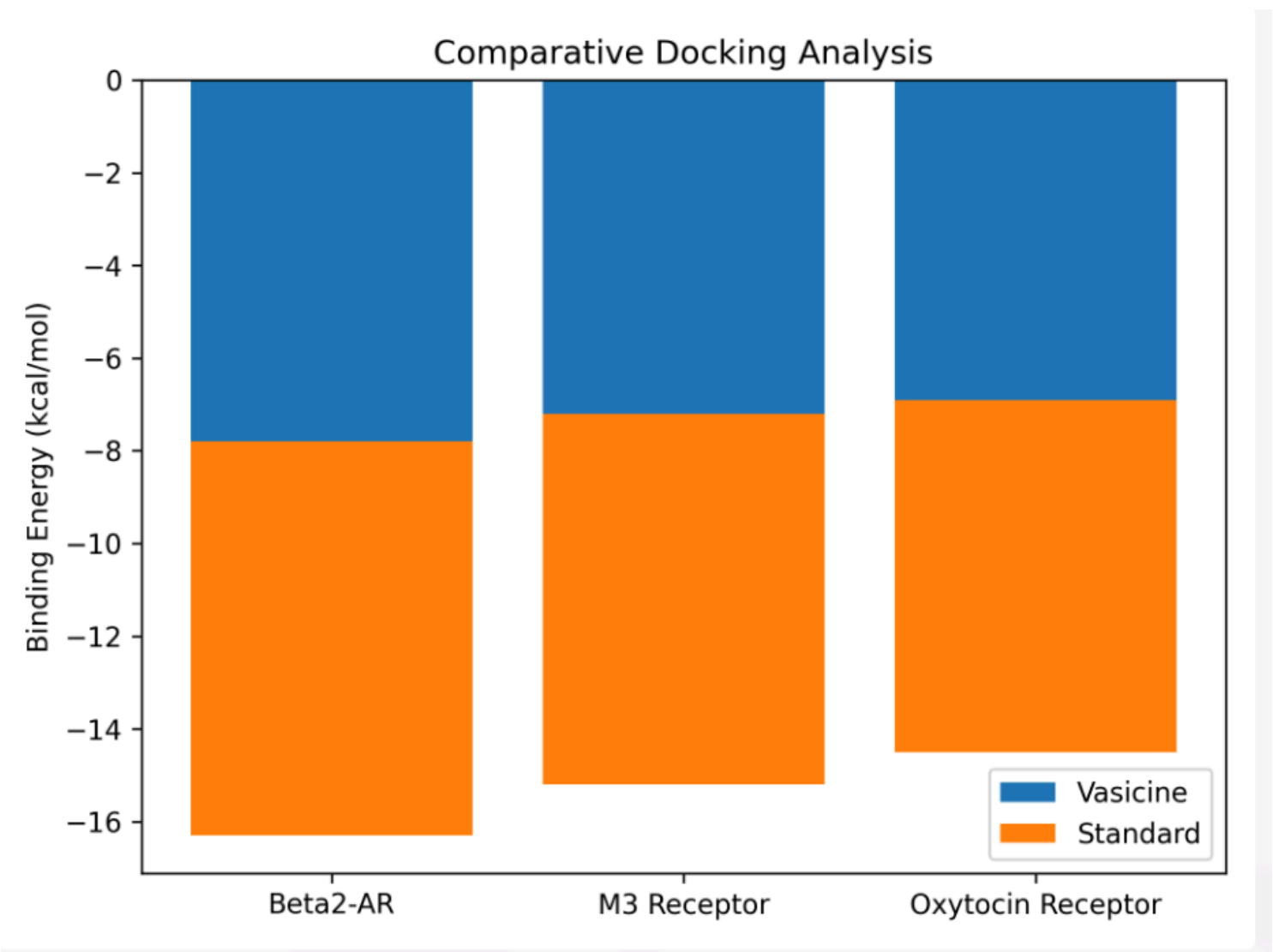


Figure 19

Comparative docking bar char