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Antioxidant Properties of Sundarban's plants: Molecular Docking, Drug-likeness, Pharmacokinetics and Toxicological Profiles of Bio-active Phytochemicals

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Abstract: Sundarbans is a mangrove forest with plants containing compounds that exhibit various pharmacological properties, including antioxidant activity. This study used computational analysis to assess the antioxidant activity, binding affinity (BA), pharmacokinetics, drug-likeness, and several toxicities of phytochemicals from Sundarbans plants for potential treatments of oxidative damage. The findings revealed that compounds such as Rutin (RTN), Amentoflavone (AFE), Procyanidin (PYN), Lutein (LTN), Asiatic Acid (AC), Lupeol Caffeate (LCE), and Ursolic Acid (UA) showed significant antioxidant activity as well as higher BA –8.3, –8.9, –10.2, –8.5, –9.9, –9.6, and –10 kcal/mol, respectively. Additionally, these compounds demonstrated higher hydrogen bond (HB) formation, which is crucial for developing new drugs. Pharmacokinetic analysis showed RTN's excellent solubility and bioavailability, while AFE, LCE, and PYN had moderate solubility. AC, AGN, and DGN exhibited high gastrointestinal absorption, with DGN having blood-brain barrier permeability, indicating neurological potential. All compounds demonstrated good intestinal absorption and Caco-2 permeability, ensuring efficient barrier crossing. None of the compounds inhibited cytochrome P450 enzymes, reducing drug-drug interaction risks. Toxicity predictions indicated most compounds were non-toxic, except UA, which showed hepatotoxicity, but no AMES toxicity or skin irritation was observed. These findings suggest that these compounds are promising bioactive agents for medicinal use, but further *in vitro* and *in vivo* studies, along with clinical investigations, are necessary to confirm their therapeutic potential and clarify their mechanisms of action.

Keywords: ADMET study; Antioxidant; *In silico*; Pharmacokinetics; Sundarbans

1. Introduction

A disruption in the equilibrium between the generation of reactive oxygen species (ROS) and antioxidant defenses is known as oxidative stress (Sachdev et al., 2021). "Reactive oxygen species" (ROS) encompass a diverse range of oxidant molecules with varying characteristics and biological functions, ranging from cellular signaling to cell damage (Sies et al., 2022). When ROS levels are excessive, they cause harmful changes to DNA, proteins, and lipids found in cells (Birben et al., 2012). Additionally, elevated ROS can lead to mtDNA mutations, unchecked growth, and carcinogenesis (Kotha et al., 2022). Oxidative stress is highly severe and can lead to significant tissue damage (Kulbacka et al., 2009). It is correlated with many fatal diseases (Sies et al., 2017). Oxidative DNA damage is already widely recognized as one factor contributing to cancer development (Hayes et al., 2020; Saha et al., 2017). Oxidative stress should be regarded as either a major or secondary cause of many CVDs, according to study findings from recent years (Dubois-Deruy et al., 2020). Numerous neurological conditions, including Parkinson's disease, Alzheimer's disease (AD), multiple sclerosis, amyotrophic lateral sclerosis (ALS), depression, and memory loss, have been connected to oxidative stress (Neves Carvalho et al., 2017). Numerous studies have demonstrated the connection between oxidative stress and lung conditions such as asthma and chronic obstructive pulmonary disease (COPD) (Sierra-Vargas et al., 2023). It is also correlated with several

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neurodegenerative conditions (Niedzielska et al., 2016).

To avoid oxidative damage, two medicinal plant extracts, *Andrographis paniculata* and *Swertia chirata,* signi[D]icantly reduce reactive oxygen species (ROS), including lipid peroxidation (Tripathi et al., 2007). Numerous studies have demonstrated the potential of plant polyphenols as antioxidants to prevent various illnesses brought on by oxidative stress (Boo, 2019; Pawlowska et al., 2019). Numerous antioxidants, including polyphenols, flavonoids, and vitamin E, are effective in preventing oxidative stress (Pizzino et al., 2017). Compounds having an antioxidant can prevent oxidative stress as well as oxidative damage (Santos-Sánchez et al., 2019). The Sundarbans has various plant species (Rahman, 2020), and they exhibit antioxidant activity.

A natural product is a chemical compound or substance produced by living organisms, including plants, animals, and microorganisms (Chowdhury & Al Hasan, 2025; Aktar et al., 2024; Bithi et al., 2025). Natural products like plant extracts, perhaps as pure chemicals or as standardized extracts, provide limitless opportunities for the discovery of novel medications (Jahan Tamanna et al., 2024). Medicinal plants have a variety of compounds that make them strong antioxidants and help to sequester ROS in functioning cells (Anbessa et al., 2024).

Sundarbans, the largest mangrove forest in the world, is biodiverse with a large number of floral species, about 334 (https://whc.unesco.org/en/list/798/). Chemical compounds derived from mangroves are used in folk and traditional medicine (Simlai & Roy, 2013). Antioxidants have shielded the body from the damaging effects of free radicals and play a vital role in reducing oxidative stress (Adwas et al., 2019; Gautam et al., 2022). They inhibit the production of free radicals, scavenge, and increase the degradation of free radicals (Jelinek et al., 2021). Synthesized antioxidants may exude toxic side effects and contraindicatory reactions, leading to problems such as allergies, irritant contact dermatitis, phototoxicity, and photoallergies (Ibrahim et al., 2021; Muflihah et al., 2021). Therefore, it is beneficial to locate natural antioxidants to lower health risks. Sundarbans plants thrive in extreme saline and oxidative stress conditions, likely enhancing their antioxidant potential beyond other natural sources (Nirjhar et al., 2017).

Computer-aided drug design (CADD) has the potential to reduce research costs by saving time and money on molecule synthesis (Abishad et al., 2021). *In silico* methods, such as molecular docking, have been extensively used in addition to analytical approaches to assess phytochemicals' capacity to block enzymes that adversely affect antioxidant activity (Kritsi et al., 2022). Furthermore, the molecule's physicochemical characteristics would offer crucial details about the early stages of drug development (Abishad et al., 2021). The study of a drug's absorption, distribution, metabolism, and excretion by the body is known as pharmacokinetics (Hedaya, 2023). Pharmacokinetic studies aim to optimize drug therapy by ensuring the drug concentration stays within the therapeutic range (Alagga et al., 2024). Although computational studies in drug discovery have limitations in model accuracy and may not fully capture biological complexity, they remain valuable for guiding experimental efforts, enhancing efficiency, and accelerating the identification of potential drug candidates (Sacan et al., 2012). The study aims to predict the antioxidant properties of Sundarbans plants using *in silico* approaches.

2. Materials and methods

2.1. In silico study

2.2. Pass prediction evaluation

Prediction of Activity Spectra for Substances (PASS) is a computational knowledge that predicts a substance's biological activity (Filimonov et al., 2018). Based on the structural formula of organic compounds, it can forecast more than 4,000 different biological activities, including pharmacological effects and methods of action (Filimonov et al., 2014). We employed a publicly available online resource in our investigation (https://www.way2drug.com/passonline/predict.php) to determine the P_a and P_i values of antioxidant activity of several compounds of Sundarbans plant. First, we evaluated over 400 phytochemicals from Sundarbans plants and performed PASS prediction based on the P_a value for antioxidant properties, followed by the docking stage. The 11 phytochemicals were selected based on their higher P_a values and lower P_i values compared to the other screened compounds.

2.3. Ligand preparation

The 3D structure of the phytochemicals AC (CID:119034), Aegicerin (AGN) (CID: 15558423), AFE (CID: 5281600), Beta Amyrone (BA) (CID: 12306160), Diosgenin (DGN) (CID: 99474), Friedeline (FDE) (CID: 91472), LCE (CID: 12149208), LTN (CID: 5281243), PYN (CID: 107876), RTN (CID: 5280805), and UA (CID: 64945) were downloaded in SDF format from the PubChem online chemical database (https://pubchem.ncbi.nlm.nih.gov/). We used Allinger's force field (MM2) method for minimization of the ligands by using the Chem3D 22.0 program package (Chowdhury et al., 2024; Al Hasan et al., 2025a). The two- dimensional structure of the chemical compounds is illustrated in **Fig. 1.**

2.4. Protein preparation

We chose the three-dimensional crystal structure of copper, zinc SOD (PDB ID: 1CB4, chain A and B) (Zhao et al., 2012), and the crystal structure of human glutathione peroxidase 7 (PDB ID: 2P31, chain A and B) (Maegawa et al., 2008) via the RCSB Protein Data Bank (https://www.rcsb.org/) After that, we eliminate any extra chains, lipids, water molecules, and other unnecessary elements by using PyMol (Bhuia et al., 2023a; Al Hasan et al., 2025b). Energy levels were then reduced using the SwissPDB Viewer program (Bhuia et al., 2023b; Jahan et al., 2025). At last, we saved the molecular docking process in PDBQT format.

2.5. Molecular docking and visualization

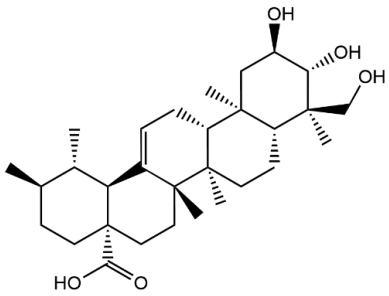
After preparing the ligands and proteins, we utilized PyRx software to determine the BA (Islam et al., 2025). The docking process involved the grid box's measurements (along the x-, y-, and z-axes, which were fixed to 85 × 80 × 75 Å) as well as the calculation involving 2000 steps for perfect docking. The protein-ligand complex was saved in CSV file format to collect the ligand in PDBQT format, and Discovery Studio software was used to visualize protein-ligand interaction as well as visualize non-bond interaction (Ghosh et al., 2025; Ferdous et al., 2024).

2.6. Determination of ADMET, Lipinski rule, pharmacokinetics, and drug likeness

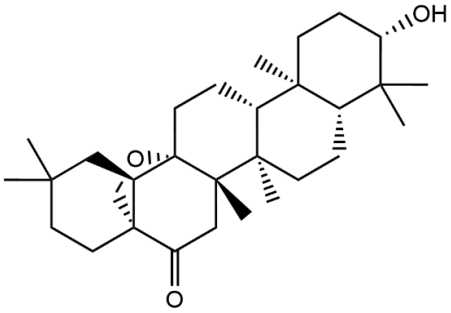
The SwissADME online platform (http://www.swissadme.ch/) are used for analysis pharmacokinetics, drug-likeness and physiological properties including solubility class, Lipinski rule and Bioavailability Score (Islam et al., 2024b; Akbor et al., 2023). Additionally, we used pkCSM (https://biosig.lab.uq.edu.au/pkcsm/prediction) online server utilized to predict ADMET evaluation (Islam et al., 2024a).

2.7. Acute toxicity prediction

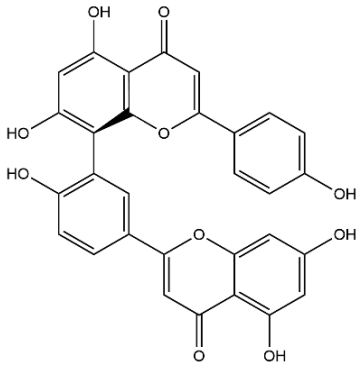
Although, various online tool involved to evaluate acute toxicity prediction but we utilized Stop Tox (https://stoptox.mml.unc.edu/) online server tool to predict various parameter such as: Acute Inhalation Toxicity, Acute Oral Toxicity, Acute Dermal Toxicity, Eye Irritation and Corrosion, Skin Sensitization and Skin Irritation and Corrosion (Al Hasan et al., 2024).



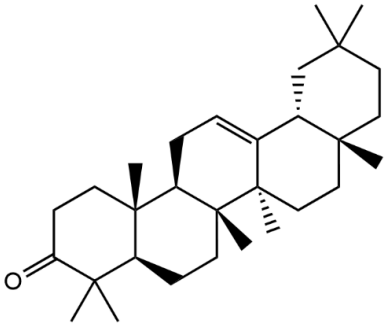
Asiatic Acid



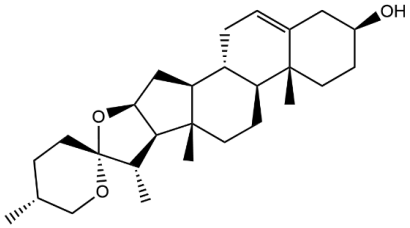
Aegicerin



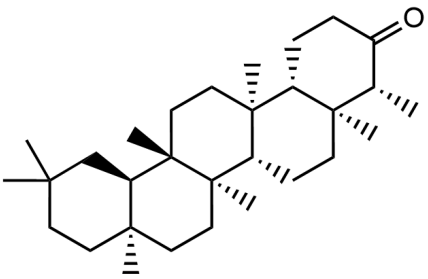
Amentoflavone



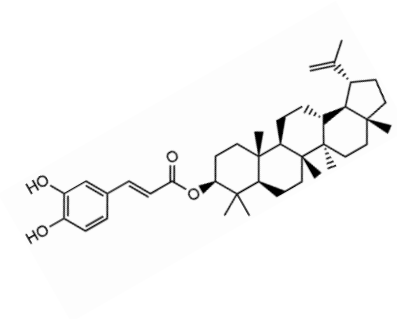
Beta Amyrone



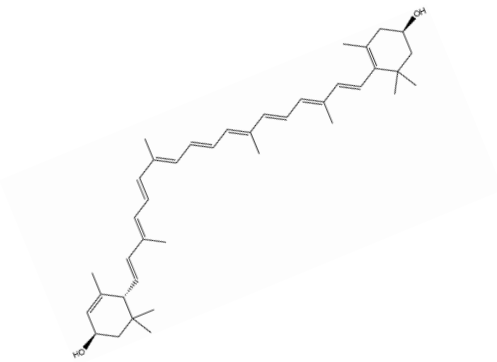
Diosgenin



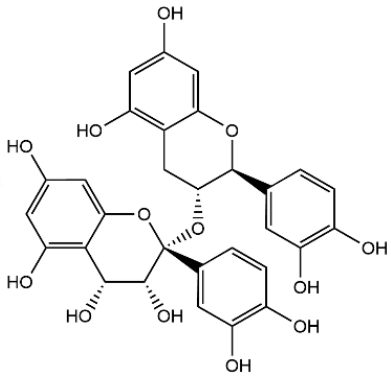
Friedeline



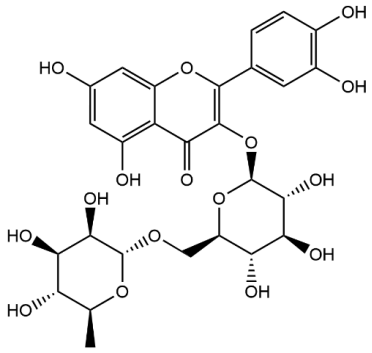
Lupeol Caffeate



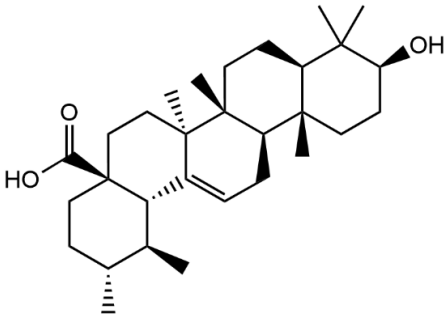
Lutein



Procyanidin



Rutin



Ursolic Acid

Fig. 1. The 2-dimentional chemical structures of Sundarbans phytochemicals.

3. Results and discussion

3.1. Pass prediction evaluation

PASS is a computational tool that predicts the biological activity of chemical compounds based on their molecular structure, using geometry to characterize buried protein regions and identify binding sites (Parasuraman, 2011). Pharmaceutical research, a laborious, high-risk procedure that takes 12 years and $800 million, tries to find new medications for illnesses (Poroikov & Filimonov, 2005). Pass prediction is essential for lowering expenses, speeding up the development process, and ranking compounds with the best chance of success (Arabi & Kawsar, 2023). We used pass prediction to evaluate the antioxidant activity of 11 compounds that were produced from Sundarbans plants. We used pass prediction to evaluate antioxidant activity that was produced from Sundarbans plants, whose values of P_a and P_i vary between 0.00 and 1.00. However, a higher P_a value indicates a higher probability of the compounds exhibiting pharmacological action (Lakhera et al., 2022). Overall, PASS is a trustworthy method for rapid screening and hypothesis generation overall, but its predictions should be carefully evaluated and supported by experimental confirmation (Lakens & DeBruine, 2021).

According to our pass prediction evaluation, RTN has the highest antioxidant activity (P_a value of 0.923), and DGN has the lowest antioxidant activity (P_a value of 0.190). Additionally, PYN, AFE, LTN, AC, and UA demonstrated significant antioxidant properties with higher P_a values 0.647, 0.652, 0.609, 0.399, and 0.302, respectively. However, the pass prediction data for all compounds is shown in **Table 1**.

Table 1. PASS calculated data of selected com-

Ligand name	PubChem CID	Antioxidant properties	
		P_a	P_i
AC	119034	0.399	0.012
AGN	15558423	0.249	0.036
AFE	5281600	0.652	0.004
BA	12306160	0.291	0.024
DGN	99474	0.190	0.061
FDE	91472	0.251	0.036
LCE	12149208	0.464	0.008
LTN	5281243	0.609	0.004
PYN	107876	0.647	0.004
RTN	5280805	0.923	0.003
UA	64945	0.302	0.023

AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid

3.2. Molecular docking and visualization of ligand-receptor interaction

3.2.1. Interaction with ICB4 receptor

In this study, we examined the binding interactions between different ligands and the ICB4 receptor. *In silico* study showed that PYN exhibited a BA of −10.2 kcal/mol, forming four HBs with LYS B: 9 (2.61), VAL B: 146 (1.90), ASN A: 51 (2.90), VAL A: 7 (2.43), CYS A: 144 (2.73), and GLY B: 54 (2.54) along with a hydrophobic interaction with LYS B: 9, LYS A: 9, VAL A: 146, and VAL B: 146. UA also showed a BA of −10 kcal/mol, forming 2 HBs with GLU A: 107 (2.92), and GLY A: 106 (2.54), in addition to a hydrophobic interaction with ALA A: 1, ALA B: 1, and ILE B: 149. DGN exhibited a BA of −9.7 kcal/mol, forming three HBs with ASP B: 11 (2.60), ASN B: 51 (2.57), and VAL B: 146 (2.16), as well as a hydrophobic interaction with VAL A: 7, VAL A: 146, and VAL B: 7. Again, AC showed a stronger BA of 9.9 kcal/mol, forming four HBs with SER A: 109 (2.52), ALA B: 1 (2.46), SER B: 109 (2.60), and GLU A: 107 (2.91), along with a hydrophobic bond with ALA A: 1, ALA B: 1, and ILE B: 149. The other two compounds FDE and LCE, also showed a BA of −9.7 kcal/mol and −9.4 kcal/mol, respectively.

3.2.1. Interaction with 2P31 receptor

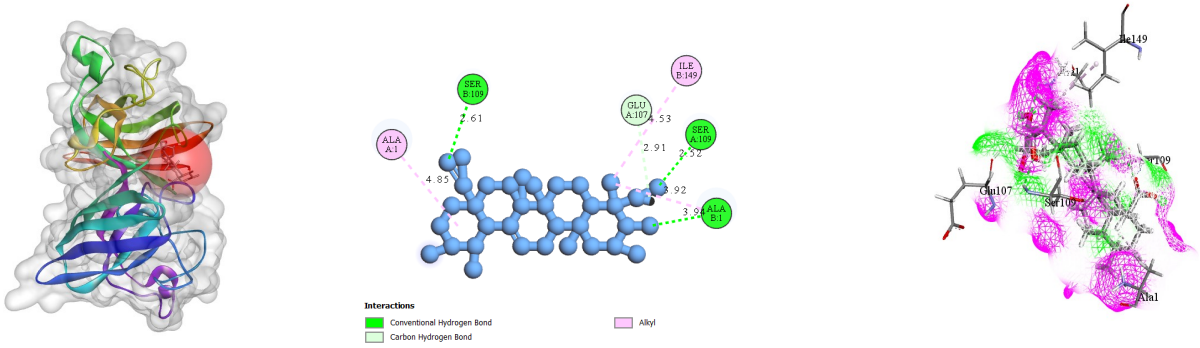
In this work, we investigated how different ligands bind to the 2P31 receptor. LCE exhibited a BA of −9.6 kcal/mol, forming two HBs with ARG B: 106 (2.45) and SER A: 102 (2.62), as well as two hydrophobic bonds with GLU B: 99 and ARG A: 106. AFE showed a BA of −8.9 kcal/mol, forming four HBs with GLU B: 56 (3.08), SER A: 102 (2.81), ARG A: 106 (2.48), and THR B: 60 (2.41), as well as 3 hydrophobic bonds: GLU B: 56, ARG A: 105, and ARG A: 106. LTN has a BA of −8.5 kcal/mol, forming one HBs with GLU B: 56 (2.46), along with five hydrophobic bonds with ARG A: 65, ALA A: 66, ARG A: 106, PHE B: 103, and TYR B: 108. BA exhibited considerable strong BA of −8.4 kcal/mol, forming two HBs with LYS B: 98 (2.60) and SER B: 102 (2.22). AGN, DGN, and RTN exhibited similar BA of −8.3 kcal/mol. RTN formed four HBs with ARG A: 106 (2.36), CYS B: 57 (2.49), GLU B: 56 (2.72), and LYS A: 98 (2.58), along with two hydrophobic bonds with ARG A: 105 and ARG A: 106, while DGN formed two HBs with ASN A: 80 (2.24) and ARG A: 105 (2.94) and AGN formed one HBs with ASP B: 61 (2.83).

BA has arguably been the most important quantitative metric to describe the interaction between a ligand and targeted proteins (Hasan et al., 2019). Drug-receptor interactions, stability, and specificity are improved by HBs in molecular docking, which guarantees strong target modulation at lower dosages for therapeutic efficacy and safety (Prottay et al., 2024). For the ICB4 receptor, PYN, DGN, AC, LCE, and UA exhibited a significant BA as well as strong HB and hydrophobic bond. Ascorbic acid, considered one of the standard antioxidants, had a BA of −7.120 against the 1CB4 receptor (Hwang & Lee, 2023; Amanat et al., 2021). Whereas, in our study, the analysis of the 2P31 receptor RTN, LTN, DGN, LCE, and AFE showed a considerable BA as well as strong HBs and hydrophobic bonds. Our final docking results indicate that RTN, LTN, DGN, AFE, PYN, AC, LCE, and UA can be options of promising medication candidates because of their improved BA, HBs and interaction profiles. All the data are given in **Table 2** and **Fig. 2**.

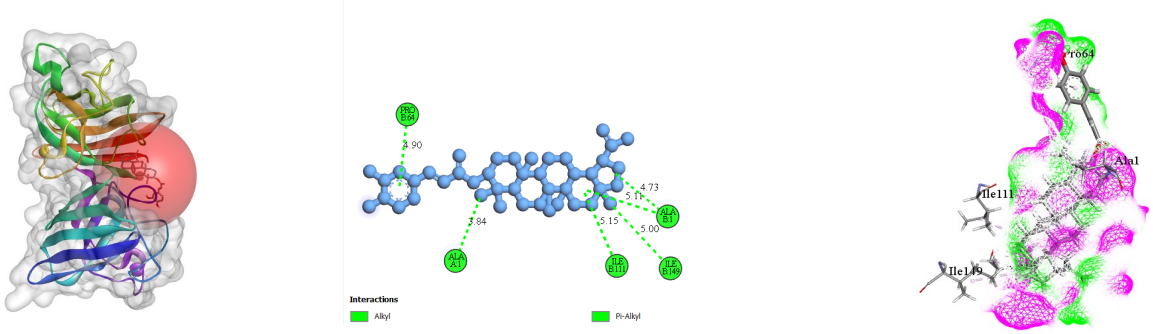
Table 2. Top selected compounds according to binding affinity and their amino acid residue inter-

PDB ID	Ligands	Binding affinity (kcal/mol)	AA Residues		
			No of HB	HB (Bond length) (A°)	Others
ICB4	AC	–9.9	4	SER A: 109 (2.52), ALA B: 1 (2.46), SER B: 109 (2.60), GLU A: 107 (2.91)	ALA A: 1, ALA B: 1, ILE B: 149
	DGN	–9.7	3	ASP B: 11 (2.60), ASN B: 51 (2.57), VAL B: 146 (2.16)	VAL A: 7, VAL A: 146, VAL B: 7
	FDE	–9.7	-	-	ALA B: 1, ILE B: 111, ILE B: 149
	LCE	–9.4	-	-	ALA A: 1, ALA B: 1, ILE B: 111, ILE B: 149, PRO B: 64
	PYN	–10.2	6	LYS B: 9 (2.61), VAL B: 146 (1.90), ASN A: 51 (2.90), VAL A: 7 (2.43), CYS A: 144 (2.73), GLY B: 54 (2.54)	LYS B: 9, LYS A: 9, VAL A: 146, VAL B: 146
	UA	–10	2	GLU A: 107 (2.92), GLY A: 106(2.54)	ALA A: 1, ALA B: 1, ILE B: 149
2P31	AGN	–8.3	1	ASP B: 61 (2.83)	ARG A: 106, LYS A: 98
	AFE	–8.9	4	GLU B: 56 (3.08), SER A: 102 (2.81), ARG A: 106 (2.48), THR B: 60 (2.41)	GLU B: 56, ARG A: 105, ARG A: 106
	BA	–8.4	2	LYS B: 98 (2.60), SER B: 102 (2.22)	ARG B: 106
	DGN	–8.3	2	ASN A: 80 (2.24), ARG A: 105 (2.94)	PRO A: 113, TYR A: 43, HIS A: 78
	LCE	–9.6	2	ARG B: 106 (2.45), SER A: 102 (2.62)	GLU B: 99, ARG A: 106
	LTN	–8.5	1	GLU B: 56 (2.46)	ARG A: 65, ALA A: 66, ARG A: 106, PHE B: 103, TYR B: 108
	RTN	–8.3	4	ARG A: 106 (2.36), CYS B: 57 (2.49), GLU B: 56 (2.72), LYS A: 98 (2.58)	ARG A: 105, ARG A: 106

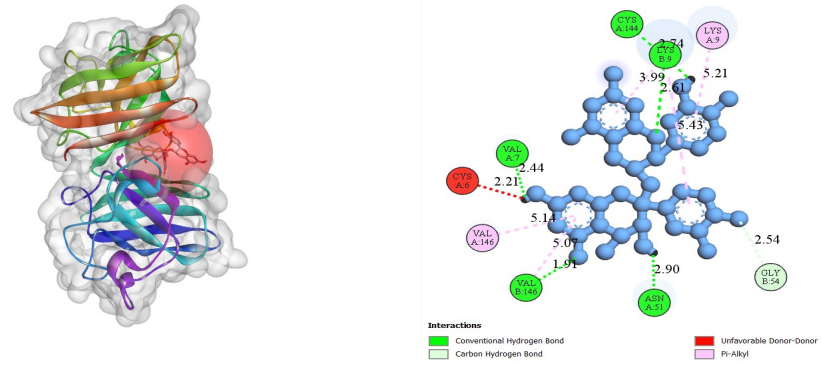
AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid



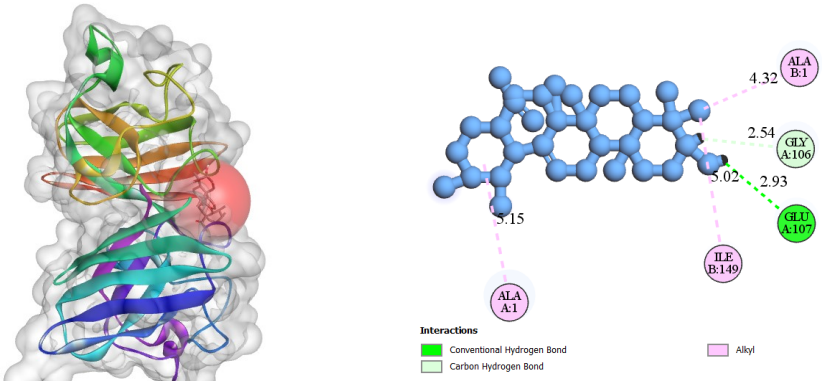
AC vs ICB4



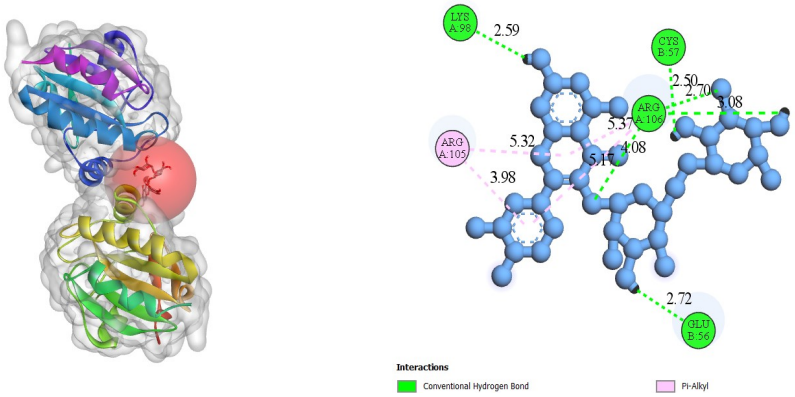
LCE vs **ICB4**



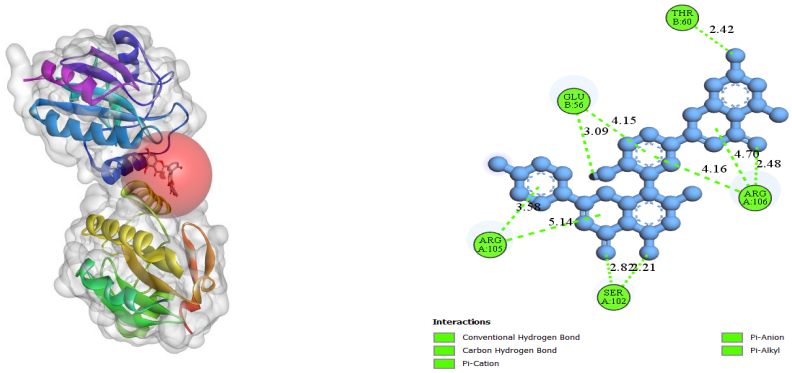
PYN vs ICB4



UA vs ICB4



RTN vs 2P31



AFE vs 2P31

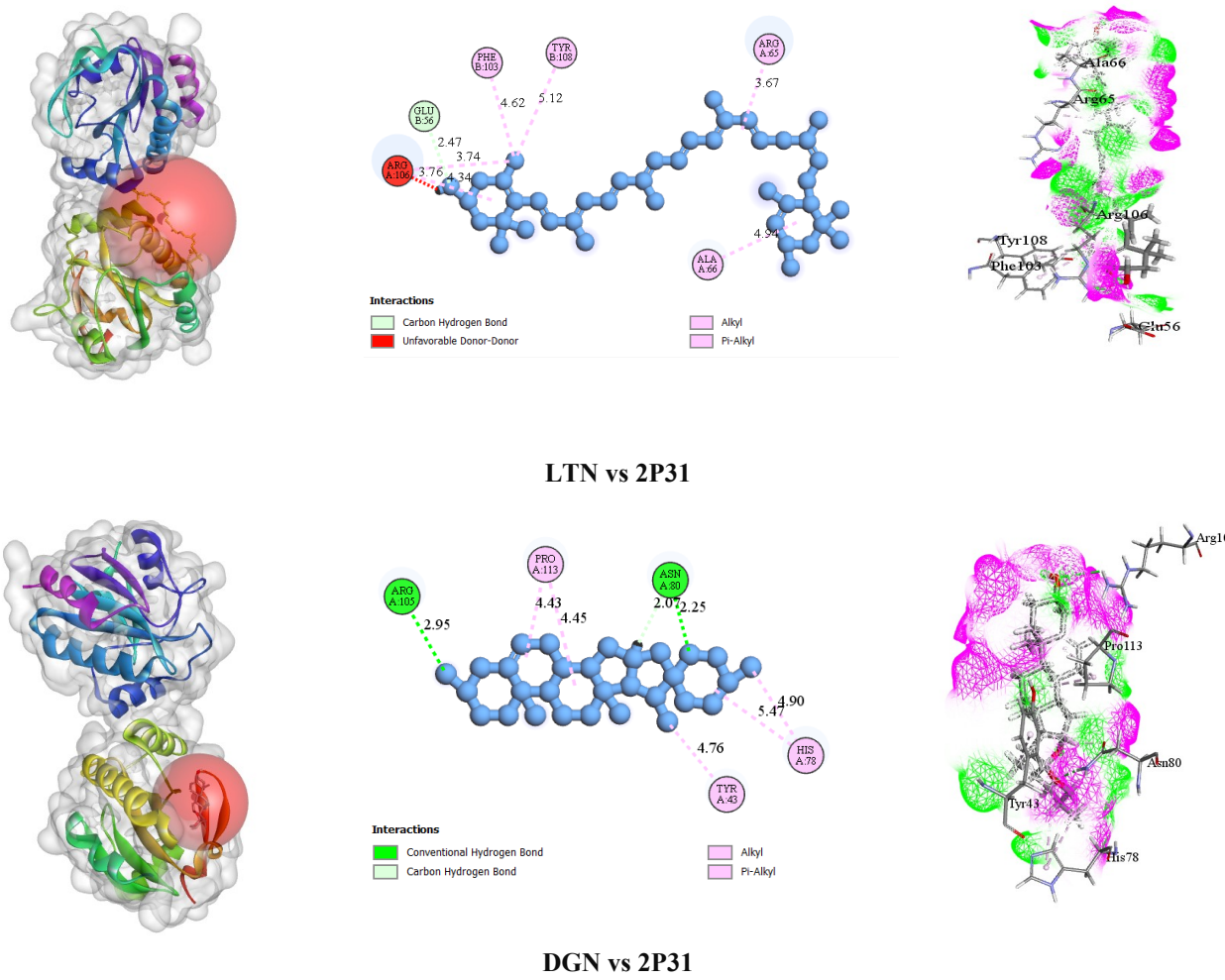


Fig. 2. The 2D and 3D non-bond interaction of selected compounds with selected ICB4 and 2P31 receptors. [AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid]

3.3. Lipinski rule, pharmacokinetics and drug likeness evaluations

Pharmacokinetics is the study of how the body reacts to drugs through metabolism, excretion, distribution, and absorption. Absorption: Explains how drugs enter the body and move from the point of administration into the blood. Distribution: Explains how the medication travels via the blood to different human tissues. Metabolism: Describes the biotransformation process of the drug by the liver, kidney, or digestive tract so that the drug can be excreted. Excretion: Describes the elimination of drug compounds from the body (Bereda, 2022; Adepu & Ramakrishna, 2021; Talevi & Bellera, 2024). Pharmacokinetics plays a critical role in drug development and clinical practice (Lin & Lu, 1997). It provides the scientific basis for determining appropriate dosing regimens, ensuring that drugs achieve therapeutic concentrations without reaching toxic levels (Gross, 1988). It also helps anticipate drug interactions and direct modifications in special populations, which eventually leads to more accurate and efficient treatment (Tannenbaum & Sheehan, 2014). The pharmacokinetic parameter was predicted using the SwissADME online tool. Our special physicochemical and ADMET features showed important differences among the 11 compounds AC, AGN, AFE, BA, DGN, FDE, LCE, LTN, PYN, RTN, and UA. The Lipinski rule of Five is a set of rules used in drug discovery to evaluate orally deliverable compounds according to characteristics such as molecular mass, clogging, and the number of donors and acceptors of HBs (Islam et al., 2024a). According to our study, all compounds adhere to Lipinski's rule except AFE, LCE, PYN, and RTN with a good bioavailability score, respectively. The molecular weights of AC, AGN, BA, FDE DGN, and UA range from 414.62 g/mol to 488.7 g/mol. The other molecules, such as AFE, LCE, LTN, PYN, and RTN, showed heavier molecular weights ranging from 538.46 g/mol to 610.52 g/mol. According to solubility, AC, AGN, AFE, BA, FDE, and UA are poorly soluble. DGN and PYN are moderately soluble. The results demonstrated that RTN is fully soluble and LCE is insoluble. The data showed that only DGN maintains BB permeability. The result also showed that all the compounds are not CYP1A2 inhibitors; also, they don't inhibit the CYP2C19 enzyme, indicating their high potential as a therapeutic drug. Our study highlights that these compounds such as RTN, AFE, PYN, LTN, AC, LCE, and UA maintain strong pharmacokinetic profiles with good bioavailability despite some exceeding Lipinski's rule limits. RTN is unique in that it is completely soluble, while AFE and PYN show moderate solubility and bioavailability. AC, AGN, and DGN express high GI absorption. The compound's potential as a therapeutic medicine is further supported by the fact that none of them inhibit CYP1A2 or CYP2C19. However, pharmacokinetics and drug likeness data show in **Table 3**.

Table 3. Data of pharmacokinetics and drug likeness properties of the selected compounds.

Parameters/ ligands	AC	AGN	AFE	BA	DGN	FDE	LCE	LTN	PYN	RTN	UA
Physiochemical properties											
Molecular mass (g/mol)	488.7	456.7	538.46	424.7	414.62	426.72	588.86	568.87	594.52	610.52	456.70
Number of aromatic heavy atoms	0	0	32	0	0	0	6	0	24	16	0
Number H-bond acceptors	5	3	10	1	3	1	4	2	13	16	3
Number H-bond donors	4	1	6	0	1	0	2	2	10	10	2
Molar Refractivity	139.24	134.56	146.97	133.92	121.59	134.39	178.54	186.76	147.52	141.38	136.91
TPSA (Å²)	97.99	46.53	181.8	17.07	38.69	17.07	66.76	40.46	229.99	269.43	57.53
Lipophilicity											
Log $P_{o/w}$ (MLOGP)	4.14	5.12	0.25	6.82	4.94	6.92	6.78	10.40	–0.60	–3.89	5.82
Water solubility											
Solubility class	Poorly soluble	Poorly soluble	Poorly soluble	Poorly soluble	Moderately soluble	Poorly soluble	Insoluble	-	Moderately soluble	Soluble	Poorly soluble
Pharmacokinetics											
GI absorption	High	High	Low	Low	High	Low	Low	-	Low	Low	Low
BBB permeant	No	No	No	No	Yes	No	No	-	No	No	No
P-gp substrate	Yes	No	No	No	No	No	No	-	No	Yes	No
CYP1A2 inhibitor	No	No	No	No	No	No	No	-	No	No	No
CYP2C19 inhibitor	No	No	No	No	No	No	No	-	No	No	No
Drug-likeness											
Lipinski	Yes; 0 vio	Yes; 1 vio	No, 2 vio	Yes; 1 vio	Yes, 1 vio	Yes; 1 vio	No; 2 vio	-	No; 3 vio	No; 3 vio	Yes; 1 vio
Bioavailability score	0.56	0.55	0.17	0.55	0.55	0.55	0.17	-	0.17	0.17	0.85

BBB: Blood-Brain Barrier; GI: Gastrointestinal; TPSA: Topological Polar Surface Area; AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid; Vio: Violation

3.4. ADME Studies

ADME is the abbreviation for Absorption, Distribution, Metabolism, and Excretion that describes how a drug moves throughout and is processed by the body (Mahalakshmi et al., 2024). Our investigation suggests that UA showed higher water solubility (–3.072 log mol/L), the highest human intestinal absorption (100%), and high Caco-2 permeability (1.171). Our ADME studies demonstrated that AC, LCE, PYN, and AFE showed higher water solubility (–3.008, –3.787, –2.892, and –2.892 log mol/L), high human intestinal absorption (62.855%, 94.06%, 55.527%, 84.356%), and moderate Caco-2 permeability (0.479, 0.507, 0.131, 0.145). Although RTN has higher water solubility (–2.892 Log mol/L), it has lower intestinal absorption and lower Caco-2 permeability. Our study also said that LTN has higher Caco-2 permeability (1.251) and high intestinal absorption (89.781%) but lower water solubility. Our result also said that none of them inhibit several metabolizing enzymes, such as CYP2D6, CYP2C19, CYP1A2, CYP2C9, and CYP3A4. Our result also suggests that RTN and LCE showed higher total clearance, about 13.3 and 8.13, suggesting rapid elimination from the body. Again, LTN, AFE, and AC showed moderate clearance with values of 0.924, 0.484, and 0.202 ml/min/kg, respectively.

Our investigation said that UA maintains the highest water solubility, intestinal absorption, and Caco-2 permeability. LCE, AC AFE, and PYN demonstrate significant solubility, moderate permeability, and high intestinal absorption. LTN also shows high permeability. RTN and LCE have the highest clearance, whereas LTN, AFE, and AC show moderate clearance. Also, all the compounds don't inhibit key metabolic enzymes. These results indicate their potentiality as a therapeutic drug. However, all the ADME results are shown in **Table 4**.

3.5. Aquatic and non-aquatic toxicity studies

Studies of aquatic toxicity evaluate the detrimental effects of chemicals on aquatic life, whereas studies of non-aquatic toxicity evaluate the impacts on terrestrial life, such as plants, animals, and soil microbes (Al Hasan et al., 2024). In this study, all the ligands, including RTN, AFE, PYN, LTN, AC, and LCE, exhibit no acute AMES toxicity and no skin sensitization, indicating that these compounds may not cause genetic mutations and allergic reactions. The result also said that all the compounds may not cause hepatotoxicity except UA. Based on aquatic and non-aquatic toxicity studies, it can be said that all the compounds, including RTN, AFE, PYN, LTN, AC, and LCE, can be potential and safe drug, as they don't show AMES toxicity, hepatotoxicity, and skin sensitization. However, aquatic and non-aquatic toxicity results are shown in **Table 5**.

Table 4. ADME properties and toxicity predictions of the selected ligands.

	Absorption			Distribution		Metabolism					Excretion	
Ligand Name	Water solubility, (Log mol/L)	Human intestinal absorption (%)	Caco-2 permeability +/--	VDss (human) (log L/kg)	BBB permeability (log BB)	CYP 2D6 inhibitor	CYP2C19 inhibitor	CYP1A2 inhibitor	CYP2C9 inhibitor	CYP3A4 inhibitor	Total clearance (ml/min/kg)	Renal OCT2 substrate
AC	−3.008	62.855	0.479	−1.600	−0.646	No	No	No	No	No	0.202	No
AGN	−5.995	94.886	1.371	0.198	0.182	No	No	No	No	No	−0.093	No
AFE	−2.892	84.356	0.145	−1.066	−1.653	No	No	No	No	No	0.484	No
BA	−6.674	97.473	1.332	0.224	0.693	No	No	No	No	No	−0.096	No
DGN	−5.539	96.565	1.293	0.426	0.200	No	No	No	No	No	0.328	Yes
FDE	−5.514	98.736	1.266	−0.272	0.720	No	No	No	No	No	−0.040	No
LCE	−3.787	94.06	0.507	1.440	−1.730	No	No	No	No	No	8.130	No
LTN	−6.822	89.781	1.251	−0.230	−0.215	No	No	No	No	No	0.924	No
PYN	−2.892	55.527	0.131	0.193	−1.783	No	No	No	No	No	−0.058	No
RTN	−2.892	23.446	−0.949	0.770	−4.610	No	No	No	No	No	13.300	No
UA	−3.072	100.00	1.171	−1.088	−0.141	No	No	No	No	No	0.083	No

BBB: Blood-Brain Barrier; VDss: Volume of Distribution at Steady State; AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid

Table 5. Aquatic and non-aquatic toxicity of the selected ligands.

Ligand name	AMES toxicity	Hepato-toxicity	Oral rat chronic toxicity (mg/kg.bw/day)	Oral rat acute toxicity (LD_{50})	Max. tolerated dose (log mg/kg/day)	T. Pyriformis toxicity (log ug/L)	Skin sensitisation
AC	No	No	0.575	2.592	0.078	0.285	No
AGN	No	No	1.551	2.004	−0.43	0.363	No
AFE	No	No	3.572	2.527	0.438	0.285	No
BA	No	No	0.868	2.261	−0.31	0.377	No
DGN	No	No	1.452	1.921	−0.559	0.399	No
FDE	No	No	0.909	2.640	−0.213	0.300	No
LCE	No	No	1.310	1.908	0.419	0.285	No
LTN	No	No	2.572	3.491	−1.068	0.335	No
PYN	No	No	3.857	2.482	0.438	0.285	No
RTN	No	No	3.673	2.491	0.452	0.285	No
UA	No	Yes	2.054	2.346	0.199	0.285	No

AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid

3.6. Acute toxicity prediction

StopTox is a computational software program that replaces *in vivo* 6-pack tests (1. Acute Inhalation Toxicity; 2. Acute Oral Toxicity; 3. Acute Dermal Toxicity; 4. Eye Irritation and Corrosion; 5. Skin Sensitization; 6. Skin Irritation and Corrosion) by predicting the toxicity hazards of tiny organic compounds using QSAR models (Borba et al., 2022). In the study of acute toxicity prediction, it is expressed that RTN, AFE, PYN, UA, AC, and LCE showed no toxicity when inhaled over a short period. Additionally, RTN, AFE, PYN, UA, LTN AC, and LCE showed no acute toxicity, suggesting that they would not cause considerable harm. Our investigation also suggests that UA, LTN AC, and LCE showed no dermal toxicity when they came into direct contact with the skin over a short period. According to our study, RTN, PYN, UA, LTN, and AC showed no eye irritation as well as skin sensitization. Our research also expressed that all the selected compounds, including RTN, AFE, PYN, UA, LTN AC, and LCE, have no skin irritation and corrosion effect, meaning that these compounds, when exposed to the skin, don't produce skin irritation or corrosion. Overall, AC, AGN, DGN, and UA are the safest compounds, as well as BA, FDE, LCE, LTN, PYN, and RTN, which can be second choices. Additionally, AFE has moderate-level toxicity, with allergic reactions and dermal and eye irritation toxicity. The acute toxicity of the selected ligands is shown in **Table 6**.

Table 6. Acute toxicity of the selected ligands.

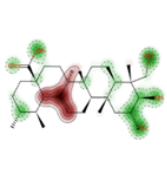
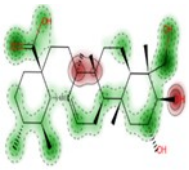
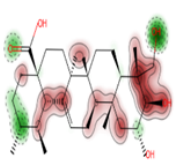
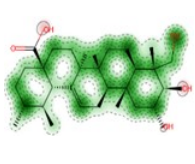
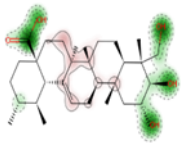
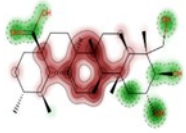
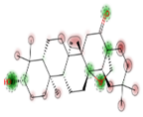
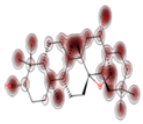
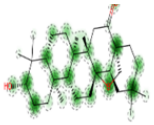
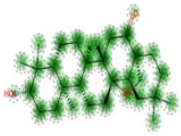
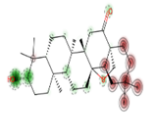
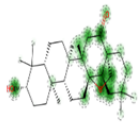
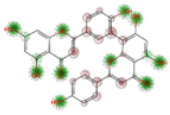
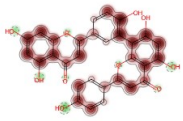
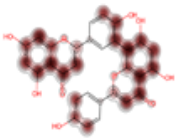
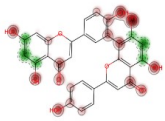
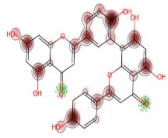
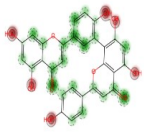
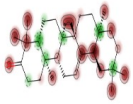
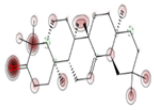
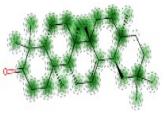
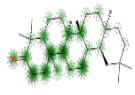
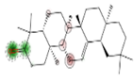
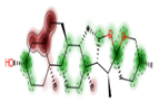
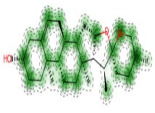
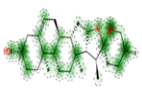
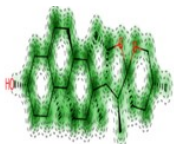
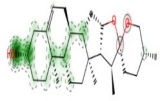
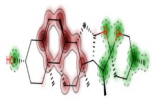
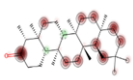
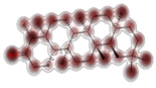
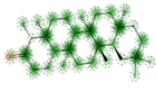
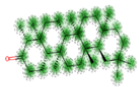
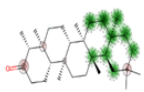
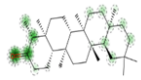
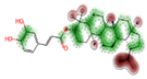
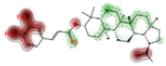
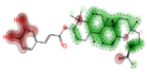
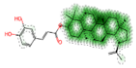
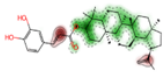
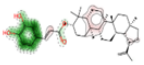
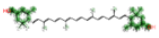
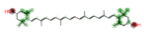
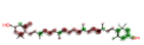
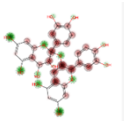
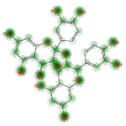
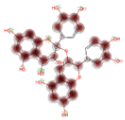
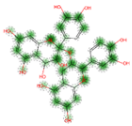
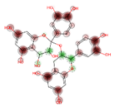
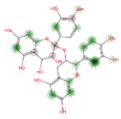
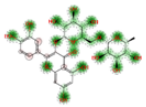
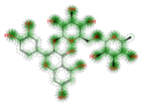
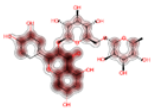
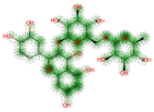
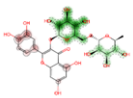
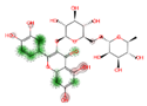
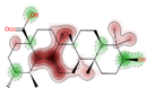
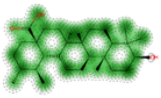
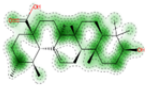
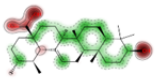
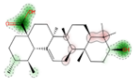
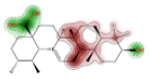
Ligand name	Acute inhalation toxicity	Acute oral toxicity	Acute dermal toxicity	Eye irritation and corrosion	Skin sensitization	Skin irritation and corrosion
AC	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Non-Sensitizer	Negative
						
AGN	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Non-Sensitizer	Negative
						
AFE	Non-Toxic	Non-Toxic	Toxic	Toxic	Sensitizer	Negative
						
BA	Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Sensitizer	Negative
						
DGN	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Non-Sensitizer	Negative
						
FDE	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Sensitizer	Negative
						

Table 6. *Continued*

Ligand name	Acute inhalation toxicity	Acute oral toxicity	Acute dermal toxicity	Eye irritation and corrosion	Skin sensitization	Skin irritation and corrosion
LCE	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Sensitizer	Negative
						
LTN	Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Non-Sensitizer	Negative
						
PYN	Non-Toxic	Non-Toxic	Toxic	Non-Toxic	Non-Sensitizer	Negative
						
RTN	Non-Toxic	Non-Toxic	Toxic	Non-Toxic	Non-Sensitizer	Negative
						
UA	Non-Toxic	Non-Toxic	Non-Toxic	Non-Toxic	Non-Sensitizer	Negative
						

AC: Asiatic Acid; AGN: Aegicerin; AFE: Amentoflavone; BA: Beta Amyrone; DGN: Diosgenin; FDE: Friedeline; LCE: Lupeol Caffeate; LTN: Lutein; PYN: Procyanidin; RTN: Rutin; UA: Ursolic Acid

4. Novelty, key findings, and limitations

Based on BA, we separated 11 phytochemicals among hundreds of thousands of phytochemicals found in 400 Sundarbans plants from various publications. We primarily identified seven chemicals in our computational investigation (AFE, LTN, PYN, RTN, AC, LCE, and UA) that have higher antioxidant activity. Although the compound's antioxidant activity has been studied previously, it is not sufficient for drug establishment. Our study describes their antioxidant activity as well as their BA, pharmacokinetic studies, ADME studies, and toxicology studies. Furthermore, we recommended doing *in vitro* and *in vivo* research to confirm these new compounds as antioxidant medications.

Our pass prediction showed that RTN exhibited the highest predicted antioxidant activity. Additionally, LCE, AFE, PYN, LTN, AC, and UA demonstrated significant antioxidant potential. Our docking score suggested that PYN exhibited the highest docking score with ICB4, forming six HBs and four hydrophobic bonds. Additionally, RTN, LCE, AFE, LTN, AC, and UA also showed strong BA with HBs. According to our pharmacokinetic research, compounds such as RTN, PYN LCE, AFE, LTN, AC, and UA have good pharmacokinetic characteristics, though some of them do not obey Lipinski's rules. ADME analysis revealed AFE, PYN, and RTN as highly water-soluble, while LCE showed the highest VDss, and UA exhibited the greatest human gastrointestinal absorption. Our toxicity prediction also said that our selected compound expresses lower toxicity. However, our study relies solely on computational predictions, which, while valuable for initial insights, have inherent limitations such as scoring function biases and lack of full biological complexity. Therefore, experimental validation (*in vitro/in vivo)* is crucial to confirm the accuracy, reliability, and real-world applicability of these predictions. Antioxidant activity of these compounds could be experimentally validated using cell-based assays, such as MTT or viability assays to evaluate cytoprotective effects and DCFH-DA (dichlorofluorescein diacetate) assays to quantify intracellular reactive oxygen species (Nwachukwu et al., 2021). Furthermore, using animal models (such as mice or rats) to induce oxidative stress with substances like carbon tetrachloride or H_2O_2 and measure biomarkers like malondialdehyde (MDA), superoxide dismutase (SOD), and catalase levels in tissues could be used to

assess *in vivo* antioxidant capability (Unsal et al., 2020; Szymonik-Lesiuk et al., 2003). A possible mechanism is shown in **Fig. 3**, which enhanced the novelty.

antioxidant activity, these compounds should be examined both *in vivo* and *in silico*. New natural treatments for oxidative damage might be created if this research is successful. It could result in safer and more effective therapeutic approaches.

5. Conclusion with future perspective

In summary, our computational study identified some compounds that have significant antioxidant activity obtained from several Sundarbans plants. These compounds demonstrated favorable pharmacokinetics and low toxicity, indicating their potential as safe drug candidates. Their properties suggest suitability for further development in pharmaceutical applications. According to our investigation, RTN, LCE AFE, PYN, LTN, AC, and UA are powerful antioxidants with high BA. Our pharmacokinetics and ADMET study also express their good pharmacokinetics with water solubility and high intestinal absorption. These findings highlight their potential as promising drug candidates. To determine their safety and antioxidant activity, these compounds should be examined both *in vivo* and *in silico*. New natural treatments for oxidative damage might be created if this research is successful. It could result in safer and more effective therapeutic approaches.

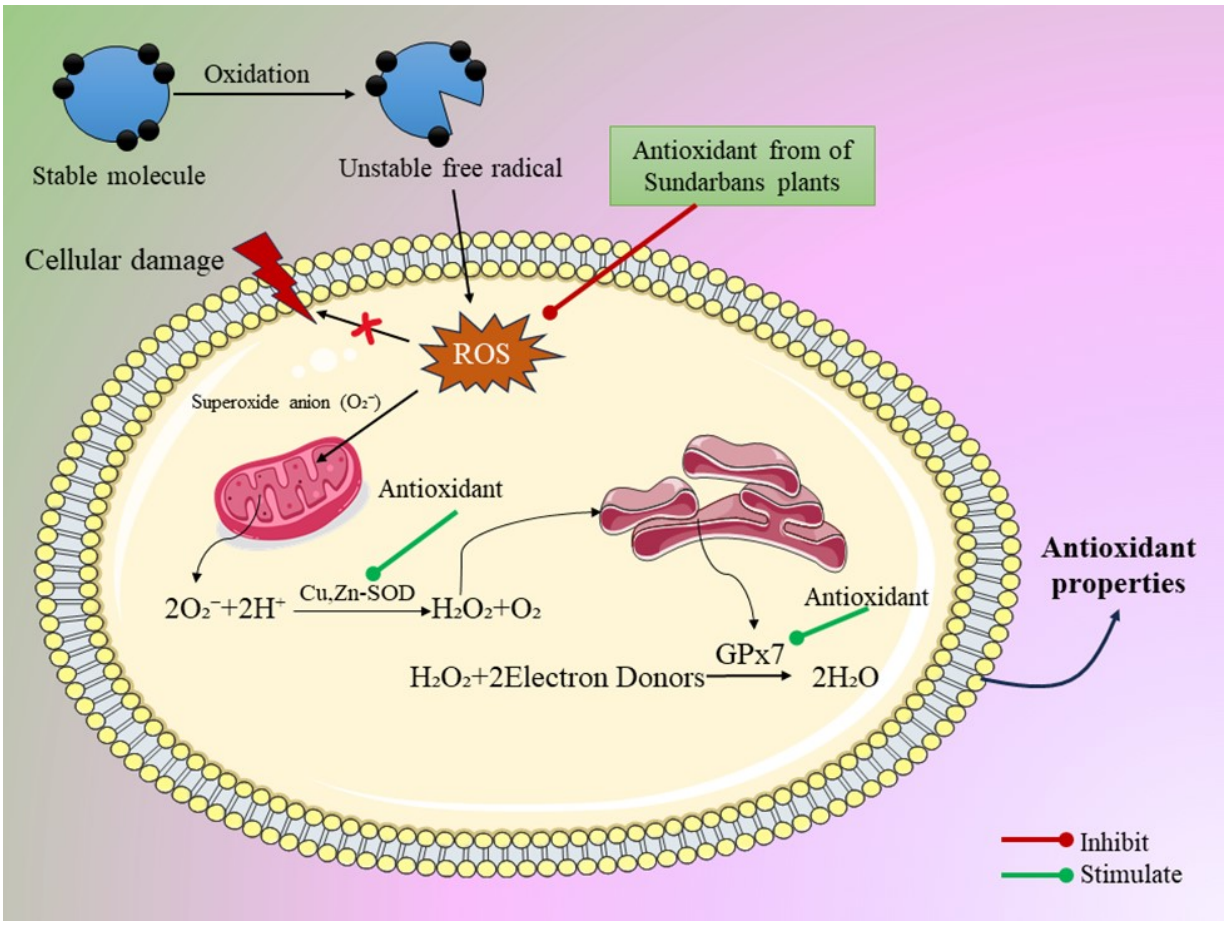


Fig. 3. The possible antioxidant mechanism of some phytochemicals of Sundarbans plants. [Phytochemicals from Sundarbans plants act as antioxidants, neutralizing reactive oxygen species (ROS) and preventing oxidative stress. They inhibit cellular damage by scavenging free radicals and enhancing antioxidant enzyme activity. Compounds stimulate superoxide dismutase (SOD) and glutathione peroxidase 7 (GPx7), converting superoxide anions and hydrogen peroxide into harmless molecules. This mechanism supports cellular defense and maintains redox balance.]

Conflict of interest

The authors declared that they have no conflict of interest.

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Acknowledgments

Not applicable.

Authorship contributions

All authors significantly contributed to the work, including its conception, study design, execution, data acquisition, analysis, interpretation, and revisions or critical reviews. They also gave final approval for the manuscript, agreed on the journal for submission, and confirmed their accountability for all aspects of the work. All authors have read and approved the final version of the manuscript.

References

Abishad, P., Niveditha, P., Unni, V., Vergis, J., Kurkure, N. V., Chaudhari, S., Rawool, D. B., & Baliram Barbuddhe, S. (2021). In silico molecular docking and in vitro antimicrobial efficacy of phytochemicals against multi-drug-resistant enteroaggregative Escherichia coli and non-typhoidal. *Springer*, *13*(5). https://doi.org/10.1186/s13099-021-00443-3

Adepu, S., & Ramakrishna, S. (2021). Controlled drug delivery systems: current status and future directions. *Molecules*, *26*(5[3]), 9[3]49. https://doi.org/10.3390/molecules26195905

Adwas, A. A., Elsayed, A., Azab, A. E., & Quwaydir, F. A. (2019). Oxidative stress and antioxidant mechanisms in human body. *J. Appl. Biotechnol. Bioeng*, *6*(1), 43–47. https://doi.org/10.15406/jabb.2019.06.00173

Akbor, M. S., Bappi, M. H., Prottay, A. A. S., Haque, M. F., Al Hasan, M. S., Ahammed, S., ... & Islam, M. T. (2023). Synergistic hypnotic effects of sesamol and thymol possibly through GABAergic interaction pathway: in vivo and in silico studies. *J. Biol. Regul. Homeost. Agents*, *37*(55), 6419-6435. https://doi.org/10.23812/j.biol.regul.homeost.agents.20233711.609

Aktar, A., Bhuia, S., Chowdhury, R., Ferdous, J., Khatun, M., Hasan, S. A., Mia, E., Hasan, R., & Islam, M. T. (2024). An Insight of Plant Source, Toxicological Profile, and Pharmacological Activities of Iridoid Loganic Acid: A ComprehensiveReview. *Chemistry & biodiversity*, *21*(12), e202400874. https://doi.org/10.1002/cbdv.202400874

Al Hasan, M. S., Bhuia, M. S., Chowdhury, R., Husain, Z., Saifuzzaman, M., Mia, E., Akbor, M. S., Yana, N. T., Islam, M. A., Ansari, S. A., Ansari, I. A., & Islam, M. T. (2025a). Tangeretin enhances sedative activity of diazepam in Swiss mice through $GABA_A$ receptor interaction: In vivo and in silico approaches. *Neuroscience*, *572*, 1–10. Advance online publication. https://doi.org/10.1016/j.neuroscience.2025.03.004

Al Hasan, M. S., Bhuia, M. S., Chowdhury, R., Shadin, M., Mia, E., Yana, N. T., ... & Islam, M. T. (2025b). Anticancer activity of Jasminum sambac and its bioactive phytochemicals against the PI3K-AKT-mTOR pathway: A literature-based in silico study. *South African Journal of Botany*, 180, 431-443. https://doi.org/10.1016/j.sajb.2025.03.004

Al Hasan, M. S., Mia, E., Yana, N. T., Rakib, I. H., Bhuia, M. S., Chowdhury, R., ... & Islam, M. T. (2024). Allium cepa bioactive phytochemicals as potent ALK (Anaplastic lymphoma kinase) inhibitors and therapeutic agents against non-small cell lung cancer (NSCLC): A computational study. *Pharmacological Research-Natural Products*, *5*, 544568. https://doi.org/10.1016/j.prenap.2024.100124

Alagga, A. A., Pellegrini, M. V., & Gupta, V. (2024). Drug absorption. In StatPearls [Internet]. StatPearls Publishing.

Amanat, M., Reza, M. S., Shuvo, M. S. R., Ahmed, K. S., Hossain, H., Tawhid, M., Saifuzzaman, M., Islam, M. S., Mazumder, T., Islam, M. A., & Daula, A. F. M. S. U. (2021). Zingiber roseum Rosc. rhizome: A rich source of hepatoprotective polyphenols. *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *139*, 555[0][1]7. https://doi.org/10.1016/j.biopha.2021.111673

Anbessa, B., Lulekal, E., Hymete, A., Debella, A., Debebe, E., Abebe, A., & Degu, S. (2024). Ethnomedicine, antibacterial activity, antioxidant potential and phytochemical screening of selected medicinal plants in Dibatie district, Metekel zone, western Ethiopia. *Springer*, *24*(5). https://doi.org/10.1186/s12906-024-04499-x

Arabi, I. I., & Kawsar, S. M. (2023). In Silico Investigations of Some Carbohydrate Derivatives: Pass Prediction, ADMET, QSAR, and Molecular Docking Studies against Pseudomonas aeruginosa. *Philippine Journal of Science*, *152*(8), 57[3][1]-1412.

Bereda, G. (2022). What the Body Does to a Drug: Pharmacokinetics. *Journal of Pharmacy and Pharmacology*, *10*, 75[0]-329. https://doi.org/10.17265/2328-2150/2022.12.002

Bhuia, M. S., Islam, T., Rokonuzzman, M., Shamsh Prottay, A. A., Akter, F., Hossain, M. I., Chowdhury, R., Kazi, M. A., Khalipha, A. B. R., Coutinho, H. D. M., & Islam, M. T. (2023a). Modulatory effects of phytol on the antiemetic property of domperidone, possibly through the D2 receptor interaction pathway: in vivo and in silico studies. 3 Biotech, 13(4), 116. https://doi.org/10.1007/s13205-023-03520-3

Bhuia, M. S., Kamli, H., Islam, T., Sonia, F. A., Kazi, M. A., Siam, M. S. H., ... & Islam, M. T. (2023b). Antiemetic activity of trans-ferulic acid possibly through muscarinic receptors interaction pathway: In vivo and in silico study. Results in Chemistry, 6, 101014. https://doi.org/10.1016/j.rechem.2023.101014

Birben, E., Sahiner, U. M., Sackesen, C., Erzurum, S., & Kalayci, O. (2012). Oxidative Stress and Antioxidant Defense. *World Allergy Organization Journal 2012 5:1*, *5*(1), 9–19. https://doi.org/10.1097/WOX.0B013E3182439613

Bithi, S. A., Al Hasan, M. S., Bhuia, M. S., Mia, E., Yana, N. T., Hasan, A. M. W., Uddin, M. B., Sayeed, M. A., Emon, Y., Hasan, R., Chowdhury, R., & Islam, M. T. (2025). Botanical sources, biopharmaceutical profile, anticancer effects with mechanistic insight, toxicological and clinical evidence of prunetin: a literature review. *Medical oncology (Northwood, London, England)*, *42*(8), [2][1]. https://doi.org/10.1007/s12032-025-02646-z

Boo, Y. C. (2019). Can plant phenolic compounds protect the skin from airborne particulate matter?. Antioxidants, 8(9), 379. https://doi.org/10.3390/antiox8090379

Borba, J. V., Alves, V. M., Braga, R. C., Korn, D. R., Overdahl, K., Silva, A. C., ... & Tropsha, A. (2022). STopTox: An in silico alternative to animal testing for acute systemic and topical toxicity. *Environmental Health Perspectives*, *130*(6), 46[1]456. https://doi.org/10.1289/EHP9341

Chowdhury, R., & Al Hasan, M. S. (2025). Assessments of membrane stabilizing and clot lysis capacity of Canna indica flower aqueous extract: In vitro study. *Journal of Phytochemical Insights*, *1*(45), 5-7. https://doi.org/10.71193/jpci.20250001

Chowdhury, R., Bhuia, S., Rakib, A. I., Al Hasan, S., Shill, M. C., El-Nashar, H. A. S., El-Shazly, M., & Islam, M. T. (2024). Gigantol, a promising natural drug for inflammation: a literature review and computational based study. *Natural product research*, 1–17. Advance online publication. https://doi.org/10.1080/14786419.2024.2340042

Dubois-Deruy, E., Peugnet, V., Turkieh, A., & Pinet, F. (2020). Oxidative stress in cardiovascular diseases. Antioxidants, 9(9), 864. https://doi.org/10.3390/antiox9090864

Ferdous, J., Bhuia, M. S., Chowdhury, R., Sheikh, S., Ansari, S. A., Bappi, M. H., & Islam, M. T. (2024). Modulatory Sedative Activity of Abrine on Diazepam in Thiopental Sodium Mediated Sleeping Mice: An In Vivo Approach with Receptor Binding Affinity of GABAergic Transmission. *ChemistrySelect*, *9*(37), e202403725. https://doi.org/10.1002/slct.202403725

Filimonov, D. A., Druzhilovskiy, D. S., Lagunin, A. A., Gloriozova, T. A., Rudik, A. V., Dmitriev, A. V., ... & Poroikov, V. V. (2018). Computer-aided prediction of biological activity spectra for chemical compounds: opportunities and limitations. Biomedical Chemistry: Research and Methods, 1(1), e00004-e00004. https://doi.org/10.18097/BMCRM00004

Filimonov, D. A., Lagunin, A. A., Gloriozova, T. A., Rudik, A. V., Druzhilovskii, D. S., Pogodin, P. V., & Poroikov, V. V. (2014). Prediction of the biological activity spectra of organic compounds using the PASS online web resource. Chemistry of Heterocyclic Compounds, 50, 444-457. https://doi.org/10.1007/s10593-014-1496-1

Gautam, V. S., Singh, A., Kumari, P., Nishad, J. H., Kumar, J., Yadav, M., Bharti, R., Prajapati, P., & Kharwar, R. N. (2022). Phenolic and flavonoid contents and antioxidant activity of an endophytic fungus Nigrospora sphaerica (EHL2), inhabiting the medicinal plant Euphorbia hirta (dudhi) L. *Archives of Microbiology*, *204*(2), 1–13. https://doi.org/10.1007/S00203-021-02650-7/TABLES/3

Ghosh, P. R., Al Hasan, M. S., Rouf, R., Chowdhury, R., Yadav, B., Mia, E., ... & Islam, M. T. (2025). Assessments of protodioscin's antinociceptive and antidiarrheal properties: in vivo and in silico investigations on macromolecule binding affinity and modulatory effects. *Naunyn-Schmiedeberg's Archives of Pharmacology*, 1-15. https://doi.org/10.1007/s00210-025-03860-2

Gross, A. S. (1998). Best practice in therapeutic drug monitoring. *British journal of clinical pharmacology*, *46*(6), [3]9-99. https://doi.org/10.1111/j.1365-2125.2001.00770.x

Hasan, M. N., Bhuiya, N. M. M. A., & Hossain, M. K. (2019). In silico molecular docking, PASS prediction, and ADME/T analysis for finding novel COX -2 inhibitor from Heliotropium indicum. *J. Comp. Med. Res*, *10*, 586-154.

Hayes, J. D., Dinkova-Kostova, A. T., & Tew, K. D. (2020). Oxidative stress in cancer. Cancer cell, 38(2), 167-197. https://doi.org/10.1016/j.ccell.2020.06.001

Hedaya, M. A. (2023). Basic pharmacokinetics. Routledge.

Hwang, S. J., & Lee, J. H. (2023). Comparison of antioxidant activities expressed as equivalents of standard antioxidant. *Food Science and Technology*, *43*, e121522.

Ibrahim, M., Oyebanji, E., Fowora, M., Aiyeolemi, A., Orabuchi, C., Akinnawo, B., & Adekunle, A. A. (2021). Extracts of endophytic fungi from leaves of selected Nigerian ethnomedicinal plants exhibited antioxidant activity. *BMC Complementary Medicine and Therapies*, *21*(1), 1–13. https://doi.org/10.1186/S12906-021-03269-3/FIGURES/9

Islam, M. T., Al Hasan, M. S., Chowdhury, R., Mia, E., Rakib, I. H., Yana, N. T., El -Nashar, H. A. S., Ansari, S. A., Ansari, I. A., Islam, M. A., Almarhoon, Z. M., Setzer, W. N., & Sharifi-Rad, J. (2024b). Unveiling the anxiolytic and analgesic effects of citronellal in Swiss mice: in vivo and in silico insights into COX and GABAA receptor pathways. *Naunyn-Schmiedeberg's archives of pharmacology*, 54.544[1] /s44654-024-03665

-9. Advance online publication. https://doi.org/10.1007/s00210-024-03665-9

Islam, M. T., Al Hasan, M. S., Ferdous, J., Mia, E., Yana, N. T., Ansari, I. A., Ansari, S. A., Islam, M. A., & Coutinho, H. D. M. (2025). GabaAergic sedative prospection of sclareol-linalool co-treatment: An antagonistic intervention through in vivo and in silico studies. *Neuroscience letters*, 845, 138060. https://doi.org/10.1016/j.neulet.2024.138060

Islam, M. T., Ferdous, J., Al Hasan, M. S., Ansari, I. A., Ansari, S. A., Islam, M. A., & Saifuzzaman, M. (2024a). Possible GABAkine-mediated antidepressant effects of phytol: molecular interventions through in vivo and in silico studies. https://doi.org/10.21203/rs.3.rs-4880848/v1

Jahan Tamanna, A., Saha, A., Hoque, M., Aktaruzzaman, M., Nahid Hasan, M., & Author, C. (2024). Evaluation of Phytochemical Screening, Antioxidant, and Thrombolytic Activity of Methanolic Extract of Phlogacanthus thyrsiflorus. *South Asian Res J Pharm Sci*, *6*(1), 5–11. https://doi.org/10.36346/sarjps.2024.v06i01.002

Jahan, N., Mandal, M., Rakib, I. H., Al Hasan, M. S., Mia, E., Hossain, M. A., Yana, N. T., Ansari, S. A., Bappi, M. H., Wasaf Hasan, A. M., Sayeed, M. A., & Islam, M. T. (2025). Assessment of Antidiarrheal Effect of Oleuropein Through μ-Oopioid Receptor Interaction Pathway: In Vivo and in Silico Studies. *Drug development research*, *86*(1), e70064. https://doi.org/10.1002/ddr.70064

Jelinek, M., Jurajda, M., & Duris, K. (2021). Oxidative stress in the brain: basic concepts and treatment strategies in stroke. *Antioxidants*, *10*(56), 1886. https://doi.org/10.3390/antiox10121886

Kotha, R. R., Tareq, F. S., Yildiz, E., & Luthria, D. L. (2022). Oxidative stress and antioxidants—A critical review on in vitro antioxidant assays. *Antioxidants*, *11*(56), $67^{2\,2}$. https://doi.org/10.3390/antiox11122388

Kritsi, E., Tsiaka, T., Ioannou, A., Mantanika, V., Sciences, I. S.-A., & 2022, undefined. (2022). In Vitro and In Silico Studies to Assess Edible Flowers' Antioxidant Activities. *Mdpi.Com*. https://doi.org/10.3390/app12147331

Kulbacka, J., Saczko, J., & Chwiłkowska, A. (2009). Oxidative stress in cells damage processes. *Polski merkuriusz lekarski: organ Polskiego Towarzystwa Lekarskiego*, *27*(59^{1}), 88-47.

Lakens, D., & DeBruine, L. M. (2021). Improving transparency, falsifiability, and rigor by making hypothesis tests machine-readable. *Advances in Methods and Practices in Psychological Science*, *4*(6), 2515245920970949. https://doi.org/10.1177/2515245920970949

Lakhera, S., Rana, M., Devlal, K., Celik, I., & Yadav, R. (2022). A comprehensive exploration of pharmacological properties, bioactivities and inhibitory potentiality of luteolin from Tridax procumbens as anticancer drug by in-silico approach. *Structural chemistry*, *33*(7), ^{1}47-719. https://doi.org/10.1007/s11224-022-01882-7

Lin, J. H., & Lu, A. Y. (1997). Role of pharmacokinetics and metabolism in drug discovery and development. *Pharmacological reviews*, *49*(8), 847-449.

Maegawa, G. H., Poplawski, N. K., Andresen, B. S., Olpin, S. E., Nie, G., Clarke, J. T., & Teshima, I. (2008). Interstitial deletion of 1p22. 2p31. 1 and medium-chain Acyl-CoA dehydrogenase deficiency in a patient with global developmental delay. American Journal of Medical Genetics Part A, 146(12), 1581-1586. https://doi.org/10.1002/ajmg.a.32255

Mahalakshmi, P. S., Peeriga, R., Chukka, K., & Vankadharu, N. S. S. (2024). Introduction to Clinical Pharmacokinetics. In *A Short Guide to Clinical Pharmacokinetics* (pp. 1-16). Singapore: Springer Nature Singapore. https://doi.org/10.1007/978-981-97-4283-7_1

Muflihah, Y. M., Gollavelli, G., & Ling, Y. C. (2021). Correlation Study of Antioxidant Activity with Phenolic and Flavonoid Compounds in 12 Indonesian Indigenous Herbs. *Antioxidants 8687,* Vol. 10, Page 1530, *10*(54), 5974. https://doi.org/10.3390/ANTIOX10101530

Neves Carvalho, A., Firuzi, O., Joao Gama, M., van Horssen, J., & Saso, L. (2017). Oxidative stress and antioxidants in neurological diseases: is there still hope?. Current drug targets, 18(6), 705-718. https://doi.org/10.2174/1389450117666160401120514

Niedzielska, E., Smaga, I., Gawlik, M., Moniczewski, A., Stankowicz, P., Pera, J., & Filip, M. (2016). Oxidative stress in neurodegenerative diseases. Molecular neurobiology, 53, 4094-4125. https://doi.org/10.1007/s12035-015-9337-5

Nirjhar Dasgupta, P. N., Sengupta, C., & Das, S. (2017). Occurrence of Secondary Metabolites and Free Radical Scavenging Ability towards Better Adaptability of Some Mangrove Species in Elevated Salinity of Indian Sundarbans. *Annals of Tropical Research*, *39*(5), 56-40.

Nwachukwu, I. D., Sarteshnizi, R. A., Udenigwe, C. C., & Aluko, R. E. (2021). A Concise Review of Current In Vitro Chemical and Cell-Based Antioxidant Assay Methods. *Molecules (Basel, Switzerland)*, *26*(5^{0}), 4865. https://doi.org/10.3390/molecules26164865

Parasuraman, S. (2011). Prediction of activity spectra for substances. Journal of pharmacology & pharmacotherapeutics, 2(1), 52. https://doi.org/10.4103/0976-500x.77119

Pawlowska, E., Szczepanska, J., Koskela, A., Kaarniranta, K., & Blasiak, J. (2019). Dietary polyphenols in age-related macular degeneration: protection against oxidative stress and beyond. Oxidative medicine and cellular longevity, 2019(1), 9682318. https://doi.org/10.1155/2019/9682318

Pizzino, G., Irrera, N., Cucinotta, M., Pallio, G., Mannino, F., Arcoraci, V., ... & Bitto, A. (2017). Oxidative stress: harms and benefits for human health. Oxidative medicine and cellular longevity, 2017(1), 8416763. https://doi.org/10.1155/2017/8416763

Poroikov, V., & Filimonov, D. (2005). PASS: prediction of biological activity spectra for substances. In *Predictive toxicology* (pp. 471-490). CRC Press.

Prottay, A. A. S., Bappi, M. H., Akbor, M. S., Asha, A. I., Bhuia, M. S., Shafin, A. A., ... & Islam, M. T. (2024). Sclareol exerts an anti-inflammatory effect, possibly through COXs inhibition pathway: In vivo and in silico studies. *Pharmaceutical Science Advances*, *2*, 54446^{3}. https://doi.org/10.1016/j.pscia.2023.100029

Rahman, M. M. (2020). Impact of increased salinity on the plant community of the Sundarbans Mangrove of Bangladesh. Community Ecology, 21 (3), 273-284. https://doi.org/10.1007/s42974-020-00028-1

Sacan, A., Ekins, S., & Kortagere, S. (2012). Applications and limitations of in silico models in drug discovery. *Bioinformatics and drug discovery*, 87-124. https://doi.org/10.1007/978-1-61779-965-5_6

Sachdev, S., Ansari, S. A., Ansari, M. I., Fujita, M., & Hasanuzzaman, M. (2021). Abiotic stress and reactive oxygen species: Generation, signaling, and defense mechanisms. Antioxidants, 10(2), 277. https://doi.org/10.3390/antiox10020277

Saha, S. K., Lee, S. B., Won, J., Choi, H. Y., Kim, K., Yang, G. M., ... & Cho, S. G. (2017). Correlation between oxidative stress, nutrition, and cancer initiation. International journal of molecular sciences, 18(7), 1544. https://doi.org/10.3390/ijms18071544

Santos-Sánchez, N. F., Salas-Coronado, R., Villanueva-Cañongo, C., & Hernández-Carlos, B. (2019). Antioxidant compounds and their antioxidant mechanism. *Antioxidants*, *10*, 5-29. https://doi.org/10.5772/intechopen.85270

Sierra-Vargas, M. P., Montero-Vargas, J. M., Debray-García, Y., Vizuet-de-Rueda, J. C., Loaeza-Román, A., & Terán, L. M. (2023). Oxidative stress and air pollution: its impact on chronic respiratory diseases. International Journal of Molecular Sciences, 24(1), 853. https://doi.org/10.3390/ijms24010853

Sies, H., Belousov, V. V., Chandel, N. S., Davies, M. J., Jones, D. P., Mann, G. E., ... & Winterbourn, C. (2022). Defining roles of specific reactive oxygen species (ROS) in cell biology and physiology. Nature reviews Molecular cell biology, 23(7), 499-515. https://doi.org/10.1038/s41580-022-00456-z

Sies, H., Berndt, C., & Jones, D. P. (2017). Oxidative stress. Annual Review of Biochemistry, 86(Volume 86, 2017), 715–748. https://doi.org/10.1146/ANNUREV-BIOCHEM-061516-045037/CITE/REFWORKS

Simlai, A., & Roy, A. (2013). Biological activities and chemical constituents of some mangrove species from Sundarban estuary: An overview. Pharmacognosy Reviews, 7(14), 170. https://doi.org/10.4103/0973-7847.120518

Szymonik-Lesiuk, S., Czechowska, G., Stryjecka-Zimmer, M., Słomka, M., Madro, A., Celiński, K., & Wielosz, M. (2003). Catalase, superoxide dismutase, and glutathione peroxidase activities in various rat tissues after carbon tetrachloride intoxication. *Journal of hepato-biliary-pancreatic surgery*, *10*(4), 309–315. https://doi.org/10.1007/s00534-002-0824-5

Talevi, A., & Bellera, C. L. (2024). Drug excretion. In *ADME Processes in Pharmaceutical Sciences: Dosage, Design, and Pharmacotherapy* (pp. 111-128). Cham: Springer Nature Switzerland. https://doi.org/10.1007/978-3-031-50419-8_6

Tannenbaum, C., & Sheehan, N. L. (2014). Understanding and preventing drug–drug and drug–gene interactions. *Expert review of clinical pharmacology*, *7*(8), 977-544. https://

doi.org/10.1586/17512433.2014.910111
Tripathi, R., Mohan, H., & Kamat, J. P. (2007). Modulation of oxidative damage by natural products. Food chemistry, 100(1), 81-90. https://doi.org/10.1016/j.foodchem.2005.09.012
Unsal, V., Cicek, M., & Sabancilar, İ. (2020). Toxicity of carbon tetrachloride, free radicals and role of antioxidants. *Reviews on environmental health*, *36*(2), 279–295. https://doi.org/10.1515/reveh-2020-0048
Zhao, Y., Sun, W., Zhang, P., Chi, H., Zhang, M. J., Song, C. Q., ... & Miao, L. (2012). Nematode sperm maturation triggered by protease involves sperm-secreted serine protease inhibitor (Serpin). Proceedings of the National Academy of Sciences, 109(5), 1542-1547. https://doi.org/10.1073/pnas.1109912109