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Original Research Article

Archachatina marginata Slime Bioactive Compounds Combat Peptic Ulcer via Inhibition of H^+/K^+-ATPase and *Helicobacter pylori* Urease: A Computational Study

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ABSRTACT

The search for natural treatment of gastric ulcers continues to attract the attention of researchers, due to the side effects of the existing synthetic antiulcer agents. The aim of this study was to examine the *in silico* inhibitory effects of *Archachatina marginata* slime on *Helicobacter pylori* urease and gastric H^+/K^+-ATPase, which are implicated in the pathophysiology of gastric ulcer. We identified the bioactive constituents of pulverized *A. marginata* slime using gas chromatography–mass spectrometry (GC –MS), and the identified ligands were docked using PyRx and BIOVIA Discovery Studio. The pharmacokinetics (ADME) and physicochemical properties of hit ligands were predicted using SwissADME, and their toxicity was assessed using pkCSM. The extracted snail slime, upon identification by GC-MS, showed twenty-three (23) peaks, corresponding to forty-three (43) compounds. Phenol, 2,6-bis(1,1-dimethylethyl)- (P26BD), benzaldehyde, 3,5-dimethyl- (BAD), 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- (SODB), and cedranoxide, 8,14- (CO) had higher binding affinity against urease (-7.4, -5.7, -6.5, -6.4 and -6.3 kcal/mol, respectively) than the standard inhibitor, N-(n-butyl) thiophosphoric triamide (NBPT) (-4.7 kcal/mol). Of all the forty-three (43) ligands, phenol, 2,4-bis(1,1-dimethylethyl)- (P24BD) with -7.4 kcal/mol) showed a predicted binding affinity close to that of the control (Omeprazole with -7.8 kcal/mol binding affinity). Phenol, 2,6-bis(1,1-dimethylethyl)- (P26BD) showed a higher binding affinity against H+/K+-ATPase (-8.0 kcal/mol) than the omeprazole (-7.89 kcal/mol), a potent proton pump inhibitor. Thus, these compounds may be potent in the treatment of gastric ulcers, since they have demonstrated strong docking affinities against the proteins implicated in gastric ulceration.

Keywords: *Helicobacter pylori*, Urease, H^+/K^+-ATPase, Docking, *Archachatina marginata* and Gastric Ulcer.

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Introduction

Peptic ulcer disease (PUD) is a gastrointestinal disorder characterized by mucosal break in the stomach or duodenum.[1] PUD is classified into duodenal and gastric ulcers, depending on the location of the ulceration. The symptoms of gastric ulcers include pain, nausea, vomiting, and weight loss.[2] *Helicobacter pylori*, a Gram-negative bacterium, is a major factor that causes chronic inflammation (60% of gastric and up to 90% of duodenal ulcers), by colonizing the antral mucosa, leading to peptic ulcer.[3] In *H. pylori*-associated gastric ulcer, the bacteria contribute to the stimulation of gastric acid production via the action of gastrin, a gastric acid-stimulating hormone secreted by the parietal cells present in the stomach.[4]

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The acid then contributes to the erosion of the mucosa.[3] By releasing urease, an enzyme that degrades urea into ammonia, *H. pylori* can resist the acidity of the stomach.[5] The ammonia produced neutralizes the stomach acid , thereby enabling survival and colonization of the bacteria.[5] This suggests that inhibition of urease may eradicate *H. pylori*, and consequently reduce ulceration due to the bacteria infection.[6] Gastric acid secretion has also been implicated in ulceration,[7] as it causes erosion or lesions in the stomach.[3] H^+/K^+-ATPase (proton pump) catalyzes the production of acid in the stomach and a decrease in its activity may ameliorate the ulceration that stems from hypersecretion of gastric acid. Proton pump inhibitors (PPIs), antiulcer agents, are prodrugs activated by acid; once activated, they bind covalently to the gastric H^+/K^+-ATPase via disulfide bonds, thereby reducing its activity.[8] However, the use of these drugs has been reported to cause serious side effects such as impotence, headache, skin rash, arrhythmias, and atrophic gastritis.[9] This necessitates the search for safer treatments for gastric ulcers. To this effect, active compound(s) from *Archachatina marginata* slime may offer a suitable option for the efficacious treatment of gastric ulcer, with little or no side effects. Molecular docking is a bioinformatics tool used to virtually screen bioactive compounds from a pool of chemicals by identifying potential inhibitors. Docking simulates the interactions between a ligand and a protein, calculates their binding energies, and predicts the binding of a compound to a pharmacological target, such as an enzyme.[6] Therefore, the aim of this study was to examine the *in silico* inhibitory effect of

Archachatina marginata slime on *H. pylori* urease and H^+/K^+-ATPase to provide predictive insight into alternative, safer, and more potent *H. pylori* eradication and proton pump inhibition strategies for the treatment of gastric ulcers (GU).

Materials and Methods

Thirty-five specimens of *Archachatina marginata* snails were obtained in Magaji Ogo Village, Adewole, Ilorin, Nigeria (latitude 8.49664 and longitude 4.54214). Acetone of analytical grade (≥ 99.5 % purity) was purchased from Sigma-Aldrich (St. Louis, MO, USA). A freeze-dryer (Labconco, Kansas City, MO, USA) was used for sample processing. GC-MS/MS analysis was performed using a Finnigan Trace DSQ GC-MS system (Thermo Fisher Scientific, Waltham, MA, USA) with NIST Library Software (Gaithersburg, MD, USA). Crystal structures of *Helicobacter pylori* urease (PDB ID: 1e9z) and human H^+/K^+-ATPase (PDB ID: 5ylv) were retrieved from the Protein Data Bank (RCSB, Piscataway, NJ, USA). PyRx version 0.8 (The Scripps Research Institute, USA) was used for docking. Canonical SMILES of bioactive compounds and standard inhibitors were retrieved from PubChem (NIH, Bethesda, MD, USA). *In silico* pharmacokinetic and toxicity predictions were conducted using SwissADME (Swiss Institute of Bioinformatics, Lausanne, Switzerland) and pkCSM (University of Queensland, Brisbane, Australia).

Preparation of Snail Slime Extract

Preparation of snail slime extract was carried out according to the method described by Nwodo *et al*.[10] The snails were washed with clean water to remove dirt and dust from their shells. Then the inner contents of the snails were mechanically separated from the shells by removing the body from which the excretory material was collected. The fleshy parts were then placed in 200 mL of water and were washed until the snail mucin was washed off. The mixture was precipitated using chilled acetone at a ratio of 4:1 (v/v, acetone: sample mixture), and the precipitate was freeze-dried to obtain greyish-brown dry flakes of snail slime. The flakes were then pulverized into powder, bottled and stored in a refrigerator.

GC-MS/MS Analysis of Extracted Snail Slime

The GC-MS of *A. marginata* mucin was carried out using the method described by Ibrahim *et al*.[11] Identification was based on comparison with the MS computer library (NIST Software Package, Finnigan) and on the respective retention indices.

Molecular Docking of Identified Compounds against Urease and H^+/k^+-ATPase

The method reported by Rahman *et al*.[12] was used for the docking of the compounds identified from *A. marginata* slime against the target proteins *Helicobacter pylori* urease (PDB ID: 1e9z) and human H^+/K^+-ATPase (PDB ID: 5ylv). BIOVIA Discovery Studio was used to remove the heteroatoms and water molecules from the proteins, leaving only chains containing the active sites. Thereafter, the ligands and the target protein (each of the enzymes) were uploaded into the virtual screening program PyRx. The target proteins were converted into pdbqt format. N-(n-butyl) thiophosphoric triamide was used as the standard inhibitor of urease while omeprazole was used for human H^+/K^+-ATPase, and the standard inhibitors were docked along with the test ligands. To perform molecular docking, the grid boxes for the two proteins were centered on the crystal structures and all other parameters were left as default. The energy of the ligands was minimized. BIOVIA Discovery Studio (2020 version) was employed to explore detailed amino acids involved in the interactions between the ligands and the enzymes. The most favorable binding poses of the ligands were analyzed by choosing the lowest free energy of binding (ΔG). For each protein, the ligands having close or higher binding affinities were selected and reported.

Evaluation of in silico Pharmacokinetics Parameters (ADMET) of Hit Compounds

In silico ADMET screening (Absorption, Distribution, Metabolism, Excretion and Toxicity) helps to predict pharmacokinetic properties and toxicities using SwissADME web server (https://www.swissadme.ch/). The web address was launched in Google Chrome, and the canonical smiles of the hit compounds downloaded from PubChem were pasted into the SwissADME dialogue box to run the ADME prediction. The toxicity of ligands was predicted using pkCSM web server (https://www.biosig.lab.uq.edu.au/). The physicochemical properties of the hit compounds were obtained using the SwissADME server used for ADME prediction.

Results and Discussion

This study identified the major bioactive constituents of *A. marginata* slime and evaluated their inhibitory potential against urease and H^+/K^+-ATPase using molecular docking and *in silico* pharmacokinetics. Because *H. pylori* eradication remains clinically important, [13] this study examined whether dual inhibition of urease and H^+/K^+-ATPase, which has been previously shown to provide antiulcer benefit, [14] could be achieved by slime-derived compounds. In the present study, snail slime, upon analysis by GC-MS, showed twenty-three (23) peaks (Figure 1) corresponding to forty-three (43) compounds (Table 1). The identified slime constituents exhibited *in silico* inhibitory potential against both urease and H^+/K^+-ATPase. This strategy offers an alternative avenue in anti-ulcer therapy, consistent with evidence that current regimens remain incomplete.[15] Previous *in vivo* findings also support anti-ulcer activity of *A. marginata* slime, reinforcing its biological relevance.[10,16] In this study, the docking scores indicated the strength and stability of ligand–enzyme interactions which are important in drug discovery.[17] This provides useful preliminary data for structure-based drug design.[18] Phenol, 2,6-bis(1,1-dimethylethyl)- (P26BD), benzaldehyde, 3,5-dimethyl- (BAD), 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- (SODB), and cedranoxide, 8,14- (CO) had higher binding affinity (-7.4, -5.7, -6.5, -6.4 and -6.3 kcal/mol, respectively) than the standard inhibitor, N-(n-butyl) thiophosphoric triamide (NBPT) (-4.7 kcal/mol), against urease (figure 2).

As shown by their predicted binding energy, phenol, 2,6-bis(1,1-dimethylethyl)- (P26BD), benzaldehyde, 3,5-dimethyl- (BAD), 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- (SODB), and cedranoxide, 8,14- (CO) had more inhibitory effects on urease than the standard inhibitor, N-(n-butyl) thiophosphoric triamide (NBPT). More negative binding energies generally reflect stronger and more stable ligand–protein interactions.[19] This implies that P26BD, BAD, BHP, SODB and CO are potential drug candidates for eradication of *H. pylori* infection due to their exhibited *in silico* inhibitory effects on urease, an enzyme needed by the bacteria to survive.[15] However, the pharmacokinetics of the compounds should be taken into consideration, as this will reveal whether they may be useful in anti-ulcer drug discovery or not.

Proton pump inhibitors act by blocking H^+/K^+-ATPase, thereby reducing gastric acid output.[20] The present study has examined the inhibitory effects of bioactive compounds obtained from *A. marginata* slime on H^+/K^+- ATPase. Of all the forty-three (43) ligands, phenol, 2,4-bis(1,1-dimethylethyl)- (P24BD, with -7.4 kcal/mol binding affinity) showed a predicted binding affinity against proton pump close to that of the control (Omeprazole with -7.8 kcal/mol binding affinity). Phenol, 2,6-bis(1,1-dimethylethyl)- (P26BD) showed a higher binding affinity (-8.0 kcal/mol) than the omeprazole (figure 3).

N-(n-butyl) thiophosphoric triamide was anchored via an ionic interaction between its phosphorus moiety and GLU B:313 (Figure 4). It also formed a hydrogen bond with PRO B:302 and hydrophobic (π-alkyl) contacts with PRO B:305 and VAL B:560, fixing the ligand within the active site. Phenol, 2,4-bis(1,1-dimethylethyl)- bound via π–π stacking with PHE B:454 and hydrophobic/π-alkyl contacts involving its tert-butyl groups with PHE B:454, ALA B:480, ALA B:485, and ALA B:489 (Figure 5). Additional stabilization was imparted through a hydrogen bond with LYS B:394 and a π-anion interaction with GLU B:33, along with hydrophobic contacts with HIS B:34. The phenol, 2,6-bis(1,1-dimethylethyl)- binding is through strong polar and electrostatic forces. The phenolic OH participates in a crucial hydrogen bond with LYS B:394.

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Table 1: GC-MS Analysis Results of Snail Slime

S/N	Peak	Compound Name	Retention Time	Area (%)
1	1	Cyclotrisiloxane, hexamethyl-	3.665	0.31
2	2	Benzaldehyde, 2-methyl-	8.032	0.99
3	2	Benzaldehyde, 4-methyl-	8.032	0.99
4	3	Benzaldehyde, 3-methyl-	8.285	0.51
5	4	Benzaldehyde, 3,5-dimethyl-	9.665	1.27
6	4	1H-Inden-5-ol, 2,3-dihydro-	9.665	1.27
7	4	Benzaldehyde, 3,4-dimethyl-	9.665	1.27
8	5	Benzaldehyde, 4-ethyl-	9.835	0.74
9	5	Isophthalaldehyde	9.835	0.74
10	6	Phenol, 2,4-bis(1,1-dimethylethyl)	11.243	0.59
11	6	Phenol, 2,6-bis(1,1-dimethylethyl)	11.243	0.59
12	6	Ethyl 4-t-butylbenzoate	11.243	0.59
13	7	4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one	11.440	0.60
14	7	Spiro[2.5]octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)-	11.440	0.60
15	7	Cedranoxide, 8,14-	11.440	0.60
16	9	4-Amino-7-diethylamino-chromen-2-one	12.511	10.75
17	9	Silane, methylidynetris[trimethyl-	12.511	10.75
18	9	p-Octylacetophenone	12.511	10.75
19	10	Z-11-Pentadecenal	13.018	0.98
20	10	1-Octadecene	13.018	0.98
21	10	Oleic Acid	13.018	0.98
22	11	cis-11-Hexadecenal	13.159	0.44
23	11	13-Tetradecenal	13.159	0.44
24	12	cis-Vaccenic acid	13.497	2.88
25	13	trans-13-Octadecenoic acid	14.060	6.13
26	13	Oleyl alcohol, trifluoroacetate	14.060	6.13
27	14	18-Nonadecenoic acid	14.201	1.36
28	14	2-Tetradecanol	14.201	1.36
29	15	Z-(13,14-Epoxy) tetradec-11-en-1-ol acetate	14.398	2.65
30	15	cis-9-Hexadecenoic acid	14.398	2.65
31	16	Cyclopentadecanone, 2-hydroxy-	14.623	2.09
32	17	Butyl 9-octadecenoate or 9-18:1	14.877	1.41
33	17	Nonadecane	14.877	1.41
34	18	9-Octadecenoic acid, (E)-	15.159	9.47
35	19	3-Octadecene, (E)-	15.553	2.94
36	19	2- Chloropropionic acid, hexadecyl ester	15.553	2.94
37	19	Hexadecane, 1-(ethenyloxy)-	15.553	2.94
38	20	Octadecane, 1-(ethenyloxy)-	16.088	3.17
39	20	Nonadecanamide	16.088	3.17
40	21	1-Nonadecene	16.370	1.41
41	22	3-Eicosene, (E)-	16.680	2.89
42	23	9-Octadecenamide, (Z)-	18.088	8.71
43	23	9-Octadecenamide	18.088	8.71

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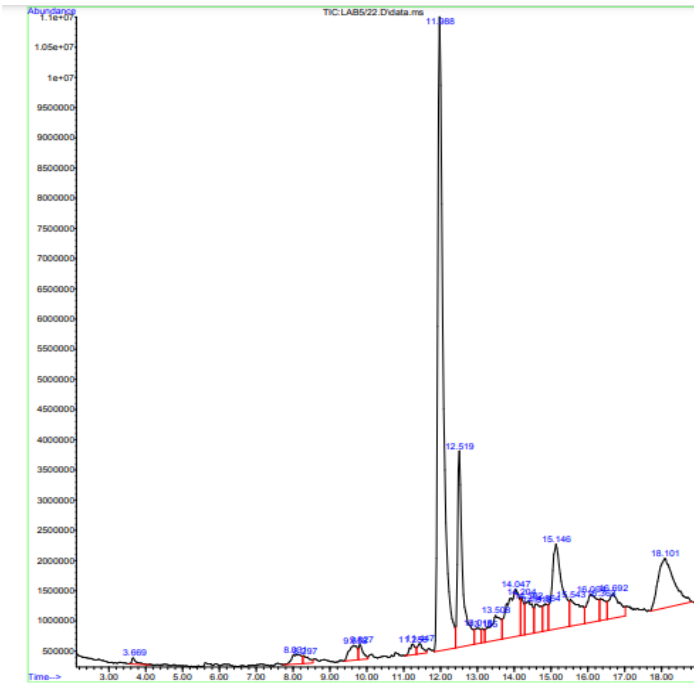

Figure 1: GC-MS Chromatogram of *A. marginata* slime

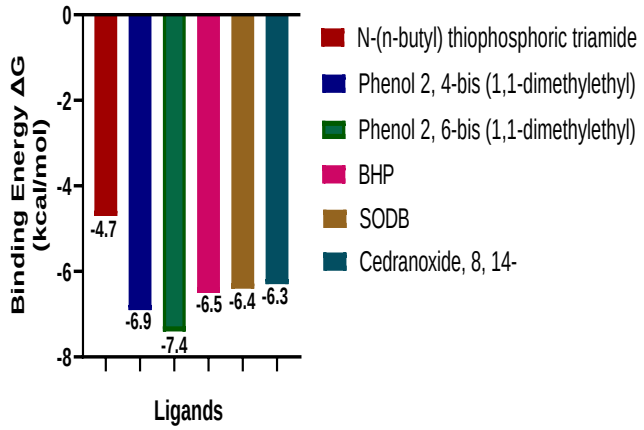

Figure 2: Docking Results of Ligands against Urease

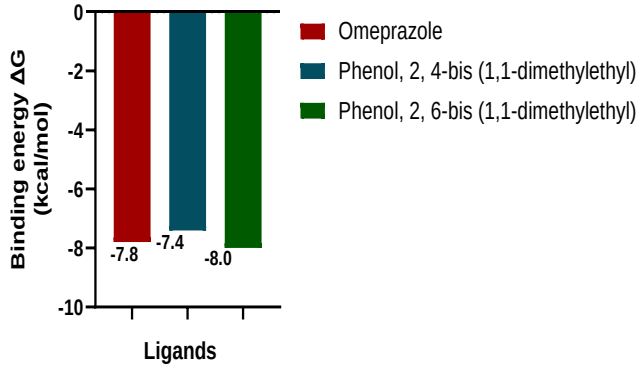

Figure 3: Docking Results of Ligands against H^+/K^+-ATPase

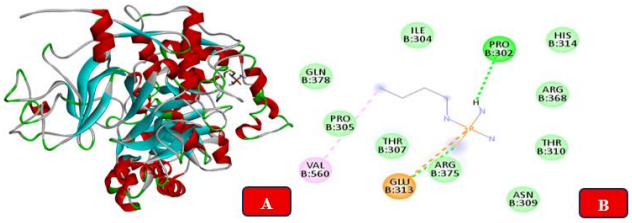

Figure 4: Interaction between N-(n-butyl) thiophosphoric triamide and urease (A: 2D structure; B: 3D structure)

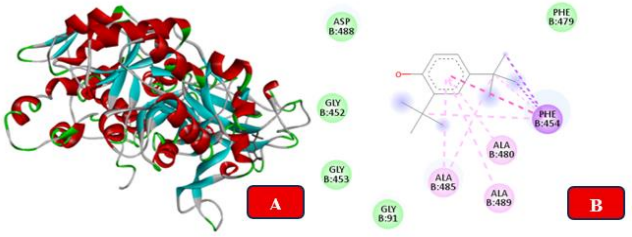

Figure 5: Interaction between Phenol, 2,4-bis(1,1-dimethylethyl)- and urease (A: 2D structure; B: 3D structure)

The aromatic ring participates in a strong π-anion interaction with the carboxylate of GLU B:33. There is a less strong hydrophobic contact with HIS B:34, stabilizing the ligand in position (Figure 6). Furthermore, 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one was stabilized through one hydrogen bond involving its C=O and GLY B:91, while its alkyl groups made hydrophobic contacts with PHE B:454, ALA B:485, ALA B:489, and LEU B:68, thereby contributing to complex stabilization (Figure 7). Cedranoxide, 8,14- was bound by a hydrogen bond to ARG B:6 and hydrophobic interactions with TYR B:9, TYR B:39, and ILE B:4, with a polar anchor supplemented by extensive nonpolar interactions. (Figure 8). Spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- was held in place mostly by hydrophobic forces. A hydrogen bond between its C=O and ILE B:4 and pi-alkyl and hydrophobic contacts with TYR B:9, TYR B:39, and ARG B:6 anchored the inhibitor (Figure 9).

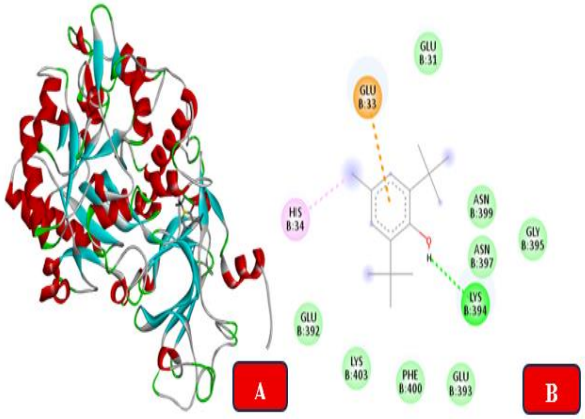

Figure 6: Interaction between Phenol, 2,6-bis(1,1-dimethylethyl) and urease (A: 2D structure; B: 3D structure)

Omeprazole, activated in acidic parietal cells, was sulfenamidated, forming covalent disulfide bonds (specifically with Cys813) on the H^+/K^+−ATPase α-subunit, irreversibly inhibiting acid secretion (Figure 10). Phenol, 2,4-bis(1,1-dimethylethyl)- bound H^+/K^+−ATPase by hydrogen bonds between CYS A:927 and GLN A:919 (Figure 11), while phenol, 2,6-bis(1,1-dimethylethyl)- had mostly hydrophobic binding, stabilized by pi interactions with PHE A:818 and PHE A:988, and alkyl/pi-alkyl contacts with TYR A:140, LEU A:817, and CYS A:822 (Figure 12).

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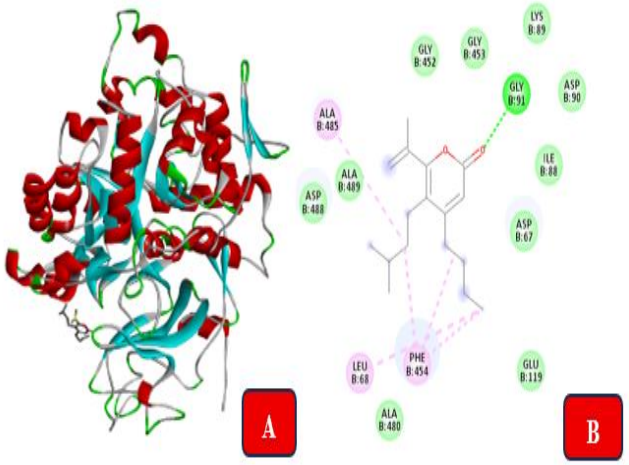

Figure 7: Interaction between 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one and urease (A: 2D structure; B: 3D structure)

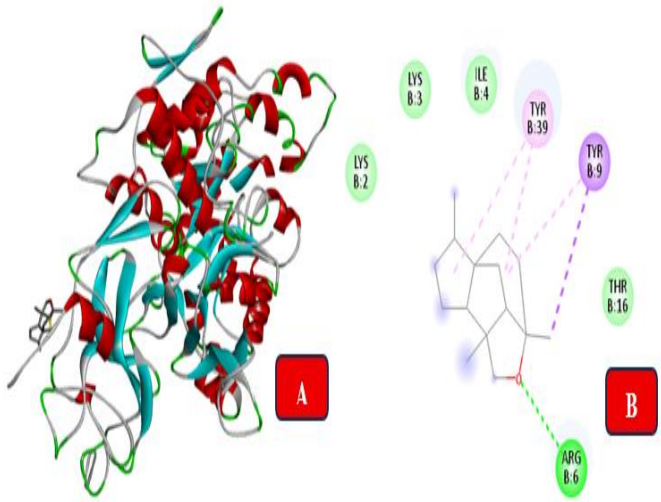

Figure 8: Interaction between Cedranoxide, 8,14- and urease (A: 2D structure; B: 3D structure)

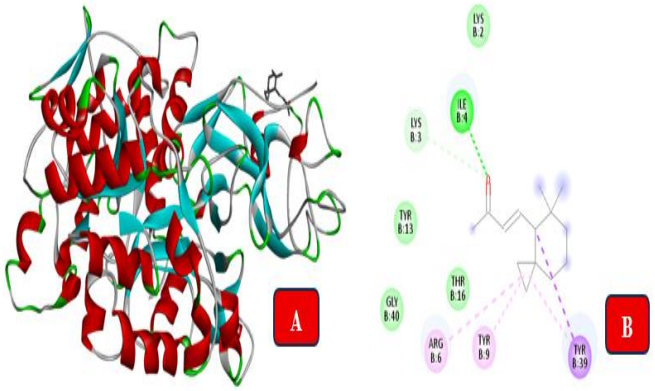

Figure 9: Interaction between Spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- and Urease (A: 2D structure; B: 3D structure)

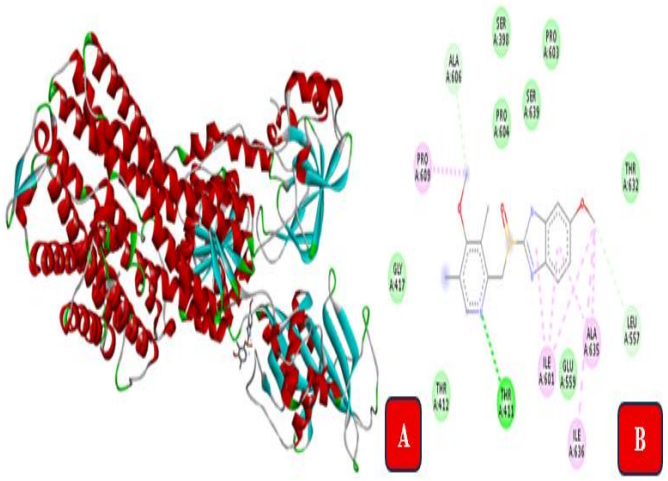

Figure 10: Interaction between omeprazole and H^+/K^+-ATPase (A: 2D structure; B: 3D structure)

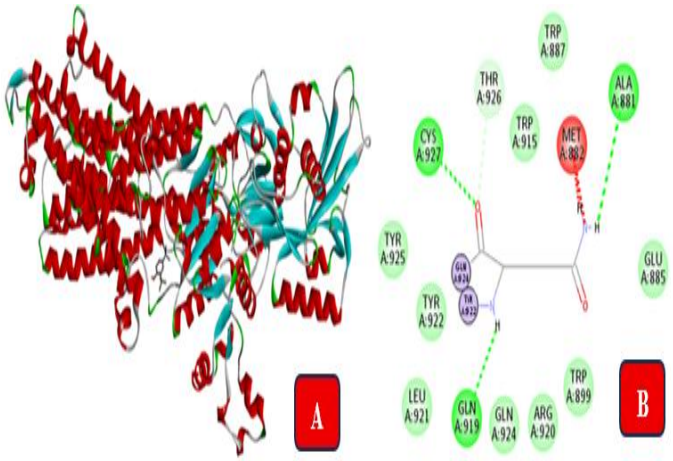

Figure 11: Interaction between Phenol, 2,4-bis(1,1-dimethylethyl)- and H^+/K^+-ATPase (A: 2D structure; B: 3D structure)

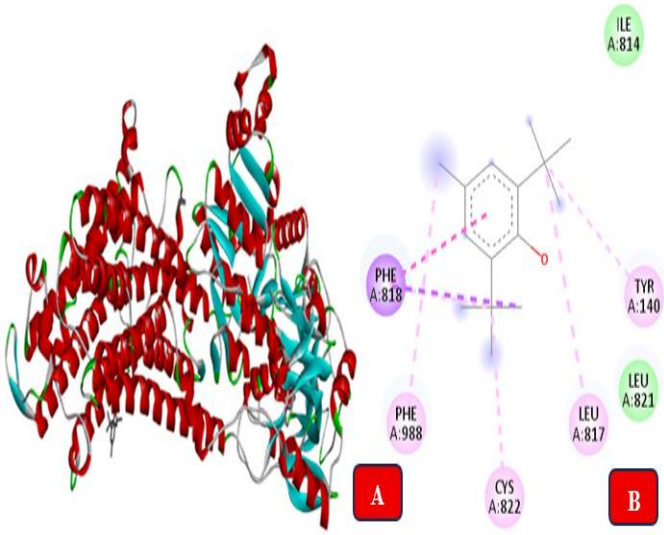

Figure 12: Interaction between Phenol, 2,6-bis(1,1-dimethylethyl) and H^+/K^+-ATPase (A: 2D structure; B: 3D structure)

Phenolic compounds, particularly tert-butylated analogues, tend to capitalize on π–π stacking with aromatic residues and hydrogen bond interactions with charged amino acids like lysine and glutamate, a model of binding also highlighted in recent docking studies of polyphenolic phytoconstituents against gastric proton pumps and urease.[21,22] Polar–aromatic interaction in 2,6-di-tert-butylphenol, where hydroxyl is engaged in hydrogen bonding and aromatic ring in π-anion interaction, is consistent with phenolic scaffold docking research showing enhanced stabilization within electrostatically charged catalytic sites.[23] Sesquiterpenoid oxides such as cedranoxide demonstrate a bi-substrate mode of binding comprising polar contacts to arginine and extensive hydrophobic contacts with aromatic residues that support the emerging consensus that polar–nonpolar complementarity governs sesquiterpenoid stabilization in ulcer-related targets.[24]

Any of these compounds with good pharmacokinetic screening results may be employed in the development of new proton pump inhibitor. The identified compounds showed different pharmacokinetic properties upon virtual prediction. Table 2 shows the pharmacokinetic parameters (absorption, distribution, metabolism, and excretion) of the hit bioactive constituents of *A. marginata* slime and standard inhibitors of urease and H^+/K^+-ATPase. ADMET prediction incorporated intestinal absorption, permeability, P-gp interaction, and BBB penetration parameters.[25] The gastrointestinal absorption of all ligands was predicted to be high and only omeprazole was predicted as p-glycoprotein substrate. 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one, N-(n-butyl) thiophosphoric triamide and omeprazole were predicted not to be blood-brain barrier (BBB) permeant, while others were predicted as BBB permeant. Only 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one and N-(n-butyl) thiophosphoric triamide showed no *in silico* properties against the cytochrome P450 isozymes. Renal organic cation transporter 2 was exhibited by omeprazole and 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one only. Omeprazole and 4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one showed predictive hepatotoxicity. The present study has shown that the gastrointestinal absorption of omeprazole is high, and that it is a P-glycoprotein substrate and it also skin permeant. The study also showed high gastrointestinal absorption and skin permeability of phenol, 2,6-bis(1,1-dimethylethyl)-, but the ligand is not a P-glycoprotein substrate. This was also the case in benzaldehyde, 3,5-dimethyl- (BAD), 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- (SODB), cedranoxide, 8,14- (CO) and n-(n-butyl) thiophosphoric triamide (NBPT). In terms of distribution, omeprazole has proven not to be blood-brain barrier (BBB) permeant, and this may account for why the drug is usually recommended with other drugs that do not only enhance the BBB permeability of the drug but also enhance its metabolism by inducing the CYP 450 isozymes. The same was the case in NBPT and BHP. Contrarily, other ligands exhibited BBB permeability. Metabolism of the compounds was predicted based on the CYP models for substrate or inhibition of the isozymes (CYP2D6, CYP3A4, CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4).[25] Among CYP enzymes relevant to drug metabolism, CYP3A4 is the most abundant and clinically significant isoform.[26] Modulation of CYP3A4 activity alters drug metabolic profiles and influences systemic exposure.[27,28] Of all the ligands whose ADMET were predicted in this study, only omeprazole showed *in silico* inhibition of CYP3A4, and at doses higher than the maximum tolerated ones, the drug can be accumulated in the liver and lead to hepatotoxicity.[28] Omeprazole showed inhibitory effects *in silico* on all CYP isozymes except CYP2C9. CYP1A2, which metabolizes caffeine, was also predicted to be inhibited by omeprazole. CYP1A2 inhibition may impair the metabolism of its substrates, including caffeine.[29] This may be accountable for advocacy against too much consumption of caffeine-containing foods by gastric ulcer patients who are on omeprazole medication. Moreover, caffeine contributes to etiology of gastric ulcer.[3] Phenol, 2,6-bis(1,1-dimethylethyl)-, benzaldehyde, 3,5-dimethyl- and cedranoxide, 8,14- are likely to behave like omeprazole (in terms of CYP1A2 inhibition) when they get developed as drugs due to the similarity in their predicted metabolism.

There was an appreciable total clearance of omeprazole, and the drug is a renal OCT 2 substrate, thereby facilitating its elimination from the body. One of the ligands from *A. marginata* slime, 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), showed almost the same *in silico* excretory property with that of omeprazole. The remaining ligands were not predicted to be substrates of renal OCT 2 but possess total clearances that project them as good drug candidates. At doses higher than the maximum tolerated doses, omeprazole has been predicted to be hepatotoxic. The same was the case of 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one (BHP), but the remaining ligands were predicted as non-hepatotoxic.

The binding affinity exhibited by benzaldehyde, 3,5-dimethyl- and spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- and their positive predicted pharmacokinetics suggest that they may be employed in drug discovery for eradication of *H. pylori* due to their *in silico* inhibitory potentials on urease, an enzyme needed by the bacteria to survive.[15] Considering the binding affinity exhibited by phenol, 2,4-bis(1,1-dimethylethyl)-, with its positive predicted pharmacokinetics, it may be employed in drug discovery as an alternative to omeprazole, as it has shown inhibitory potentials on proton pump *in silico.* The solubility and lipophilicity of the hit compounds suggest good predictive physicochemical properties of a good drug candidate, since high solubility of a drug enables it to be readily absorbed in various sites of absorption in the body.[30]

The physicochemical profiles of the compounds align with established drug-likeness criteria.[31] Table 3 shows the physicochemical properties of the hit ligands, and those of the standard ligands. Phenol, 2,6-bis(1,1-dimethylethyl)-, benzaldehyde, 3,5-dimethyl-, 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one and phenol, 2,4-bis(1,1-dimethylethyl)- were predicted as 'moderately soluble', while omeprazole, spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)- and cedranoxide, 8,14- were predictively soluble. N-(n-butyl) thiophosphoric triamide was predicted as 'very soluble'. No ligand violated the Lipinski's rule of five.

Drug solubility strongly influences oral absorption and systemic availability.[32] Phenol, 2,6-bis(1,1-dimethylethyl)-, benzaldehyde, 3,5-dimethyl-, 4-butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one and phenol, 2,4-bis(1,1-dimethylethyl)- were predicted as moderately soluble, suggesting moderate absorption and bioavailability of the compounds. Omeprazole, spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)-, and cedranoxide, 8,14- were predicted as soluble, while N-(n-butyl) thiophosphoric triamide was predicted as very soluble, implying that the ligands have high bioavailability and absorption. The predicted medicinal chemistry showed no alert for pan-assay interference compounds (PAIN), and of all the ligands, only omeprazole, which was the standard used for docking the ligands against H^+/K^+-ATPase, showed lead-likeness. None of the ligands was predicted to violate the Lipinski rule of five. These promising docking scores and pharmacokinetics suggest that the compounds may be employed in drug discovery for eradication of *H. pylori* due to their *in silico* inhibitory potentials on urease. Amelioration of gastric ulcer by dual inhibition of urease and proton pump has also been supported by the findings of Alabi *et al*.[33] The combined docking, pharmacokinetic, and physicochemical results support the potential of selected slime-derived compounds as dual inhibitors of urease and H^+/K^+-ATPase.

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Table 2: Pharmacokinetic Properties and Toxicity of the Hit Compounds

	Omeprazole	Phenol, 2,6-bis(1,1-dimethylethyl)-	Benzaldehyde, 3,5-dimethyl-	BHP	SODB	Cedranoxide, 8,14-	N-(n-butyl) thiophosphoric triamide	Phenol, 2,4-bis(1,1-dimethylethyl)-
GIA	High	High	High	High	High	High	High	High
Pg-Substrate	+	-	-	-	-	-	-	-
BBB Perm.	-	+	+	-	+	+	-	+
CYP1A2I	+	+	+	-	-	+	-	-
CYP2C19I	+	-	-	-	-	+	-	-
CYP2C9I	-	-	-	-	-	+	-	-
CYP2D6I	+	+	-	-	-	-	-	+
CYP3A4I	+	-	-	-	-	-	-	-
R.OCT.	+	-	-	-	+	-	-	-
HT	+	-	-	+	-	-	-	-

GIA: Gastrointestinal absorption; pg-sub: P-glycoprotein substrate; BBB Perm: blood-brain barrier permeability; CYP1A2I: CYP1A2 Inhibitor; CYP2C19I: CYP2C19 Inhibitor; CYP2C9I CYP2C9 Inhibitor; CYP2D6I: CYP2D6 Inhibitor; CYP3A4I: CYP3A4 Inhibitor; R. OCT2: Renal OCT2; HT: Hepatotoxicity.

Table 3: Physicochemical Properties and Drug likeness of Bioactive Components of *A. marginata* Slime extract

S/N	**Compounds**	**Water solubility (ESOL)**	**Solubility Class**	**Lipophilicity (ILOGP)**	**PAINS**	**Lead Likeness**	**Lipinski Drug likeness**
1	Omeprazole	-3.52	Soluble	1.64	-	+	0 violation
2	Phenol, 2,6-bis(1,1-dimethylethyl)-	-4.38	Moderately soluble	3.07	-	-	0 violation
3	Benzaldehyde, 3,5-dimethyl-	-4.29	Moderately soluble	4.01	-	-	0 violation
4	4-Butyl-5-(3-methylbutyl)-6-(1-methylethenyl)-2H-pyran-2-one	-4.58	Moderately soluble	3.64	-	-	0 violation
5	Spiro [2.5] octane, 3,3-dimethyl-2-(1-buten-3-on-1-yl)-	-3.52	Soluble	2.84	-	-	0 violation
6	Cedranoxide, 8,14-	-3.51	Soluble	3.03	-	-	0 violation
7	N-(n-butyl) thiophosphoric triamide	-1.01	Very Soluble	0.47	-	-	0 violation
8	Phenol, 2,4-bis(1,1-dimethylethyl)-	-4.55	Moderately Soluble	3.08	-	-	0 violation

P: PAINS: Pan-assay Interference compounds; LL: Lead Likeness

Conclusion

This study has revealed the predictive inhibitory effects of *A. marginata* slime bioactive constituents such as phenol, 2,6-bis(1,1-dimethylethyl) and phenol, 2,4-bis(1,1-dimethylethyl), the potent PPI and *H. pylori* urease inhibitors which may be developed as crucial therapies for gastric ulcers. These compounds have shown pharmacokinetic and physicochemical properties *in silico*. *In vitro* and *in vivo* studies are therefore, recommended to confirm the antiulcerogenic potential of *A. marginata*, as the slime may proffer another fruitful direction for gastric ulcer treatment.

Conflict of interest

The authors declare no conflict of interest

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them

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References

1. Sverdén E, Lars A, Jason M, Dunn M, Jesper L. Peptic ulcer disease. Brit Med J. 2019; 367 (3): 1-8. https://10.1136/bmj.l5495
2. Majumdar D, Looi S. *Helicobacter pylori* infection and peptic ulcers. Medicine (Abingdon). 2024; 52(3):152–160. https://doi.org/10.1016/j.mpmed.2023.12.006
3. Collatuzzo G, Dajti E, Secco M, Bazzoli F, Boffetta P, Zagari RM. Burden of gastric cancer attributable to *Helicobacter pylori* in 27 countries from seven geographic regions in 2022. Gastric Cancer. 2025; 28(1):1–11. https://doi.org/10.1007/s10120-025-01677-9
4. Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse effects associated with proton pump inhibitor use. Cureus. 2021; 13(1): 1-6 https://doi.org/10.7759/cureus.12759
5. Ghouri YA, Aslam S, Jafri W. *Helicobacter pylori* infection. Cleve Clin J Med. 2021; 88(6):347-354. https://doi.org/10.3949/ccjm.88a.20193
6. Rani L, Ramakrishnan LM, Vinodhin D, Krishnaaveni GP, Bhuvaneshwari B, Sudarvizhi M, Reena J, Priyanka Ramya T. Molecular docking study of lead compounds from *Elathy Chooranam* a Siddha formulation against *Helicobacter pylori* urease. J Pharm Negat Results. 2023; 14(3):1470-1477.
7. Jaiswal F, Rai AK, Wal P, Wal A, Singh SP. Peptic ulcer: a review on etiology, pathogenesis and treatment. Asian J Pharm Educ Res. 2021; 10(4):1-17.
8. Merkhan M, Mustafa Y, Hassan E. Safety and efficacy of proton-pump inhibitors are relevant to their distinctive chemical structures and physicochemical properties. Int J Pharm Stud. 2022; 6(2):1–11.
9. Gheorghe C, Pascu O, Iacob R. Adverse effects associated with proton pump inhibitor therapy. Maedica (Bucur). 2012; 7(4):309-314.
10. Nwodo NJ, Okota JM, Ezugwu CO, Attama AA. Anti-ulcer potentials of phylum *mollusca* (tropical snail) slime. Asian Pac J Trop Med. 2009; 2(3):23-28.
11. Ibrahim M, Mohammed H, Warra Z, Abdulrahman A, Sabo Y, Ibrahim I, Jajere GU, Victor A, Oyi R. Physicochemical and genetic diversity studies of Vitellaria paradoxa in Northern Nigeria. J Curr Biomed Res. 2022; 2(1):19–37. https://doi.org/10.54117/jcbr.v2i1.4
12. Rahman N, Khalil N, Khan S, Almutairi MH, Almutairi BO, Alam M. Multispectroscopic and molecular docking studies on the interaction of diltiazem hydrochloride with bovine serum albumin and its application to the quantitative determination of diltiazem hydrochloride. J King Saud Univ Sci. 2021; 34 (4): 1-8.
13. Kuipers EJ, Thijs JC, Festen HPM. The pathogenesis of peptic ulcer disease. N Engl J Med. 2021; 384(25):2406–2416. https://doi.org/10.1056/NEJMra2028892
14. Li B, Lan X, Wang L, Zhao J, Ding J, Ding H, Lei J, Wei Y, Zhang W. Proton-pump inhibitor and amoxicillin-based triple therapy containing clarithromycin versus metronidazole for *Helicobacter pylori*: a meta-analysis. Microb Pathog. 2020; 142 (1):1-8. https://doi.org/10.1016/j.micpath.2020.104075
15. Kamada T, Satoh K, Itoh T, Ito M, Iwamoto J, Okimoto T, Kanno T, Sugimoto M, Chiba T, Nomura S, Mieda M, Hiraishi H, Yoshino J, Takagi A, Watanabe S, Koike K. Evidence-based clinical practice guidelines for peptic ulcer disease 2020. J Gastroenterol. 2021; 56(5):459–473. https://doi.org/10.1007/s00535-021-01769-0
16. Amah AK, Ewa O, Karimah MR, Elendu MU, Yunusa Z. Effect of *Archachatina marginata* mucin on the aggressive factors of gastric ulcer challenged Wistar rat stomach tissue. Biol Pharm Sci. 2019; 9(1):77–82.
17. Mehrotra R, Agarwal S. An overview of molecular docking. JSM Chem. 2016; 4(2):1024.
18. Guedes IA, Magalhães CS, Dardenne LE. Receptor–ligand molecular docking. Biophys. Rev. 2014; 6 (6): 75-87.
19. Du X, Li Y, Xia YL. Insights into protein-ligand interactions: mechanisms, models, and methods. Int J Mol Sci. 2016; 17(2):1-34.
20. Kawade D, Nikhil S, Payal B, Payal H, Nidhi D. Peptic ulcer: a review on its etiology, pathogenesis and pharmacotherapy. World J Pharm Res. 2020; 9(5):558-583.
21. Khan A, Abbasi SW, Shah FA, Rasheed F, Qazi NG, Pervez S, Khalil AAK, Ali F, Aziz N, Seo SY. Ethnopharmacological basis of *Rumex hastatus* D. Don in gastrointestinal diseases with focusing effects on H^+/K^+-ATPase, calcium channels, and PDE inhibition. Molecules. 2022; 27(18):5919. https://doi.org/10.3390/molecules27185919
22. Gonfa YH, Beshah F, Tadesse MG, Bachheti A, Bachheti RK. Phytochemical investigation and potential pharmacologically active compounds of Rumex nepalensis: an appraisal. Beni-Suef Univ J Basic Appl Sci. 2021; 10(18):1–11.
23. Panigrahi N, Pasha A, Mondal S. Synthesis of novel aryl (4-aryl-1H-pyrrol-3-yl) (thiophen-2-yl) methanone derivatives: molecular modelling, in silico ADMET, and anti-ulcer activities. Anti-Inflamm Anti-Allergy Agents Med Chem. 2021; 20(2):135–147. https://doi.org/10.2174/1871520620666201120161327
24. Laloo D, Sinha SK, Prasad SK, Hemalatha S. Gastric H^+/K^+-ATPase inhibitory effects of the active constituent isolated from Potentilla fulgens roots: An *in vivo* and *in silico* molecular docking studies. Phytomedicine Plus. 2021; 1(1):1–10.
25. Han Y, Zhang J, Hu CQ, Zhang X, Ma B, Zhang P. In silico ADME and toxicity prediction of ceftazidime and its impurities. Front Pharmacol. 2019; 10:434.
26. Rendic S, Di Carlo FJ. Human cytochrome P450 enzymes: a status report summarizing their reactions, substrates, inducers, and inhibitors. Drug Metab Rev. 1997; 29 (2):413-580.
27. Ohno Y, Hisaka A, Suzuki H. General framework for the quantitative prediction of CYP3A4-mediated oral drug interactions based on the AUC increase by coadministration

of standard drugs. Clin Pharmacokinet. 2007; 46 (8):681-696.
28. Busti AJ, Herrington JD, Daves BJ, McKeever GC. What is the process to determine if medications are to be classified as weak, moderate or strong inhibitors of CYP3A4? PW Drug Interact Newsl. 2009; 1(39):1-3.
29. Hebert MF. Impact of pregnancy on maternal pharmacokinetics of medications. Clin Pharmacol Pregnancy. 2013; 20(3):17-39.
30. Savjani KT, Gajjar AK, Savjani JK. Drug solubility: importance and enhancement techniques. ISRN Pharm. 2012; 2 (1): 1-10. https://doi.org/10.5402/2012/195727
31. Jia C, Li J, Hao G, Yang G. A drug-likeness toolbox facilitates ADMET study in drug discovery. Drug Discov Today. 2020; 25(1):248-258. https://doi.org/10.1016/j.drudis.2019.10.014
32. Meanwell NA. Improving drug candidates by design: a focus on physicochemical properties as a means of improving compound disposition and safety. Chem Res Toxicol. 2011; 24(6):1420–1456.
33. Alabi MA, Abiola MM, Yakub NT, Ajani EO. *In vitro* anti-inflammatory and anti-ulcerogenic potential of ethanol extract of *Carica papaya* leaves: phytochemical and molecular docking studies. Trop J Phytochem Pharm Sci. 2025; 4(8):341–354. http://www.doi.org/10.26538/tjpps/v4i8.1/5