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Article

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In-silico molecular studies of the phytochemicals in ethanolic extract of *Chromolaena Odorata* against H^+/K^+-*ATPase* enzyme for Proton Pump inhibitor

Chinyere B.C. Ikpa,[1*] Oluwatosin Maduka Tochukwu[2]

[1]*Department of Chemistry, Imo State University, Owerri, Imo State, Nigeria.* [2]*Graduate School of Engineering, Saitama University, 255 Shimo Okubo, Sakura-ku, Saitama City, Saitama. Japan.*

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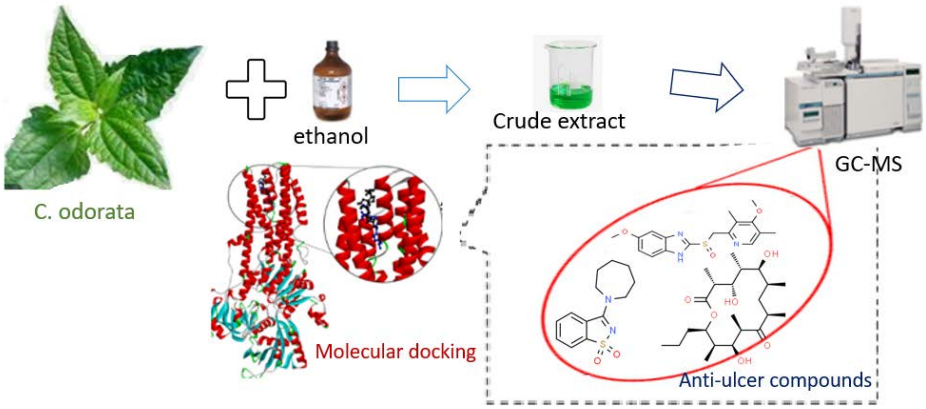
ABSTRACT



Chromolaena odorata popularly called devil weed (independent leaves) is a subtropical flowering shrub in the family of Asteraceae that has been used for the herbal treatment of wounds, burns, skin infections, and relieving painful stomach ulcers. It has antimicrobial, wound healing, hemostatic, antioxidant, anti-inflammatory, platelet protective, anticancer, hypoglycemic, hypolipidemic, insecticidal, and anti-anemic properties. This study investigated the phytochemical components and the anti-ulcer (gastric pump inhibition) properties of the ethanolic extract of the plant using GC-MS and in silico molecular docking. The GC-MS results from this study detected thirty (30) retentions with fifty-one (51) library/ID-suggested compounds. The docking of the detected compounds against gastric proton pump for the treatment of ulcer revealed that among the ligands that were docked with the enzyme (H^+/K^+-ATPase); (3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide) had better (high) binding energy value (-8.4kcal/mol) compared to the standard anti-ulcer drug (omeprazole; −8.0 kcal/mol). The strong bonding of 3-(Azepan-1-yl)-1,2-benzothiazole-1,1-dioxide to the receptor suggests that the compound may possess better gastric proton pump inhibitory potential than omeprazole. This result may also validate the traditional use of the plant for gastric ulcer-relieving activity.

Keywords: Omeprazole, gastric pump, ulcer, in-silico, inhibitory

INTRODUCTION

Chromolaena odorata is an herbaceous perennial plant that forms dense tangled bushes of herbs 1.5-2.0 m in height with long rambling (but not twining) branches. C. *odorata* is a tropical and subtropical specie of flowering shrub in the family Asteraceae.[1] Several parts of this plant have been widely used in Africa to treat wounds, burns, and skin infections. For instance, in Ghana and Nigeria (Benin), the infusion from fresh *Chromolaena odorata* leaves is used to treat malaria and internal hemorrhage.[2] Other parts of the world have equally reported the effective use of this plant in herbal treatment. Examples include Vietnamese folk medicine, where the plant has been widely used for gastric ulcer treatment,[3] while in Thailand and Guatemala, the leaves are used to quench external hemorrhage and as an antimicrobial agent respectively,[4,5] The leaf extract of the plant has been reported to contain very high-value nutritional potency with a rich source of mineral elements,[6] as well as it also possesses anticancer, antidiabetic, anti-hepatotoxic, anti-inflammatory, antimicrobial, and antioxidant properties.[6]

The digestive system's stomach is the organ that transports food from the esophagus to the small intestine, where it is further processed. It produces acid and a number of enzymes to break down food into simpler compounds.[7,8] The interior wall of the stomach is protected from acid and enzymes by a mucous layer. An imbalance between the digestive juices in the stomach and the various

*Corresponding Author: Ikpa, Chinyere, Department of Chemistry, Imo State University, Imo State, Owerri Nigeria.
Tel: 234 806 430 5552; Email: ikpacbc@gmail.com

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elements that help to protect its lining results in lesions called ulcers.[9] Peptic ulcer disease (PUD) is characterized by discontinuation in the inner lining of the gastrointestinal (GI) tract because of gastric acid.[8] The main risk factors for Peptic ulcer disease are Helicobacter pylori (H. pyroli) and non-steroidal anti-inflammatory drugs (NSAID) use.[10,11] Helicobacter pylorus is a gram-negative bacillus that is found within the gastric epithelial cells. Almost half of the world's population is colonized by *H. pylori*, an organism that is usually acquired in childhood and persists until treated. *H. pylori* diseases can also be transmitted from person to person through oral-to-oral or fecal-to-oral routes, drinking water, and other environmental sources.[12,13] Risk factors for acquiring the infection can generally classified as lower socioeconomic status and unsanitary conditions or crowding.[8] The organism has a wide spectrum of virulence factors allowing it to adhere to and inflame the gastric mucosa. This results in hypochlorhydria or achlorhydria, leading to gastric ulceration.[14,15] *H. pylori* eradication promotes peptic ulcer healing and reduces the incidence of complications,[16] and is also a primary preventive measure for gastric cancer. However, with the widespread use of antibiotics, the resistance of H. pylori to antibiotics has gradually increased in recent years,[17] which has become the main reason for the failure of H. pylori eradication.[18]

NSAIDs including low-dose aspirin are some of the most commonly used anti-inflammatory drugs. They have good efficacy and a long history of clinical use like analgesic and anti-inflammatory properties,[19] but NSAIDs can also induce mucosal injury by several mechanisms. Peptic ulcers caused by these drugs may have fatal complications.[20,21] The majority of NSAIDs are weak acids that become protonated and easily cross lipid membranes to enter epithelial cells when exposed to acidic gastric juice and thus can result in a topical injury, rapid epithelial cell death, superficial hemorrhage, and erosions.[3] The other major mechanism by which NSAIDs cause mucosal injury is by inhibition of cyclooxygenase-1 (COX-1), thereby blocking prostaglandin synthesis and resulting in decreased gastric mucus and bicarbonate production and a decrease in mucosal blood flow.[22,23,24]

Various medications including proton pump inhibitors and H2 receptor antagonist are available for the treatment of gastric ulcers, however clinical assessment of these medications have demonstrated side effects, the incidence of relapses, drug interactions and inadiquate drug solubility in oral administration[25] thus, there is a necessity to identify effective and safe anti-ulcer agent. The rapidly growing research in this field suggests that, with remedial and nutritional advances, gastric ulcers may become preventable within the next decade. This can be done by strengthening the defense mechanisms of the gastric mucosa and, in parallel, limiting the factors resulting in gastric ulceration. Plants have been reported to be a better treatment for ulcers due to posing little to no side effects when compared to modern medications.[22] Plants from the Fabaceae family are the most frequently studied and reported to have promising wound healing, antioxidant, anti-inflammatory, cytoprotective, gastric secretion inhibition, mucus production improvement, HSP70 up-regulation, Bax protein down-regulation, anti-secretory and anti-H. pylori effects.[22] C. *odorata* has been extensively used as a herbal remedy for PUD treatment in local medicines around the world. Some researchers have reported the *In vivo* anti-ulcer potentials of the crude ethanolic,[23] and Methanol/Methylene Chloride extract[24] of the plant in rats and mice respectively. With the discovery of H+/K+ ATPase as the primary gastric proton pump, inhibition of H+/K+ ATPase as a means of controlling gastric pH has gained extensive interest in recent years. Hence, the present study aimed to identify the mechanism of C. *odorata* anti-ulcer action by inhibition of H+/K+ ATPase. This study was carried out by first identifying the phytochemicals present in the ethanolic crude extract using GCMS, subsequently, the mechanism of action of the phytochemicals was investigated by docking against crystal structure of the gastric proton pump.

MATERIALS AND METHODS

Plant material collection

The leaves of Chromolaena odorata were collected in May 2021 from behind the New Science Laboratory of Imo State University, Imo state, Nigeria. The plant was authenticated by Professor Mbagwu of the Plant Science and Biotechnology Department at Imo State University. The leaves were shade-dried at room temperature, and powdered with mortar and pestle kept in an amber colour container prior to analysis.[26]

Preparation of the crude extract

The Chromolaena odorata powder was extracted by percolating 500 g of the sample with 750 ml of redistilled ethanol (92%) for 72 hours with occasional agitation. The extract was filtered and concentrated with rotary evaporator (Stuart, SO1, UK), and dried at 45°C in a Genlab oven.[27]

Gas chromatography-mass spectrometry (GC–MS) analysis:

The sample (1g) was dissolved in ethanol and injected in an Agilent (Agilent 19091-433HP, USA) GC-MS coupled to a mass spectrophotometer MS (Agilent Technologies) by auto injection at the Multi-User Science Research Laboratory, Ahmadu Bello University, Zaria in Kaduna State, Nigeria. The following were the GC-MS operating conditions for the analysis: Temperature in the oven: 50°C for 2 minutes, then 100°C at 10°C/min, then 200°C and held isothermally for 10 minutes. The sample injection volume was 2µliters, and the carrier gas was helium at a rate of 1 mL per minute. The sample components were ionized at a voltage of 70 eV. The GC ran for a total of 24.50 minutes. The structures of the identified compounds were then compared to those in the NIST database using NIST14.Library (2018). The retention durations and mass spectra of the compounds were compared to those of already known compounds in the NIST library.[25] The reported data includes the compound, name, retention time, and concentration. The structures, molecular weight, and pubchem ID were derived from the PubChem database.[28]

Molecular docking studies

Protein-ligand docking study of compounds identified in chromolaena odorata was conducted in oder to investigate the interaction between the active site of H+/K+-ATPase enzyme and the ligands using Auto dock vina virtual screening software, and Discovery studio software.

Ligands preparation for docking

The 3D structure of the compounds was downloaded from the PubChem server. Those compounds without 3D structures, 2D structures were downloaded, and were later converted to 3D structures, all in SDF format using Open babel software In the command line environment. Hydrogen bonds were added, charges were added by converting the compounds to MOL2 format and they were further converted to PDBQT format and energies were minimized using the MMFF94 in the same command line environment.

Preparation of receptor

The crystal structure of the gastric proton pump complexed with tegoprazan (PDB code: 7w47) was downloaded from Protein Databank (PDB). The 3D structure receptor was prepared by discarding water molecules and cofactors using Discovery Studio software30 and saved as Pdb. The binding site of tegoprazan was selected as the active site of the receptor.

Docking of the ligands with the receptor

The docking of the ligands and the receptor was performed using Autodock vina[29] since the receptor and the ligand separate after carrying out the docking with autodock. The complexes interactions were visualized using Discovery studio software.[30-35]

RESULTS AND DISCUSSION

Gas chromatography-mass spectrometry (GC–MS) result:

The gummy, dark green ethanolic extract of chromolaena odorata leaves gave thirty (30) retentions on GC-MS analysis with fifty-one (51) library/ID-suggested compounds. The result comprises forty-nine (49) aliphatic compounds, one alicyclic compound; Oxacyclotetradecane-2,11-dione, -methyl- and one aromatic heterocyclic compound; 3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide. The result presented in Table 1S in the supplementary data shows the peaks, compounds name, retention time, percentage composition, molecular weight, molecular formula, PubChem ID, and their structures. The compounds with the highest docking scores are presented on Table 1.

Table 1: GC-MS result of ethanolic extract of chromolaenaodorata leaves showing 10 compounds with the highest binding affinities

Sr. No.	PK#	Compounds Name	RT	% AREA	MF & MW	Pubchem id
1	25a	3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide	34.475	11.05	$C_{13}H_{16}N_2O_2S$ 264.35	535203
2	11a	13-methyl-Oxacyclotetradecane-2,11-dione	19.762	0.13	$C_{14}H_{24}O_3$ 240.34	543408
3	27a	9-Octadecenoic acid (Z)-, 2,3-dihydroxypropyl ester	34.777	6.74	$C_{21}H_{40}O_4$ 356.5	5283468
4	13a	9,12-Octadeca dienoic acid (Z,Z)-, methyl ester	23.378	0.27	$C_{19}H_{34}O_2$ 294.5	5284421
5	16b	9-Octadecenoic acid	24.886	0.23	$C_{18}H_{34}O_2$ 282.5	637517
6	21a	(Z)-Decyl icos-9-enoate	29.993	0.69	$C_{30}H_{58}O_2$ 450.8	76964864
7	13b	9,15-Octadecadienoic acid, methyl ester, (Z,Z)-	23.378	0.27	$C_{19}H_{34}O_2$ 294.5	5362738
8	17a	9,12-Octadecadienoyl chloride, (Z, Z)-	25.152	0.13	$C_{18}H_{31}ClO$ 298.9	86740353
9	2a	9,12-Octadecadienal	10.329	2.21	$C_{18}H_{32}O$ 264.4	5283383
10	9c	3-Eicosene, (E)-	13.367	0.10	$C_{20}H_{40}$ 280.5	5365051

Molecular docking result

Peptic ulcer disease is one of the life-threatening diseases that affect a large population of the world, over the past two centuries with high morbidity as well death rate. According to the latest WHO data published in 2020 Peptic Ulcer Disease Deaths in Nigeria reached 5,846 or 0.39% of total deaths. Gastric proton/potassium pump (H+/K+-ATPase) is a phosphoenzyme resting and concentrated in the parietal cells, is responsible for the excess secretion of gastric acid into the stomach lumen, leading to acid-related disorders. Therefore, this enzyme is unique to the parietal cells, it is considered as a good validated hit for anti-ulcer agents, because the proton pump inhibitors reduce acid secreted by the stomach via restraining the function of the enzyme. Molecular docking studies of 51 compounds identified in the ethanolic extract of chromolaena odorata were carried out targeting the protein and the docking scores of the compounds were presented on the Table 2. The result showed that the docking scores fall within the range of −4.8 to −8.4 kcal/mol. All the Compound were found to strongly inhibit the H+/K+-ATPase enzyme by totally inundating the binding site in the target protein. More also Fig. 2, Fig 3, and Fig. 4 depict the visuals of the best low binding energy (high binding energy values) for the docked ligands. Among the ligands that were docked with the enzyme (H+/K+-ATPase), ligand 3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide is the most potent with the highest docked score followed by 13-methyl-Oxacyclotetradecane-2,11-dione with docked score of −7.1 kcal/mol. The result of docking analysis also showed that (3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide) have lower energy value (high binding energy value) (-8.4kcal/mol) compared to the standard anti-ulcer drug (omeprazole) with it binding energy value of −8.0 kcal/mol. The compound 3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide display hydrogen interactions with TYR799, and ALA335 and pi-sigma interactions with ALA335 which it used in stabilizing its aromatic nucleus, more interactions observed were 4 alkyl interactions and 7 Van Der Waal's interactions with the active site amino acid residues, these hydrophobic interactions indicated that the compound bind deep in the core of active site. Hydrophobic interactions were observed from the second highest binder, 13-methyl-Oxacyclotetradecane-2,11-dione. The interactions observed include pi-alkyl interactions at residues PHE 818, and ALA 144. Further interactions were van der waal interactions with 7 amino acid residues. The interactions of the control compound (Omeprazole) was also identified, it interacted using hydrogen bonding with ASN138, and CYS813, it also had pi Interactions with ASP132, TYR799, and ALA335, further interactions observed were 16 van der waal's interactions with residues at the active site.

This visualized interactions from the compounds gives the reason for the high binding energies identified in the results.

Table 2: Binding energies of the compounds on the protein target

s/n	PK#	Compounds	Pubchem id	Binding Energy kcal/mol
Cntr		Control (Omeprazole)	4594	-8.0
47	25a	3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide	535203	-8.4
23	11a	Oxacyclotetradecane-2,11-dione, -methyl-	543408	-7.1

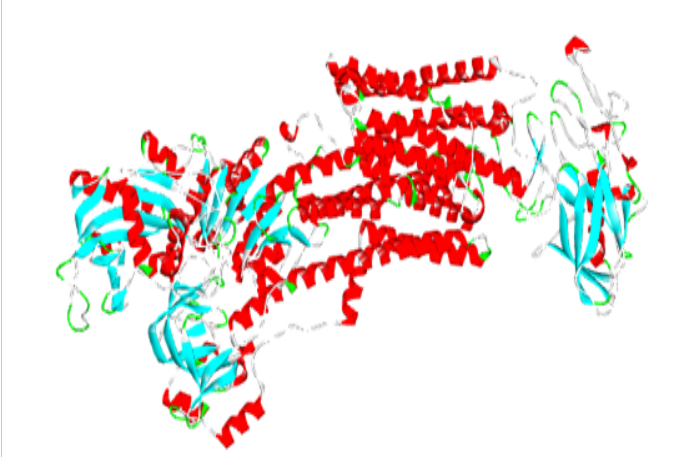
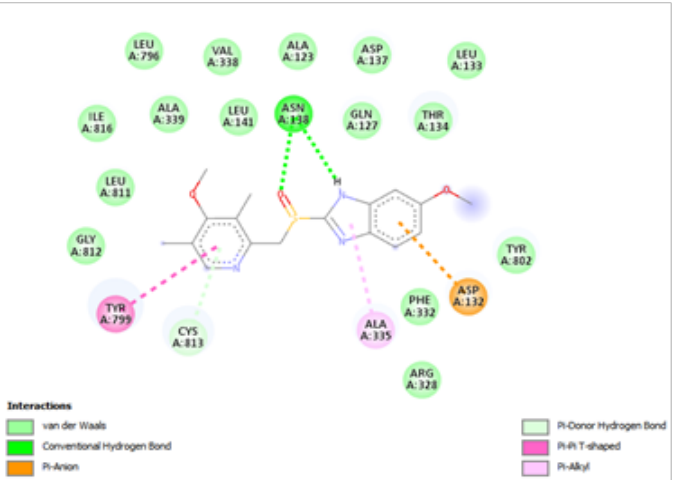


Figure 1: Crystal structure of the gastric proton pump. (PDB ID: 7w47).



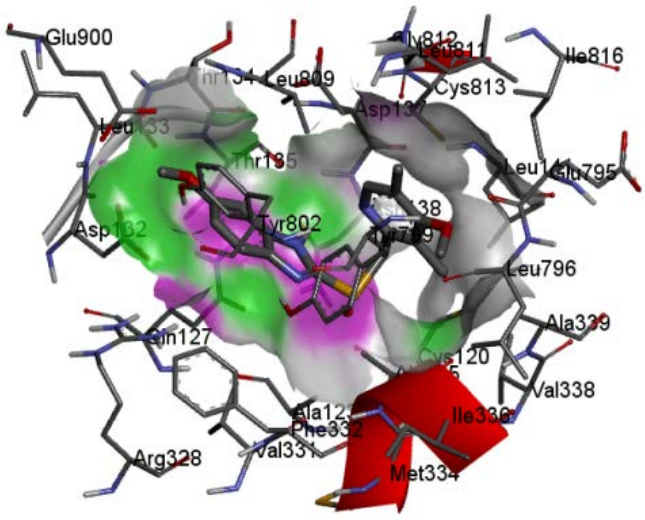
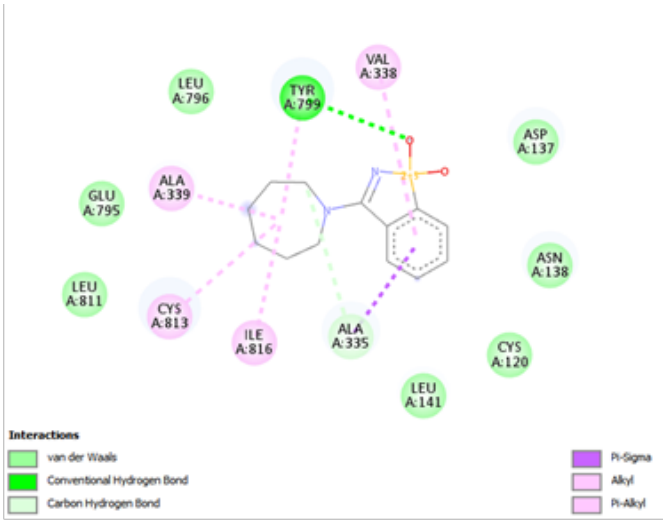


Figure 2: 2d and 3d interaction of the gastric proton pump with the control Omeprazole.



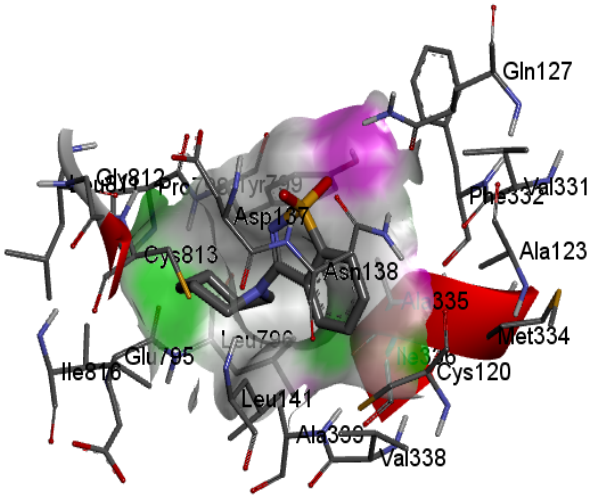


Figure 3: 2d and 3d interaction of the gastric proton pump with 3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide

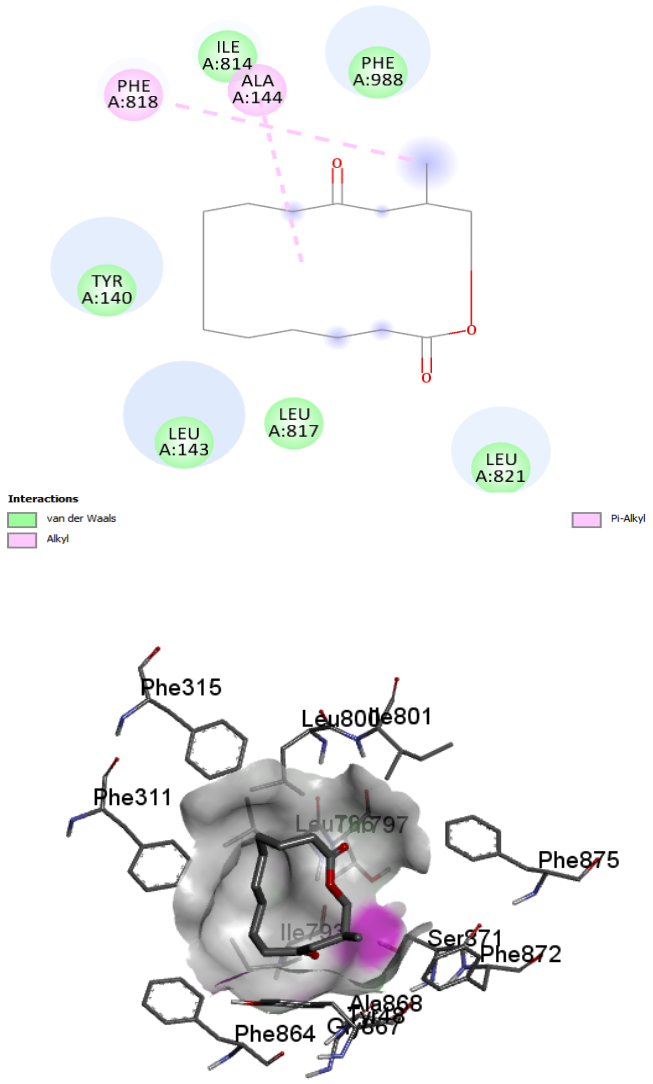


Figure 4: 2d and 3d interaction of the gastric proton pump with Oxacyclotetradecane-2,11-dione, -methyl-

CONCLUSION

The inhibitory actions of the ethanolic extract of Chromolaena Odorata against gastric proton pump for the treatment of gastric ulcer indicates that C. odoranta is a very good herbal supplement for the treatment if gastric ulcer. The GCMS result of the sample`s ethanolic extract showed presence of fifty-one (51) compounds. The in-silico molecular docking of the extracts showed that only the two cyclic compounds in the GC-MS result revealed inhibitory properties against gastric proton/potassium pump (H+/K+-ATPase) that is comparable to the commonly used synthetic drug (omeprazole). The excellent docking score of 3-(Azepan-1-yl)-1,2-benzothiazole 1,1-dioxide (−8.4 kcal/mol) as compared to omeprazole (-8.0 kcal/mol) suggest that the plant probably may exhibit better gastric proton pump inhibitory properties than omeprazole.

CONFLICT OF INTEREST

Authors declare no conflict of interest is there for publication of this work.

SUPPLEMENTARY INFORMATION FILE

The Table 1S having the peaks, compounds name, retention time, percentage composition, molecular weight, molecular formula, PubChem ID, and their structures have been provided as the supplementary data file and can be downloaded from article page.

REFERENCES AND NOTES

1. G.L. Nesom. Grindelia. En Flora of North America Editorial Committee (Ed.). Flora of North America North of Mexico, 20: 424-436, **2006**.
2. F. Olawale, K. Olofinsan, O. Iwaloye. Biological activities of Chromolaena odorata: A mechanistic review. *South African Journal of Botany* **2022**, 144, 44–57.
3. L.D. Vu, H.T. Nguyen, D.H. Le, M.T. Nguyen, T.X. Nguyen. Anti-Ulcer Effect on Indomethacin-Induced Ulcerated Mice of Chromolaena odorata Leaf from Vietnam and its Secondary Metabolites. *Tropical Journal of Natural Product Research* **2023**, 7 (5).
4. M. Zahara. Description of Chromolaena odorata LRM King and H. Robinson as medicinal plant: A Review. In *IOP Conference Series: Materials Science and Engineering*; IOP Publishing, **2019**; Vol. 506, p 012022.
5. Z.F. Tonzibo, E. Wognin, J.C. Chalchat, Y.T. N'Guessan. Chemical Investigation of *Chromolaena odorata* L. King Robinson from Ivory Coast. *Journal of Essential Oil Bearing Plants***2007**, 10 (2), 94–100.
6. N. Nwinuka, B. Nwiloh, J. Eresama. Nutritional and potential medicinal value of Chromolaena odorata leaves. *International Journal of Tropical Agriculture and Food Systems* **2009**, 3 (2).
7. S.O. Onoja, G.C. Ezeh, N.E. Udeh, et al. Anti-ulcer property of methanol fraction of Callichilia subsessilis leaf extract in albino rats. *Notulae Scientia Biologicae* **2021**, 13 (1), 10886–10886.
8. G.V. Papatheodoridis, A.J. Archimandritis. Role of Helicobacter pylori eradication in aspirin or non-steroidal anti-inflammatory drug users. *World journal of gastroenterology: WJG* **2005**, 11 (25), 3811.
9. K.B. Abbas. The Major Causes of Peptic Ulcer Disease (PUD) and its Diagnosis. *Journal of Clinical Gastroenterology and Hepatology* **2023**, 7 (1), 13–14.
10. A. Sonnenberg, J.E. Everhart. The prevalence of self-reported peptic ulcer in the United States. *Am J Public Health***1996**, 86 (2), 200–205.
11. K. Ramakrishnan, R.C. Salinas. Peptic ulcer disease. *American family physician* **2007**, 76 (7), 1005–1012.
12. Epidemiology of Helicobacter pylori Infection - Magalhães Queiroz - 2006 - Helicobacter - Wiley Online Library https://onlinelibrary.wiley.com/doi/full/10.1111/j.1478-405X.2006.00429.x (accessed Dec 30, 2023).
13. W. Delport, S.W. van der Merwe. The transmission of Helicobacter pylori: the effects of analysis method and study population on inference. *Best practice & research Clinical gastroenterology* **2007**, 21 (2), 215–236.
14. T.F. Malik, K. Gnanapandithan, K. Singh. Peptic ulcer disease. **2018**.
15. M. Narayanan, K.M. Reddy, E. Marsicano. Peptic ulcer disease and Helicobacter pylori infection. *Missouri medicine* **2018**, 115 (3), 219.
16. P.E. Arkkila, K. Seppälä, T.U. Kosunen, et al. Helicobacter pylori eradication as the sole treatment for gastric and duodenal ulcers. *European journal of gastroenterology & hepatology* **2005**, 17 (1), 93–101.
17. C.A. Fallone, S.F. Moss, P. Malfertheiner. Reconciliation of recent Helicobacter pylori treatment guidelines in a time of increasing resistance to antibiotics. *Gastroenterology* **2019**, 157 (1), 44–53.
18. L. Wang, J. Zhang, M. Hu, X. Pang. Comparison of Drug Resistance of Helicobacter pylori Between Children and Adults in Jilin, China. *Turk J Gastroenterol* **2021**, 32 (12), 1012–1018.
19. Somasundaram, Sigthorsson, Simpson, et al. Uncoupling of intestinal mitochondrial oxidative phosphorylation and inhibition of cyclooxygenase are required for the development of NSAID-enteropathy in the rat. *Aliment Pharmacol Ther* **2000**, 14 (5), 639–650.

20. M. Sharifi-Rad, P.V.T. Fokou, F. Sharopov, et al. Antiulcer agents: From plant extracts to phytochemicals in healing promotion. *Molecules* **2018**, 23 (7), 1751.
21. I.E. Peter, M.T.O. Akachukwu, F.N. Mbaoji, M.N. Ofokansi, C.S. Nworu. Evaluation of the Antiulcer Activity of Methanol/Methylene Chloride Leaf Extract of Chromolaena odorata (L.) in Rats. *Trends Nad. Prod. Res* **2020**, 1 (2), 87–98.
22. A. Lanas, F.K. Chan. Peptic ulcer disease. *The Lancet* **2017**, 390 (10094), 613–624.
23. Á. Lanas, P. Carrera-Lasfuentes, Y. Arguedas, et al. Risk of upper and lower gastrointestinal bleeding in patients taking nonsteroidal anti-inflammatory drugs, antiplatelet agents, or anticoagulants. *Clinical Gastroenterology and Hepatology* **2015**, 13 (5), 906–912.
24. J.-Q. Huang, S. Sridhar, R.H. Hunt. Role of Helicobacter pylori infection and non-steroidal anti-inflammatory drugs in peptic-ulcer disease: a meta-analysis. *The Lancet* **2002**, 359 (9300), 14–22.
25 R. Gulia, S. Singh, S. Arora, N. Sharma. Recent advancements in solubilization and Gastroretentive techniques for Oral Drug Delivery of Proton Pump inhibitors: A comprehensive review. *Chem. Biol. Lett.* **2023**, 10 (3), 546.
26. C.C.B. Ikpa, T.O.D. Maduka. Antimicrobial Properties of Methanol Extract of Dacryodes edulis Seed and Determination of Phytochemical Composition Using FTIR and GCMS. *Chemistry Africa* **2020**, 3 (4), 927–935.
27. C.B. Ikpa, U.J. Ikezu, M.C. Maduwuba. In Silico Docking Analysis of Anti-malaria and Anti-typhoid Potentials of Phytochemical Constituents of Ethanol Extract of Dryopteris dilatata. *Tropical Journal of Natural Product Research* **2022**, 6 (5).
28. I.A. Duru, C.E. Duru. Identification and quantification of phytochemicals from Carica papaya Linn (Caricaceae) root extract using GC-FID. *Journal of Chemical Society of Nigeria* **2019**, 44 (7).
29. O. Trott, A.J. Olson. AutoDock Vina: Improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. *J Comput Chem* **2010**, 31 (2), 455–461.
30. C.B.C. Ikpa, N.N. Chidozie-Ikpa. Molecular docking of phytochemical compounds in cucurbita maxima with anti-prostrate cancer activity. *J. Mol. Chem.* **2024**, 4(1), 685.
31. S. Sharma, Y. Monga, A. Gupta, S. Singh. In silico screening and molecular docking study of quinoline based compounds with Human kallikrein 7 in complex with 1,4-diazepane-7-one 1-acetamide derivative receptor target for potential antibacterials. *J. Mol. Chem.* **2023**, 3 (1), 585.
32. S.P. Gurjar, A. Gupta, A. Roy. Molecular docking studies of phytocompounds from Artemisia monosperma against ERK2 kinase in lung cancer. *J. Mol. Chem.* **2023**, 3 (2), 591.
33. V.K. Maurya, S. Kumar, M. Singh, V. Saxena. Molecular docking and dynamic studies of novel phytoconstituents in an investigation of the potential inhibition of protein kinase C- beta II in diabetic neuropathy. *J. Mol. Chem.* **2023**, 3 (2), 589.
34. K. Kuriki, R. Matsumoto, C. Ijichi, J. Taira, S. Aoki. Establishment of in silico prediction methods for potential bitter molecules using the human T2R14 homology-model structure. *Chem. Biol. Lett.* **2022**, 9 (3), 351.
35. V. Chandel, M. Srivastava, A. Srivastava, S. Asthana, D. Kumar. In-silico interactions of active Phytochemicals with c-MYC EGFR and ERBB2 oncoproteins. *Chem. Biol. Lett.* **2020**, 7 (1), 47–54.