



Therapeutic Potentials of Phytoconstituents of *Asparagus racemosus* and *Ocimum gratissimum* Plants for Treatment of Peptic Ulcer Disease

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ABSTRACT: Peptic ulcer disease is due to hyperacid secretion. Various factors have been linked to this disease and hence are targets of conventional drugs for the treatment of this condition. Hence, this paper investigated the therapeutic potential of the phytoconstituents of *Asparagus racemosus* and *Ocimum gratissimum* plants for treatment of peptic ulcer disease using *in silico* techniques using literature sources; their phytoconstituents' 3D structure data file format was obtained from PubChem and prepared. Proteins with co-crystallized ligands were obtained from protein data bank (RCSBPDB) and prepared. Prepared ligands were docked against the proteins using maestro12.8. The drug-likeness and toxicity profiles of the ligands with similar binding affinities as the reference ligands were evaluated using ADMETLAB3.0 webserver. Post-docking analysis was done using Maestro12.8. Phytoconstituents from *A. racemosus* (1), *O. gratissimum* (11) had comparable binding affinity with the standard soraprazan (-9.01 kcal/mol) when docked against proton pump 7W49; also, *A. racemosus* (6), *O. gratissimum* (17) compared to standards famotidine (-6.86kcal/mol) and ranitidine (-7.49kcal/mol) when docked against proton histamine H2 receptor 7UL3; *A. racemosus* (2), *O. gratissimum* (6) compared to standard pirenzepine (-9.07kcal/mol) when docked against muscarinic M1 receptor 5CXV. Further analysis of pharmacokinetics profiles yielded two ligands active against 7W49: eight for 7UL3 and three for 5CXV as potential leads for the treatment of peptic ulcer disease. However, *in silico* studies like molecular dynamics simulation and pharmacophore modeling as well as *in vivo* and *in vitro* studies need to be done to validate these claims.

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Peptic ulcer disease is a medical condition that occurs because of the disruption or imbalance between the aggressive factors (gastric acid, pepsin, bile salt, *Helicobacter pylori* and the use of Non-Steroidal Anti-Inflammatory Drugs); and the mucosal defense mechanism (mucosal blood flow, mucosal bicarbonate secretion, and mucosal cells reconstitution. (Goodman and Gillman, 2006). Peptic ulcer disease is one of the most common chronic

gastrointestinal disorders in the modern era. Now it has become a common global phenomenon affecting many people worldwide and still a major cause of morbidity and mortality (Chan and Leung, 2002). Inhibiting stomach acid secretion to improve gastric protection, promote epithelial cell proliferation, or halt apoptosis to promote an efficient healing process is the modern method of treating the disease condition. (Bandhopadhyay *et al.*, 2002). Traditional

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medications aim to address the different physiological and extrinsic variables that contribute to the development of peptic ulcer disease. They are used to; Decrease stomach acid production; Reduce mucosa irritation; Increase mucosa prostaglandin production; Increase mucosal blood flow; Increase mucosal bicarbonate production; Relax the gastrointestinal smooth muscles. These drugs are grouped into Proton pump inhibitors, H₂ receptor antagonists, prostaglandin E₂ analogues, Muscarinic M₁ receptor antagonists, and antibiotics. Although the pathophysiology of the disorder is not identical, the inhibition of gastric acid secretion is pivotal to alleviating symptoms of discomfort and improving quality of life. Moreover, acid-related damage to the oesophagus and other situations may involve the progression of cancer and other late complications of these conditions. (Sach, 2001). Also, prostaglandin E, which is present in the gastric mucosa is a powerful inhibitor of gastric acid secretion and a stimulus for gastric acid secretion. (Park *et al.*, 1992.). *Ocimum gratissimum* L., is an aromatic herbaceous plant also known as basil, basil-clove, or alfavaca. It belongs to the Lamiaceae family. (Nweze and Eze, 2009). *Ocimum gratissimum* is a perennial and odoriferous shrub found in tropical regions such as Brazil, India, Vietnam, Rwanda, Nigeria (Lahlau *et al.*, 2008), Cameroon, Togo, Côte d'Ivoire, Kenya, Benin (Kpoviessi *et al.*, 2014), and South Africa (Venuprasad *et al.*, 2014). Popularly known as scent leaf, it is one of the discovered medicinal plants with the potential to serve as an alternative therapy for the treatment of various ailments or as a source of a new drug. It is also used in traditional medicine for the treatment of several ailments such as cough, pneumonia, fever, inflammation, anaemia, diarrhoea, pains, and fungal and bacterial infections (Akara *et al.*, 2021). *Asparagus racemosus* is a climber that has stems up to about 4m long. It has both tuberous and fibrous roots (Clifford *et al.*, 2020). It grows 1-2 M tall and has pine-needle-like phylloclades that are uniform and shiny green. It produces minute, white flowers on short spiky stems in July and fruits in September producing blackish-purple globular berries. Various parts of the plants have been used in the treatment of various diseases due to various pharmacological activities which include the galactagogue effect, antisecretory and anti-ulcer, antitussive, adaptogenic, antibacterial activity, antiprotozoal activity, gastrointestinal (promote gastric emptying and ulcer treatment; particularly duodenal ulcers) (Hassan *et al.*, 2016), uterine activity, antihepatotoxic, antineoplastic, and molluscicidal effect, cardiovascular, immunomodulatory and central nervous system depressants activity, anticonvulsant, antioxidant,

antilithiatic, anti-amnesia, anti- inflammatory, aphrodisiac, diuretic, anti-hepatocarcinogenesis, anti-stress, anti-diabetic, female tonic, antidiarrhoeal analgesic and cytotoxic activity (Alok *et al.*, 2013). Hence, this paper investigates the therapeutic potentials of the phytoconstituents of *Asparagus racemosus* and *Ocimum gratissimum* plants in the treatment of peptic ulcer disease using *in silico* techniques

MATERIALS AND METHOD

Personal computer system with; Operating system: Windows 10 Pro, Processor: intel Core i7, 1.99GHz, 16 GB RAM, System type: 64-bit, Mouse. Data bases: PDB, PUBCHEM. Webserver: ADMETLAB3.0 Software: Schrodinger's Suite (Maestro 12.8).

Preparation of Target Proteins: The target protein molecules 3D structures were obtained from the Protein Data Bank. Using the protein preparation function of the maestro 12.8 of Schrodinger's suite the downloaded proteins were singly preprocessed with commands to assign bond orders, use the CCD database, add hydrogen, create zero-order bonds to metals, create disulfide bonds and generate het states using Epik at pH off 7±2. They were further optimized and then minimized. The target proteins obtained alongside their PDB ID are proton pump (H⁺/Na⁺K⁺ATPase) 7W49 bound to soraprazan; histamine H₂ receptor 7UL3 bound to famotidine, Nb6M, NabFab; Muscarinic receptor M₁ 5CXV bound to tiotropium; Prostaglandin E₂ receptor 6M9T bound to misoprostol.

Identification And Preparation of Ligands: The 3D structured data file formats of the various plants' ligands (metabolites and natural products) were obtained from the PUBCHEM database. They were then imported into the maestro workspace and using the Ligprep inbuilt function, the ligands were prepared at a maximum ligand size of 500 atoms, OPLS4 forcefield, ionisation at a pH of 7 ±2, using Epik, desalt, and generating tautomers and set to generate 5 stereoisomers per ligand retaining their specific chiralities and output in the Maestro format. This was then run simultaneously for all ligands.

Identification Of Binding Sites: Using the site map feature of Schrodinger's suite Maestro 12.8, the binding sites on the receptors were identified, and each was assessed. Also, the binding site where the co-crystallized ligand was bound was noted. The active amino acids were identified.

Target Grid Generation: Using the receptor grid

function of the docking program, the grid of the various receptors was generated showing the receptor's active site for which the docking is to be conducted. This was done by selecting the co-crystallized ligand present on each receptor with a scaling factor of 1 and partial charge cut off at 0.25.

Ligand/Molecular Docking: The generated library underwent docking into the active sites of the proteins utilizing standard precision with non-refined sample screening. To anticipate binding affinity and molecular interactions, co-crystallized ligands were docked into the active site of each protein's produced compound.

Pharmacokinetics Profiling Predictions: Using *in silico* integrative model Admetlab3.0, the absorption, distribution, metabolism, excretion, and toxicity (ADMET) properties of the test compounds were ascertained. The filter based on the Lipinski rule was used to evaluate drug likeness.

RESULTS AND DISCUSSION

These plants studied in the research have been used ethnomedicinally in the treatment of peptic ulcer diseases and hence the need to evaluate their claims of efficacy. Also, the adverse effects of conventional drugs create room for higher studies of better compounds with better pharmacokinetic properties.

Molecular Docking: The aim of molecular docking of a set of ligands against a receptor is to generate a docking score in Kcal/mol which predicts the binding affinities of the different compounds and then the activity and interaction of the compound with the receptor. In these studies, these interactions are usually due to pi-alkyl bonds, pi-pi stacking, pi-anion, hydrogen-bond, pi-donor, pi-sigma bond, van-Der Waal forces, carbon-hydrogen bond, and the unfavorable acceptor-acceptor. The phytoconstituents of *Asparagus racemosus*, *Ocimum sanctum* were obtained from literature alongside standard ligands (misoprostol, enprostil, soraprazan, Famotidine, ranitidine, pirenzepine). These standards and phytoconstituents were then prepared, and evaluated against the prepared prostaglandin E2 receptor, muscarinic m1 receptor, Histamine2 receptor, and proton pump using the Schrodinger's Maestro 12.8 suite. The results of the docking score (binding affinities) are shown in Tables 1, 2. The compounds showing proximity and higher docking scores were further selected as in Table 3.4 and then analyzed for their pharmacokinetic parameters (absorption, distribution, metabolism, excretion, and toxicological properties) to further check suitability for leads. This

is done to ensure the efficacy and safety of the potential leads. The Lipinski rule of five serves as a key parameter in the evaluation of the oral absorptivity and hence oral activity of these candidates. It is a set of four rules which states that a compound will only be suitable for oral activity if it does not violate more than one of i. No more than 5 hydrogen bond donors (the total number of nitrogen-hydrogen and oxygen-hydrogen bonds) ii. No more than 10 hydrogen bond acceptors (all nitrogen or oxygen atoms) iii. A molecular mass of less than 500 Daltons iv. A calculated octanol-water partition coefficient (Clog P) that does not exceed 5. Also, the pharmacokinetic properties as well as the toxicity profile of the resultant compound with binding affinities higher and closer to the standard ligands were evaluated using the online server ADMETLAB3.0. Results are shown in Tables 3, 4 and 5.

Asparagus racemosus: A total of 86 phytoconstituents (standards inclusive) were docked against the receptors 5cxv, 7ul3, and 7w49. The phytochemicals gave docking scores for most ligands on each receptor as in Table 1. For the proton pump (7w49) one phytochemical with PUBCHEM CID of 5380805 gave a docking score of -9.7697 Kcal/mol higher than that of the standard soraprazan with a score of - 9.013. 3Kcal/mol. For the histamine 2 receptor, 5 phytochemicals were obtained with proximity and higher docking scores compared to the standards (famotidine and ranitidine). The PUBCHEM CID of these phytochemicals are 5029, 52325853, 5311225, 162955816, 5042. For the prostaglandin E2 receptor 6M9T, all phytoconstituents gave docking scores less than and not close to the standards (5282381 and 5311225) docking scores. For the muscarinic M1 receptor (5CXV) two ligands (53350155 and 162985356) gave docking scores close to and higher than the standard (pirenzepine). The results of the docking scores and the corresponding binding affinities are shown in Tables 1, 2 and 3. Also, the pharmacokinetic parameters as well as the toxicity profile of the compounds with binding affinities closer to or higher than the standard ligands for each receptor were evaluated using the online version of ADMETLAB 3.0 and results were as shown in Tables 4, 5 and 6. ***Ocimum gratissimum:*** For the proton pump, a total of eleven ligands with PUBCHEM CID of (14104302, 9064, 65084, 162980641, 162979504, 146798, 5316673, 439533, 5991, 133612286, 44258710). For the histamine 2 receptor 7UL3, *Ocimum* gave a total of 18 ligands with binding affinities closer to or higher than the standards (famotidine and ranitidine). These ligands

include (1794427, 1794425, 163005955, 439533, 5042, 162934828, 370, 10883321, 162934831, 101992980, 133612286, 11824948, 162896256, 162896258, 72, 5322089, 162934830, 5311225). For the prostaglandin E2 receptor 6M9T, no ligand gave a docking score close to or higher than the standard ligands (enprostil and misoprostol).

Table 1: Molecular docking results of phytochemical constituents of *Asparagus racemosus* against selected protein targets in kcal/mol

PUBCHEM CID	7W49	7UL3	6M9T	5CXV
1183	-6.75	-4.44	-6.09	-4.98
4848	-7.69	-2.03	-5.90	-9.90
5029	-6.87	-5.16	-8.16	-7.81
5042	-6.96	-7.18	-8.31	-6.29
7431	-5.44	-5.62	-7.32	-5.91
10569	-7.43	-5.60	-7.00	-7.53
213054	-9.01	-2.42	-7.56	-9.38
220338	-6.22	#N/A	-7.65	-8.30
564727	-7.18	-6.14	-6.53	-7.48
3001055	-6.08	-5.17	-5.66	-5.90
5282199	-6.82	-4.70	-7.50	-7.25
5282381	-7.04	-4.77	-10.71	-6.59
5311225	-8.15	-6.45	-10.22	-7.91
5702160	-6.01	-5.68	-6.36	-5.81
10760330	-6.02	-3.48	-6.54	-8.43
11358117	-8.71	-5.43	-7.55	-7.87
14017925	-7.32	-4.71	-8.61	-7.90
14017925	-7.32	-4.71	-8.61	-7.90
15715176	-7.72	-4.32	-7.01	-8.85
26183540	-6.12	-4.21	-8.58	-8.67
38347252	-5.52	-5.00	-7.21	-6.64
46895238	-4.96	-3.94	-6.31	-7.31
46895239	-5.08	-4.62	-6.73	-7.97
49871253	-7.42	-5.48	-7.02	-7.77
52325853	-8.22	-6.33	-8.23	-7.82
53350155	-5.78	-2.62	-7.18	-5.90
86049451	-7.70	-2.32	-7.75	-5.00
91884799	-7.76	-4.75	-6.96	-8.07
101521440	-4.84	#N/A	-7.20	-8.06
162922769	-3.82	-0.66	-7.21	-4.35
162955816	-8.18	-6.69	#N/A	-5.05
162985356	-6.44	-6.13	-8.03	-9.01
162998739	-6.33	-4.82	-7.79	-8.51
163105420	-5.98	-2.67	-6.23	-5.37

Key: #N/A = Not Ascertained; 7w49=Proton Pump; 7ul3=H2 Receptor; 6m9t= Prostaglandin E2 Receptor ;5cxv= Muscarinic M1

Table 2: Molecular docking results of phytochemical constituents of *Ocimum gratissimum* against selected protein targets in kcal/mol

PUBCHEM CID	7W49	7UL3	6M9T	5CXV
72	-6.44	-6.59	-7.25	-6.86
126	-6.71	-5.39	-4.88	-6.42
135	-6.25	-5.44	-6.85	-6.76
370	-6.53	-7.05	-4.42	-6.49
802	-6.79	-6.36	-9.07	-7.41
1183	-6.75	-5.83	-5.52	-6.41
2537	-5.87	-4.91	-6.08	-7.20
3314	-5.85	-5.24	-5.16	-5.76
4848	-7.69	-4.58	-4.21	-9.90
5029	-6.87	-6.32	-6.08	-7.81
5042	-6.96	-7.18	-8.31	-6.29
5991	-9.31	-5.29	-8.01	-8.79
6128	-6.14	-3.34	-6.39	-9.09
6508	-6.41	-5.22	-6.49	-6.00

6549	-3.92	-3.16	-5.93	-4.70
6616	-6.34	-5.92	-6.11	-7.01
6654	-6.35	-5.32	-5.62	-6.78
7127	-5.57	-5.06	-4.66	-6.05
7428	-6.95	-5.75	-4.17	-6.31
7462	-6.22	-5.97	-6.48	-6.92
8742	-6.29	-6.42	-6.84	-6.59
8815	-4.98	-4.54	-4.43	-5.60
9064	-9.63	-6.07	-6.99	-9.05
9984	-6.32	-5.57	-4.49	-6.53
10364	-7.51	-6.24	-7.23	-6.90
11230	-6.13	-6.15	-6.47	-7.06
11463	-6.23	-5.38	-5.69	-6.96
11467	-6.42	-5.72	-6.93	-7.38
11850	-3.84	-4.61	-5.09	-3.05
13250	-7.03	-5.40	-4.13	-6.40
16822	-6.17	-5.74	-5.42	-5.79
17100	-5.76	-5.60	-6.04	-6.87
22311	-5.41	-4.66	-5.19	-6.36
31253	-2.21	-2.65	-3.62	-3.52
31261	-5.17	-4.36	-5.36	-5.01
31261	-5.17	-4.36	-5.36	-5.01
65084	-9.63	-5.88	-4.57	-8.35
69867	-7.49	-5.43	-7.51	-7.16
73160	-8.56	-6.07	-7.95	-10.27
73399	-5.71	-6.13	-8.11	-8.90
75142	-5.75	-5.60	-5.38	-6.17
82227	-6.16	-5.56	-5.92	-6.45
82452	-5.36	-5.05	-5.18	-5.91
96539	-5.75	-4.83	-6.88	-6.40
114776	-7.65	-4.61	-4.65	-5.00
119205	-7.68	-6.27	-8.33	-9.80
136330	-6.90	-5.47	-6.33	-7.22
146798	-9.53	#N/A	#N/A	#N/A
154407	-7.54	-4.49	-3.56	-7.82
160521	-7.85	-4.65	-6.91	-9.37
161131	-6.56	-5.35	-6.32	-8.15
162350	-6.84	-4.86	-5.64	-5.18
162464	-6.53	-5.16	-7.49	-5.95
164619	-6.27	-5.15	-5.90	-5.51
165225	-5.54	-5.04	-5.08	-6.26
171401	-5.05	-4.48	-4.91	-5.09
188323	-6.73	-5.36	-7.14	-5.81
213054	-9.01	-5.19	-4.30	-9.38
394846	-6.67	-6.32	-8.09	-9.56
439533	-9.35	-7.19	-4.77	-8.93
439711	-6.03	-5.94	-6.60	-7.41
440186	-6.02	-4.08	-8.60	-6.63
440917	-5.60	-5.09	-5.16	-6.17
440967	-6.26	-5.64	-6.15	-6.64
440968	-6.35	-5.32	-5.62	-6.78
442461	-6.74	-5.91	-6.12	-6.89
442484	-6.51	-5.85	-6.63	-6.81
443156	-6.34	-5.65	-6.12	-6.99
443158	-3.92	-3.16	-5.93	-4.70
443160	-6.55	-5.95	-5.77	-6.73
443161	-5.80	-5.66	-6.61	-6.79
445713	-6.07	-5.86	-9.18	-7.15
445858	-5.75	-5.98	-6.61	-5.87
447277	-6.84	-5.23	-8.16	-8.03
524200	-6.40	-5.90	-5.97	-6.90
576718	-6.83	-5.65	-5.98	-6.93
589098	-8.15	-5.15	-5.91	-6.96
592986	-6.65	-5.70	-5.68	-6.96
630253	-6.92	-5.24	-7.07	-5.72
637563	-5.75	-5.02	-5.12	-6.20
637566	-4.47	-3.56	-4.17	-4.93
689043	-6.05	-5.96	-6.45	-6.43
1742210	-6.47	-5.69	-5.94	-7.83
1794427	-6.90	-7.62	-7.41	-5.01

2724161	-6.13	-6.15	-6.47	-7.06	14332899	-8.86	-6.08	-8.01	-8.47
3001055	-6.08	-7.49	-4.45	-8.17	14427336	-6.94	-5.16	-6.92	-7.81
3084296	-7.24	-5.17	-6.06	-8.47	14585506	-7.99	-4.56	-6.75	-5.86
5280441	-8.62	-4.53	#N/A	-5.92	14705598	-4.33	-5.04	-7.41	-8.23
5280443	-8.81	-5.76	-5.58	-8.80	14830071	-6.75	-0.80	-5.46	-6.88
5280445	-7.44	-5.71	-4.84	-8.72	15747360	-7.40	-4.79	-6.38	-7.84
5280457	-8.10	-5.83	-6.99	-8.37	23271974	-7.39	-4.94	-7.94	-7.06
5280536	-6.32	-5.19	-4.49	-5.88	25231264	-6.13	-4.08	-6.50	-5.72
5280637	-7.37	-6.03	-7.05	-8.65	44258710	-9.01	-5.18	-7.30	-7.81
5280666	-7.88	-5.66	-5.07	-8.96	44630107	-6.42	-5.04	-6.53	-7.74
5280704	-7.25	-5.98	-8.63	-7.81	45266909	-6.28	-5.40	-5.26	-5.89
5280794	-5.11	-2.82	-7.89	#N/A	45278176	-7.41	-5.33	-7.44	-7.08
5281416	-7.40	-5.53	-4.39	-7.35	51136357	-7.36	-5.79	-7.53	-7.45
5281417	-7.94	-4.61	-4.81	-8.25	52325853	-8.22	-6.33	-8.23	-7.82
5281515	-6.79	-6.01	-6.19	-8.28	52325855	-6.26	#N/A	-6.61	-7.89
5281516	-2.95	-2.08	-2.49	-3.92	52325861	-7.51	#N/A	-7.04	-8.01
5281520	-7.29	#N/A	-6.58	-8.09	74409819	-6.13	-4.93	-6.50	-7.59
5281520	-7.29	#N/A	-6.58	-8.09	90743708	-7.12	-5.51	-6.91	-7.65
5281525	-3.12	-1.33	-3.42	-3.85	91129494	-7.11	-5.36	-7.84	-8.01
5281553	-3.92	-3.07	-4.37	-3.96	92261496	-7.77	#N/A	-6.95	-8.64
5281675	-8.75	-5.48	#N/A	-4.33	98052623	-6.15	-6.24	-6.54	-7.05
5281792	-7.18	-5.45	-7.46	-6.55	101198558	-6.30	-5.91	-6.05	-6.30
5282199	-6.82	-4.70	-7.50	-7.25	101651530	-6.22	-5.21	-4.70	-6.48
5282381	-7.04	-4.77	-10.71	-6.59	101992980	-7.29	-7.04	-8.45	-7.84
5288573	-7.25	-5.50	-6.95	-8.55	101992982	-5.31	-3.88	-8.66	-8.61
5311225	-8.15	-6.45	-10.22	-7.91	101992983	-6.71	-4.90	#N/A	-6.35
5316673	-9.39	-3.43	-5.71	-8.67	101992984	-7.19	-5.02	#N/A	-5.66
5316750	-6.54	-5.23	-7.84	-7.89	102499957	-5.58	-4.23	#N/A	-7.78
5317471	-7.52	-5.49	-5.45	-3.42	130740339	-5.23	-5.42	-5.75	-6.15
5317570	-6.59	-6.39	-6.73	-8.18	131178377	-6.09	-4.26	-5.77	-5.87
5319484	-7.97	-4.52	-8.75	-7.21	134687947	-7.29	#N/A	-6.60	-8.13
5319484	-7.97	-4.52	-8.75	-7.21	154496877	-7.56	#N/A	-6.72	-8.26
5320250	-3.64	-3.39	-2.64	-4.32	162843160	-7.15	-4.77	-7.42	-5.61
5320521	-7.80	-5.46	-6.37	-8.12	162844436	-6.26	-5.86	-8.39	-7.82
5322089	-7.45	-6.53	-8.29	-6.96	162855418	-7.12	-6.11	-6.16	-6.85
5372312	-6.99	-5.68	-7.69	-8.06	162868108	-5.51	-6.10	#N/A	-9.18
5702160	-6.01	-6.86	-5.02	-6.59	162872299	-7.06	-5.35	-8.51	-9.77
5922634	-7.23	-4.54	-6.92	-8.35	162892257	-7.26	-5.58	#N/A	-7.22
6918391	-6.54	-5.46	-5.60	-7.26	162892258	-8.27	-6.62	#N/A	-5.90
9548706	-6.32	-5.33	-6.30	-7.74	162896256	-7.67	-6.84	-7.61	-8.11
9840292	-6.15	-4.64	-7.77	-5.64	162905105	-8.11	#N/A	-6.74	-8.13
9874426	-6.54	-5.94	-7.95	-6.97	162906021	-7.71	-5.16	-4.08	-6.58
9930064	-6.84	-5.38	-7.59	-8.70	162910549	-6.32	-5.45	-7.69	-6.35
9934142	-7.06	-6.41	-5.17	-5.94	162915510	-5.49	-5.67	-6.12	-7.04
10006384	-7.72	-3.64	#N/A	#N/A	162918552	-7.35	-5.86	-6.57	-7.19
10290825	-6.07	-5.83	-6.07	-6.54	162930638	-7.83	-5.46	-8.57	-7.14
10856614	-7.58	-5.55	-6.17	-8.02	162934828	-7.23	-7.10	-7.71	-7.69
10883321	-6.91	-7.04	-7.33	-7.49	162934830	-7.05	-6.45	-7.72	-8.28
11063784	-5.35	-4.95	-6.71	-6.46	162934831	-7.06	-7.04	-8.18	-6.90
11148775	-6.79	-5.12	-6.74	-8.99	162947737	-4.22	-4.73	-7.77	-7.57
11220007	-4.98	-4.12	-6.91	-7.64	162954979	-6.75	-5.71	-3.80	-5.35
11378474	-5.77	-5.26	-5.28	-6.27	162954980	-7.06	-5.63	-5.79	-5.90
11726019	-7.05	-4.62	-7.27	-5.92	162970571	-5.86	#N/A	#N/A	-8.28
11793120	-6.28	-4.60	-8.19	-7.73	162977897	-8.33	#N/A	#N/A	-8.86
11824948	-6.25	-6.89	-8.25	-8.06	162979504	-9.61	-4.45	-6.71	-8.09
11966109	-6.07	#N/A	-6.83	-9.21	162980641	-9.61	#N/A	#N/A	#N/A
12310250	-6.04	-4.73	-6.56	-5.83	163005955	-6.10	-7.25	#N/A	#N/A
12313020	-7.27	-5.81	-6.79	-8.17	163014945	-6.10	#N/A	#N/A	-9.43
12447832	-5.71	-3.95	-4.92	-7.06	163033098	-7.06	-5.23	-5.06	-6.78
13118571	-4.24	-2.60	-3.93	-4.23	163036208	-4.45	-4.59	-5.51	-7.43
13660470	-5.90	-4.96	-4.83	-6.06	163037164	-6.69	-5.67	-6.20	-7.69
13844658	-6.98	-6.29	-5.22	-8.74	163037512	-7.51	-3.33	#N/A	-6.07
13893597	-8.46	-5.40	-8.69	-7.93	163044773	-7.37	-4.52	-6.92	-7.72
13894537	-6.92	-6.02	-6.36	-8.21	163075841	-6.80	-4.94	-7.59	-6.87
13916049	-6.23	-4.85	-7.89	-5.56	163084237	-7.67	-2.29	#N/A	-6.69
14104302	-11.00	-4.38	-5.96	#N/A	163089925	-7.20	-6.41	-7.10	-9.02
14132337	-6.80	-4.49	-8.90	-6.88	163106339	-6.59	-6.33	-6.34	-8.19
14135399	-5.55	-4.89	-7.80	-9.53	133612286	-9.02	-6.94	#N/A	-7.90
14282775	-7.09	-6.42	-4.42	-6.36	Key: #N/A = Not Ascertained; 7w49= Proton Pump; 7ul3= H2 Receptor; 6m9t= Prostaglandin E2 Receptor ;5cxv= Muscarinic M1				
14314225	-6.01	-6.13	-6.80	-7.64					

Table 3: Likely leads with proximity and higher docking scores to standard ligands

7W49	docking score	7UL3	docking score	6M9T	docking score	5CXV	docking score
5280805	-9.77	52325853	-6.33	5282381	-10.71	4848	-9.9
213054	-9.01	5311225	-6.45	5311225	-10.22	53350155	-9.89
14104302	-11	162955816	-6.69	5282381	-10.71	213054	-9.38
9064	-9.63	5702160	-6.86	5311225	-10.22	4848	-9.07
65084	-9.63	5042	-7.18			162985356	-9.01
162980641	-9.61	3001055	-7.49			73160	-10.27
162979504	-9.61	1794427	-7.62			4848	-9.9
146798	-9.53	3001055	-7.49			119205	-9.8
5316673	-9.39	163005955	-7.25			162872299	-9.77
439533	-9.35	439533	-7.19			394846	-9.56
5991	-9.31	5042	-7.18			14135399	-9.53
133612286	-9.02	162934828	-7.1			163014945	-9.43
213054	-9.01	370	-7.05				
44258710	-9.01	10883321	-7.04				
		162934831	-7.04				
		101992980	-7.04				
		133612286	-6.94				
		11824948	-6.89				
		162896256	-6.84				
		162892258	-6.62				
		72	-6.59				
		5322089	-6.53				
		5702160	-6.47				
		162934830	-6.45				
		5311225	-6.45				

Table 4: Pharmacokinetic properties of selected ligands of *Asparagus racemosus*, *Ocimum grattissimum* against proton pump target protein

PUBCHEM ID	MW	Lipinski	BBB	CYP3A4-inh	CYP3A4-sub	cl-plasma	t0.5	DILI	RT	H-HT	NT	OT	HT	NPT	GT
5280805	610.2	1.0	0.0	0.0	0.0	1.6	4.6	0.9	0.0	0.4	0.0	0.9	0.0	0.1	0.9
14104302	452.1	1.0	0.2	0.0	0.0	4.2	3.1	0.7	0.0	0.6	0.0	0.9	0.0	0.4	0.8
9064	290.1	0.0	0.1	0.0	0.0	16.5	2.4	0.2	0.6	0.6	0.1	0.7	0.0	0.1	0.9
65084	306.1	0.0	0.0	0.0	0.0	12.1	2.3	0.4	0.6	0.5	0.0	0.9	0.0	0.0	1.0
162980641	556.2	0.0	0.0	0.6	0.0	6.5	1.7	0.4	0.5	0.7	0.6	0.8	0.4	0.8	0.1
162979504	466.1	1.0	0.0	0.0	0.0	3.2	2.9	0.2	0.0	0.5	0.0	0.9	0.0	0.3	0.5
146798	578.1	1.0	0.0	0.0	0.0	6.6	4.6	0.6	0.8	0.9	0.0	1.0	0.0	0.1	1.0
5316673	432.1	0.0	0.0	1.0	0.0	2.9	3.3	0.9	0.3	0.5	0.0	0.5	0.1	0.1	1.0
439533	304.1	0.0	0.0	1.0	0.0	13.4	2.1	0.5	0.7	0.5	0.0	0.7	0.1	0.1	1.0
5991	296.2	0.0	0.9	0.6	1.0	5.6	2.1	0.0	1.0	0.6	0.6	0.8	0.0	0.3	0.0
133612286	578.2	1.0	0.0	0.0	0.0	1.6	4.3	0.9	0.0	0.4	0.0	1.0	0.0	0.0	0.9
44258710	314.1	0.0	0.0	0.3	0.0	8.7	1.6	0.7	0.6	0.4	0.1	0.2	0.1	0.0	0.9

Key: mw= molecular weight; bbb= blood brain barrier; inh= inhibition; sub= substrate; t0.5= halflife; dili=drug induced liver injury; rt= respiratory toxicity; nt= neurotoxicity; ot= ototoxicity; ht=hepatotoxicity; npt=nephrotoxicity gt=genotoxicity. For the classification endpoints, the prediction probability values are transformed into six symbols: 0-0.1 (---), 0.1-0.3 (--), 0.3-0.5 (-), 0.5-0.7 (+), 0.7-0.9 (++), and 0.9-1.0 (+++).

OGBEIDE, U. M; SAMSON, C. C

Table 5: Pharmacokinetic properties of selected ligands of *Asparagus racemosus*, *Ocimum gratissimum* against histamine receptor target protein.

Pubchem cid	MW	Lipinski	BBB	CYP3A4-inh	CYP3A4-sub	cl-plasma	t0.5	DILI	RT	H-HT	NT	OT	HT	NPT	GT
52325853	318.2	0.0	0.0	0.0	1.0	3.4	1.3	0.4	0.9	0.5	0.1	0.5	0.5	0.9	0.6
5311225	400.2	0.0	0.0	0.0	0.0	8.3	0.9	0.2	0.7	0.4	0.2	0.7	0.1	0.7	0.0
162955816	478.1	1.0	0.0	0.0	0.0	3.7	3.7	0.9	0.0	0.7	0.0	0.9	0.2	0.5	0.9
5042	370.1	0.0	0.1	0.0	1.0	1.3	1.5	0.9	0.3	0.6	0.7	0.5	0.5	0.9	1.0
1794427	354.1	0.0	0.0	0.0	0.0	3.3	2.8	0.3	0.1	0.5	0.0	0.9	0.0	0.4	0.2
163005955	610.1	1.0	0.0	0.5	0.0	5.0	3.2	0.9	0.0	0.6	0.0	0.8	0.0	0.1	1.0
439533	304.1	0.0	0.0	1.0	0.0	13.4	2.1	0.5	0.7	0.5	0.0	0.7	0.1	0.1	1.0
162934828	346.1	0.0	0.0	0.0	0.0	3.3	2.5	0.2	0.0	0.6	0.1	0.9	0.1	0.5	0.5
370	170.0	0.0	0.0	0.0	0.0	5.4	2.2	0.7	0.5	0.4	0.0	0.8	0.1	0.1	0.8
10883321	376.1	0.0	0.0	0.0	0.0	1.9	3.0	0.5	0.0	0.6	0.1	1.0	0.2	0.9	0.4
162934831	346.1	0.0	0.0	0.0	0.0	2.6	2.3	0.1	0.0	0.5	0.0	0.8	0.0	0.7	0.3
101992980	344.1	0.0	0.0	0.0	0.0	3.2	2.2	0.4	0.1	0.5	0.1	0.8	0.3	0.5	0.2
133612286	578.2	1.0	0.0	0.0	0.0	1.6	4.3	0.9	0.0	0.4	0.0	1.0	0.0	0.0	0.9
11824948	376.1	0.0	0.0	0.0	0.0	2.2	2.7	0.3	0.1	0.6	0.0	0.9	0.3	0.6	0.2
162896256	346.1	0.0	0.0	0.0	0.0	2.6	2.6	0.2	0.0	0.6	0.0	1.0	0.2	0.3	0.2
162892258	526.2	1.0	0.0	0.0	0.7	2.6	2.6	0.4	0.0	0.8	0.0	1.0	0.2	0.9	0.0
72	154.0	0.0	0.0	0.0	0.0	4.9	2.3	0.6	0.5	0.4	0.1	0.6	0.2	0.1	0.4
5322089	390.1	0.0	0.0	0.1	0.0	2.6	3.0	0.6	0.0	0.7	0.0	0.7	0.1	0.6	0.8
162934830	346.1	0.0	0.0	0.0	0.0	2.1	2.5	0.1	0.0	0.4	0.0	1.0	0.0	0.7	0.2

Key: mw= molecular weight; bbb= blood brain barrier; inh= inhibition; sub= substrate; t0.5= half-life; dili=drug induced liver injury; rt= respiratory toxicity; nt= neurotoxicity; ot= ototoxicity; ht=hepatotoxicity; npt = nephrotoxicity gt=genotoxicity. For the classification endpoints, the prediction probability values are transformed into six symbols: 0-0.1 (---), 0.1-0.3 (--), 0.3-0.5 (-), 0.5-0.7 (+), 0.7-0.9 (++), and 0.9-1.0 (+++).

Table 6: Pharmacokinetic properties of selected ligands of *Asparagus racemosus*, *Ocimum gratissimum* against muscarinic m1 receptor target protein.

Pubchem CID	MW	Lipinski	BBB	CYP3A4-inh	CYP3A4-sub	cl-plasma	t0.5	DILI	RT	H-HT	NT	OT	HT	NPT	GT
53350155	292.1	0.0	0.0	0.0	0.0	6.9	1.7	0.8	0.4	0.7	0.0	0.3	0.2	0.3	0.9
213054	367.2	0.0	1.0	0.0	1.0	9.1	1.4	0.8	0.8	0.8	0.6	0.8	0.3	0.9	0.9
162985356	364.2	0.0	0.0	0.0	0.0	8.6	2.2	0.0	0.1	0.7	0.1	1.0	0.1	0.6	0.0
73160	290.1	0.0	0.0	0.2	0.2	14.3	2.2	0.3	0.7	0.7	0.2	0.6	0.1	0.2	1.0
119205	358.1	0.0	0.0	1.0	1.0	6.7	1.5	0.9	0.6	0.9	0.8	0.6	0.6	0.9	1.0
162872299	330.2	0.0	0.0	0.4	0.9	7.5	1.6	0.2	0.3	0.8	0.2	0.8	0.4	0.6	0.0
394846	374.1	0.0	0.0	1.0	1.0	6.7	2.0	0.6	0.4	0.9	0.6	0.5	0.4	0.8	1.0
14135399	388.2	0.0	0.0	0.0	1.0	4.2	2.1	0.4	0.0	0.6	0.0	0.9	0.5	0.5	0.3
163014945	524.2	1.0	0.0	0.6	0.4	2.7	2.5	0.6	0.0	0.6	0.0	0.9	0.1	0.9	0.1

Key: mw= molecular weight; bbb= blood brain barrier; inh= inhibition; sub= substrate; t0.5= half-life; dili=drug induced liver injury; rt= respiratory toxicity; nt= neurotoxicity; ot= ototoxicity; ht=hepatotoxicity; npt = nephrotoxicity gt=genotoxicity. For the classification endpoints, the prediction probability values are transformed into six symbols: 0-0.1 (---), 0.1-0.3 (--), 0.3-0.5 (-), 0.5-0.7 (+), 0.7-0.9 (++), and 0.9-1.0 (+++).

Finally, for the Muscarinic M1 receptor, only six ligands gave docking scores higher and near the standard pirenzepine. These include (73160, 119205, 162872299, 394846, 14135399, 163014945). The docking score showing the degree of affinities of the ligands and standards to the receptors were derived as in Tables 1, 2 and 3. The pharmacokinetic parameters of the ligands with resultant docking scores closer to or higher than that of the standard for each of the receptors

were then analyzed using the webserver ADMETLAB3.0. as shown in Tables 4, 5 and 6. Further Screening with criteria of solubility, ability to cross the blood-brain barrier, cytochrome complex interactions, and toxicity in terms of cardiotoxicity, hepatotoxicity, neurotoxicity, nephrotoxicity, genotoxicity, carcinogenicity, hematotoxicity, ototoxicity, and respiratory toxicity were considered. . *Proton Pump*: Succinctly, a total of 13 ligands gave OGBEIDE, U. M; SAMSON, C. C

higher scores higher than the standard test compound soraprazan. *Ocimum* gave the higher number of ligands. These compounds were further tested for their pharmacokinetics properties and the results are seen in Table 4. The interactions and further toxicity screening yielded three compounds which were from *Ocimum gratissimum*.

The results showed that the receptor integrated with the majority of receptors from all the plants and then further toxicity assessment yielded only plant ligands from *Ocimum gratissimum*.

Histamine H2 receptor: For the Histamine H2 receptor, the interactions with ligands from the two plants yielded a total of 21 ligands with docking scores higher or of very close proximity to the standard. Upon further toxicity screening, a total of 9 compounds were obtained. Asparagus yielded one, eight were from *Ocimum*. The interactions of the ligands from the two plants with the prostaglandin E2 receptor yielded no compound with a docking score close to or higher than that of the standards and hence no further screening was conducted here. Results are shown in Table 5

Table 7: Summary of interaction mechanism between selected ligands and proton pump receptor amino acids

ligands	proteins	Interactions	with what
213054	TYR 799	PI	NH ₂
9064	GLH 795	HB	OH
	LEU 811	HB	OH
	VAL 331	HB	OH
162979504	THR 135	HB	OH
	ASP 137	HB	OH
	CYS 813	HB	OH
	VAL 331	HB	OH
	LEU 811	HB	OH
439533	VAL 331	HB	OH
	GLH 795	HB	OH
	LEU 811	HB	OH

Table 8. Summary of interaction mechanism between selected ligands and histamine 2 receptor amino acids

ligands	proteins	Interactions	with what
5311225	PHE 254	PPS	BENZENE
	VAL 176	HB	O
	ASP 98	HB	OH
1794427	ARG 257	HB	O
		SB	O ⁻
	ASP 98	HB	OH
439533	ASP 186	HB	OH
	TYR 250	HB	OH
	ASP 98	HB	OH
	GLU 270	HB	OH
162934828	GLN 77	HB	OH
	ASP 186	HB	OH
	ARG 257	HB	OH
	CYS 174	HB	OH
162934831	ASP 98	HB	OH
	TYR 250	HB	OH
		HB	O
101992980	CYS 174	HB	OH
	ASP 186	HB	OH
	PHE 254	PPS	BENZENE
	TYR 250	HB	O
11824948	ASP 98	HB	OH
	LYS 174	HB	OH
	ASP 186	HB	OH
	TYR 250	HB	OH/O
162896256	ARG 257	HB	OH
	CYS 174	HB	OH
	ASP 98	HB	OH
	ASP 98	HB	OH
	TYR 94	HB	OH
	GLN 79	HB	OH
72	GLU 270	HB	OH
	ARG 257	SB	O ⁻
		HB	O
	TYR 250	HB	O
	ASP 98	HB	OH
	ARG 257	SB	O ⁻
		HB	O

Keys: PI= pi interactions; HB= hydrogen bonding; PPS= pi-pi stacking.; SB= salt bridge.

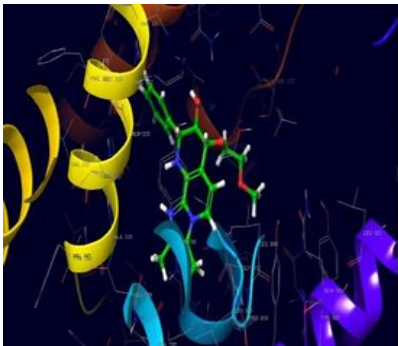


Fig 1: 3D and 2D molecular interaction of the standard ligand 213054 against proton pump

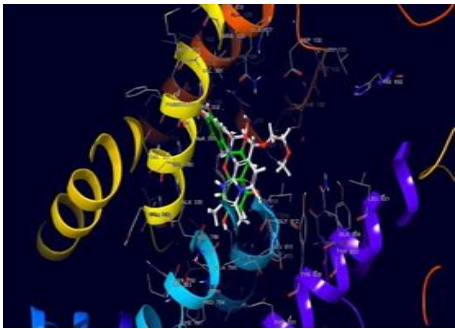
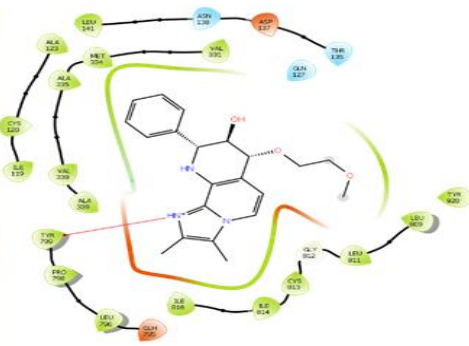
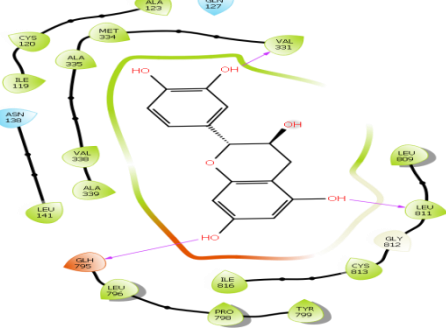
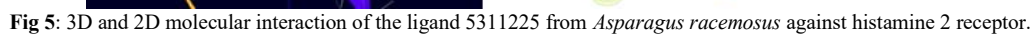
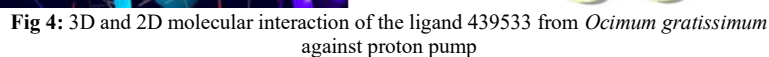
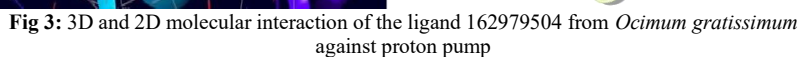


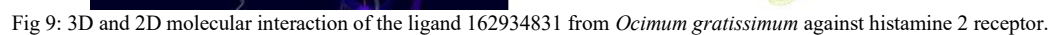
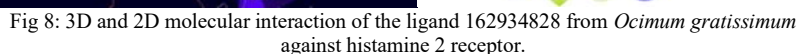
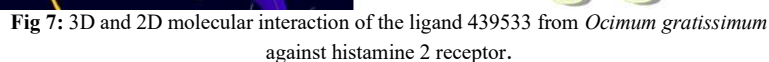
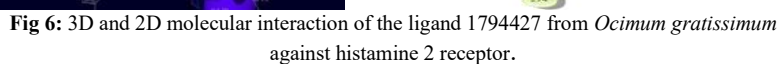
Fig 2: 3D and 2D molecular interaction of the ligand 9064 from *Ocimum gratissimum* against proton pump.





ligands	proteins	Interactions	with what
73160	TYR 404	HB	OH
	SER 109	HB	OH
	THR 192	HB	OH
	ASN 382	HB	OH
162872299	TRP 378	PPS	BENZENE
	TYR 404	PPS	BENZENE
		HB	OH
	THR 189	HB	OH

KEYS:pi= pi interactions; hb= hydrogen bonding; pps= pi~pi stacking.; sb= salt bridge.



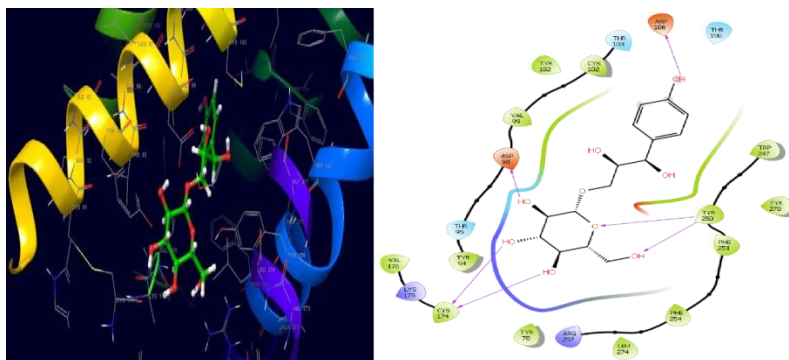


Fig 10: 3D and 2D molecular interaction of the ligand 101992980 from *Ocimum gratissimum* against histamine 2 receptor.

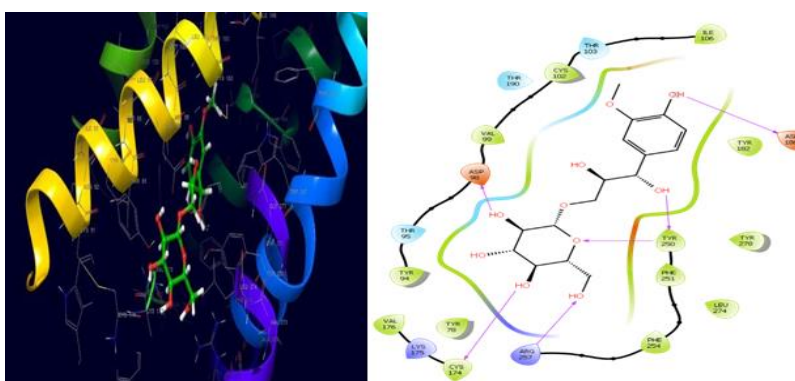


Fig 11: 3D and 2D molecular interaction of the ligand 11824948 from *Ocimum gratissimum* against histamine 2 receptor.

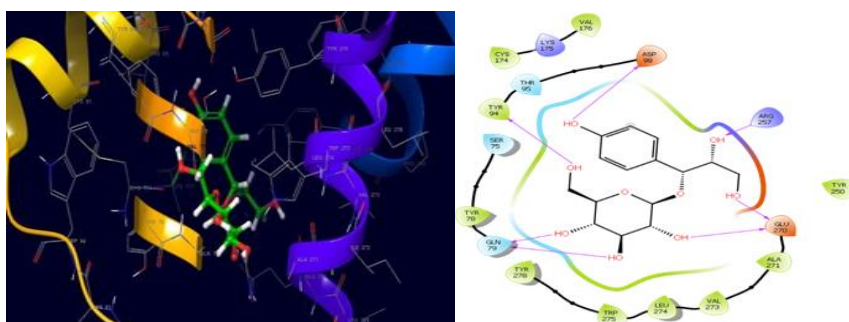


Fig 12: 3D and 2D molecular interaction of the ligand 162896256 from *Ocimum gratissimum* against histamine 2 receptor.

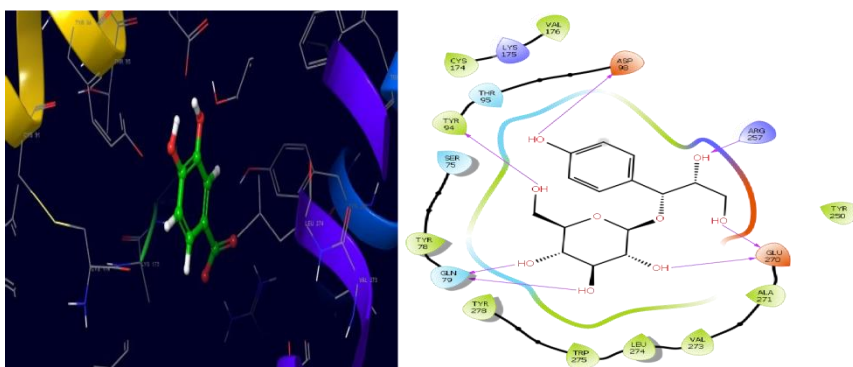


Fig 13: 3D and 2D molecular interaction of the ligand 72 from *Ocimum gratissimum* against histamine 2 receptor.

Muscarinic m1 receptor: In the docking of ligands from the two plants with the muscarinic M1 receptor, 10 compounds of proximity and higher docking scores were derived. *Asparagus* yielded four compounds, *Ocimum* with six as seen in **Table 6**.

Further pharmacokinetic screening of these compounds gave a total of two different ligands from two *Ocimum gratissimum*. The plant *Asparagus* yielded no safe ligands upon further analysis.

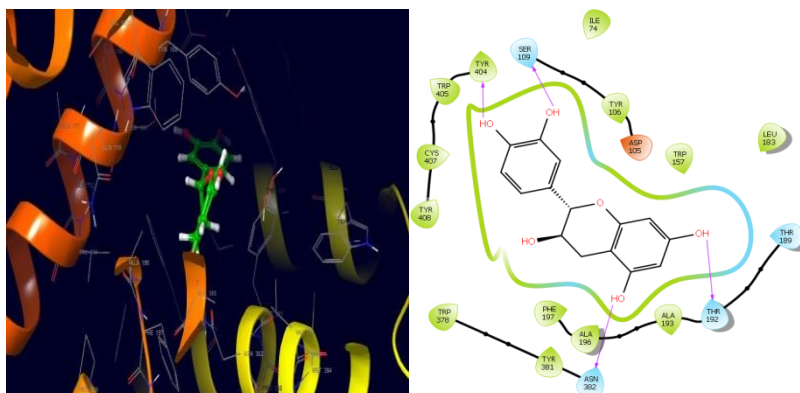


Fig 14: 3D and 2D molecular interaction of the ligand 73160 from *Ocimum gratissimum* against muscarinic m1 receptor.

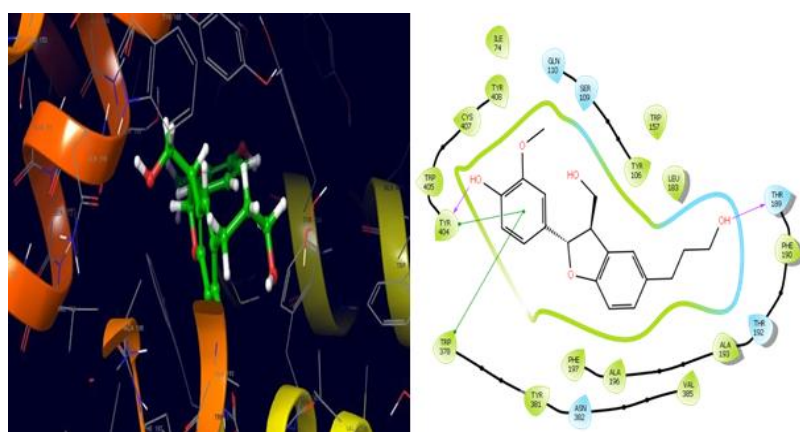


Fig 15: 3D and 2D molecular interaction of the ligand 162872299 from *Ocimum gratissimum* against muscarinic m1 receptor.

The binding affinities and interaction with active site residues of the protein target, proton pump possessed by 9064 (cianidanol), 162979504 in *Ocimum gratissimum* showed the potential of these ligands as lead compounds for the treatment of peptic ulcer disease. Also, the binding affinities and interaction with active site residues of the protein target, histamine H2 receptor possessed by 1794427(chlorogenic acid), 439533(taxifolin), 162934828, 162934831, 101992980, 11824948, 162896256, 72(3,4-dihydroxyl benzoic acid) in *Ocimum gratissimum* showed the potential of these ligands as lead compounds for treatment of peptic ulcer disease.

Moreso, the binding affinities and interaction with active site residues of the protein target muscarinic M1 receptor, possessed by 73160(catechin), 637584(epi pinoresinol), 162872299 present in *Ocimum gratissimum* showed the potentials of these ligands as lead compounds for the treatment of peptic

ulcer disease. It is worth noting that not all ligands docked returned docking scores. This could be due to factors pertinent to the receptor and ligand structures, software, and computer systems. These factors include ligand size and flexibility, receptor site issues, clashing or steric issues, scoring function limitations, computational resource limitations, software bugs and errors, docking algorithm limitations, and ligand and receptor preparation issues.

Conclusion: *Ocimum gratissimum* and *scoparia dulcis* possesses phytoconstituents that have potential in the treatment of peptic ulcer disease. Although many compounds showed a high and proximal binding affinity to conventional drugs for each receptor, most of them were shown to be toxic. However, studies such as molecular dynamics simulations, *in vitro* and *in vivo* studies using appropriate animal models need to be done to further

validate their use as drugs for the treatment of peptic ulcer disease.

Declaration of Conflict of Interest: The authors affirm that none of the work described in this publication was influenced by any known conflicts of interest or personal ties.

Declaration of Data Availability Statement: The data can be obtained upon request from the corresponding author

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