ASSESSMENT OF THE THERAPEUTIC POTENTIALS OF THE PHYTOCONSTITUENTS OF SOME HERBAL PLANTS USED FOR THE TREATMENT OF PEPTIC ULCER DISEASE USING *IN-SILICO* METHODS

BY

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UNIVERSITY OF BENIN

BENIN CITY

FEBRUARY, 2025.

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A DISSERTATION SUBMITTED TO THE DEPARTMENT OF PHARMACEUTICAL CHEMISTRY, FACULTY OF PHARMACY, UNIVERSITY OF BENIN, BENIN CITY IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR THE AWARD OF DOCTOR OF PHARMACY DEGREE HONOURS IN PHARMACY

FEBRUARY, 2025.

CERTIFICATION

This is to certify that this work was done by **Christian Chukwuebuke Samson** in the Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Benin, Benin City, Nigeria in partial fulfilment of the requirement of the award of the Doctor of Pharmacy Degree (Pharm D).

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CHRISTIAN C. SAMSON. **Date**

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DR. U.M. OGBEIDE **Date**

Supervisor

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DR. V. IMIEJE **Date**

Head of Department

DEDICATION

This work is dedicated to God almighty, for His faithfulness and for being my source throughout my journey in this great institution of learning and to my parents Mr. and Mrs. Samson Ossai for their unwavering support and guidance.

ACKNOWLEDGEMENT

My sincere gratitude goes to God almighty for His grace, mercy, love, provision, and strength throughout the course of my project work.

My heartfelt gratitude also goes to my supervisor, Dr. Uyi M. Ogbeide whose understanding, patience, friendliness, experience, and invaluable guidance made the entire work a huge success.

My special appreciation goes to my parents, Mr. and Mrs. Samson Ossai, and my siblings Basil, Maxwell, and Nduka who encouraged and supported me throughout my sojourn in the School of Pharmacy.

I also want to thank my friends who have turned siblings, who have always been supportive through school; Anointed, Chinedu, Esther, Ayomide, Ekene, Osato, Anatolia, Bunmi, Austin, Mighty, Jenifer, Divine, Ama, Jessica and Benedict for being of immense help, encouragement, support and cheers.

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ABSTRACT

Peptic ulcer disease is due to hyperacid secretion. Various factors and agents have been linked to these disease conditions and as such these factors and agents have been the target of major conventional drugs used in the treatment and management of these conditions. This study aims to assess the therapeutic potentials of the phytoconstituents of some plants used in the treatment of peptic ulcer disease using *in silico* techniques.

The phytoconstituents of *Ocimum gratissimum(275), Scoparia dulcis(102), Solanum nigrum(192), and Asparagus racemosus(86)* were obtained from literature sources; The 3D structure data file format of the phytoconstituents were obtained from PubChem and prepared using the ligrep domain of Maestro. Proteins with cocrystallized ligands were obtained from a protein data bank (RCSBPDB)and then prepared using the protein preparation domain of Maestro. These prepared ligands were docked against the proteins using Maestro 12.8. The drug-likeness and toxicity profiles of the ligands with similar binding affinities as the reference standards were assessed using the Admetlab 3.0 web server. The post-docking analysis was done using Maestro12.8.

Phytoconstituents from these plants; *A. racemosus* (1), *O. grattisimum* (11) *S. dulcis* (1), and *S. nigrum* (10) had a comparable binding affinity with the standard soraprazan (9.01kcal/mol) when docked against proton pump 7W49. Also, phytoconstituents from these plants; *A. racemosus* (6), *O. grattisimum* (17) *S dulcis* (4), and *S. nigrum* (6) had comparable docking score values with the standards famotidine (-6.86kcal/mol) and ranitidine (-7.49kcal/mol) when docked against proton histamine H2 receptor 7UL3. For the phytoconstituents from these plants; *A. racemosus* (2), *O. grattisimum* (6) *S, dulcis* (5), and *S. nigrum* (6) had comparable docking score values with the standard pirenzepine (-9.07kcal/mol) when docked against muscarinic M1 receptor 5CXV. Further analysis of pharmacokinetics profiles yielded six ligands active against 7W49; eleven for

7UL3 and four for 5CXV as potential leads for the treatment of gastrointestinal acid disorders. However, more 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 the claim.

CHAPTER ONE

INTRODUCTION/ LITERATURE REVIEW

1.0 PEPTIC ULCER DISEASE

Peptic ulcer disease is a medical condition that occurs as a result 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 defence 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 a large number of people worldwide and also 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)

1.1 CONVENTIONAL DRUGS IN PEPTIC ULCER DISEASE TREATMENT.

These traditional medications aim to address the different physiological and extrinsic variables that contribute to the development of gastro-oesophageal reflux disease and peptic ulcer disease. They are accustomed to;

i. Decrease stomach acid production

ii. Reduce mucosa irritation

iii. Increase mucosa prostaglandin production

iv. Increase mucosal blood flow

v. Increase mucosal bicarbonate production

vi. Relax the gastrointestinal smooth muscles.

Although the pathophysiology of the disorders 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 mucosal is a powerful inhibitor of gastric acid secretion and a stimulus for gastric acid secretion. (Sill *et al.,*1992.).

These drugs are grouped into Proton pump inhibitors, H2 receptor antagonists, Prostaglandin E2 analogues, Muscarinic M1 receptor antagonists, and Antibiotics.

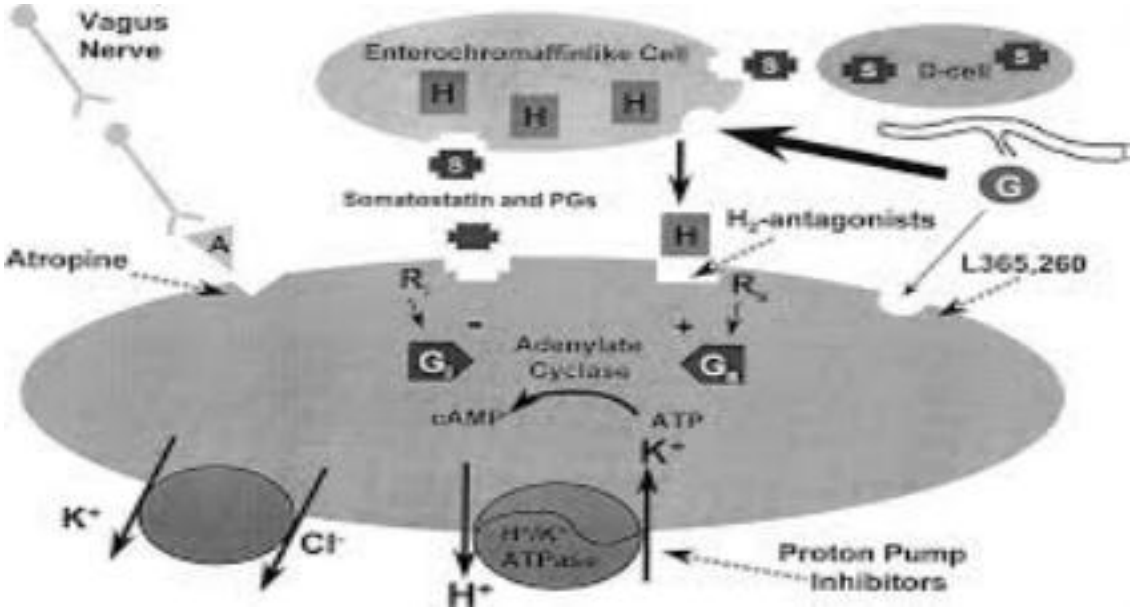


Figure 1.1: Diagram showing targets and mechanism of action for proton pump inhibitors, prostaglandin analogues, and muscarinic M1 receptor antagonists. (Wolfe *et al.,*2000)

1.1.1. **Proton Pump Inhibitors**

Proton pump inhibitors are the commonly used drugs in the treatment of peptic ulcer disease and gastro-oesophageal reflux disease. Blockade of the gastric acid pump, hydrogen potassium adenosine Triphosphatase (H^+k^+ATPase) by proton pump inhibitors is one of the most effective treatments for gastro-oesophageal reflux disease and peptic ulcer disease (Sachs, 2001).

Central to the acid secretion mechanism are the parietal cells of the stomach. These cells secret hydrogen ions into the gastric lumen under the control of neurocrine, paracrine, and endocrine pathways. (Wolfe *et al.,*2000)

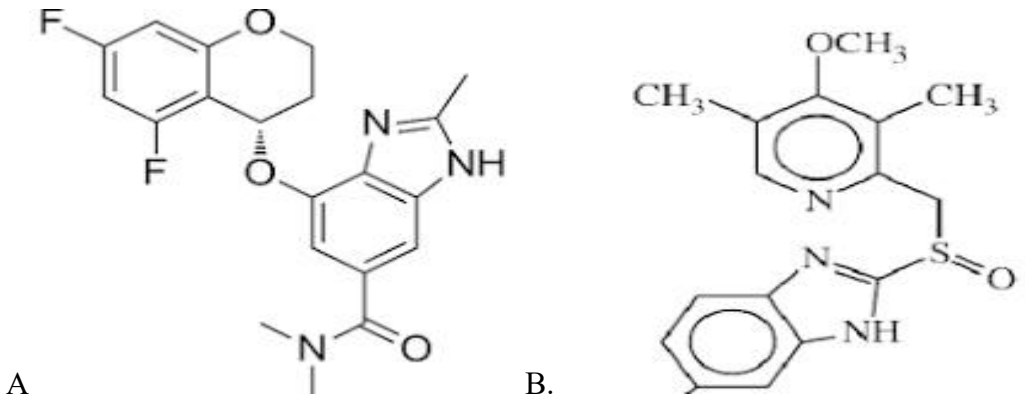
All these pathways interact to either stimulate hydrogen ion generation by the parietal cells or inhibition through a negative feedback mechanism as in Figure1.1. (Wolfe *et al.,*1988).

The main target here is the H^+K^+ATPase of the active parietal cells. These cells constitute the primary and final acid sources for the gastrointestinal tract- the acid secretory canaliculus and the acid pump itself. Therefore, drugs designed to inhibit at this level showed a greater promise of efficacy and specificity. (George Sachs. 2001) and hence the proton pump inhibitors.

They are similar concerning their chemical structures, which consist of substituted pyridyl methyl sulfonyl benzimidazoles (Wolfe *et al.,*2000)

These proton pump inhibitors work by inhibiting the H^+K^+ATPase enzyme and hence gastric acid production. Also to note here is the Prazans which are a new class of drugs known as potassium-competitive acid blockers as they competitively inhibit the H^+K^+ATPase directly and it is dependent on the concentration of potassium.

Examples of the conventional proton pump inhibitors are omeprazole, rabeprazole, pantoprazole, lansoprazole, esomeprazole, dexlansoprazole etc. while the new class of Prazans include tegoprazan, soraprazan, revaprazan and vonoprazan.



A B.

Figure1.1.1. Chemical structures A.tegoprazan and B.omeprazole respectively.

1.1.2. **Histamine 2 Receptor Antagonists.**

Histamine, a paracrine factor released by the enterochromaffin-like cells, stimulates parietal acid secretion via histamine 2 (H2) receptors. Engagement of the receptors stimulates H+ release via the production of cyclic adenosine -3'5'- monophosphate (cAMP). The endocrine pathway is also regulated by the production of gastrin by antral G cells which stimulates acid production via the stimulation of histamine production by enterochromaffin-like cells. (Sachs, 2000)

H2 receptor antagonists inhibit acid secretion with an effect that lasts for four to eight hours with a single dose, decreasing stimulated acid production by 70%. (Colin-Jones, 1995)

They work by competitively binding to H2 receptor sites on the surface of the parietal cells and inhibit the common pathway that histamine and other substances must travel to stimulate the proton pump activity and promote gastric acid secretion. This results in reduced gastric acid secretion, gastric volume, and H^+ concentration (figure 1.1) (Myrna, 2023.)

Examples of H2 receptor antagonists include ranitidine, cimetidine, famotidine, and nizatidine.

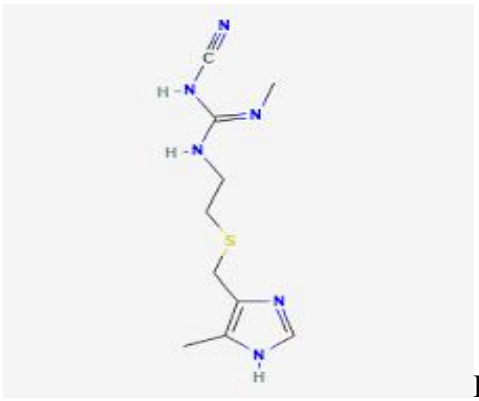
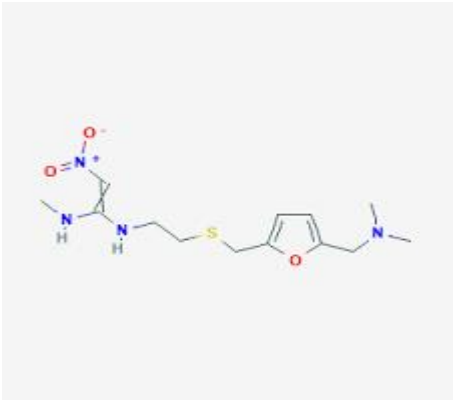
A.  B 

Figure1.1.2. Chemical structure of A. cimetidine and B. ranitidine

1.1.3. **Prostaglandin Analogues (E1and E2)**

While endogenous Prostaglandin generally protects the stomach against cold restraint stress mediated by PGI2/IP receptors and partly EP4 receptors, Prostaglandin prevents acid reflux oesophagitis and indomethacin-induced gastric lesions through EP1 receptors. (Takeuchi *et al.,*2011)

Endogenous Prostaglandins produced from arachidonic acid by the two isoforms of cyclo-oxygenase play a vital role in maintaining mucosal integrity by modulating various functions of the gastrointestinal tract and Prostaglandin E2 is most effective in this activity through its four specific G- protein-coupled receptor subtypes EP1- EP4.

Prototyped by misoprostol, misoprostol is indicated as a tablet to reduce the risk of NSAID-induced gastric ulcers but not duodenal ulcers in high-risk patients. It is a synthetic Prostaglandin E1 analog that stimulates PGE1 receptors on the parietal cells in the stomach to reduce gastric acid secretion. Mucus and bicarbonate are also increased along with the thickening of the mucosa bilayer so that the mucosa can generate new cells.

Synthetic Prostaglandin E2 analogue, enprostil also possesses gastric anti secretary(acid), cytoprotective (COX2 generation), gastrin lowering properties and also wound healing in ulcer management.

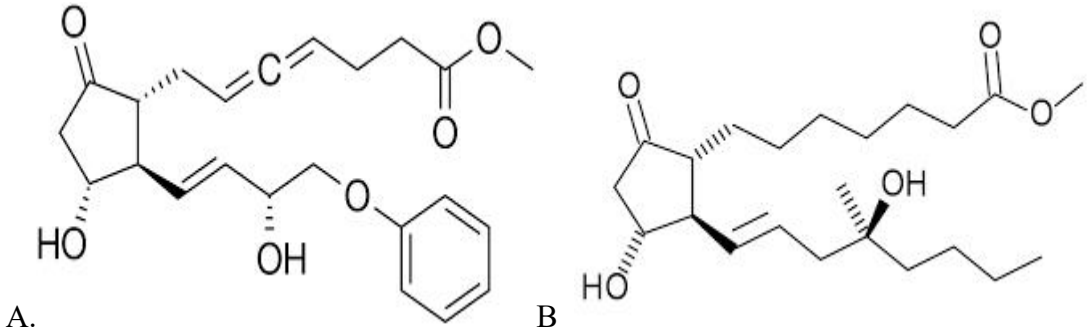


Figure1.1.3. Chemical structures of A. enprostil and B. misoprostol.

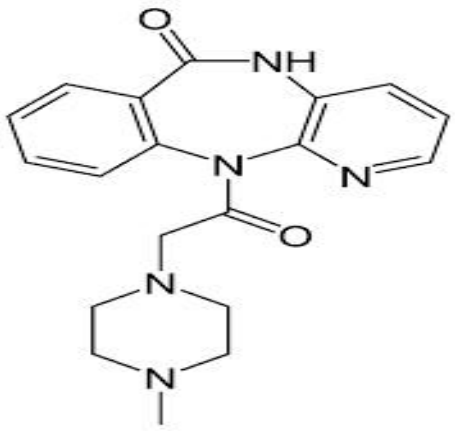
1.1.4. **Muscarinic Receptors M1 and M2 antagonists.**

These agents(antimuscarinics) decrease the amount of gastric acid secretion in the stomach known for causing and worsening peptic ulcer disease and gastro-oesophageal reflux disease. An example is pirenzepine.

It treats duodenal, gastric and peptic ulcers. It binds to muscarinic acetylcholine receptors. The muscarinic acetylcholine receptors mediate various physiological and cellular responses including inhibition of adenylyl cyclase, breakdown of phosphoinositides and modulation of potassium channels through the actions of G-proteins.

Of about 400 papers reviewed on anticholinergic drugs use in the treatment and management of peptic ulcer and gastro-oesophageal reflux diseases; only a dozen or so reasonably well-controlled studies could be found to show any reduction of basal or histamine-stimulated acid secretion in man by anticholinergic drugs given orally. In many of the cases, the mean reduction in basal acid output was about 50%. As most subjects were hypersecretors with duodenal ulcers, this degree of reduction in acid output resulted in an output in the normal range. (Ivey *et al.,*1975)

The use of an anticholinergic in peptic ulcer disease is based on the role of the vagus nerve in the control of gastric acid secretion and therapy aims to reduce gastric acid secretion. (Ivey *et al.,*1975). The basal or continuous secretion of gastric juice in normal men and animals is almost entirely caused by tonic impulses in the vagus nerves.



1.1.4. Chemical structure of pirenzepine

1.1.5. **Antibiotics**

Since the implication of the Gram-negative Bacterium *Helicobacter pylori* as a major causative factor in the generation, proliferation and prevention of wound healing in peptic ulcer disease, it has become relevant to address the bacteria involved with the use of antibiotics.

According to the 2017 American College of Gastroenterology, treatment guideline for peptic ulcers indicative of H. *pyroli*, the following antibiotics are used alongside proton pump inhibitors, and bismuth salts in a 10 to 14 days regimen; tetracycline, nitroimidazoles (tinidazole and metronidazole), amoxicillin, clarithromycin, levofloxacin and rifabutin.

1.2. MEDICINAL PLANTS FOR PEPTIC ULCER DISEASE TREATMENT.

The use of plants in religious ceremonies as well as for magic and medicinal purposes is very commonplace and widespread. Plants and phytoconstituents are better choices to treat diseases

than allopathic drugs. Most of the medications used in primitive medicine originated from plants and are the earliest and principal natural source of medicine. The drugs from plants are fairly innocuous and relatively free from toxic effects. Nature has provided us various medicinal plants which became the storehouse of remedies to cure all ailments of mankind. In the modern era, many plant-derived compounds have been used as drugs, either in their original or semi-synthetic form. Peptic ulcer disease is a widespread health problem nowadays. Generation of free radicals, decrease in mucosal defensive factor, or increase in mucosal injurious factor causes peptic ulcer. (Saikat *et al.,*2009)

Various plants amongst which include *Ocimum sanctum, Asparagus racemus, Anogeissus latifolia, Centaurea solstistialis, Scoparia dulcis, Solanum nigrum* and their phytoconstituents proved active in antiulcer therapy. (Saikat *et al.,*2009).

Many plants have been discovered to be beneficial in peptic ulcer disease gastro-oesophageal reflux disease and other gastrointestinal and acid secretion disorders. Most of these plants and their constituents have been used with and in time and have been transferred from one human generation to another but without scientific evaluation and supportive data hence the need for scientific evaluation and data support to these claims.

1.2.1. **Ocimum gratissimum**

Ocimum gratissimum L., popularly known as scent leaf, 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 a widespread and commercially viable perennial herbaceous plant with a very strong aromatic smell. It belongs to the family of Lamiaceae and is found in Africa, Asia, and South America (Tanko *et al.,*2008; Akara *et al.,*2021). It is used as a natural flavouring agent, condiment, or vegetable in the preparation of fish, meat, soup, and stew. 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). As seen in figure 1.2.1 available At https://en.wikipedia.org/wiki/Ocimum_gratissimum

Figure 1.2.1. picture of *Ocimum gratissimum* from Wikipedia

Botanical description

Ocimum gratissimum is an aromatic herbaceous plant also known as basil, basil-clove, or alfavaca. It belongs to the Lamiaceae family (genus *Ocimum* and species *gratissimum*) (Nweze and Eze, 2009). It is about 1–3 cm tall, has an erect stem, and is branched, round-quadrangular, and woody at the base, with opposite, slender, and marginalized leaves.

Geographic location

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).

Phytoconstituents:

Polyphenols and flavonoids found in *Ocimum gratissimum*: The phenolic compounds found in *Ocimum gratissimum* include rosmarinic acid, sinapic acid, salvigenin, gallic acid, catechins, methyl eugenol, caffeic acid, L-caftaric, ellagic acid, trans-ferulic acid, L-chicoric acid, and flavonoids such as xanthomicrol, cirsimaritin, rutin, apigenin, kaempferol, vicenin-2, luteolin 5-O-glucoside, luteolin 7-O-glucoside, 7,4′-dimethyl ether, vitexin, isovitexin, nepetoidin A, quercetin 3-O-glucoside, nevadensin, cirsimaritin, hymenoxin, myricetin, basilimoside, morin, isothymusin (Grayer *et al.,*2000; Costa *et al.,*2012; Ouyang *et al.,*2013; Casanova *et al.,*2014;venuprasad *et al.,*2014; Ajayi *et al.,*2013), epicatechin, quercitrin, quercetin (Irondi *et al.,*2016), and triterpenes (oleanolic, pomolic acid, ursolic acids, and tormentic acid) (Dzoyem *et al.,*2021).

Chemical constituents of essential oil present in *O. gratissimum:* Compounds present in the essential oil of *O. gratissimum* include hydrocarbonated monoterpenes such as camphene, α-thujene, α-pinene, sabinene, β-pinene, β-myrcene, α and β-phellandrene, δ-3-carene, limonene, α-terpinene, p-cymene, trans-β-ocimene, γ-terpinene, terpinolene, p-cymenene, and p-menthane-1,3,8-triene; oxygenated monoterpenes such as 1.8-cineole, cis-sabinene hydrate, linalool, trans-sabinene hydrate, trans-thujone, citronellal, umbellulone, borneol, terpinen-4-ol, p-cymen-8-ol, α-terpineol, thymol methyl ether, estragol, p-cymen-7-ol, thymol, and carvacrol; hydrocarbonated sesquiterpenes such as α-copaene, β-elemene, γ-elemene, β-caryophyllene, α-trans-bergamotene, α-humulene, β-bourbunene, α-guaiene, δ-cadinene, germacrene D, γ-selinene, β-selinene, α-selinene, (Z,E)-α-farnesene, and 7-epi-α-selinene; and oxygenated sesquiterpenes such as caryophyllene oxide, 1,2-epoxydehumulene, and 3,7-(11)-eudesmadiene, spathulenol (Vieira *et al.,*2001; Pessoa *et al.,*2002; Lahlau *et al.,*2004; Tchoumbougnang *et al.,*2005;Lesmos *et al.,*2005;Benitez *et al.,*2009; Kpoviessi *et al.,*2012; Nguemtchouin *et al.,*2013; Aguiar *et*

*al.,*2015; Mohr *et al.,*2015; Chimnoi *et al.,*2018; Melo *et al.,*2019;Onyebuchi and Kavaz 2020; Essoung *et al.,*2020).

Trado medicinal uses

Ocimum gratissimum has been described as a plant easily available to communities and commonly utilized for the treatment of a plethora of diseases in numerous ethnopharmacological surveys (Ajayi *et al.,*2017). This perennial and odoriferous plant is now found in all continents and possesses generally acknowledged medicinal properties. Its medicinal potential in Africa is incredibly vast and varies by country (Kpoviessi *et al.,*2014). Its infusions are regarded as tonic and pectoral in Cameroon, and the juice of its sheets is used to treat giddiness, headaches, colds, and coughs. In Côte d'Ivoire, several formulations of this plant are used to treat ear infections, dermatoses, and ophthalmias (Kpoviessi *et al.,*2014).). In Nigeria, it is recommended for diarrhoea therapy (Kpoviessi *et al.,*2014).), while Sofowora (1970) recommended it for respiratory ailments and use as an anthelminthic. It was also used to treat headaches, fevers, and ophthalmic and skin problems, as well as pneumonitis. In Togo, the plant's infusion is used to relieve cough (antitussive). The fresh juice from its leaves has antidiarrheic and antimesenteric properties, and its aqueous maceration is used to treat haematuria and purulent urethritis (Kpoviessi *et al.,*2014).). In Benin Republic, the aqueous maceration of its pulp or aerial portions is used to treat dystopias, pelvic aches, colic, candidoses, digestive dysmenorrhoea, emesis, haemorrhoid (pile), and diarrhoea. Its stem decoction is used to treat hepatitis, cough, asthma, and wound infections (Chal *et al.,*2006; Kpoviessi *et al.,*2014).). The juice from its leaves is used to treat angina, cephalgias, headaches, fever, and malnutrition. Its inflorescences are utilized as aromatizers in a variety of meals.

Several studies have shown that this type of basil has anaesthetic, anti-stress, anti-inflammatory, anthelminthic, antidiarrhoeal (Offiah *et* Chikwendu, 1999), antipyretic, anti-mutagenic, anti-ulcerative, gastroprotective, hepatoprotective, sedative, and fungicidal properties, validating its widespread medical use (Priyanka *et al.,*2018; Martins *et al.,*2018). *O*. *gratissimum* is antiseptic and has found widespread applications in the preparation of toothpaste mouthwash and topical therapies (Pessoa *et al.,*2002). It is an excellent wash for sore throat and tonsillitis. It is also used as an expectorant and as a cough suppressant. The plant extract is used to treat gastrointestinal helminths in both animals and humans (Chitwood *et al.,*2002). Reports on *O*. *gratissimum* revealed that the plant extract may be used as a medicinal resource for people living with the human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) (Priyanka *et al.,*2018). It is used as a febrifuge and as a component in several malarial treatments in West Africa (Chal *et al.,*2006). Crushed leaves of the plant are used to cure conjunctivitis, while the oil extracted from the leaves is considered highly antimicrobial and has been used in wound dressing, the preparation of mouthwash, and the prevent postnatal sepsis (Chal *et al.,*2006). Furthermore, fresh aerial portions are consumed directly as vegetables in traditional soups, while dried and powdered aerial parts are utilized in a variety of traditional dishes (Kpoviessi *et al.,*2014).

1.2.2. Scoparia dulcis

Freeze-dried aqueous extract of the aerial parts of *Scoparia dulcis* L. produced reduction gastric hypersecretion and ulcers in rodents (Messia-Vela *et al.,*2007) as seen in figure 1.2.2 available at https://portal.wiktrop.org/species/show/550.

Figure 1.2.2. picture of *Scoparia dulcis*(WIKTRO)

Botanical description:

Scoparia dulcis L. (Scrophulariaceae), syn. *Scoparia grandiflora, Capraria dulcis, Gratiola micrantha*. Other common names: Vassourinha, amruti, bitter-broom, boroemia, broomweed, Brum sirpi, cancharagua, escobilla, gadadahana, mastuerzo, ñuñco pichana, and sweet broom. *S. dulcis* is a small erect annual in the foxglove family. It grows up to 0.5 m high and produces serrated leaves and small white flowers. (Melania *et al.,*2008)

Geographical location

This plant is found in abundance in South America and the Amazon rainforest and is widely distributed in many tropical countries in the world. The traditional use has been recorded in herbal medicine systems in the following parts of the world: Asia-Pacific, Africa, Central America, South America, and India. (Melania *et al.,*2008)

Phytoconstituents:

The plant contains a lot of metabolites as well as natural products which are classified into; nitrogen-containing compounds, flavonoids, diterpenoids, triterpenoids, steroids, phenolics and other aliphatic compounds. (Abere *et al.,*2015)

Nitrogen-containing compounds: Nitrogen-containing compounds, of which alkaloids are the most important, are very commonly found in plants. 2-Hydroxy-2H-1,4-benzoxazol-3-one, Benzoxazine, Coixol, 1-Hydroxy-6-methoxy-2-benzoxazolinon, 3,6-Dimethoxy-benzoxazolin-2(3H)-one, (2R)-2-(β-D-Glucopyranosyloxy)-7-methoxy-2H-1,4-benzoxazin-3(4H)-one, (2R)-2-(β-D-Glucopyranosyloxy)-4,7-dimethoxy-2H-1,4-benzoxazin-3(4H)-one, (2R)-7-Methoxy-2H-1,4-benzoxazin-3(4H)-one 2-O-β-galactopyranoside, 7-Methoxy-2,4-hydroxy-1,4-benzoxazin-3(2H)-one, Dextromoramide, 2-Heptadecyl-2-imidazoline, 1-Methyl-2-pyrrolidinone, N^1-Acetylspermine, Cyclohexylamine, Procaine, Epinephrine, Norepinephrine.(Zikang *et al.,* 2021)

Flavonoids: Flavonoids are compounds composed of two benzene rings (A ring and B ring) with phenolic hydroxyl groups connected through three central carbon atoms, creating a compound composed of C_6–C_3–C_6 units. The flavonoids in S. dulcis can be grouped into flavones, flavonols, flavan-3-ols, and flavanones which includes the following; Scutellarin methylester, Scutellarin, 5,7,8,3′,4′,5′-Hexahydroxy-flavone glucuronide, 5-Hydroxy-6,7-dimethoxyflavone-4′-O-β-glucose, iso-Vitexin, 5,7-Dihydroxy-3′4′,6,8-tetrametoxyflavone, Acerosin, Nevadensin, 5,6,4′-Trihydroxyflavone 7-O-α-L-2,3-di-O-acetylrhamnopyranosyl-(1→6)-β-D-glucopyranoside, Apigenin 7-O-α-L-2,3-di-O-acetylrhamnopyranosyl-(1→6)-β-D-glucopyranoside, Apigenin 7-O-α-L-3-O-acetylrhamnopyranosyl-(1→6)-β-D-glucopyranoside, Acacetin, Apigenin, Cirsimarin, Cynaroside, Homoplantaginin, Linarin, Pectolinarin, Isorhoifolin, Vicenin-2, Vitexin, Luteolin, Scutellarein, Hispidulin, Apigenin-8-C-α-L-arabinopyranoside, Apigenin-7-O-glucuronide, Hispidulin-7-O-glucuronide, Cirsimaritin, Cirsiliol, Salvigenin, Scutellarein 7-O-α-glucuronamide, Morin, Dihydroxy-dimethoxyflavone, Hydroxy-tetramethoxyflavone, Dillenetin 3-O-(6″-O-p-coumaroyl)-β-D-glucopyranoside, Rutin, Quercetin, Quercetin, Catechin, Naringin.(Zikang *et al.,* 2021)

Terpenoids: This refers to the diterpenoids and the triterpenoids which contain in their molecular structure four isoprene (twenty carbon atoms) and six isoprenoids (thirty carbon atoms) units respectively. Scopadulcic acid A, 4-epi-Scopadulcic acid B, Scopadulcic acid B, Scopadulciol, iso-Dulcinol, Scopadulcic acid C, Dulcidiol, Dulcinodal, Dulcinodiol, Scopadiol decanoate, 4-epi-7α-O-Acetylscoparic acid A, 7α-Hydroxyscopadiol, (7S)-4-epi-7-Hydroxyscoparic acid A, 7α-O-Acetyl-8,17β-epoxyscoparic acid A, neo-Dulcinol, Dulcinodal-13-one, 4-epi-7α-Hydroxydulcinodal-13-one, Scoparic acid A, Scoparic acid B, Scoparic acid C, Scoparic acid E, Scoparicol A, Scoparicol B, Scoparic acid D, Scopadulin, Scopanolal, Scopadiol, Phytol, Friedelin, Glutinol, α-Amyrin, Dulcioic acid, Betulinic acid, Lupeol, Ifflaionic acid, Glutenol, Glutinone, Taraxerol. (Zikang *et al.,* 2021)

Steroids: Due to few studies on the steroid components of *Scoporia dulcis*, only a few of the steroid components of the plant have been discovered and studied. Amongst these include; Daucosterol, Stigmasterol, and β-Sitosterol.

Phenolics: The chemical component of the plant is responsible for the characteristic odour of the plant. Although these compounds produce aromatic odours, they include; Chlorogenic acid, Caffeic acid, Ferulic acid, Sinapic acid, p-coumaric acid, Forsythoside G, Acteoside, Ferruginoside C, and Gentisic acid.

Other aliphatic compounds: These compounds include the following; Mannitol, Hexalure, 2-Hexyldecanoic acid, 5Z-Eicosenoic acid, Methyl arachidate, Stearic acid, Methyl stearate.

Tradomedicinal uses

The plant has been in use for several purposes in the tradomedical scene and these uses include; antibacterial and immunomodulatory (Alli *et al.,*2013), and anti-inflammatory effects (Ahmed *et*

*al.,*2022). Antidiabetic, antimalarial, analgesic and anti-inflammatory, antiviral, anticancer, diuretics, neurotic activity, sedation prolongation. (Krishna *et al.,*2012).

1.2.3. Solanum nigrum

Botanical source: *Solanum nigrum* Linn. is a common edible medicinal herb of the Solanaceae family as seen in figure 1.1.2. available at https://apps.lucidcentral.org/plants_se_nsw/text/entities/solanum_nigrum.htm

Figure 1.2.3. picture of *Solanum nigrum*. (Australian Plant Image Index), photographer Murray Fagg, Booroowa-Crookwell Road

Geographical location

Solanum nigrum complex species such as S. sabrum S. viltosum, S. americanum, S. eldoretti, S. florulentum, S. physalifolium, S. nigrum, S. grossidentatum, S. retroflerum have been regarded as African nightshades due to their origin and naturalization in Africa (Suphosanele *et al.,*2022)

Phytoconstituents.

Solanum nigrum contains various compounds of structural varieties which include classes of metabolites and natural products such as steroids, alkaloids, organic acid phenylpropanoids and

their glycosides and flavonoids. The steroids are both steroidal saponins or alkaloids which are the main compounds of pharmacological importance (Xufei *et al.,*2022). These constituents generally includes Degalactotigonin, Pterosterone, 12-keto-porrigenin, 28-*O*-*β*- d-glucopyranosyl betulinic acid 3*β*-*O*-*β*-D glucopyranoside, *β*-daucosterol, (25*R*)-5*α*-furost-3*β*, 22*α*-diol-12-one-26-carboxylicacid-3-*O*-*β*-D-glucopyranosy-(1→4)-[*O*-*β*-d-glucopyranosyl, (1→2)]-*O*- *β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, Tigogenin3-*O*-*β*-d-glucopyranosyl-(1→2)-[*O*-*β*-d-xyloyranosyl-(1→3)]-*O*-*β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, Uttroside A, Uttroside B, (22*α*, 25*R*)-26-*O*-*(β*-d-glucopyranosyl)-22-methoxy-furost-Δ5-3*β*, 26-diol-3-*O*-*β*-d-glucopyranosyl-(1→2)-*O*-[*β*-d-xylopyranosyl-(1→3)]-*O*-*β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, (22*α*, 25*R*)-26-*O*-(*β*-d-glucopyranosyl)-22-hydroxy-furost-Δ5-3*β*, 26-diol-3-*O*-*β*-d-glucopyranosyl-(1→2)-*O*-[*β*-d-xylopyranosyl-(1→3)]-*O*-*β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, (5*α*, 22*α*, 25*R*)-26-*O*-(*β*-d-glucopyranosyl)-22-methoxy-furostan-3*β*, 26-diol-3-*β*-d-glucopyranosyl-(1→2)-*O*-[*β*-d-glucopyranosyl-(1→3)]- *O*-*β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, (5*α*, 22*α*, 25*R*)-26-*O*-(*β*-d-glucopyranosyl-22-hydroxy-furost-3*β*,26-diol-3-*β*-d-glucopyranosyl-(1→2)-*O*-[*β*-d-glucopyranosyl-(1→3)]-*O*-*β*-d-glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, Solanigroside I, Solanigroside J, Solanigroside K, Solanigroside L, Solanigroside M, Solanigroside N, Solanigroside R, Solanigroside S, Solanigroside T, Hypoglaucin H, 5*α*-pregn-16-en-3*β*-ol-20-one-lycotetraoside, Solanigroside A, Solanigroside B, (5*α*, 20*S*)-3*β*, 16*β*-dihydroxy pregn-22-carboxylic acid (22, 16)-lactone-3-*O*-*β*-d-glucopyranosyl-(1→2)-*O*-[*β*-D-xylopy ranosyl-(1→3)]-*O*-*β*-d- glucopyranosyl-(1→4)-*O*-*β*-d-galactopyranoside, Solanigroside U, Solanigroside V, Solanigroside W, Solanigroside X, Nigrumnin I, Solanigroside C, Solanigroside D, Solanigroside E, Solanigroside F, Solanigroside G, Solanigroside O, Nigroside A, Tigogenin/(25*R*)-5*α*-spirostan-3*β*-ol, (25*R*)-26-*O*-*β*-d-

glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16,22-dione-3-*O*-*α*-l-rhamnopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-galactopyranoside, (25*R*)-26-*O*-*β*-d-glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16,22-dione-3-*O*-*α*-l-rhamnopyranosyl-(1→4)-*β*-d-glucopyranoside, (25*S*)-26-*O*-*β*-d-glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16, 22-dione-3-*O*-*α*-l-rhamnopyranosyl-(1→2)-[*α*-Lrhamnopyranosyl-(1→4)]-[*β*-d-glucopyranosyl-(1→6)]-*β*-d-glucopyranoside, (25*R*)-26-*O*-*β*-d-glucopyranosyl-(1→2)-*β*-d-glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16, 22-dione-3-*O*-*α*-Lrhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-[*β*-d-glucopyranosyl-(1→6)]-*β*-d-glucopyranoside, (25*S*)-26-*O*-*β*-d-glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16, 22-dione-3-*O*-*β*-d-glucopyranosyl-(1→6)-*β*-d-glucopyranosyl-(1→3)-[*α*-l-rhamnopyranosyl-(1→2)]-*β*-d-galactopyranoside, (25*R*)-26-*O*-*β*-d-glucopyranosyl-(1→2)-*β*-d-glucopyranosyl-cholest-5(6)-en-3*β*, 26-diol-16, 22-dione-3-*O*-*α*-l-rhamnopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-galactopyranoside, (25*R*)-26-*O*-*β*-d-glucopyranosyl-cholest-5*α*-3*β*, 26-diol-16, 22-dione-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside, Stigmast-5, 22-dien-3β-ol, Inunigroside A, Solanigroside Y1, Solanigroside Y2, Solanigroside Y3, Solanigroside Y4, Solanigroside Y5, Solanigroside Y6, Solanigroside Y7, Solanigroside Y8, Solanigroside Y9, (25*R*)-26-*O*-*β*-D-glucopyranosylfurost-5(6)-ene-3*β*, 22*α*, 26-triol-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside, (25*R*)-26-*O*-*β*-Dglucopyranosylfurost-5(6)-ene-3*β*, 22*α*, 26-triol-3-*O*-*α*-l-rhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-*β*-d-glucopyranoside, (25*R*)-26-*O*-*β*-D-glucopyranosylfurost-5(6)-ene-16*α*-methoxy-3*β*, 26-diol-3-*O*-*α*-l-rhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-*β*-d-glucopyranoside, (25*R*)-26-*O*-*β*-d-glucopyranosyl-5*α*-furost-3*β*, 22*α*, 26-triol-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside, (25*S*)-26-*O*-*β*-d-glucopyranosyl-5*α*-furost-3*β*,

22*α*, 26-triol-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside, (25*R*)-26-*O*-*β*-Dglucopyranosyl-22*α*-methoxy-5*α*-furost-3*β*, 26-diol-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-glucopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside, Uttroside B ((25*R*)-26-*O*-*β*-d-glucopyranosyl-5*α*-furost-3*β*, 22*α*, 26-triol-3-*O*-*β*-d-glucopyranosyl-(1→2)-[*β*-d-xylopyranosyl-(1→3)]-*β*-d-glucopyranosyl-(1→4)-*β*-d-galactopyranoside), *β*-sitosterol, *β*-carotene glycosides, Tigogenin, Uttronin A,, Uttronin B, Dumoside, Nigrumnin II, Solanigroside H, Cholesterol, , *β*1-solasonine, *β*2-solasonine, Solamargine, *β*2solamargine, Solanigroside P, Solanigroside Q, (3*β*, 12*β*, 22*α*, 25*R*)-3, 12-dihydroxy-spirosol-5-en-27-oic acid, Solaoic acid, (25*R*)-22*α*N-4-nor-spirosol-5(6)-en-3*β*-ol-6-al-3-*O*-l-rhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-*β*-d-glucopyranoside, (25*R*)-22*α*N-spirosol-5(6)-en-3*β*-ol-7-oxo-3-*O*-l-rhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-*β*-d-glucopyranoside, (25*R*)-22*α*N-spirosol-4(5)-en-3*β*-ol-6-oxo-3-*O*-*α*-Lrhamnopyranosyl-(1→2)-[*α*-l-rhamnopyranosyl-(1→4)]-*β*-d-glucopyranoside, Solasodine, N-methylsolasodine, Tomatidenol, Solanocapsine, Solanaviol, Solasodine-3-*O*-*β*-d-glucopyranoside, 12*β*-hydroxysolasodine *β*-solatrioside, 12*β*, 27-dihydroxy solasodine *β*-chacotrioside, 23-*O*-acetyl-12*β*-hydroxysolasodine, (3*β*, 22*α*, 25*R*)-spirosol-5-en-3yl-*O*-*α*-l-Rhamanopyranosyl-(1-2)-[*O*-*β*-d-glucopyranosyl(1–3)]-*O*-*β*-d-galactopyranoside, 15*α*-hydroxysolasodine, *α*-Solanine, Solasonine, Leptinine I, (7*R*, 8*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-{4-{2-[N-2-(4-hydroxyphenyl)ethyl]Carbamoylehenyl-2-methoxyphenoxyl}}-1, 3-propanodiolnamed, (7*S*, 8*R*)-1-(4-hydroxy-3-methoxyphenyl)-2-{4-{2-[N-2-(4-hydroxyphenyl)ethyl]Carbamoylehenyl-2-methoxyphenoxyl}}-1, 3-propanodiolnamed, (7*R*, 8*R*)-1-(4-hydroxy-3-methoxyphenyl)-2-{4-{2-[N-2-(4-hydroxyphenyl)ethyl]Carbamoylehenyl-2-methoxyphenoxyl}}-1, 3-propanodiolnamed, (7*S*,8*S*)-1-(4-hydroxy-3-methoxyphenyl)-2-{4-{2-[N-2-(4-

hydroxyphenyl)ethyl]Carbamoylehenyl-2-methoxyphenoxyl}}-1, 3-propanodiolnamed, 7′*S*, 8′*R*-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-N^2, N^3-bis(4-hydroxyphenethyl)-6-methoxy-1, 2-dihydronaphthalene-2, 3-dicarboxamide, 7′*R*, 8′*S*-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-N^2, N^3-bis(4-hydroxyphenethyl)-6-methoxy-1, 2-dihydronaphthalene-2, 3-dicarboxamide, 7′*R*, 8′*S*-7-(4-hydroxy-3,5-dimethoxyphenyl)-3′-hydroxymethyl-1′-[N-7″-(4″-hydrxyphenyl)ethyl] carbamoylethenyl-3′-methoxybenzodihydrofuran, 7′*S*, 8′*R*-7-(4-hydroxy-3, 5-dimethoxyphenyl)-3′-hydroxymethyl-1′-[N-7″-(4″-hydrxyphenyl)ethyl]carbamoylethenyl-3′-methoxybenzodihydrofuran, (7′*R*,8′*R*)-2-(4-Hydroxy-3-methoxyphenyl)-3-[N-2-(4-hydroxyphenyl)ethyl]carbamoyl-5-[N-2-(4-hydroxyphenyl)ethyl]carbamoylethenyl-7-methoxybenzodihydrofurn, (7′*S*, 8′*S*)-2-(4-Hydroxy-3-methoxyphenyl)-3-[N-2-(4-hydroxyphenyl)ethyl]carbamoyl-5-[N-2-(4-hydroxyphenyl)ethyl]carbamoylethenyl-7-methoxybenzodihydrofurn, Cannabisin F, Adenine, Pyroglutamic acid, Nicotinic acid, 9-aminononane-1,3,9-tricarboxylic acid, Glutarylcarnitine, (6*S*)-3-((1H-imidazol-4-yl)methyl)-6-amino-1, 4-diazocane-2, 5, 8-trione, 3-Indoleacrylic acid, 6-Hydroxypurine, Uridine, Ethyl 4-glycylbenzoate, Adenosine, Dihydrocapsaicin, Choline, Betaine, Allantoin,, Uracil, Trigonelline, (2-acetoxyethyl)trimethylammonium, Glycyl-l-leucine, GABA, FMoc-Asn(Trt)-OPfp, Phenylpropanoids, *Trans*-4-Hydroxycinnamic acid, *Cis*-4, Hydroxycinnamic acid, Ethyl 3, 4-dihydroxycinnaMate, *Cis*-caffeic acid ethyl ester, *Trans* ferulic acid, *Cis*-ferulic acid, Caffeic acid, 4-(4-hydroxyphenyl)-2-methylenebutyrolactoneChlorogenic acid, 3-caffeoylquinic acid methyl ester, Scopoletin, (−)-5′-methoxyisolariciresinol-3*α*-*O*-*β*-d-glucopyranoside, (+)-isolariciresinol-3*α*-*O*-*β*-d-glucopyranoside, Cinnacassoside A, Pinoresinol, Pinoresinol-4-*O*-*β*-d-glucopyranoside, Syringaresinol, Syringaresinol-4-*O*-*β*-d-glucopyranoside, Medioresinol, Acanthoside D, (+)-medioresonol-di-*O*-*β*-d-glucopyranoside, Quercetin, Quercitrin, Isoquercitrin,

Quercetin-3-*O*-*β*-d-glucopyranosyl(1-2)-*β*-d-glucopyranoside, Quercetin-3-*O*-*β*-d-galactopyranosyl-(1→6)-*β*-d-glucopyranoside, Quercetin-3-gentiobioside, Quercetin-3-O-*α*-l-rhaopyranosyl(1→4)-*O*-*β*-d-glucopyranosyl-(1→6)-*O*-*β*-d-glucopyranoside, 6-Hydroxyluteolin 7-sophoroside, Kaempferol, (8-hydroxy-3′-*β*-d-galactosyl-isoflavone)-2′-8″-(4‴-hydroxy-flavone)-biflavone, 2′, 3′, 5-trihydroxy-5″-methoxy-3″-O- *α*-glucosyl-3-4‴-*O*-biflavone, Benzoic acids, Gallic acid, 2, 4-Dihydroxybenzoic acid, Protocatechuic acid, Vanillic acid, 4-Hydroxybenzoic acid, Salicylic acid, 2, 5-Dihydroxybenzoic acid, Galacturonic acid, Pyruvic acid, Formic acid, Succinic acid, Fumaric acid, Ursolic acid, Linolenic acid, Oleic acid, Linoleic acid, Palmitic acid, 1-monolinolenin,Lignoceric acid, (*E*)-docosyl-3-(4-hydroxy-3-methoxyphenyl)acrylate, *α*-carotene, *β*-carotene, Xanthophyll. (Chen *et al.,*2022).

Ethnomedicinal uses

These African species are not only beneficial for their nutritional values as sources of proteins, energy, fibres, minerals, and vitamins; they also possess phytochemicals with anti-inflammatory, antioxidant, antidiabetic, anticancer, and hepatoprotective activities (Siphonanele *et al.,*2022).

It is also used in combination with Amaranth to feed people with HIV/AIDS. Treatment of people with malnutrition and promotion of healthy diet. (Linguya *et al.,* 2015)

According to Chen *et al.,*2022, several Chinese classical books of Traditional Chinese medicines record that S. nigrum is used in sore healing, poison, skin eczema, poor urination, chronic tonsilitis, chronic bronchitis, excessive leucorrhea, prostatitis, dysentery, clearing away heat, detoxification, dispersion of knots and detumescence and can be in preparations such as pills, tablets, granules, powders, and decoctions.

1.2.4. Asparagus racemosus

Botanical description

Asparagus racemosus is a climber having stems up to about 4m long. It has both tuberous and fibrous roots (Clifford *et al.,*2020)

It grows 1-2m 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 as seen in figure 1.2.4 as seen in figure 1.2.4 available at https://en.wikipedia.org/wiki/Asparagus_racemosus.

Figure 1.2.4. picture of *Asparagus racemosus* (Wikipedia)

Ethnomedical uses

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 (Shashi *et al.,*2013)

Phytoconstituents

The plant contains a wide range of constituents ranging from carbohydrates, vitamins steroids, saponins, alkaloids, spiranositoside, aliphatics, sterols, furans, flavonoids, kaempferol and others**.** *Asparagus racemosus* is rich in phytoestrogens (Joshi, 2016). Steroidal saponins, known as shatvarins. Shatvarin I to VI are present. Shatvarin I is the major glycoside with 3-glucose and rhamnose moieties attached to sarsapogenin. Oligospirostanoside referred to as Immunoside is also present. Polycyclic alkaloid-Aspargamine A; Isoflavones-8-methoxy-5, 6, 4-trihydroxy isoflavone-7-0-beta-D-glucopyranoside .Cyclic hydrocarbon-racemosol, dihydrophenantherene; Furan compound-Racemofuran; Carbohydrates-Polysacharides, mucilage; Flavanoids-Glycosides of quercitin, rutin and hyperoside are present in flower and fruits; Sterols-Roots also contain sitosterol, 4, 6-dihydryxy-2-O (-2-hydroxy isobutyl) benzaldehyde and undecanyl cetanoate; Trace minerals are found in roots-zinc, manganese, copper, cobalt along with calcium, magnesium, potassium zinc and selenium; Kaepfrol-Kaepfrol along with Sarsapogenin from woody portions of tuberous roots could be isolated; others are Essential fatty acids-Gamma linoleinic acids, vitamin A, diosgenin, quercetin 3-glucourbnides.

1.3 RECEPTOR TARGETS OF CONVENTIONAL DRUGS FOR TREATMENT OF GASTROINTESTINAL ACID DISORDERS

1.3.1. H+/K+ ATPase

In all eukaryotes, the plasma membrane potential and secondary transport systems are organized by the activity of p-type ATPase membrane proteins, H+ ATPase (the proton pump) in plants

and animals; and Na+/K+ ATPase (the sodium-potassium pump) in humans. (Bjørn *et al.,*2007). Therefore, in humans, this activity is carried out by a combined effect of both the proton pump and the sodium-potassium pump. The proton pump belongs to the type III p-type subfamily while the sodium-potassium pump belongs to the type II p-type subfamily.

Proton pump inhibitors inhibit the H+/K+ ATPase via the covalent bonding to cysteine residues on the proton pump. (Sachs *et al.,*2007)

The receptor is present in the cytoplasmic membrane of the resting parietal cells, upon activation, it migrates or translocates to the canalicular membrane where it pumps out H+ ions in exchange for k+ ions.

Gastric acid secretion by the parietal cells is controlled by the food stimulation and neuroendocrine pathways involving the activities of gastrin, histamine, acetylcholine, and pituitary adenylate cyclase-activating peptide and therefore controlling one or all of these pathways affecting these neurotransmitters will control the stimulation of gastric acid secretion. (Sachs *et al.,*2007)

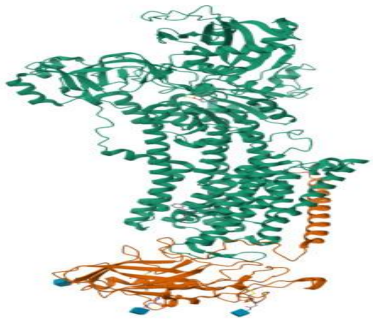


Figure1.3.1 3D Crystal structure of the gastric proton pump complexed with tegoprazan

1.3.2. **Histamine H2 Receptors**.

The histamine receptor H2 is also present in the parietal cells of the gastrointestinal tract lining. It is a member of the seven transmembrane G-protein-linked receptors. H2 receptor antagonists

bind to the receptor and inhibit its upregulation of cAMP to bring about the acid secretion activity in the basolateral membrane of the gastric parietal cells.

The H2 receptor also appears to regulate gastrointestinal tract motility and secretion and also plays a possible role in cell growth and differentiation.

The activity of the receptor is mediated by G proteins which activate adenylate cyclase and through a separate G protein-dependent mechanism, the phosphoinositol/ protein kinase signalling pathway.

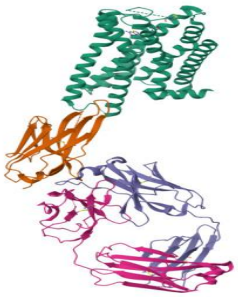


Figure 1.3.2. 3D CryoEM Structure of Inactive H2R Bound to Famotidine, Nb6M, and NabFab

1.3.3. **Prostaglandin Receptors**

The prostaglandin analogues bind to and antagonists or agonize at the different receptors and receptor subtypes which are prostacyclin receptor (antagonists) prostaglandin E2, E1, E3 and E4 receptors. These receptors are either inhibitory or stimulation G protein-coupled receptors.

In peptic ulcer disease and gastro-oesophageal reflux disease management and treatment, the prostaglandin analogues bind the prostaglandin E1 and E2 receptors to inhibit basal and nocturnal mucosal parietal cells' gastric acid secretion through direct stimulation of prostaglandin E1 receptor and a further increase in bicarbonate secretion and thickening of mucosal bilayer against so the mucosa can generate new cells. (Krugh M *et al.,*2024)

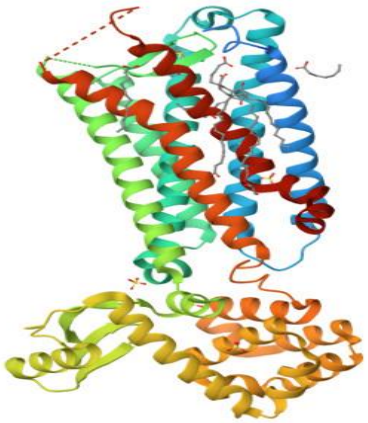


Figure 1.3.3. 3D Crystal structure of EP3 receptor bound to misoprostol-FA

1.3.4. **Muscarinic M1 Receptors.**

The muscarinic receptors generally are ligand-gated G protein-coupled receptors that are present in the parasympathetic nervous system pathway except that which occurs in the sweat glands. They are names due to their sensitivity to the activities of Muscatine. The molecule acetylcholine activates muscarinic receptors allowing for a parasympathetic reaction in an organism hence its involvement in gastrin acid secretion (Megan *et al.,*2023).

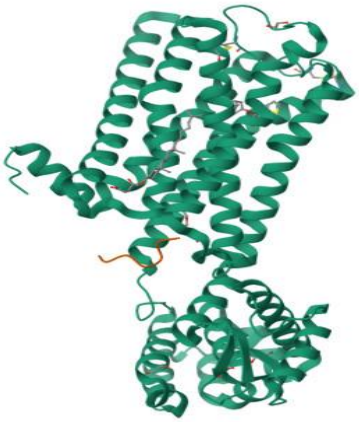


Figure 1.3.4. 3D Structure of the human M1 muscarinic acetylcholine receptor bound to antagonist Tiotropium

1.4 *IN SILICO* DRUG DISCOVERY AND DESIGN

The main goal of drug discovery is to get compounds which have a particular or a plethora of activities on a biological target. Amongst the techniques used today is high-throughput screening in which automated assays are used to test large databases of a very large number of compounds for a desired biological and pharmacological activity. (Lill, 2013)

In silico drug discovery, virtual screening and computer-aided drug design encompass techniques and technology now adopted for the high throughput screening for compounds with active and biological activity against specified targets. Computer and various software are used and it is easier, less expensive, time conservative, efficient and cost-reducing compared to the conventional method.

This Insilco drug discovery and design involved processes which use a computational technique called molecular docking to predict how ligands (drug-like small molecules) bind and interact with the binding site of a target receptor, usually a protein structure. (Lill, 2013)

Software, web servers, and databases used in this study include;

1.4.1 **RCSB PDB**

The global Protein Data Bank database of 3D structures for big biological molecules, including proteins, DNA, and RNA, is housed in the Research Collaboratory for Structural Bioinformatics Protein Data Bank (RCSB PDB), the US data centre for this resource. It serves as a source of experimental data that is essential to making scientific discoveries. Understanding the three-dimensional structure of biological macromolecules is crucial for comprehending their significance in various aspects of global sustainability as well as their involvement in human and animal health and disease. (https://rcsb.org).

The 3D structures of the proton pump inhibitor, muscarinic M1 receptor, histamine 2 receptor, cholecystokinin 1 receptor and the pi3k receptor with various bound complexes were obtained from the RCSBPDB database. All proteins obtained, and their PDB ID are in Table 3.1.

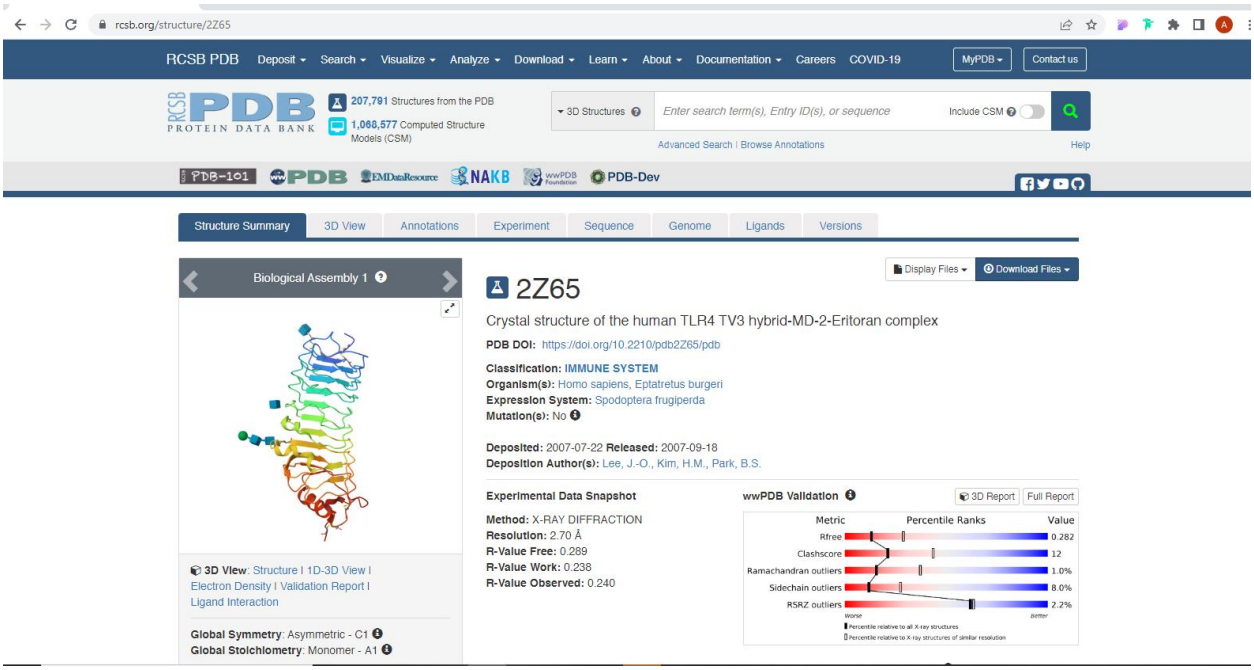


Figure 2.0.1. Image of RSCB Protein Data Bank.

2.0.2.PUBCHEM

Launched in 2004 as part of the US National Institute of Health's Molecular Libraries Roadmap Initiatives, Pubchem is a public repository for data on chemicals and their biological properties (Kim and Bolton, 2015). BioAssay, Compound, and Substance are the three main public databases that make up PubChem, an open archive. It includes details on a wide variety of chemical entities, such as nucleic acid and amino acid sequences that have undergone chemical modification, tiny molecules, lipids, and carbohydrates. Utilizing special IDs known as

SubstanceID (SID), CompoundID (CID), and AssayID (AID), respectively, the chemical structures of the substances, compounds, and bioassays in the database are retrieved.

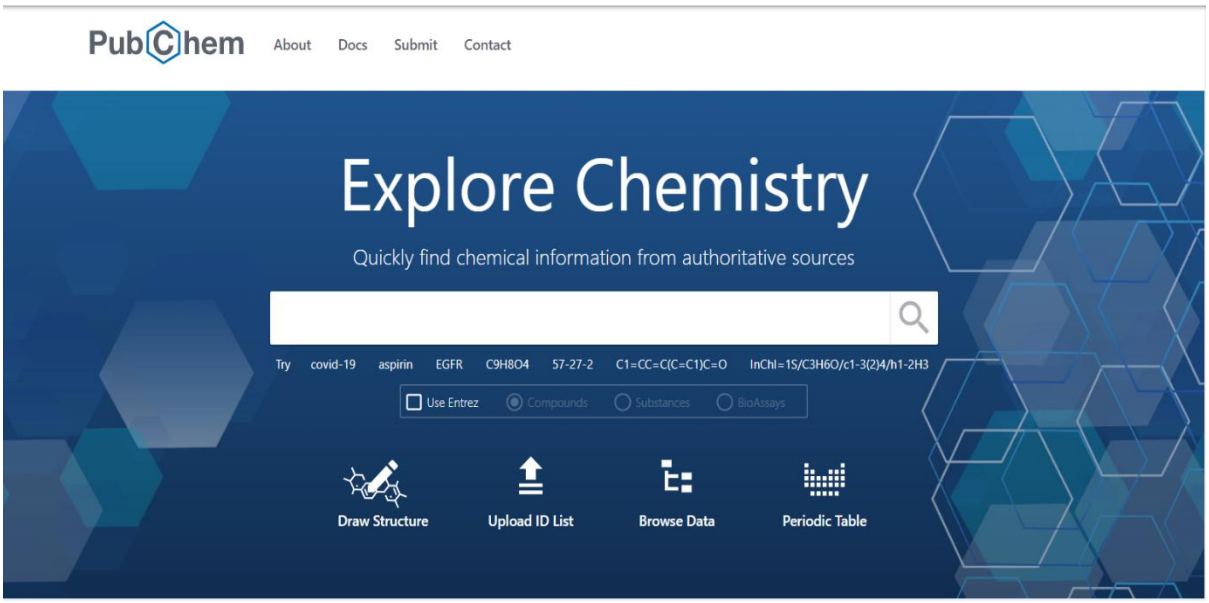


Figure 2.0.2. Image of PubChem Database web server interface

2.0.3 MAESTRO 12.8 (Schrodinger's suite)

Schrödinger's simplified gateway to cutting-edge predictive computer modelling and machine learning processes for molecular discovery is called Maestro. Maestro offers a unified entry point for users of all expertise levels to obtain unique molecular insights to guide their study, thanks to its sophisticated and accessible graphical user interface. (https://www.schrodinger.com/platform/products/maestro/)

This program was used as the docking suite for the protein target and ligand docking as it supports simultaneous multiple molecular docking.

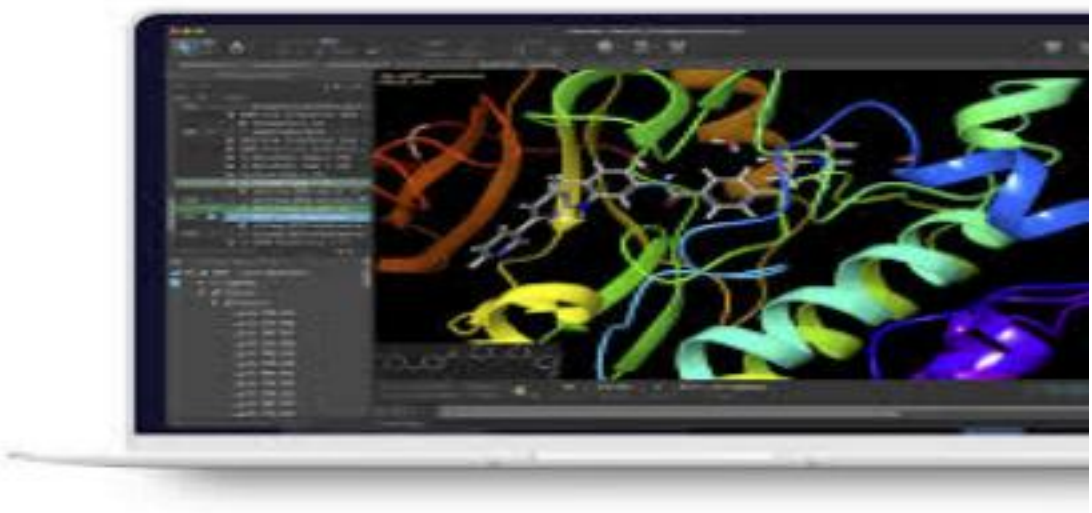
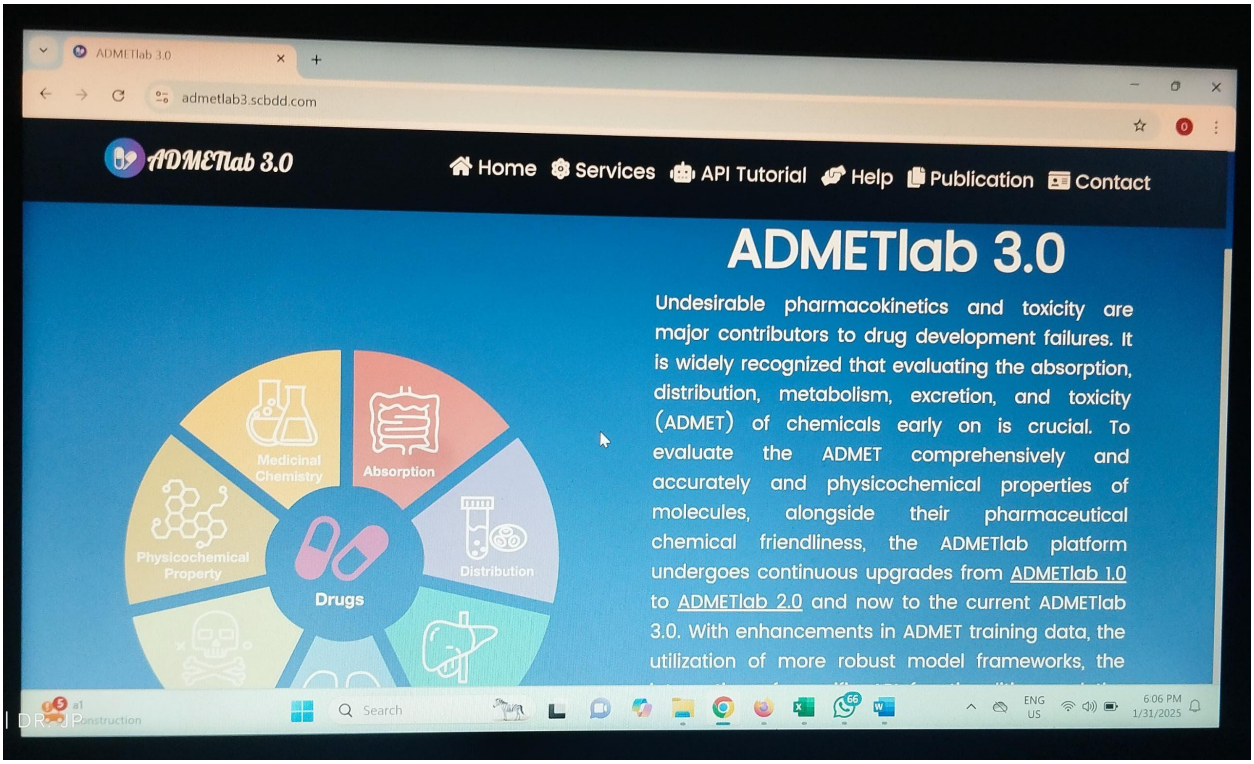


Figure 2.0.3. Image of Schrodinger suite maestro 12.8 interface.

2.0.4. ADMETLAB 3.0

In the process of developing new drugs, absorption, distribution, metabolism, excretion, and toxicology (ADMET) are evaluated at progressively earlier stages of the discovery phase, when the number of potential compounds is high but physical sample access is constrained. Within that framework, computer simulations are legitimate substitutes for experiments. (Antoine *et al.,*2017) Here, the Admetlab3.0 web service, which provides free access to a collection of quick yet reliable predictive models for drug-likeness, pharmacokinetics, physicochemical qualities, and medicinal chemistry friendliness was used.

Figure 2.0.4. Image of ADMETlab3.o webserver interface



1.5 **MOLECULAR DOCKING AND STRUCTURE-BASED VIRTUAL SCREENING.**

The structural-based drug design discovery involved three main ingredients; the target structure; the database of potential ligands and the docking software. All processes are followed in every research, the implementation is usually problem-specific and dependent.

The result is usually a hit or lead compound with activity against the target on the macromolar range; although a few hits with nanomolar-level activity have been discovered. Also, pharmacophore modelling, quantitative structure-activity relationship, Insilco absorption, distribution, metabolism and toxicological studies are carried out. (Lill, 2013).

1.5.1 **Steps involved in molecular docking and virtual screening**.

1. **Preparation of ligands and targets**: the amount and accuracy of the information available on the target protein will determine the relevance and accuracy of the structural-based drug discovery and design. The target must be "druggable" to allow for the binding of small ligands to its binding site. Very large/ shallow and/or highly charged binding sites are generally considered

difficult for drug discovery. The ligands are the chemical compounds usually in 3d which are being screened for pharmacological activity. They could be obtained from experimentally solid X-ray crystallography, nuclear magnetic resonance or homology. Structures from X-ray crystallography are usually preferred. The targets and ligands can be sourced from sources such as in figures 2.0.1 and 2.0.2 respectively.

2. **Preparation of ligands and targets**. Before screening, the ligands' structure must be carefully calculated and one or more 3D conformers must be generated for each ligand with correct chirality, tautomerization and protonation state. In preparation of targets, the extent of the binding site as well as conditions such as protonation state, and solvation, needs to be defined by the program because the pka values of some amino acids are affected by their local environments.

3. **Pre-filtering:** this filters the ligand database before screening to remove compounds which are unsuitable and aimed at reducing the size of the compound and time wastage.

4. **Molecular docking**. This is the central step in structure-based virtual screening. It is the simulation of the binding of the ligands to proteins to form a non-covalent complex revealing the electrostatic and steric complementarity between them. This exemplified the lock and key model of protein binding. Docking programs predict both a binding mode (position and orientation of the ligand relative to the target) and a score (quantitative measure of how well the ligand fits into and interacts with the target binding site.)

5. **Scoring functions and post-docking analysis**: the docking program evaluates using scoring to provide quantitative measures of induced fit quality. Scoring functions include knowledge-based, empirical and force field. Compounds are then selected based on these scores for further post-docking analysis.

1.5.2 **Limitations of *In silco* drug discovery and design**

1. Absence of protein flexibility: the induced fit effect of the protein on binding is not replicated in this software and confirmational changes that occur when ligands bind to proteins are not considered.

2. Modelling solvation. At times there may be water molecules at the site of binding and these water molecules may take part in binding with affinities as strong as that of the receptor components proteins. In the preparation stage, these waters are removed.

3. Predict binding affinity. At the moment available programs only predict binding affinity and fail to predict the free energies involved in binding.

1.5.3. **Applications of molecular docking**. (Lill, 2013)

1. Throughput screening and selection of natural products for further testing and analysis.

2. Lead optimization.

3. Remediation

1.6. AIMS AND OBJECTIVES

The study aims to assess the therapeutic potentials of phytoconstituents of *Ocimum grattisimum, Scoparia dulcis, Solanum nigrum* and *Asparagus racemosus* in the treatment of peptic ulcer disease using *in silico* techniques.

1.7 SPECIFIC OBJECTIVES.

1. Obtain ligands from various literature sources and their 3D SDF structures from Pubchem.

2. obtain proposed proteins from protein data bank

2. Carry out molecular docking studies of the phytoconstituents against the proposed protein targets.

3. Carry out ADMET profiling to Predict the absorption, distribution, metabolism and toxicological properties using admetlab3.0.

4. Identify lead compounds for the treatment of peptic ulcer disease using *in silico* techniques

CHAPTER 2

MATERIALS AND METHOD

2.0 MATERIALS

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: Schrondinger's Suite (Maestro 12.8)

2.1 METHOD

2.1.1 **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 pomp (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.

2.1.2. **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 generate tautomers and set to generate 5 stereoisomers per ligand whole retaining their specific chiralities and output in the Maestro format. This was then run simultaneously for all ligands.

2.1.3 **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 particular binding site where the cocrystallized ligand was bound was noted. The active amino acids were identified.

2.1.4. **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 cocrystallized ligand present on each receptor with a scaling factor of 1 and partial charge cut off at 0.25.

2.1.5. **Ligand/Molecular Docking**

The generated library underwent docking into the active sites of the proteins utilizing standard precision with non refined sample screening. In order to anticipate binding affinity and molecular interactions, cocrystallized ligands were docked into the active site of each protein's produced compound.

2.1.6. **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.

CHAPTER THREE

RESULTS

Tables 3.0 , 3.1, 3.2, 3.3 shows the results of the docking scores of the phytoconstituents of the Asparagus racemosus, Ocimum gratissimum, Scoparia dulcic and Solanum Nigrum against the receptors respectively.

Table 3.4 shows the ligands from each plant with docking similar to that of the reference standards.

Tables 3.5, 3.6, 3.7 shows the drug likeness and toxicity profile of the various ligands with similar docking score with ligand against proton pump, histamine h2 receptor and muscarinic m1 receptor

Table 3.8 shows the interaction mechanism between the ligands with similar affinity and the receptors

Table 3.0: Molecular docking results of phytochemical constituents of *Asparagus racemosus* against selected protein targets in kcal/mol

PUBCHEM CID	PROTON PUMP(7W49)	H2 RECEPTOR(7UL3)	PGE2 RECEPTOR(6M9T)	MUSCARINIC M1(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 3.1: Molecular docking results of phytochemical constituents of *Ocimum gratissimum* against selected protein targets in kcal/mol

PUBCHE	PROTON	H2	PGE2	MUSCARINIC

M CID	PUMP(7W49)	RECEPTOR(7UL3)	RECEPTOR(6M9T)	M1(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
3001055	-6.08	-7.49	-4.45	-8.17
3084296	-7.24	-5.17	-6.06	-8.47
5280441	-8.62	-4.53	#N/A	-5.92
5280443	-8.81	-5.76	-5.58	-8.80
528044	-7.44	-5.71	-4.84	-8.72

5				
5280457	-8.10	-5.83	-6.99	-8.37
5280536	-6.32	-5.19	-4.49	-5.88
5280637	-7.37	-6.03	-7.05	-8.65
5280666	-7.88	-5.66	-5.07	-8.96
5280704	-7.25	-5.98	-8.63	-7.81
5280794	-5.11	-2.82	-7.89	#N/A
5281416	-7.40	-5.53	-4.39	-7.35
5281417	-7.94	-4.61	-4.81	-8.25
5281515	-6.79	-6.01	-6.19	-8.28
5281516	-2.95	-2.08	-2.49	-3.92
5281520	-7.29	#N/A	-6.58	-8.09
5281520	-7.29	#N/A	-6.58	-8.09
5281525	-3.12	-1.33	-3.42	-3.85
5281553	-3.92	-3.07	-4.37	-3.96
5281675	-8.75	-5.48	#N/A	-4.33
5281792	-7.18	-5.45	-7.46	-6.55

5282199	-6.82	-4.70	-7.50	-7.25
5282381	-7.04	-4.77	-10.71	-6.59
5288573	-7.25	-5.50	-6.95	-8.55
5311225	-8.15	-6.45	-10.22	-7.91
5316673	-9.39	-3.43	-5.71	-8.67
5316750	-6.54	-5.23	-7.84	-7.89
5317471	-7.52	-5.49	-5.45	-3.42
5317570	-6.59	-6.39	-6.73	-8.18
5319484	-7.97	-4.52	-8.75	-7.21
5319484	-7.97	-4.52	-8.75	-7.21
5320250	-3.64	-3.39	-2.64	-4.32
5320521	-7.80	-5.46	-6.37	-8.12
5322089	-7.45	-6.53	-8.29	-6.96
5372312	-6.99	-5.68	-7.69	-8.06
5702160	-6.01	-6.86	-5.02	-6.59
5922634	-7.23	-4.54	-6.92	-8.35
691839	-6.54	-5.46	-5.60	-7.26

1				
9548706	-6.32	-5.33	-6.30	-7.74
9840292	-6.15	-4.64	-7.77	-5.64
9874426	-6.54	-5.94	-7.95	-6.97
9930064	-6.84	-5.38	-7.59	-8.70
9934142	-7.06	-6.41	-5.17	-5.94
10006384	-7.72	-3.64	#N/A	#N/A
10290825	-6.07	-5.83	-6.07	-6.54
10856614	-7.58	-5.55	-6.17	-8.02
10883321	-6.91	-7.04	-7.33	-7.49
11063784	-5.35	-4.95	-6.71	-6.46
11148775	-6.79	-5.12	-6.74	-8.99
11220007	-4.98	-4.12	-6.91	-7.64
11378474	-5.77	-5.26	-5.28	-6.27
11726019	-7.05	-4.62	-7.27	-5.92
11793120	-6.28	-4.60	-8.19	-7.73
11824948	-6.25	-6.89	-8.25	-8.06

11966109	-6.07	#N/A	-6.83	-9.21
12310250	-6.04	-4.73	-6.56	-5.83
12313020	-7.27	-5.81	-6.79	-8.17
12447832	-5.71	-3.95	-4.92	-7.06
13118571	-4.24	-2.60	-3.93	-4.23
13660470	-5.90	-4.96	-4.83	-6.06
13844658	-6.98	-6.29	-5.22	-8.74
13893597	-8.46	-5.40	-8.69	-7.93
13894537	-6.92	-6.02	-6.36	-8.21
13916049	-6.23	-4.85	-7.89	-5.56
14104302	-11.00	-4.38	-5.96	#N/A
14132337	-6.80	-4.49	-8.90	-6.88
14135399	-5.55	-4.89	-7.80	-9.53
14282775	-7.09	-6.42	-4.42	-6.36
14314225	-6.01	-6.13	-6.80	-7.64
14332899	-8.86	-6.08	-8.01	-8.47
144273	-6.94	-5.16	-6.92	-7.81

36				
14585506	-7.99	-4.56	-6.75	-5.86
14705598	-4.33	-5.04	-7.41	-8.23
14830071	-6.75	-0.80	-5.46	-6.88
15747360	-7.40	-4.79	-6.38	-7.84
23271974	-7.39	-4.94	-7.94	-7.06
25231264	-6.13	-4.08	-6.50	-5.72
44258710	-9.01	-5.18	-7.30	-7.81
44630107	-6.42	-5.04	-6.53	-7.74
45266909	-6.28	-5.40	-5.26	-5.89
45278176	-7.41	-5.33	-7.44	-7.08
51136357	-7.36	-5.79	-7.53	-7.45
52325853	-8.22	-6.33	-8.23	-7.82
52325855	-6.26	#N/A	-6.61	-7.89
52325861	-7.51	#N/A	-7.04	-8.01
74409819	-6.13	-4.93	-6.50	-7.59
90743708	-7.12	-5.51	-6.91	-7.65

91129494	-7.11	-5.36	-7.84	-8.01
92261496	-7.77	#N/A	-6.95	-8.64
98052623	-6.15	-6.24	-6.54	-7.05
101198558	-6.30	-5.91	-6.05	-6.30
101651530	-6.22	-5.21	-4.70	-6.48
101992980	-7.29	-7.04	-8.45	-7.84
101992982	-5.31	-3.88	-8.66	-8.61
101992983	-6.71	-4.90	#N/A	-6.35
101992984	-7.19	-5.02	#N/A	-5.66
102499957	-5.58	-4.23	#N/A	-7.78
130740339	-5.23	-5.42	-5.75	-6.15
131178377	-6.09	-4.26	-5.77	-5.87
134687947	-7.29	#N/A	-6.60	-8.13
154496877	-7.56	#N/A	-6.72	-8.26
162843160	-7.15	-4.77	-7.42	-5.61
162844436	-6.26	-5.86	-8.39	-7.82
162855	-7.12	-6.11	-6.16	-6.85

418				
162868108	-5.51	-6.10	#N/A	-9.18
162872299	-7.06	-5.35	-8.51	-9.77
162892257	-7.26	-5.58	#N/A	-7.22
162892258	-8.27	-6.62	#N/A	-5.90
162896256	-7.67	-6.84	-7.61	-8.11
162905105	-8.11	#N/A	-6.74	-8.13
162906021	-7.71	-5.16	-4.08	-6.58
162910549	-6.32	-5.45	-7.69	-6.35
162915510	-5.49	-5.67	-6.12	-7.04
162918552	-7.35	-5.86	-6.57	-7.19
162930638	-7.83	-5.46	-8.57	-7.14
162934828	-7.23	-7.10	-7.71	-7.69
162934830	-7.05	-6.45	-7.72	-8.28
162934831	-7.06	-7.04	-8.18	-6.90
162947737	-4.22	-4.73	-7.77	-7.57
162954979	-6.75	-5.71	-3.80	-5.35

162954980	-7.06	-5.63	-5.79	-5.90
162970571	-5.86	#N/A	#N/A	-8.28
162977897	-8.33	#N/A	#N/A	-8.86
162979504	-9.61	-4.45	-6.71	-8.09
162980641	-9.61	#N/A	#N/A	#N/A
163005955	-6.10	-7.25	#N/A	#N/A
163014945	-6.10	#N/A	#N/A	-9.43
163033098	-7.06	-5.23	-5.06	-6.78
163036208	-4.45	-4.59	-5.51	-7.43
163037164	-6.69	-5.67	-6.20	-7.69
163037512	-7.51	-3.33	#N/A	-6.07
163044773	-7.37	-4.52	-6.92	-7.72
163075841	-6.80	-4.94	-7.59	-6.87
163084237	-7.67	-2.29	#N/A	-6.69
163089925	-7.20	-6.41	-7.10	-9.02
163106339	-6.59	-6.33	-6.34	-8.19
133612	-9.02	-6.94	#N/A	-7.90

286	

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

Table 3.2: Molecular docking results of phytochemical constituents of *Scoparia dulcis* against

PUBCHEM CID	PROTON PUMP(7W49)	H2 RECEPTOR(7UL3)	PGE2 RECEPTOR(6M9T)	MUSCARINIC M1(5CXV)
322	-5.70	-6.10	-8.39	-5.99
4848	-7.69	-4.58	-5.90	-6.38
5029	-6.87	-6.32	-8.16	-6.33
5042	-6.96	-7.18	-8.31	-6.29
5746	-8.39	-5.52	-5.45	-8.20
5816	-6.78	-5.55	-6.63	-7.01
6043	-7.11	-5.92	-6.92	-6.27
8417	-6.27	-4.77	-7.48	-7.11
10772	-7.36	-5.91	-7.33	-6.53
159460	-7.10	-5.58	#N/A	-5.96
162350	-6.84	-4.86	-7.43	-5.18
171488	-6.30	-5.12	-7.49	-6.05
177696	-3.83	-5.24	-7.18	-6.12
185617	-5.19	-6.67	-7.25	-7.87
213054	-9.01	-5.19	-7.56	-7.86
220401	-7.85	-4.13	-6.86	-7.66
637542	-5.70	-6.10	-6.70	-5.99
3001055	-6.08	-7.49	-5.66	-5.90
3084296	-7.24	-5.17	-6.06	-8.47
3084390	-8.86	-5.33	-8.24	-8.10
5280441	-8.62	-4.53	#N/A	-5.92
5280442	-7.01	-5.79	-7.17	-8.36
5280443	-8.81	-5.76	-7.81	-8.80
5280443	-8.81	-5.76	-7.81	-8.80
5280445	-7.44	-5.71	-7.67	-6.60

5280445	-7.44	-5.71	-7.67	-6.60
5280637	-7.37	-6.03	-7.05	-8.65
5281430	-6.60	-3.21	#N/A	-8.05
5281628	-6.32	-5.37	-6.95	-3.51
5281697	-8.76	-6.04	-8.61	-8.23
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
5318083	-8.57	-6.13	-6.49	-6.37
5318869	-8.56	-4.22	-6.70	-7.86
5321190	-6.23	#N/A	#N/A	-7.28
5702160	-6.01	-6.86	-6.36	-6.44
11445323	-9.51	#N/A	#N/A	#N/A
11575632	-5.70	-3.95	-7.24	-5.50
13093776	-7.75	-4.84	-8.77	-8.75
13964545	-6.57	-4.56	-7.45	-5.89
21672082	-5.70	1.15	#N/A	-5.97

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

Table 3.3: Molecular docking results of phytochemical constituents of *Solanum nigrum* against selected protein targets in kcal/mol

PUBCHEM CID	PROTON PUMP(7W49)	H2 RECEPTOR(7UL3)	PGE2 RECEPTOR(6M9T)	MUSCARINIC M1(5CXV)
72	-6.44	-6.59	-7.25	-6.86
135	-6.25	-5.44	-6.85	-6.76
187	-4.54	-3.78	-3.92	-5.52

750	-3.30	-2.83	-2.79	-3.21
932	-8.88	-5.50	-7.77	-5.82
1203	-7.58	-5.26	-7.07	-9.57
1249	-7.54	-5.40	-7.65	-6.16
1287	-7.15	-5.13	-6.11	#N/A
2518	-6.13	-6.15	-8.09	-6.18
3469	-6.55	-6.96	-6.78	-6.40
4848	-7.69	-4.58	-5.90	-6.38
5029	-6.87	-6.32	-8.16	-6.33
5042	-6.96	-7.18	-8.31	-6.29
8468	-6.34	-6.04	-7.62	-6.31
9064	-9.63	-6.07	-6.99	-9.05
10742	-5.95	-5.16	-7.19	-6.30
60961	-6.88	-6.16	-6.91	-7.32
65064	-7.57	-5.56	#N/A	-6.03
65133	-6.87	-5.42	-5.60	-6.48
66883	-7.08	-5.76	-6.46	-7.20
72276	-7.58	-5.26	-7.07	-9.57
72277	-7.54	-5.40	-7.65	-6.16
72281	-9.30	-5.61	-6.98	-4.73
73160	-8.56	-6.07	-7.95	-10.27
73160	-8.56	-6.07	-7.95	-10.27
73399	-5.71	-6.13	-8.11	-8.90
100067	-5.38	-5.43	-7.78	-6.32
125213	-6.56	-5.96	-7.75	-5.11
159894	-7.12	-5.41	-5.84	-4.57
181681	-5.88	-5.69	-8.19	-5.08
182232	-8.12	-7.05	-8.03	-8.87
199472	-7.15	-5.13	-6.11	#N/A
213054	-9.01	-5.19	-7.56	-7.86
332425	-5.88	-5.69	-8.19	-5.08
332426	-5.72	-6.08	-6.39	-6.46
439246	-8.88	-5.50	-7.77	-5.82

443023	-5.72	-6.08	-6.39	-6.46
445858	-5.75	-5.98	-6.61	-5.87
588705	-7.54	-5.64	-6.74	-6.85
637541	-5.84	-5.02	-7.05	-6.23
637584	-6.11	-5.97	-7.20	-10.12
667495	-8.61	-5.54	-7.12	-6.25
689043	-6.05	-5.96	-6.45	-6.43
689043	-6.05	-5.96	-6.45	-6.43
736681	-6.87	-5.26	-5.59	-6.48
1549106	-5.27	-5.67	-8.39	-6.22
1549111	-6.13	-6.15	-8.09	-6.18
1794425	-6.97	-7.35	-8.92	-6.63
1794427	-6.90	-7.62	-7.41	-5.01
3001055	-6.08	-7.49	-5.66	-5.90
3702506	-6.25	-5.44	-6.85	-6.76
4546425	-6.36	-4.45	-7.51	-6.34
5257127	-3.30	-2.83	-2.79	-3.21
5280343	-9.16	-5.56	-7.24	-5.28
5280343	-9.16	-5.56	-7.24	-5.28
5280460	-6.67	-5.28	-7.32	-4.38
5280537	-6.56	-5.96	-7.75	-5.11
5280794	-5.11	-2.82	-7.89	#N/A
5280805	-9.77	#N/A	#N/A	#N/A
5280863	-8.79	-5.55	-6.87	-5.37
5281643	-10.56	-4.51	-6.22	-5.13
5281643	-10.56	-4.51	-6.22	-5.13
5281672	-6.99	-5.76	-7.29	-3.32
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
5317238	-7.08	-5.76	-5.92	-7.32
5321318	-7.12	-5.41	-5.84	-4.57
5702160	-6.01	-6.86	-6.36	-5.72

5867807	-3.04	-3.44	-7.36	-3.52
10425234	-6.63	-5.32	-7.96	-5.52
11085279	-7.23	-5.44	-7.84	-8.08
11336841	-7.73	-6.30	-8.02	-5.97
11604108	-5.38	-5.43	-7.78	-6.32
11994876	-6.25	-5.09	-7.65	-5.93
12309636	-5.87	-4.94	-8.07	-8.30
12309637	-6.62	-5.74	-6.61	-9.43
17750970	-5.71	-6.13	-8.11	-8.90
18413781	-1.17	-2.03	-4.92	-1.58
19818056	-6.40	-5.74	-5.60	-3.42
44134699	-8.96	-5.09	-7.54	-4.36
51402807	-9.66	-0.44	-4.29	#N/A
52914864	-1.26	-2.96	-5.43	-1.59
54732806	-7.41	-5.24	-6.28	-7.49
1010039 62	-4.70	-5.43	-7.77	-7.15
10149030 1	-6.08	-4.06	-5.73	-7.47

101490302	-5.62	-3.63	-4.79	-6.16
130770324	-5.30	-4.88	-6.24	-6.65
138454555	-7.73	-6.36	-8.05	-5.97
162886346	-6.16	-4.58	-7.93	-6.02
162942605	-9.46	#N/A	#N/A	#N/A
162949100	-4.99	-5.14	-7.41	-7.92
162949100	-4.99	-5.14	-7.41	-7.92

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

Table 3.4: Likely leads with close proximity and higher docking scores to standard ligand's.

7W49	docking score	7UL3	docking score	6M9T	docking score	5CXV	docking score
ASPARAGUS		**ASPARAGUS**		**ASPARAGUS**		**ASPARAGUS**	
5280805	-9.77	5029	-6.32	5282381	-10.71	4848	-9.90
213054	-9.01	52325853	-6.33	5311225	-10.22	53350155	-9.89
OCIMUM		5311225	-6.45	**OCIMUM**		213054	-9.38
141043029064	-11.00	5702160	-6.47	5282381	-10.71	4848	-9.07
	-9.63	162955816	-6.69	5311225	-10.22	162985356	-9.01
65084	-9.63	5702160	-6.86	**SCOPARIA**		**OCIMUM**	
162980641	-9.61	5042	-7.18	5282381	-10.71	73160	-10.27
162979504	-9.61	3001055	-7.49	5311225	-10.22	4848	-9.90
146798	-9.53	**OCIMUM**		**SOLANUM**		119205	-9.80
5316673	-9.39	1794427	-7.62	5282381	-10.71	16287229	-9.77

						9	
439533	-9.35	3001055	-7.49	5311225	-10.22	394846	-9.56
5991	-9.31	163005955	-7.25			14135399	-9.53
133612286	-9.02	439533	-7.19			163014945	-9.43
213054	-9.01	5042	-7.18			**SCOPARIA**	
44258710	-9.01	162934828	-7.10			5280637	-8.65
SCOPARIA		370	-7.05			5280445	-8.72
11445323	-9.51	10883321	-7.04			5280445	-8.72
213054	-9.01	162934831	-7.04			13093776	-8.75
SOLANUM		101992980	-7.04			5280443	-8.80
74089792	-11.48	133612286	-6.94			5280443	-8.80
5281643	-10.56	11824948	-6.89			4848	-9.07
5281643	-10.56	5702160	-6.86			213054	-9.38
5280805	-9.77	162896256	-6.84			4848	-9.90
51402807	-9.66	162892258	-6.62			**SOLANUM**	
9064	-9.63	72	-6.59			73160	-10.27
162942605	-9.46	5322089	-6.53			73160	-10.27
72281	-9.30	5702160	-6.47			637584	-10.12
5280343	-9.16	162934830	-6.45			5281672	-9.94
5280343	-9.16	5311225	-6.45			4848	-9.90
213054	-9.01	**SCOPARIA**				667495	-9.77
		3001055	-7.49			1203	-9.57
		5042	-7.18			72276	-9.57
		5702160	-6.86				
		185617	-6.67				
		5702160	-6.47				
		5311225	-6.45				
		SOLANUM					
		1794427	-7.62				
		3001055	-7.49				
		1794425	-7.35				

5042	-7.18
182232	-7.05
3469	-6.96
5702160	-6.86
14215566	-6.79

Table 3.5: Pharmacokinetic properties of selected ligands of *Asparagus racemosus, Ocimum grattisimum, Scoparia dulcis and Solanum nigrum* against proton pump target protein.

pubchem cid	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
11445323	678.2	1.0	0.0	0.0	0.0	2.1	3.9	1.0	0.0	0.5	0.0	0.8	0.1	0.6	0.9
74089792	917.3	1.0	0.0	0.0	0.0	0.9	5.3	1.0	0.1	0.9	0.0	0.8	0.0	0.0	1.0
5281643	464.1	1.0	0.0	0.3	0.0	3.5	2.8	0.9	0.1	0.6	0.0	0.7	0.1	0.1	1.0
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
51402807	464.1	1.0	0.0	0.4	0.0	3.7	2.5	0.7	0.0	0.4	0.0	0.7	0.0	0.0	0.9
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
162942605	626.2	1.0	0.0	0.1	0.0	1.7	4.7	0.8	0.0	0.5	0.0	1.0	0.0	0.1	0.8
72281	302.1	0.0	0.0	0.9	0.0	4.4	1.7	0.8	1.0	0.7	0.5	0.3	0.1	0.5	1.0
5280343	302.0	0.0	0.0	0.9	0.0	8.3	1.6	0.8	0.7	0.3	0.0	0.2	0.0	0.0	1.0

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 3.6: Pharmacokinetic properties of selected ligands of *Asparagus racemosus, Ocimum grattisimum, Scoparia dulcis and Solanum nigrum* 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	0.6	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
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
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
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
185617	462.1	1.0	0.0	0.0	0.0	1.9	3.7	0.9	0.1	0.4	0.0	0.5	0.1	0.5	0.9
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
1794425	354.1	0.0	0.0	0.0	0.0	3.4	3.1	0.0	0.2	0.5	0.0	0.9	0.0	0.4	0.0
182232	290.1	0.0	0.0	0.1	0.0	15.1	2.4	0.1	0.6	0.7	0.1	0.8	0.0	0.1	0.9
3469	154.0	0.0	0.0	0.0	0.0	13.9	1.7	0.3	0.8	0.4	0.2	0.3	0.2	0.4	0.6
14215566	390.4	0.0	0.0	0.0	0.0	5.2	0.4	0.0	0.8	0.4	0.0	0.2	0.0	0.4	0.0

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 3.7: Pharmacokinetic properties of selected ligands of *Asparagus racemosus, Ocimum gratissimum, Scoparia dulcis and Solanum nigrum* 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
5280637	448.1	1.0	0.0	0.0	0.0	3.6	3.8	1.0	0.0	0.6	0.0	0.9	0.1	0.2	1.0
5280445	286.1	0.0	0.0	1.0	0.0	8.5	1.4	0.8	0.7	0.4	0.0	0.2	0.0	0.0	1.0
13093776	448.1	1.0	0.0	0.0	0.0	3.4	4.0	0.9	0.0	0.4	0.0	0.9	0.0	0.1	0.8
5280443	270.1	0.0	0.0	1.0	0.0	5.9	1.2	0.7	0.8	0.4	0.1	0.1	0.0	0.0	1.0
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
637584	358.1	0.0	0.0	0.6	1.0	8.5	2.0	0.7	0.5	0.7	0.3	0.2	0.3	0.5	0.8
5281672	318.0	0.0	0.0	1.0	0.0	6.8	1.6	0.8	0.7	0.3	0.0	0.5	0.0	0.0	1.0
667495	272.1	0.0	0.0	0.9	0.0	8.7	1.3	0.5	0.9	0.8	0.7	0.3	0.1	0.4	1.0
1203	290.1	0.0	0.1	0.1	0.0	14.9	2.1	0.2	0.5	0.5	0.1	0.7	0.0	0.1	0.8
72276	290.1	0.0	0.1	0.0	0.0	15.8	2.3	0.4	0.8	0.6	0.1	0.6	0.1	0.1	1.0

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 (+++).

Tab 3.8: 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
51402807	ASP 137	HB	OH
	ASN 138	HB	OH
	GLN 127	HB	OH
	GLH 795	HB	OH
	LEU 811	HB	OH
51402807	ASP 137	HB	OH
	ASN 138	HB	OH

	GLN 127	HB	OH
	GLH 795	HB	OH
162942605	GLU 900	HB	OH
	GLN 924	HB	OH
	ASN 138	HB	OH
	NBL 331	HB	OH
	TYR 799	PPS	Hct
5280343	VAL 331	HB	OH
	GLH 795	HB	OH
	LEU 811	HB	OH

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

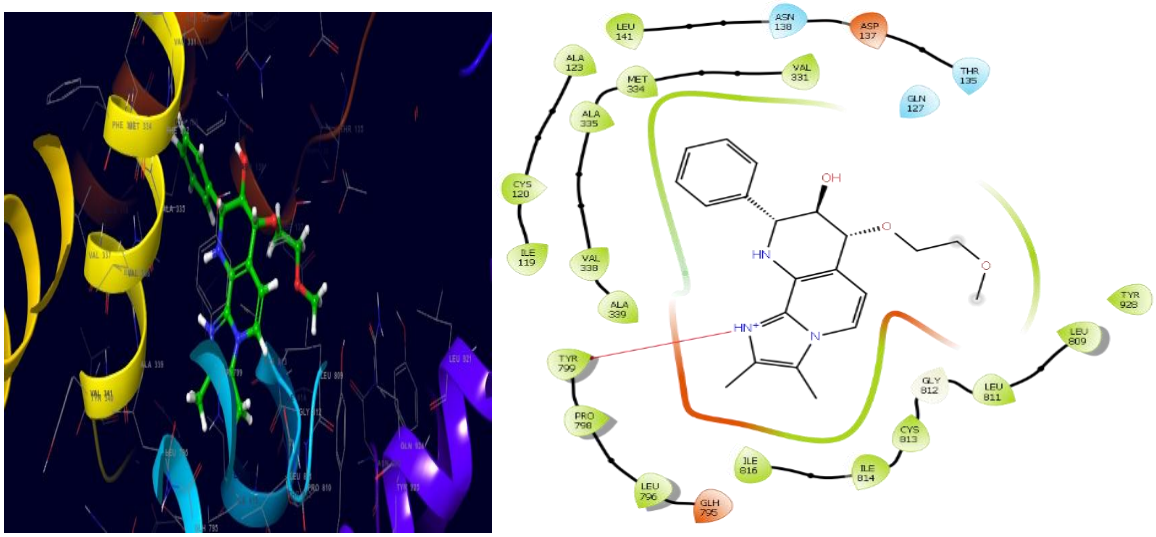


Figure 3.5: 3D and 2D molecular interaction of the standard ligand 213054 from *Ocimum gratissimum* against proton pump

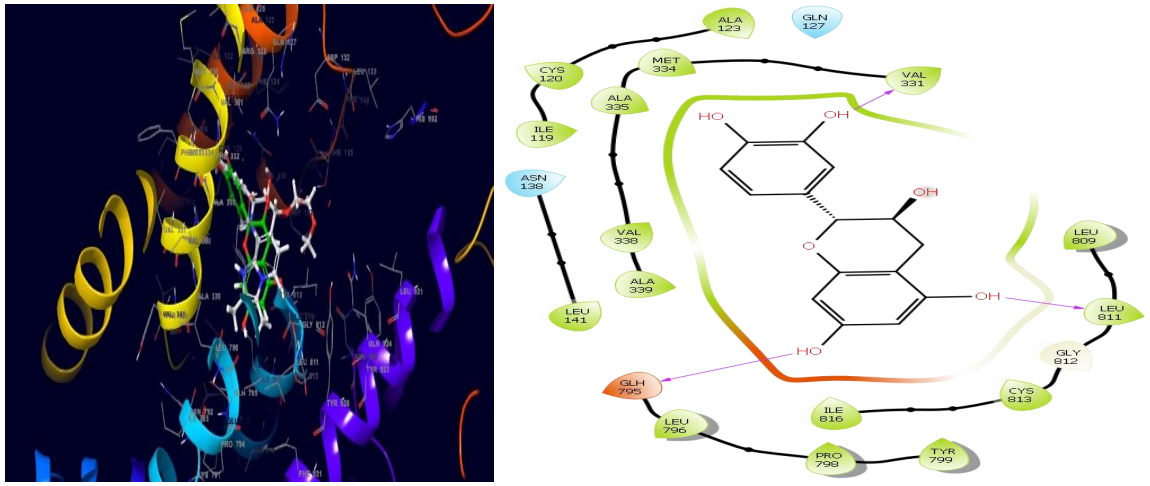


Figure 3.6: 3D and 2D molecular interaction of the ligand 9064 from *Ocimum gratissimum* and *Solanum nigrum* against proton pump.

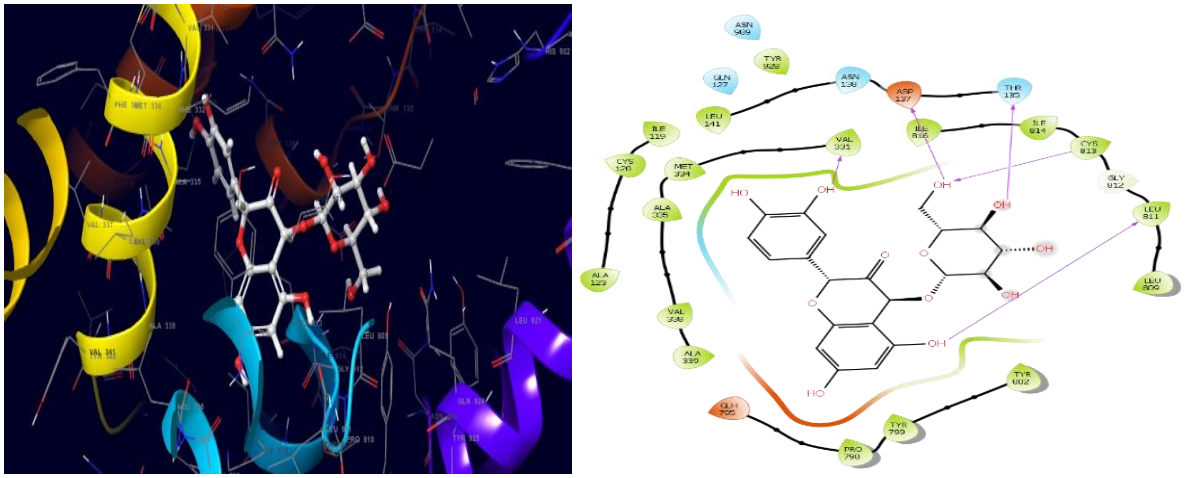


Figure 3.7: 3D and 2D molecular interaction of the ligand 162979504 from *Ocimum gratissimum* against proton pump

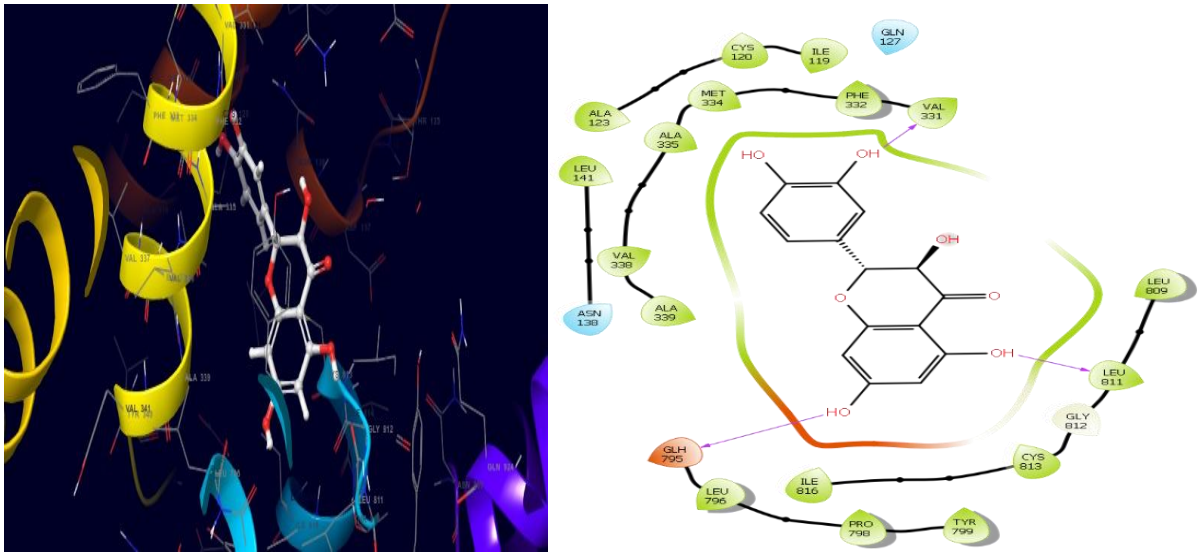


Figure 3.8: 3D and 2D molecular interaction of the ligand 439533 from *Solanum nigrum* against proton pump

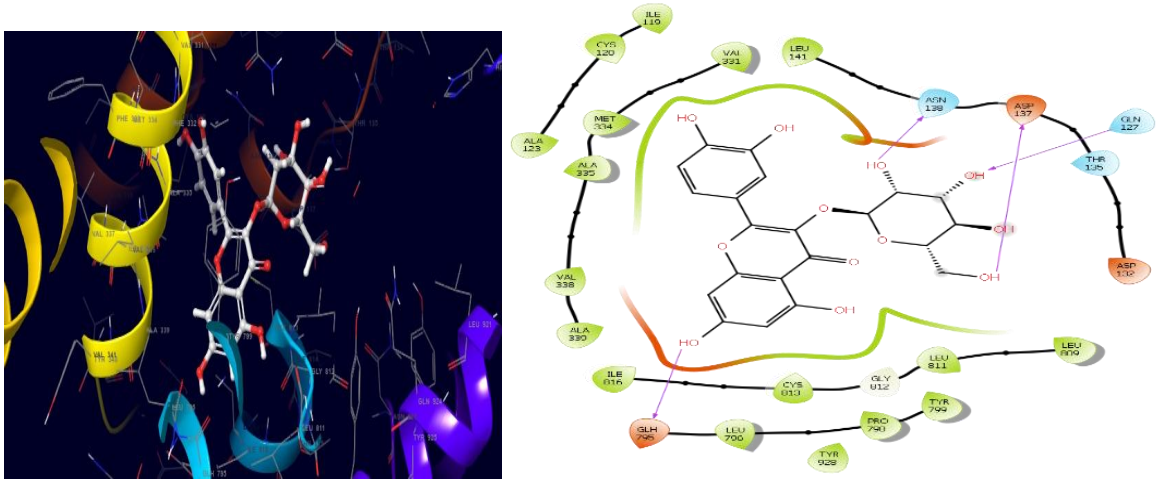


Figure 3.9: 3D and 2D molecular interaction of the ligand 51402807 from *Solanum nigrum* against proton pump

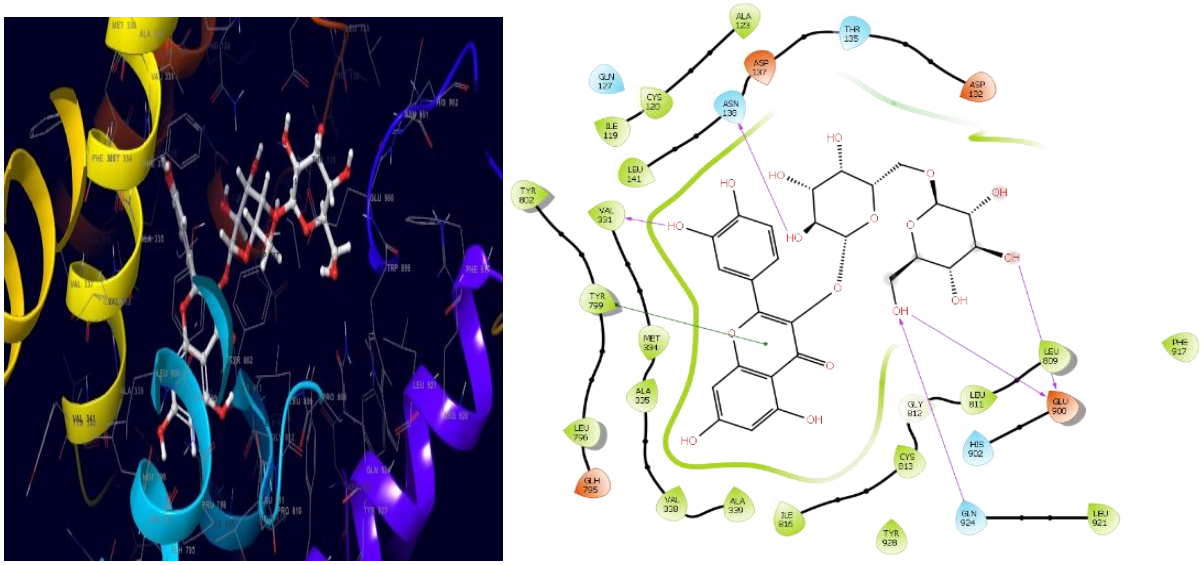


Figure 3.10: 3D and 2D molecular interaction of the ligand 162942605 from *Solanum nigrum* against proton pump

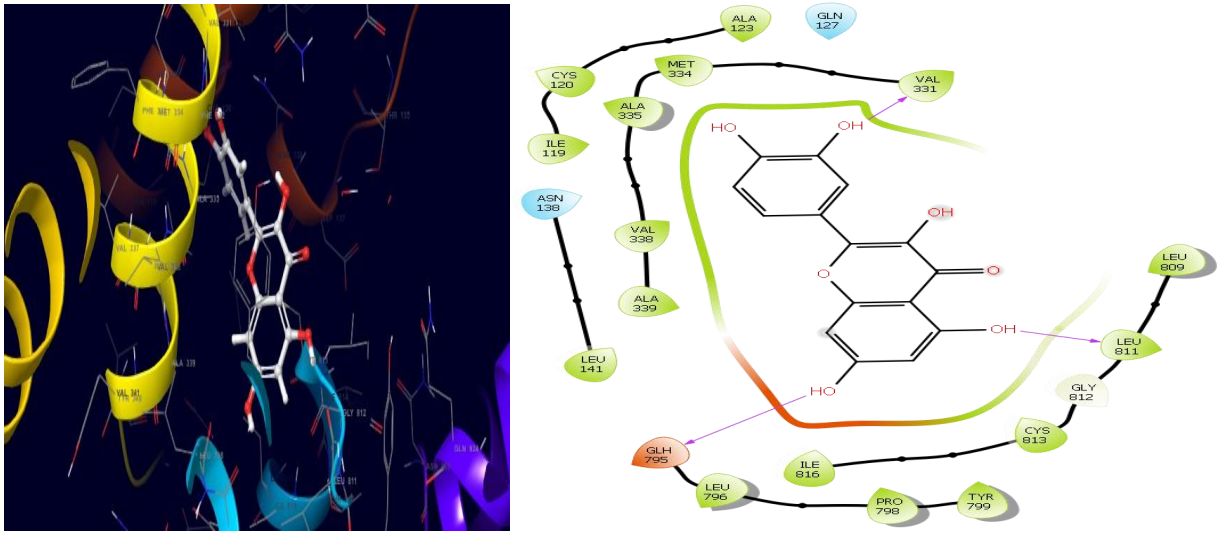


Figure 3.11: 3D and 2D molecular interaction of the ligand 5280343 from *Solanum nigrum* against proton pump

Table 3.9. 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
	ASP 186	HB	OH
439533	TYR 250	HB	OH
	ASP 98	HB	OH
	GLU 270	HB	OH
	GLN 77	HB	OH
162934828	ASP 186	HB	OH
	ARG 257	HB	OH
	CYS 174	HB	OH
	ASP 98	HB	OH
162934831	TYR 250	HB	OH
		HB	O
	CYS 174	HB	OH
	ASP 186	HB	OH
101992980	PHE 254	PPS	BENZENE
	TYR 250	HB	O
	ASP 98	HB	OH
	LYS 174	HB	OH
11824948	ASP 186	HB	OH
	TYR 250	HB	OH/ O
	ARG 257	HB	OH
	CYS 174	HB	OH
	ASP 98	HB	OH
162896256	ASP 98	HB	OH
	TYR 94	HB	OH
	GLN 79	HB	OH
	GLU 270	HB	OH
72	ARG 257	SB	O^-
		HB	O
	TYR 250	HB	O
	ASP 98	HB	OH
	ARG 257	SB	O^-
		HB	O
1794425	PHE 254	PPS	BENZENE
	ARG 257	SB	O^-
		HB	O

	ASP 98	HB	OH
	ASP 186	HB	OH
3469	ARG 257	SB	O^-
		HB	O
	CYS 174	HB	OH
	TYR 250	HB	OH
142155663	TYR 250	HB	O
	ARG 257	SB	O^-
		HB	O
	VAL 176	SB	O^-

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

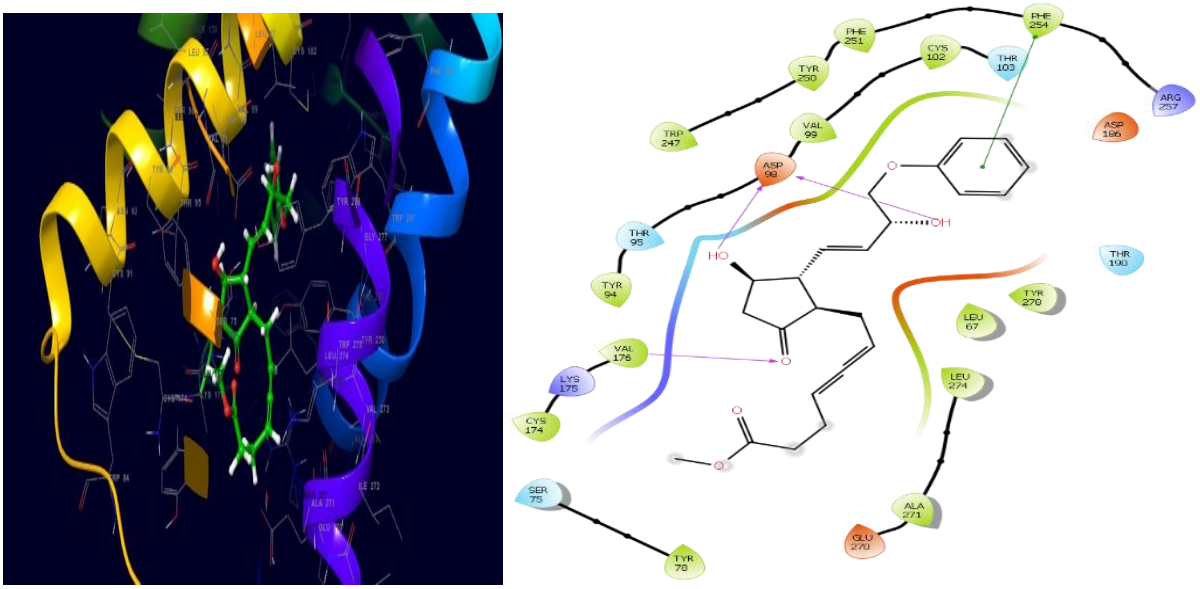


Figure 3.12: 3D and 2D molecular interaction of the ligand 5311225 from *Asparagus racemosus* against histamine 2 receptor.

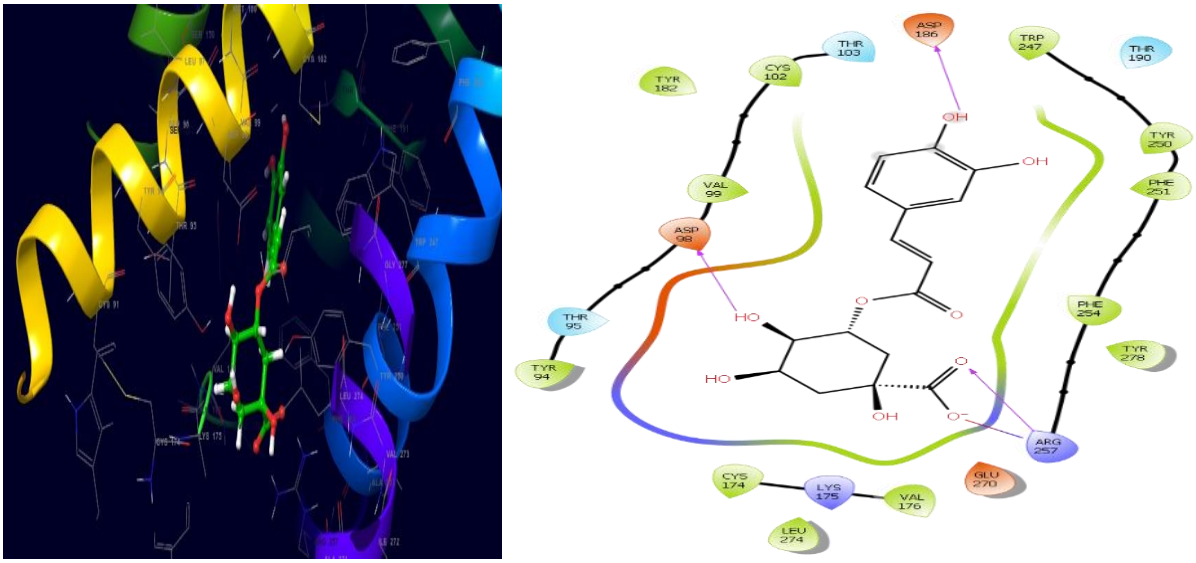


Figure 3.13: 3D and 2D molecular interaction of the ligand 1794427 from *Ocimum gratissimum and Solanum nigrum* against histamine 2 receptor.

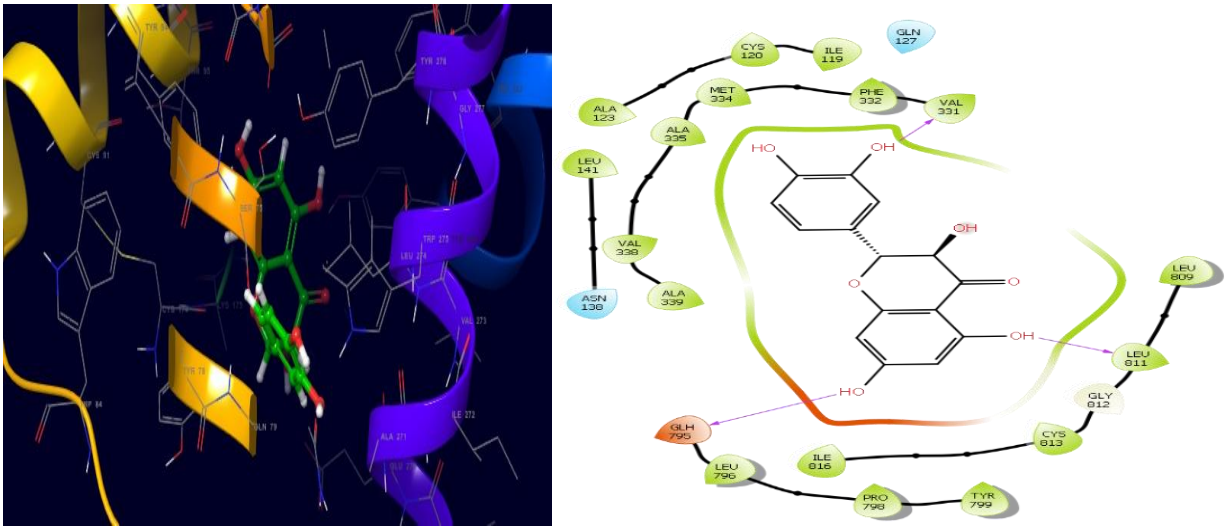


Figure 3.14: 3D and 2D molecular interaction of the ligand 439533 from *Ocimum gratissimum* against histamine 2 receptor.

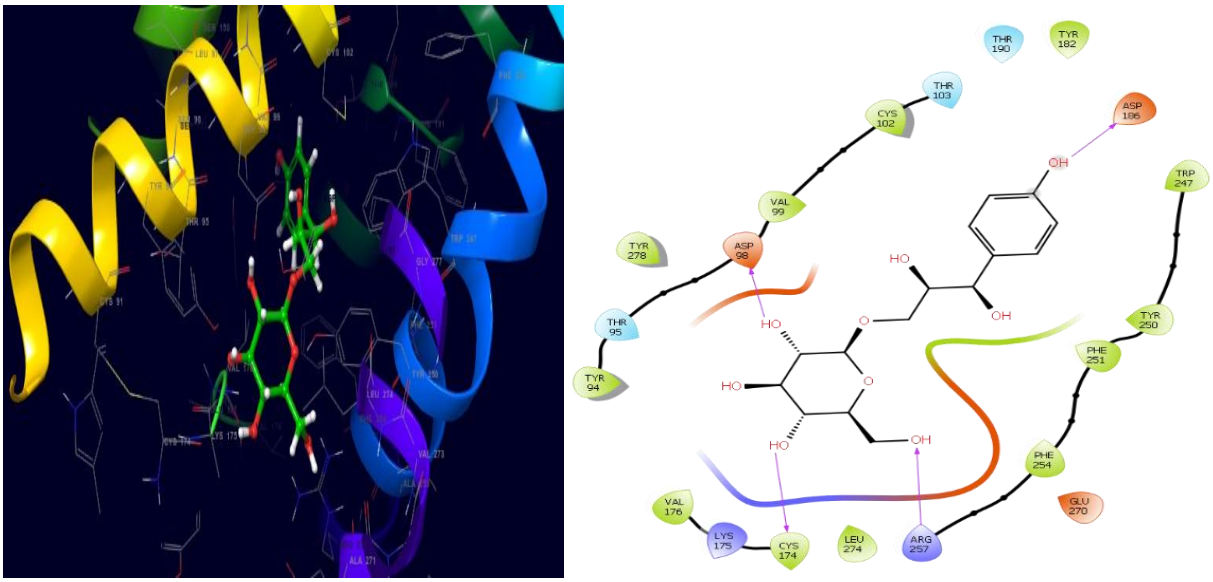


Figure 3.15: 3D and 2D molecular interaction of the ligand 162934828 from *Ocimum gratissimum* against histamine 2 receptor.

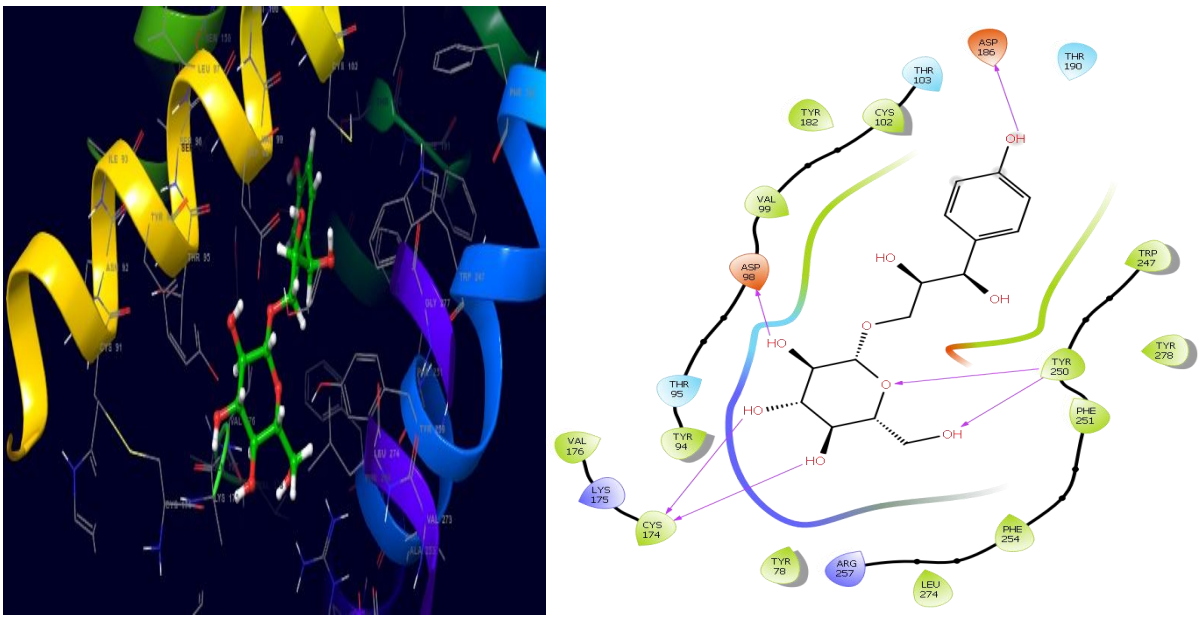


Figure 3.16: 3D and 2D molecular interaction of the ligand 162934831 from *Ocimum gratissimum* against histamine 2 receptor.

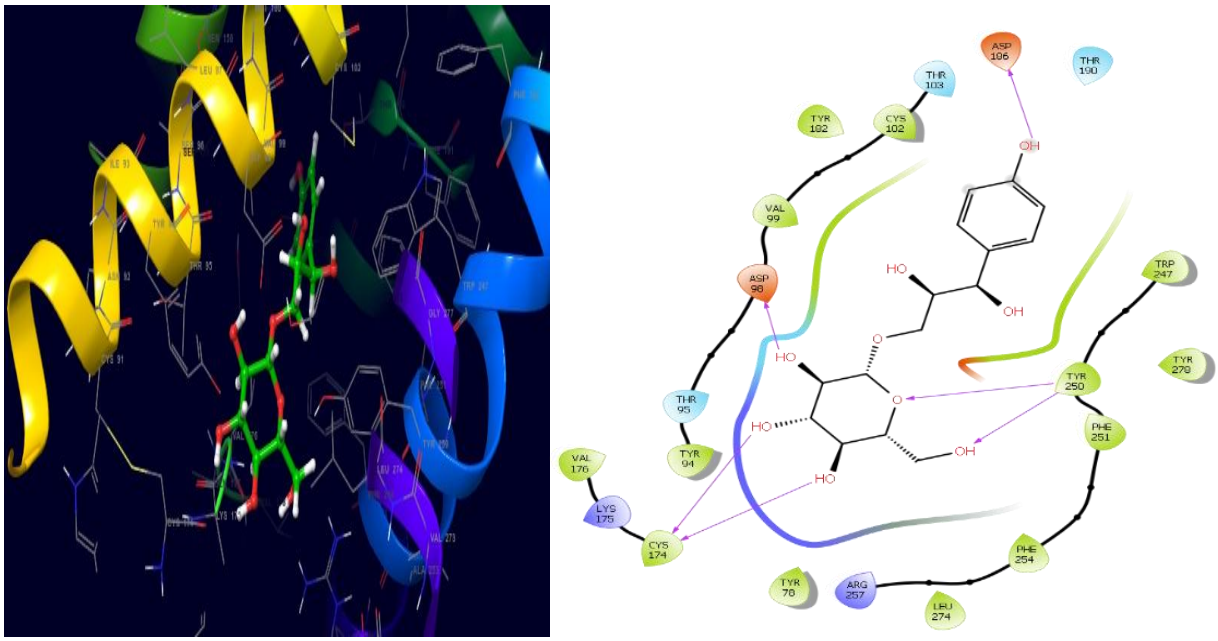


Figure 3.17: 3D and 2D molecular interaction of the ligand 101992980 from *Ocimum gratissimum* against histamine 2 receptor.

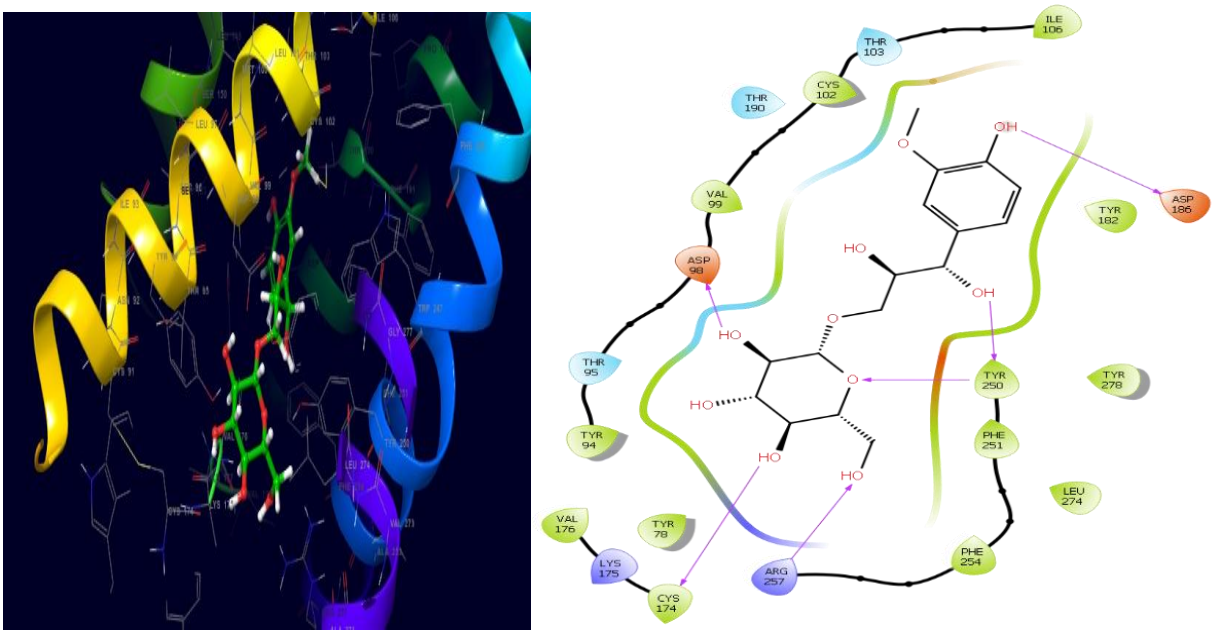


Figure 3.18: 3D and 2D molecular interaction of the ligand 11824948 from *Ocimum gratissimum* against histamine 2 receptor.

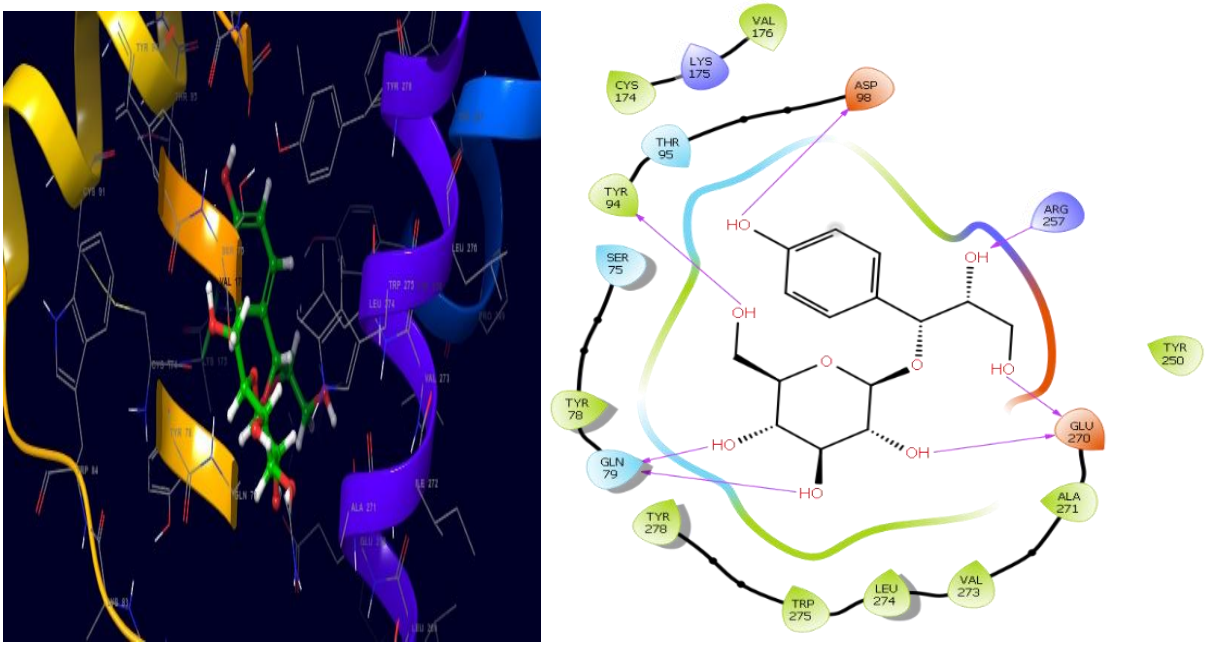


Figure 3.19: 3D and 2D molecular interaction of the ligand 162896256 from *Ocimum gratissimum* against histamine 2 receptor.

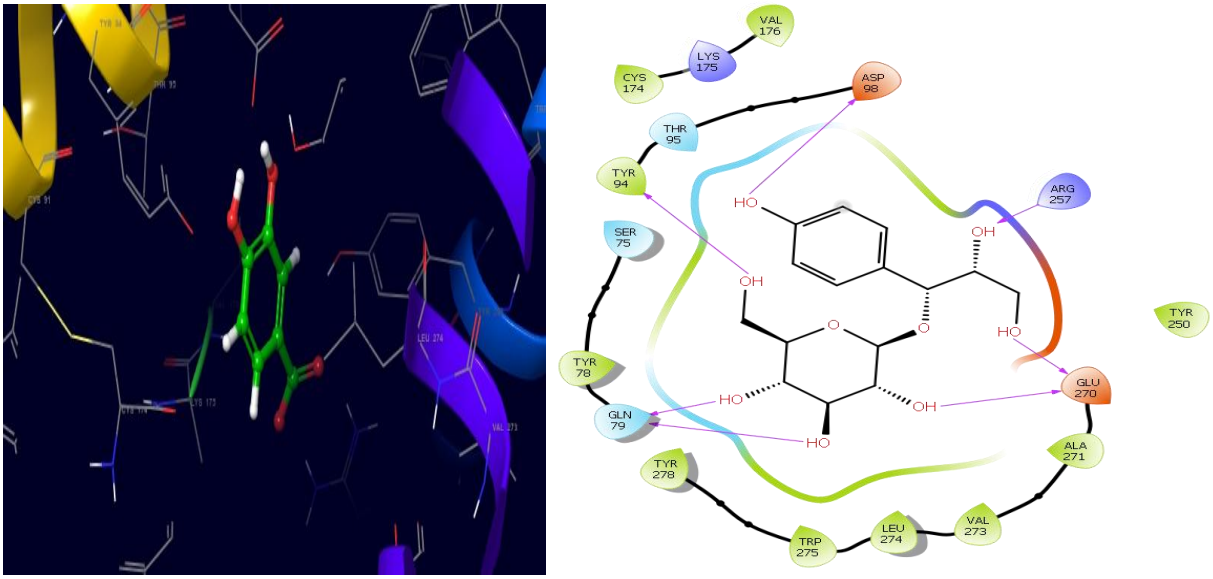


Figure 3.20: 3D and 2D molecular interaction of the ligand 72 from *Ocimum gratissimum* against histamine 2 receptor.

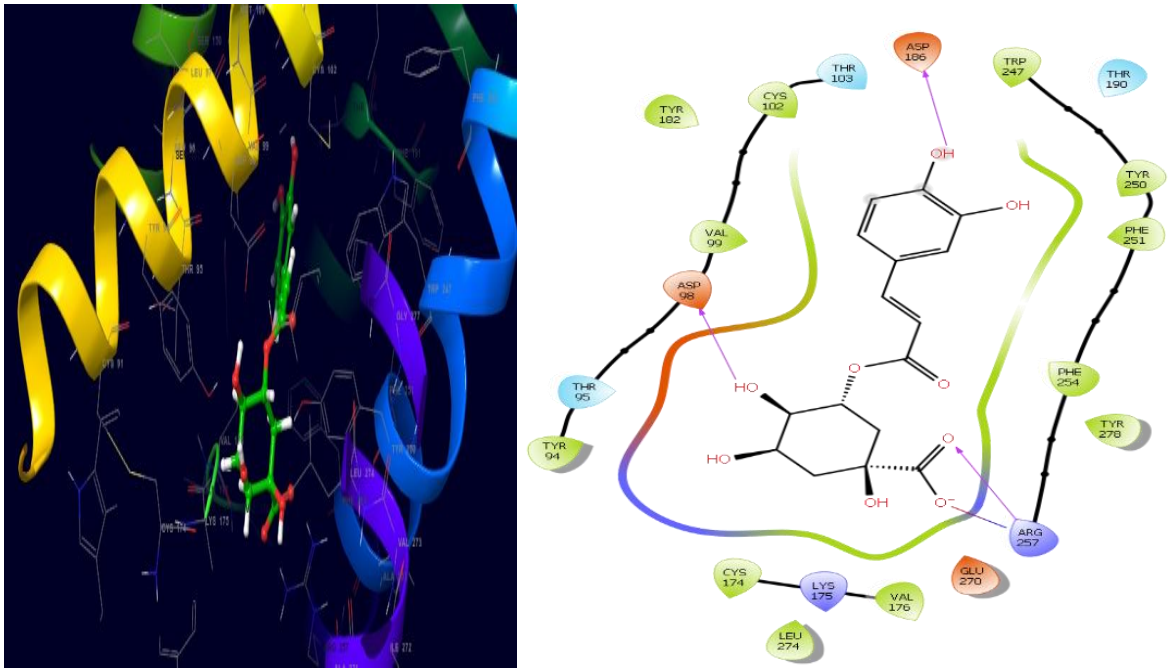


Figure 3.21: 3D and 2D molecular interaction of the ligand 1794427 from *Solanum nigrum* against histamine 2 receptor.

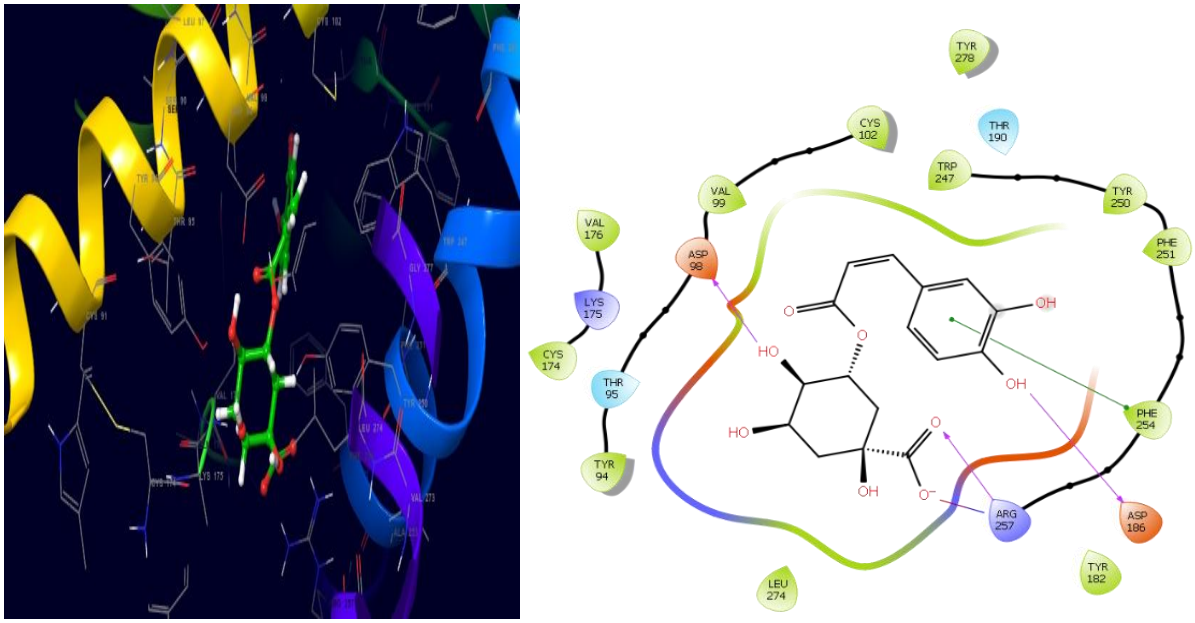


Figure 3.22: 3D and 2D molecular interaction of the ligand 1794425 from *Solanum nigrum* against histamine 2 receptor.

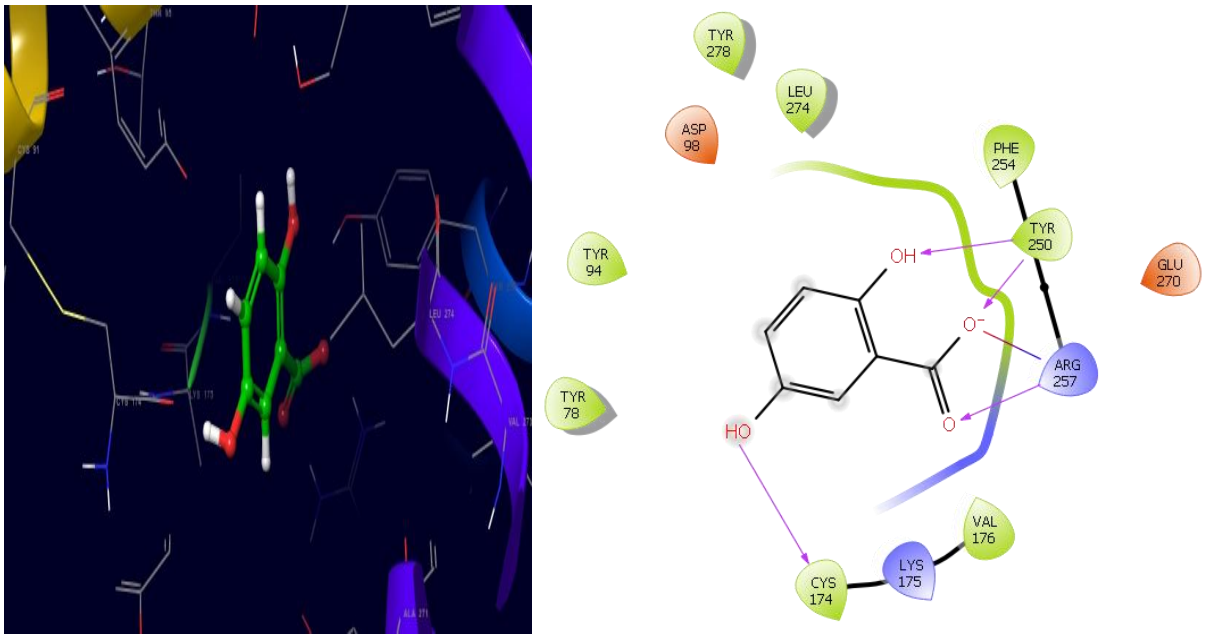


Figure 3.23: 3D and 2D molecular interaction of the ligand 3469 from *Solanum nigrum* against histamine 2 receptor.

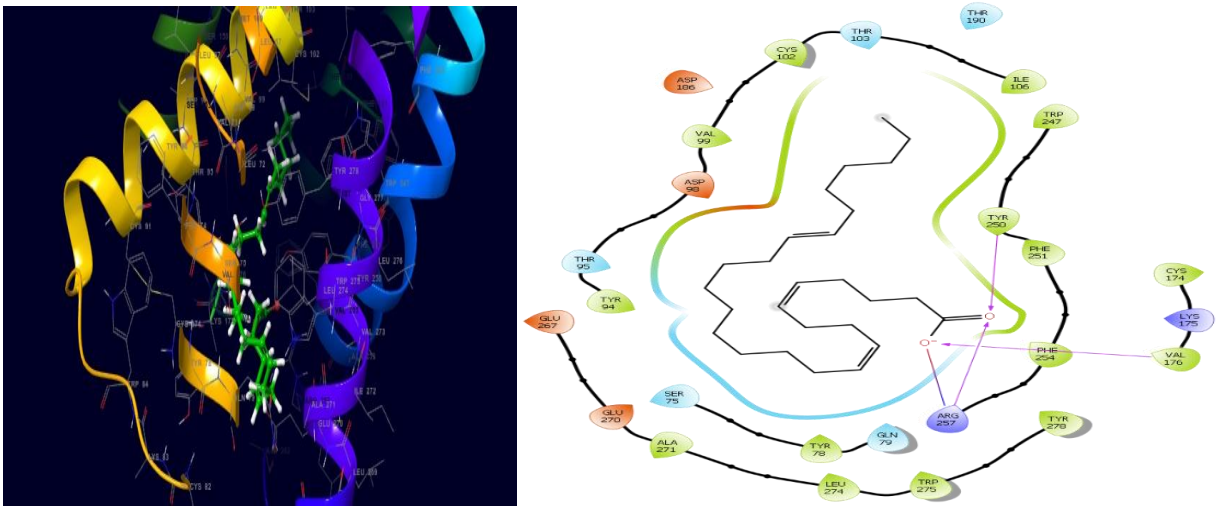


Figure 3.24: 3D and 2D molecular interaction of the ligand 14215566 from *Solanum nigrum* against histamine 2 receptor.

Table3.10: Summary of interaction mechanism between selected ligands and muscarinic m1 receptor amino acids.

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
1203	TRP 157	PPS	BENZENE
	THR192	HB	OH
	ASN 382	HB	OH
	TYR 106	HB	OH
637584	TYR 404	HB	OH
	TRP378	PPS	BENZENE
	ASN 382	HB	OH
	THR192	HB	OH

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

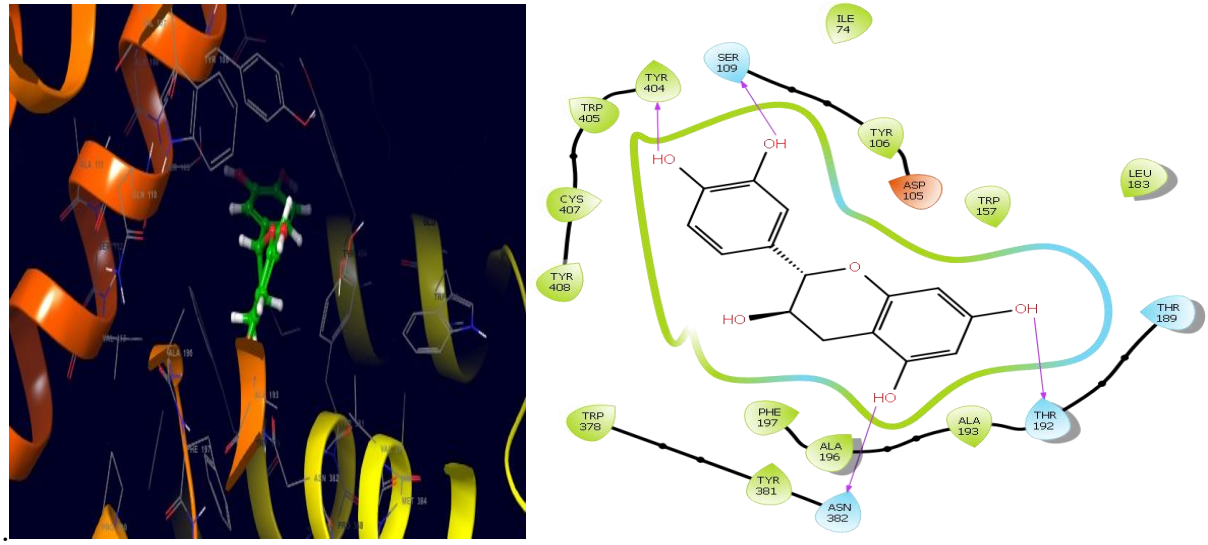


Figure 3.25: 3D and 2D molecular interaction of the ligand 73160 from *Ocimum gratissimum* and *Solanum nigrum* muscarinic m1 receptor

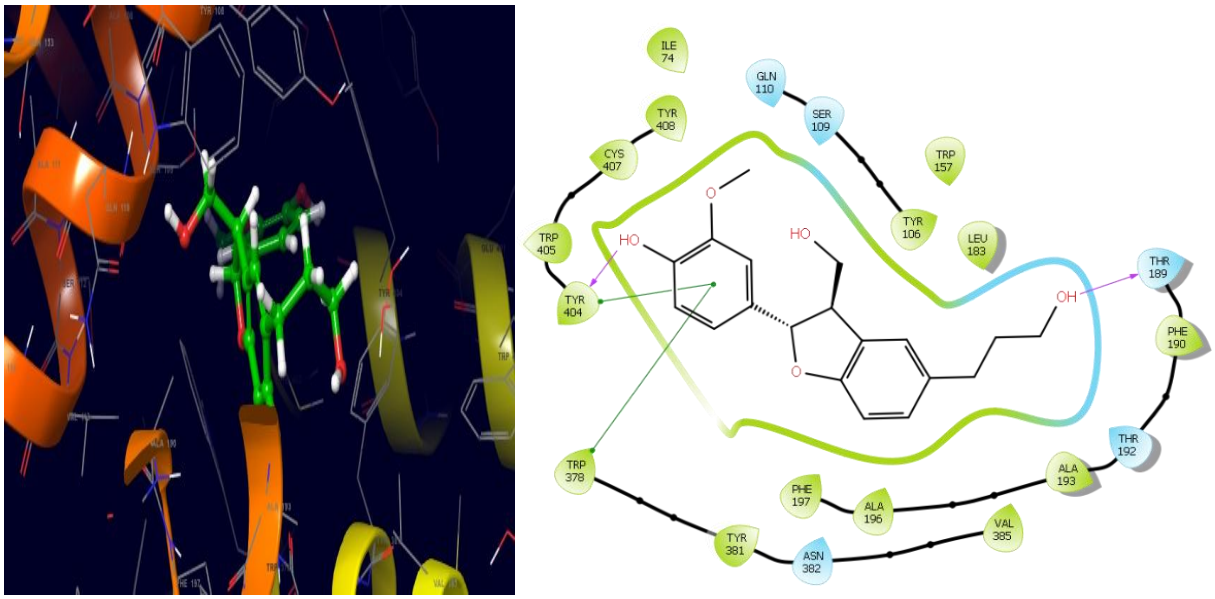


Figure 3.26: 3D and 2D molecular interaction of the ligand 162872299 from *Ocimum gratissimum* muscarinic m1 receptor.

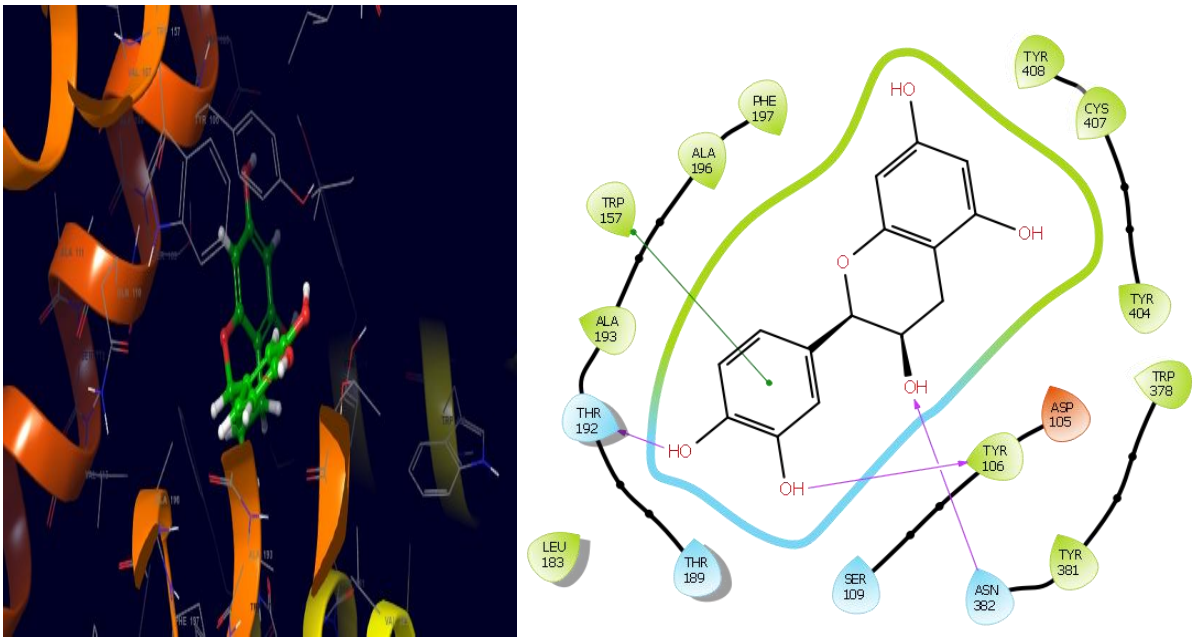


Figure 3.27: 3D and 2D molecular interaction of the ligand 1203 from *Solanum nigrum* muscarinic m1 receptor

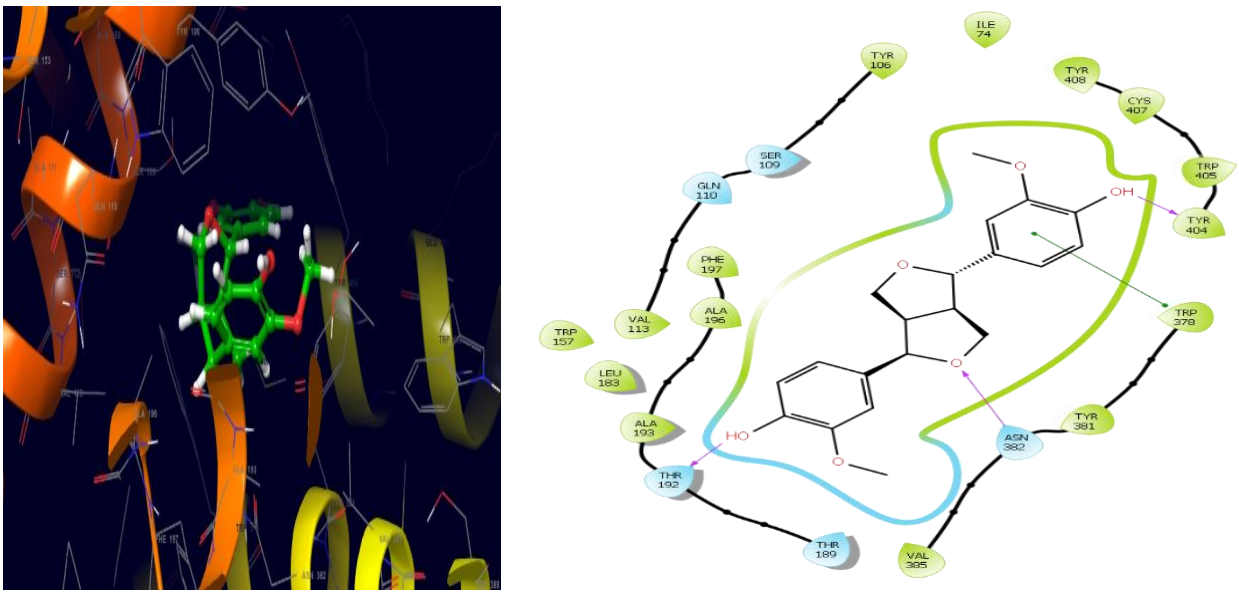


Figure 3.28: 3D and 2D molecular interaction of the ligand 637584 from *Ocimum gratissimum and Solanum nigrum* muscarinic m1 receptor

CHAPTER FOUR

DISCUSSION

Gastrointestinal disorders due to hyperacidity are diseases, mainly gastroesophageal reflux disease and peptic ulcer disease. These conditions are usually due to hypersecretion of acid in the stomach. Several factors, such as non-steroidal anti-inflammatory drugs used, erosion of the stomach mucosa, and Helicobacter pylori, amongst others, have been involved in peptic ulcer disease . Hence, the main drugs used to treat these diseases target correcting the aftermath effects of these factors.

The proton pump inhibitors target the proton pump (H/K ATPase), the prostaglandin analogues target the prostaglandin E2 receptors, the Muscarinic antagonist target the muscarinic M1 receptor the H2 receptor blockers target H2 receptors. By induction of these receptors, these ligands mediate the actions of endothelial cytoprotection, mucosa production, and ulcer healing.

These plants studied in the research have been used in the treatment of disease conditions of the gastrointestinal tract due to hyperacidity 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.

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, Scoparia dulcis,* and *Solanum nigrum* were obtained from literature alongside standard ligands (misoprostol, enprostil, rabeprazole, soraprazan, Famotidine, ranitidine). 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 3.0, 3.1, 3.2, and 3.3**.

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 Admetlab. Results are shown in **Tables 3.5, 3.6, and 3.7.**

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 **Tables 3.0, 3.1, 3.2, and 3.3.** 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 -9.0133Kcal/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).

A total of 275 ligands including the standards were generated from the literature source and then docked against the receptors and their docking scores were generated. The results of the docking scores and the corresponding binding affinities are shown in Tables 3.0, 3.1, 3.2, and 3.3. 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 table3.5, 3.6, and 3.7.

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). 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). A total of 97 ligands and standards were obtained from literature sources and then docked against the receptors 7w49, 7ul3, and 5cxv. The docking score showing the degree of affinities of the ligands and standards to the receptors were derived as in **Tables 3.0, 3.1, 3.2, and 3.3.**

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 3.5, 3.6, and 3.7.** For the proton pump(7w49) only one ligand 11445323 gave a docking score higher than the standard.

For the Histamine2 receptor 7UL3, *Scoparia dulcis* gave 4 ligands with docking scores close to or higher than the standard ligands. These ligands are 5042, 185617, 5702160, and 5311225. For the prostaglandin E2 receptor, no ligands gave a docking score closer to or higher than that of the standard ligands. For the muscarinic M1 receptor 5CXV, a total of five ligands gave a docking score closer and higher than that of the standard pirenzepine. These are 5280637,5280445, 13093776, 5280443, 213054.

A total of 185 ligands including the standards were downloaded from the literature source and then docked against the receptors and their docking scores were generated. The results of the docking and the corresponding binding affinities are shown in **Tables 3.0, 3.1, 3.2, and 3.3**. 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 3.5, 3.6, and 3.7**.

For the proton pump, a total of eight ligands with pub chem cid of (74089792, 5281643, 5280805, 51402807, 9064, 162942605, 72281, 5280343). 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, 5042, 182232, 3469,14215566). For the prostaglandin E2 receptor 6M9T, no ligand gave a docking score close to or higher than the standard ligands (enprostil and misoprostol). Finally, for the Muscarinic M1 receptor, only six ligands gave docking scores higher and near the standard pirenzepine. These include (73160, 637584, 5281672, 667495, 1203, 72276)

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.

4.7 **PROTON PUMP**

Succinctly, a total of 24 ligands gave higher scores higher than the standard test compound soraprazan. Ocimum gave the higher number of ligands and then solanum and then asparagus and scoparia. These compounds were further tested for their pharmacokinetics properties and the results are seen in table 3.5. The interactions and further toxicity screening yielded seven compounds of which three were from *Ocimum grattisimum*, and four were from *Solanum nigrum*. 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 grattisimum* and *Solanum nigrum*.

4.8. **HISTAMINE H2 RECEPTOR.**

For the Histamine H2 receptor, the interactions with ligands from the four plants yielded a total of 33 ligands with docking scores higher or of very close proximity with the standard; six from *Asparagus racemosus,* eighteen from *Ocimum grattisimum*, three from *Scoparia dulcis*, and then eight from *Solanum nigrum*. Upon further toxicity screening, a total of 13 compounds were obtained. Asparagus yielded one, eight were from Ocimum while Solanum yielded four. Here, only the compounds from Scoparia did not pass the screening test. The interactions of the ligands from the four 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 3.6.**

4.9 **MUSCARINIC M1 RECEPTOR**

In the docking of ligands from the four plants with the muscarinic M1 receptor, 21 compounds of proximity and higher docking scores were derived. Asparagus yielded five compounds, Ocimum with six, Scoparia with five, and then Solanum yielding six as seen in **Table 3.7**. Further pharmacokinetic screening of these compounds gave a total of four different ligands: one from two Ocimum grattisimum and two (one co-occurring as in Ocimum) in Solanum nigrum. The plant Asparagus and Scoparia yielded no safe ligands upon further analysis. 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.

Although results are reliable, it is worth noting that cases, where ligands show mild to moderate toxicity scores on organs such as the ear and skin but are safe on the other essential organs such as the liver, heart, and kidney with low or no carcinogenicity and genotoxicity, such compound, can be readily selected and used. Results of pharmacokinetic analysis and toxicological screening may differ from clinical studies induced fit nature of proteins and receptors may affect results which may be rigid in *in-silico* methods, waters in the environment body homeostasis, etc.

CHAPTER FIVE.

5.0 CONCLUSION

The phytoconstituents isolated from the plants were obtained, and molecular docking was carried out against the proton pump, prostaglandin E2 receptor muscarinic m1 receptor, and histamine h2 receptor; post-docking analysis was carried out, and the ADMET properties of selected ligands were determined.

The binding affinities and interaction with active site residues of the protein target, proton pump possessed by cianidanol(9064) present in both *Ocimum grattisimum* and *Solanum nigrum,*162979504 in *Ocimum grattisimum* and taxifolin(439533), isoquercitrin(51402807), sophoretin(5280343), 162942605 in *Solanum nigrum* showed the potentials of these ligands as lead compounds for the treatment of peptic ulcer disease and gastro-oesophageal reflux disease.

Also, the binding affinities and interaction with active site residues of the protein target, histamine H2 receptor possessed by chlorogenic acid (1794427) present in both *Ocimum grattisimum* and *Solanum nigrum;* taxifolin(439533), 162934828, 162934831, 101992980, 11824948, 162896256, 3,4-dihydroxyl benzoic acid(72) in *Ocimum grattisimum* and cis-chlorogenic acid(1794425), 2,5-dihydroxyl benzoic acid(3469), 142155663, in *Solanum nigrum* showed the potentials of these ligands as lead compounds for treatment of peptic ulcer disease and gastro-oesophageal reflux disease.

Moreso, the binding affinities and interaction with active site residues of the protein target muscarinic M1 receptor, possessed by catechin(73160), epi pinoresinol(637584) present in both *Ocimum grattisimum* and *Solanum nigrum,*162872299 in *Ocimum grattisimum* and

epicatechin(1203) in *Solanum nigrum* showed the potentials of these ligands as lead compounds for treatment of peptic ulcer disease and gastro-oesophageal reflux disease

Succinctly, it is obvious that none of the plant's ligands works through the prostaglandin E2 receptor.

However, studies such as molecular dynamics simulations, invitro and invivo studies using appropriate animal models need to be done to further validate their use as drugs for the treatment of peptic ulcer disease and gastro-oesophageal reflux disease.

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