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IN-SILICO ANTI-ULCERATIVE ACTIVITY EVALUATION OF SOME BIOACTIVE COMPOUNDS FROM *CASSIA TORA* AND *BUTEA MONOSPORA* THROUGH MOLECULAR DOCKING APPROACH

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Keywords:

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ABSTRACT: Background and Aim: *In-silico* approach is commonly the method for predicting and confirming drug design. Hence the present study was undertaken to evaluate *in-silico* the anti-ulcerative activity of some bioactive compounds from *Cassia tora* and *Butea monospora* through a molecular docking approach. **Method:** Docking is performed using 22 runs of the Lamarckian Genetic Algorithm with the grid box sized x, y, and z coordinates of (20.7075) X (38.7045) X (–33.7057) and spacing of 0.375 Å on Autodock suits software 2. The docking data are then evaluated with the Autodock Tools suite software, and the interaction is displayed with the Biovia Discovery Studio Visualizer. **Result:** Kaempferol (5280863) and Gallic acid (370) of *Cassia tora* and *Butea monospora* showed that the value -8.7 kcal/mol and -8.3 kcal/mol for binding energy, respectively, though binding energy of standard of ligand ranitidine (3001055) is -5.4 kcal/mol. Kaempferol and gallic acid are strongly tied to GLU374 ARG846 ARG775 PHE778 ASP779 LEU843 ARG949 ASP851 and TYR799 CYS813 LEU811, respectively, on the active site of the receptor. **Conclusion:** Kaempferol and Gallic acid displayed interactions with the residue, indicating an excellent inhibitory ability. The compounds providing an anti-ulcerative effect have the lowest binding energy to the receptor, binding to the residual binding as native ligands. Therefore, Kaempferol and Gallic acid of *Cassia tora* and *Butea monospora* produce a better conformation of the ligand-receptor complex.

INTRODUCTION: In India peptic ulcer disease (PUD) has become common. An estimated 15,000 deaths occur each year as a consequence of PUD. Antacids and antiulcer medications account for 6.2 billion rupees in the Indian pharmaceutical business, accounting for 4.3 percent of the market. There are two basic techniques for treating peptic ulcers nowadays. The first concern is lowering stomach acid production, while the second concerns reinforce gastric mucosal protection.

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The majority of the research focuses on novel and improved pharmacological treatments. These have been made feasible largely by the availability of proton pump inhibitors, histamine H2 receptor blockers, mucosal barrier medicines and prostaglandin analogues.

However, clinical trials of these medications revealed the development of tolerance and an increased rate of relapses and adverse effects, making their usefulness questionable. This is the logic for creating novel antiulcer treatments, including natural medicines. Indian medicinal herbs and derivatives have shown to be a great source of therapeutic compounds for various illnesses, including PUD. The key thrust area of current research is an indigenous medication with fewer side effects, aiming for a better and safer approach to managing PUD [1, 2].

In addition to hazardous human behaviours, the development or proliferation of dangerous microbes has resulted in various human illnesses. As a result, there is an ongoing hunt for drugs to treat these illnesses.

Herbal remedies have been used to treat various disorders for millennia, long before the discovery of most contemporary pharmaceuticals. As a result, herbal medications are regarded to have higher cultural acceptability and fewer harmful and antagonistic effects [3].

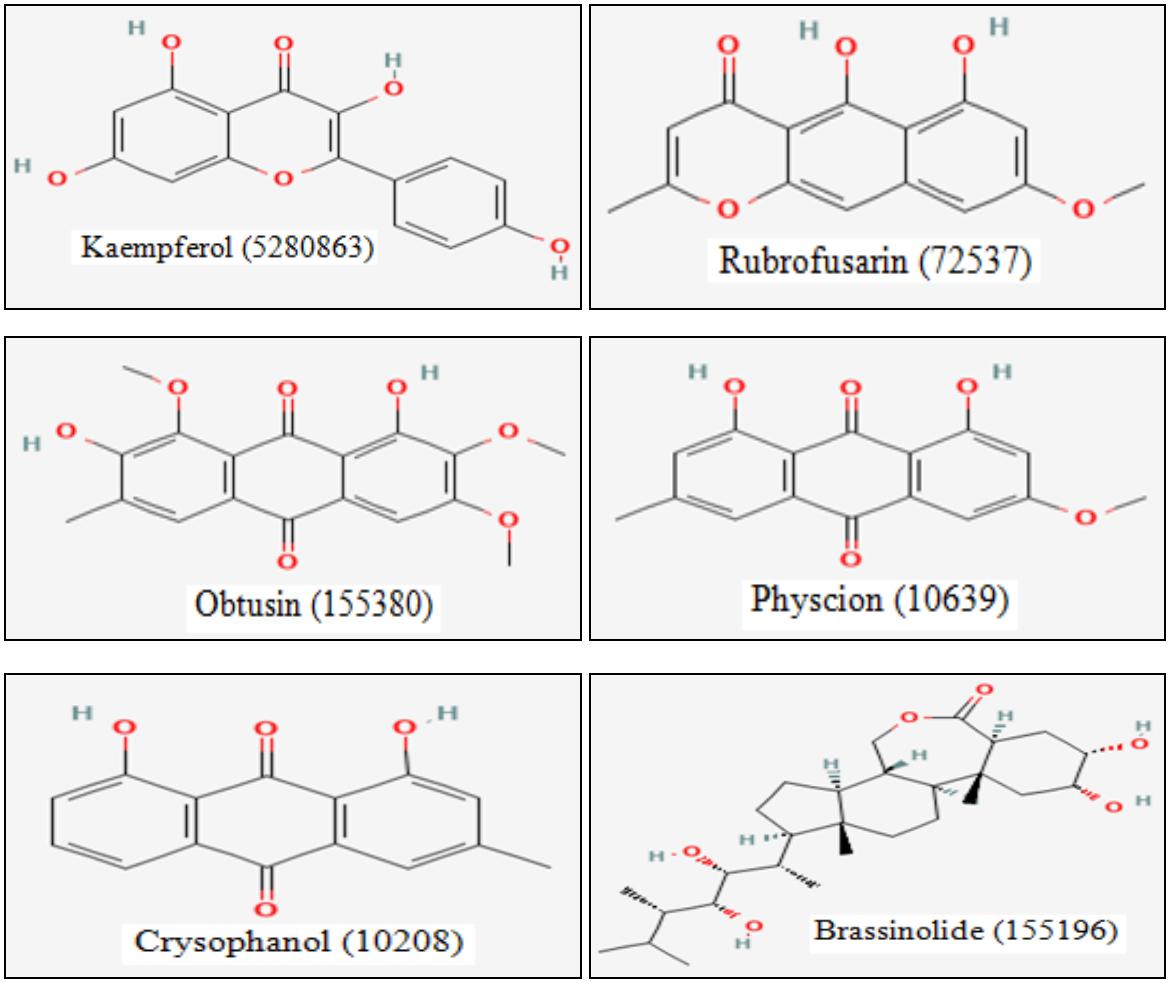
Interestingly, plant-based medications are recognized to be among the most appealing sources of novel therapeutics, with promising outcomes in treating various disorders, including peptic ulcers. Several potential medicinal plants for treating peptic ulcers have been examined and described in the literature worldwide [4]. *In-silico* approach is commonly the method for prediction and confirmation of drug design.

Hence, the present study was undertaken to evaluate *in-silico* anti-ulcerative activity of some bioactive compounds from *Cassia tora* and *Butea monospora* through a molecular docking approach.

METHODS: The macromolecule used in this study is chain A of Gastric H(+), K(+)- ATPase (PDB ID: 2XZB)5. The macromolecule is then prepared, and minimization of energy of targeted protein is done using spdb viewer. The ligands used were selected from the PubMed database and minimized by pyrx software.

Docking is performed using 22 runs of the Lamarckian Genetic Algorithm with the grid box sized x, y, and z coordinates of (20.7075) X (38.7045) X (–33.7057) and spacing of 0.375 Å on Autodock suits software 6. The docking data are then evaluated with the Autodock Tools suite software, and the interaction is displayed with the Biovia Discovery Studio Visualizer. The structure of ligands is listed below in **Fig. 1.**

Cassia tora:



Butea monospora:

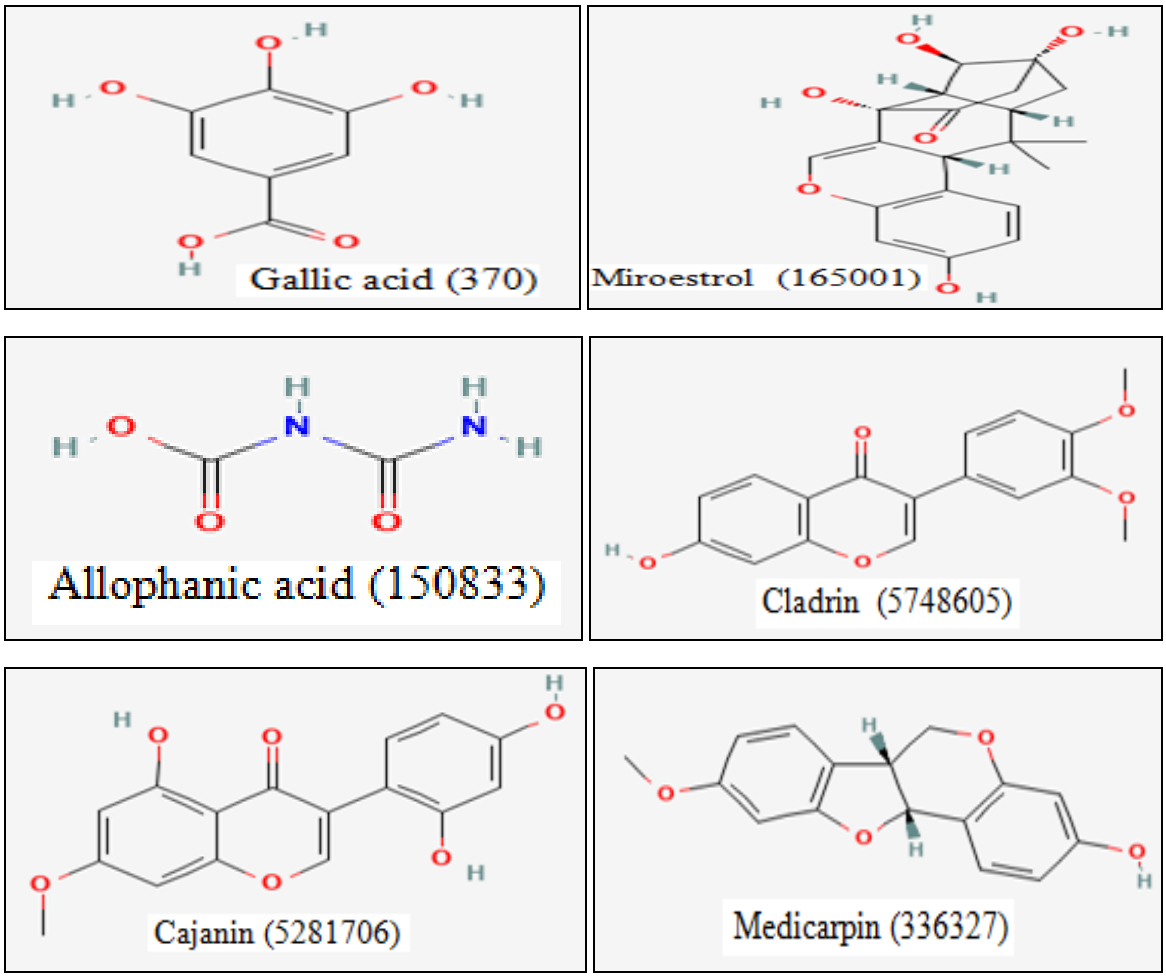


FIG. 1: STRUCTURES OF THE BIOACTIVE COMPOUND OF *CASSIA TORA* AND *BUTEA MONOSPORA*

RESULT AND DISCUSSION: *In-silico* approach is commonly the technique for predicting and confirming drug design. This approach offers advantages such as being less costly, taking less time, and minimizing the separation of inactive chemicals [7].

TABLE 1: ANALYSIS OF INHIBITING POTENCY OF BIOACTIVE COMPOUND FROM *CASSIA TORA* AND *BUTEA MONOSPORA* AGAINST THE 2XZB RECEPTOR WITH IN SILICO APPROACH

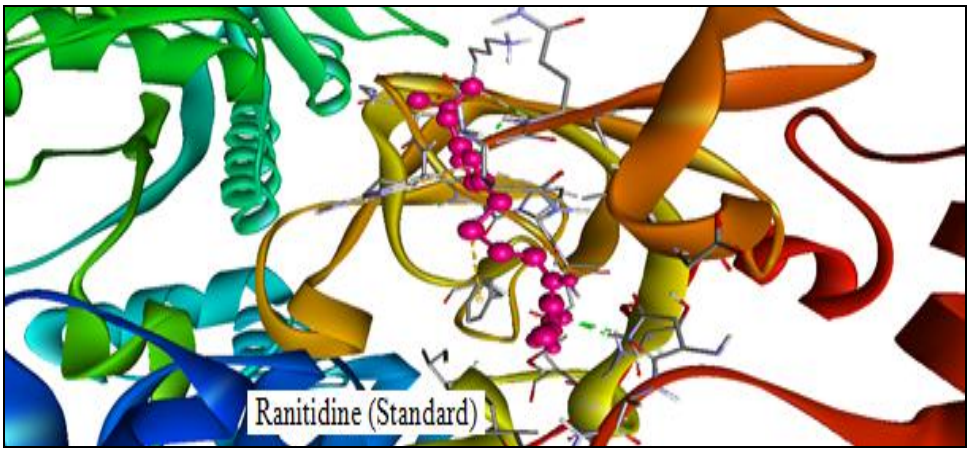
Drug/ phytocompounds	Binding Affinity (kcal/mol)	Amino acid Interaction
Ranitidine (3001055)	-5.4	ASN87 GLY271 PRO209 ARG207 GLN177 ALA191 PHE254
Cassia tora		
Kaempferol (5280863)	-8.7	GLU374 ARG846 ARG775 PHE778 ASP779 LEU843 ARG949 ASP851
Rubrofusarin (72537)	-7.6	ASN475 GLU470 MET477 ALA476 ARG454
Obtusin (155380)	-7.3	LEU307 ALA860 ALA859 PHE311 TYR340 LEU796 ILE793 TYR863
Physcion (10639)	-7.7	TYR340 TYR863 LEU307 ALA859 ALA860 PHE311
Crysophanol (10208)	-8.1	TYR157 GLY153 LYS100 PHE101 GLU160
Brassinolide (155196)	-8.0	TYR802 LEU809 GLN924 ASN986
Butea monospora		
Gallic acid (370)	-8.3	TYR799 CYS813 LEU811
Miroestrol (165001)	-5.7	CYS813 LEU809
Allophanic acid (150833)	-5.4	ARG394 ASP602 THR387 LYS386 SER231
Cladrin (5748605)	-7.6	ILE793 PHE311 LEU307 PHE864 ALA859 ALA860 GLU856
Cajanin (5281706)	-7.6	ARG949 ASP851 TYR103 LYS782 LEU843
Medicarpin (336327)	-7.8	GLY774 ARG846 ILE840 ASP851 LEU843 ARG844 ARG775

The study has performed using MGL Tools-based Autodock software between the selected phytoconstituents from *Cassia tora* and *Butea monospora* and Gastric H(+), K(+)- ATPase (proton pump) (PDB ID: 2XZB).

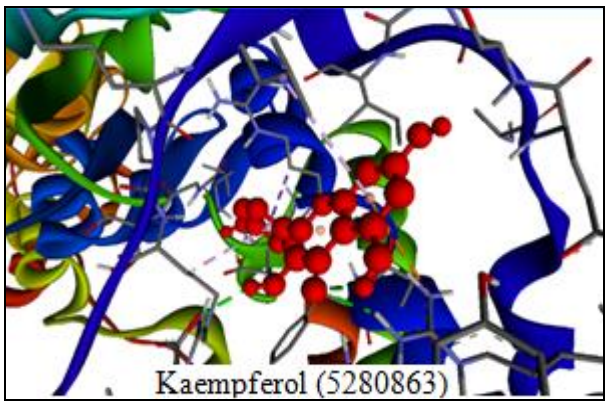
The final result is linked to the reference standard of ligand ranitidine (3001055). Method validation was performed before the commencement of the research to assure data accuracy. During the validation process, the grid box was set to x, y, and z coordinates of (20.7075) X (38.7045) X (–33.7057) and spacing of 0.375 Å.

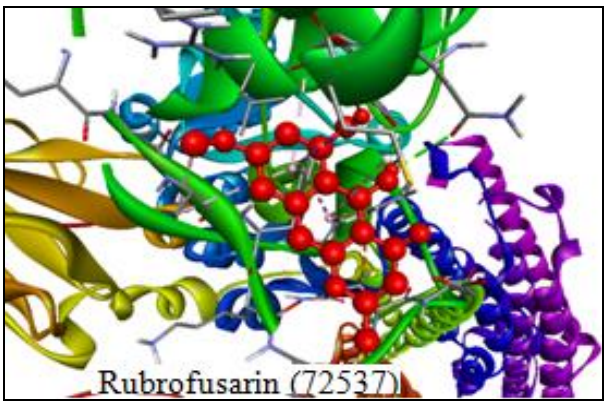
The selected phytoconstituents were summarized from the previous study [8]. LGA was used to provide a score to molecules.

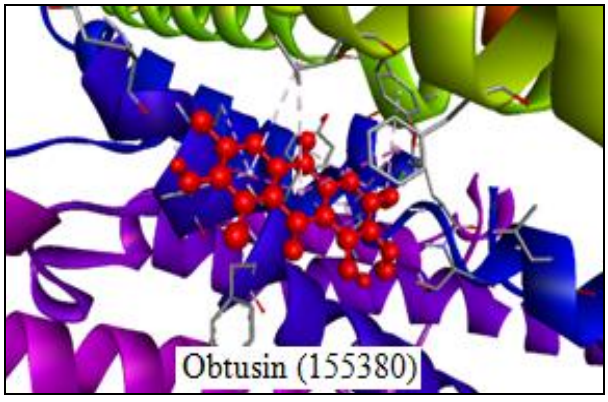
The lowest energy of the complex was analyzed using Biovia Discovery Studio after the molecular docking simulation method generated binding energy information. The result of molecular docking simulation between every 6 compounds from *Cassia tora* and *Butea monospora* to the gastric H(+), K(+)- ATPase receptor (proton pump) is given in **Table 1.**

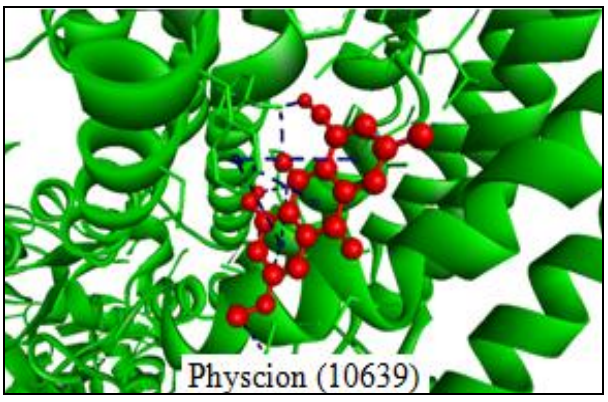


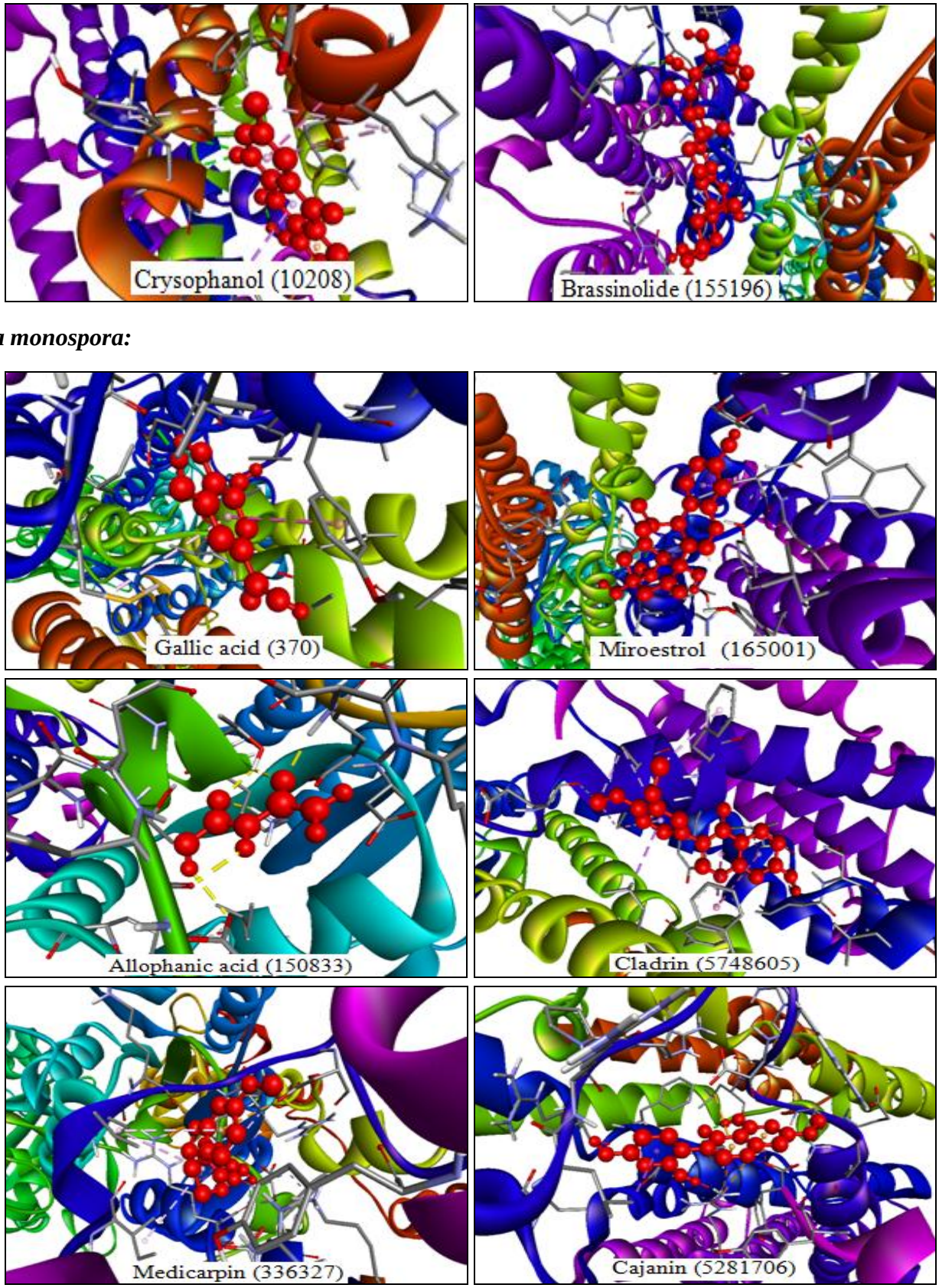
Cassia tora:









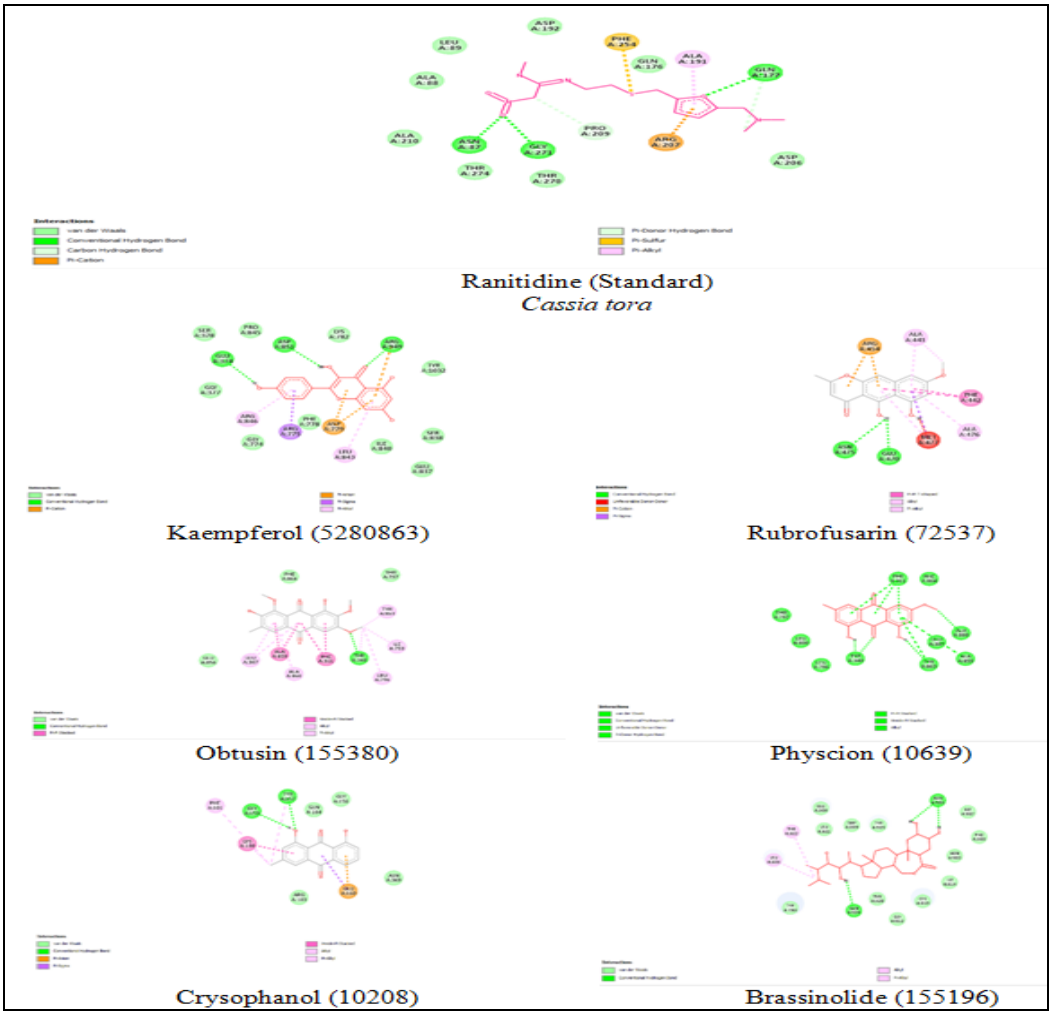


Butea monospora:

FIG. 2: DOCKED POSES OF LIGANDS WITH TARGETED PROTEIN POCKET

Previous research found that extracts from traditional medicinal herbs suppressed ulcerative processes on the proton pump [9]. The bioactive components from the medicinal plant hinder the performance of the gastric H (+), K (+) - ATPase receptor in this pathway. As we understand, the

proton pump is a crucial mediator in the membrane ulceration process. The antihistaminic group is predicted to be replaced by chosen phytocompounds from *Cassia tora* and *Butea monospora*. Antihistaminic medicines have long-term harmful effects; thus, a plant-derived drug offers an option [10]. Because the usage of bioactive substances from the plant can limit unpleasant side effects to a few. Based on **Table 1**, Kaempferol (5280863) and Gallic acid (370) of *Cassia tora* and *Butea monospora* demonstrated that the values of -8.7 kcal/mol and -8.3 kcal/mol for binding energy, respectively, though binding energy of standard of ligand ranitidine (3001055) is -5.4 kcal/mol. Ranitidine (3001055) as a reference standard inhibitor resulted in bounding through ASN87 GLY271 PRO209 ARG207 GLN177 ALA191 and PHE254 residues. The bioactive compound kaempferol, rubrofusarin, obtusin, physcion, crysophanol, brassinolide of *Cassia tora* and gallic acid, miroestrol, allophanic acid, cladrin, cajanin, medicarpin of *Butea monospora* exhibited the binding energy close to and lesser the standard reference compound (ranitidine). Whereas the binding energy of kaempferol and gallic acid are lesser than the reference ligand; as a result, these phytoconstituents can block the gastric H (+)., K (+) - ATPase receptor. Kaempferol and gallic acid are strongly tied to GLU374 ARG846 ARG775 PHE778 ASP779 LEU843 ARG949 ASP851 and TYR799 CYS813 LEU811, respectively, on the receptor's active site. The binding energy of kaempferol, rubrofusarin, obtusin, physcion, crysophanol, brassinolide of *Cassia tora* and gallic acid, miroestrol, allophanic acid, cladrin, cajanin, medicarpin of *Butea monospora* phytoconstituents are -8.7, -7.6, -7.3, -7.7, -8.1, -8.0 and -8.3,-5.7,-5.4,-7.6,-7.6, -7.8 kcal/mol respectively. The existence of lactone and keto groups at the molecule might result in interaction with the receptor. The 2D and 3D visualizations of phytocompounds and standards were demonstrated in **Fig. 2** and **3**.



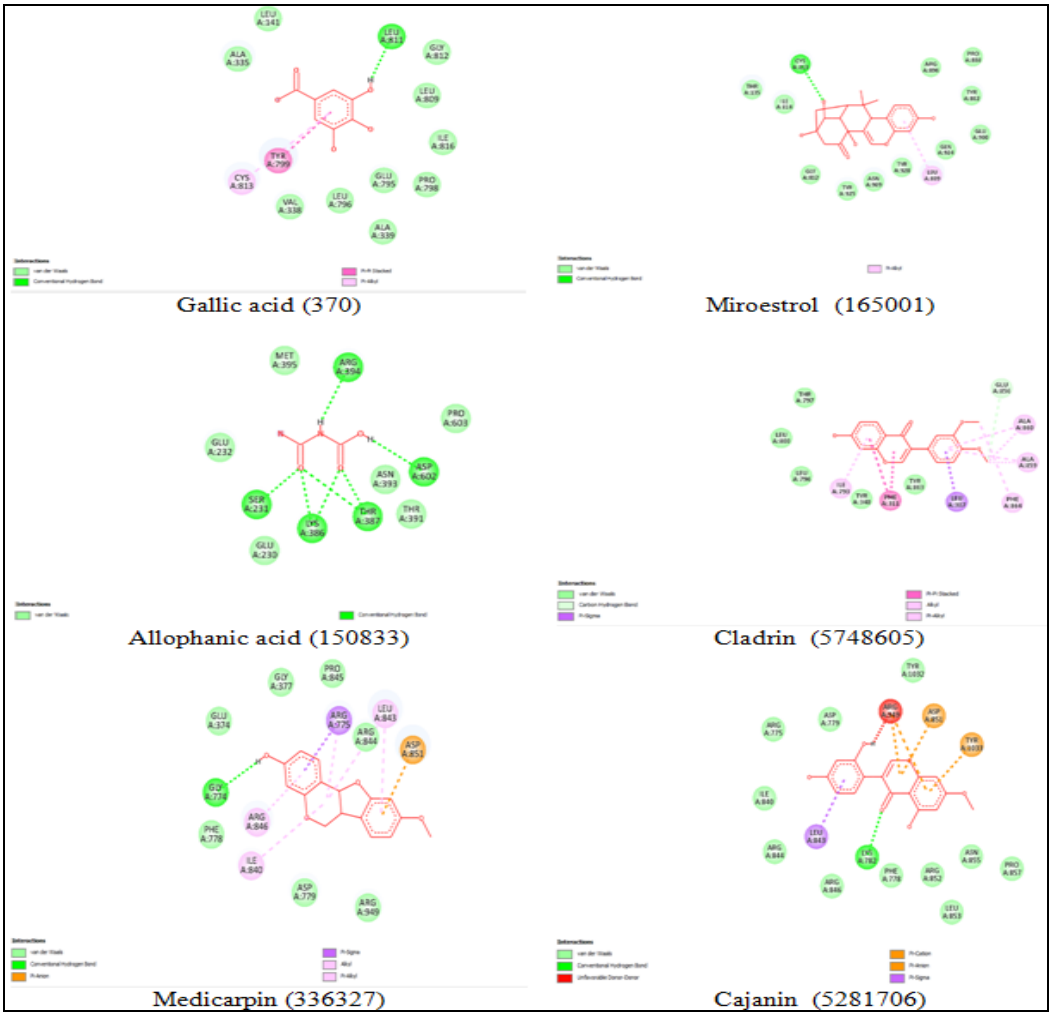


FIG. 3: INTERACTION OF LIGANDS AND TARGETED PROTEIN

The "binding energy" of rubrofusarin, obtusin, physcion, crysophanol, brassinolide of *Cassia tora* and miroestrol, allophanic acid, cladrin, cajanin, medicarpin of *Butea monospora* is highest negative than standard reference, ligand but it is not tied to residue on the "active site of the protein". In vivo study reported kaempferol and gallic acid could inhibit the formation of proton on gastric H (+), K (+) - ATPase receptors [11]. Instead, kaempferol and gallic acid derived from *Cassia tora* and *Butea monospora* offered an excellent antiulcerative activity, and the activity is as effective as ranitidine, the selective gastric H (+), K (+) - ATPase receptor inhibitor [12].

CONCLUSIONS: The molecular docking simulation performed by Autodock 4.2 is extremely useful in predicting and validating the composition of a therapeutic candidate derived from *Cassia tora* and *Butea monospora* as an anti-ulcerative agent. The selected phytoconstituents from *Cassia tora* and *Butea monospora* have docked to the gastric H (+), K (+) - ATPase receptor and Kaempferol (5280863) and Gallic acid (370) of *Cassia tora* and *Butea monospora* respectively, has the lowermost binding energy (-8.7 kcal/mol and -8.3 kcal/mol) than the standard of ligand ranitidine (3001055) is -5.4 kcal/mol. The smaller binding energy at the complexes, therefore, offers more enormous potential as an inhibitor of the gastric enzyme. However, other phytoconstituents of *Cassia tora* and *Butea monospora* did not display any interaction with the residue of the gastric H (+), K (+) - ATPase receptor. While Kaempferol and Gallic acid displayed interactions with the residue, it indicated an excellent inhibitory ability.

The compounds providing an anti-ulcerative effect have the lowest binding energy to the receptor and it binds to the residual binding as native ligands. Therefore, Kaempferol and Gallic acid of *Cassia tora* and *Butea monospora* generate the best conformation of the ligand-receptor complex.

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CONFLICTS OF INTEREST: Declared None

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