International Journal of Botany Studies
www.botanyjournals.com
ISSN: 2455-541X
Received: 04-09-2021, Accepted: 21-09-2021, Published: 05-10-2021
Volume 6, Issue 5, 2021, Page No. 1009-1014

Exploration of the anti-inflammatory potential of polar extract of *Alhagi pseudalhagi* through docking studies

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Abstract
Pharmacologically active molecules exhibit therapeutic anti-inflammatory effects due to cyclooxygenase-2 inhibition whereas cyclooxygenase-1 inhibition is the cause of unpleasant side effects. More selective cyclooxygenase-2 inhibitors have lesser side effects. Molecular docking is a bioinformatics modelling that involves an interaction between two molecules to create a stable adduct. The 3 dimensional structure of every complex depends on the ligand and target binding properties. Molecular docking generates several possible adduct structures, which are identified using the software scoring function and categorized. Plants of the Alhagi family have been commonly used for cure of a range of diseases including gastroenteritis, headaches, toothache, diarrhoea, rheumatoid arthritis and liver disease. In the current study, we explored the phytochemicals present in polar extract of *Alhagi pseudalhagi*: Kaempferol, rhamnetin, ombuine, isorhamnetin, tamarixetin, rutin, isoquercitrin, 1-*O*-β-methyl-glucoside, isoswertianolin, isorhamnetin-3-*O*-β-D-rutinoside, stigmasterol and tyramine were screened against Cyclooxygenase- 2 receptor (5KIR) using Autodock and Discovery studio. The docked phytochemicals exhibited significant binding with the cyclooxygenase- 2 receptor (5KIR) and paved the path for the development of polar extracts of *Alhagi pseudalhagi* as anti-inflammatory agent.

Keywords: autodock, discovery studio, anti-inflammatory, cyclooxygenase-2, *Alhagi pseudalhagi*

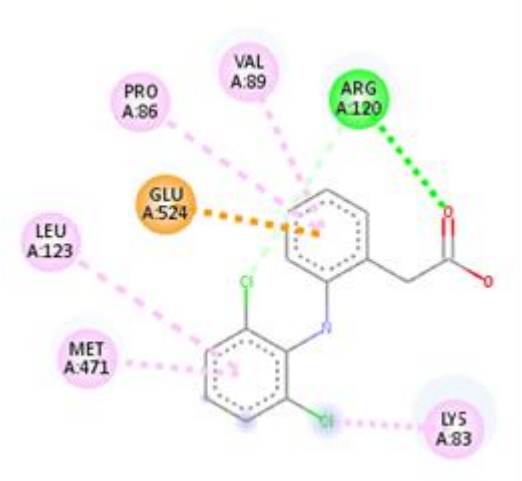
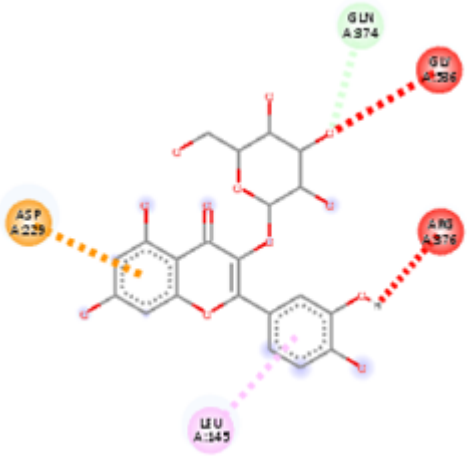
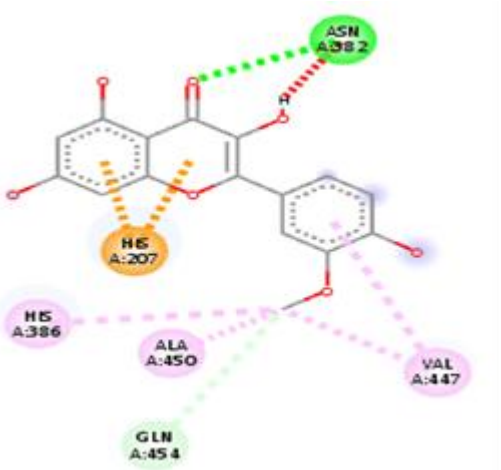
Introduction

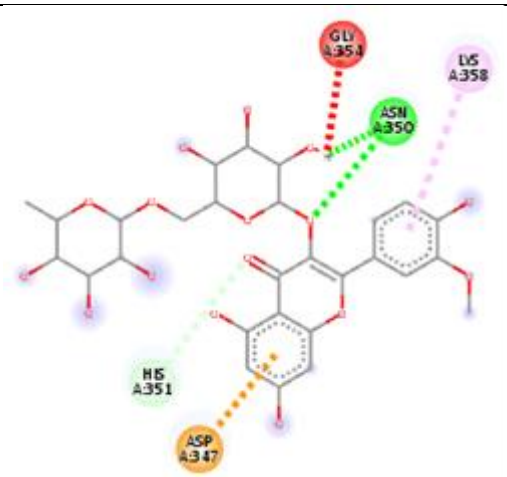
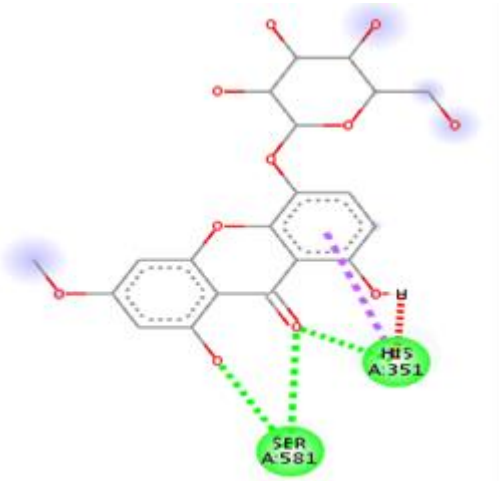
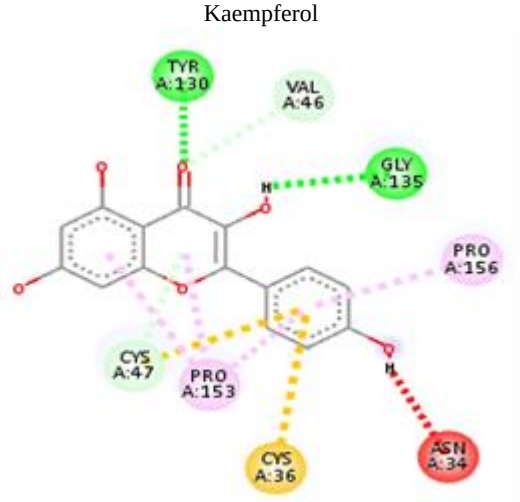
Discovery of novel chemical enetities [1, 2] such as competitive inhibitors of cyclooxygenase (COX) are anti-Inflammatory drugs that promote the bioconversion of arachidonic acid into inflammatory prostaglandin. Their use is associated with negative consequences of gastrointestinal and renal damage. Based on a range of selective COX-2 inhibitors [3] (Rofecoxib, Celebrcoxib and Valdecoxib), safer NSAIDs have been developed with an improved stomach safety profile. Rofecoxib has been withdrawn from the market due to cardiovascular side effects which motivate the researchers to detect and try alternative COX-2 templates. Natural products are a rich source of phytochemicals [4] and nearly all Alhagi are recognised for their potential medicinal applications. Plants of the Alhagi family have been commonly used for cure of a range of diseases including antibacterial [5], gastroenteritis [6], antioxidant [7], headaches, toothache, diarrhea, joint pain [8] and liver disease. It has been also identified as cytotoxic [9], anti-inflammatory [10] and antiulcer agent. Alhagi species are safe and rich sources of biologically active compounds [11] such as flavanone glycosides [12] with low toxicity [13]. An important technique in structural molecular biology [14] and computer aided medicine design is molecular docking. The objective of ligand protein docking is to anticipate a ligand's main binding mode(s) with a known 3D protein. Successful docking techniques efficiently search high dimensional spaces using a scoring system which classifies candidate dockings properly. Docking is useful technique to investigate the different characteristics related with protein ligand interactions [15]. In other words, the research shows how two or more molecules fit together, for example, ligand and protein. It is widely recognised that molecular binding of one (the ligand) molecule into the pocket of another (the receptor), which is often a protein, causes exact pharmacological action. Molecular docking has shown to be a highly effective method to find new drugs for protein targeting. Due to its applicability in the pharmaceutical business, protein-ligand docking is of particular interest among various kinds of docking. Protein ligand docking involves searching for precise ligand conformances inside a target protein when the protein structure is known. AutoDock/Vina used the Broyden-Fletcher-Goldfarb-Shanno method for docking purposes and improves substantially average binding mode predictions compared with AutoDock 4.

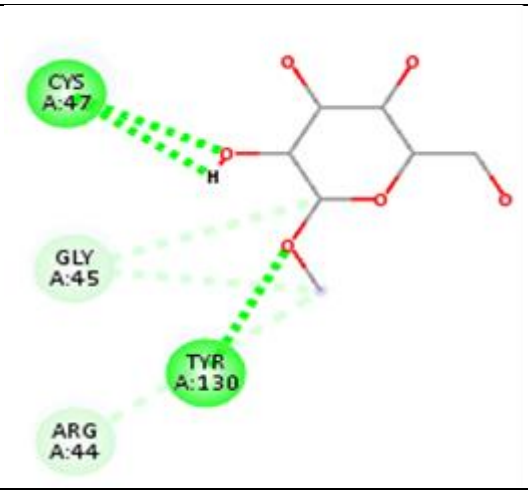
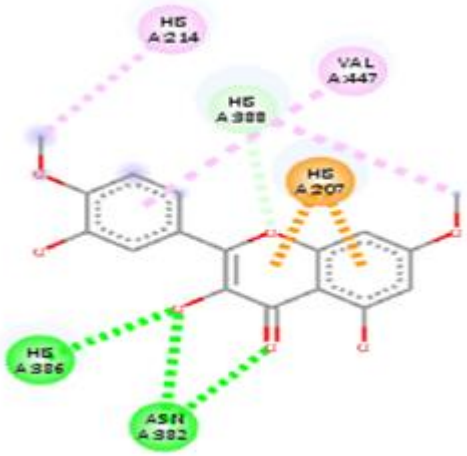
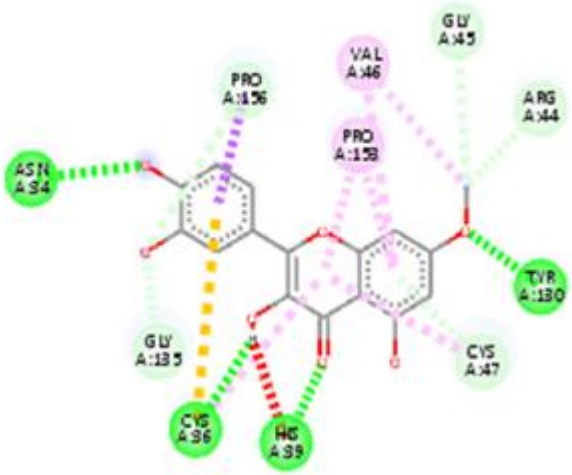
In silico screening

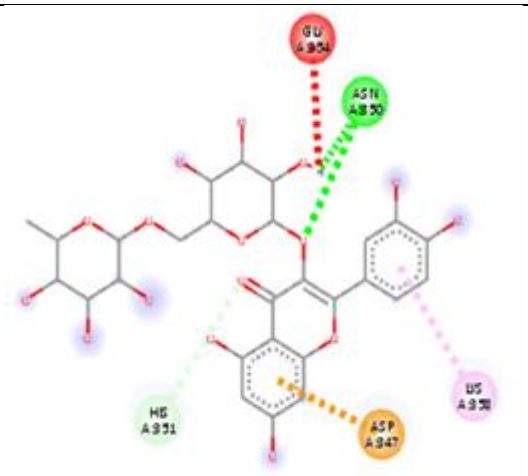
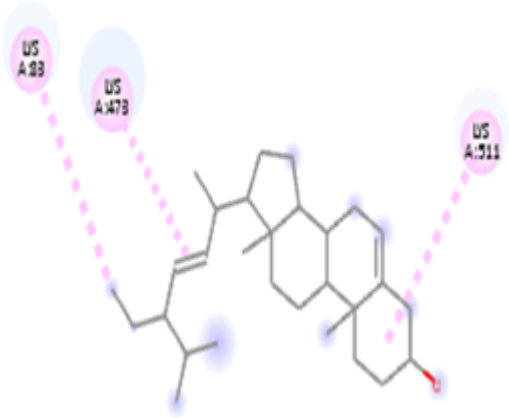
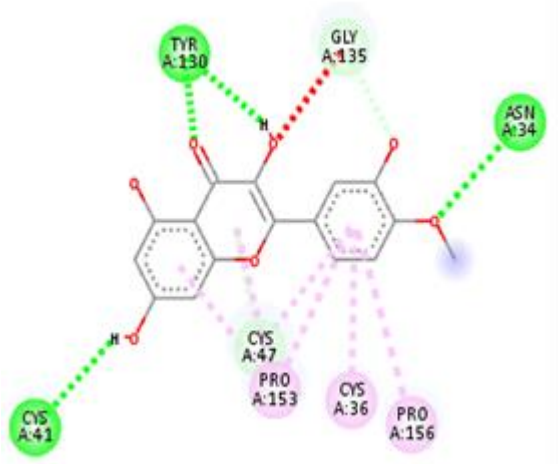
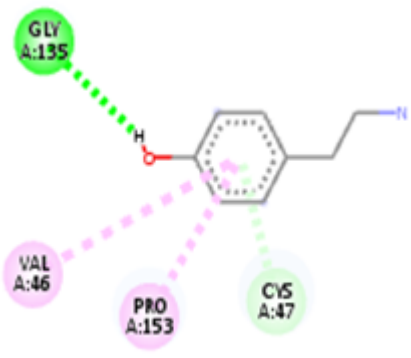
Receptor structure was download as pdb file from RCSB PDB: Homepage. After editing (Add Polar hydrogen and Delete water), it was converted into pdbqt file using Autodock Tools. It was selected as the grid for the active sites of receptor and the coordinates of the grid were mentioned in the configuration file. Ligand structure was drawing as cdx file using chem draw and further converted into PDB file using chem draw 3D. Pdb file was edited (rotatable bonds made non-rotatable bonds) and saved as PDBQT file using Autodock Tools. Ligand receptor interaction was executed [16] (C\hp>desktop>cd docking>."\program files (x86)\ the scripps research institute\ vina\ vina.exe" --config conf.txt --log log.txt) using Autodock Vina. Ligand and receptor interactions were visualized using discovery studio.

Table 1: Screening of phytochemicals against cyclooxygenase- 2 receptor (5KIR)

Ligand-Receptor Interactions	Mode	Affinity (Kcal/Mol)
Diclofenac 	1.	-11.7
	2.	-11.5
	3.	-11.5
	4.	-11.4
	5.	-11.3
	6.	-11.3
	7.	-11.3
	8.	-11.2
	9.	-11.2
Isoqercitin 	1.	-10.0
	2.	-10.0
	3.	-9.9
	4.	-9.8
	5.	-9.8
	6.	-9.7
	7.	-9.5
	8.	-9.2
	9.	-9.1
Isorhamnetin 	1.	-9.0
	2.	-8.6
	3.	-8.4
	4.	-8.3
	5.	-8.1
	6.	-8.0
	7.	-7.9
	8.	-7.8
	9.	-7.8
Isorhamnetin 3_O_rutinoside	1.	-10.9
	2.	-10.8
	3.	-10.5
	4.	-10.5
	5.	-10.0
	6.	-10.0
	7.	-9.7
	8.	-9.7
	9.	-9.3

		
Isoswertianolin 	1.	-10.0
	2.	-9.4
	3.	-9.2
	4.	-9.1
	5.	-9.1
	6.	-8.9
	7.	-8.8
	8.	-8.8
	9.	-8.4
Kaempferol 	1.	-10.1
	2.	-9.2
	3.	-8.5
	4.	-8.4
	5.	-8.2
	6.	-7.8
	7.	-7.7
	8.	-7.7
	9.	-7.6
Methyl glucoside	1.	-7.1
	2.	-6.5
	3.	-6.3
	4.	-6.1
	5.	-6.1
	6.	-6.1
	7.	-6.0
	8.	-6.0
	9.	-6.0

		
Ombuin 	1. 2. 3. 4. 5. 6. 7. 8. 9.	-8.9 -8.2 8.1 -8.0 -7.9 -7.8 -7.7 -7.5 -7.5
Rhamnetin 	1. 2. 3. 4. 5. 6. 7. 8. 9.	-10.6 -9.0 -8.6 -8.6 -8.5 -8.4 -8.3 -8.1 -8.1
Rutin	1. 2. 3. 4. 5. 6. 7. 8. 9.	-11.0 -10.6 -10.4 -10.4 -9.6 -9.6 -9.5 -9.4 -9.4

		
Stigmasterol	1.	-8.5
	2.	-8.4
	3.	-8.2
	4.	-8.2
	5.	-8.1
	6.	-8.0
	7.	-7.9
	8.	-7.9
	9.	-7.9
Tamarixetin	1.	-10.9
	2.	-8.8
	3.	-8.6
	4.	-8.5
	5.	-8.0
	6.	-8.0
	7.	-7.9
	8.	-7.8
	9.	-7.7
Tyramine	1.	-5.8
	2.	-5.6
	3.	-5.6
	4.	-5.5
	5.	-5.3
	6.	-5.2
	7.	-5.2
	8.	-5.1
	9.	-5.0

Results and Discussions

Molecular docking is an attractive scaffold for understanding drug-biomolecular interactions for the purposes of the rational design by placing a molecule (ligand), mainly in a non-covalent manner, on a favoured binding site for a specific DNA/protein region and forming a stable complex of possible effectiveness and specificity. Since molecules have a propensity to be discovered in their lowest form of energy, the energy minimization of the ligand was performed using chem draw 3D software. The affinity (Kcal/Mol) data generated by the docking process indicates the complex stability (Table 1). The primary aim of molecular docking is to create ligand receiver complex with optimal conformation and with the aim of having reduced binding free energy. Diclofenac exhibited maximum affinity followed by rutin. Other phytochemicals also exhibited significant binding affinity with the cyclooxygenase -2 receptor. The ligand–receptor interaction sites visualized using discovery studio showed that both hydrogen bonding and hydrophobic interactions play an important role in binding the ligand with the receptor and the screened phytochemicals may act as a powerful inhibitor for cyclooxygenase -2 receptor.

Conclusion

Alhagi pseudalhagi has a range of pharmacologically active secondary metabolites with an array of biological activities such as antioxidant, antiulcer, anti-inflammatory and antifungal. Phenolic compounds have different biological properties [17]. The polar phytochemicals may be responsible for the anti-inflammatory activity especially through cyclooxygenase – 2 inhibition.

Conflict of interest

The authors declare no conflict of interest.

Acknowledgments

Garima Verma is a Ph.D. Research Scholar at IFTM University. Authors are grateful to the IFTM University, Moradabad; Rameesh Institute of Vocational and Technical education, Greater Noida and Galgotias University, Gautam Buddh Nagar for providing the necessary facilities for carrying out this research.

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