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Molecular Docking Analysis of Bergenin and 11-o-gallyl Bergenin from *Mallotus philippensis* against Anti-oxidant Proteins

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ABSTRACT: One of the critically endangered medicinally significant plants used in traditional systems of medicine is *Mallotus philippensis*, which has the potential for cultivation. It is a significant Ayurvedic medicinal shrub, and the entire plant is loaded with secondary metabolites. The plant's various parts are used to treat conditions like cancer, diabetes, diarrhea, urinogenital infection, bronchitis, abdominal disease, jaundice, malaria, antifungals, tape-worms, and eye disease. Additionally, it possesses a variety of pharmacological properties, including antioxidant, antimicrobial, anti-filarial, anti-leukemic, anti-tumor, anti-HIV, and hepatoprotective properties. We aimed in this study to perform molecular docking to two compounds from *Mallotus philippensis* against two anti-oxidant proteins SOD and GPX. The results showed that 11-o-galloylbergenin has a high docking score and binding affinity to both protein receptors as compared to bergenin. The demonstrated biological potentials declared that compounds could be the better natural antioxidant candidate. The resulting data is extremely valuable for phytotherapeutics continued development as a cancer treatment.

Keywords: *Mallotus philippensis,* Molecular docking, SOD, GPX. 11-o-galloylbergenin, bergenin.

INTRODUCTION

India holds a special significance worldwide in the traditional system of medicine and has a rich biodiversity of medicinal and aromatic plants (Mishra, 2011). Due to their biological advantages in the treatment of various diseases, such as their anti-inflammatory and antioxidant properties, medicinal plants have been used throughout history. According to the World Health Organisation, three-quarters of the world's population still uses medicinal plants; this is due to their affordability and availability, particularly in countries that are developing. Numerous diseases have been successfully treated using medicinal plants, their extracts, or the isolated, purified constituents. Utilizing specific medicinal plant parts like leaves, seeds, stems, bark, flowers, and roots, Ayurveda uses a variety of medicinal preparations to treat both external and internal illnesses. The scavengers of free radicals known as antioxidants can stop, stop, or limit the spread of such damage (Finkel and Holbrook 2000; Knight 1995). The majority of natural products are currently processed and being developed as potential pharmacological agents with powerful antioxidative, antimitotic, anti-infective, anti-inflammatory, antiangiogenic, and anticarcinogenic properties (Ramana *et al.,* 2014).

The Euphorbiaceae family of plants includes the widely used medicinal herb *Mallotus philippensis* (also known as the Kamala tree) (Sharma and Varma 2011). It has long been used as an antioxidant, hepatoprotective, antiviral, antibacterial, anti-inflammatory, and anticancer agent (Kumar *et al*., 2020). Major natural compounds found in this genus include phenols, diterpenoids, steroids, flavonoids, cardenolides, triterpenoids, coumarin, isocoumarin, and many more that are yet to be discovered.

The two organic compounds are bergenin and 11-O-galloylbergenin. In the literature, the biological and pharmacological effects of bergenin have been extensively studied Takahashi *et al*. (2003); Piegen (1980); Jahromi *et al*. (1992); Piacente *et al*. (1996); Pu *et al*. (2002); Zhang *et al.* (2003); Lim *et al.* (2000); Lim *et al*. (2001); Lee *et al*. (2005); Nazir *et al*. (2007); Li *et al.* (2005). However, there hasn't been much research on the biological effects of 11-O-galloylbergenin reported Uddin *et al*. (2014); Arfan *et al*. (2010). Lipid peroxidation can start the oxidation process when ROS are present. To prevent further oxidation processes, the body has a system of intracellular ROS scavengers, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), and others (Lu *et al.,* 2010; Rahman, 2007).

A chemical molecule and a protein, or a protein and a protein, can interact intramolecularly, and this can be predicted by molecular docking (Razak *et al.,* 2021). The main objective of molecular docking was to reactivate the computational process of molecule identification and arrive at an ideal conformation that reduced the free energy of the entire system (Durga *et al.,* 2023). Thus, using *in silico* molecular docking analysis against superoxide dismutase (SOD) and glutathione peroxidase (GPX) as protein targets with the two organic compounds from *Mallotus philippensis*.

MATERIAL AND METHODS

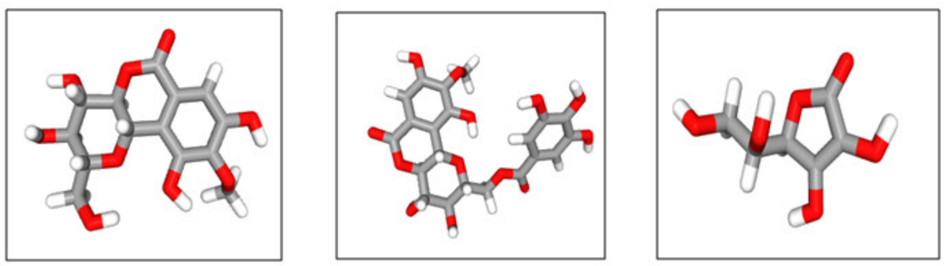
Preparation of Protein and Ligands: The 3D structure proteins SOD (5YTO) and GPX (2F8A) used in the study were retrieved from a protein data bank (https://pdb101.rcsb.org/). The two organic compounds from bergenin and 11-O-galloylbergenin and standard (Ascorbic acid) were downloaded from (https://pubchem.ncbi.nlm.nih.gov/). The water molecules and the other ligands were removed from the protein and pure protein was used for molecular docking. The grid parameters were 40×40×40, spacing 0.375, for GPX (X=-15.155, Y=19.499, Z=27.867) for SOD (X=69.14, Y=80.47, Z=-17.06).

Molecular Docking: The molecular docking of three ligands listed in Table 1 with the two proteins was performed by Autodock vina (Dubey and Pradhan 2021). The visualization was done by using the BIOVIA discovery studio (Fitrilia *et al.,* 2020).

RESULTS AND DISCUSSION

In the present study, we used two compounds along with the standard (ascorbic acid) as ligands with their PubChem IDs shown Fig. 1 and were listed in Table 1. The 3D structure of the two protein were shown in Fig. 2. We investigated the precise intermolecular interactions between the ligand and the target protein using an automated docking program called Auto Dock Vina. The molecular docking results were shown in Table 3 with their interacting residues in Fig. 3 and 4.

From the results obtained, 11-O-galloylbergenin showed (-9.1 Kcal/mol) binding affinity towards SOD and (-7.6 Kcal/mol) binding affinity towards GPX protein, when compared to standard (ascorbic acid) (Khan *et al*., 2016). Suggests that these two compounds have antioxidant and antiplasmodial activity but among these two 11-O-galloylbergenin showed potent activity similar to our results. Hence, it can be used as a drug candidate (Tripathi *et al.,* 2018) review explains that this plant has many medicinal importance in curing several diseases.

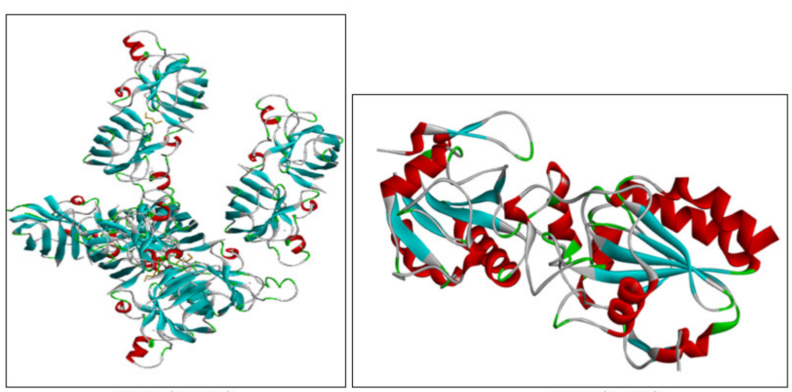


Bergenin 11-o-gallylbergenin Ascorbic acid

Fig. 1. The structure of ligands selected for this study.

Table 1: The list of ligands selected for the study.

Ligand name	Pubchem ID
Bergenin	66065
11-o-gallylbergenin	56680102
Ascorbic acid (Standard)	54670067



SOD (5YTO) GPX (2F8A)

Fig. 2. The pure protein structure of SOD and GPX.

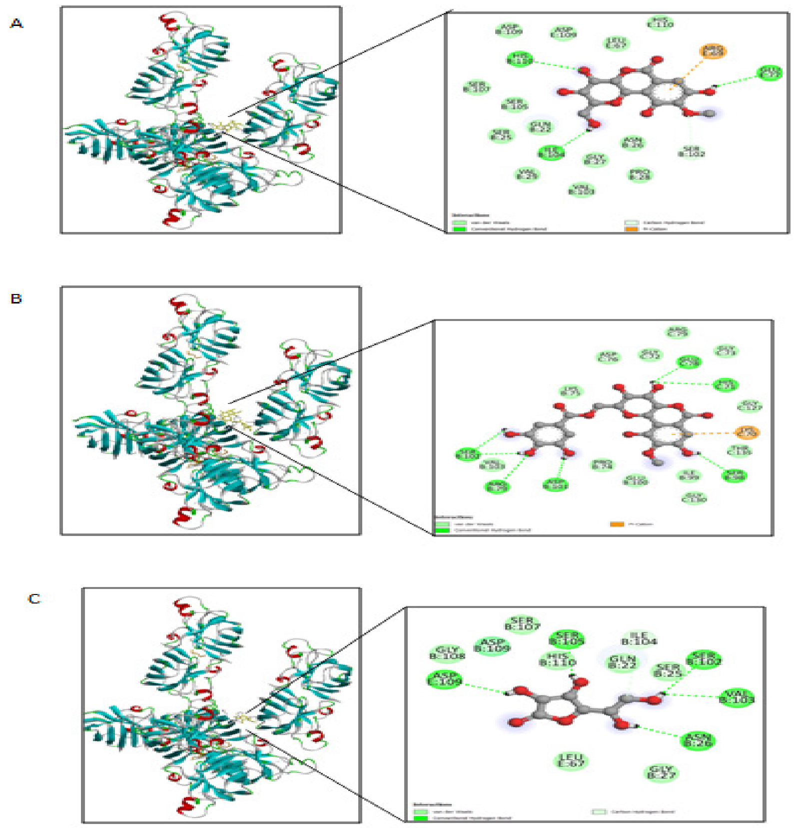


Fig. 3. The SOD protein with ligands A) 66065, B) 5680102, and C) 54670067 with their interacting residues.

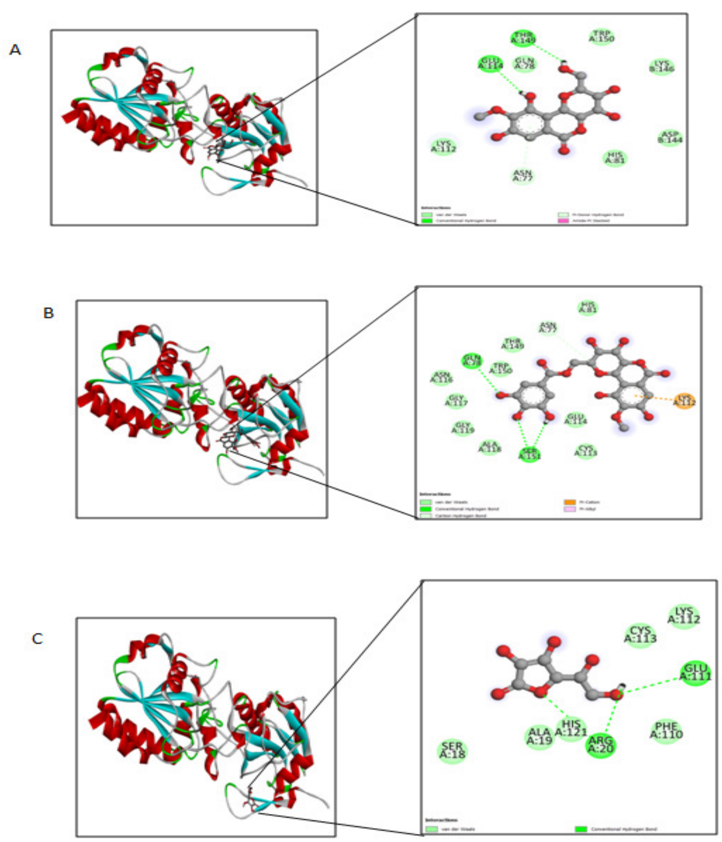


Fig. 4. The GPX protein with ligands A) 66065, B) 5680102, and C) 54670067 with their interacting residues.

Table 2: The proteins with ligands A) 66065, B) 5680102 and C) 54670067 with their docking score and interacting residues.

Protein	Ligand name	Docking score (Kcal/mol)	Interacting Residues
SOD(5YTO)	Bergenin	**-7.5**	ASP 109, LEU 67, HIS 110, ARG 69, GLU 77, SER102, SER107, ASN 26, PRO 28, VAL 103, GLY 27, ILE 104, VAL 29, SER 25, GLN 22 AND SER 105.
	11-o-gallylbergenin	-9.1	ASP 76, GLY 72, GLU 78, GLY 73, HIS 71, GLY 121, LYS 70, THR 135, SER 98, ILE 99, GLY 130, GLU 100, PRO 74, ASP 101, VAL 103, SER 102 AND LYS 75.
	Ascorbic acid (Standard)	-6.3	ASP 109, SER 105, HIS 110, GLN 22, SER 25, SER 102, VAL 103, ASN 26, GLY 27, LEU 67, SER 107 AND GLY 108.
GPX(2F8A)	Bergenin	-6.0	THR 249, TRP 150, LYS 146, ASP 144, GLN 78, GLU 514, ASN 77AND LYS 112.
	11-o-gallylbergenin	-7.6	HIS 81, LYS 112, GLU 114, CYS 113, SER 151, ALA 118, GLY 219, GLY 117, ASN 116, GLN 78, TRY 150, THR 149 AND ASN 77
	Ascorbic acid (Standard)	-4.3	ALA 19, HIS 121, ARG 20, PHE 110, GLU 111, CYS 113, LYS 112 AND SER 18.

CONCLUSIONS

In the present study, two biologically active compounds from *M. philippensis* were Bergen in and 11-O-galloylbergenin. Therefore, it is concluded that the isolated compounds' proven medicinal properties could be used as building blocks for the creation of advanced natural products and may be crucial for the development of new drugs.

FUTURE SCOPE

The presence of a variety of bioactive chemicals supports the effectiveness of how traditional healers have used plant parts to treat a variety of diseases. These Compounds can be isolated and further *in-vitro* studies will be carried out.

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Conflict of Interest. None.

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