



[Science Archives \(ISSN:2582-6697\)](http://www.sciencearchives.org)

Journal homepage: www.sciencearchives.org



<https://doi.org/10.47587/SA.2022.3403>

Research Article



Molecular docking of putative phytochemicals in aqueous *Moringa oleifera* leaf extracts with three cytochrome P450 enzyme involved in xenobiotic metabolism

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Received: Oct 9, 2022/ Revised: Nov 11, 2022/ Accepted: Nov 14, 2022

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Abstract

The Indian plant *Moringa oleifera* is found in tropical and subtropical climates across the globe. It is frequently cultivated for its embryonic seed pods and leaves, that are consumed as vegetables and also for herbal remedies. Using *in silico* computational techniques and three CYP450 enzymes, this study assessed the potential hepatoprotective effects of probable metabolites in watery *M. oleifera* leaf extracts. All quantities of aqueous *M. oleifera* leaf extract were subjected to several qualitative phytochemical analyses. The flavonoid galangin demonstrated the strongest interactions with the majority of cytochrome P450 enzymes in accordance with the predicted binding affinity, followed by caffeic acid. Galangin also outperformed the bulk of other known CYP450 enzyme inhibitors. These results suggest that the hepatoprotective effects of *M. oleifera* leaf extract on CYP450 may be due to galangin. In comparison to galangin and caffeine acid, two reference substances, 1H-indazole, and alpha-naphthoflavone, were shown to have energy values with all three receptors between -4.6 and -4.8. The *in silico* screening data showed that when docked to CYP1A2, CYP2E1, and CYP2D6, all compounds had a greater binding affinity. Therefore, additional studies are necessary to support these findings.

Keywords: CYP450 enzymes, Galangin, Enzyme inhibitors, Caffeine acid, Binding affinity

Introduction

The Indian plant *Moringa oleifera* is found in tropical and subtropical climates across the globe. It is frequently cultivated for its embryonic seed pods and leaves, which are consumed as vegetables and also for herbal remedies (Au et al., 2011). Due to the great nutritive value of each part of the tree, it can be used for mainly commercial or medicinal purposes. The leaves, seeds, and all parts are full of important compounds, vitamins, and minerals. It is utilized as potent pharmacological agent for microbiological, anticancer, anti-inflammatory, including anti-inflammatory functions (Asrani et al., 2019; Melo et al., 2017). Phytosterols like stigmasterol, sitosterol, and kampesterol, which are hormone precursors, are abundant in moringa (Kerr et al., 2012). The synthesis of oestrogen is increased by these substances (Arooj et al., 2013). Among the several elements found in moringa that are crucial for growth and development, calcium is regarded as one of the key minerals for human growth (Azam et al., 2013). Because *M. oleifera* is natural, dependable, and safe in known quantities, it can be employed as an antitumor agent

(Balimane et al., 2000). According to reports, moringa can act as an anti-neoproliferative agent, which prevents cancer cells from proliferating (Beaulieu et al., 1999; Beeching et al., 2014). Numerous investigations have shown that it has impacts on immunological response, antioxidant defence, cytotoxicity, antibacterial defence, antiproliferative defence, antiplatelet aggregation defence, antihypertensive defence, cardioprotective defence, anti-inflammatory defence, and mineral homeostasis defence (Benet et al., 2002; Bissantz et al., 2000; Gasteiger et al., 1998).

A family of monooxygenase enzymes known as cytochrome P450 (CYPs) enzymes is in charge of the oxidative metabolism of xenobiotics as well as lipophilic medicines (Irvine et al., 1999). These enzymes are critical for the elimination of many substances, as well as for the production and breakdown of hormones (Sarkar et al., 2022). In mammals, they oxidise steroids, fatty acids, and xenobiotics (Sarkar, 2021). The active site of cytochrome P450 seems to have a heme-iron cluster. The iron is bonded to the protein via a cysteine thiolate partner. Human CYPs are generally

membrane associated proteins which found in the endoplasmic reticulum of cells or in the inner membrane of mitochondria (Loprinzi et al., 2011).

Numerous endogenous and exogenous substances are metabolised by CYPs. The primary enzymes involved in drug metabolism are CYPs. Since variations in CYP enzyme activity potentially impact the metabolism as well as clearance of many medications, effects on CYP isozyme activity are a primary cause of unfavourable treatment options. Natural substances can also stimulate or inhibit CYP activity (Sarkar et al., 2022). The highest range of drug biotransformation is demonstrated by the CYP450 enzymes CYP3A4 and CYP2D6 which metabolise over than 50% of therapeutically used medicines. Each member of the CYP450 family is specialised in the metabolization of particular classes of medications. CYP2E1, CYP1A2, CYP2D6, and CYP3A4 are the four main enzymes in the CYP450 system that break down acetaminophen in the liver (Ramalingam et al., 2011; Roe et al., 2013). The primary enzyme involved in the metabolism of acetaminophen, CYP2E1, comprises between 30 to 78% (Wadapurkar et al., 2018). Using in silico computational techniques and three CYP450 enzymes, this study assessed the potential hepatoprotective effects of probable metabolites in watery *M. oleifera* leaf extracts.

Materials and methods

Collection and drying of plants

Fresh *M. oleifera* leaves were procured in a nearby Howrah location. Young leaves were cleaned with water to eliminate dust and debris. They were crushed, weighed, and stored in airtight jar coated with plastic bags and silica desiccants after being air-dried until brittle undercover. They were kept out of direct sunlight in a cold, dry atmosphere (Morris et al., 2009; Sarkar, 2022).

Leaf extract preparation and storage

The aqueous leaf extract preparation procedure was largely modified from prior work. Four concentration was prepared (%w/v). For this, 10, 20, 40, and 100 mg of dry *M. oleifera* leaf were dissolved in 1L of dH₂O and therefore 1%, 2%, 4%, and 10% (%w/v) concentrations were created. They were separated into individual amber bottles and steeped in boiling water for 5 minutes with periodic shaking. They were then allowed to soak for 24 hours, filtered, and stored at 4°C until use (Sarkar et al., 2023; Rothman et al., 2008).

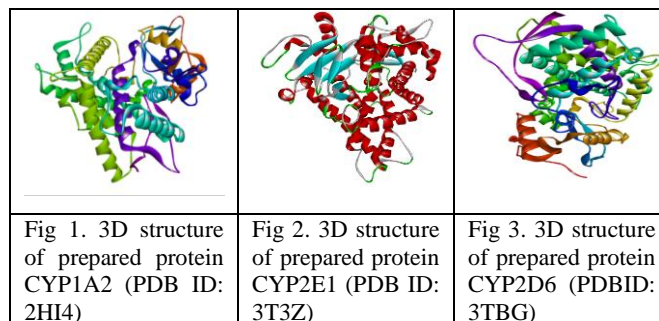
Screening of phytochemicals from the extract

Qualitative phytochemical analysis for proteins, carbohydrates, and secondary metabolites including phenols,

tannins, flavonoids, alkaloids, and saponins was performed at the Department of Physiology Laboratory, University of Kalyani, Kalyani, Nadia, West Bengal, India. The methodology was adapted from earlier research (Nas et al., 2021; Yoon et al., 2016).

Molecular docking study

Following the collection of the data from the phytochemical analysis, a bibliographic study was carried out to pinpoint particular probable phytochemical components found in aqueous *M. oleifera* leaf extract. The three-dimensional structures of these phytonutrients were derived PubChem database. Protein Data Bank was used to obtained 3D structure of 3 different cytochrome P450 enzymes and these were CYP2E1 (PDB ID: 3T3Z), CYP1A2 (PDB ID: 2HI4), and CYP2D6 (PDBID: 3TBG). These 3 were selected because prior research has linked them to hepatotoxicity. The AutoDock Tools v1.5.6 programme was used for in silico molecular docking (Grant, 1991; Alsenz et al., 1998). Here first we uploaded protein structure and then one by one all selected bioactive compounds (ligand). Software after minimized ligand energy converted it into pdbqt format. Started docking after creating a grid box to screen best fitted bioactive compounds based on negative energy value, resulting in 10 docked conformations. Intra-molecular associations such as hydrogen bonds, van der Waals contacts, plus hydrophobic correlations with such an individual bioactive molecule have really been clearly examined using Discovery Studio software.



Results and discussion

Different qualitative phytochemical assays were conducted on all aqueous *M. oleifera* leaf extract concentrations, and the results are shown in Table 1. Results for phenols, tannins, saponins, alkaloids, and flavonoids were all found +ve. Positive outcomes showed a change in the colour of the precipitation, the solution, or both (Yang et al., 2012). The outcomes also demonstrate that the identified phytochemicals were unaffected by the different *M. oleifera* leaf extract concentrations.

Table 1. Phytochemical analysis of *M. oleifera* leaf extract at various concentration

SI No	Test of Phytochemicals	Name of the compounds	<i>M. oleifera</i> leaf extract 1%	<i>M. oleifera</i> leaf extract 2%	<i>M. oleifera</i> leaf extract 3%	<i>M. oleifera</i> leaf extract 4%
1	Iodine test for starch	Starch	-ve	-ve	-ve	-ve
2	Fehling test	Reducing sugar	+ve	+ve	+ve	+ve
3	Molisch test	Carbohydrates	+ve	+ve	+ve	+ve
4	Ninhydrin test	Ammonia	+ve	+ve	+ve	+ve
5	Biuret test	Protein	-ve	-ve	-ve	-ve
6	5% FeCl ₃ test	Phenols	+ve	+ve	+ve	+ve
7	10% FeCl ₃ test	Tannins	+ve	+ve	+ve	+ve
8	Foam layer test	Saponins	+ve	+ve	+ve	+ve
9	Mayer test	Alkaloids	+ve	+ve	+ve	+ve
10	Lead Acetate test	Flavonoids	+ve	+ve	+ve	+ve

The bioavailability of oral medications is evaluated using Lipinski's Rule of Five utilizing the molecular weight, log P value, and quantity of acceptors and donors of H-bonds (Pu et al., 2015; Basheer et al., 2015). As can be shown in Table 2, none of the examined phytochemicals specifically broke any rules. Their molecular weights ranged from 154.12 to 270.24

(g/mol). The range of log P values was 0.7–2.3. They had between three and four H-bond donors and between four and five H-bond acceptors. Quinidine (PubChem CID: 441074) and alpha-Naphthoflavone (PubChem CID: 11790) were used as controls.

Table 2. ADMET prediction of all studied phytochemicals

SL No	Phytomolecule with Chemical formula and PubChem ID	Molecular Wt (g/mol)	No of H acceptor	No of H donor	Log P _{o/w}	Log S	Lipinski violation
1	Protocatechulic Acid C ₇ H ₆ O ₄ ID 72	154.12	4	3	0.65	-1.86	0
2	Gallic Acid C ₇ H ₆ O ₅ ID 370	170.12	5	4	0.21	-1.64	0
3	Methyl Gallate C ₈ H ₈ O ₅ ID 7428	184.15	5	3	0.57	-1.73	0
4	Caffeic Acid C ₉ H ₈ O ₄ ID 689043	180.16	4	3	0.93	-1.89	0
5	Galangin C ₁₅ H ₁₀ O ₅ ID 5281616	270.24	5	3	1.99	-3.46	0
6	1H-Indazole C ₇ H ₆ N ₂ ID 9221	118.14	1	1	1.60	-2.72	0
7	Alpha- Naphthoflavone C ₁₉ H ₁₂ O ₂ ID 11790	272.30	3	0	4.09	-5.20	0

CYP2E1, CYP1A2, and CYP2D6 docking scores with number of hydrogen bonds and interacting residues for suspected *M. oleifera* leaf extract phytoconstituents and known Cytochrome P450 inhibitors were displayed in Table 3. Fig. 4 to 24 indicates 3D and 2D diagram of molecular docking between all putative compounds with CYP2E1, CYP1A2, and CYP2D6 respectively. There were detectable amounts of phenols, tannins, saponins, alkaloids, and flavonoids in the aqueous *M. oleifera* leaf extract. In a comparable experiment, ethanolic and methanolic *M. oleifera* leaf extract extracts were performed to check present similar phytoconstituents or not.

The phytoconstituents classes found in the leaf extracts matched those in the aqueous *M. oleifera* leaf extract. Additionally, they stated that the preparations contained glycosides and sterols, saponins, tannins, triterpenes, steroids, as well as flavonoids. All of these, nevertheless, were not examined in this investigation. Such studies have emphasized the value and significance of secondary plant metabolites, especially those from the phenol and flavonoid groups (Tsai et al., 2015). We looked through numerous online journal papers about *M. oleifera* leaf extract to determine the possible identities of the compounds (Sansen et al., 2007; Sevrioukova et al., 2017). These investigations, however, were restricted to isolating particular phenols, flavonoids, and triterpenes.

Triterpenes were not found in the extract, according to the qualitative phytochemical test results, hence they were not included in the subsequent experiment. The list was further trimmed down to only include substances extracted by aqueous means. The alleged compounds contained four phenols: Caffeic acid, methyl gallate, and gallic acid, protocatechuic acid and one flavonoid (Galangin). Every single enzyme used in the study are members of the cytochrome P450 family. Protocatechuic acid (PCA) has anti-inflammatory and antioxidant properties. Gallic Acid is a phenolic acid. Methyl gallate also is a phenolic chemical and it is gallic acid's methyl ester. A chemical substance known as caffeine is categorised as a hydroxycinnamic acid. A flavonoid called galangin is a flavonol. The Gibbs free energy, which gives information regarding the stability of the crystal docked form, is represented by the docking score that was reported (Sevrioukova et al., 2013; Porubsky et al., 2008).

The lower the docking value, the lower the free energy, and the higher the affinity for binding between the protein and the ligand. In this investigation energy range was found in between - 5.8 to -7.1 Kcal/mol (Table 3). Galangin showed the highest interaction score (-7.1 Kcal/mol) with CYP1A2 and CYP2D6 (Table 3, Fig. 16, 18). Covalent bonds, conventional hydrogen bonds, Alkyl, and van der Waals bonding were found there. The second highest interaction (-6.0 Kcal/mol) was found for Caffeic Acid with CYP1A2 (Table 3, Fig. 13). Van der Waals, conventional hydrogen bonds, Pi-sulfur, Pi-Sigma, and covalent bonds were found to be involved in this interaction. Two reference compounds 1H-Indazole and Alpha- Naphthoflavone found to have energy values with all three receptors between -4.6 to -4.8 which is much lower than Galangin and Caffeic Acid (Table 3). All substances displayed a higher binding affinity when docked to CYP1A2, CYP2E1, and CYP2D6, according to the *in silico* screening data.

Table 3. Overview of results for CYP proteins and respective ligand binding with the binding affinity and number of residues in interaction as well as number of hydrogen bond involved in the interaction

SL No	Phytomolecule with Chemical formula and PubChem ID	Docking enzyme	Binding affinity (Kcal/mol)	Interaction residues	No. of H bonds	Bonds involved in interaction	Fig. No
1	Protocatechulic Acid C ₇ H ₆ O ₄ ID 72	CYP1A2	-5.8	Leu 475, Ile 474, Leu 347, Gln 478, Arg 356, Pro 357, Arg 355, Arg 353, Phe 512, Leu 476, Leu 479, Ala 473, Leu 472	4	Van der Waals, conventional hydrogen bond, carbon hydrogen bond, covalent bond	4
		CYP2E1	-5.5	Glu 241, Asn 238, Asn 206, Glu 205, Tyr 201, Asn 204, Arg 198, Phe 203, Leu 199, Met 200, Val 242	3	Van der Waals, conventional hydrogen bond, Alkyl, Covalent bond	5
		CYP2D6	-5.5	Glu 346, Gly 348, Phe 454, Ala 351, Met 353, Thr 357, His 352, Met 347, Asp 349	3	Van der Waals, conventional hydrogen bond, covalent bond	6
2	Gallic Acid C ₇ H ₆ O ₅ ID 370	CYP1A2	-5.8	Lys 170, leu 470, Glu 163, Leu 161, Glu 162, Glu 163, His 164, Lys 167, Glu 168, Val; 165, Ala 169	2	Van der Waals, conventional hydrogen bond, covalent bond	7
		CYP2E1	-5.8	Glu 241, Asn 238, Asn 206, Glu 205, Tyr 201, Asn 204, Arg 198, Phe 203, Leu 199, Met 200, Val 242,	3	Van der Waals, conventional hydrogen bond, covalent bond, Alkyl	8
		CYP2D6	-5.5	Gly 348, Met 347, Gln 350, Asp 349, His 352, Met 353,	1	Van der Waals, conventional hydrogen bond, covalent bond	9

3	Methyl Gallate C ₈ H ₈ O ₅ ID 7428	CYP1A2	-5.9	Tyr 189, Val 192, Val 193, Val 196, Phe 319, Thr 321, Val 322, Thr 324, Asp 320, Ile 326, ala 325, Ser 327		Van der Waals, conventional hydrogen bond, covalent bond, carbon hydrogen bond	10
		CYP2E1	-5.8	Arg 198, Phe 179, Leu 170, Leu 202, Leu 197, Leu 199, Met 200, Asn 204, Glu 205, Lys 234	2	Van der Waals, conventional hydrogen bond, Pi-Cation, covalent bond	11
		CYP2D6	-5.9	Leu 448, Glu 150, Leu 149, Val 153, Met 347, Phe 454, Leu 455, Phe 456, Leu 453, Glu 452, Arg 450, Pro 442, Ala 449	4	Van der Waals, conventional hydrogen bond, Alkyl, covalent bond	12
4	Caffeic Acid C ₉ H ₈ O ₄ ID 689043	CYP1A2	-6.0	Leu 144, ala 464, Leu 463, Val 462, Glu 461, Cys 458, Ile 459	3	Van der Waals, covalent bond, conventional hydrogen bonds	13
		CYP2E1	-5.9	Lys 234, Arg 198, Phe 170, Leu202, Leu 197, Leu 199, Met 200, Phe 203, Asn 204, Glu 205	2	Van der Waals, conventional hydrogen bond, Pi-cation, covalent bond	14
		CYP2D6	-5.5	Leu 149, Glu 150, Val 153, Met 347, Phe 454, Leu 455, Phe 456, Leu 453, Arg 450, Pro 447, Ala 449	4	Van der Waals, conventional hydrogen bond, Alkyl, Covalent bond	15
5	Galangin C ₁₅ H ₁₀ O ₅ ID 5281616	CYP1A2	-7.1	Lys 170, Ala 169, Arg356, Pro 357, Phe 471, Leu 472, Leu 470, Ala 473, Gln 478, Gln 477, Leu 475, Leu 476, Ile 173	3	Covalent bond, conventional hydrogen bond, Alkyl, van der Waals	16
		CYP2E1	-6.0	Arg 194, Phe 170, Leu 202, Leu 197, Leu 199, Met 200, Phe 203, Asn 204, Glu 205, Lys 234	2	Van der Waals, conventional hydrogen bond, Pi-Cation, covalent bond	17
		CYP2D6	-7.1	Ser 459, Thr 356, Gln 350, Asp 349, Pro 345, Glu 346, Met 353, Met 347, Ile 360, Leu 455, Arg 450, Met 451, Glu 452, Leu 453, Phe 456	3	Van der Waals, conventional hydrogen bond, Pi-sulfur, Pi-Sigma, covalent bond	18
6	1H-Indazole C ₇ H ₆ N ₂ ID 9221	CYP1A2	-4.8	Arg 511, Ile 173, Gln 427, Arg 353, Arg 356, Leu 475, Leu 476, Ile 474, Arg 510, Leu 479, Phe 512	4	Van der Waals, conventional hydrogen bond, carbon hydrogen bond, covalent bond	19
		CYP2E1	-4.8	Leu 189, Val 185, Val 153, Met 451, Glu 452, Arg 450, Ala 449, Pro 447, Gly 445, Glu 446, Leu 149, Leu 139, Leu 189	3	Van der Waals, Conventional hydrogen bond, Alkyl, covalent bond	20

		CYP2D6	-4.8	Arg 198, Phe 170, Leu 202, Leu 197, Leu 199, Met 200, Phe 203, Asn 204, Glu 205, Lys 234	2	Van der Waals, conventional hydrogen bond, Pi-Cation, Covalent bond	21
7	Alpha-Naphthoflavone C ₁₉ H ₁₂ O ₂ ID 11790	CYP1A2	-4.8	Arg 511, Ile 173, Gln 477, Arg 353, Arg 356, Leu 475, Ile 474, Leu 476, Arg 510, Phe 512, Leu 479	4	Van der Waals, conventional hydrogen bond, covalent bond, carbon hydrogen bond	22
		CYP2E1	-4.6	Asp 349, arg 343, Ile 339, Gly 340, Glu 334, Asp 337, Asp 336, Ile 335, Met 353, His 352	3	Van der Waals, conventional hydrogen bond, Alkyl, covalent bond	23
		CYP2D6	-4.8	Arg 198, Phe 170, Leu 202, Leu 197, Leu 199, Met 200, Phe 203, Asn 204, Glu 205, Lys 234	2	Van der Waals, conventional hydrogen bond, covalent bond, Pi-Cation	24

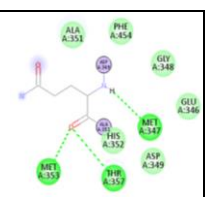
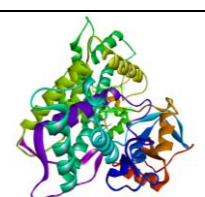
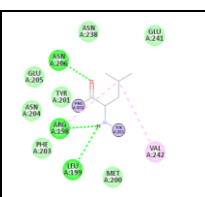
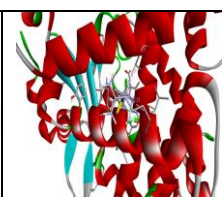
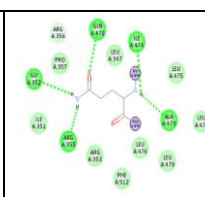
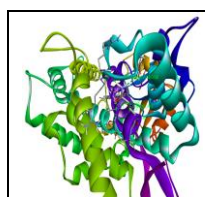


Fig 4. 3D and 2D interaction between Protocatecholic Acid with CYP1A2

Fig 5. 3D and 2D interaction between Protocatecholic Acid with CYP2E1

Fig 6. 3D and 2D interaction between Protocatecholic Acid with CYP2D6

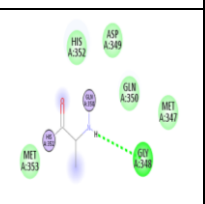
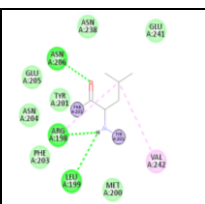
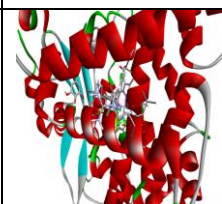
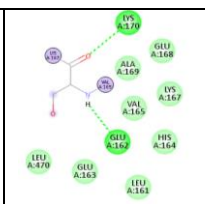
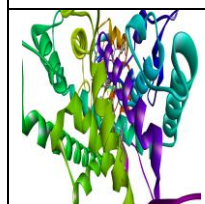


Fig 7. 3D and 2D interaction between Gallic Acid with CYP1A2

Fig 8. 3D and 2D interaction between Gallic Acid with CYP2E1

Fig 9. 3D and 2D interaction between Gallic Acid with CYP2D6

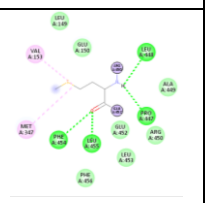
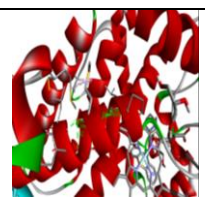
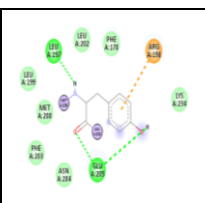
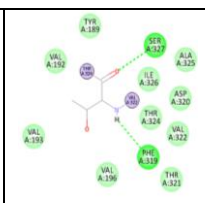
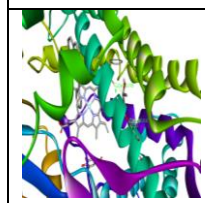


Fig 10. 3D and 2D interaction between Methyl Gallate with CYP1A2

Fig 11. 3D and 2D interaction between Methyl Gallate with CYP2E1

Fig 12. 3D and 2D interaction between Methyl Gallate with CYP2D6

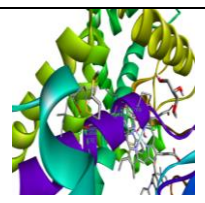
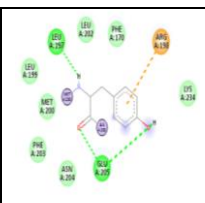
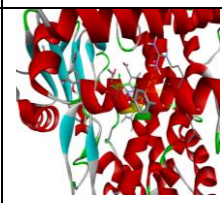
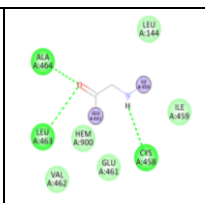
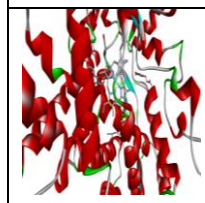


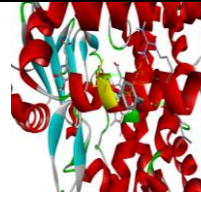
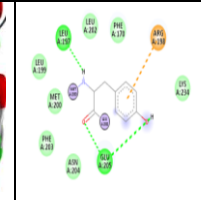
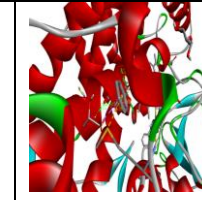
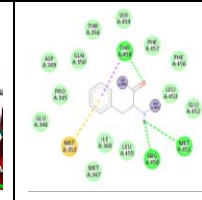
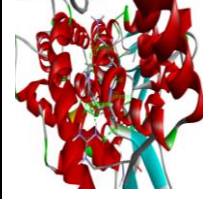


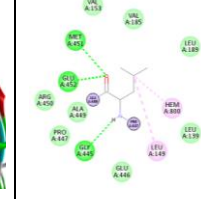
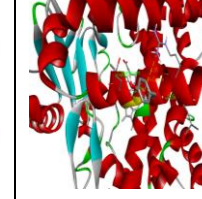
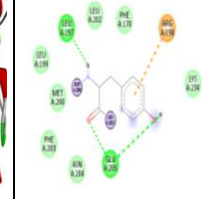


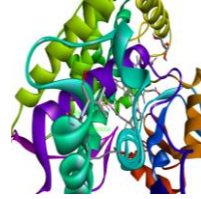
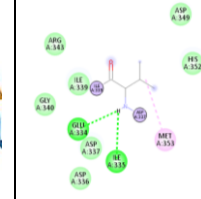
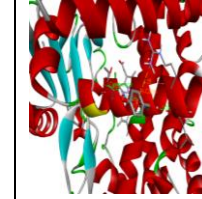
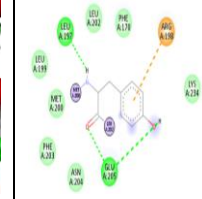


Fig 13. 3D and 2D interaction between Caffeic Acid with CYP1A2

Fig 14. 3D and 2D interaction between Caffeic Acid with CYP2E1

Fig 15. 3D and 2D interaction between Caffeic Acid with CYP2D6

					
Fig 16. 3D and 2D interaction between Galangin with CYP1A2		Fig 17. 3D and 2D interaction between Galangin with CYP2E1		Fig 18. 3D and 2D interaction between Galangin with CYP2D6	
					
Fig 19. 3D and 2D interaction between 1H-Indazole with CYP1A2		Fig 20. 3D and 2D interaction between 1H-Indazole with CYP2E1		Fig 21. 3D and 2D interaction between 1H-Indazole with CYP2D6	
					
Fig 22. 3D and 2D interaction between Alpha-Naphthoflavone with CYP1A2		Fig 23. 3D and 2D interaction between Alpha-Naphthoflavone with CYP2E1		Fig 24. 3D and 2D interaction between Alpha-Naphthoflavone with CYP2D6	

Conclusion

All quantities of aqueous *M. oleifera* leaf extract were subjected to several qualitative phytochemical analyses. The flavonoid galangin demonstrated the strongest interactions with the majority of cytochrome P450 enzymes in accordance with the predicted binding affinity, followed by caffeic acid. Galangin also outperformed the bulk of other known CYP450 enzyme inhibitors. These results suggest that the hepatoprotective effects of *M. oleifera* leaf extract on CYP450 may be due to galangin. In comparison to galangin and caffeine acid, two reference substances, 1H-indazole and alpha-naphthoflavone, were shown to have energy values with all three receptors between -4.6 and -4.8. The *in silico* screening data showed that when docked to CYP1A2, CYP2E1, and CYP2D6, all compounds had a greater binding affinity. As a result, additional studies are necessary to validate these results.

Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

Funding support

The author declares that they have no funding support for this study.

References

- Alsenz, J., Steffen, H., Alex, R. (1998). Active apical secretory efflux of the HIV protease inhibitors saquinavir and ritonavir in Caco-2 cell monolayers. *Pharm Res*. 15(3):423-8. doi: 10.1023/a:1011924314899.
- Arooj, M., Sakkiah, S., Kim, S., Arulalapperumal, V., & Lee, K. W. (2013). A combination of receptor-based pharmacophore modeling & QM techniques for identification of human chymase inhibitors. *PLoS One*, 8(4), e63030.
- Asrani, S.K., Devarbhavi, H., Eaton, J., Kamath, P.S. (2019). Burden of liver diseases in the world. *J Hepatol*. 70(1):151-71. doi: 10.1016/j.jhep.2018.09.014.
- Au, J.S., Navarro, V.J., Rossi, S. (2011). Review article: Drug-induced liver injury—its pathophysiology and evolving diagnostic tools. *Aliment Pharmacol Ther*. 34(1):11-20. doi: 10.1111/j.1365-2036.2011.04674.x.
- Azam, S. S., & Abbasi, S. W. (2013). Molecular docking studies for the identification of novel melatoninergic inhibitors for acetylserotonin-O-methyltransferase using different docking routines. *Theoretical Biology and Medical Modelling*, 10(1), 1-16.
- Balimane, P. V., Chong, S., & Morrison, R. A. (2000). Current methodologies used for evaluation of intestinal permeability and absorption. *Journal of pharmacological and toxicological methods*, 44(1), 301-312.
- Basheer, L., Kerem, Z. (2015). Interactions between CYP3A4 and dietary polyphenols. *Oxid Med Cell Longev*. 015:854015. doi: 10.1155/2015/854015.
- Beaulieu, D., & Ohemeng, K. A. (1999). Patents on bacterial tRNA synthetase inhibitors: January 1996 to March 1999. *Expert Opinion on Therapeutic Patents*, 9(8), 1021-1028.
- Beeching, N. J., Fenech, M., & Houlihan, C. F. (2014). Ebola virus disease. *BMJ* 349: g7348.
- Benet, L. Z., & Hoener, B. A. (2002). Changes in plasma protein binding have little clinical relevance. *Clinical Pharmacology & Therapeutics*, 71(3), 115-121.
- Bissantz, C., Folkers, G., & Rognan, D. (2000). Protein-based virtual screening of chemical databases. 1. Evaluation of different docking/scoring combinations. *Journal of medicinal chemistry*, 43(25), 4759-4767.

- Gasteiger, J., & Marsili, M. (1980). Iterative partial equalization of orbital electronegativity—a rapid access to atomic charges. *Tetrahedron*, 36(22), 3219-3228.
- Grant, D.M. (1991). Detoxification pathways in the liver. *J Inherit Metab Dis*. 14(4):421-30. doi: 10.1007/BF01797915.
- Irvine, J. D., Takahashi, L., Lockhart, K., Cheong, J., Tolan, J. W., Selick, H. E., & Grove, J. R. (1999). MDCK (Madin–Darby canine kidney) cells: a tool for membrane permeability screening. *Journal of pharmaceutical sciences*, 88(1), 28-33.
- Kerr, T. A., Davidson, N. O. (2012). Cholesterol and NAFLD: Renewed focus on an old villain. *Hepatology (Baltimore, Md.)*; (v):56(5):1995.
- Loprinzi, C. L., Barton, D. L., & Qin, R. (2011). Nonestrogenic management of hot flashes. *Journal of Clinical Oncology*, 29(29), 3842-3846.
- Melo, A. P. S., França, E. B., Malta, D. C., Garcia, L. P., Mooney, M., Naghavi, M. (2017). Mortality due to cirrhosis, liver cancer, and disorders attributed to alcohol use: Global Burden of Disease in Brazil, 1990 and 2015. *Rev Bras Epidemiol*. 20 Suppl(Suppl 01):61-74. doi: 10.1590/1980-5497201700050006.
- Morris, G. M., Huey, R., Lindstrom, W., Sanner, M. F., Belew, R. K., Goodsell, D. S., & Olson, A. J. (2009). AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. *Journal of computational chemistry*, 30(16), 2785-2791.
- Nas, J. S., Sanchez, A., Bullago, J.C., Fatalla, J.K., Gellecanao, Jr. F. (2021). Molecular interactions of cyanidin-3-glucoside with bacterial protein S modulate the virulence of selected pathogens in *Caenorhabditis elegans*. *Asian J Biol Life Sci*. 10(1):150-8. doi: 10.5530/ajbls.2021.10.22.
- Porubsky, P. R., Meneely, K. M., Scott, E. E. (2008). Structures of human cytochrome P-450 2E1. Insights into the binding of inhibitors and both small molecular weight and fatty acid substrates. *J Biol Chem*. 283(48):33698-707. doi: 10.1074/jbc.M805999200. 18818195.
- Pu, Q. H., Shi, L., Yu, C. (2015). Time-dependent inhibition of CYP3A4 by gallic acid in human liver microsomes and recombinant systems. *Xenobiotica*. 45(3):213-7. doi: 10.3109/00498254.2014.973470.
- Ramalingam, S., Babu, P. D. S., Periandy, S., & Fereyduni, E. (2011). Vibrational investigation, molecular orbital studies and molecular electrostatic potential map analysis on 3-chlorobenzoic acid using hybrid computational calculations. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, 84(1), 210-220.
- Roe, D. R., & Cheatham III, T. E. (2013). PTRAJ and CPPTRAJ: software for processing and analysis of molecular dynamics trajectory data. *Journal of chemical theory and computation*, 9(7), 3084-3095.
- Rothman, R. B., Baumann, M. H., Prisinzano, T. E., & Newman, A. H. (2008). Dopamine transport inhibitors based on GBR12909 and benzotropine as potential medications to treat cocaine addiction. *Biochemical pharmacology*, 75(1), 2-16.
- Sansen, S., Yano, J. K., Reynald, R. L., Schoch, G. A., Griffin, K. J., Stout, C. D., et al. (2007). Adaptations for the oxidation of polycyclic aromatic hydrocarbons exhibited by the structure of human P450 1A2. *J Biol Chem*. 282(19):14348-55. doi: 10.1074/jbc.M611692200.
- Sarkar, D. (2021). Molecular Docking study to Identify Potent Fungal Metabolites as Inhibitors against SARS-CoV-2 Main Protease Enzyme. *Int J Pharm Sci*.12(2), b78-85 <http://dx.doi.org/10.22376/ijpbs.2021.12.2.b78-85>
- Sarkar, D. (2022). In-silico research to screen various phytochemicals as potential therapeutics against beta glucan synthase enzyme from black fungus endangering COVID patients in India. *Intern. J. Zool. Invest*. 8(1): 320-337 <https://doi.org/10.33745/ijzi.2022.v08i01.035>
- Sarkar, D., Ganguly, A. (2022). Molecular Docking Studies with Garlic Phytochemical Constituents To Inhibit The Human EGFR Protein For Lung Cancer Therapy. *Int J Pharm Sci*.13(2), B1-14 <http://dx.doi.org/10.22376/ijpbs.2022.13.2.b1-14>.
- Sarkar, D., Maiti, A. K. (2023). Virtual Screening and Molecular Docking Studies with Organosulfur and Flavonoid Compounds of Garlic Targeting the Estrogen Receptor Protein for the Therapy of Breast Cancer. *13(1)*, 2023, 49 <https://doi.org/10.33263/BRIAC.131.049>
- Sarkar, D., Maiti, A. K., Rawaf, A., Babu, J. (2022). In silico Approach to Identify Potent Bioactive Compounds as Inhibitors against the Enoyl-acyl Carrier Protein (acp) Reductase Enzyme of Mycobacterium tuberculosis. *12(5)*, 7023–7039. <https://doi.org/10.33263/BRIAC.125.70237039>
- Sevrioukova, I. F. (2017). High-level production and properties of the cysteine-depleted cytochrome P450 3A4. *Biochemistry*. 56(24):3058-67. doi: 10.1021/acs.biochem.7b00334.
- Sevrioukova, I. F., Poulos, T. L. (2013). Understanding the mechanism of cytochrome P450 3A4: Recent advances and remaining problems. *Dalton Trans*. 42(9):3116-26. doi: 10.1039/c2dt31833d.
- Tsai, M. S., Chien, C. C., Lin, T. H., Liu, C.C., Liu, R. H., Su, H. L. (2015). Galangin prevents acute hepatorenal toxicity in novel propacetamol-induced acetaminophenoverdosed mice. *J Med Food*. 18(11):1187-97. doi: 10.1089/jmf.2014.3328.
- Wadapurkar, R. M., Shilpa, M. D., Katti, A. K. S., & Sulochana, M. B. (2018). In silico drug design for *Staphylococcus aureus* and development of host-pathogen interaction network. *Informatics in Medicine Unlocked*, 10, 58-70.
- Yang, Y., Engkvist, O., Llinàs, A., Chen, H. (2012). Beyond size, ionization state, and lipophilicity: Influence of molecular topology on absorption, distribution, metabolism, excretion, and toxicity for druglike compounds. *J Med Chem*. 55(8):3667-77. doi: 10.1021/jm201548z.
- Yoon, E., Babar, A., Choudhary, M., Kutner, M., Pyrsopoulos, N. (2016). Acetaminophen-induced hepatotoxicity: A comprehensive update. *J Clin Transl Hepatol*. 4(2):131-42. doi: 10.14218/JCTH.2015.00052.

How to cite this article

Sarkar, D. (2022). Molecular Docking of Putative Phytochemicals in Aqueous *Moringa Oleifera* leaf Extracts with Three Cytochrome P450 Enzyme Involved in Xenobiotic Metabolism. *Science Archives*, Vol. 3(4), 255-262. <https://doi.org/10.47587/SA.2022.3403>

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