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CHEMICAL, ANTIOXIDANT AND ANTIBACTERIAL STUDIES OF *Monodora* myristica SEED EXTRACT AND MOLECULAR DOCKING OF THE PROMINENT COMPOUNDS

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ABSTRACT

Petroleum ether extract of the seed endosperms of *Monodora myristica* was subjected to GC/MS analysis and twelve compounds were identified. The compounds were classified as fatty acids (38.897 %), terpenes and terpenoids (29.133 %), salicyclohydrazine (19.626 %), carboxylic acid (8.124 %) flavonoid (2.352 %), benzoic acid ester (1.166 %), and phenolic compound (0.700 %). The extract showed significant antioxidant activities of 72.51 and 96.22 % at minimum and maximum concentrations of 25 and 400 µg/ml, respectively. The antioxidant activity results obtained are comparable to that of vitamin C used as a standard antioxidant agent. The extract also showed antibacterial potency against five strains of bacteria organisms which included *Escherichia coli* (gram-negative), *Klebsiella pneumonia*e (gram-negative), *Shigella flexneri* (gram-negative), *Streptococcus pneumonia* (gram-positive) and *Staphylococcus epidermidis* (gram-positive). The highest inhibition was shown against *S. flexneri* while the lowest inhibition was against *S. pneumoniae*. Gentamicin was used as a standard antibacterial agent and the results showed the extract to be far more efficacious than gentamicin against the bacteria organisms tested. The extract of the seeds of *M. myristica* could be used as antioxidant and antibacterial agent for the treatment of diseases caused by these pathogens as well as diseases mediated by free radicals. Molecular docking simulation showed that all the test compounds gave negative binding affinities which indicated that they were successfully docked to the receptors. The compounds' *in-silico*ADME and drug-likeness predictions demonstrated good pharmacokinetic characteristics, including high blood-brain barrier absorption, oral bioavailability, and water solubility. The results of this study make these compounds much more relevant as viable lead prospects for treating bacteria that are resistant to several drugs. This could aid medicinal chemists and other pharmaceutical specialists in developing and synthesising even more effective drug candidates.

Keywords: *Monodora myristica*; Phytochemicals; GC/MS; Antioxidants; Antibacterials; Molecular docking

INTRODUCTION

Plants remain the greatest source of bioactive compounds which can be developed and used as drugs [1]. The rainforest vegetation of Nigeria is a habitat for a lot of medicinal and economic plants used by the natives and the country at large and there is an increasing effort to harness its therapeutic potentials [2]. One of such plants primarily known for its usage as a spice is *Monodora myristica* Dunal. It is a perennial plant that belongs to the family Annonaceae and mostly found in the evergreen forests of West Africa [3]. It is known as African nutmeg but

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commonly called Efuru (Ehuru) in Eastern Nigeria. The seed has been reported to be used in herbal medicine for the treatment of headache, hypertension and infections while the stem bark is used in the treatment of stomachache, hemorrhoids and eye diseases [4].

Certain diseases such as cardiovascular and inflammatory diseases, cataract and cancer are mediated by free radicals [5]. Antioxidant compounds scavenge free radicals such as peroxide, hydroperoxide or lipid peroxyl and thus reduce the level of oxidative stress and slow or prevent the development of complications associated with oxidative stress-related diseases [6]. These antioxidants prevent free radical induced tissue damage by preventing the formation of radicals, scavenging them, or by promoting their decomposition [4].

It was recently discovered [7] that the *in-silico* method can help in addressing the molecular mechanism of action of small compounds with proteins. Molecular docking and pharmacokinetic (ADME) experiments were conducted on notable *M. myristica* seed compounds to characterize their binding affinity and interactions. These investigations included assessing the "drug-likeness" of the compounds using Lipinski's rule of five.

This research aimed to use GC/MS technique to investigate the chemical constituents of the seed extract of *M. myristica*, to determine its antioxidant and antibacterial efficacies as well as the molecular docking studies of the two most prominent compounds identified in the extract. It should be noteworthy that the use of the seed extract in herbal medicine for the treatment of infections, hypertension and cataract which are mediated by free radicals necessitated a probe into its antibacterial and antioxidant potency.

MATERIALS AND METHODS

Collection of Plant Sample

The seeds of *M. myristica* were bought from Orie-ugba market in Umuahia North, Abia State, Nigeria, in the month of March, 2023. They were identified and authenticated at the Taxonomy Section, Forestry Department, Michael Okpara University of Agriculture, Umudike.

Sample Preparation

The seed endosperms were obtained and washed thoroughly with water and allowed to dry. They were milled using an electric blender and was thereafter stored in an airtight container prior to extraction.

Extraction of Phytochemicals

Soxhlet extraction method was used. 20 g of the pulverized sample was wrapped in a porous paper (Whatman No.1 filter paper). The wrapped sample was put in a soxhlet reflux flask containing 200 ml of petroleum ether. The upper end of the reflux flask was connected to a condenser. By heating the solvent in the flask

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through an electro-thermal heater, it vaporizes and condensed into the reflux flask. The wrapped sample was completely immersed in the solvent and remained in contact with it until the flask filled up and siphoned over thus carrying the extracts from the sample down to the boiling flask. This process was allowed to go on repeatedly for about 4 h. The solvent was recovered using rotary evaporator and the extract was dried in the oven at 600 ℃ for 3 min to remove any residual solvent.

Gas Chromatography/Mass Spectrometry Analysis

An Agilent 6890N gas chromatography equipped with an auto-sampler connected to an Agilent mass spectrophotometric detector was used. 1 µl of sample extract was injected in the pulsed spitless mode onto a 30 m x 0.25 mm id DB 5MS coated fused silica column with a film thickness of 0.15 µm. Helium gas was used as a carrier gas and the column head pressure maintained at 20 psi to give a constant of 1 ml/min. Other operating conditions were preset. The column temperature initially held at 55 ℃ for 0.4 min, was increased to 200 ℃ at a rate of 25 ℃/mins, then to 280 ℃ at a rate of 8 ℃/mins and to final temperature of 300 ℃ at a rate of 25 ℃/mins, held for 2 mins. All solvents used were of analytical grade and were procured from Merck, Germany. The components of the extract were identified by matching the peaks with computer Wiley MS libraries and confirmed by comparing mass spectra of the peaks and those from literature as well as using the database of National Institute of Standards and Technology (NIST).

Antioxidant Activity Determination

The free radical scavenging activity of the sample was determined using the 1,1-diphenyl-2-picrylhydrazyl (α, α-diphenyl-β-picrylhydrazyl; DPPH) method reported by Igwe and Onuoha, [8]. 1.0 g of DPPH, a stable radical was dissolved in 100 ml of methanol. 3.0 ml of different concentrations of the test sample were added to 3.0 ml of a 0.004 % methanol solution of DPPH and incubated for 30 minutes at room temperature. The decrease in absorbance of the solution brought about by the test samples was measured at 517 nm using a spectrophotometer. Ascorbic acid, which is a known antioxidant [9], was used as a reference standard. The radical scavenging activity was calculated as the percentage inhibition of DPPH discoloration using the equation below:

$$\%\ Inhibition of DPPH radical = \left[\frac{(A_{blank} - A_{sample})}{A_{blank}}\right] \times 100$$

Where; A_{blank} is the absorbance of the control reaction solution (containing all reagents except the test sample); A_{sample} is the absorbance of the test sample.

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Antibacterial Activity Screening

Cell Concentration Assay

The bacteria organisms used for the *in vitro* antibacterial screening were *Escherichia coli* (Gram-negative), *Klebsiella pneumonia* (Gram-negative), *Shigella flexneri* (Gram-negative), *Streptococcus pneumonia* (Gram-positive) and *Staphylococcus epidermidis* (Gram-positive).The test organisms were clinical isolates of human pathogens obtained from stock cultures at the Federal Medical Centre, Umuahia, Abia State, Nigeria. Tenfold serial dilution of the samples was prepared. Sterile water was used as diluent. A 9.0 mL amount of diluent was placed into each of 9 sterile test-tubes. The samples were mixed uniformly and with a sterile 1-mL micropipette, 1.0 mL was transferred into the first tube of diluent. This was done for the remaining dilutions in the same way, using a fresh pipette tip for each. Starting with the greatest dilution, 1.0mL amounts of each dilution was pipetted into each of the three test tubes. 10mL of clear nutrient broth and yeast extract broth melted and cooled to 45-50℃ was then poured aseptically into each of the test tubes and mixed for about ten seconds. The broth was allowed to set and incubated for 24 h at 37℃ in an incubator (Gallenkamp England).The viable cell concentration of bacterial isolates was evaluated after 24 h incubation through tracking the optical density of the cell colonies at 600 nm (OD600) using a UV spectrophotometer (K300, Jenway England), from the bacterial broth culture [10]. Gentamicin was used as a standard antibacterial agent. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values for the extract were determined.

Preparation of Receptors and Prominent Compounds

The crystal structures of *S. pneumoniae* (PDB ID: 2BRW), *S. epidermidis* (PDB ID: 4HBL), *S. flexneri* (PDB ID: 4A5P), *K. pneumoniae* (PDB ID: 5O79), and *E. coli* (PDB ID: 6GCM) (Figures 2a–e) were obtained from the RCSB Protein Databank. Water molecules and the cofactors were removed using the molecular molegroviewer software (CLC Bio, 2012). The PDBs of the most abundant compounds, p-cymene and n-Hexadecanoic acid, were downloaded from PubChem. They have been abbreviated as CMN and HDA, respectively.

In silico Studies

The compounds were docked to the receptors using the PyRx visual screening tool [11]. The macromolecules were uploaded, and the ligands were uploaded through Open Babel embedded in PyRx. The interactions of all docked complexes were visualized using the protein-ligand interaction profiler (PLIP) server [12]. We also docked gentamycin (GNT) (the standard drug) with the receptors as a control to validate the docking protocol in this work. Drug-likeness

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prediction study, Lipinski's Rule of Five (RO5), pharmacokinetic analysis, and ADME were assessed using the web server of Swiss ADME [13].

RESULTS AND DISCUSSION

The GC/MS chromatogram of the seed extract of *M. myristica* is shown in Figure 1. Twelve phytochemical compounds were identified (Table 1) comprising fatty acids (38.897 %), terpenes and terpenoids (29.133 %), salicyclohydrazine (19.626 %), carboxylic acid (8.124 %) flavonoid (2.352 %), benzoic acid ester (1.166 %), and phenolic compound (0.700 %). The two most prominent compounds were n-hexadecanoic acid and p-cymene with equal composition of 24.831 %.

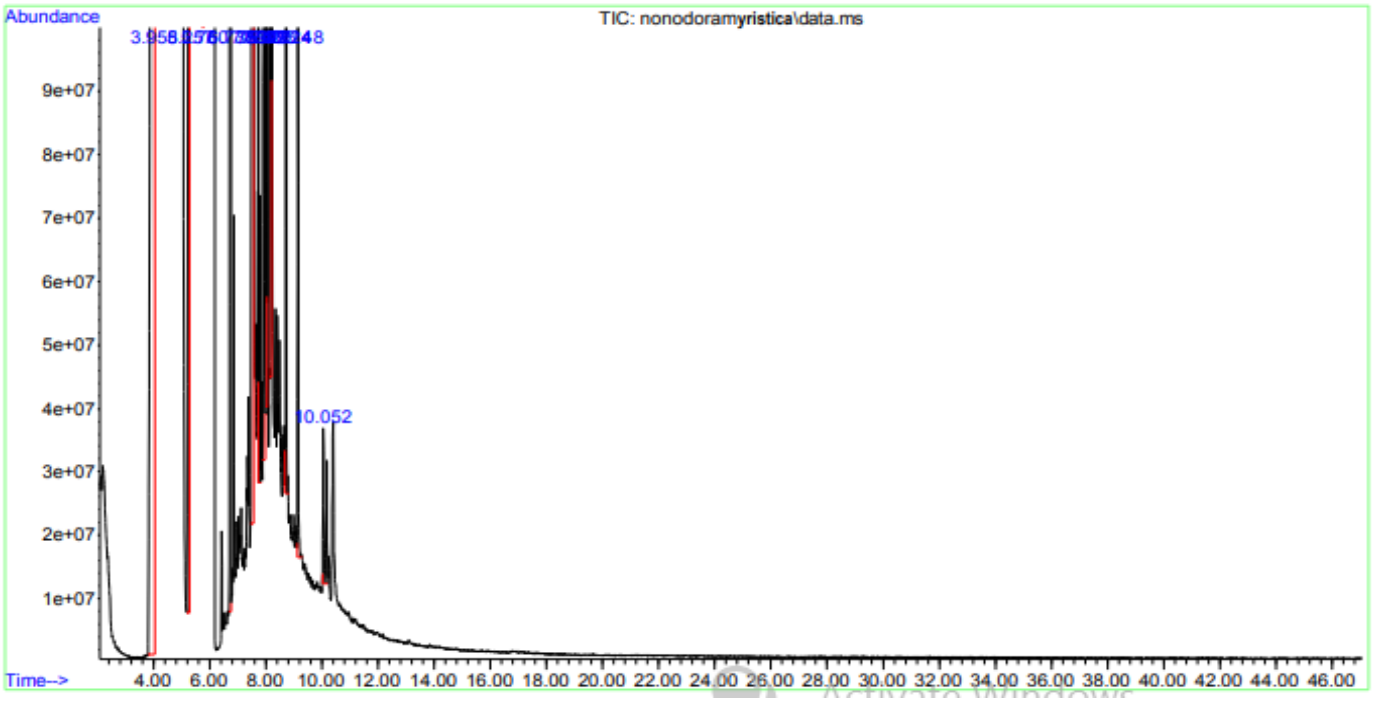


Fig. 1: GC/MS chromatogram of *M. myristica* seed extract

Table 1: Phytochemicals from the GC/MS analysis of *M. myristica* seed extract

Peak No.	Phytochemical Components	Retention Time (min.)	Class of Compound	Percentage Composition (%)
1	n-Hexadecanoic acid	3.958	Saturated fatty acid	24.831
2	Eicosanoic acid	5.257	Saturated fatty acid	14.066
3	D-Catechin	5.760	Flavonoid	2.352
4	Salicyl hydrazide	6.739	Salicyclohydrazine	19.626
5	p-cymene	7.534	Monoterpene	24.831

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6	Salicylic acid benzyl ester	7.740	Benzoic acid ester	1.166
7	Eugenol	7.923	Monoterpenoid	2.478
8	β-Myrcene	8.020	Monoterpene	1.824
9	3-phenyl-2-propenoic acid	8.175	Carboxylic acid	3.193
10	4-hydroxy-3-methoxy benzoic acid	8.724	Carboxylic acid	3.351
11	Gentisic acid	9.148	Carboxylic acid	1.580
12	2-Methyl-5-(1-methylethyl)-phenol	10.052	Phenolic compound	0.700

Hexadecanoic acid has been reported to possess antioxidant, antimicrobial and anti-inflammatory activities [14]. Terpenes and their derivatives are generally used as flavouring and medicinal agents and in perfumery. They are used by the food industry to give flavour to drinks and foods and are also a component for the pharmaceutical industry for the preparation of drugs, soaps, perfumes and other cosmetics as well as for home cleaning products [15]. The presence of p-cymene, eugenol and β-myrcene constituting 29.133 % of the extract is an indication that the extract is rich in terpenes hence its uses as a spice and also in herbal medicine. D-catechin identified in the extract is a flavonoid compound. D-catechin and other phenolic compounds have been reported as known antioxidant agents [16].

Table 2: Antioxidant activity of *M. myristica* seed extract

Concentration (µg/ml)	**Antioxidant activity (%)**	
	Seed extract	**Vitamin C**
25	72.51 ± 0.82	80.90 ± 4.34
50	83.32 ± 1.04	95.16 ± 1.55
100	90.42 ± 1.03	97.63 ± 0.07
200	92.68 ± 0.46	97.81 ± 0.10
400	96.22 ± 0.00	98.28 ± 0.31

Data are mean ± standard deviation of triplicate determinations

The antioxidant activity of the seed extract of *M. Myristica* is shown in Table 2. The extract showed significant antioxidant activities of 72.51 and 96.22 % at minimum and maximum concentrations of 25 and 400 µg/ml, respectively. The antioxidant activity results obtained are comparable to that of vitamin C used as a standard antioxidant agent. Antioxidant activity increased with increase in doses suggesting a dose-dependent pattern. This pattern had been reported by Igwe and Onuoha [8] for *Citrullus lanatus* seed extract.

The antibacterial activity of *M. Myristica* seed extract is shown in Table 3. The extract showed antibacterial potency against five strains of bacteria organisms which included *E. coli* (gram-negative), *K. pneumonia*e (gram-negative), *S. flexneri* (gram-negative), *S. pneumoniae* (gram-

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positive) and *S. epidermidis* (gram-positive). The highest inhibition was shown against *S. flexneri* while the lowest inhibition was against *S. pneumoniae*. Gentamicin was used as a standard antibacterial agent and the results showed the extract to be far more potent than gentamicin against the bacteria organisms tested. The contributory antibacterial activities of the phytochemicals in the extract probably gave rise to this commendable antibacterial potency since many phytochemicals have been reported to possess antibacterial activities [17].

The antioxidant and antibacterial activities shown by *M. Myristica* seed extract could be as a result of the synergistic contributory roles of the terpenoid molecules, flavonoid and phenolic compounds identified in the GC/MS analysis of the extract.

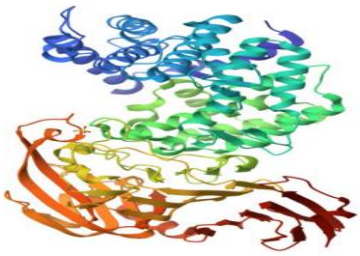
Table 3: Antibacterial activity of *M. myristica* seed extract

Test Microorganism	***M. myristica* seed extract**	**Gentamicin**	**Water**	**MIC**	**MBC**
E. coli	0.494±0.260	0.133±0.045	0.000	0.250	0.500
K. pneumoniae	0.585±0.145	0.050±0.026	0.000	0.250	0.500
S. flexneri	0.756±0.172	0.043±0.020	0.000	0.125	0.250
S. pneumoniae	0.456±0.156	0.026±0.003	0.000	0.125	0.250
S. epidermidis	0.589±0.212	0.051±0.018	0.000	0.125	0.250

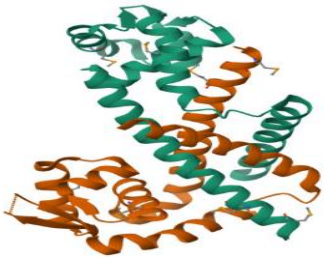
Data are mean ± standard deviation of triplicate determinations

The crystal structures of the bacterial receptors are presented in Figure 2(a–e). Table 4 depicts the binding energies (Kcal/mol) of *M. myristica* seed compounds docked with bacterial receptors. The PLIP 3D interactions of the complexes are presented in Figure 3. Table 5 represents the drug-likeness prediction of prominent compounds present in *M. myristica* seed. Some ADME parameters for the prediction of prominent compounds present in *M. myristica* seed are presented in Table 6. The interaction of prominent compounds present in *M. myristica* seed with cytochrome P450 (CYP) is depicted in Table 7.

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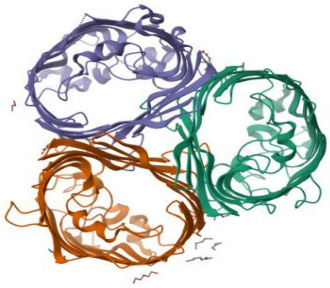
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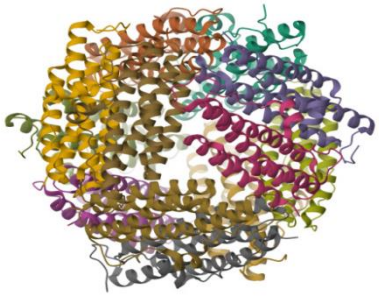
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c



d



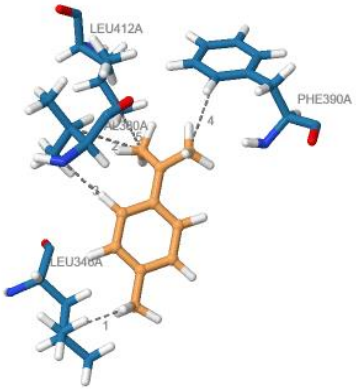
e

Figures 2: Crystal structures of (a) *S. Pneumoniae (b)S.epidermidis (c) S.flexneri (d) K. pneumonia (e) E. coli*

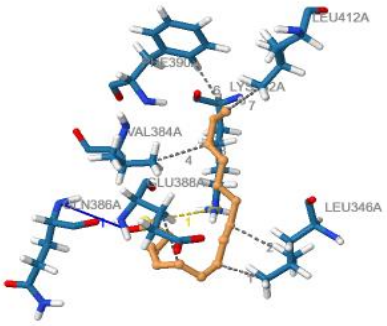
Table 4: Binding energies (Kcal/mol) of *M.myristica*seed compounds with bacterial receptors

Compound	**Receptors**				
	2BRW	4HBL	4A5P	5079	6GCM
CMN	-4.9	-5.8	-4.9	-5.8	-5.1
HDA	-4.5	-5.8	-5.7	-5.8	-5.3
GNT	-7.1	-9.3	-8.4	-6.2	-8.9

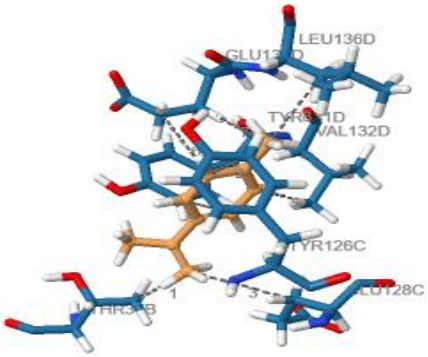
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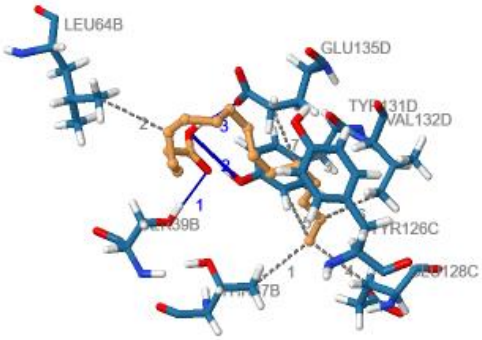
2BRW-CMN



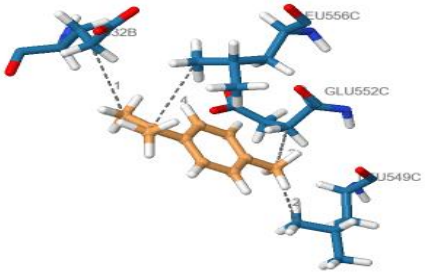
2BRW-HDA



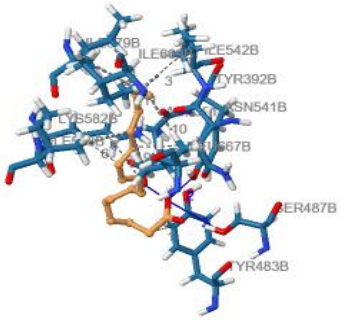
4HBL-CMN



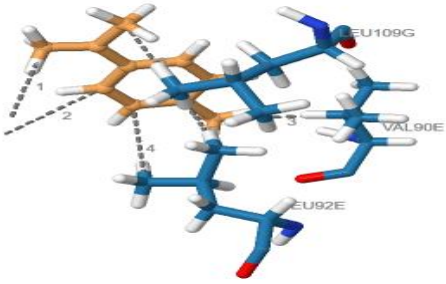
4HDL-HDA



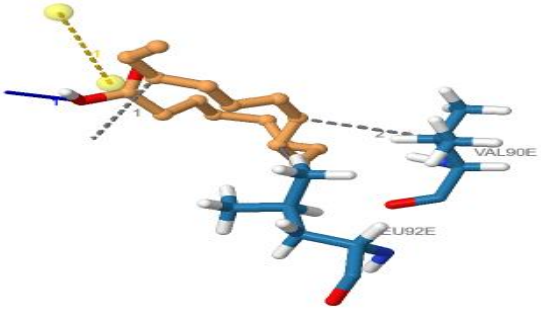
4A5P-CMN



4A5P-HDA

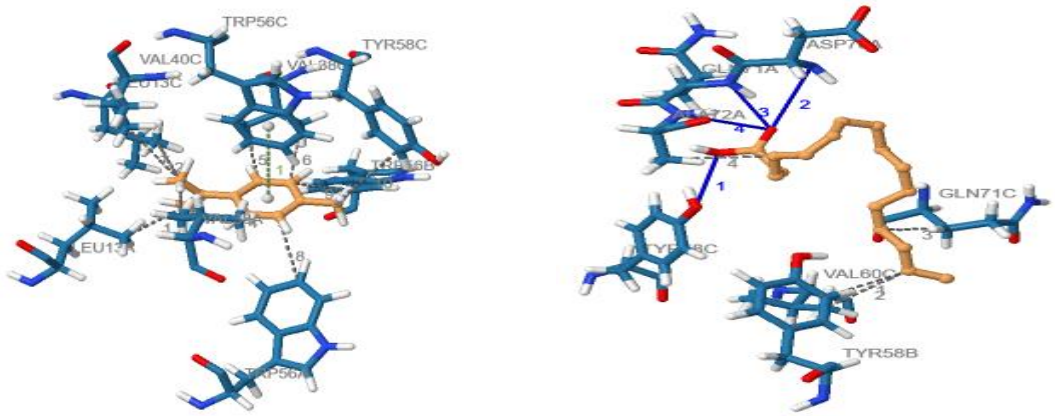


6GCM-CMN



6GCM-HDA

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5079-CMN 5079-HDA

Figure 3: PLIP 3D interactions of the docked complexes

Table 5: Drug-likeness prediction of prominent compounds present in *M.myristica* Seed

Compounds	Mol. weight (g/mol.)	HB Acceptor	HB Donor	Lipophilicity LogP	Molar refractivity	No. of violations
CMN	134.22	0	0	4.47	45.99	1 MLOGP>4.15
HDA	256.42	2	1	4.19	80.80	1 MLOGP>4.15

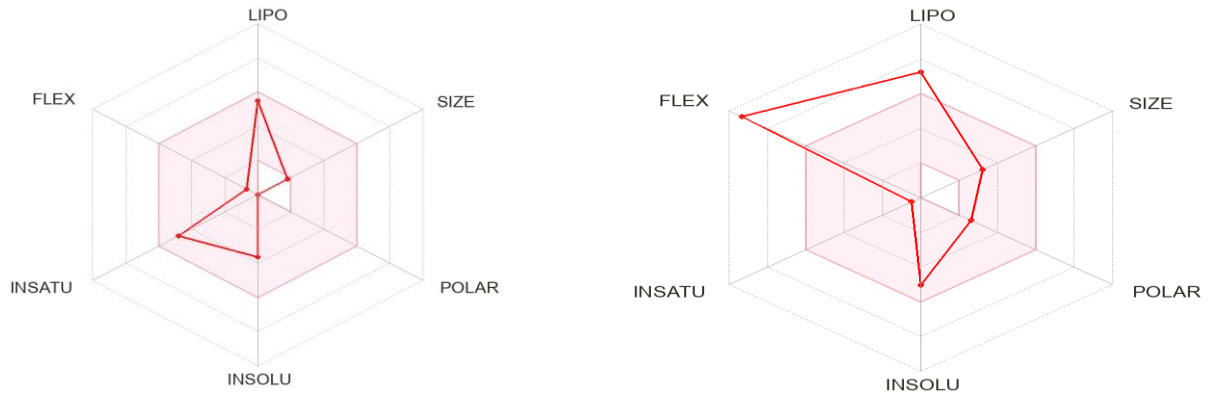
Table 6: Some ADME Parameters predictions of prominent compounds present in *M. myristica* seed

Compound	TPSA (Å²)	Water Solubility Log *S* (ESOL)	Bio. Avail. Score	Med. Chem. (PAIN) alert	Synthetic Accessibility
CMN	0.00	-3,63	0.55	0	1.00
HDA	37.30	-5.02	0.85	0	2.31

Table 7: Interaction of prominent compounds present in *M. myristica* seed with cytochromes P450 (CYP)

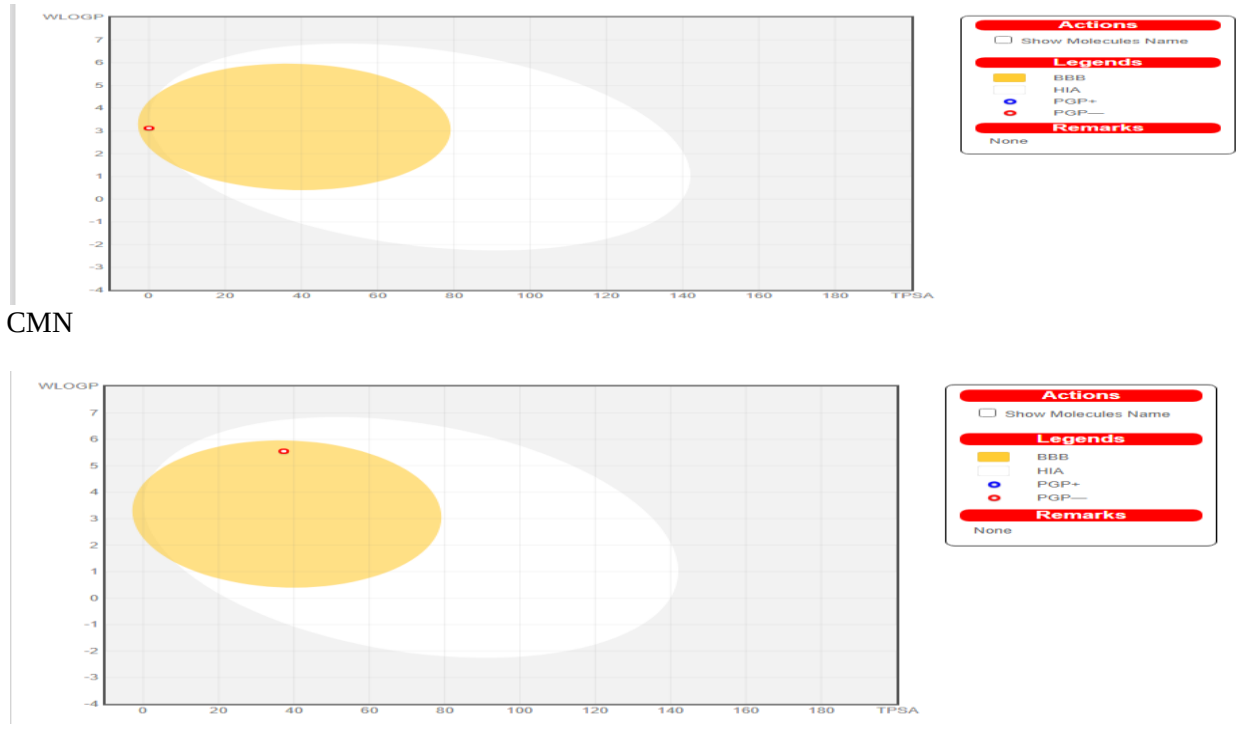
Compounds	CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4	Log K_p (skin permeation) (cm/s)
			Inhibitor			
CMN	No	No	No	Yes	No	-4.21
HAD	Yes	No	Yes	No	No	-2,77

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CMN HAD

Figure 4: The Bioavailability Radar of the prominent compounds from *M. myristica*seed



CMN

HDA

Figure 5: BOILED-Egg diagram of the prominent compounds from *M. myristica* seed

The binding energies of CMN and HDA with the receptors (Table 4) suggested that the docking process was feasible. The antibacterial activities of the compounds against the bacterial species look promising. However, the standard drug,

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GNT, showed better binding energies when compared to CMN and HDA for all the receptors.

The 3D molecular interactions (Figure 3) represent the bonds between the receptors and the ligands. For the 2BRW-CMN 3D interactions, hydrophobic interactions were observed with the amino acids LEU 346A, VAL 380A, PHE 390A, and LEU 412. Hydrophobic interactions were also observed in the 2BRW-HDA complex with residues LEU 346A, LYS 382A, VAK 384A, GLU 388A, PHE 390A, and LEU 412A. The presence of a salt bridge was observed with LYS 382A. A hydrogen bond was observed with the amino acid GLN 386A.

For the 4HBL-CMN docked complex, the amino acids THR 37B, TYR 126C, GLU 125C, TYR 131D, VAL 132D, GLU 135D, and LEU 136D were involved in hydrophobic interactions. For the 4HBL-HDA docked complex, the receptor's amino acids THR 37B, LEU 64B, TYR 126C, GLU 128C, TYR 131D, VAL 132D, LEU 136D, and GLU 135D were involved in hydrophobic interactions. The residues SER 39B, TYR 131D, and GLU 135D formed hydrogen bonds with the ligands.

Some of the interactions between the 4A5P-CMN 3D complex showed that it had hydrophobic interactions with the amino acids GLU 532B, LEU 549C, GLU 552C, and LEU 536C. The 4A5P-HDA 3D complex interactions showed the presence of hydrophobic interactions with amino acids TYR 483B, ASN 541B, ILE 542B, ILE 579B, LYS 582B, LYS583B, LEU 667B, and ILE 669B. Hydrogen bonds were observed with ASP 391B, TYR 392B, and SER 487B.

The 5O79-CMN 3D complex interactions showed the presence of hydrophobic interactions with the amino acids LEU 13A, LEU 13C, VAL 38A, VAL 38C, VAL 40C, TRP 56A, TRP 56B, and TYR 58C. A π-stacking bond was observed with TRP 56C. The 5O79-HDA 3D complex interactions showed the presence of hydrophobic interactions with amino acids TYR 58C, ASP 70A, GLN 7IC, and ALA 72A. Hydrogen bonds were observed with TYR 58C, ASP 70A, GLN 71A, and ALA 72A.

The 6GCM-CMN 3D complex interactions showed the presence of hydrophobic interactions with amino acids TYR 16J, VAL 90E, LEU 92E, and LEU 109G. Hydrogen bonds were observed with TYR 16J, GLU 31E, and ASN 130B. The 6GCM-HDA 3D complex interactions showed the presence of hydrophobic interactions with amino acids TYR 16J, VAL 90E, and LEU 92E. A hydrogen bond was observed with THR 17J. There was a salt bridge between the ligand and LYS 26J.

Molecular docking is very helpful since it reduces the expense of conducting research in wet labs, saves time, money, and animals, and correctly directs the selection and synthesis of medications. Anticipating a ligand's binding affinity with a protein and the most stable complex is the aim of molecular docking simulation; the more negative

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or lower the binding affinity, the better. For pharmaceutical researchers, molecular docking simulation has made drug modeling and design easier and more reliable. It has also been verified *in vivo* and *in vitro* [7,18,19 20,21,22,23]. The RO5, created by Lipinski, is a heuristic that aids in assessing if a substance with a specific bioactivity has the necessary chemical and physical characteristics to be used as an oral medication. For every molecule in the drug-likeness forecast, there was only one violation (Table 5). All docked compounds meet RO5 requirements. Minimal compound attrition is anticipated for the test compounds for future drug development research [7].

For the Lipinski rule [24], a good drug should have a topological polar surface area (TPSA) of less than 140 Å2. This is one of the most significant chemical descriptors that correlate strongly with pharmacokinetic parameters. The test compounds' TPSA was less than 140 Å2 (Table 6).

It is much easier to handle and formulate drugs when the molecule is soluble [25]. This is one of the main benefits of solvent-based drug development. According to [26], solubility is a significant factor affecting absorption in research efforts that aim for oral delivery. According to [27], a medication intended for parenteral administration must also have high water solubility in order to provide an adequate amount of the active ingredient in the tiny amount of the prescribed pill. An ESOL model water solubility profile [28] for the test compounds is shown in Table 6. The solubility profile indicated that the compounds were soluble.

The bioavailability score [29] calculates the probability that a chemical will have at least 10% oral bioavailability in rats using the predominant charge of a rat model at biological pH. This predicts the probability that a material will have F > 10%. Martin [29] stated that a molecule is generally considered a potential therapeutic candidate if its bioavailability score is at least 0.10. The oral bioavailability of CMN and HDA was predicted to be 0.55 and 0.85, respectively.

PAINS (pan assay interference compounds), which are also known as frequent hits or promiscuous compounds, are molecules with substructures that show strong reactions in assays no matter what protein target they are tested against. Our results showed that there are no promiscuous compounds that can cause drug interference.

The score is normalised between 1 (easy synthesis) and 10 (extremely difficult synthesis) for synthetic accessibility. The test compounds CMN and HDA are anticipated to be easily synthesised based on the synthetic accessibility test score (Table 7).

Understanding the interactions between chemicals and cytochromes P450 (CYP) is also crucial. This isoenzyme superfamily plays a crucial role in drug clearance via metabolic

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biotransformation. Research suggests that P-gp and CYP can work together to metabolise small compounds in a way that enhances tissue and organism protection [30]. One main reason for pharmacokinetics-related drug-drug interactions [31] is inhibition of these isoenzymes. This can cause toxic or other unwanted side effects because the drug or its metabolites don't get cleared out as quickly or as much [32]. It has been determined that there are several CYP isoform inhibitors. Some substances selectively target particular isoenzymes, while others impact distinct CYP isoforms [33]. Predicting which isoforms will be impacted and the likelihood that the compounds will inhibit CYPs to create meaningful drug interactions are therefore crucial steps in the drug discovery process. Our research indicated that CMN did not inhibit CYP1A2, CYP2C19, CYP2C9, CYP3A4, and CYP3A4. HDA inhibited CYP2C19, CYP2D6, and CYP3A4.

Potts and Guy [34] reported that the more negative the log Kp (with Kp in cm/s), the less skin permeant the molecule is. Log Kp values for CMN and HDA were negative. This suggested that they were not skin-permeable.

Figure 4 displays the bioavailability radar for a quick assessment of drug-likeness. The following six physicochemical characteristics were considered: size, polarity, solubility, flexibility, saturation, and lipophilicity. Descriptors taken from Ritchie *et al*. [35] and Lovering *et al.* [36] were used to create a physicochemical range on each axis. A pink area delineates the range within which a molecule's radar plot must fall completely in order to qualify as drug-like. In our research work, CMN was orally bioavailable, while HDA was not orally bioavailable because it was too flexible and had high lipophilicity.

By using the BOILED-Egg (Figure 5), it is easy to get a sense of how the positions of the molecules in the WLOGP-versus-TPSA referential affect the blood-brain barrier (BBB) and human gastrointestinal absorption (HIA). The possibility of brain penetration is higher in the yellow zone (yolk) than in the white area, which has a high chance of passive absorption by the gastrointestinal tract [35,36]. White areas and yolk areas are not mutually exclusive. Also, the spots are red if they are thought to not bind to P-gp (PGP−) and blue if they are thought to be actively pushed out by the permeability glycoprotein P-gp (PGP+). CMN and HDA had significant BBB absorption in this study and were predicted to be non-substrates of P-gp (PGP−).

CONCLUSION

M. myristica seed compounds have been reported to exhibit antioxidant and antibacterial activity. The outcomes of docking simulations, drug-likeness, and ADME tests demonstrated the importance of hydrophobic contacts and hydrogen bonds. Each of the compounds has demonstrated favourable characteristics for Lipinski's criteria, including good permeability in biological membranes and the blood-brain

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barrier, as well as good solubility in the aqueous medium (Log S) and TPSA<140. The exhibited experimental antioxidant and antibacterial activity was in good agreement with the accuracy of the *in silico* prediction. This work has significance not only for the design and synthesis of antibacterial inhibitors but also for our understanding of the mechanism by which *M. myristica* seed compounds inhibit the tested bacterial species.

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