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Chemical and bioprotective studies of *Xylopia aethiopica* seed extract and molecular docking of doconexent and cryptopinone as the prominent compounds

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Abstract

Fourteen phytochemical compounds were identified in the gas chromatography/mass spectrometry (GC/MS) analysis of the petroleum ether extract of the seeds of *Xylopia aethiopica*. The compounds comprised of terpenoids (56.027 %), unsaturated fatty acids (30.081 %), alcohol (9.385 %) and saturated fatty acid (4.507 %). The extract showed high antioxidant activity in a dose dependent pattern at a minimum and maximum concentrations of 25 and 400 μg/ml respectively and could be compared with that of ascorbic acid used as a standard antioxidant agent. The antibacterial activity screening of the extract against five pathogenic bacteria organisms indicated that the extract possessed more antibacterial activity than gentamicin used as a standard antibacterial agent. The trend of activity was *Klebsiella pneumonia*e (gram-negative) > *Shigella flexneri* (gram-negative) > *Staphylococcus epidermidis* (gram-positive) > *Escherichia coli* (gram-negative) > *Streptococcus pneumoniae* (gram-positive). The presence of high amount of terpenoids in the extract of *X. aethiopica* could be the reason for the high antioxidant and antibacterial activities shown by the extract and also suggests why the seed extract of the plant is used in herbal medicine for the treatment of diseases and infections. All of the test compounds had negative binding affinities, indicating that the compounds had been successfully docked to the receptors. The compounds showed good pharmacokinetic properties, such as high blood-brain barrier absorption, oral bioavailability, and water solubility, in the *in-silico* ADME and drug-likeness predictions. These findings significantly increase the relevance of these compounds as promising first targets for the treatment of drug resistant bacteria.

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1. Introduction

Phytochemicals are naturally occurring plant chemicals. The early use of these chemicals in phytomedicine gave rise to the modern drugs that abound today [1]. Hence there is an ongoing effort to profile the phytochemical constituents of Nigerian herbal plants and their bioactivity studies [2]. *Xylopia aethiopica* is one of such plants which belongs to the family Annonaceae and grows up to 15-30 m high. The plant is a tall, slim, aromatic and evergreen tree predominantly found in the savanna regions of Africa such

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as Nigeria, Senegal, Cameroon and Ghana [3]. *X. aethiopica* is primarily used as a spice in southeast Nigeria but has been reported to be used in herbal medicine for the treatment of cough, syphilis, diabetes, hemorrhoids, uterine fibroid, female infertility, malaria, amenorrhea and dysentery [4]. A decoction of the seeds is used in the treatment of epilepsy, numbness, anemia and to enhance postpartum placental expulsion [3]. The antiviral activity of the aqueous extract of *X. aethiopica* has also been reported [5].

The most important oxygen-containing free radicals in many disease states are hydroxyl radical, superoxide anion radical, hydrogen peroxide, oxygen singlet, hypochlorite, nitric oxide radical, and peroxynitrite radical [6]. Free radicals attack important macromolecules leading to cell damage and homeostatic disruption [6, 7]. Many synthetic antioxidants have shown toxic and mutagenic effects, which have shifted attention towards naturally occurring antioxidants [8]. Many herbal plants have been reported to possess antioxidant activities. Some of them include *Tetrapleura tetraptera* [9], *Citrullus lanatus* [10] and *Cocos nucifera* [11].

The *in-silico* approach has been shown to be useful in addressing the molecular mechanism of action of small drugs involving proteins [12]. To assess the binding affinity and interactions of significant *X. aethiopica* seed compounds, molecular docking and pharmacokinetic (ADME) tests were performed. The ”drug-likeness” of the compounds was evaluated in this research by applying Lipinski’s rule of five.

The use of *X. aethiopica* in herbal medicine for the treatment of cough, syphilis and dysentery which are mostly caused by bacteria organisms and for the treatment of diabetes which is mediated by free radicals prompted this research. Hence, we report herein, the chemical, antioxidant and antibacterial studies of the seed extract of *X. aethiopica* and molecular docking investigations of the two most prominent compounds identified in the extract.

2. Materials and methods

2.1. Collection of plant sample

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

2.2. Sample preparation

The seed endosperms were obtained and washed thoroughly with distilled water and allowed to dry under a shade. These seed endosperms were milled using an electric blender and the milled sample was thereafter stored in an airtight container prior to extraction.

2.3. Extraction of phytochemicals

The extraction process followed the procedure reported by Igwe and Echeme [13] with minor modifications. 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 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 °C for 3 min to remove any residual solvent.

2.4. 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 $\times$ 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 °C for 0.4 min, was increased to 200 °C at a rate of 25 °C/mins, then to 280 °C at a rate of 8°C/mins and to final temperature of 300 °C at a rate of 25 °C/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).

2.5. Antioxidant activity determination

The free radical scavenging activity of the sample was determined using the 1,1-diphenyl-2picrylhydrazyl (α, α-diphenyl-β-picrylhydrazyl; DPPH) method as reported by Igwe and Onuoha [10]. 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 [14] was used as a reference standard. The radical scavenging activity was calculated as the percentage inhibition of DPPH discoloration using equation (1).

$$\% \text{ Inhibition of DPPH radical} = \left[\frac{A_{\text{blank}} - A_{\text{sample}}}{A_{\text{blank}}}\right] \times 100, \tag{1}$$

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.

2.6. Antibacterial activity screening

2.6.1. Cell concentration assay

The bacteria organisms used for the *in vitro* antibacterial screening were *Escherichia coli* (Gramnegative), *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, 1.0 mL amounts of each dilution was pipetted into each of the three test tubes. 10 mL of clear nutrient broth and yeast extract broth melted and cooled to 45-50 °C 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 °C 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 [15]. Gentamicin was used as a standard antibacterial agent. The minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values for the extract were determined.

2.7. 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 1a–e) were obtained from the RCSB Protein Databank. Water molecules and the cofactors were removed using the molecular viewer software [16]. The PDBs of the most abundant compounds, cryptopinone and doconexent, were downloaded from PubChem. They have been abbreviated as CTP and DNX, respectively.

2.8. In silico studies

The compounds were docked to the receptors using the PyRx visual screening tool [17]. 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 [18]. We also docked gentamycin (GNT) (the standard drug) with the receptors as a control to validate the docking protocol in this work. Drug-likeness prediction study, Lipinski's Rule of Five (RO5), pharmacokinetic analysis, and ADME were assessed using the web server of Swiss ADME [19].

3. Results and discussion

The GC/MS chromatogram of *X. aethiopica* seed extract is shown in Figure 1. The GC/MS result showed fourteen phytochemical compounds (Table 1) comprising of terpenoids (56.027 %), unsaturated fatty acids (30.081 %), alcohol (9.385 %) and saturated fatty acid (4.507 %). The two most prominent compounds in the extract were doconexent (15.425 %) which is an unsaturated fatty acid and cryptopinone (11.141 %) which is a diterpenoid.

Out of the fourteen phytochemical compounds identified in the seed extract of *X. aethiopica*, nine are terpenoid compounds constituting 56.027 % of the total extract. Little wonder the plant seed is used as a spice. Terpenes and their derivatives are generally used as flavouring and medicinal agents and in perfumery. These terpenoid compounds possess marked physiological effects and have been reported to possess antioxidant, anti-inflammatory and antibacterial effects [20].

The antioxidant activity of *X. aethiopica* seed extract is shown in Table 2. The extract showed high antioxidant activity in a dose dependent pattern at a minimum and maximum concentrations of 25 and 400 μg/ml respectively and could be compared with that of ascorbic acid used as a standard antioxidant agent. This dose-dependent pattern had been reported by Igwe and Ugwunnaji [11] for endosperm tissues of *Cocos nucifera* L.

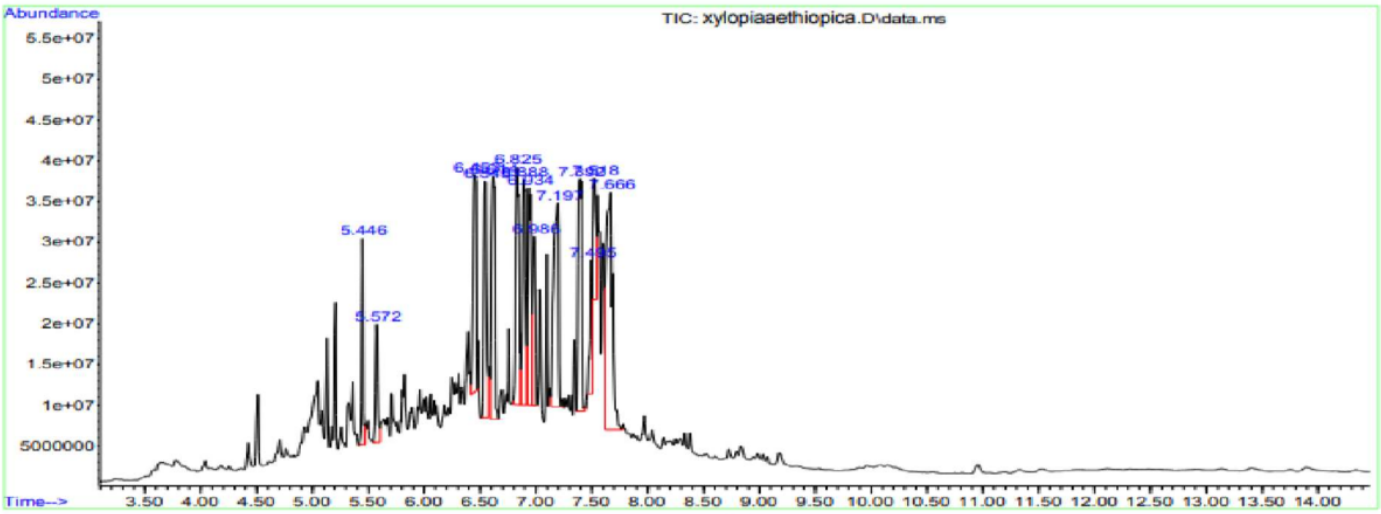


Figure 1: GC/MS chromatogram of *X. aethiopica* seed extract.

Table 1: Phytochemicals from the GC/MS analysis of *X. aethopica* seed extract.

Peak No.	Phytochemical components	Retention time (min.)	Class of compounds	Percentage composition (%)
1	β-ylangene	5.446	Sesquiterpenoid	3.693
2	D-Germacrene	5.572	Sesquiterpenoid	2.835
3	(-)-Spathulenol	6.453	Sesquiterpenoid	7.713
4	Trans-Z-α-Bisabolene epoxide	6.545	Sesquiterpenoid	6.937
5	Caryophyllene oxide	6.614	Sesquiterpenoid	8.674
6	Manoyl oxide	6.825	Diterpenoid	8.142
7	9,12-Octadecadienoic acid (linoleic acid)	6.888	Unsaturated fatty acid	7.136
8	9-Octadecenoic acid (oleic acid)	6.934	Unsaturated fatty acid	7.520
9	n-Hexadicanoic acid (palmitic acid)	6.986	Saturated fatty acid	4.507
10	Cryptopinone	7.197	Diterpenoid	11.141
11	1-Heptatriacotanol	7.392	Alcohol	9.385
12	Kaur-16-ene	7.495	Diterpenoid	3.287
13	β-Pimaric acid	7.518	Diterpenoid	3.605
14	Doconexent	7.666	Unsaturated fatty acid	15.425

Table 2: Antioxidant activity of *X. aethiopica* seed extract.

Concentration (μg/ml)	Antioxidant activity (%)	
	Seed extract	Vitamin C
25	17.60 ± 0.43	80.90 ± 4.34
50	71.21 ± 0.13	95.16 ± 1.55
100	78.13 ± 1.00	97.63 ± 0.07
200	81.33 ± 1.92	97.81 ± 0.10
400	82.12 ± 1.03	98.28 ± 0.31

Data are mean ± standard deviation of triplicate determinations.

The antibacterial activity of *X. aethiopica* extract is shown in Table 3. The antibacterial activity screening of the extract against five pathogenic bacteria organisms indicated that the extract possessed more antibacterial activity than gentamicin used as a standard antibacterial agent. The trend of activity was *Klebsiella pneumonia*e (gram-negative) > *Shigella flexneri* (gram-negative) > *Staphylococcus epidermidis* (gram-positive) > *Escherichia coli* (gram-negative) > *Streptococcus pneumoniae* (gram-positive). The minimum inhibitory concentration ranged from 0.25 to 0.50. The presence of high amount of terpenoids which had been reported to possess marked antioxidant and antibacterial activities [20] in the extract of *X. aethiopica* could be the reason for the high antioxidant and

Table 3: Antibacterial activity of *X. aethiopica* seed extract.

Test Microorganism	*X. aethiopica* seed extract	Gentamicin	Water	MIC	MBC
E. coli	0.392±0.227	0.133±0.045	0.000	0.250	0.500
K. pneumoniae	0.593±0.166	0.050±0.026	0.000	0.250	0.500
S. flexneri	0.544±0.096	0.044±0.020	0.000	0.125	0.250
S. pneumoniae	0.385±0.186	0.026±0.003	0.000	0.125	0.250
S. epidermidis	0.519±0.306	0.051±0.018	0.000	0.125	0.250

Data are mean ± standard deviation of triplicate determinations.

Table 4: Antibacterial activity of *X. aethiopica* seed extract.

Compound	Receptors				
	2BRW	4HBL	4A5P	5079	6GCM
CTP	-6.0	-8.9	-6.8	-3.5	-8.3
DNX	-5.0	-6.9	-6.6	-6.8	-6.8
GNT	-7.1	-9.3	-8.4	-6.2	-8.9

Table 5: Drug-likeness prediction of prominent compounds present in *X. aethiopica* seed.

Compound	Mol. weight (g/mol.)	HB acceptor	HB donor	Lipophilicity Log P	Molar refractivity	No. of violations
CTP	286.45	2	1	4.65	90.38	1 MLOGP>4.15
DNX	328.49	2	1	6.55	106.80	1 MLOGP>4.15

Table 6: Some ADME Parameters prediction of prominent compounds present in *X. aethiopica* seed.

Compound	TPSA (Å^2)	Water solubility Log S (ESOL)	Bio. Avail. Score	Med. Chem. (PAIN) Alert	Synthetic accessibility
CTP	17.07	-4.94	0.55	0	4.73
DNX	37.30	ND	ND	0	ND

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

Compound	CYP1A2	CYP2C19	CYP2C9	CYP2D6	CYP3A4	Log K_p (skin permeation) (cm/s)
	Inhibitor					
CTP	No	Yes	Yes	No	No	-4.16
DNX						

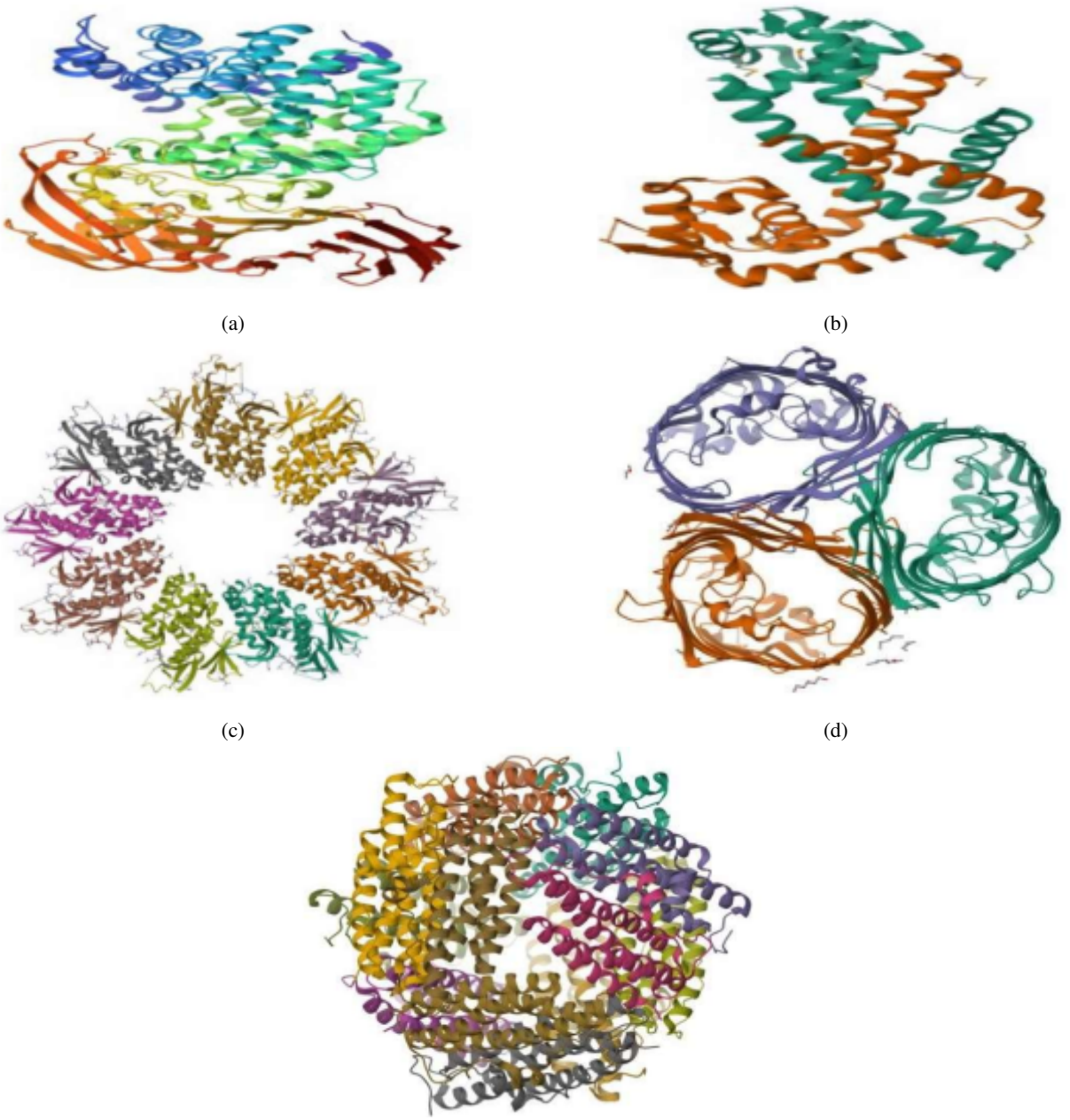
antibacterial activities shown by the extract and also suggests why the seed extract of the plant is used in herbal medicine for the treatment of diseases and infections.

The crystal structures of the bacterial receptors are presented in Figure 2(a–e). Table 4 depicts the binding energies (Kcal/mol) of X. *aethiopica* 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 *X. aethiopica* seed. Some ADME parameters for the prediction of prominent compounds present in *X. aethiopica* seed are presented in Table 6. The interaction of prominent compounds present in *X. aethiopica* seed with cytochrome P450 (CYP) is depicted in Table 7.

Binding energies (Kcal/mol) of *X. aethiopica* seed compounds with bacterial receptors

The binding energies of CTP and DNX 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, GNT, showed better binding energies when compared to CTP and DNX for all the receptors except *K. pneumonia*. The 3D molecular interactions (Figure 3) represent the bonds between the receptors and the ligands. For the 2BRW-CTP 3D interactions, hydrophobic interactions were observed with the amino acids GLN 379A and LYS 382A. Hydrogen bonds were observed with LYS 344A. Hydrophobic interactions were also observed in the 2BRW-DNX complex with residues LYS 382A, LEU 383A, ASP 433A, LYS 434A, GLN 436A, THR 437A, and HIS 440A. The presence of a salt bridge was observed with LYS 434A.

For the 4HBL-CTP docked complex, the amino acids LEU 64B, THR 68B, and GLU 135D were involved in hydrophobic



(a) (b) (c) (d) (e)

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

interactions. The residues ARG 21A, SER 39B, and GLU 125C formed hydrogen bonds with the ligands. The π-stacking bonds were involved with TYR 126C and TYR 131D. A salt bridge was also observed with GLU 125C and GLU 135D. For the 4HBL-DNX docked complex, the receptor's amino acids PHE 14B, ALA 24A, TYR 27A, GLU 25A, LEU 31A, TYR 38A, PRO 118C, and GLN 119C were involved in hydrophobic interactions. The residues GLN 25A and GLU 120C formed hydrogen bonds with the ligands. A salt bridge was also observed with ARG 21A.

Some of the interactions between the 4A5P-CTP 3D complex showed that it had hydrophobic interactions with the amino acids GLU 532B and LEU 556C. A hydrogen bond was observed with ARG 536B. The 4A5P-DNX 3D complex interactions showed the presence of hydrophobic interactions with amino acids ASN 495B, GLU 532B, GLN 535B, ARG 536B, LEU 556C, ILE 565B, and VAL 568B. A hydrogen bond was observed with ASN 495B. The 5O78-CTP 3D complex interactions showed the presence of hydrophobic interactions with the amino acids GLN 61C and TRP 73C. Hydrogen bonds were observed with GLN 61C and ASN 63C. The 5O78-DNX 3D complex interactions showed the presence of hydrophobic interactions with amino acids TYR 58A, VAL 60B, GLN 71A, GLN 71B, GLN 71C, ALA 72A, and ALA 72C. Hydrogen bonds were observed with TYR 58B, GLN 61C, and

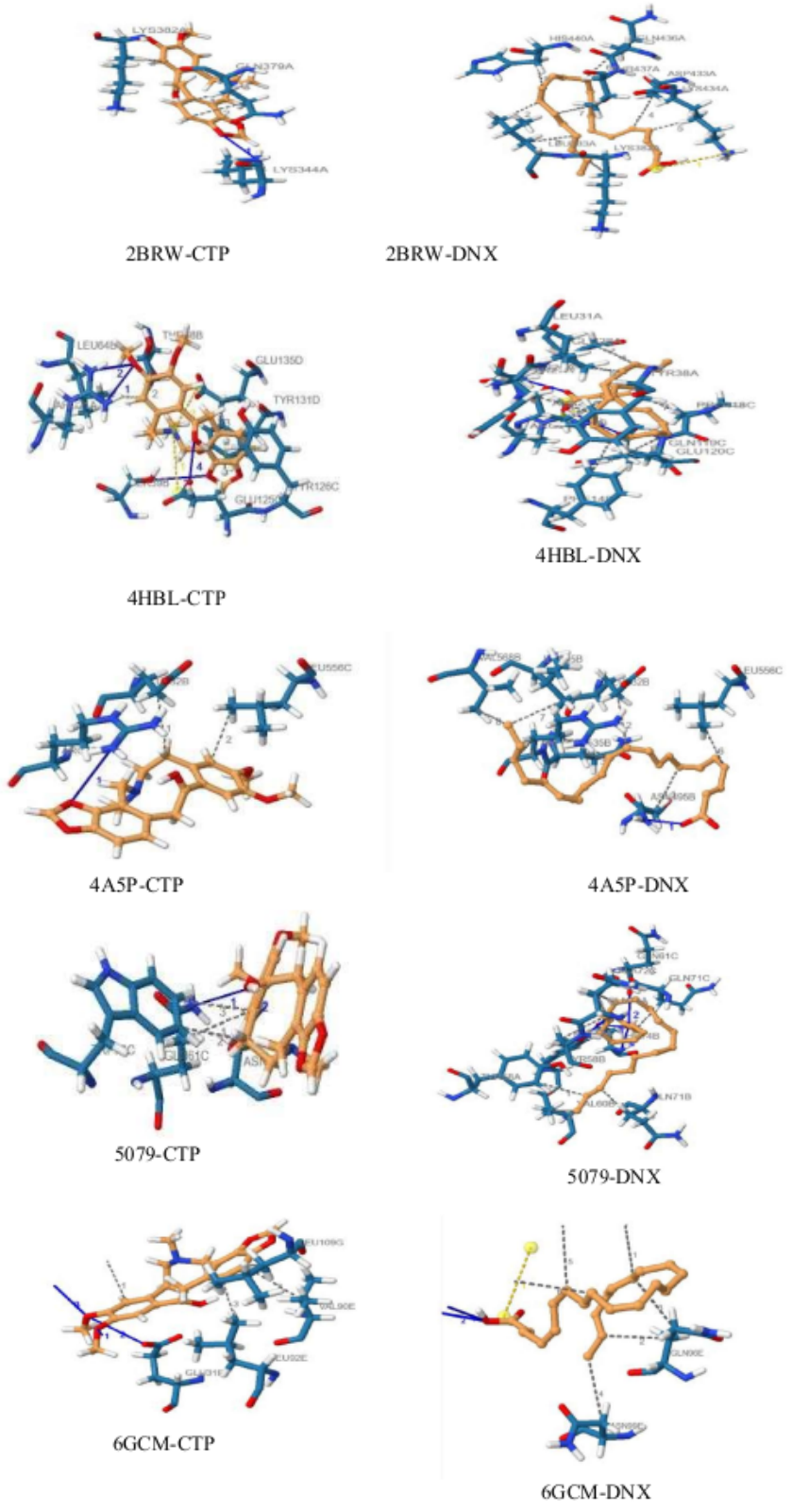
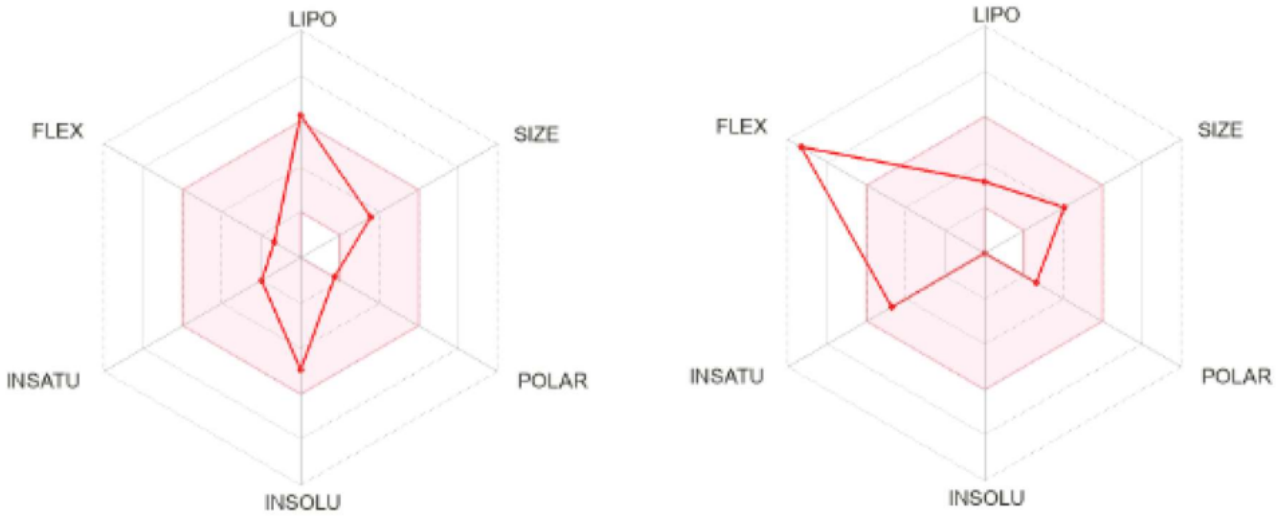


Figure 3: PLIP 3D interactions of the docked complexes.

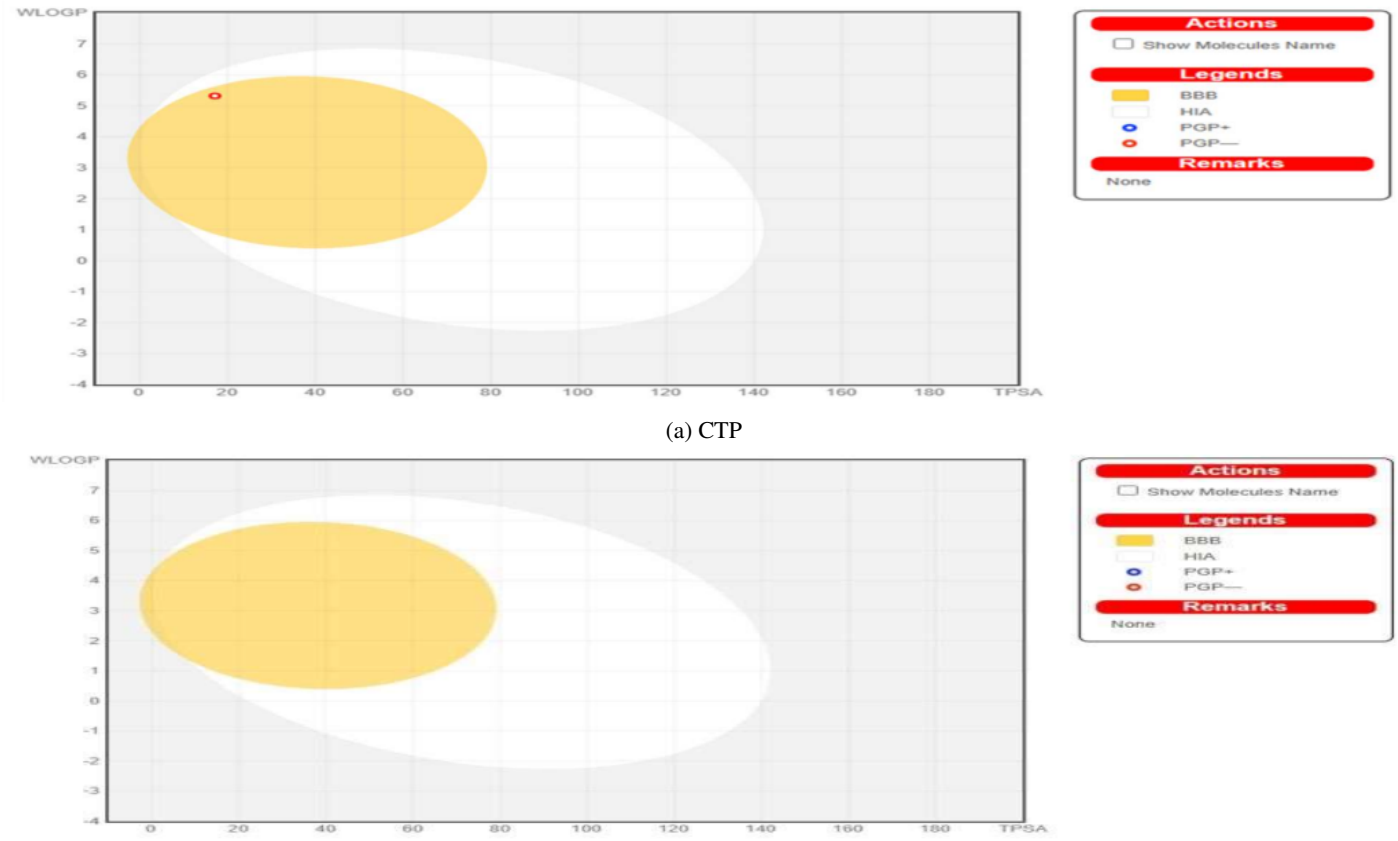
THR 74B.

The 6GCM-CTP 3D complex interactions showed the presence of hydrophobic interactions with amino acids ASP 20J, VAL 90E, LEU 92E, and LEU 109G. Hydrogen bonds were observed with TYR 16J, GLU 31E, and ASN 130B. The 6GCM-DNX 3D



(a) CTP (b) DNX

Figure 4: The Bioavailability Radar of the prominent compounds from *X. aethiopica* seed.



(a) CTP

(b) DNX

Figure 5: BOILED-Egg diagram of the prominent compounds from *X. aethiopica* seed.

complex interactions showed the presence of hydrophobic interactions with amino acids LEU 15J, GLN 96E, ASN 99E, HIS 121I, and ASN 131I. Hydrogen bonds were observed with GLY 56I and SER 164B. There was a salt bridge between the ligand and ARG 55I.

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 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* [12, 21–26]. 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 [12].

For the Lipinski rule [27], a good drug should have a topological polar surface area (TPSA) of less than 140 $Å^2$. This is one of the most significant chemical descriptors that correlates strongly with pharmacokinetic parameters. The test compounds' TPSA was less than 140 $Å^2$ (Table 6).

It is much easier to handle and formulate drugs when the molecule is soluble [28]. This is one of the main benefits of solvent-based drug development. According to Ottaviani *et al*. [29], solubility is a significant factor affecting absorption in research efforts that aim for oral delivery. According to Savjani *et al*. [30], 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 [31] for the test compounds is shown in Table 3. DNX solubility could not be predicted. The solubility profile indicated that CTP was soluble.

The bioavailability score [32] 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 [32] states that a molecule is generally considered a potential therapeutic candidate if its bioavailability score is at least 0.10. The oral bioavailability of CTP was predicted. In contrast, DNX was not found. The CTP had a strong bioavailability score of 0.55.

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 normalized between 1 (easy synthesis) and 10 (extremely difficult synthesis) for synthetic accessibility. The test substance CTP is anticipated to be easily synthesized based on the synthetic accessibility test score (Table 7), but the synthetic DNX cannot be detected.

Understanding the interactions between chemicals and cytochromes P450 (CYP) is also crucial. This isoenzyme superfamily plays a crucial role in drug clearance via metabolic biotransformation. Research suggests that P-gp and CYP can work together to metabolize small compounds in a way that enhances tissue and organism protection [33]. One main reason for pharmacokinetics-related drug-drug interactions [34] 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 [35]. It has been determined that there are several CYP isoform inhibitors. Some substances selectively target particular isoenzymes, while others impact distinct CYP isoforms [36]. 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 CTP did not inhibit CYP1A2, CYP2D6, or CYP3A4. DNX's inhibitory actions were not observed.

Potts & Guy [37] reported that the more negative the log Kp (with Kp in cm/s), the less skin permeant the molecule is. Log Kp values for CTP were negative. This suggested that CTP was not skin-permeable. There was no discernible skin permeant value for DNX.

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.* [38] and Lovering *et al*. [39] 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, CTP was orally bioavailable, while DNX was not orally bioavailable because it was too flexible.

By using the BOILED-Egg (Figures 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 [38, 39]. 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+). CTP had a significant BBB absorption in this study and was predicted to be a non-substrate of P-gp (PGP-). DNX was not detectable.

4. Conclusion

Compounds found in *X. aethiopica* seeds have antibacterial and antioxidant properties. The high concentration of terpenoids in the *X. aethiopica* extract may account for the plant's strong antibacterial and antioxidant properties. It also explains why the plant's seed extract is utilized in herbal medicine to treat infections and illnesses. Drug-likeness, ADME, and docking simulation results all showed how crucial hydrophobic interactions and hydrogen bonds are. All of the compounds have shown positive properties for Lipinski's requirements, such as good solubility in the aqueous medium (Log S) and TPSA<140, as well as good permeability in

biological membranes and the blood-brain barrier. The *in silico* prediction's accuracy and the experimentally demonstrated antioxidant and antibacterial properties agreed well. This work is important for understanding the mechanism by which *X. aethiopica* seed compounds inhibit the tested bacterial species as well as for the design and manufacturing of antibacterial inhibitors.

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