FUDMA Journal of Sciences (FJS)
ISSN online: 2616-1370
ISSN print: 2645 - 2944
Vol. 10 No. 3, February, 2026, pp 119 – 129
DOI: https://doi.org/10.33003/fjs-2026-1003-4601

MOLECULAR DOCKING AND THEORETICAL TOXICITY ASSESSMENT OF BIOACTIVE CONSTITUENTS OF LEAF AND ROOT BARK ESSENTIAL OILS FROM *Spondia dulcis*

***[1, 2]Israel Azogor Ekoro and [2]Oluwakayode Olubunmi Odeja**

[1]Department of Chemistry, Federal University of Medical and Health Sciences, Kwale, Delta State, Nigeria.
[2]Department of Chemistry, Federal University of Petroleum Resources, Effurun, Delta State, Nigeria.

*Corresponding author: israelekoro@gmail.com

ABSTRACT

Spondias dulcis (*S. dulcis*) belongs to the *Anacardiaceae* family that is also called *Ambarella* or golden apple. The medicinal uses of the plant have been reported. This study was conducted to investigate the phytochemical profile, antioxidant activity and the *in silico* drug discovery capability of the essential oil of the leaf and root bark of *Spondia dulcis*. Essential oils were obtained by hydro-distillation, and their compositions were determined using gas chromatography-mass spectrometry (GC-MS). The essential oil of the leaf (SDLEO) was found to be comprised of 30 compounds, with linalool and trans-β-ionone as major constituents, with concentrations of 35.06 and 11.48% respectively. In contrast, the SDREO contained 19 compounds, comprising p-cymene (44.03%) and o-acetyl-p-cresol (14.36%) as major compounds. Theoretical toxicity prediction on the pkCSM platform showed that several compounds were non-hepatotoxic and non-carcinogenic. Molecular docking of the antioxidant protein xanthine oxidase (PDB ID: 3NRZ) demonstrated good binding affinities, in which neophytadiene -5.6 kcal/mol) and farnesol -5.4 kcal/mol) had good binding affinities as compared to ascorbic acid -5.8 kcal/mol). These results indicate that *S. dulcis* essential oils displayed high antioxidant activity, and they contain bioactive non-toxic constituents for future pharmacological development.

Keywords*:* Antioxidant, Essential oil, Molecular dock*ing*, *Spondia dulcis*, Toxicity

INTRODUCTION

Oxidative stress due to the disproportion between the formation of reactive oxygen species (ROS) and the antioxidant response of the body is associated with the pathogenesis of various chronic diseases, such as cancer, cardiovascular diseases, and neurodegenerative disorders (Al-Kufaishi et al., 2025). Antioxidants are molecules which are capable of counteracting ROS, so that they do not cause cell damage (Kıran et al., 2023). They can be either endogenous (synthesized by the body) or exogenous (in diet) (Adwas et al., 2019). Antioxidants have various modes of action including the scavenging of free radicals, chelation of metal ions and the modulation of signaling pathways (Günther & Bednarczyk-Cwynar, 2025). Further research is required to develop effective antioxidant-based therapeutics.

Medicinal plants have been a part of therapeutic activities worldwide for thousands of years (Jiang et al., 2020). Approximately 40% of healthcare around the world is based on traditional medicine, and about 85% of these are based on plant-based remedies (Monib & Monib, 2024). Several plants in Africa have been scientifically investigated and documented for their therapeutic potential in the management of diseases such as malaria, typhoid fever, diabetes and epilepsy (Aloke et al., 2023). Nigeria as a country with a variety of ecological zones is particularly endowed with medicinal plant resources. Traditional medicine has remained a significant part of the country and is being used to offer healthcare to over 70% of the population (Abdulrahman et al., 2021; Agu et al., 2025). Ethnobotanical surveys in various regions provide a record of the different plants used and the ailments they treat, often the knowledge having been gathered through engagement with the community (Lawal et al., 2022). Essential oils (EOs) refer to natural volatile secondary metabolites produced by aromatic plants (Joujeh et al., 2024). Terpenes and their oxygenated derivatives such as alcohols, aldehydes, esters, ketones, phenols and oxides are the major constituents of EOs and these compounds are responsible for their characteristic aroma, volatilities and lipophilicity (Paul et al., 2020; Singh et al., 2022). The composition of EOs depends on a particular plant part and species (Pino et al., 2023). The EOs has a wide range of applications in various industries. They are used as natural preservatives in the food industry to increase shelf life and avoid microbial contamination (Noshirvani et al., 2024). They are used in cosmetics as antioxidants, antimicrobials, and anti-inflammatory (Cunha et al., 2022). In medicine, essential oils have been explored as therapeutic agents against a variety of diseases and conditions (Mehdizadeh & Moghaddam, 2018). The increased interest in natural drug substitutes to synthetic drugs has led to further research on essential oils.

Theoretical techniques play a central role in contemporary drug discovery as they provide low cost pre-clinical evaluation of bioactivity interaction mechanism (Islam et al., 2025). ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) is an important in silico methodology that is used to analyze the pharmacokinetic and safety profile of a potential drug candidate (Gu et al., 2024). The tool utilizes various algorithms, such as quantitative structure-activity relationship (QSAR) models and machine learning techniques. Computer-based drug design and discovery applications are also based on molecular docking, which predicts a protein or other biomolecule's binding mode and affinity to small molecules, e.g., ligands or inhibitors (Ansari et al., 2025). Virtual screening is an approach that involves screening large libraries of compounds using molecular docking and reduces the number of compounds that need to be experimentally tested (Ahmed et al., 2024). The combination of ADMET profiling and molecular docking offer researchers an opportunity to simplify the drug discovery process, minimize costs of drug development, and improve the chances of finding safe and effective drug candidates.

Spondias dulcis (*S. dulcis*) belongs to the Anacardiaceae family that is also called Ambarella or golden apple (Gomasta et al., 2025). It is a medium-sized tree which grows rapidly as it can reach a height of 20 meters (Mohammed et al., 2017).

Its fruits turn yellow. It is cultivated due to the edible fruits; however, it is also reported to have medical uses in tropical regions like the Caribbean, Southeast Asia as well as Africa (Fernandes et al., 2024). *S. dulcis* is known to have medicinal properties that are attributed to the fact that the plant contains a variety of bioactive compounds. These include ellagitannins, hydroxybenzoic acids, hydroxycinnamic acids, flavonols, flavanones and flavanonols (Sinan et al., 2021). There is absence of comprehensive stuidies on the antioxidant activity, and molecular interactions of essential oils from *Spondia dulcis*. This study aims to identify the chemical components of *Spondia dulcis* essential oils, determine the antioxidant and toxicity potential using theoretical methods. This research will help contribute to the discovery of new active compounds relevant in drug discovery and the theoretical predictions will provide a guide for future experimental analysis.

MATERIALS AND METHODS

Collection and Preparation of Plant Material

The fresh leaf and root of *S. dulcis* were collected from the botanical garden of the University of Ibadan, Oyo State, Nigeria. Specimens were identified and authenticated at the Forest Research Institute of Nigeria (FRIN), Oyo State, where a voucher specimen with herbarium number FHI 112667 was deposited in the FRIN herbarium. The fresh plant materials were chopped into small sizes respectively and the essential oils were immediately collected from the fresh plants material by hydro-distillation on a Clevenger-type apparatus for 4 hours. The essential oils were collected and stored at 4oC before analysis.

Gas Chromatography–mass Spectrometry (GC–MS) Analysis

About 1.5 mL of n-hexane was added to the GC vial and approximately 1.0 µL of the essential was added, centrifuged for about 5 min. Te constituents of the stem essential oil of E. speciosa were identifed on an Agilent 7809A gas chromatograph hyphenated with an Agilent mass detector featuring a split/splitless injector interfaced to a mass selective detector operating at 70 eV. With a 1428 amu/sec scan rate, the ion source temperature was 200 °C with a mass spectral range of m/z 50–700. A 30 m long HP-5MS column with an internal diameter of 0.25 mm and a film thickness of 0.25 m was installed in the GC column. Te oven temperature was adjusted as follows: 80°C at first for 2 min, then 10°C/min up to 240 °C/6 min. Helium was used as the carrier gas, with a 1 mL/min fow rate. Injection volume, linear velocity and pressure were adjusted at 1.0 µL, 362 cm/s and 56.2 kPa, respectively. The oven temperature was set at 60°C, hold for 1 min to 180°C for 3 min at 10 °C/min, then the fnal temperature was 280°C for 2 min at 10 °C/min. Both injector and detector temperatures were fixed at 250 °C. Based on their retention indices, which were calculated using homologous series of normal alkane and comparing the mass spectral fragmentation patterns (NIST data/ base/Chemstation data system) with information previously published in the literature, the constituents of essential oil were identifed (Ibok et al., 2023).

Theoretical Prediction of Toxicity

The ligands (compounds) used in prediction of toxicity were all the identified constituents of *Spondia dulcis* essential oils (leaf and root) obtained from the GC-MS analysis. This is a computational methodology that offers an effective tool to filter compounds with possible toxicity, which reduces the ethical, time, and cost of the use of conventional animal models (Rajeshkumar et al., 2022). The PubChem database (https://pubchem.ncbi.nlm.nih.gov) was searched to find the chemical structures of the compounds. Theoretical predictability of toxicity was evaluated in the pkCSM web server (https://biosig.lab.uq.edu.au/pkcsm/) that provides an array of predictive models of different toxicological endpoints (Gentile et al., 2020). The platform makes it possible to predict essential ADMET parameters that are essential in drug discovery and drug development at an early stage (Chikhale et al., 2024; Pyka et al., 2024). The software offers a prediction system of various forms of toxicity, such as mutagenicity and cardiotoxicity (Mansour et al., 2020). The PkCSM web server also offers the prediction of the maximum tolerated dose, oral rat acute toxicity, and oral rat chronic toxicity, providing a more in-depth insight into the adverse effects of a compound (Hariyono et al., 2022).

Molecular Docking Protocol

PyRx was utilized for the molecular docking (Kumar et al., 2020). The reference antioxidant (ascorbic acid) and GC-MS components were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The protein receptor (PDB ID: 3NRZ), was obtained from the RCSB database (https://www.rcsb.org/). The selection of PDB ID: 3NRZ was justified by the relevance of xanthine oxidase in oxidative stress and related disorders, which supports its use as a target protein for for antioxidant molecular docking studies (Ardjani & Mekelleche, 2017). Molecular docking studies have demonstrated that various compounds exhibit significant binding affinity scores to this protein, indicating their potential as effective antioxidants. Compounds like methyl gallate have shown high binding affinity (-7.45 kcal/mol) to 3NRZ, suggesting strong antioxidant potential (Sutomo et al., 2020). The receptor was cleaned and prepared for docking using the discovery studio tool (DS) (Ayodele et al., 2023). The result of docking and interactions using blind docking protocol were also visualized in the DS tool. Ekoro et al. (2025) described blind docking as protocol without prior knowledge of the binding site and explains how the ligand is interacted across the entire protein surface.

RESULTS AND DISCUSSION

GC-MS Composition of Essential Oils

The essential oil obtained from the leaves of *S. dulcis* (SDLEO) was a rich and complex blend volatile component (30) accounting for 99.97% of the overall composition as presented by the GC-MS data (Figure 1) (Table 1). Several chemical classes such as fatty acid esters, monoterpenes and sesquiterpenes were identified in the essential oil. The EO is chemically diverse and consists of monoterpenes, sesquiterpenes and fatty acid esters. Limonene, pinene, linalool and other volatile organic compounds which occur in plants have been identified by GC-MS (Petretto *et al*., 2023; Shao *et al*., 2022). According to previous research (Cruz *et al*., 2023; Dev & Moj, 2024), caryophyllene and farnesene are some of the sesquiterpenes present in essential oils. This study found that linalool made up 35.06% of the total composition of the leaf essential oil and had a retention time of 4.70 minutes. This monoterpene alcohol has a nice floral aroma (Dev & Moj, 2024) and has been widely reported to have antimicrobial, anti-inflammatory, and antioxidant properties in different plants (Fillipova *et al*., 2021; Tian *et al*., 2022). Trans-β-ionone (11.48%) was the second most abundant component and eluted at 8.981 minutes. β-ionone is also one of the volatile compounds from extracts reported in plants

such as *Dunaliella salina* extract (Valdés *et al*., 2024) and various types of green tea (Shao *et al*., 2022). Hexahydrofarnesyl acetone which eluted at 8.34 minutes was the third most abundant compound (7.01 %). Several fatty acid methyl esters such as methyl palmitate at 4.68% (RT: 12.98 minutes), methyl isomyristate at 2.62% (RT: 11.258 minutes), methyl stearate at 2.44% (RT: 14.57 min) and methyl vaccenate at 1.70% (14.39 minutes) were also contained in the SDLEO. *S. dulcis* root bark oil (SDREO) had a different chemical profile than its leaf oil, and was mainly dominated by high levels of aromatic monoterpenes and derivatives. The oil from the root bark of *S. dulcis* (SDREO) had 19 components with a total composition of 99.97 % (Figure 2) (Table 2). The major component identified from the oil was the p-cymene with a value of 44.03% and a retention time of 3.59 min. P-Cymene is an aromatic monoterpene that possesses antimicrobial properties and has been found in many essential oils (Dodoš et al., 2024; Makangara *et al*, 2024). The o-acetyl-p-cresol was the second highest component with 14.36% of the essential oil at a retention time of 6.96 minutes. Dodoš *et al*. (2024) reported that carvacrol and thymol are phenolic compounds with strong antibacterial, antioxidant, and antifungal properties and occur in essential oils. Neral, which is an isomer of citral, was also found in the essential oil with a retention time of 6.23 minutes (10.91% component). Neral is an acyclic monoterpenoid aldehyde; significant in fragrance formulations (Fillipova *et al*., 2021) Linalool is a monoterpenoid alcohol with floral-citrusy odour. It was present at 4.31% with a retention time of 4.44 minutes. The amount is much lower than what is usually found in leaf oils (Shaji *et al*., 2023). The essential oil of the root bark of *Spondia dulcis* also contained oxygenated monoterpenes like borneol 2.62% geraniol 2.12% and isogeranial 3.04%. Borneol is a bicyclic monoterpene alcohol (Pradhan *et al*., 2022). Geraniol refers to an acyclic monoterpenoid alcohol. It has a fragrance similar to rose; hence it's used in the production of perfumes and cosmetics (Makangara *et al*., 2024). Isogeranial also contributed to the volatile oil profile. Terpene alcohols, in general, present very specific characteristics as compared to the non-oxidized terpene analogs (Zongo *et al*., 2024). The presence of numerous monoterpenes and its derivatives suggested the potential bioactivities of *Spondia dulc*is root bark essential oil, which are in line with similar findings obtained from other plant essential oils rich in these compounds (Tejada-Muñoz *et al*., 2024). In comparison, SDLEO was dominated by linalool and also presented fatty acid methyl esters, while SDREO was mainly represented by p-cymene and also showed a higher percentage of aromatic monoterpenes. SDLEO and SDREO shared certain components, like linalool and caryophyllene, in extremely different concentrations.

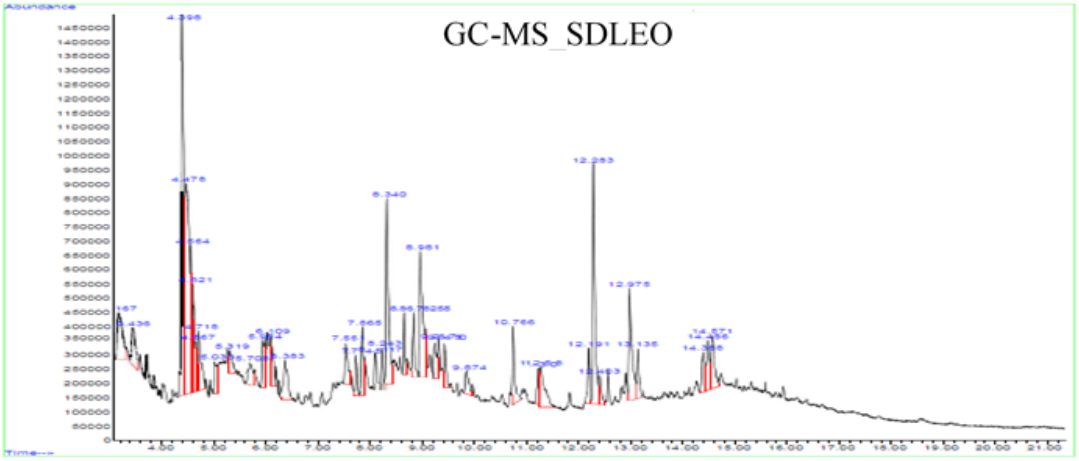

Figure 1: GC-MS Spectrum of SDLEO

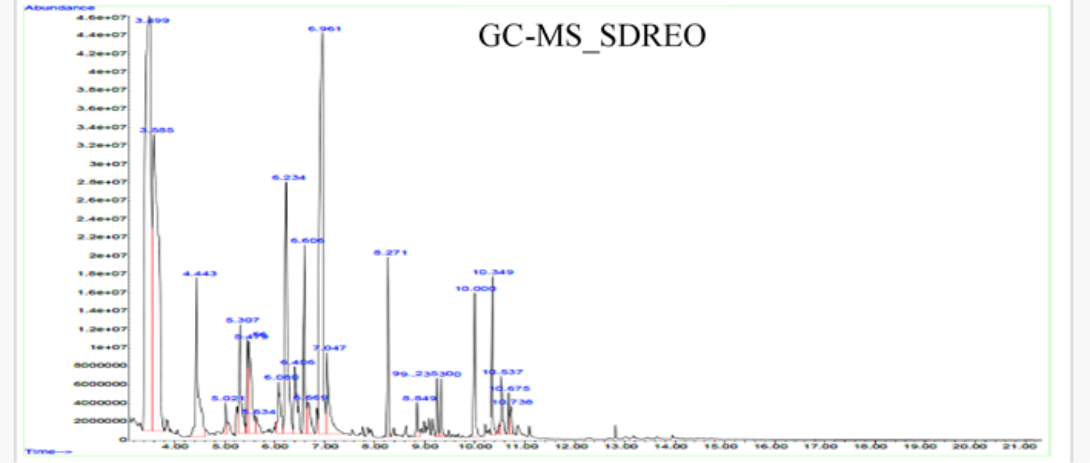

Figure 2: GC-MS Spectrum of SDREO

Table 1: SDLEO Components Identified by GC-MS

S/N	Compounds	Area %	RT (min)	CID
1.	Linalool	35.06	4.70	6549

2.	trans-β-Ionone	11.48	8.98	638014
3.	Hexahydrofarnesyl acetone	7.01	8.34	10408
4.	Methyl Palmitate	4.68	12.98	8181
5.	Methyl isomyristate	2.62	11.26	21204
6.	Methyl stearate	2.44	14.57	8201
7.	8-Heptadecene	2.44	10.77	5364555
8.	1-Octen-3-yne	2.34	6.38	140268
9.	α-Terpineol	2.29	5.71	131875736
10.	p-mentha-1(7),8-diene	2.16	6.11	26300
11.	4-Ethyl-O-Xylene	2.03	3.43	13629
12.	β-Damascenone	1.98	7.87	5366074
13.	11,13-Dimethyl-12-tetradecen-1-ol acetate	1.96	14.49	549821
14.	camphene	1.90	4.62	6616
15.	β-Santalene	1.75	8.86	10534
16.	Methyl vaccenate	1.70	14.39	5364432
17.	Dehydro-ar-ionene	1.51	7.55	121677
18.	1-Methoxy-9-octadecene	1.35	13.14	5366217
19.	Humulene epoxide II	1.33	9.45	564746
20.	Santalol	1.30	8.67	5281532
21.	p-Menth-3-en-7-al	1.22	5.95	15601950
22.	Neophytadiene	1.22	12.19	10446
23.	2,4-tert-butylphenol	1.16	9.27	7311
24.	copaene	1.06	7.75	12303902
25.	Farnesol	1.04	9.87	445070
26.	Geosmin	1.03	8.12	29746
27.	8-methyl-1-undecene	1.0	11.23	522552
28.	4-Methyl-1,4-heptadiene	1.0	12.40	5362810
29.	Caryophyllene	0.96	8.24	5281515
30.	(6E)-8-hydroxylinalool	0.95	5.32	5280678
	Total	99.97		

Key: CID- Compound Identifier

Table 2: SDREO Components Identified by GC-MS

S/N	Compounds	Area %	RT (min)	CID
1.	p-Cymene	44.03	3.59	7463
2.	o-Acetyl-p-cresol	14.36	6.96	15068
3.	Neral	10.91	6.23	643779
4.	Linalool	4.31	4.44	6549
5.	Isogeranial	3.04	5.48	6428928
6.	Borneol	2.62	5.31	64685
7.	Biosol	2.48	7.05	18597
8.	Caryophyllene	2.48	8.27	5281515
9.	Caryophyllene oxide	2.21	10.00	1742210
10.	Geraniol	2.12	6.41	637566
11.	Longifolene	2.12	10.35	1796220
12.	α-Amorphene	2.29	8.85	101708
13.	O-Methylthymol	1.65	6.08	14104
14.	4-Carvomenthenol	1.60	5.46	11230
15.	α-Humulene	1.17	10.54	595137
16.	Camphor	0.59	5.02	2537
17.	γ-Selinene	0.58	10.74	521334
18.	Spirojatamol	0.57	10.68	11053257
19.	Cyclofenchene	0.55	5.63	79022
	Total	99.97		

Key: CID- Compound Identifier

Theoretical Toxicity Analysis

The toxicity evaluation of the essential oil constituents from *Spondia dulcis* dulcis was performed in an attempt to predict their safety profile using two toxicity parameters (liver injury and carcinogenic potential). Liver injury, or hepatotoxicity, is

a major issue in the field of toxicology, because the liver plays a key role in metabolism, detoxification, and excretion (Sheng *et al*., 2024]. The tremendous metabolic activity of the liver makes it especially susceptible to ROS-induced damage, which can result in lipid peroxidation; protein modification and DNA damage (Oyeyemi *et al*., 2024). Carcinogenicity is the property of a substance to cause cancer, a complex process with several phases such as initiation, promotion and progression (Bhat *et al*., 2024). The results are given in Table 3. The analysis showed that both the leaf (SDLEO) and root (SDREO) essential oils contained compounds of different levels of predicted toxicity. Some compounds were classified as "Safe", meaning that there was a low risk of causing liver damage or being carcinogenic, while others were classified as "Toxic", which means that there is a possibility that the compound has adverse effects. For the leaf essential oil (SDLEO), several compounds such as CIDs 6549, 10408, 8181, 21204, 5364555, 8201 and 1742210 were predicted to be safe according to both parameters. These compounds were found to be non-hepatotoxic and non-carcinogenic and hence were suitable for further pharmacological evaluation. Also, compounds such as CIDs 638014, 140268, 5281515, 131875736, 26300, and 595137 were classified as potentially toxic in both categories, suggesting a potential health hazard. A similar pattern was observed in the essential oil of the roots (SDREO). Compounds such as CIDs 15068, 643779, 6549, 6428928, 64685, 18597, 5364432 and 7311 were determined to be safe and others, such as CIDs 10703, 5281515, 12303902 and 5362810 were determined to be toxic. A few compounds showed mixed results as they were safe under one parameter but toxic under the other, which could be the sign of conditional or environment-dependent toxicity. On the toxicity assessment, *S. dulcis* essential oils were found to have a variety of bioactive compounds, some of which were safer for therapeutic use than others. Consequently, only the compounds that were safe according to both toxicity parameters (non-hepatotoxic and non-carcinogenic) were used in further computational assessments. A systematic exclusion of toxic compounds according to either or both criteria was performed in order to assure that only non-toxic and pharmacologically acceptable substances went through in subsequent biological interpretation.

Table 3: Theoretical Toxicity Analysis of *S. dulcis* EOs

	SDLEO			SDREO	
CID	**Liver Injury**	**Carcinogenesis**	**CID**	**Liver Injury**	**Carcinogenesis**
6549	Safe	Safe	10703	Toxic	Toxic
638014	Toxic	Toxic	15068	Safe	Safe
10408	Safe	Safe	643779	Safe	Safe
8181	Safe	Safe	6549	Safe	Safe
21204	Safe	Safe	6428928	Safe	Safe
5364555	Safe	Safe	64685	Safe	Safe
8201	Safe	Safe	18597	Safe	Safe
140268	Toxic	Toxic	5281515	Toxic	Toxic
131875736	Toxic	Toxic	1742210	Safe	Safe
26300	Toxic	Toxic	637566	Safe	Safe
13629	Toxic	Toxic	1796220	Toxic	Safe
5366074	Safe	Toxic	101708	Toxic	Toxic
549821	Safe	Safe	14104	Safe	Safe
6616	Toxic	Safe	11230	Safe	Safe
10534	Toxic	Safe	595137	Toxic	Toxic
5364432	Safe	Safe	2537	Toxic	Toxic
121677	Toxic	Toxic	521334	Toxic	Toxic
5366217	Safe	Safe	11053257	Toxic	Safe
564746	Toxic	Toxic	79022	Toxic	Safe
5281532	Toxic	Safe	-	-	-
15601950	Safe	Toxic	-	-	-
10446	Safe	Safe	-	-	-
7311	Safe	Safe	-	-	-
12303902	Toxic	Toxic	-	-	-
445070	Safe	Safe	-	-	-
29746	Toxic	Safe	-	-	-
522552	Toxic	Safe	-	-	-
5362810	Toxic	Toxic	-	-	-
5281515	Toxic	Toxic	-	-	-
5280678	Safe	Safe	-	-	-

Molecular Docking Interaction Analysis

The molecular docking analysis was conducted to visualize the possible interactions of the non-toxic components of *Spondias dulcis* leaf and root essential oils (SDLEO and SDREO, respectively) and the antioxidant protein target (PDB ID: 3NRZ). The resulting grid box parameters from the blind docking was centered at x = 41.55, y = −17.67, z = 29.47 Å, with dimensions of 38.54 × 46.22 × 54.75 Å^3. The docking results obtained (Table 3) provided insight into the binding affinity of the compounds with the selected receptor. Figures 4-10 shows the interaction patterns of the top three compounds with the best affinities each for SDLEO and

SDREO. Among the examined ligands, Neophytadiene (CID 10446) of SDLEO showed the highest docking affinity with a binding energy of -5.6Kcal/mol showing a good and favorable interaction with the active site of the protein (Figure 3). The Interactive profile showed that the Neophytadiene was stabilized mainly through hydrophobic interactions (alkyl interactions) with residues such as Val88, Pro118 and Val121, Phe107. These nonpolar interactions were likely responsible for excellent conformational fit of the ligand into the receptor pocket. 6E-8-hydroxylinalool (CID 5280678) showed a binding energy of -5.5 Kcal/mol (Figure 4), which suggested that the hydroxyl functional group could have been involved in hydrogen bond formation, and increased its affinity for the active site. This compound was found to form a hydrogen bond with residue Asn146, whereas hydrophobic interactions were detected with Phe143, Ile156 and Leu157. Farnesol (CID 445070) also interacted with the receptor (Figure 6) with a docking score of -5.3Kcal/mol. In comparison, the reference antioxidant Ascorbic acid (CID 54670067) had a docking score of -5.8Kcal/mol (Figure 6) which was slightly higher (more negative) than those of the essential oil constituents. The docking pose showed several hydrogen bonds with Thr52, Ser69, Ser123 and Asn 146, which indicated its high binding polarity. The network of hydrogen bonds in ascorbic acid was probably responsible for its better affinity and was the validation of the docking protocol. The similar affinities of Neophytadiene and Farnesol with the standard compound implied that the phytochemicals may have significant antioxidant activities owing to similar binding mechanisms. In the SDREO profile, the compound Linalool (CID 6549) had a -5.2 kcal/mol docking score (Figure 7), which was quite high in comparison to the root oil compounds. Linalool formed hydrophobic interactions with components amino acids such as Ile120 and Tyr153. O-Methyl-Thymol (CID 14104) had obtained a docking score of -4.9Kcal/mol (Figure 13). Geraniol (CID 637566) had a binding energy of -4.7Kcal/mol (Figure 8). Other constituents from SDREO such as compounds with CIDs 15068, 643779, and 6428928 had relatively lower binding affinities (-4.0 to -4.6Kcal/mol), indicating weaker stabilizing interactions in comparison to the dominant ligands. The binding affinities of SDLEO constituents were generally higher than the SDREO suggesting that the essential oil of the leaves contained more potent antioxidant ligands in terms of molecular binding behavior. SDLEO compounds' hydroxyl substituents, unsaturated aliphatic chains, and hydrophobic moieties seemed to improve the stability of their interactions with the protein receptor (Okpala *et al*., 2024). A variety of binding modes, characterized by hydrogen and hydrophobic interactions, were revealed by the docking poses displayed in Figures 3–9; these modes all contributed to the stability of the ligand-receptor complex. There was a correlation between the observed binding trends and the essential oils' antioxidant potential. Therefore, a mechanistic understanding of the experimental antioxidant results was provided by the molecular docking study, which showed that certain phytoconstituents interacted with the antioxidant target protein in an efficient manner to potentially have biological effects.

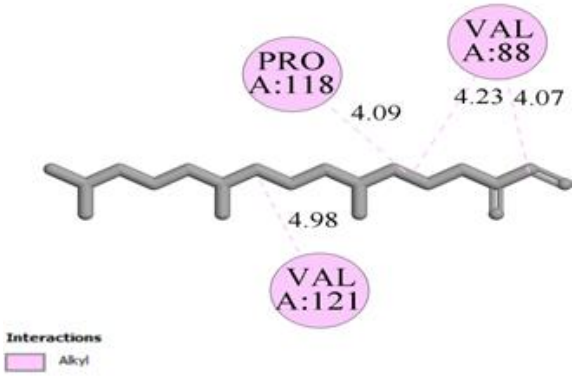

Figure 3: Docking Interactions of Protein 3NRZ and SDLEO-Neophytadiene (CID 10446)

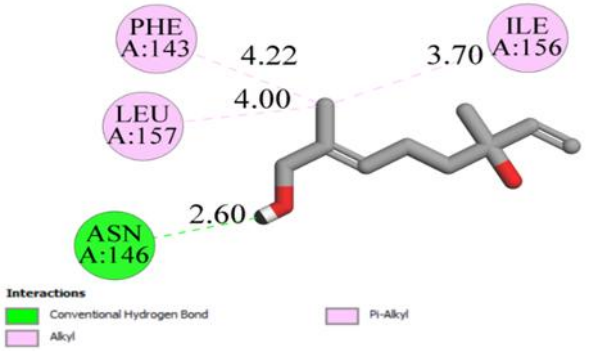

Figure 4: Docking Interactions of Protein 3NRZ and SDLEO-6E-8-hydroxylinalool (CID 5280678)

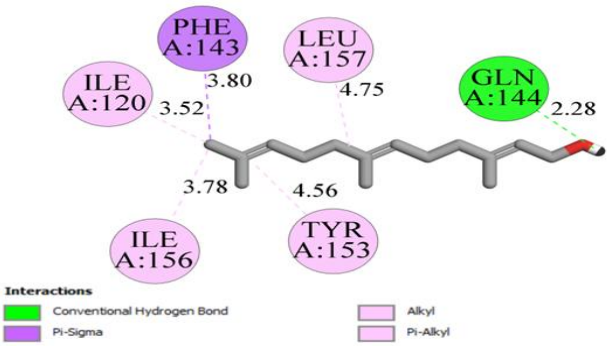

Figure 5: Docking Interactions of Protein 3NRZ and SDLEO-Farnesol (CID 445070)

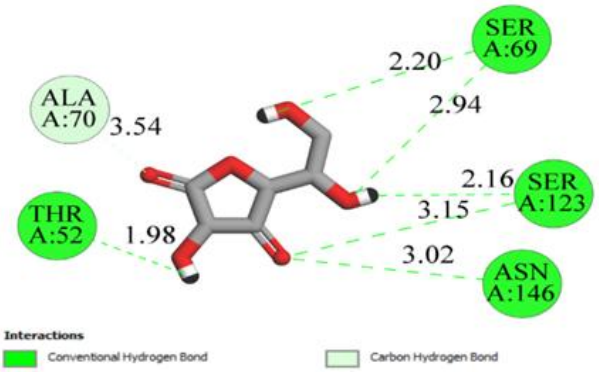

Figure 6: Docking Interactions of Protein 3NRZ and Reference-Ascorbic Acid (CID 54670067)

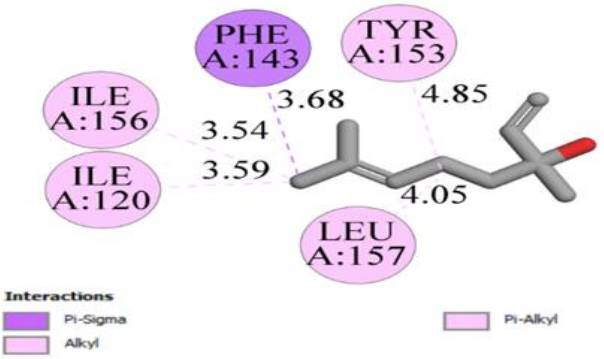

Figure 7: Docking Interactions of Protein 3NRZ and SDREO-Linalool (CID 6549)

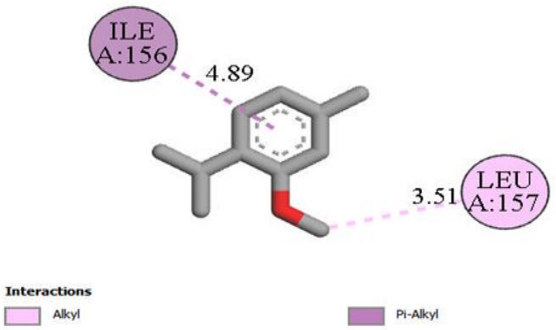

Figure 8: Docking Interactions of Protein 3NRZ and SDREO-O-Methyl-Thymol (CID 14104)

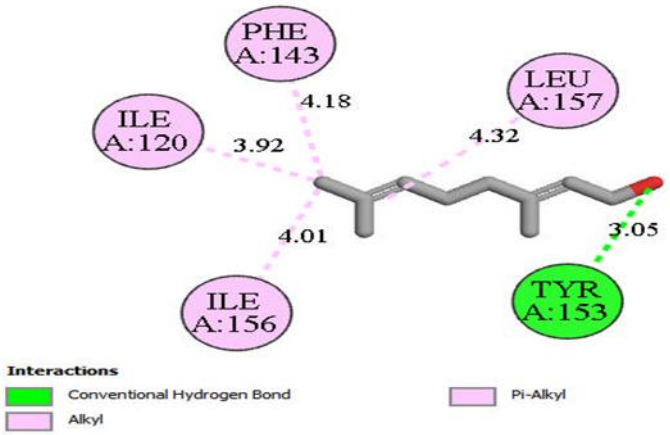

Figure 9: Docking Interactions of Protein 3NRZ and SDREO-Geraniol (CID 637566)

Table 1: Docking Score of *S. dulcis* EOs

SDLEO		SDREO	
CID	DOCKING SCORE (Kcal/mol)	CID	DOCKING SCORE (Kcal/mol)
6549	-5.2	15068	-4.0
10408	-5.3	643779	-4.6
8181	-4.3	6549	-5.2
21204	-4.6	6428928	-4.5
5364555	-4.5	64685	-4.1
8201	-4.2	18597	-4.0
549821	-4.6	1742210	-4.0
5364432	-4.1	637566	-4.7
5366217	-4.3	14104	-4.9
10446	-5.6	11230	-4.2
7311	-5.3	–	–
445070	-5.4	–	–
5280678	-5.5	–	–
# 54670067	-5.8	# 54670067	-5.8

Key: # Ascorbic acid

CONCLUSION

The present study focused on the phytochemical profile, as well as the in silico the antioxidant properties of the essential oils of leaf and root bark of *Spondia dulcis*. The results of the GC-MS analysis showed that linalool (35.06%) and trans-b-ionone (11.48%) were the main compounds in the leaf essential oil (SDLEO). In comparison, the essential oil extracted from root barks (SDREO) comprised of p-cymene (44.03%), o-acetyl-p-cresol (14.36%) as the major constituents. Toxicity analysis through theoretical approach showed that some of the compounds were not hepatotoxic and carcinogenic indicating that oils were safe to use in event of pharmacological application. Molecular docking study demonstrated that the identified compounds such as neophytadiene, farnesol and linalool had good binding affinities with the antioxidant enzyme xanthine oxidase (PDB ID: 3NRZ) as compared to ascorbic acid indicating a potential therapeutic significance. The findings signified that the essential oils of *Spondia dulcis* has potential natural antioxidants and contain bioactive compounds which are non-toxic and can be used in drug discovery and development of plant based medicinals. Future research should involve *in vitro*, *in vivo* and clinical assessments to validate the antioxidant activity and safety of *Spondia dulcis* essential oils in biological systems. To determine their precise methods of antioxidant action, major bioactive substances such farnesol, neophytadiene, and linalool should be isolated and structurally studied. Further investigations should study various biological activities such as anti-inflammatory, anticancer, and antibacterial characteristics to extend the pharmacological scope of *Spondia dulcis* essential oil.

Author Contributions

I. A. Ekoro: Final draft, *in silico* Methodology, and Experiment. **O. O. Odeja:** Experiment**,** Analysis, First draft.

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