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Identification, Molecular Docking and Pharmacokinetic Evaluation of Bioactive Flavonoids from *Dennettia tripetala* Baker. f. (Annonaceae) Root

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Dennettia tripetala Baker f. (Annonaceae) is a medicinal plant traditionally used for treating ailments such as pain, inflammation, diabetes, and respiratory conditions. This study focused on isolating and characterizing bioactive compounds from the ethyl acetate fraction of *D. tripetala* root extract and evaluating their potential therapeutic properties through molecular docking analysis. The plant material was sourced from Itak Ikot Akap village in Ikono local government area of Akwa Ibom State, Nigeria. The roots were thoroughly cleaned, air-dried, and ground into a fine powder. An extraction was performed using 70% aqueous methanol, followed by partitioning into various solvent fractions to separate the compounds based on their polarity. Open-column chromatography and preparative thin-layer chromatography (TLC) were employed to isolate rutin, which was identified and characterized using ^{1}H NMR, ^{13}C NMR, and FTIR spectroscopy. Molecular docking studies were performed to evaluate the binding affinities of rutin, quercetin, vitexin, and aspirin (standard) against analgesic and anti-inflammatory protein targets, including TRPV1, μ-opioid receptor, and phospholipase A2. Pharmacokinetic properties were assessed using Lipinski's rule of five and *in silico* tools. The spectroscopic data obtained showed that the compound isolated was rutin, a flavonoid with strong antioxidant and anti-inflammatory properties. Molecular docking revealed that rutin exhibited higher binding affinities compared to aspirin for several protein targets, suggesting its potential as a natural analgesic and anti-inflammatory agent. However, pharmacokinetic analysis indicated poor oral bioavailability due to Lipinski rule violations, emphasizing the need for alternative delivery strategies. This study highlights *D. tripetala* root as a valuable source of bioactive compounds, particularly rutin, with promising therapeutic applications.

Keywords: Dennettia tripetala; anti-inflammatory; analgesic; phytochemical properties; isolation; molecular docking.

1. INTRODUCTION

Dennettia tripetala, commonly known as pepper fruit, is a plant native to the rainforests of West Africa, particularly Nigeria. It belongs to the family Annonaceae and was first described by the botanist Baker F. The plant is a small woody shrub or tree that typically reaches a height of 12 to 18 meters. It features a fibrous bark with a strong characteristic scent. Its leaves are elliptic in shape, measuring approximately 3 to 6 inches in length and 1.5 to 2.5 inches in width, with a shortly acuminate tip and a broadly rounded base. The plant produces fruits between March and May. *D. tripetala* is traditionally utilized in African medicine for various ailments. Its applications include the treatment of diabetes, fever, cough, catarrh, asthma, diarrhea, and pain. The fruits are specifically used to clear the throat, reduce excessive saliva, and enhance appetite. In postpartum care, similar to the use of *Tetrapleura tetraptera*, the fruits are incorporated into women's diets to promote uterine contraction (Iseghohi, 2015).

Beyond its traditional uses, *Dennettia tripetala* has been studied for its pharmacological properties. Various parts of the plant have demonstrated potential as antioxidants, antidiabetic, antimicrobial, analgesic, anti-inflammatory, and anticancer agents. Phytochemical analyses of the fruits and leaves have identified numerous bioactive compounds, including alkaloids, tannins, saponins, flavonoids, terpenoids, steroids, and cardiac glycosides. Additionally, compounds such as quercetin, uvariopsine, stephenanthrine, and 2-methylphenol have been isolated from different parts of the plant. Gas Chromatography-Mass Spectrometry (GC-MS) analysis of the essential oils from the fruit and leaves has further revealed a variety of compounds contributing to its biological activities (Oyemitan et al., 2006; Elekwa et al., 2011).

The root of *D. tripetala* is furnished with dennetine (2, 6-dimethoxychromone), 3-phenanthrene alkaloids-uvariopsine, stephenanthrine, argentinine and vanillin; the fruit essential oil gave 2-phenylnitroethane (72.41%), linalool (18.0%) and (6E) – nerolidod (4.51%), o-cymene, β-ocimene, copaene, -farnescene, caryophyllene and its oxide, eudesmol. *D. tripetala* fruit essential oils contain 1-nitro-pentane, α- and β-cinene, camphene, β-myrcene, α-phellandrene, p-cymene, (+)-4-carene, β-ocimene, linalool, α-terpinene, phenylethyl-alcohol, borneol, terpin-4-ol, α-terpineol, safrole, 2-methylphenyl formate, elemene, caryophyllene, humulene, α-farnescene, caryophyllene oxide, copaene, 4-epi-cubenol, guaiol, α-eudesmol, trans-cadinol, azulen-5-ol, ascorbic acid 2,6-

dihexadecanoate and 9-octadecenoic acid. Leaf fatty acid composition, caprylic, capric, lauric, myristic (tetradecanoic), myristoleic (Tetradec-9-enoic), palmitic, palmitoleic (hexadec-9-enoic), stearic, oleic (cis-9-Octadecenoic), linoleic (cis, cis-9, 12-octadecadienoic), linolenic (cis, cis-9,12,15-octadecatrienoic) acid (Egharevba and Idah, 2015; Oyemitan et al., 2008).

The increasing prevalence of chronic diseases like cancer, inflammations and pains as well as the resistance to synthetic treatments like the use of nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids as well as their associated side effects creates an urgency for novel therapeutic alternatives of natural origin (Pahwa et al., 2021). This study aims to isolate and characterize bioactive constituents from the ethyl acetate fraction of the root of *D. tripetala* and evaluate their therapeutic properties through molecular docking.

2. MATERIALS AND METHODS

2.1 Plant Collection and Identification

The root of *D. tripetala* was collected from Itak Ikot Akap village in Ikono Local Government Area, Akwa Ibom State, Nigeria. The plant was identified by Dr Imeh Imoh Johnny of the Department of Pharmacognosy and Natural Medicine, Faculty of Pharmacy, University of Uyo, Uyo and authenticated by Prof Mrs. M.E Bassey of the Department of Botany and Ecological Studies, Faculty of Biological Sciences, University of Uyo, Uyo and a voucher specimen deposited in the herbarium. The voucher number UUPH A2(i) was assigned.

2.2 Extraction and Partitioning

The root of *D. tripetala* were air-dried and coarsely powdered with a hammer mill. About 3 kg of each of the powdered plant material was extracted in 70% aqueous methanol. The extract was dried and weighed, and stored in a refrigerator. The dried extract was then partitioned using various solvents including n-hexane (9.7g), dichloromethane (22.5g), ethyl acetate (14.0g), and n-butanol (17.3g), aqueous (19.8g), respectively to obtain the respective fractions after drying.

2.3 Isolation of Rutin

About 18g of the ethylacetate fraction was subjected to open column chromatography for isolation and purification of sample. Gradient elution using solvents including n-hexane, dichloromethane, ethyl acetate, and methanol, were utilized. A total of 76 eluates were collected and grouped based on their Rf from Thin Layer Chromatography (TLC). TLC was carried out using different solvent systems, such as n-hexane: dichloromethane (1:9, 3:7, 50:50), 100% dichloromethane, dichloromethane: ethyl acetate (9:1, 7:3), 100% ethyl acetate, and ethyl acetate: methanol (9:1, 9:2)., respectively. Based on the TLC report, the fractions were bulked into three groups: ETQ (1-29) (2654 mg), EQZ (65-69) (1488 mg), and EQ1 (1533 mg) (70-76), respectively. The focus then shifted to EQZ1 (1533 mg), which was subjected to a second round of open column chromatography. This process involved a fresh gradient elution of solvents again using n-hexane, dichloromethane, ethyl acetate, and methanol in various ratios of increasing order of polarity. The fractions from this column were grouped into four new bulked categories: EQ1 (5-19), EQ2 (20-38), EQ3 (41-64), and EQ4 (65-95).

EQ3 (248 mg) was further purified by preparative thin-layer chromatography (TLC) using a solvent system of ethyl acetate: methanol (9:1). This procedure revealed four distinct spots on the TLC plate. These spots were scraped off, dissolved in methanol, and labeled for subsequent analysis. One of these spots, designated as EQ3A (49 mg), was selected for additional purification via preparative TLC, utilizing the same solvent system. This purification step yielded three spots, which were again scraped and dissolved in methanol. One of these spots, identified as QY, underwent further TLC analysis using various solvent systems, including 100% ethyl acetate and ethyl acetate: methanol (9:1, 9:2). The consistent appearance of a single spot across all solvent systems confirmed the purity of QY, with its final weight recorded as 8.6 mg.

2.4 *In silico* Molecular Docking Analysis

In silico studies were conducted using the AutoDock 4.2.6 software program, AutoDockTools v.1.5.6, BIOVIA Discovery Studio 2021 (BIOVIA, 2021), MarvinSketch (ChemAxon, 2021), Notepad++ v7.5.9, Pymol 2.4.1, Ligplot + (The Scripps Research Institute, US), Visual Molecular Dynamics, and Avogadro). The RCSB Protein Data Bank was used to derive 3D structural protein receptors in .pdb format. The 2D structures of the ligand (SDF) molecules were

retrieved from the PubChem database and the NIST Chemistry WebBook, while compounds not in the database were drawn with the MarvinSketch tool. The ligands Quercetin, Vitexin, and Rutin were docked with; Transient receptor potential vanilloid 1 (PDB Code 3J5R), μ- Opioid Receptor (PDB Code 4DKL) and Cannabinoid Receptor (PDB Code 5XR8) for the analgesic properties, while Phospholipase A2 (PDB Code 1BP2), Iterleukin -1, (PDB Code 1HIB) and Nuclear factor -kappa(PDB Code 1NF1) was used for the anti-inflammatory properties The molecular properties were obtained using Moleinspiration (https://www.molinspiration.com/cgi-bin/properties), and the pharmacokinetic properties were obtained at the PKCSM website using (http://biosig.unimelb.edu.au/pkcsm/prediction). Lipinski's rule of 5 was used to determine the drugability of the synthesized products.

3. RESULTS

The ^{1}H NMR spectrum (Fig. 1) and corresponding data (Table 1) exhibit several distinct signals. Hydroxyl protons are observed at δ 12.3, 10.5, 9.5, and 9.1, consistent with phenolic or hydroxyl functionalities, characteristic of flavonoids such as rutin. In rutin, hydroxyl groups are located on the flavonoid core and the sugar moiety. The aromatic region (δ 6.9–7.7) indicates a substituted benzene ring, in agreement with the expected structure of the flavone core in rutin. Coupling patterns further support the substitution positions.

Signals in the aliphatic and sugar region (δ 3.3–5.1) suggest a glycosidic structure, which is a defining feature of rutin (quercetin conjugated with a disaccharide unit). The anomeric proton, appearing at δ 5.12, confirms the presence of a glycosidic linkage, while the signal at δ 1.14 corresponds to a methyl group.

The ^{13}C NMR data further corroborate this structure. Carbonyl carbons resonate at δ 178.0, while aromatic carbons appear between δ 164.6 and 93.5, indicative of multiple substituted aromatic rings. The chemical shifts in the δ 70–76 region suggest the presence of carbons within a sugar or polyol framework, whereas the resonance at δ 16.5 is consistent with a methyl carbon.

Overall, these spectral characteristics strongly support a complex structure incorporating aromatic, hydroxyl, and sugar moieties, consistent with rutin. Comparison with literature data (Guvenalp et al., 2006) confirms the identification of the compound as rutin, with the chemical shifts of both ^{1}H and ^{13}C nuclei assigned to their respective atoms in the molecular structure (Fig. 4).

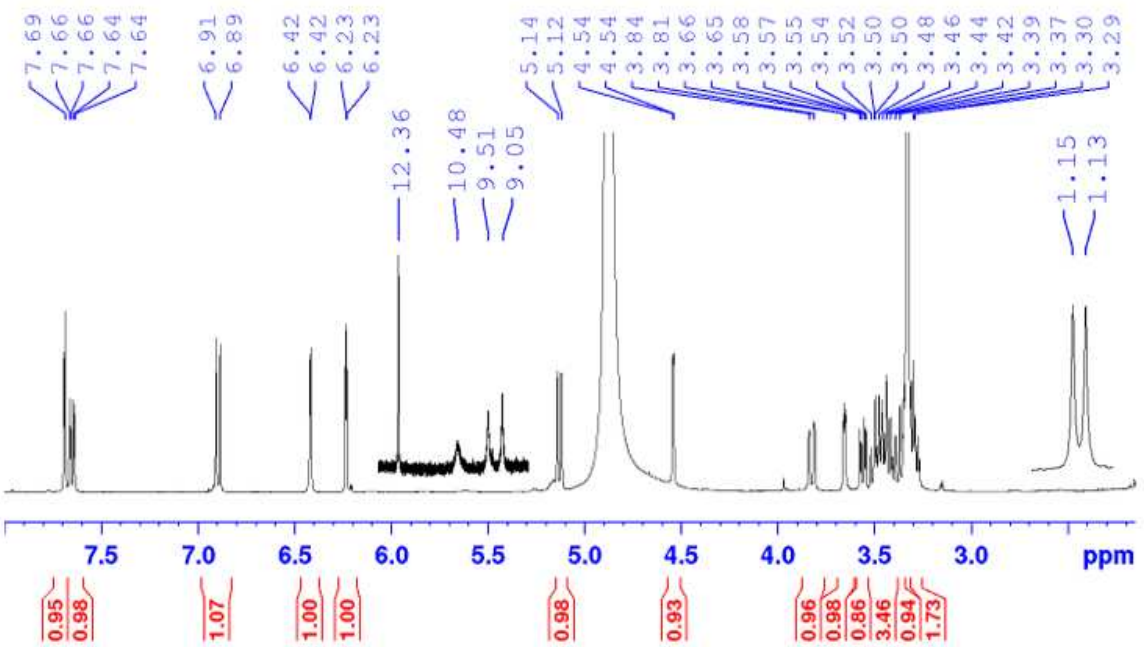

Fig. 1. ^{1}H NMR of sample QY

Table 1. ^{1}H NMR Data for Sample QY

Peak (δ ppm)	Multiplicity	Coupling Constant (J, Hz)	Functional Group/Assignment	Significant Peaks for Identification
12.3	s	-	Hydroxyl group (-OH)	Yes, confirms hydroxyl group
10.5	b	-	Hydroxyl group (-OH)	Yes, confirms hydroxyl group
9.5	b	-	Hydroxyl group (-OH)	Yes, confirms hydroxyl group
9.1	b	-	Hydroxyl group (-OH)	Yes, confirms hydroxyl group
7.69	d	2.2	Aromatic proton	Yes, confirms aromatic group
7.65	dd	8.4, 2.2	Aromatic proton	Yes, confirms aromatic group
6.90	d	8.4	Aromatic proton	Yes, confirms aromatic group
6.42	d	2.1	Aromatic proton	Yes, confirms aromatic group
6.23	d	2.1	Aromatic proton	Yes, confirms aromatic group
5.12	d	7.6	Sugar proton	Yes, confirms glycoside unit
4.54	d	1.6	Sugar proton	Yes, confirms glycoside unit
3.82	dd	10.8, 1.0	Sugar proton	Yes, confirms glycoside unit
3.66	dd	3.4, 1.6	Sugar proton	Yes, confirms glycoside unit
3.56	dd	9.5, 3.4	Sugar proton	Yes, confirms glycoside unit
3.48	m	-	Sugar proton	Yes, confirms glycoside unit
3.47	m	-	Sugar proton	Yes, confirms glycoside unit
3.45	m	-	Sugar proton	Yes, confirms glycoside unit
3.40	m	-	Sugar proton	Yes, confirms glycoside unit
3.34	m	-	Sugar proton	Yes, confirms glycoside unit
3.30	m	-	Sugar proton	Yes, confirms glycoside unit
3.29	m	-	Sugar proton	Yes, confirms glycoside unit
1.14	d	6.3	Methyl group	Yes, confirms methyl group

Source: Experimental data (2024)

Table 2. ^{13}C NMR data for sample QY

Peak (δ ppm)	Literature Range (if available)	Functional Group/Assignment	Significant Peaks for Identification
178.0	176–180	Carbonyl group (C=O)	Yes, confirms carbonyl group
164.6	162–165	Aromatic carbon attached to -OH	Yes, confirms hydroxyl group

Peak (δ ppm)	Literature Range (if available)	Functional Group/Assignment	Significant Peaks for Identification
161.5	160–162	Aromatic carbon attached to -OH	Yes, confirms hydroxyl group
157.9	156–159	Aromatic carbon	No, general aromatic signal
157.1	156–158	Aromatic carbon	No, general aromatic signal
148.4	146–150	Aromatic carbon	No, general aromatic signal
144.4	143–145	Aromatic carbon	No, general aromatic signal
134.2	132–135	Aromatic carbon	No, general aromatic signal
122.1	120–123	Aromatic carbon	No, general aromatic signal
121.7	120–122	Aromatic carbon	No, general aromatic signal
116.3	115–117	Aromatic carbon	No, general aromatic signal
114.7	113–116	Aromatic carbon	No, general aromatic signal
104.2	103–105	Aromatic carbon	No, general aromatic signal
103.3	102–104	Aromatic carbon	No, general aromatic signal
101.0	100–102	Aromatic carbon	No, general aromatic signal
98.6	97–99	Aromatic carbon	No, general aromatic signal
93.5	92–94	Aromatic carbon	No, general aromatic signal
76.8–67.1	67–77	Sugar carbons (glycoside unit)	Yes, confirms glycoside unit
16.5	15–17	Methyl carbon	Yes, confirms methyl group

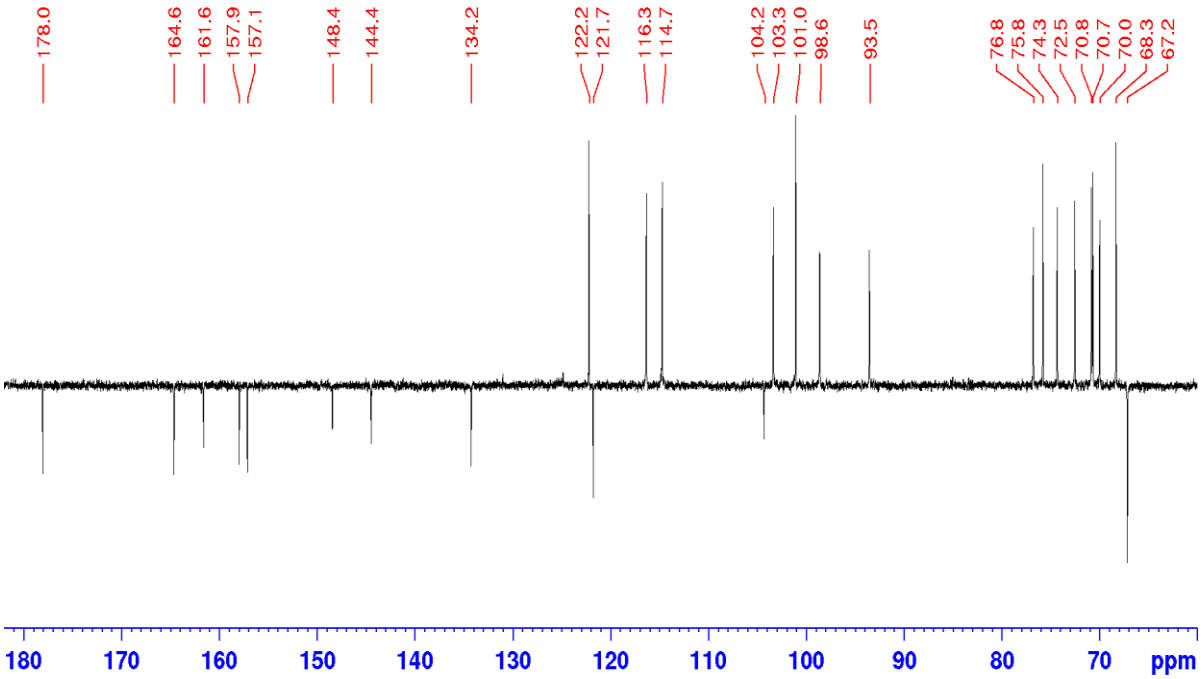

Fig. 2. ^{13}C NMR spectra of sample QY

Table 3. FTIR Data for sample QY

Peak (cm^{-1})	Functional Group/Assignment	Significant Peaks for Identification
3400–3200	Hydroxyl group (-OH)	Yes, confirms hydroxyl group
1720–1700	Carbonyl group (C=O)	Yes, confirms carbonyl group
1600–1500	Aromatic C=C	Yes, confirms aromatic group
1200–1000	C-O (alcohol or glycoside linkage)	Yes, confirms glycoside unit

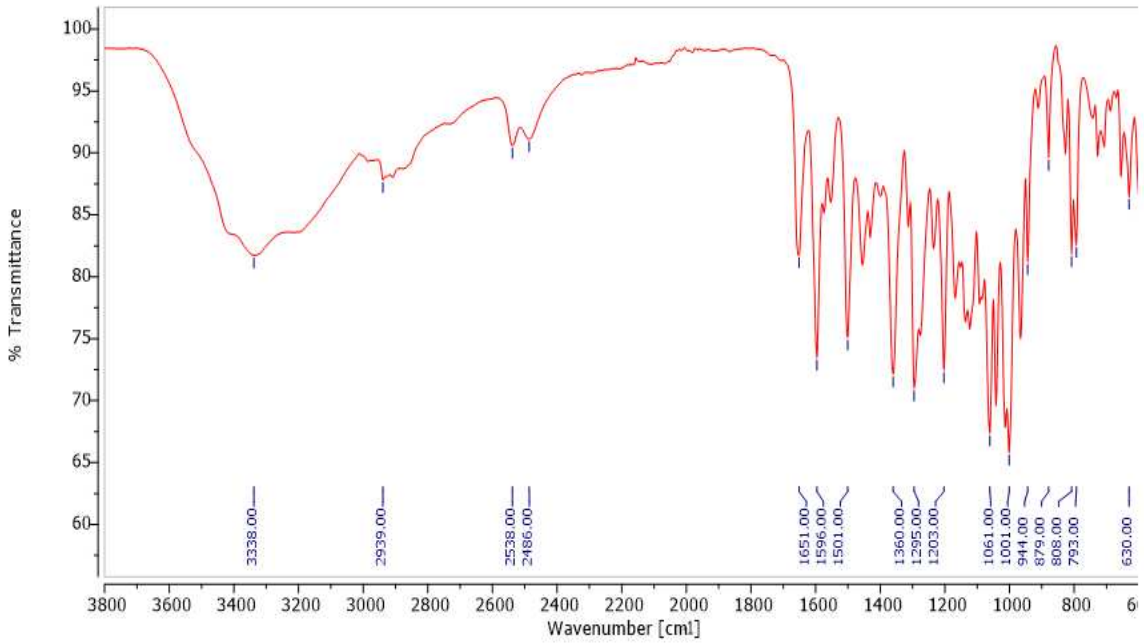

Fig. 3. FTIR spectra of sample QY

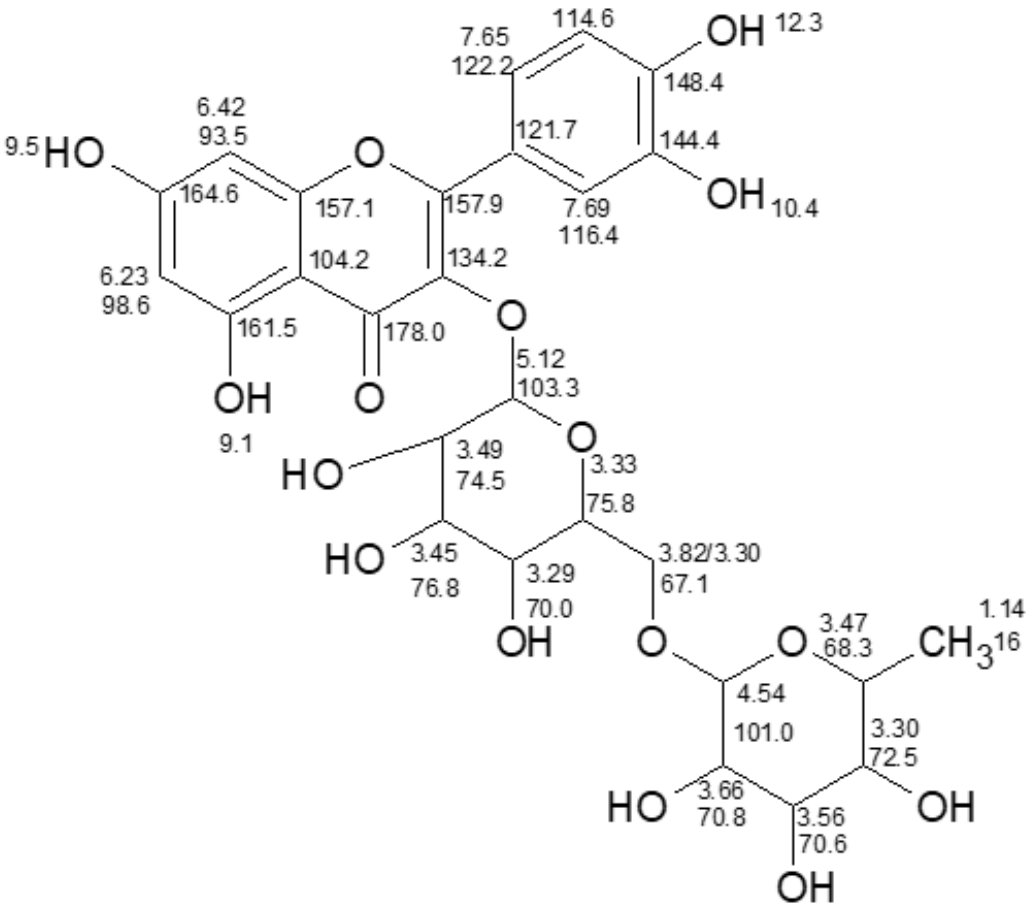

Fig. 4. Chemical structure of rutin (sample QY)

Table 4. Binding interaction of ligands with proteins

S/N	Ligands	Analgesic	Anti-inflammatory					Residue involved in H-bond interaction
		Binding Affinities of Targets (kcal/mol)						
		TRPV1 (PDB Code 3J5R)	μ- Opioid Receptor (PDB Code 4DKL)	Cannabinoid Receptor (PDB Code 5XR8)	Phospholipase A2(PDB Code 1BP2)	Iterleukin -1 (PDB Code 1HIB)	NF-Kβ (PDB Code 1NF1)	
1	Quercetin (E-380.43)	-8.9	-7.1	-9.5	-8.1	-5.0	-6.1	Ala, His, Phe,
2	Vitexin (E-409.01)	-9.7	-7.0	-8.2	-7.9	-4.0	-7.4	Glu, Arg, Thr, Asp.
4	Rutin (E-751.59)	-10.6	-7.6	-8.2	-7.7	-3.4	-7.1	Gln, Thr,Tyr,Arg
7	Aspirin	-5.4	-5.7	-5.2	-5.8	-5.5	-5.4	Leu, Lys, Arg

Table 5. Pharmacokinetic properties of quercetin, vitexin, rutin, vanillin, 4- hydroxybutyric acid, methyl 3-octenoate and aspirin

Ligands	Intestinal absorption (human) in %	Fraction unbound (human) (Fu)	CYP3A4 inhibitor	Total Clearance (log ml/min/kg)	AMES toxicity	Max. tolerated dose (human) (log mg/kg/day)	LD_{50} (mol/kg)	Oral Rat Chronic Toxicity	Hepatotoxicity	Water solubility (log mol/L
Quercetin	77.207	0.206	No	0.407	No	0.499	2.471	2.612	No	-2.925
Vitexin	46.695	0.242	No	0.444	No	0.577	2.595	4.635	No	-2.845
Rutin	23.446	0.187	No	-0.369	No	0.452	2.491	3.673	No	-2.892
Aspirin	76.938	0.481	No	0.72	No	1.016	2.286	1.956	No	-1.868

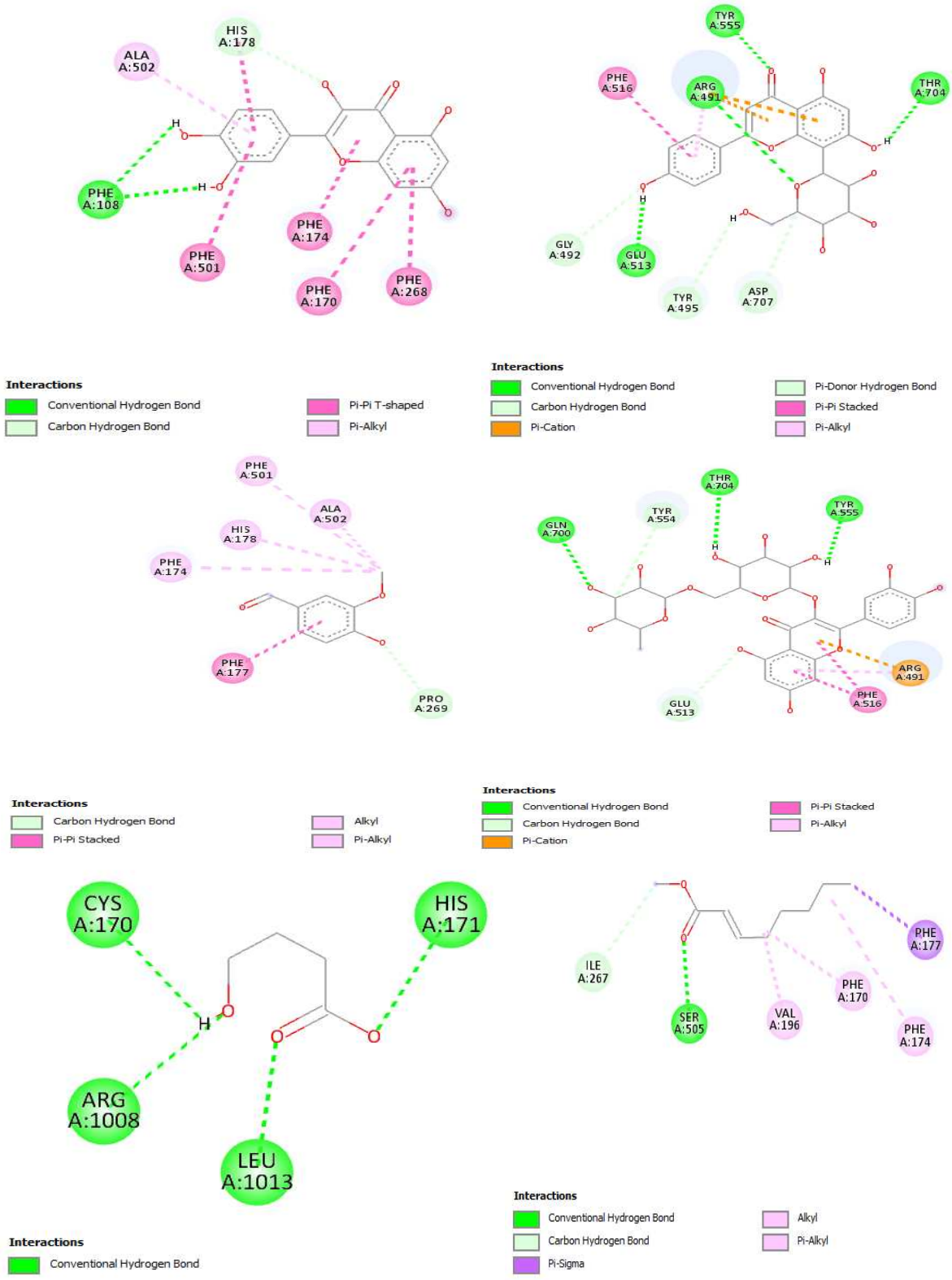

Fig. 5. The 2D visualization results of ligands: quercetin (e-380.43), vitexin (e-409.01), vanillin (e- 79.79), rutin (e- 751.59), 4- hydroxybutyric acid (e-36.35), and methyl 3-octenoate (e- 37.98) with analgesic target proteins

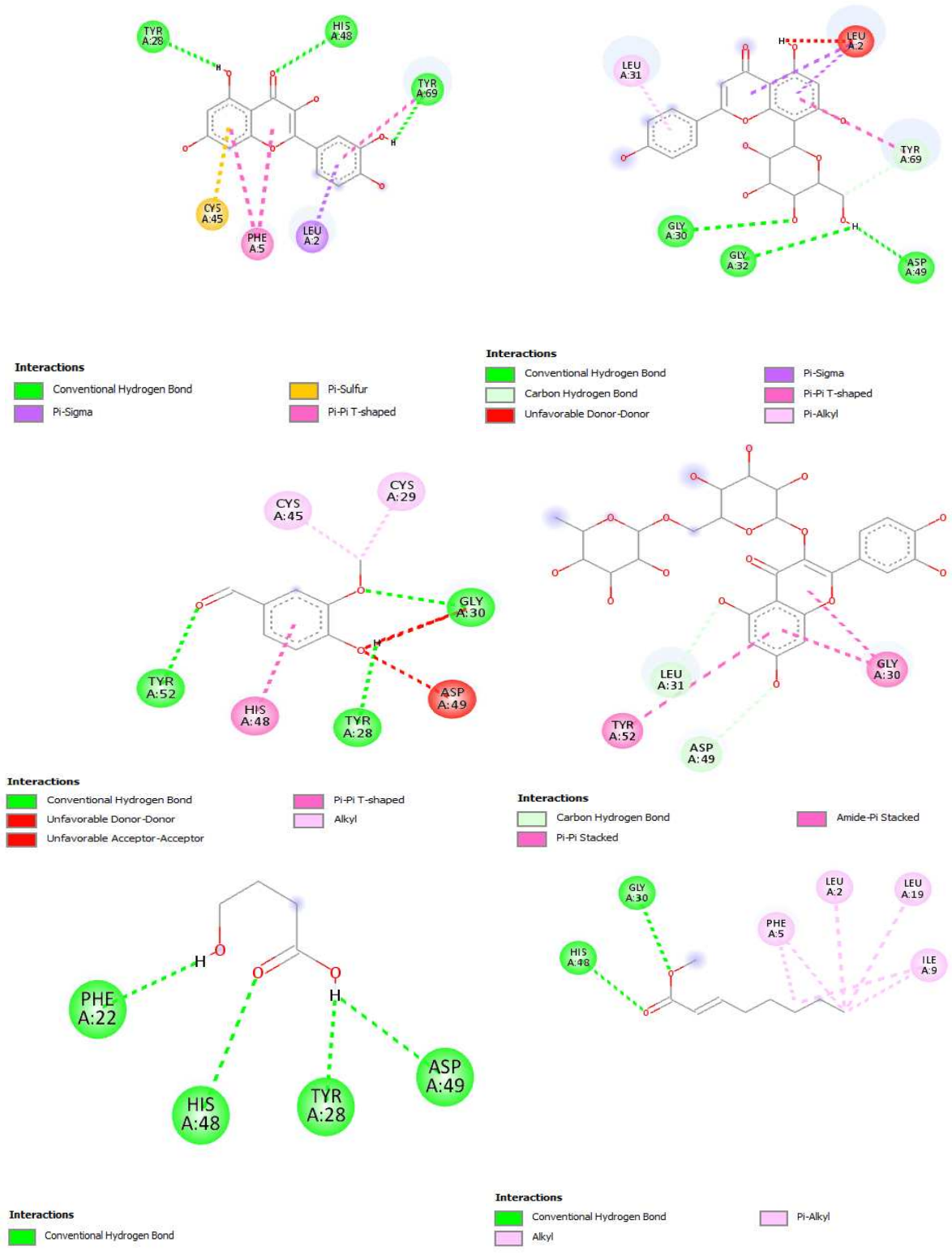

Fig. 6. The 2D visualization results of ligands: quercetin (e-380.43), vitexin (e-409.01), vanillin (e- 79.79), rutin (e- 751.59), 4- hydroxybutyric acid (e-36.35), and methyl 3-octenoate (e- 37.98) with anti-inflammatory target proteins

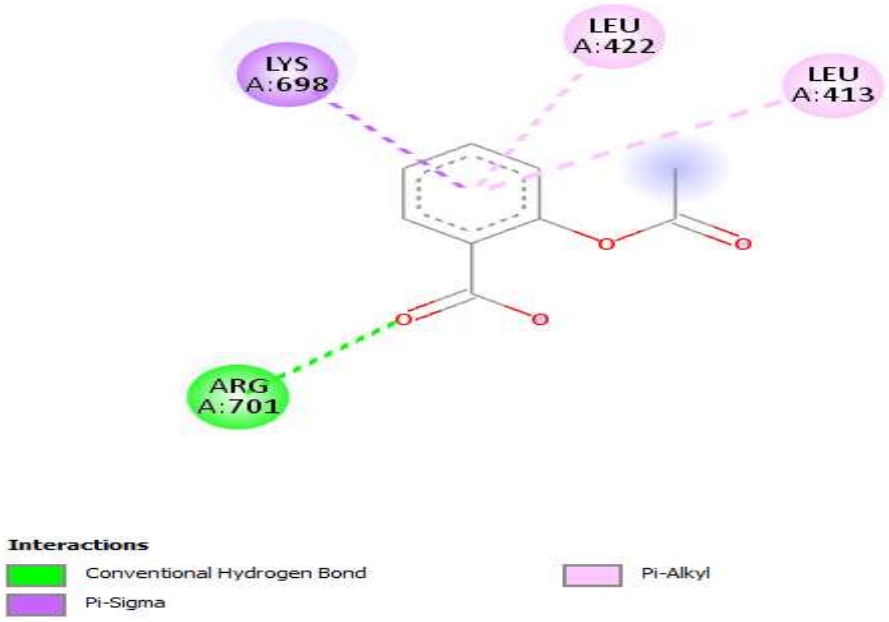

Fig. 7. The 2D visualization results of aspirin with the transient receptor potential vanilloid 1 (PDB code 3J5R)

Table 6. Characterization of drug-likeness molecular docking results

Ligand	Lipinski rule parameter					
	logP	MW	Surface area	nHBD(acceptors)	nOHDB(donors)	n Violators
Quercetin	1.98	302.24	122.21	7	5	0
Vitexin	0.09	423.38	133.99	10	5	0
Rutin	-1.69	610.52	240.90	16	10	4
Aspirin	1.31	180.51	74.76	3	1	0

4. DISCUSSION

4.1 Rutin

Rutin is known for its antioxidant and anti-inflammatory properties. It can scavenge free radicals and inhibit inflammatory pathways, making it beneficial in managing oxidative stress and inflammation (Bezerra et al., 2016). Rutin, also known as quercetin-3-O-rutinoside, is a well-known bioactive compound with antioxidant, anti-inflammatory, and other pharmacological properties. Studies have shown that it can inhibit key inflammatory mediators and protect against oxidative stress (Kim et al., 2015). This compound's isolation from *D. tripetala* underscores the plant's therapeutic potential. It can inhibit microglial activation and reduce the production of pro-inflammatory cytokines (Kimura et al., 2018). The isolation of rutin from *D. tripetala* highlights the plant's potential in developing natural anti-inflammatory agents.

4.2 Molecular Docking Analysis

The compounds were successfully docked onto the active site of target proteins (Transient receptor potential vanilloid-1, μ- Opioid Receptor, Cannabinoid Receptor, Phospholipase A2, Iterleukin -1 and Nuclear factor –kappa). Table 4 shows the binding energy, amino acid residues in H-Bond, and Hydrophobic Interactions in docking experiments. The lower binding energies seen between the ligands and the target proteins compared to the positive control (Aspirin) confirms the anti-inflammatory and analgesic potential *in silico*. The amino acid residues were essential components of protein active sites and played a role in hydrophobic interactions and hydrogen bond formation.

Table 6 reveals the results of the drug-likeness study performed using Lipinski's rules on the docked compounds. Rutin had four violations of the Lipinski rule out of the 7 drug-likeness

compounds, with molecular weight, hydrogen bond donors, surface area and Number of hydrogen bond acceptors greater than 500, 5, 140 and 10 respectively. These violations indicate that Rutin may have poor oral bioavailability due to its size, polarity, and ability to form hydrogen bonds. Such properties can affect its ability to cross cell membranes and be absorbed in the gastrointestinal tract. Despite this, compounds that violate Lipinski's rules can still have biological activity and therapeutic potential, particularly if they are administered via non-oral routes (e.g., injection) or are designed to target specific sites. Lipinski's rule states that in general, oral active drugs must not have more than one violation of the following criteria Molecular weight <500, Number of hydrogen bond donors (nHBD) ≤5, Number of hydrogen bond acceptors (nHBA) ≤10, Calculated Log p ≤5 and Polar surface area (PSA) < 140 Å 2). Quercetin, Vitexin and Aspirin violated none of the Lipinski's rules. Thus are good oral anti-inflammatory and analgesic candidates.

The pharmacokinetics study (Table 5) confirmed that the intestinal absorption, Fraction unbound (human) (Fu), Total Clearance (log ml/min/kg), AMES toxicity, L_{50} (mol/kg), Hepatotoxicity and most especially water solubility (log mol/L) are satisfactory.

5. CONCLUSION

This study revealed the therapeutic potential of *D. tripetala* due to its rich phytochemical constituents. The molecular docking analysis showed that rutin exhibits strong binding affinities with key analgesic and anti-inflammatory protein targets, such as TRPV1, μ-opioid receptor, and cannabinoid receptor. These findings validate the compound's potential as a natural alternative for managing pain and inflammation. Despite rutin's notable bioactivity, its Lipinski rule violations suggest limited oral bioavailability, highlighting the need for innovative delivery methods or structural optimization to enhance its pharmacokinetic profile. Beyond rutin, this research also reinforces the broader pharmacological significance of *D. tripetala* as a reservoir of bioactive compounds with diverse medicinal properties.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

Bezerra, D. P., Militao, G. C. G., de Morais, M. C., & de Sousa, D. P. (2016). The dual antioxidant/prooxidant effect of eugenol and its action in cancer development and treatment. *Nutrients, 8*(11), 682.

Egharevba, H. O., & Idah, E. A. (2015). Major compounds from the essential oil of the fruit and comparative phytochemical studies of the fruits and leaves of *Dennettia tripetala* Baker f. found in North Central Nigeria. *International Journal of Pharmacognosy and Phytochemical Research, 7*(6), 1262-1266.

Elekwa, I., Okereke, S. C., & Chukwudoruo, C. S. (2011). Phytochemical screening and GC-MS analysis of the essential oil of *Dennettia tripetala* (pepper fruit) seeds. *ABSU Journal of Environment, Science and Technology, 1*, 93-98.

Guvenalp, Z., Kilic, N., Kazaz, C., Kaya, Y., & Demirezer, L. O. (2006). Chemical constituents of *Galium tortumense*. *Turkish Journal of Chemistry, 30*, 515-523.

Iseghohi, S. O. (2015). A review of the uses and medicinal properties of *Dennettia tripetala* (Pepperfruit). *National Library of Medicine, 3*(4), 104-111.

Kim, H. J., Kim, J. H., & Kim, J. H. (2015). Anti-inflammatory effects of methyl 2-octenoate in lipopolysaccharide-stimulated RAW264.7 cells. *Journal of Ethnopharmacology, 174*, 1-8.

Kimura, I., Ozawa, K., Inoue, D., Imamura, T., Kimura, M., & Maeda, T. (2018). The gut microbiota suppresses insulin-mediated fat accumulation via the short-chain fatty acid receptor GPR43. *Nature Communications, 4*.

Oyemitan, I. A., Iwalewa, E. O., Akanmu, M. A., & Olugbade, T. A. (2008). Antinociceptive and anti-inflammatory effects of essential oil of *Dennettia tripetala* G. Baker (Annonaceae) in rodents. *African Journal*

of Traditional Complementary and Alternative Medicine, 5(4), 355-362.

Oyemitan, I. A., Iwalewa, E. O., Akanmu, M. A., Asa, S. O., & Olugbade, T. A. (2006). The abusive potential of habitual consumption of the fruits of *Dennettia tripetala* G. Baker (Annonaceae) among the people in Ondo township (Nigeria). *Nigerian Journal of Natural Products Medicine, 10*(1), 55-62.

Pahwa, R., Amandeep, G., Pankaj, B., & Jialal, I. (2021). Chronic inflammation. In *StatPearls Publishing*. Retrieved August 2021, from https://www.ncbi.nlm.nih.gov/books/NBK493173/

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