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Phenolics, Antioxidants and Minerals in Fermented vs Unfermented *Terminalia catappa*

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ABSTRACT

Background and Objective: There has been growing interest in preventing oxidative stress, and investigating the potential of medicinal plants to combat it has gained momentum. This study explores the antioxidant properties, phenolic compositions, and mineral content of both fermented and unfermented *T. catappa* leaf extracts. **Materials and Methods:** *Terminalia catappa* leaves were divided into two portions of which one was wrapped with plantain leaves to facilitate fermentation. Both samples were air-dried and milled into powder. Ethanolic extracts (5 g/100 mL) of each sample were prepared to determine the above-mentioned assays. Statistical significance was evaluated using a One-way Analysis of Variance (ANOVA), followed by Dunnett's *post hoc* test. Data points correspond to the mean of independent experiments and error bars; the level of significance was set at $p<0.05$. **Results:** The unfermented extract exhibited a higher significant difference ($p<0.05$) in antioxidant properties and phenolic contents. The HPLC analysis also followed the same trend with the presence of higher contents of quercetin, caffeic acid, ferulic acid, maleic acid, p-coumaric acid, and naringenin in unfermented *T. catappa*. However, the fermented extract was observed to contain additional bioactive compounds such as salicylic acid and apigenin, which are also known for antioxidant potential. In addition, the fermented extract was also observed to have a higher content ($p<0.05$) of potassium and manganese, while calcium, magnesium, iron, copper, sodium, and zinc were higher in the unfermented extract. The overall results of the analysis showed that the unfermented extract of *T. catappa* had higher antioxidant activity, phenolic contents, minerals, and HPLC-identified contents. **Conclusion:** However, the contents of fermented extract unique compounds suggest that fermentation not only alters the phytochemical profile but can also enhance the production of additional components that are needed for health benefits, which could be adopted in managing oxidative stress and related chronic diseases.

KEYWORDS

Antioxidant properties, bioactive compounds, fermentation, extraction, oxidative stress

INTRODUCTION

Free radicals, also known as reactive oxygen species, are constantly generated in the body as byproducts of different biochemical processes. Under normal conditions, the body's antioxidant systems neutralize and eliminate these radicals. However, when these protective mechanisms are impaired, an accumulation of free radicals can occur, contributing to the development of various diseases[1].

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Plants have long been a vital source of medicinal compounds, significantly contributing to global health[2]. Plants and their compounds have been used globally for the prevention and treatment of various diseases[3]. The plant *Terminalia catappa* has been extensively studied for its medicinal properties, owing to its diverse chemical composition[4,5]. *Terminalia catappa* leaf extracts demonstrate various biological activities, such as antioxidant effects, due to compounds like punicalagin, punicalin, Terflavin A and B, chebulic acid, benzoic acid, coumaric acid, and their derivatives[6,7], antidiabetic (β-carotene)[8], anticancer (punicalagin)[9], antiviral (ellagic acid)[10], anti-inflammatory (triterpenic acids, especially ursolic acid and its derivatives)[11], antimicrobial (flavones and flavonols)[12,13], and hepato-protective activities (punicalagin, punicalin)[14,15]. *Terminalia catappa* leaf plasters are used in India to treat leprosy lesions, scabies, and other skin conditions[13]. Traditionally, it has been used to treat fever and diarrhea, particularly in Malaysia, the Philippines, and India[12]. *Terminalia catappa* was chosen for this study to analyze the antioxidant properties, mineral composition, and phytochemicals in its leaves, both qualitatively and quantitatively, to scientifically validate its medicinal properties and health benefits.

MATERIALS AND METHODS

Study area: The research was carried out in the Ondo State Region of Akungba-Akoko, a semi-rural settlement where the major occupation of the populace is farming and trading of food items. Ondo State has boundaries with neighboring on East-Edo and Delta, on West-Ogun and Osun, on the North-Ekiti and Kogi, and South-bright Atlantic Ocean. Ondo State is located on the Latitude 5°45' and 7°52' and Longitude 4°20' and 6°05'E. Every analysis was carried out between the months of May to July, 2024 at the Adekunle Ajasin University, Department of Biochemistry in Akungba-Akoko, Ondo State, Nigeria.

Chemicals and reagents: All chemicals and reagents used for this were of analytical grade, Quercetin, Gallic acid, ethanol, Folin-Ciocalteu reagent, Sodium Carbonate (Na_2CO_3), Potassium Acetate, Aluminum Chloride ($AlCl_3$), Methanol, Iron (III) Chloride ($FeCl_3$), Potassium Ferricyanide ($K_3Fe(CN)_6$), Trichloroacetic Acid (TCA) were purchased from Sigma-Aldrich, Inc. (St Louis, USA). The distilled water used was obtained from the Biochemistry Department at Adekunle Ajasin University, Akungba Akoko, Ondo State, Nigeria. Optical absorbance was measured with a UV-visible spectrophotometer.

Plants collection: The leaf of *Terminalia catappa* was obtained from Akungba Akoko, Ondo State, Nigeria. It was identified by Dr. (Mrs.) Shodehinde of the Department of Biochemistry, Adekunle Ajasin University, Akungba Akoko, Ondo State, Nigeria.

Preparation of extracts: The fresh leaves of *Terminalia catappa* were cut and washed with potable water to remove all contaminants, after which they were spread under the shade to drain completely. A portion of the drain samples was wrapped with plantain leaves to facilitate fermentation, while the remaining samples were left unwrapped and air-dried at room temperature for three weeks. The dried leaves samples were pulverized into powdered form and stored in air-tight containers for extraction. A total of 100 g of both fermented and unfermented powdered leaves were separately soaked in 1000 mL of ethanol (1:10). The mixtures were left to steep in their respective containers for 72 hrs. After this period, the resulting solutions were filtered using a sieve. The residue was allowed to dry, while the filtrate was left to evaporate for approximately two weeks before proceeding with further processing. After the filtrate dried, it was processed by adding 100 mL of distilled water to 5 g of each of the dried filtrate from the fermented and unfermented samples, respectively, in separate sample bottles. The mixtures were then shaken in a shaking water bath to achieve uniform homogeneity. The resulting mixtures were then filtered using filter paper and the filtrate was subsequently used for biochemical assays to evaluate the antioxidant activity of the samples *in vitro*.

***In vitro* assay determination**

Determination of total phenolic content: The total phenolic content was determined according to the method of Singleton *et al.*[14]. Briefly, appropriate dilutions of the extracts were oxidized with 2.5 mL of 10% Folin-Ciocalteu's reagent (v/v) and neutralized by 2.0 mL of 7.5% sodium carbonate. The reaction mixture was incubated for 40 min at 45°C and the absorbance was measured at 765 nm. The total phenolic content was subsequently calculated as gallic acid equivalent (GAE).

Determination of flavonoids content: The total flavonoid content of the extract was determined using a slightly modified method reported by Meda *et al.*[15]. Briefly, 0.5 mL of appropriately diluted sample was mixed with 0.5 mL methanol, 50 µL of 10% $AlCl_3$, 50 µL of 1M potassium acetate, and 1.4 mL water, and allowed to incubate at room temperature for 30 min. Thereafter, the absorbance of the reaction mixture was subsequently measured at 415 nm. The total flavonoids were calculated using quercetin as standard.

Determination of ferric reducing antioxidant property: The reducing property of the extracts will be determined by assessing the ability of the extract to reduce $FeCl_3$ solution as described by Oyaizu[16]. As 2.5 mL aliquot was mixed with 2.5 mL of 200 mM sodium phosphate buffer (pH 6.6) and 2.5 mL of 1% potassium ferricyanide. The mixture was incubated at 50°C for 20 min. Then 2.5 mL of 10% trichloroacetic acid was added. The mixture was centrifuged at 650 rpm for 10 min. As 5 mL of the supernatant was measured with an equal volume of water and 1 mL of 0.1% ferric chloride. The absorbance was measured at 700 nm. The ferric-reducing antioxidant property was subsequently calculated.

HPLC analysis: The High-Performance Liquid Chromatography (HPLC) analysis of the both fermented and unfermented *Terminalia catappa* (TC) sample was performed using a NIMR 1260LC instrument equipped with a Poroshell 120 EC C18 column (4 µm, 150×4.6 mm). The mobile phase consisted of acetonitrile (ACN) and 0.1% formic acid in a 70:30 ratio. The flow rate was maintained at 0.700 mL/min, while the column temperature was set to 28°C. The detection was carried out at a wavelength of 257 nm using a diode array detector (DAD). For each injection, a sample volume of 20 µL was used. Standard compounds such as caffeic acid, ferulic acid, maleic acid, salicylic acid, apigenin, naringin, and p-coumaric acid were identified based on their retention times. The data was analyzed using the ChemStation software, and the retention times were compared against reference standards to confirm the identity of the compounds present in the sample.

Atomic absorption spectroscopy methodology: The Principle of operation of an atomic absorption spectrometer using a flame ionization detector (FID) requires a liquid (digested) sample to be aspirated, aerosolized, and mixed with combustible gases, such as acetylene and air or acetylene and nitrous oxide (this test utilizes acetylene and air). The mixture is ignited in a flame whose temperature ranges from 2100 to 2800°C. During combustion, atoms of the element of interest in the sample are reduced to free, unexcited ground-state atoms, which absorb light at characteristic wavelengths. To provide element-specific wavelengths, a light beam from a lamp whose cathode is made of the element being determined is passed through the flame. A photomultiplier detects the amount of reduction of the light intensity due to absorption, and this is directly related to the amount of the element in the sample. A series of standard solutions for each metal ion was prepared using deionized distilled water and stock solutions (1000 ppm); 0.00, 0.20, 0.50, 0.60, and 1.00. To obtain accurate quantitative data, the regression coefficient of the standard calibration curve for each element was greater than 0.9960. The Buck Scientific Atomic Absorption Spectrometer Model 210 VGP was used for this analysis.

Digestion procedure: About 1 g of the sample was taken into A 250 mL conical flask, 10 mL of conc. Nitric acid was added and the mixture was placed on (hot plate) for about 35 min until the brown fumes started forming and the fume changed gradually to whitish which shows that the samples have been completely digested. The digested samples were allowed to cool and later made up to 25 mL mark with purified water, the mixture was filtered through a micro glass filter or clean filter paper and the samples were ready for AAS analysis.

Some measures of QA/QC were put in place in the course of the analysis:

- Replicate determination of samples was carried out to ascertain the degree of reproducibility of the data
- Blank determination was carried out at intervals to prevent carryover of the samples
- A known standard concentration was analyzed like a sample to check the accuracy of the machine

Statistical analysis: GraphPad Prism 8 was used for the statistical analysis, statistical significance was evaluated using a One-way Analysis of Variance (ANOVA), followed by Dunnett's *post hoc* test. Data points correspond to the mean of independent experiments and error bars (SEM); the level of significance was set at $p<0.05$.

RESULTS

The total phenolic content (Fig. 1) of *Terminalia catappa* leaves was evaluated in both fermented and unfermented forms, with gallic acid serving as the standard for comparison. The results demonstrate a statistically significant variation in phenolic content across the samples. Gallic acid exhibited the highest total phenolic content. The unfermented *T. catappa* sample and fermented sample show significant differences ($p<0.05$) when compared to the gallic acid but non-significant differences ($p>0.05$) when compared to each other, indicating that both samples show moderate phenolic contents.

Figure 2 indicates significant differences between the flavonoid content of Quercetin (standard), unfermented *Terminalia catappa*, and fermented *Terminalia catappa*. Quercetin, exhibits the lowest flavonoid content among the samples, with a total flavonoid value significantly lower than both the fermented and unfermented *Terminalia catappa* samples, signifying that its flavonoid content is statistically different ($p<0.05$) from the unfermented and the fermented samples.

The ferric reducing antioxidant property of *Terminalia catappa* leaf as shown in Fig. 3 above was evaluated in both fermented and unfermented samples in comparison to the standard (ascorbic acid). The results demonstrate a not-statistically significant variation in antioxidant properties across the samples.

HPLC analysis: The analysis of polyphenolic contents in fermented *Terminalia catappa* leaves revealed a wide range of concentrations in Fig. 4, with saponin being the most abundant compound at 1009.24 mg/g, followed by p-coumaric acid (436.95 mg/g), apigenin (72.27 mg/g), and naringenin (61.08 mg/g). Other compounds such as quercetin (53.50 mg/g), salicylic acid (14.59 mg/g), and ferulic acid (7.08 mg/g) were present in moderate amounts, while caffeic acid (2.05 mg/g) was the least concentrated. This variation underscores the rich polyphenolic profile of the fermented leaves, highlighting their potential as a source of bioactive compounds shown in Table 1.

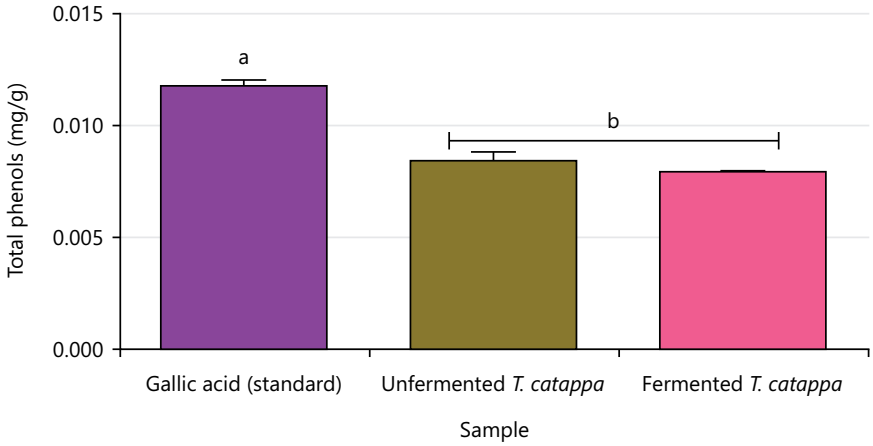

Fig. 1: Total phenolic content of fermented and unfermented *Terminalia catappa* leaf

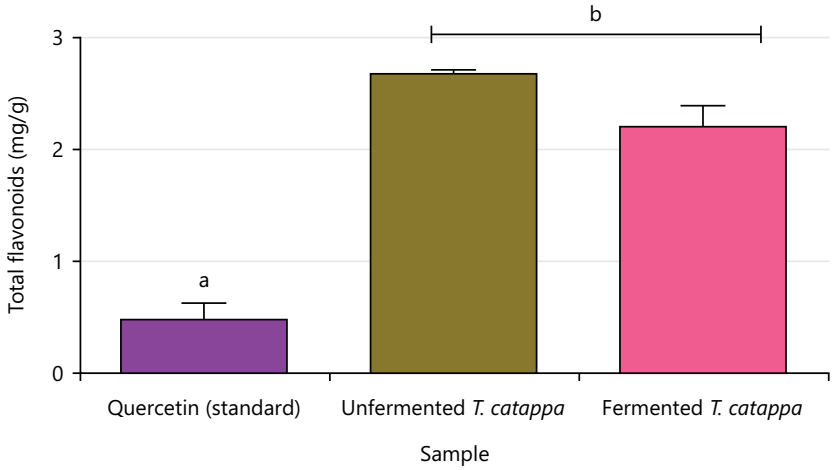

Fig. 2: Total flavonoids content of fermented and unfermented *Terminalia catappa* leaf

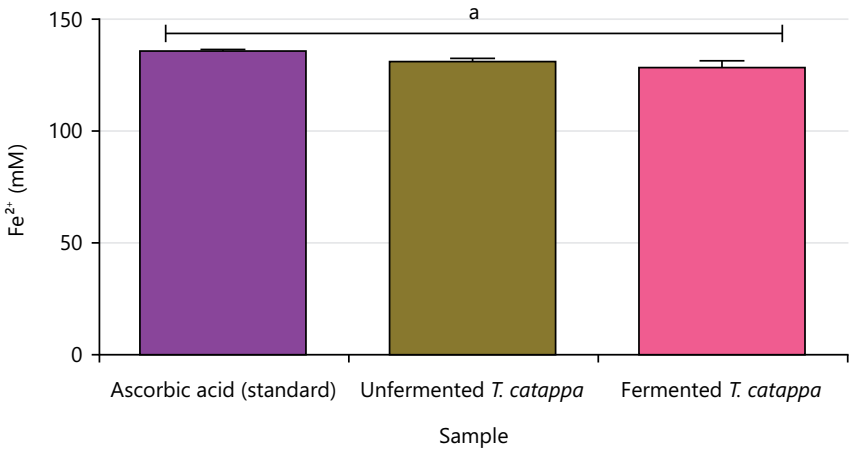

Fig. 3: Ferric reducing antioxidant property of fermented and unfermented *Terminalia catappa* leaf

Table 1: Concentration of polyphenolic contents in fermented *Terminalia catappa* leaf

Compound	Concentration (mg/g)
Caffeic acid	2.05
Ferulic acid	7.08
Tannic acid	4.12
Maleic acid	4.49
Salicylic acid	14.59
Apigenin	72.27
Naringenin	61.08
Quercetin	53.50
p-Coumaric acid	436.95
Saponin	1009.24

Table 2: Concentration of polyphenolic contents in unfermented *Terminalia catappa* leaf

Compound	Concentration (mg/g)
Caffeic acid	7.14
Ferulic acid	8.13
Tannic acid	5.24
Maleic acid	6.76
Naringenin	56.14
Quercetin	217.81
p-Courmaric acid	552.02
Saponin	1666.03

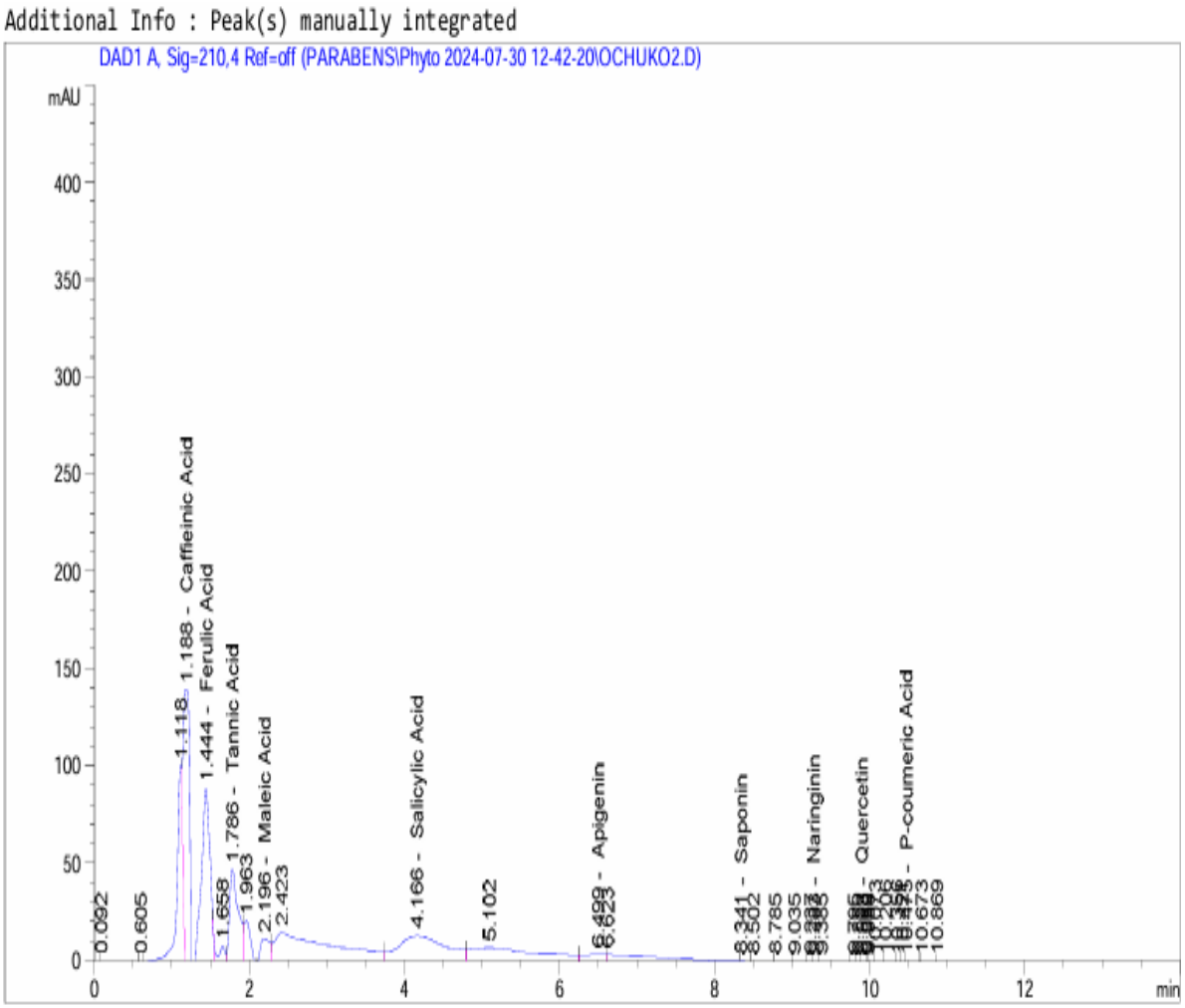

Fig. 4: HPLC chromatogram of the compounds present in fermented *Terminalia catappa* leaf
x-axis: Retention time and y-axis: Absorbance

Table 3: Concentration of minerals in both fermented and unfermented *Terminalia catappa* leaf

Mineral content (mg/kg)	Calcium	Magnesium	Iron	Copper	Manganese	Potassium	Sodium	Zinc
Fermented *T. catappa*	68.78	20.64	1.06	0.95	4.02	2.86	4.06	35.65
Unfermented *T. catappa*	90.50	25.68	2.56	1.16	3.85	2.56	5.62	55.05

The analysis of polyphenolic contents in unfermented *Terminalia catappa* leaf revealed (Fig. 5) that saponin exhibited the highest concentration (1666.03 mg/g), followed by p-coumaric acid (552.02 mg/g) and quercetin (217.81 mg/g). Among the other compounds, naringenin was moderately abundant (56.14 mg/g), while caffeic acid, ferulic acid, tannic acid, and maleic acid were present in lower concentrations, ranging from 5.24 to 8.13 mg/g. These findings highlight the dominance of saponin and p-coumaric acid in the polyphenolic profile of the leaf shown in Table 2.

Mineral analysis: The analysis of mineral content in *Terminalia catappa* leaves revealed a decrease in most mineral concentrations following fermentation. Unfermented leaves exhibited higher levels of calcium (90.50 mg/kg), magnesium (25.68 mg/kg), iron (2.56 mg/kg), copper (1.16 mg/kg), potassium (2.56 mg/kg), sodium (5.62 mg/kg), and zinc (55.05 mg/kg) compared to fermented leaves, which showed lower values for these minerals. However, manganese content slightly increased post-fermentation, from 3.85 to 4.02 mg/kg, highlighting a potential variation in nutrient availability due to fermentation.

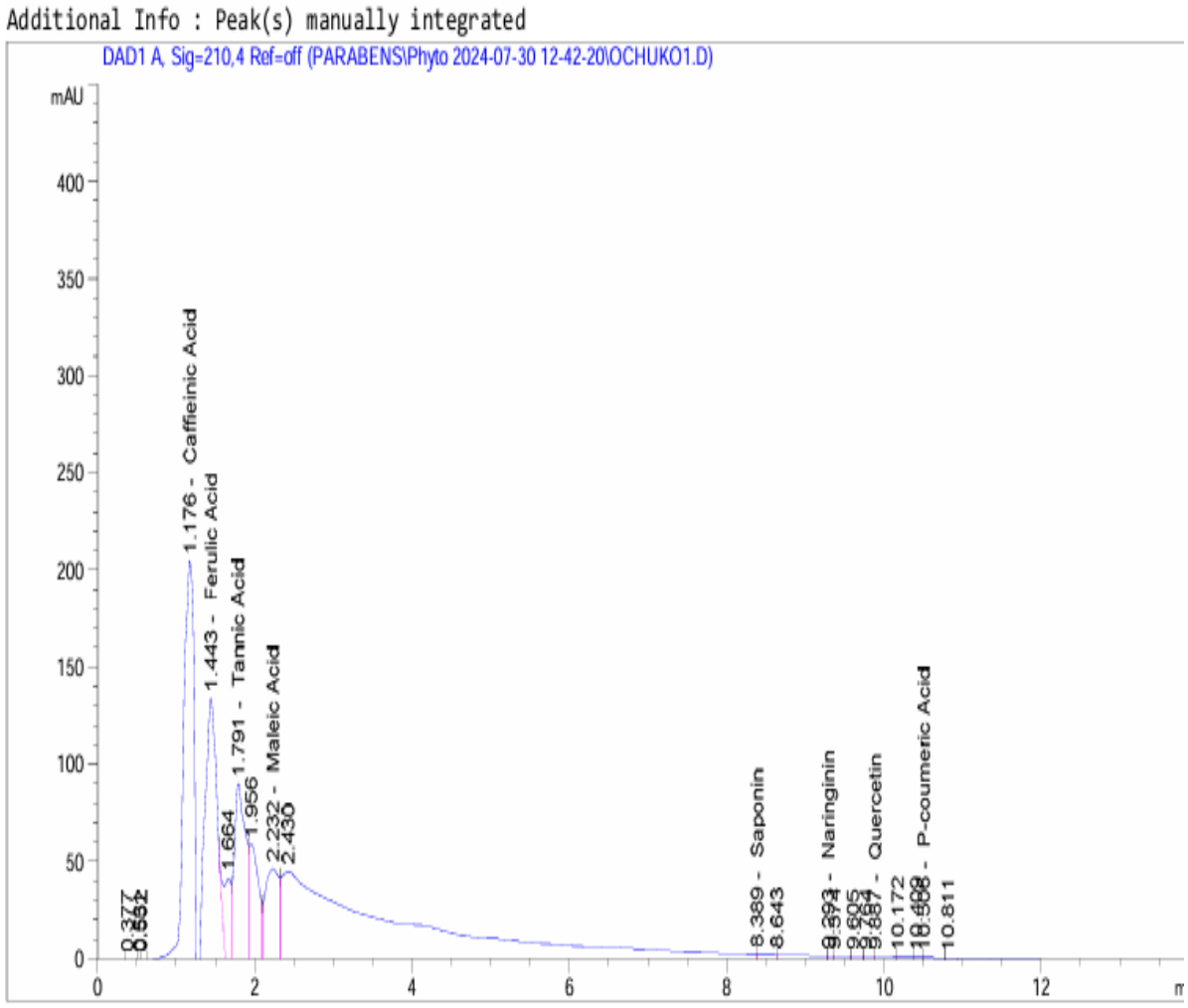

Fig. 5: HPLC chromatogram of the compounds present in unfermented *Terminalia catappa* leaf
x-axis: Retention time and y-axis: Absorbance

DISCUSSION

In recent times, there has been a notable focus on investigating natural substances for possible medicinal qualities, and an intriguing source of these compounds is plant extracts. The plant *Terminalia catappa* Linn has been the subject of numerous medicinal investigations due to its diverse chemical composition[3,4]. *Terminalia catappa* leaf extracts demonstrate a range of biological activities, including antioxidant properties. Understanding the phytochemical composition and mineral content of *T. catappa* can shed light on the bioactive compounds responsible for these therapeutic effects. Given the role of oxidative stress in chronic diseases such as diabetes, hypertension, cancer, and studying the antioxidant potential of plant extracts like *T. catappa* could lead to novel treatments or supplements for managing oxidative stress-related conditions. Natural antioxidants are known for their ability to neutralize reactive oxygen species (ROS) and reactive nitrogen species (RNS), preventing cellular damage. The choice of both ethanolic extract of fermented and unfermented *Terminalia catappa* leaf in this study allows for a comprehensive examination of its antioxidant properties, phytochemical profile, mineral composition, and how fermentation enhances the liberation and reduction of specific bioactive compounds, providing a more refined understanding of the effect of fermentation on the plant medicinal potential.

The total phenolic content analysis (Fig. 1) showed no significant differences ($p>0.05$) when both the fermented and unfermented samples were compared to each other, indicating that both samples show moderate phenolic content, but statistically significant ($p<0.05$) when compared to the gallic acid

standard. Phenolic compounds constitute a diverse category of phytochemicals that are extensively distributed within the plant kingdom[1]. They possess a wide spectrum of biochemical properties, including antioxidant, antimutagenic, and anticancer activities, along with the ability to modulate gene expression[17]. Additionally, phenolic compounds represent the largest group of phytochemicals, contributing predominantly to the antioxidant capacity of plants and their derived products[18]. Plant polyphenols, known as dietary antioxidants, may play a protective role against oxidative damage in human health and disease. Several studies have shown that phenolic compounds are the most abundant dietary antioxidants in typical human diets. Recently, they have gained considerable attention due to growing evidence of their potential role in preventing various human diseases[19-21]. According to the result shown in Fig. 2, both samples demonstrated the highest flavonoid content when compared to the quercetin standard ($p<0.05$). Flavonoids are recognized for their diverse biological activities, including antioxidant, anti-inflammatory, and anticancer properties, and play an essential role in safeguarding cells from oxidative damage[22]. The results presented in Fig. 3, indicate no significant difference ($p>0.05$) in the ferric-reducing antioxidant property between fermented and unfermented *Terminalia catappa* leaves when compared to the standard (ascorbic acid) and each other. The findings show a non-statistically significant variation in antioxidant activity across the samples. The presence of well-documented antioxidants such as quercetin, which modulates signaling pathways related to oxidative stress and inflammation, and caffeic acid, known for its ability to reduce oxidative damage in biological systems, in high concentration, reinforces the therapeutic potential of the unfermented *Terminalia catappa* extracts. High-Performance Liquid Chromatography (HPLC) analysis identified a diverse array of phytochemicals, including ferulic acid, tannic acid, saponins, caffeic acid, maleic acid, naringenin, quercetin, p-coumaric acid in both fermented and unfermented extracts (Table 1 and 2) all recognized for their antioxidant properties. Antioxidants exhibit a broad spectrum of biological and pharmacological effects and are widely valued for promoting nutrition and enhancing health[23]. Ferulic acid plays an important role in protecting fatty acids within cell membranes from harmful autoxidation. As a secondary metabolite, it and its derivatives can bind to copper and iron ions, thereby inhibiting the formation of harmful hydroxyl radicals that can cause cellular damage[24]. The p-coumaric acid, a hydroxylated derivative of cinnamic acid, helps prevent the oxidation of low-density lipoproteins and decreases the risk of stomach cancer[25]. Naringenin offers numerous health benefits, including enhancing carbohydrate metabolism, boosting antioxidant defenses, eliminating reactive oxygen species, regulating immune system functions, and exhibiting anti-cancer, anti-inflammatory, and anti-atherosclerotic properties[26].

However, fermentation introduced new compounds, such as salicylic acid and apigenin, while reducing others like caffeic acid, ferulic acid, tannic acid, maleic acid, naringenin, quercetin, p-coumaric acid, and saponin. Salicylic acid is well known for its anti-inflammatory properties, and apigenin has been associated with neuroprotection and cancer modulation, suggesting that fermentation may produce or enhance bioactive compounds that provide additional health benefits.

Although the unfermented extract demonstrates superior antioxidant activity the fermented extract presents distinct advantages, particularly in terms of mineral content. Mineral analysis (Table 3) revealed the presence of minerals including calcium, magnesium, iron, copper, manganese, potassium, sodium, and zinc in both fermented and unfermented extracts. Calcium contributes to the health of bones and teeth, the nervous system, and muscles. Therefore, it plays a prominent role in children's nutrition and health[27] and sodium which is one of the most abundant elements on the earth's crust regulates the amount of fluid in the body[28]. Copper, an essential mineral, occurs naturally in certain foods and is also available as a dietary supplement. Copper (Cu) is a vital trace element for humans, serving as an essential cofactor in electron transfer reactions, particularly in the brain, where the demand for metals is notably high[29]. The role of iron in the body includes making hemoglobin, a protein in red blood cells that carries oxygen throughout the body. Magnesium has an important role in the functioning of the immune system,

muscles, heart health, and nerves[30]. Magnesium in addition to potassium and other macro elements including calcium and sodium are required by the body in higher amounts and are more important than any other minerals. However, the concentrations of potassium and manganese was found to be higher (Table 3) only in the fermented extract. Manganese also plays a role in blood clotting and hemostasis in conjunction with vitamin K[31]. Manganese is a vital trace element found naturally in many foods and available as a dietary supplement. It serves as a cofactor for several enzymes, such as manganese superoxide dismutase, arginase, and pyruvate carboxylase[32]. Potassium is one of the most important minerals and its role in muscle balance and nerve function is well documented[33], potassium is essential for maintaining proper electrolyte balance and cardiovascular health. However, manganese in addition to copper, iron, and zinc are regarded as microelements that are required in trace amounts for healthy growth and development. These changes in mineral content suggest that the fermented extract may offer enhanced bioavailability of these nutrients, making it particularly beneficial for certain health conditions.

CONCLUSION

The study demonstrated that the unfermented extract of *T. catappa* exhibited significantly higher antioxidant activity, phenolic contents, and mineral composition. However, fermentation led to the production of additional bioactive compounds, such as salicylic acid and apigenin, which are known for their antioxidant properties. These findings suggest that fermentation can modify the phytochemical profile, potentially enhancing health benefits. Future research should focus on optimizing fermentation conditions to maximize beneficial compound production and investigating the bioavailability and therapeutic effects of both extracts *in vivo*.

SIGNIFICANCE STATEMENT

This study highlights the distinct therapeutic potential of fermented and unfermented *Terminalia catappa* leaf extracts. Fermentation-enhanced bioactive compounds like salicylic acid and apigenin, along with minerals such as potassium and manganese, are beneficial for cardiovascular and immune health. Conversely, the unfermented extract demonstrated superior antioxidant activity due to its higher phenolic and flavonoid content, showcasing the complementary health benefits of both forms. Future studies should focus on the clinical evaluation of *Terminalia catappa* extracts to confirm their therapeutic efficacy and explore their potential in managing oxidative stress-related diseases.

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