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RESEARCH

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Antimicrobial, antioxidant and anti-inflammatory activities of the root extracts and fractions of *Terminalia avicennioides* Guill. and Perr.

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Abstract

Background Infectious diseases remain a major source of death and sickness globally. Their management entails use of antimicrobials. However, emergence of microbial resistance to these agents is on the increase. Inflammation and oxidative stress also accompany disease states. Newer agents to counter microbes, inflammation and oxidative stress are needed. *Terminalia avicennioides* Guill and Perr. is regularly exploited as a traditional remedy to numerous complaints, comprising infections, inflammation and enhancement of well-being. This study was intended to examine the effects of the root extracts and fractions of *T. avicennioides* against select bacteria and fungi as well as their anti-inflammatory and antioxidant potentials. Antimicrobial, anti-inflammatory and antioxidant assessments were conducted with broth microdilution technique, lipoxygenase and 2,2-diphenyl-1-picryhydrazyl (DPPH) assays, respectively.

Results All the bacteria displayed varying susceptibility to the different extracts. The extracts caused good antibacterial activity towards *Staphylococcus aureus, Salmonella typhimurium, Stenotrophomonas maltophilis, Enterobacter cloaca, Klebsiella pneumoniae*, *Echinococcus faecalis and Escherichia coli*, but moderate for *Proteus mirabilis and Pseudomonas aeruginosa*. Antifungal action varied from good to moderate against *Fusarium spp*, moderate against *Aspergillus niger* but inactive against *Candida albicans.* Anti-inflammatory and antioxidant activities were dose-dependent, recording robust activity at higher concentrations. The *n*-butanol fraction manifested the highest anti-inflammatory and antioxidant activities, then ethylacetate while methanol extract showed better activities among hot and cold water extracts.

Conclusions The analysis of the biological activities of *T. avicennioides* root extracts and fractions revealed encouraging antibacterial, antioxidant and anti-inflammatory activities, which were dose reliant. The different extracts and fractions displayed variable grades of activity. The plant showed good antibacterial but weak antifungal action. These activities could be credited to polyphenols and other plant constituents. This report may explain some of the traditional medicinal uses of the plant and could open the door for further studies in search of newer compounds against microbial organisms, inflammation and/or oxidative stress.

Keywords Antimicrobial, Anti-inflammatory, *Terminalia avicennioides*, Minimum inhibitory concentration, Oxidative stress, Total antibacterial activity

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Background

Infectious diseases, especially bacterial, are a leading source of death the world over, with developing countries having the utmost tolls. Relatively recently, about 13.7 million people died from infections in 2019 alone, with bacteria accounting for 7.7 million of the mortalities (Gray and Sharara 2022). Antibiotics have been extensively utilized in the cure of bacterial infections as well as improving the average survival proportion of infected subjects (Aslam et al. 2018). Sickness and death, principally in developing countries with inadequate or absent healthcare facilities, are also substantially reduced by antibiotics (Rossolini et al. 2014). However, the continuous and haphazard use and abuse of antibiotics have caused emergence of increased resistance by microbial agents (Aslam et al. 2018). Antibiotic resistance is a normal process entailing generated adaptive mechanisms, which currently epitomizes a very significant problem (Popa et al. 2022). Therapy against infections initiated by multidrug resistant pathogens is a hugely tasking endeavour due to the narrow choice of effective antibiotics as well as absence of excellent alternate treatment options (Tietgen et al. 2022). Antibiotic resistance has turn out to be a severe hazard to human community health globally (Zhang et al. 2022) which has prompted the intense search for alternative sources of antimicrobial agents (Anand et al. 2019).

Oxidative stress is a biological state caused by a disparity amid pro-oxidants and antioxidants in favour of the oxidants, resulting in a perturbation of redox signaling mechanism and/or molecular damage (Sies 2020). Reactive oxygen species (ROS) damage important molecules such as lipids, proteins and DNA. Oxidative stress is a key element in the pathogeneses of a range of diseases comprising cancer, diabetes mellitus, cardiovascular, neurodegenerative and inflammatory diseases among others (Arika et al 2019; Pham et al. 2022). Cross-talk exists between oxidative stress and inflammation during the course of several pathological states. Oxidative damage may result in cellular infiltration and spread of inflammation via triggering release of cytokines and initiation of enzymes as lipoxygenases from cellular effectors (Yu et al. 2022). Inflammation is an active defensive response to counter mechanical injuries, burns, infections or other toxic stressors, which is intended to be beneficial, but could itself be deleterious, especially chronically (Deng et al. 2022). Persistent inflammatory responses could result in chronic illnesses including inflammatory bowel, circulatory or neurodegenerative diseases (Hussain et al. 2020).

The body maintains a steady equilibrium amid pro-oxidants and antioxidants in a normal physiologic state, through an intricate system harbouring enzymatic and non-enzymatic routes, to counter stress and thereby ensuring a healthy being (Arika et al. 2019). Oxidative stress may be controlled with synthetic phenolic antioxidant chemicals including butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), or propyl gallate (PG), which, however, may produce detrimental hepatotoxic and carcinogenic effects (Wang et al. 2021). These agents are also not easily accessible, exorbitant, and labile, thus hindering their use (Moriasi et al. 2020). Therefore, the need for safer, easily accessible and potent alternatives such as medicinal plants is paramount (Anand et al. 2019).

Medicinal plants are believed to be safer, affordable and accessible alternative therapy for microbial infection and/or management of oxidative stress-related conditions including inflammatory processes (Goyal and Suleria 2019). Herbs remain the origin of most of the presently used orthodox drugs, while studies have affirmed their prospect in the development of novel agents to counter a variety of conditions (Agidew 2022). Plants continue to be utilized as medicaments from ancient times (Rojas et al. 2022). The World Health Organization (WHO) stated that over 75% of the world populace uses plant materials as medicaments, especially those in rural areas (Agidew 2022). Several studies have indicated medicinal plants to encompass constituents such as saponins, flavonoids, phenolic compounds, alkaloids, steroids, tannins, glycosides and anthraquinones among others (Agidew 2022).

Terminalia sp., family Combretaceae, harbours about 250 species and has a worldwide distribution. Several plants in the genus are extensively utilized as traditional medicines (Cock 2015; Das et al. 2020). Analysis of the phytochemicals contained within 39 select species had revealed 368 compounds, comprising terpenoids, tannins, flavonoids, phenylpropanoids, simple phenolics, among other chemicals (Zhang et al. 2019). Several of these plants have been reported to exhibit free-radical scavenging, antioxidant and anticancer activities (Salau et al. 2015). Other noteworthy properties described for these plants include antidiabetic and antiobesity, anti-inflammatory, antimicrobial as well as antimalarial activities (Das et al. 2020).

Terminalia avicennioides Guill. and Perr. is plentiful in the West African savannah. The root bark extracts of *Terminalia avicennioides* have been described to comprise flavonoids, tannins, phenols, saponins, alkaloids and other phytochemicals (Salau et al. 2013; Aliyu-Amoo et al. 2021). The aim of this study was to evaluate the antibacterial, antifungal, anti-inflammatory and antioxidant potential of the root extracts and fractions of *Terminalia avicennioides*. The antimicrobial activity, anti-inflammatory potential and antioxidant capacity were appraised

utilizing broth microdilution technique, lipoxygenase (LOX) inhibition assay and 2, 2-diphenyl-1-picryhydrazyl (DPPH) assay, respectively.

Methods

Plant collection, identification and extraction

The root of *Terminalia avicennioides* was sourced from the nearby bushes in Zaria, Nigeria, during dry season in November. Samples of the leaves, fruits and seeds of the plant were taken to the Herbarium, Department of Biological Sciences, Ahmadu Bello University, Zaria, for authentication. A verification number, VIN 900239, was allotted by Mr. Namadi Sunusi. The root sample collected was washed and dried away from the sun, after which it was milled into fine particles, with the aid of a laboratory mill. Roughly 4 kg of the pounded plant substance was placed in a polythene container and kept. An amount (240 g) of the prepared substance was distributed in 6 equivalent lots, and respectively extracted by way of infusion with acetone, absolute ethanol, 30% ethanol and methanol, as well hot and cold water, over 24 h. The resultant extracts were filtered using Whatman filter paper No: 1. The filtrates were dried to solid extracts. Another measure (2 kg) of the plant matter was methodically extracted by mixing with methanol over 24 h and sifted to yield the methanol extract (ME). The ME was dried in vacuo in a Rotary evaporator, at reduced pressure, yielding the solid ME, which was fractionated.

Fractionation of extract

For the fractionation, 50 g methanol extract was liquefied in 500 ml distilled water and mixed with similar volume of *n*-hexane. The mixture was smoothly shaken during few minutes and the pressure that developed inside the flask was released by turning upside down the funnel and opening the tap at the base. The process was repeated for a number of times. The resultant suspension was left idle over 10 min before the lower aqueous portion was evacuated into a container. The residual *n*-hexane fraction was placed in another beaker. The aqueous methanol fraction was again partitioned, consecutively, in similar fashion, first in chloroform then in *n*-butanol. The fractions acquired were dried by vapourization using a fast current of air.

Phytochemical analysis

Phytochemical components in the plant extracts were identified according to Trease and Evans (2002) as described below.

Test for alkaloids

Two hundred milligram (0.2 g) of extract was mixed with 10 ml acid alcohol, boiled and filtered. To 5 ml of the solution, 2 ml of dilute ammonia and chloroform (5 ml) were added to this mixture and agitated lightly. To this mixture, 10 ml of acetic acid was added. This was apportioned into two. To one portion, Dragendorff's reagent was added. A change to reddish or brown precipitate is suggestive of alkaloids.

Test for flavonoids

In 0.5 ml filtrate of extract, 5 ml dilute ammonia was added, followed by the addition of 1 ml concentrated sulphuric acid. The existence of flavonoids is manifested as yellowish colouration of the solution which vanishes on standing.

Test for phenolics

A little quantity of extract was liquefied in 2 ml distilled water in a tube. A few drops of 10% aqueous ferric chloride solution were added to it. Generation of a blue or green hue denotes the existence of phenols.

Test for saponins

The extract was blended with 5 ml distilled water in a test tube and agitated strongly during 30 s. Generation of a honeycomb-like froth that persists over 10–15 min specifies the presence of saponins.

Test for tannins

To about 2 ml of the extract in a tube, 3–5 drops of ferric chloride (FeCl3) solution were introduced. A blue or brownish-blue precipitate is a manifestation of hydrolysable tannins.

Test for terpenoids

One millilitre acetic anhydride was added into a tube containing 2 ml of the extract and was mixed with concentrated sulphuric acid (H2SO4). Appearance of a pink or violet hue designates terpenoids in the extract.

Characterization of bacterial isolates

Enterobacteriaceae strains which include *Stenotrophomonas maltophilia, Enterobacter cloacae, Klebsiella pneumoniae,* and *Proteus mirabilis* were isolated from the shell, albumin and yolk of poultry eggs using the standard World Health Organization (gold standard) culture and isolation techniques. These include pre-enrichment of samples in non-selective media which was buffered with peptone water (BPWSelecta-MEDIA, South Africa), enrichment of sample-broth in selective media, tetrathionate (SelectaMEDIA, South Africa), isolation of sample on selective solid agar media, xylose lysine deoxycholate (XLD-MERCK, South Africa) and confirmation of presumptive bacterial isolates using biochemical tests and molecular techniques, Matrix Assisted Laser Desorption/

Ionization Time-of-Flight (MALDI-TOF) and polymerase chain reaction (PCR) (Mellman et al. 2008; WHO 2010). The bacterial isolates were stored in the University of Pretoria Phytomedicine Laboratory, Faculty of Veterinary Science, Onderstepoort, Gauteng, South Africa.

Antimicrobial susceptibility test

Preparations (10%) of the extract or fraction of *T. avicennioides* each were done via liquefying 150 mg of the sample in 15 ml acetone. The antimicrobial activities of the samples were appraised by broth microdilution technique. Antibacterial test was carried out on nine (9) bacteria viz; *Pseudomonas aeruginosa* (ATCC27853), *Escherichia coli* (ATCC25922), *Staphylococcus aureus* (ATCC29213), *Echinococcus faecalis* (ATCC29212) and *Salmonella typhimurium* (ATCC39183). Others were *Stenotrophomonas maltophilis, Enterobacter cloacae, Klebsiella pneumoniae* and *Proteus mirabilis.* Gentamicin and distilled water were the positive and negative controls, respectively. The antifungal test was carried out on three fungal species which include *Candida albicans, Fusarium spp* and *Aspergillus niger.* Amphotericin B and distilled water were positive and negative controls, respectively. Stock cultures of the microbes were sustained at 4 °C on slopes of Müller-Hinton agar. To make inocula, loopfuls of an overnight culture were suspended in distilled water and adjusted to 0.25 McFarland turbidity standard corresponding to 0.75×10^8 CFU/ml. Antibacterial action was assessed with Müller-Hinton broth culture medium in 96 well plates. Two-fold serial dilutions were made with solutions of crude extracts and fractions. One hundred millilitres of inoculum, diluted 100 times, were added into each well. Plates were incubated at 37 °C during 24 h. After incubation, growth was visualized with colorimetric technique by means of *p*-iodonitrotetrazolium violet (INT) (Sigma®). Viable bacteria transform the yellow colour of INT to pink. For a particular extract or fraction, the lowest concentration at which no discernible colour transformation occurred was deemed the minimum inhibitory concentration (MIC). The assay was done in triplicate in three independent experiments.

The total antibacterial activity (TAA) was calculated as a function of the extraction yield in gram (g) of plant material and the minimum inhibitory concentration (MIC), mg/ml. TAA specifies the volume of water or solvent, which after adding to 1 g of the extract that will still impede the growth of the pathogen (Eloff 2000).

DPPH radical scavenging assay for antioxidant potential

The capacity of the extracts to mop-up free radicals was confirmed using DPPH assay according to Blois (1958) and Desmarchelier et al. (1997). The DPPH test assesses the capability of antioxidants to mop-up free radicals. The capacity by the plant extracts to contribute a hydrogen atom was revealed via transformation in colour in the extract solution. DPPH reagent yields a violet/purple colour in methanol solution which diminishes to tints of yellow when antioxidants are present. A preparation of DPPH was made in 95% methanol (0.1 mmol/l). One millilitre was added each to 3 ml of different concentrations (0.78 to 100 µg/ml) of the test material and the control. Thirty minutes were allowed to elapse before measuring the absorbance at 517 nm. The reduction in DPPH absorption specifies the capability of the extract in mopping up radicals.

The percentage inhibition was computed as follows:

$$\% \text{ Inhibition} = [(AB - AA)/AB] \times 100$$

where AB = Absorbance of blank DPPH solution, AA = Absorbance of test extract.

The effective concentration at which DPPH¨ radicals are scavenged by 50% (EC50 in µg/ml) was determined with plot of per cent inhibition versus log of concentration.

The 15-lipoxygenase (15-LOX) inhibitory assay

The technique by Pinto del Carmen et al. (2007) was employed to spectrophotometrically assess LOX activity with minor adjustments. The test estimated the inhibition of soybean 15-lipoxygenase activity by the extracts using linoleic acid as substrate to produce Fe3 + /xylenol orange composite detected at 560 nm. Linoleic acid (140 µM) was made in Tris–HCl buffer (50 mM, pH 7.4). Test samples (10 mg/ml) were made in DMSO (100%) and mixed with Tris–HCl making 2 mg/ml. Lipoxygenase enzyme (40 µl) mixed with icy Tris–HCl buffer (final concentration, 0.2 U/ml), was each added to 20 µl of diverse concentrations (0.78 to 100 µg/ml) of extract and fractions or quercetin (positive control) at 25 °C during 5 min. Linoleic acid (40 µl) was placed into the mix followed by additional incubation at 25 °C over 20 min in the dark. To terminate the reaction, stop solution made of 100 µl of fresh FOX reagent [sulphuric acid (30 mM), xylenol orange (100 µM), iron (II) sulphate (100 µM) in methanol/water (9:1)] was added. Tris–HCl buffer, 15-LOX solution, substrate and FOX reagent constituted the negative control while the blanks contained the enzyme 15-LOX and buffer.

The impediment to LOX activity was found by working out the percentage of the impairment of hydroperoxide formation via variations in absorbance at 560 nm after 30 min at 25 °C as presented as follows:

15 − LOX inhibition (%) = Absorbance (control) − Absorbance (sample) /Absorbance (control) x 10(

The half-maximal inhibitory concentration (IC50) was calculated from the non-linear regression of percentage inhibition against log concentration.

Data analysis

Data obtained were presented as mean ± SD and subjected to analysis of variance (ANOVA), Tukey's post hoc test was used to determine the *p*-values for the differences observed between tested samples and controls. Statistical analysis was carried out with GraphPad prism (Version 5.0, San Diego, CA, USA). Values of $p < 0.05$ were set for statistical significance.

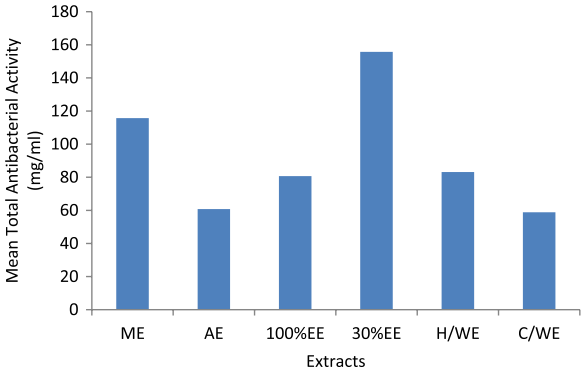

Fig. 1 Mean total antibacterial activity (TAA) of all the bacteria tested. *ME* Methanol extract, *AE* Acetone extract, *EE* Ethanol extract, *H/WE* Hot water extract, *C/WE* Cold water extract

Results

Analysis of phytochemical composition of all the extracts and fractions showed presence of flavonoids, phenols, saponins and tannins.

The MIC values for the extracts and fractions of the root of *Terminalia avicennioides* on tested bacteria are presented in Table 1. *Echinococcus faecalis* had the lowest MIC for all the extracts (0.02 mg/ml), representing the highest degree of susceptibility to all the extracts. Gentamicin as positive control was inactive against *S. aureus* and *E. faecalis* each with MIC values of 2.5 mg/ml.

For total antibacterial activity (TAA) of the extracts, 30% ethanol showed the highest mean of 155.72 ml/g, followed by methanol (115.74 ml/g), hot water (83.13 ml/g), 100% ethanol (80.71 ml/g), acetone (60.76 ml/g) and cold water (58.84 ml/g) (Fig. 1).

Table 2 Minimum inhibitory concentration values (mg/ml) of the root extracts of *Terminalia avicennioides* and controls on the three fungal isolates evaluated

Extracts	*Candida albicans*	*Fusarium spp*	*Aspergillus niger*
Methanol	1.25^{I}	0.16 ± 0.05^{M}	0.63 ± 0.15^{W}
Acetone	0.63 ± 0.14^{W}	0.16 ± 0.01^{M}	1.25^{I}
100% Ethanol	0.63 ± 0.15^{W}	0.16 ± 0.04^{M}	1.25^{I}
30% Ethanol	2.5^{I}	0.16 ± 0.05 M	0.31 ± 0.14^{M}
Hot water	0.63 ± 0.14^{W}	0.08 ± 0.06^{G}	0.31 ± 0.14^{M}
Cold water	2.5^{I}	0.08 ± 0.06^{G}	0.16 ± 0.05^{M}
Amphotericin B	1.25^{I}	0.02^{G}	2.5^{I}
Water	2.5^{I}	2.5^{I}	2.5^{I}

Different superscript letters denote dissimilar degrees of activity from good (G), to moderate (M), weak (W) or inactive (I)

Table 1 Minimal inhibitory concentration (MIC) values (mg/ml) of extracts of the root of *Terminalia avicennioides* and controls on select bacterial organisms

Extracts	S. aur	S. typ	S. mal	E. clo	K. pne	P. mir	E. fae	P. aer	E. col
Meth	**0.08 ± 0. 02**	**0.04 ± 0.00**	**0.08 ± 0.00**	**0.04 ± 0.01**	**0.08 ± 0.02**	*0.16 ± 0.11*	**0.02 ± 0.00**	*0.16 ± 0.13*	**0.08 ± 0.01**
Ace	*0.16 ± 0. 12*	**0.04 ± 0.00**	**0.08 ± 0.00**	**0.04 ± 0.01**	**0.08 ± 0.00**	**0.08 ± 0.01**	**0.02 ± 0.00**	*0.16 ± 0.11*	**0.08 ± 0.00**
100% Eth	**0.08 ± 0. 00**	**0.04 ± 0. 01**	**0.08 ± 0.00**	**0.04 ± 0.01**	**0.08 ± 0.01**	*0.16 ± 0.11*	**0.02 ± 0.00**	*0.16 ± 0.13*	**0.08 ± 0.03**
30% Eth	**0.08 ± 0.00**	**0.04 ± 0.01**	**0.08 ± 0.00**	**0.04 ± 0.02**	**0.08 ± 0. 02**	*0.16 ± 0.11*	**0.02 ± 0.00**	*0.16 ± 0.13*	**0.08 ± 0.03**
H/W	**0.08 ± 0.02**	**0.04 ± 0. 01**	**0.08 ± 0.15**	**0.04 ± 0.02**	**0.08 ± 0.05**	*0.16 ± 0.15*	**0.02 ± 0.00**	0.63 ± 0.23^{W}	**0.08 ± 0.05**
C/W	**0.08 ± 0.02**	**0.04 ± 0.01**	**0.08 ± 0.05**	**0.04 ± 0.02**	**0.08 ± 0.05**	*0.16 ± 0.15*	**0.02 ± 0.00**	1.25^{I}	**0.08 ± 0.05**
Gent	2.5^{I}	**0.02**	**0.02**	**0.02**	**0.02**	**0.02**	2.5^{I}	**0.02**	**0.02**
D/W	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}	2.5^{I}

Different degrees of antibacterial activity are denoted by different formatted values from good (bold), to moderate (italics), weak (w) or inactive (I). Values were mean ± SD of assay done in triplicates

S. aur = *Staphylococcus aureus,* S. typ = *Salmonella typhimurium,* S. mal = *Stenotrophomonas maltophilis,* E. clo = *Enterobacter cloacae,* K. pne = *Klebsiella pneumonae,* P. mir = *Proteus mirabilis,* E. fae = *Echinococcus faecalis,* P. aer = *Pseudomonas aeruginosa,* E. c = *Escherichia coli.* Meth = methanol, Ace = acetone, Eth = ethanol, H/W = hot water, C/W = cold water, Gent = gentamicin, D/W = distilled water

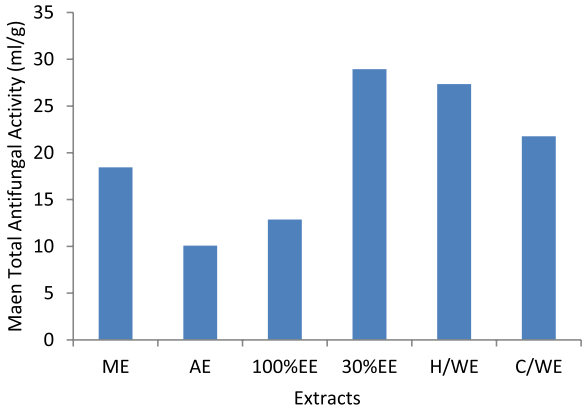

Fig. 2 Mean total antifungal activity of extracts against the tested fungi. *ME* Methanol extract, *AC* Acetone extract, *EE* Ethanol extract, *H/WE* Hot water extract, *C/WE* Cold water extract

The MIC values for the root extracts of *T. avicennioides* on tested fungal organisms are presented in Table 2. *Fusarium* spp showed the most susceptibility to the extracts with MIC of 0.08–0.16 mg/ml.

For the total antifungal activity among the extracts, 30% ethanol had the highest action, with activity of 28.94 ml/g, followed by hot water (27.35 ml/g), cold water (21.77 ml/g), methanol (18.45 ml/g), 100% ethanol (12.87 ml/g) and acetone (10.08 ml/g) (Fig. 2).

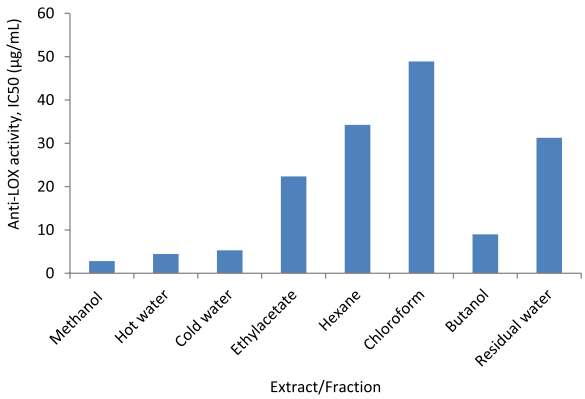

Fig. 3 Anti-LOX activity (IC50 = µg/ml) of extracts (methanol, hot and cold water) and fractions (ethylacetate, hexane, chloroform, butanol and residual water) of the root of *T. avicennioides*

Amphotericin B was inactive against *C. albicans* and *A. niger* with MIC values of 1.25 mg/ml and 2.5 mg/ml, respectively, but the drug was very active against *Fusarium spp* with MIC value of 0.02 mg/ml.

Among the extracts, 30% ethanol had the highest mean TAA (28.94) for all the fungi tested, followed by H/WE (27.35 ml/g), C/WE (21.77 ml/g), ME (18.45 ml/g), 100% EE (12.87 ml/g) and AE (10.08 ml/g).

Lipoxygenase inhibition assay

Results for LOX inhibitory activity as a measure of anti-inflammatory potential of the extract and fractions of *T. avicennioides* are presented in Fig. 3. Inhibitory effect on lipoxygenase enzyme by the extracts and fractions generally revealed a dose-dependent activity. Among the extracts, methanol showed the highest inhibition of LOX (IC50 = 2.81 µg/ml), followed by hot water (IC50 = 4.45 µg/ml) then cold water (IC50 = 5.30 µg/ml) as displayed in Fig. 3. For the fractions, *n*-butanol caused the greater inhibition of LOX (IC50 = 8.97 µg/ml) followed by ethylacetate (IC50 = 22.36 µg/ml) while chloroform fraction had the lowest inhibition of LOX and highest IC50 (48.90 µg/ml) (Fig. 3).

DPPH assay

The results for DPPH assay as a measure of antioxidant capacity of the extracts and fractions of *T. avicennioides* are presented in Table 3. The antioxidant effect by the extracts was variable and dose-dependent. Higher extract concentrations caused greater activity for each extract. N-Butanol fraction manifested the highest activity (11.53 µg/ml) as presented in Table 3.

Discussion

The study evaluated the antimicrobial effect of the root extracts of *Terminalia avicennioides* against bacteria and fungi as well as their antioxidant and anti-inflammatory capacity. This was based on the ethnobotanical usage of the plant. Values of MIC as well as total antimicrobial activity revealed the antibacterial and antifungal efficacy of the extracts. This study also considered plant extracts having MIC values lesser than 0.1 mg/ml for the microbes as good antimicrobial activity; those with

Table 3 Antioxidant activity (IC50 = µg/ml) of the root extracts and fractions of *Terminalia avicennioides* as determined using the DPPH assay

	Extracts			Fractions				
	Methanol	Hot water	Cold water	Ethylacetate	Hexane	Chloroform	Butanol	Residual water
IC50 (µg/ml)	35.91	84.91	155.45	21.94	206.35	100.26	11.53	401.04

values of 0.1 to 0.5 mg/ml moderately active; values 0.5 to 1 mg/ml weakly active, while MIC greater than 1 mg/ml indicate inactive extract as reported earlier (Holetz et al. 2002).

The bacteria tested in this study were susceptible to the root extracts of *T. avicennioides* to varying degrees. The extracts and fractions displayed robust activity against all the bacteria except for *Proteus* and *Pseudomonas* were the antibacterial activity was moderate. The dissimilarity in the activities of the extracts but also fractions in all probability are related to variations in composition of each extract and/or differences in susceptibility by the microbes to the extracts. The activity of the extracts in this study was highest against *Echinococcus faecalis* followed by *Salmonella typhimurium*, *Enterobacter cloaca, Stenotrophomonas maltophilis, Klebsiella pneumonia, Escherichia coli, Staphylococcus aureus, Proteus mirabilis* and *Pseudomonas aeruginosa* in that order. Similar to this study, previous reports had indicated the plant to have antimicrobial effect (Mann 2012; Yimta et al. 2014). The ethyl acetate extract of the root bark of the plant elsewhere demonstrated inhibitory action towards methicillin-resistant *Staphylococcus aureus* (MRSA) (Adim et al. 2018). Root bark extract of *T. avicennioides* also exhibited effect on *Salmonella typhi, S. dysentriae, S. aureus* and *Pseudomonas aeruginosa* (Usman et al. 2018). Also, Issah et al. (2020) reported antibacterial activity by methanol and ethanol extracts of the stem bark and leaves of *Terminalia avicennioides* against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, with the greatest activity displayed towards *Escherichia coli*. Extracts of *T. avicennioides* reduced the load of *S. typhi* in vivo in rats (Famen et al. 2021). A related plant, *Terminalia ferdinandiana* Exell demonstrated strong antibacterial action towards numerous pathogenic bacteria (Cheesman et al. 2019). In another study, ethanol extract of *Terminalia ferdinandiana* Exell displayed robust antibacterial action towards *Bacillus cereus* and MRSA (Akter et al. 2019). *Terminalia superba* was also recently described as having robust antibacterial action towards *E. coli*, *S. typhi*, *S. aureus*, *K. pneumonia* and *Streptococcus pyogenes*, which was attributable to fatty acids with amphiphilic function disrupting cell wall of bacteria (Ani et al. 2023).

Some of the tested bacteria had recorded variable degrees of susceptibility to extracts from different plants in previous studies. Elisha et al. (2017) reported good antibacterial activity against a number of bacteria including *E. coli* by extracts of some South African plants. The extracts in our study harbour different constituents from the above referenced studies. The dose-dependent variations in the activities of the extracts might be from differences in the quantity of the phytochemicals they harbour (Otun et al. 2015). Similarly, the differences exhibited by the extracts of different solvents could imply that the extracts with higher activities extracted more of the active principles (Babayi et al. 2004). The antibacterial activity displayed by *T. avicennioides* in this study was most likely mediated by similar constituents identified in the report by Adim et al. (2018) as the plant in their study was sampled from the same location as ours. However, while our study utilized both crude extracts and fractions, Adim et al. (2018) described ethylacetate extract.

No difference in antibacterial action by the extracts was noted between the Gram positive and Gram negative bacteria. Eloff (2000) in his study of plant extracts had suggested antibacterial activity to be unconnected with dissimilarities in cell wall structure between the two bacteria classes. It is plausible the extracts of *T. avicennioides* in our study exerted their action against the bacteria through a mechanism not related with bacterial cell wall.

The bacteria in this study were chosen due to their medical importance. Enterobacter is an important pathogen, accounting for many of the nosocomial infections of wound, blood, respiratory and urinary tracts (Hafiz et al. 2023). *Salmonella typhimurium* infections are mostly associated with the intake of unclean animal products including eggs and meat (Sun et al. 2021). *Klebsiella pneumoniae,* an opportunistic pathogen, remains the Gram negative bacteria most frequently causing a range of infections, comprising urinary tract infections, pneumonia, abdominal infections and septicaemia in different healthcare systems. Several descriptions of MDR *K. pneumoniae* have been made (Tietgen et al. 2022). *Stenotrophomonas maltophilia* has been documented as a major nosocomial microbe infecting many body parts and prosthetic devices particularly in very ill or patients with weak immunity (Hafiz et al. 2022). Thus, the susceptibility of these bacteria to the plant extracts used in this study further affirms the importance of the plant.

The extracts exhibited good through moderate to no antifungal activity against the fungi tested. The good to moderate antifungal action was against *Fusarium species*. Similar to our findings, *Terminalia ivorensis* A.Chev. and *T. mantaly* H. Perrier bark extracts were described as having inhibitory effect (MIC = 0.025–0.050 mg/ml) on *Fusarium* sp. (Kouassi et al. 2019). Hot and cold water extracts showed good activity while acetone, ethanol and methanol extracts exhibited moderate action. It is apparent the polarity of the solvents influenced the antifungal efficacy of the extracts. The antifungal constituents were contained more in the aqueous extracts. Similarly, against *Aspergillus niger*, the water extracts exhibited higher action, producing moderate effect compared to the weak activity caused by methanol to no activity by

acetone and 100% ethanol extracts. Further, it is plausible that higher concentrations of extracts/fractions were needed for robust antifungal activity to be displayed against the fungi. This study utilized 10% preparations. At these concentrations, the antimicrobial activity of the plant was only good against bacteria. It was previously reported that ethanol extracts of the bark of *T. catappa* L. showed antifungal action (MIC) towards *Candida albicans* (0.25 mg/ml) and *C. glabrata* (0.25 mg/ml) (Gonçalves 2019). Similarly, antifungal action due to ethanol extract of the fruit of *Terminalia chebula* Retz. was displayed against *Candida albicans* (MIC = 0.25 mg/ml) and *C. glabrata* (MIC = 0.25 mg/ml) (Vidya et al. 2019). Among the fungi, *Candida albicans* was resistant to the effect of the extracts. Candida seems resilient as it was not vulnerable to the normal antifungal agent amphotericin B. In another study on antifungal effect of South African Terminalia species by Masoko and Eloff (2005), it was observed that the greatest antifungal activity rested with the acetone extract among hexane, methanol and dichloromethane.

From accessible literature, no work has been described supporting the anti-inflammatory activity of *Terminalia avicennioides* as believed in traditional medicine. However, potent anti-inflammatory activity has been described for some members of the *Terminalia* genus. Earlier, Khan et al. (2018) described dose reliant anti-inflammatory activity by methanol extract of *Terminalia coriacea* (Roxb.) in rats, which they ascribed to identified flavonoids including apigenin, kaempferol, luteolin among others. Furthermore, *Terminalia* sp. extracts dose-dependently supressed pro-inflammatory cytokines, an effect they attributed to vitexin, chebulinic acid as well as other similar constituents (Fahmy et al. 2017). In this study, *T. avicennioides* produced a dose-dependent anti-inflammatory activity which may be the first description in this particular species. The higher the concentration, the greater the inhibitory effect of the extracts and fractions on the lipoxygenase enzyme. Several studies had reported on anti-inflammatory effect of extracts, fractions or identified compounds from many plants in the Genus Terminalia. Some of the reports have identified the mechanism by which the compounds bring forth their anti-inflammatory activity. *Terminalia ferdinandiana* fruit displayed anti-inflammatory action in lipopolysaccharide-activated murine macrophages, via impeding COX-2 and inducible nitric oxide synthase (iNOS) besides hindering the synthesis of prostaglandin E2 (Tan et al. 2011). Nair et al. (2012) had reported a selective inhibition of COX-2 by the ethanol extract of *T. phanerophlebia* and its isolated compound β-sitosterol. *Terminalia superba* was also recently reported to exert anti-inflammatory effect via capric acid to inhibit pro-inflammatory cytokines including interleukin-6 (Ani et al. 2023).

This study did not identify a particular constituent or mechanism responsible for the anti-LOX activity observed. However, we could speculate on the relationship between LOX inhibition and (total) phenolic content of plants. Since LOX inhibition is positively correlated to total phenolics (Das et al. 2020), it is sound to suggest that greater inhibition of the enzyme was instigated by larger quantities of flavonoids and tannins contained by *T. avicennioides* root extracts. Phytochemical content analysis of *T. avicennioides* (Aliyu-Amoo et al. 2021) indicated the presence of flavonoids and tannins in the plant, which suggests that the plant could mediate anti-inflammatory action through a similar manner.

Different fractions exhibited varying degrees of anti-inflammatory action. The n-butanol fraction showed the greater activity (8.97 µg /ml) among the fractions then ethylacetate (22.36 µg /ml).

Owing to the composite nature of plants having diverse phytochemical components, the antioxidant capability of plant extracts could be deemed a rough estimate since one assay method was utilized. Multiple assay techniques could have offered a finer estimate. In the current work, the DPPH assay was employed to gauge the antioxidant capacity of *T. avicennioides* root bark extracts and fractions. Of all the research conducted on *Terminalia* sp. from 2010 to 2020, antioxidant studies were the least in number (Das et al. 2020). Anokwuru et al. (2018) assessed the antioxidant capacity of ethanol extracts of all the different parts of *Terminalia sericea* Burch. ex DC. from South Africa, wherein some demonstrated high antioxidant action majorly attributable to gallic acid and resveratrol.

The ethylacetate and butanol fractions presented the best antioxidant activity while the crude methanol, hot and cold water extracts demonstrated low antioxidant function as revealed in the DPPH assay. The hexane, chloroform and residual water fractions showed the lowest activity. These results suggest that the antioxidant compounds extracted from *T. avicennioides* are more concentrated in the ethyl acetate and butanol fractions. Kim et al. (2022) reported greater antioxidant effects (determined with DPPH assay) by the butanol and ethylacetate fractions of *Brassica oleracea* L. methanol extract, which were positively correlated with the total phenolic content of the plant. It is evident that the more functional fractions harbour more of antioxidant constituents which are polyphenolic in *T. avicennioides*. However, Basu et al. (2017) in their study showed polar fractions to have more antioxidant action. Akter et al. (2019) also showed more polar (methanol and water) extracts to have the highest antioxidant activity, contrary to our study.

For the butanol fraction, the IC50 obtained in this study (11.51 µg/ml) was higher than that reported for broccoli (IC50 = 0.524 ± 0.09 µg /ml) by Kim et al. (2022) which signifies that *T. avicennioides* manifested lower antioxidant potential than broccoli.

The differences in the hot versus cold water extracts though not significant ($p > 0.05$) could be due to influence of temperature on the extraction process. Temperature has been reported to affect phytochemicals content (polyphenols) during extraction (Antony and Farid 2022). *Terminalia species* contain great amounts of phytoconstituents with established antioxidant action including terpenes, flavonoids, besides phenolic acids (Das et al. 2020).

Conclusions

It can be concluded that analysis of the biological activities of *T. avicennioides* root extracts and fractions revealed encouraging antibacterial, antioxidant and anti-inflammatory activities, which were dose reliant. The different extracts and fractions displayed varying degrees of activity. The plant showed good antibacterial activity but the antifungal action was weak. N-Butanol and ethylacetate fractions as well as crude methanol extract displayed the best anti-inflammatory and antioxidant action. These activities might be credited partially to the polyphenols as well as other components within the extracts and fractions. Consequently, this report on antimicrobial, antioxidant and anti-inflammatory potentials of *Terminalia avicennioides* has re-affirmed the importance of the plant and the findings may partly explain some of its traditional uses against a number of ailments.

Abbreviations

ATCC	American type culture collection
BHA	Butylated hydroxyanisole
BHT	Butylated hydroxytoluene
COX	Cyclo-oxygenase
DPPH	Diphenyl-1-picryhydrazyl
g	Gram
h	Hour
iNOS	Inducible nitric oxide synthase
IL-6	Interleukin-6
INT	Iodonitrotetrazolium violet
LOX	Lipoxygenase
MALDI-TOF	Matrix assisted laser desorption ionization time-of-flight
ME	Methanol extract
mg	Milligram
ml	Millilitre
MIC	Minimum inhibitory concentration
MRSA	Methicillin resistant *Staphylococcus aureus*
nm	Nanometre
OD	Optical density
PCR	Polymerase chain reaction
PG	Propyl gallate
ROS	Reactive oxygen species
SD	Standard deviation
TAA	Total antibacterial activity
TLC	Thin layer chromatography
VIN	Voucher identification number
WHO	World Health Organization
XLD	Xylose lysine deoxycholate

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Author contributions

Author HAA conceived and designed the work. HAA and HII prepared the extracts, conducted the preliminary screening and performed the experiments. HII analysed the data. The original manuscript was drafted by HAA while HII revised the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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