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Curtisia dentata: a review of its botany, medicinal uses, phytochemistry and biological activities

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Abstract

Curtisia dentata is a medium-sized to large tree widely used as traditional medicine in South Africa. This study is aimed at providing a critical review of the botany, biological activities, phytochemistry and medicinal uses of *C. dentata*. Documented information on the botany, biological activities, medicinal uses and phytochemistry of *C. dentata* was collected from several online sources which included BMC, Scopus, SciFinder, Google Scholar, Science Direct, Elsevier, Pubmed and Web of Science. Additional information on the botany, biological activities, phytochemistry and medicinal uses of *C. dentata* was gathered from pre-electronic sources such as book chapters, books, journal articles and scientific publications obtained from the University library. This study showed that the bark and leaves of *C. dentata* are mainly used to "purify blood", as aphrodisiac, ethnoveterinary medicine and as traditional medicine for hypertension, cancer, obesity, sexually transmitted infections and stomach problems. Phytochemical compounds identified from the leaves, roots and stem bark of *C. dentata* include β-sitosterol, 2α-hydroxyursolic acid, betulinic acid, betulinic acid acetate, linoleic acid, lupeol, ursolic acid, ursolic acid acetate, alkaloids, amines, anthocyanins, anthraquinones, essential oils, flavonoids, glycosides, phenols, quinones, saponins and tannins. Pharmacological research revealed that *C. dentata* extracts and compounds isolated from the species have anthelmintic, antibacterial, antimycobacterial, antifungal, anti-inflammatory, antioxidant, glucose utilization and cytotoxicity activities. Future research should focus on evaluating the phytochemical, pharmacological and toxicological properties of *C. dentata* crude extracts as well as compounds isolated from the species.

Keywords: Cornaceae, *Curtisia dentata*, Curtisiaceae, ethnopharmacology, herbal medicine, indigenous pharmacopeia

INTRODUCTION

Curtisia dentata (Burm.f.) C.A. Sm. is a medium-sized to large evergreen tree belonging to the Curtisiaceae family. The species is traditionally placed in family Cornaceae but recent cladistics and molecular systematic studies support placement of the genus *Curtisia* Aiton in family Curtisiaceae.[1-4] Phylogenetic studies based on molecular data grouped genus *Curtisia* close to genus *Grubbia* P.J. Bergius, a genus of three species endemic to southern South Africa, and it has been suggested that both genera should be placed in the Grubbiaceae family mainly because of their morphological similarities, however, the fruits of the two genera are completely different.[2-5] Therefore, Curtisiaceae is a family of a single genus and species, *C. dentata*.[3-5] *Curtisia dentata* is a multipurpose species widely used in southern Africa as traditional medicine and often planted as an ornamental plant and hedge.[5] *Curtisia dentata* is one of the valuable medicinal plant species in South Africa, and the species is included in the book "medicinal plants of South Africa," a photographic guide to the most commonly used herbal medicines in the country, including its botany, major medicinal applications and active phytochemical compounds.[6] Research by Van Wyk[7,8] showed that the bark of *C. dentata* have commercial potential as aphrodisiac and tonic, and traditional medicine for inflammation and diarrhoea in South Africa. The bark of *C. dentata* is sold as herbal medicine in informal herbal medicine markets in the Eastern Cape, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga and Western Cape provinces in South Africa, that is, 66.7% of provinces in the country.[9-23] In South Africa, *C. dentata* is in the Red Data List of threatened plants, categorized as Near Threatened as the species has been over-exploited over most of its South African geographical range due to timber extraction for wagon spokes and furniture, and bark harvesting for the traditional medicine trade.[15,24-30] It is within this context that this review was undertaken aimed at reviewing the botany, medicinal uses, phytochemical and biological activities of *C. dentata* so as to provide baseline data required in evaluating the therapeutic potential of the species.

Botanical profile of *Curtisia dentata*

The genus name "*Curtisia*" is in honour of William Curtis (1746-1799), an English botanist, entomologist and founder of a unique botanical magazine first published in 1787 and which is still published today.[24] The specific name "*dentata*" is a Latin word meaning "toothed" in reference to toothed and serrated leaves of the species.[24] *Curtisia dentata* is a medium-sized to large evergreen tree which can be 20 metres in height.[31] The bole is usually cylindrical, up to 180 cm in diameter without buttresses.[5] The bark of *C. dentata* is brown in colour and smooth in younger trees, becoming dark brown and square-fissured in older trees. The leaves of *C. dentata* are simple, opposite, oblong, broadly elliptic to almost circular in shape. The younger leaves are leathery and covered with dense, woolly grey or rusty hairs. The upper surface of mature leaves are shiny, dark green in colour and hairless with conspicuous pale veins while the under-surface is light green in colour with woolly hairs and very prominent veins covered with short soft grey, rusty or brown hairs. The leaf apex is broadly tapering to rounded while the base is broadly tapering to square with strongly and coarsely toothed margins. The flowers are small and inconspicuous which are cream in colour with all floral parts covered with light grey soft hairs. The flowers are often parasitized so that only a few of the many in an inflorescence are normally fertilized and produce seed.

The fruit is white or tinged with pink, small, round or oval, crowned with four small points which are the remains of the calyx and enclosing two to four seeds.[24] *Curtisia dentata* has been recorded in evergreen forests, grassland on mountain slopes and coastal scrub forest in Mozambique, South Africa, Swaziland and Zimbabwe at an altitude ranging from 60 m to 3050 m above sea level.[4,5,31-33]

Medicinal uses of *Curtisia dentata*

The bark and leaves of *C. dentata* are mainly used to "purify blood", as aphrodisiac, ethnoveterinary medicine and as herbal medicine for hypertension, cancer, obesity, sexually transmitted infections and stomach problems (Table 1, Figure 1). In the Eastern Cape Province in South Africa, the bark of *C. dentata* is mixed with those of *Rapanea melanophloeos* (L.) Mez and used as ethnoveterinary medicine for heartwater in cattle.[34-44]

Table 1: Medicinal uses of *Curtisia dentata*

Medicinal use	Parts used	References
Aphrodisiac	Bark	Yembaturova et al.[4]; Lemmens[5]; Van Wyk et al.[6]; Grace et al.[20]; Shai et al.[37]; Shai et al.[38]; Shai et al.[39]; Shai et al.[40]; Doughari et al.[41]; Oyedemi et al.[42]; Wintola and Afolayan[43]; Wintola and Afolayan[44]; Jujol[45]; Hutchings et al.[46]; Notten[47]; Van Wyk and Gericke[48]; Bisi-Johnson et al.[49]; Nielsen et al.[50]; Otang et al.[51]; Afolayan and Wintola[52]; Fadipe et al.[53]; Olaokun et al.[54]; Van Wyk and Prinsloo[55]
Blood purification	Bark	Yembaturova et al.[4]; Lemmens[5]; Van Wyk et al.[6]; Grace et al.[20]; Shai et al.[37]; Shai et al.[38]; Shai et al.[39]; Shai et al.[40]; Doughari et al.[41]; Oyedemi et al.[42]; Wintola and Afolayan[43]; Wintola and Afolayan[44]; Jujol[45]; Hutchings et al.[46]; Notten[47]; Van Wyk and Gericke[48]; Nielsen et al.[50]; Otang et al.[51]; Afolayan and Wintola[52]; Fadipe et al.[53]; Van Wyk and Prinsloo[55]; Soyingbe et al.[56]
Cancer	Bark and leaves	Olaokun et al.[54]; Soyingbe et al.[56]; Koduru et al.[57]
Diabetes	Bark	Afolayan and Mbaebie[58]
Emetic	Bark	Cocks and Dold[35]
Hypertension	Bark	Afolayan and Mbaebie[58]; Olaokun et al.[54]
Malaria	Bark	Fadipe et al.[59]
Obesity	Bark	Oyedemi et al.[42]; Olaokun et al.[54]; Afolayan and Mbaebie[58]
Skin problems (acne, eczema, oesopharyngeal candidiasis, pimples and rash)	Bark	Lemmens[5]; Shai et al.[39]; Shai et al.[40]; Doughari et al.[41]; Wintola and Afolayan[44]; Otang et al.[51]; Afolayan and Wintola[52]; Grierson and Afolayan[60]; Sagbo and Mbeng[61]
Purgative	Bark	Wintola and Afolayan[44]; Fadipe et al.[53]; Fadipe et al.[62]
Sexually transmitted infections	Bark	Wintola and Afolayan[44]; Fadipe et al.[53]; Van Wyk and Prinsloo[55]; Soyingbe et al.[56]; Fadipe et al.[59]; Fadipe et al.[62]
Stomach problems (diarrhoea and dysentery)	Bark	Yembaturova et al.[4]; Lemmens[5]; Van Wyk et al.[6]; Grace et al.[20]; Shai et al.[37]; Shai et al.[38]; Shai et al.[39]; Shai et al.[40]; Doughari et al.[41]; Oyedemi et al.[42]; Wintola and Afolayan[43]; Wintola and Afolayan[44]; Jujol[45]; Hutchings et al.[46]; Notten[47]; Van Wyk and Gericke[48]; Bisi-Johnson et al.[49]; Nielsen et al.[50]; Otang et al.[51]; Afolayan and Wintola[52]; Fadipe et al.[53]; Olaokun et al.[54]; Van Wyk and Prinsloo[55]; Soyingbe et al.[56]; Afolayan and Mbaebie[58]; Fadipe et al.[59]; Fadipe et al.[62]; McGaw et al.[63]; Olajuyigbe and Afolayan[64]
Tuberculosis	Bark	Fadipe et al.[59]
Ethnoveterinary medicine (heartwater)	Bark mixed with that of *Rapanea melanophloeos* (L.) Mez	Dold and Cocks[34]; Cocks and Dold[35]; McGaw and Eloff[36]; Shai et al.[37]; Shai et al.[38]; Shai et al.[39]; Shai et al.[40]; Doughari et al.[41]; Oyedemi et al.[42]; Wintola and Afolayan[43]; Wintola and Afolayan[44]

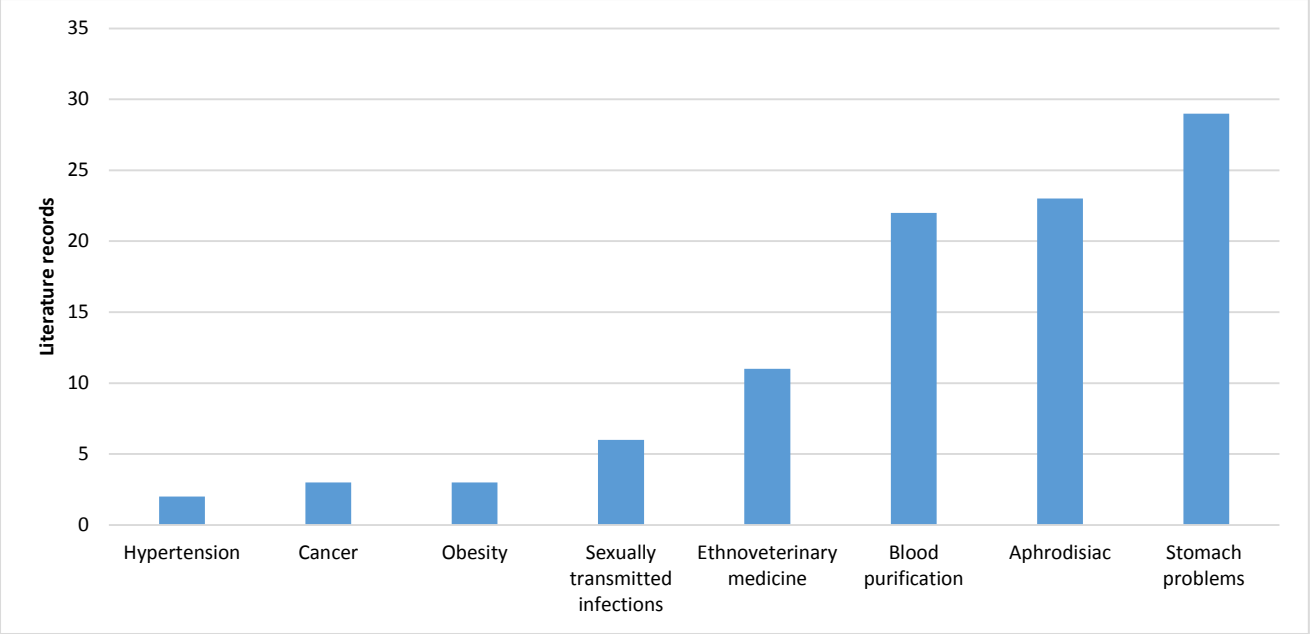

Figure 1. Medicinal applications of *Curtisia dentata* derived from literature records

Phytochemistry and biological activities of *Curtisia dentata*

Curtisia dentata contains several phytochemical compounds (Table 2) including β-sitosterol, 2α-hydroxyursolic acid, betulinic acid, betulinic acid acetate, linoleic acid, lupeol, ursolic acid and ursolic acid acetate.[37,40-43,53,54,59,62,65,66] Doughari et al.[41], Wintola and Afolayan[43] and Doughari et al.[67] identified alkaloids, amines, anthocyanins, anthraquinones, carboxyllic acids, essential oils, flavonoids, glycosides, phenols, quinones, saponins, steroids and tannins from the leaves, roots and stem bark of *C. dentata*. The following biological activities have been reported from the bark, leaf, root, stem, stem bark and twig extracts of *C. dentata* and compounds isolated from the species: anthelmintic,[40] antibacterial,[37-39,41-43,50,53,56,62,63,67] antimycobacterial,[59] antifungal,[37-39,50,53,62,66] anti-inflammatory,[54] antioxidant,[41-43,53,54,62] glucose utilization[54] and cytotoxicity[37,42,53,62,66] activities.

Table 2: Phytochemical composition of *Curtisia dentata*

Phytochemical	Value	Plant part	Reference
β-sitosterol	-	Leaves	Fadipe et al.[53]; Fadipe et al.[59]; Fadipe et al.[62]
2α-hydroxyursolic acid	-	Leaves	Shai et al.[37]
Alkaloids (mg/g)	<0.5	Stem bark	Wintola and Afolayan[43]
Betulinic acid	-	Leaves	Shai et al.[37]; Shai et al.[40]; Fadipe et al.[53]; Fadipe et al.[59]; Fadipe et al.[62]; McGaw et al.[66]
Betulinic acid acetate	-	Leaves	Fadipe et al.[59]
Flavonoids (mg/g)	4.2 - 12.5	Stem bark	Wintola and Afolayan[43]
Linoleic acid	-	Leaves	Breuer et al.[65]
Lupeol	-	Leaves	Shai et al.[37]; Shai et al.[40]; Fadipe et al.[53]; Fadipe et al.[59]; Fadipe et al.[62]; McGaw et al.[66]
Proanthocyanidin (mg/g)	0.2 – 1.6	Stem bark	Wintola and Afolayan[43]
Saponin (mg/g)	0.2 – 3.1	Stem bark	Wintola and Afolayan[43]
Steroids (%)	1.4	Stem bark	Oyedemi et al.[42]
Tannin (mg/g)	10.4 – 12.2	Stem bark	Wintola and Afolayan[43]
Total flavonoids (mg quercetin equivalent /g)	13.6 – 27.7	Leaves and stem bark	Oyedemi et al.[42]; Olaokun et al.[54]
Total phenolic content (mg GAE/g)	8.6 - 125.1	Leaves, roots and stem bark	Doughari et al.[41]; Oyedemi et al.[42]; Wintola and Afolayan[43]; Olaokun et al.[54]
Ursolic acid	-	Leaves	Shai et al.[37]; Shai et al.[40]; Fadipe et al.[53]; Fadipe et al.[59]; Fadipe et al.[62]
Ursolic acid acetate	-	Leaves	Fadipe et al.[59]

Anthelmintic activities

Shai et al.[40] evaluated the anthelmintic activities of the acetone and dichloromethane leaf extracts of *C. dentata* and the compounds betulinic acid, lupeol and ursolic acid isolated from the leaves of the species against *Caenorhabditis elegans*, *Haemonchus contortus* and *Trichostrongylus colubriformis*. The acetone and dichloromethane extracts were active against all nematodes at concentrations as low as 160 µg/ml. Betulinic acid and lupeol were active against the parasitic nematodes only at the high concentrations of 1000 µg/ml and 200 µg/ml, respectively. All compounds were effective against *Caenorhabditis elegans* with active concentrations as low as 8 µg/ml. The acetone and dichloromethane extracts were active against *Caenorhabditis elegans* with a concentration of 0.3 mg/ml resulting in almost 80% inhibition of larval motility.[40]

Antibacterial activities

McGaw et al.[63] evaluated the antibacterial activities of aqueous, ethanol and hexane bark extracts of *C. dentata* against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* using the disc-diffusion assay with neomycin (5 µg) as the positive control. Ethanol and water extracts were active against *Bacillus subtilis* with minimum inhibitory concentration (MIC) values of 0.8 mg/ml and 3.1 mg/ml, respectively.[63] Shai et al.[37] evaluated the antibacterial activities of the compounds lupeol, betulinic acid, ursolic acid and 2α-hydroxyursolic acid isolated from the leaves of *C. dentata* against *Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Escherichia coli* using the serial microplate method with gentamicin as a positive control. The compounds exhibited activities with MIC values ranging from 4.0 µg/ml to 250.0 µg/ml.[37] Shai et al.[38] evaluated the antibacterial activities of n-hexane, dichloromethane and acetone leaf extracts of *C. dentata* against *Staphylococcus aureus*, *Escherichia coli*, *Enterococcus faecalis* and *Pseudomonas aeruginosa* using the microplate dilution method with gentamicin as a positive control. The extracts exhibited activities with MIC values ranging from 0.05 mg/ml to 2.5 mg/ml and total activity ranging from 8.0 ml to 2600.0 ml.[38] Shai et al.[39] evaluated the antibacterial activities of acetone leaf, stem bark and twig extracts of *C. dentata* against *Staphylococcus aureus*, *Enterococcus faecalis*, *Pseudomonas aeruginosa* and *Escherichia coli* using the microplate dilution method. The extracts exhibited activities with MIC values ranging from 0.09 mg/ml to 0.6 mg/ml and total activity values ranging from 210.0 µg/l to 1311.0 µg/l.[39] Doughari et al.[41] and Doughari et al.[67] evaluated the antibacterial activities of the stem bark ethanol extracts of *C. dentata* against strains of *Acinetobacter haemolyticus*, *Acinetobacter lwoffii* and *Escherichia coli* using the broth dilution method. The extract exhibited activities with relative inhibition zone diameters ranging from 8% to 30% and MIC values ranging from 100.0 µg/ml to 2500.0 µg/ml.[41,67] Nielsen et al.[50] evaluated antibacterial activities of methanol leaf and stem extracts of *C. dentata* against *Citrobacter*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Mycobacteria smegmatis* using the micro-broth dilution method with gentamicin and ciprofloxacin as positive controls. The extracts exhibited weak activities with MIC values ranging from 78.1 µg/ml to 1250 µg/ml which were much higher than MIC values 0.3 µg/ml to 19.5 µg/ml exhibited by the controls.[50] Oyedemi et al.[42] evaluated the antibacterial activities of hydroalcoholic stem bark extract of *C. dentata* against *Bacillus cereus*, *Bacillus pumilus*, *Pseudomonas aeruginosa*, *Serratia mercescens*, *Acinectobacter calcaocenticus*, *Klebsiella pneumoniae*, *Proteus vulgaris*, *Enterobacter faecalis*, *Staphylococcus aureus* and *Escherichia coli* using agar dilution method with norfloxacin and streptomycin as positive controls. The extract exhibited activities against majority of the tested pathogens with the exception of *Bacillus pumilus*, *Acinectobacter calcaocenticus* and *Escherichia coli* with MIC values ranging from 19.5 mg/L to 512.0 mg/L.[42] Fadipe et al.[53] evaluated the antibacterial activities of ethanol, chloroform, ethyl acetate and acetone leaf extracts of *C. dentata* and the compounds β-sitosterol, betulinic acid, lupeol and ursolic acid isolated from the leaves of the species against E*scherichia coli*, *Pseudomonas aeruginosa*, *Mycobacterium smegmatis*, *Mycoplasma hominis*, *Moraxella catarrhalis*, *Proteus mirabilis* and *Staphylococcus aureus* using micro plate broth dilution assay with streptomycin sulphate as a positive control. The extracts and compounds exhibited activities with MIC values ranging from 0.01 mg/ml to >12.5 mg/ml and minimum bactericidal concentration (MBC) values ranging from 0.05 mg/ml to >12.5 mg/ml.[53] Fadipe et al.[62] evaluated the antibacterial activities of ethanol, chloroform, ethyl acetate and acetone leaf extracts of *C. dentata* and the compounds lupeol, betulinic acid and ursolic acid and β-sitosterol isolated from the species against *Escherichia coli*, *Pseudomonas aeruginosa*, *Mycobacterium smegmatis*, *Mycoplasma hominis*, *Moraxella catarrhalis*, *Proteus mirabilis* and *Staphylococcus aureus* using the micro dilution assay. The compounds lupeol, betulinic acid and ursolic acid and β-sitosterol exhibited moderate antibacterial activities with MIC values ranging from 0.2 mg/ml to 6.3 mg/ml. Furthermore, the ethanol extract and the four isolated compounds revealed MIC index of less than 4 suggesting that their effect is bactericidal. The ethanol extract also revealed the best total activity of 2400 ml/g against *Mycoplasma hominis* compared to other extracts.[62] Wintola and Afolayan[43] evaluated the antibacterial activities of aqueous, acetone and ethanol stem bark extracts of *C. dentata* against *Salmonella typhimurium*, *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus cereus*, *Shigella sonnei*, *Streptococcus pyogens*, *Bacillus subtilis*, *Shigella flexneri*, *Vibrio cholerae*, *Klebsiella pneumoniae* and *Staphylococcus aureus* using agar well diffusion and broth micro-dilution techniques with ciprofloxacin as a positive control. The extracts exhibited activities against tested pathogens with zone of inhibition ranging from 10 mm to 25 mm which were comparable to 20 mm to 25 mm

exhibited by the positive control. The MIC values exhibited by the extracts ranged from 0.01 mg/mL to >5.0 mg/mL.[43] Soyingbe et al.[56] evaluated antibacterial activities of acetone, ethyl acetate, methanol and water leaf extracts of *C. dentata* against *Enterococcus avium, Staphylococcus aureus, Streptococcus agalactiae, Bacillus cereus, Enterococcus hirae, Enterococcus faecalis, Enterococcus gallinarium, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Proteus vulgaris, Klebsiella pneumoniae, Acinetobacter calcoaceuticus anitratus* and *Salmonella typhi* using the agar well diffusion and micro plate dilution assays with ciprofloxacin as a positive control. Soyingbe et al.[56] also evaluated the MBC, lactate dehydrogenase (LDH) release and rhodamine 6G intake assays to ascertain the antibacterial activities of the extracts. The extracts exhibited activities with zone of inhibition ranging from 7 mm to 18 mm against 21 mm to 35 mm exhibited by the positive control. The MIC values ranged from 0.3 mg/ml to >10.0 mg/ml which were comparable to MIC values of 0.3 mg/ml to 5.0 mg/ml exhibited by the positive control. The MBC values exhibited by the extracts ranged from 2.5 mg/ml to >10.0 mg/ml which were higher than 0.2 mg/ml to 5.0 mg/ml exhibited by the positive control. The ethyl acetate extract revealed 53% inhibition of rhodamine 6G inside the cell against Escherichia coli in a cytosolic lactate dehydrogenase assay.[56]

Antimycobacterial activities

Fadipe et al.[59] evaluated antimycobacterial activities of acetone, chloroform, ethanol and methanol extracts of the leaves of *C. dentata* using and the compounds β-sitosterol, betulinic acid, ursolic acid, lupeol, betulinic acid acetate and ursolic acid acetate isolated from the species using the microplate alamar blue assay against *Mycobacterium tuberculosis* with bedaquiline (TMC207), isoniazid, rifampicin and streptomycin as positive controls. The methanol extract had the lowest MIC value of 22.2 µg/ml while ursolic acid acetate was the most active compound with MIC value of 3.4 µg/ml.[59]

Antifungal activities

McGaw et al.[66] evaluated antifungal activities of leaf extracts of *C. dentata* and the compounds betulinic acid and lupeol isolated from the species against *Candida albicans* and *Cryptococcus neoformans* using a broth microdilution assay. Betulinic acid presented higher activities against *Candida albicans* and *Cryptococcus neoformans* with MIC values of 16.0 µg/ml and 32.0 µg/ml compared to 250.0 µg/ml and 180.0 µg/ml lupeol, respectively.[66] Shai et al.[37] evaluated the antifungal activities of crude extracts of *C. dentata* and compounds lupeol, betulinic acid, ursolic acid and 2α-hydroxyursolic acid isolated from the leaves of the species against *Sporothrix schenckii, Microsporum canis, Aspergillus fumigatus, Candida albicans, Cryptococcus neoformans, Candida guilliermondi* and *Candida spicata* using the serial microplate method with amphotericin B as a positive control. The extracts and compounds exhibited activities with MIC values ranging from 8.0 µg/ml to 250.0 µg/ml.[37] Shai et al.[38] evaluated the antifungal activities of n-hexane, dichloromethane and acetone leaf extracts of *C. dentata* against *Aspergillus fumigatus, Micrococcus canis, Candida albicans, Sporothrix schenckii* and *Cryptococcus neoformans* using the microplate dilution method with amphotericin B as a positive control. The extracts exhibited activities with MIC values ranging from 0.02 mg/ml to 2.5 mg/ml and total activity ranging from 33.0 ml to 6500.0 ml.[38] Shai et al.[39] evaluated the antifungal activities of acetone leaf and stem bark extracts of *C. dentata* against *Candida albicans* using the microplate dilution method with amphotericin B as a positive control. The leaf and stem bark extracts exhibited activities with MIC values of 0.1 mg/ml and 0.6 mg/ml, respectively and total activity of 1072.0 µg/l and 190.0 µg/l, respectively.[39] Nielsen et al.[50] evaluated antifungal activities of methanol leaf and stem extracts of *C. dentata* against *Candida albicans* and *Microsporum audouinii* using the micro-broth dilution method with nystatin as a positive control. The extracts exhibited weak activities with MIC values ranging from 78.1 µg/ml to >2500 µg/ml which were much higher than MIC value of 19.5 µg/ml exhibited by the control.[50] Fadipe et al.[53] evaluated the antifungal activities of ethanol, chloroform, ethyl acetate and acetone leaf extracts of *C. dentata* and the compounds β-sitosterol, betulinic acid, lupeol and ursolic acid isolated from the leaves of the species against *Candida albicans* using micro plate broth dilution assay. The extracts and compounds exhibited activities with MIC values ranging from 0.008 mg/ml to 4.2 mg/ml and minimum fungicidal concentration (MFC) values ranging from 0.02 mg/ml to 3.8 mg/ml.[53] Fadipe et al.[62] evaluated the antifungal activities of ethanol, chloroform, ethyl acetate and acetone leaf extracts of *C. dentata* and the compounds lupeol, betulinic acid and ursolic acid and β-sitosterol isolated from the species against *Candida albicans* using the micro dilution assay. The acetone extract exhibited lowest MIC value of 0.01 mg/ml in comparison with other extracts. The compounds lupeol, betulinic acid, ursolic acid and β-sitosterol exhibited moderate activities with MIC values ranging from 0.20 mg/ml to 6.25 mg/ml.[62]

Anti-inflammatory activities

Olaokun et al.[54] evaluated the anti-inflammatory activities of acetone leaf extracts of *C. dentata* using the inhibition of 5-lipoxygenase assay with quercetin as a positive control. The extract exhibited activities with half maximal inhibitory concentration (IC_{50}) value of 95.4 µg/ml which was higher than IC_{50} value of 9.0 µg/ml exhibited by the positive control quercetin.[54]

Antioxidant activities

Doughari et al.[41] evaluated the antioxidant activities of acetone leaf, root and stem extracts of *C. dentata* using the 2,2'-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay and by determining the reducing power of the different extracts. The DPPH radical scavenging activities ranged from 14.7% to 62.4%, while reducing power activities ranged from 1.0% to 41.3%.[41] Oyedemi et al.[42] evaluated the antioxidant activities of hydroalcoholic

stem bark extract of *C. dentata* using ferric reducing power, DPPH, 2,2'-azino-bis-3-ethylbenzothiazoline-6-sulfonic-acid (ABTS), nitric oxide (NO), hydrogen peroxide (H2O2) and lipid peroxidation (LPO) assays with butylated hydroxytoluene (BHT), gallic acid and rutin as positive controls. The extract exhibited activities with IC_{50} values against DPPH of 0.02 mg/mL, ABTS (0.02 mg/mL), H_2O_2 (0.2 mg/mL), LPO (0.06 mg/mL), NO (0.05 mg/mL) and the reducing power of the extract was found to be concentration dependent.[42] Fadipe et al.[53] evaluated the antioxidant activities of acetone and ethyl acetate leaf extracts of *C. dentata* using the DPPH free radical scavenging assay with ascorbic acid as a positive control. The acetone extract exhibited better inhibition of DPPH than ethyl acetate extract, while ascorbic acid completely inhibited DPPH at lower concentrations.[53] Fadipe et al.[62] evaluated the antioxidant activities of ethyl acetate and acetone leaf extracts of *C. dentata* using the DPPH free radical scavenging assay. The acetone extract exhibited 53.6% inhibition against DPPH at a concentration of 1 mg/100 ml.[62] Olaokun et al.[54] evaluated the antioxidant activities of acetone leaf extracts of *C. dentata* using the DPPH free radical scavenging assay with ascorbic acid and trolox as positive controls. The extracts exhibited activities with IC_{50} value of 22.6 µg/ml which was higher than IC_{50} values of 0.2 µg/ml and 0.5 µg/ml exhibited by the positive controls ascorbic acid and trolox, respectively.[54] Wintola and Afolayan[43] evaluated the antioxidant activities of aqueous, acetone and ethanol stem bark extracts of *C. dentata* using ferric reducing power, DPPH, ABTS and nitric oxide (NO) with ascorbic acid, BHT and gallic acid as positive controls. The extracts exhibited activities with IC_{50} values against DPPH of 0.1 mg/mL, ABTS (0.2 mg/mL), NO (0.2 mg/mL to 0.3 mg/mL) and ferric reducing power with IC_{50} values of 0.3 mg/mL to 0.7 mg/mL.[43]

Glucose utilization activities

Olaokun et al.[54] evaluated the glucose utilization activities of acetone leaf extracts of *C. dentata* using the C2C12 muscle cells glucose utilization and 3T3-L1 adipocytes glucose utilization assays. The extract enhanced dose-dependent glucose utilization activity of muscle cells and adipocytes with glucose utilization of 3T3-L1 adipocytes at 63.7% at the highest concentration of 500 µg/ml.[54]

Cytotoxicity activities

McGaw et al.[66] evaluated cytotoxicity activities of leaf extracts of *C. dentata* and the compounds betulinic acid and lupeol isolated from the species against the Vero cells using a tetrazolium-based colorimetric assay (MTT). The compounds were relatively cytotoxic with selectivity index values less than 1.[66] Shai et al.[37] evaluated the cytotoxicity activities of crude extracts of *C. dentata* and compounds lupeol and betulinic acid isolated from the leaves of the species against Monkey kidney (Vero) cells using a MTT assay. The crude extracts and compounds exhibited activities with median lethal concentration (LC_{50}) values ranging from 10.9 µg/ml to 89.5 µg/ml and selectivity index ranging from 0.1 to 7.4.[37] Oyedemi et al.[42] evaluated the cytotoxicity activities of hydroalcoholic stem bark extract of *C. dentata* using a brine shrimp (*Artemia salina*) lethality bioassay with cyclophosphamide and vincristine sulfate as positive controls. The extract had no toxic effects against brine shrimp with LC_{50} values of 0.3 mg/mL compared to the standard cyclophosphamide and vincristine sulfate which exhibited LC_{50} values of 16.3 and 0.52 µg/mL, respectively.[42] Fadipe et al.[53] evaluated the cytotoxicity activities of the compounds β-sitosterol, betulinic acid, lupeol and ursolic acid isolated from the leaves of *C. dentata* against the human embryonic kidney (HEK293) and human hepatocellular carcinoma (HepG2) cells using the MTT assay. Ursolic acid exhibited the lowest median lethal dose (LD_{50}) value of 122.4 µg/ml against HEK293 cell line while lupeol exhibited LD_{50} values of 278.8 and 289.4 µg/ml against HEK293 and HepG2, respectively.[53] Fadipe et al.[62] evaluated the cytotoxicity activities of the compounds lupeol, betulinic acid, ursolic acid and β-sitosterol isolated from the leaves of *C. dentata* against the human embryonic kidney (HEK293) and human hepatocellular carcinoma (HepG2) cell lines using the MTT assay. Ursolic acid exhibited the lowest LD_{50} value of 122.4 µg/ml against HEK293 cell line, while lupeol exhibited LD_{50} value of 278.8 and 289.4 µg/ ml against HEK293 and HepG2, respectively.[62] Soyingbe et al.[56] evaluated cytotoxicity activities of acetone, ethyl acetate, methanol and water leaf extracts of *C. dentata* using MTT cell proliferation assay against MCF-7, human colorectal carcinoma cells (Caco-2), A549 and HeLa cancerous cell lines with doxorubicin hydrochloride as a positive control. The extracts exhibited IC_{50} values ranging from 41.6 µg/ml to >100.0 µg/ml which were higher than IC_{50} values of 1.3 µg/ml to 2.8 µg/ml exhibited by the positive control.[56]

CONCLUSION

The present review summarizes the botany, medicinal uses, phytochemistry and biological activities of *C. dentata*. But there is not yet enough data on ethnopharmacological evaluation and clinical research on the species and no evaluations of target-organ toxicity have been documented. Since *C. dentata* contain potentially toxic compounds, future studies should include the identification of toxic compounds, possible side effects caused by taking *C. dentata* as herbal medicine, and mechanisms of how potential toxic components of the species can be managed. Detailed studies on the pharmacokinetics, in vivo and clinical research involving both extracts and compounds isolated from the species are required.

Conflict of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

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