

A REVIEW OF BOTANY, THERAPEUTIC VALUE, PHYTOCHEMISTRY, AND PHARMACOLOGY OF *CUSSONIA PANICULATA*

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ABSTRACT

Cussonia paniculata is a small tree widely used as herbal medicine throughout its distributional range in southern Africa. This study is aimed at providing a critical review of the botany, biological activities, phytochemistry, and medicinal uses of *C. paniculata*. Documented information on the botany, biological activities, medicinal uses, and phytochemistry of *C. paniculata* 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. paniculata* was gathered from pre-electronic sources such as book chapters, books, journal articles, and scientific publications sourced from the University library. This study showed that the bark, fruits, leaves, roots, and stems of *C. paniculata* are used as emetic, immune booster, and herbal medicine for dysmenorrhea, intestinal parasites and worms, mental problems, boils, shingles and skin diseases, indigestion and stomach complaints, sores, and wounds. Phytochemical compounds identified from the leaves of *C. paniculata* include acetylated triterpene glycosides, unacetylated triterpene glycosides, flavonoid, steroidal saponin, and triterpenoid saponins. Pharmacological research revealed that *C. paniculata* extracts have analgesic, antibacterial, anticancer, anti-inflammatory, antiplasmodial, antiprotozoan, A β 42 protein reduction, and cytotoxicity activities. Future research should focus on evaluating the phytochemical, pharmacological, and toxicological properties of *C. paniculata* crude extracts as well as compounds isolated from the species.

Keywords: *Araliaceae*, *Cussonia paniculata*, Ethnopharmacology, Herbal medicine, Indigenous pharmacopeia.

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INTRODUCTION

Cussonia paniculata Eckl. and Zeyh. is a member of the *Araliaceae* or ginseng or ivy family. Ginseng is a common name for several herbaceous plants used in traditional medicines such as Asian ginseng (*Panax ginseng* C.A. Meyer) [1-6], American ginseng (*Panax quinquefolius* L.) [4,7-14], and Japanese ginseng (*Panax japonicus* (T.Nees) C.A. Meyer) [4,15-21]. Ivy is a common name for *Hedera* L. species grown as ornamental plants and house plants throughout the world [22-24]. Several *Hedera* species are used as herbal medicines for respiratory, skin problems, and other health-related conditions [25-32]. *Hedera* species are also characterized by several phytochemical and biological activities which include antimicrobial, anti-inflammatory, antiarthritic, antioxidant, antispasmodic, anti-allergic, and antitumor activities [29,33-39]. The genus *Cussonia* Thunb. comprises about 22 species which are mainly trees or shrubs or occasionally subshrubs recorded in grasslands, woodlands, and forests of sub-Saharan Africa, the Arabian Peninsula (Yemen), and the Comoro Islands [40-46]. *C. paniculata* is widely used as a decorative and ornamental plant, as the species is frost-resistant and therefore recommended for rockeries, bonsai, and other gardens [42,47-55]. *C. paniculata* is domesticated in home gardens in South Africa [56], and the thick tuberous roots are peeled and eaten raw as an emergency food, as a source of water or snack in South Africa and Swaziland [57-59]. In South Africa, research by Makunga *et al.* [60] showed that the flowers, leaves, and roots of *C. paniculata* are used in the production of essence and tinctures. Local communities in the Eastern Cape province in South Africa described *C. paniculata* as "rare" in the Eastern thorn bushveld [61], an observation which has important implications for conservation and sustainable use of the species. It is against this background that this study was undertaken aimed at appraising the botany, medicinal uses, phytochemistry, and biological activities of *C. paniculata*.

TAXONOMY AND BOTANICAL DESCRIPTION OF *C. PANICULATA*

The genus name *Cussonia* is in honor of Pierre Cusson (1727–1783), a French botany professor at the University of Montpellier who specialized

in the plant group Umbrelliferae [50,62,63]. The specific name "*paniculata*" refers to the paniculate or branched inflorescence which terminates the growth of the species' branches. The English common name of *C. paniculata* is "mountain cabbage tree," mainly because the species is associated with dry stony hills and the thick, often blue-green leaves resemble those of a cabbage (*Brassica oleracea* L.) [49]. The leaves of *C. paniculata* are gray-green or blue-green in color which is probably due to the thick waxy layers on the leaves. These waxy layers are believed to protect the leaves from severe frost in winter [49]. Two subspecies of *C. paniculata* are recognized subsp. *paniculata* and subsp. *sinuata* (Reyneke and Kok) De Winter [64]. The subsp. *paniculata* is characterized by entire leaflet margins, confined to the southern Karoo, Eastern Cape, KwaZulu-Natal, Northern Cape, and Western Cape provinces of South Africa at an altitude ranging from 300 m to 2000 m above the sea level [41,64]. The subsp. *sinuata* is characterized by shallowly to deep lobed and waxy (sinuate) leaflet margins and widely distributed and recorded in Botswana, Lesotho, Swaziland, the Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, and North West provinces of South Africa at an altitude ranging from 900 m to 1980 m above the sea level [41,64]. However, most ethnobotanical and ethnopharmacological literature do not separate *C. paniculata* into specific subspecies but rather to *C. paniculata sensu lato*, and this is the approach that has been adopted in this study. Synonyms associated with *C. paniculata* include *C. paniculata* Eckl. and Zeyh. var. *paniculata* and *C. paniculata* Eckl. and Zeyh. var. *sinuata* Reyneke and Kok. [64].

C. paniculata is an evergreen small tree with a sturdy trunk which is sparsely branched, rarely exceeding 5 m in height [41,63,65-68]. The stem is reddish gray to gray, rough, corky, swollen at the base and roughly 3.5 cm in diameter, the branches marked with prominent leaf scars as the species usually sheds old leaves while new flush of leaves are being produced. The branches have a mop-like crown of leathery, green, frequently blue-green leaves, composed of several leaflets on short stalks springing from the same point at the end of a stout common stalk. The leaves are bi-digitate, oblong in shape, apex and base tapering, margin

sparingly to distinctly toothed. The flowers are a branched panicle of spikes which are greenish yellow in color. The fruits are fleshy, almost globose in shape, pale purplish in color, and closely clustered along the spikes. *C. paniculata* has been recorded in Botswana, Lesotho, South Africa, and Swaziland [41,63,66-68] in bushveld, wooded grassland, usually in rocky places at an altitude ranging from 300 m to 2000 m above the sea level [64].

MEDICINAL USES OF *C. PANICULATA*

The bark, fruits, leaves, roots, and stems of *C. paniculata* are used as herbal medicines against 32 human diseases in southern Africa (Table 1). *C. paniculata* is mainly used as emetic, immune booster, and herbal medicine for dysmenorrhea, intestinal parasites and worms, mental problems, boils, shingles and skin diseases, indigestion and stomach complaints, sores, and wounds (Fig. 1). In Lesotho, the leaves of *C. paniculata* are mixed with those of *Searsia divaricata* (Eckl. and Zeyh.) Moffett and *Scabiosa columbaria* L. as herbal medicine for menstrual problems [69].

PHYTOCHEMISTRY OF *C. PANICULATA*

Several researchers such as Dovgii *et al.* [93], Grishkovets *et al.* [94], Adedapo *et al.* [95], and Thakur *et al.* [76] identified acetylated triterpene glycosides, unacetylated triterpene glycosides, flavonoid, steroidal saponin, and triterpenoid saponins from the leaves of *C. paniculata* (Table 2). Some of these phytochemical compounds may be responsible for the pharmacological properties associated with *C. paniculata*. For example, research by Panche *et al.* [96] revealed that flavonoids are associated with acetylcholinesterase, antioxidant, steroid-genesis modulating, xanthine oxidase modulating, countering antibiotic resistance, and disease-combating activities. Research by Careaga *et al.* [97] and Bahrami and Franco [98] showed that acetylated triterpene glycosides have induction of caspase, antiproliferative, apoptosis, hemolytic, cytotoxicity, anticancer, antifungal, and antibacterial properties. While saponins have demonstrated anti-viral, anti-inflammatory, hepatoprotective, anti-ulcer, antibacterial, hypoglycemic, anti-fertility, anticancer, antimalarial, anthelmintic, and antioxidant activities [99-103].

BIOLOGICAL ACTIVITIES OF *C. PANICULATA* EXTRACTS

Biological activities of *C. paniculata* extracts include analgesic [95], antibacterial [104], anticancer [105,106], anti-inflammatory [52,75,95], antiplasmodial [52,75,104], antiprotozoan [104], A β 42 protein reduction [76], and cytotoxicity [104] activities.

Analgesic activities

Adedapo *et al.* [95] evaluated the analgesic activities of aqueous extract of the stem bark of *C. paniculata* using the formalin test by treating male Wistar rats with 50 mg/kg, 100 mg/kg, and 200 mg/kg of extract; 10 mg/kg of indomethacin; and 2 ml/kg of normal saline, and the licking time and frequency of the injected paw were recorded for 30 min. In the acetic acid-induced writhing model, the extract showed a good analgesic effect characterized by reduction in the number of writhes when compared to the control. The extract caused dose-dependent decrease of licking time and licking frequency in rats injected with 2.5% formalin, signifying its analgesic effect [95].

Antibacterial activities

De Villiers *et al.* [104] evaluated antibacterial activities of aqueous and methanol leaf extracts of *C. paniculata* subsp. *paniculata* and *C. paniculata* subsp. *sinuata* against *Enterococcus faecalis*, *Escherichia coli*, *Neisseria gonorrhoeae*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa* using the microplate bioassay with ciprofloxacin (0.01 mg/mL) as a positive control. The extract exhibited activities with minimum inhibitory concentration values ranging from 0.3 mg/mL to 16.0 mg/mL [104].

Anticancer activities

Fouché *et al.* [105] evaluated anticancer activities of dichloromethane leaf extracts of *C. paniculata* against sixty human cancer cell lines organized into subpanels representing leukemia, melanoma, and cancer of the lung, colon, kidney, ovary, and central nervous system. The extracts exhibited a moderate growth inhibition of above 50% for two or more of the cell lines (GI₅₀) with values ranging from >0 μ g/mL to 1.1 μ g/mL [105]. Similarly, Fouché *et al.* [106] evaluated anticancer

Table 1: Medicinal uses of *Cussonia paniculata*

Medicinal use	Plant part used	Country	References
Anemia	Bark	Lesotho	[70]
Bladder problems	Bark	Lesotho	[71-74]
Breast and cervical cancer	Leaves	Lesotho	[69,74]
Cardiovascular problems	Bark	Lesotho	[70]
Cleanses blood	Bark	Lesotho	[70]
Colic	Bark	South Africa	[52,75,76]
Dysmenorrhea	Bark	South Africa	[52,75,76]
Menstrual problems	Leaves mixed with those of <i>Searsia divaricata</i> (Eckl. and Zeyh.) Moffett and <i>Scabiosa columbaria</i> L.	Lesotho	[69]
Emetic	Bark and leaves	Lesotho and Swaziland	[57,71-74]
Heartburn	Bark	Lesotho	[70-73,77]
Human immunodeficiency virus opportunistic infections	Bark and leaves	South Africa	[78-80]
Immune booster	Bark, leaves, and roots	Lesotho and South Africa	[77-81]
Intestinal ulcers	Leaves	Lesotho	[71-74,77]
Intestinal parasites and worms	Bark, fruits, roots, and stems	Lesotho and South Africa	[70,82,83]
Kidney problems		Lesotho	[71-74]
Loss of appetite	Roots	Lesotho	[77]
Malaria	Roots	South Africa	[78,79,84-86]
Mental problems	Leaves	South Africa and Swaziland	[52,57,58,75,82,87,88]
Nervous problems	Leaves	South Africa	[52,75,76,82,87,89]
Phlegm	Bark	Lesotho	[70]
Pellagra	Bark	Lesotho	[70]
Purgative	Leaves	South Africa	[78,79]
Rheumatism and swollen limbs	Leaves	South Africa	[75,76,90]
Boils, shingles, and skin diseases	Bark and leaves	Lesotho and South Africa	[71-74,78-81]
Indigestion and stomach complaints	Leaves and roots	Lesotho and South Africa	[71-74,77-79,84,91]
Tonic	Bark and leaves	South Africa	[78-80]
Sores and wounds	Bark and leaves	Lesotho and South Africa	[70-74,82,90,92]

activities of dichloromethane: methanol (1:1) leaf extracts of *C. paniculata* against sixty human cancer cell lines organized into subpanels representing leukemia, melanoma and cancer of the lung, colon, kidney, ovary, and central nervous system. The extracts exhibited activities against leukemia RPMI-8226, colon HCT-116, and colon KM12 with total growth inhibition (TGI) values of 1.0 µg/ml, 1.5 µg/ml, and 2.7 µg/ml, respectively [106].

Anti-inflammatory activities

Tetyana [52] and Tetyana *et al.* [75] evaluated anti-inflammatory activities of bark, leaves, roots, and stems ethanolic, ethyl acetate and water extracts of *C. paniculata* using the cyclooxygenase-1 (COX-1) assay. The extracts inhibited COX in the COX-1 assay with 85.0%

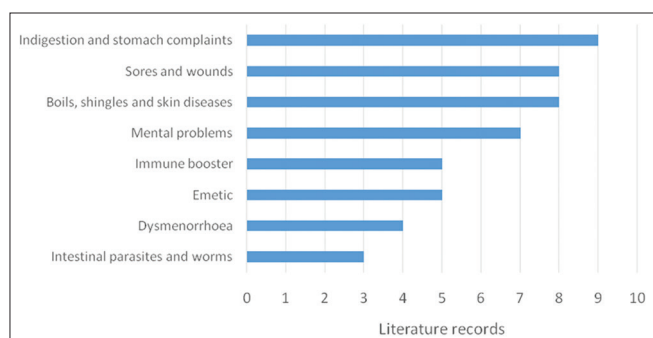


Fig. 1: Medicinal applications of *Cussonia paniculata* derived from literature records

being the highest inhibition [52,75]. Adedapo *et al.* [95] evaluated the anti-inflammatory activities of aqueous extract of the stem bark of *C. paniculata* using the carrageenan-induced rat paw edema and histamine-induced rat paw edema assays with indomethacin and cyproheptadine as positive controls. The extract at 50 mg/kg, 100 mg/kg, and 200 mg/kg body weight reduced significantly, the formation of edema induced by carrageenan and histamine [95].

Antiplasmodial activities

Tetyana [52] and Tetyana *et al.* [75] evaluated antiplasmodial activities of the bark ethanolic, ethyl acetate and water extracts of *C. paniculata* against *Plasmodium falciparum* in an *in vitro* assay, a slightly modified version of the parasite lactate dehydrogenase assay with chloroquine as a positive control. The extracts exhibited weak inhibitory activities ranging from 10% to 35% at a concentration of 200 mg/ml [52,75]. De Villiers *et al.* [104] evaluated antiplasmodial activities of aqueous and methanol leaf extracts of *C. paniculata* subsp. *paniculata* and *C. paniculata* subsp. *sinuata* using the (G-³H) hypoxanthine incorporation assay against the chloroquine-sensitive (3D7) strain of *P. falciparum* as the test organism. The extracts exhibited moderate antiplasmodial activities with half maximal inhibitory concentration (IC₅₀) value of >50.0 mg/mL [104].

Antiprotozoan activities

De Villiers *et al.* [104] evaluated antiprotozoan activities of aqueous and methanol leaf extracts of *C. paniculata* subsp. *paniculata* and *C. paniculata* subsp. *sinuata* against protozoan pathogen associated with urogenital or sexually transmitted infections, *Trichomonas vaginalis* using the microplate bioassay with ciprofloxacin

Table 2: Phytochemical compounds identified from *Cussonia paniculata* leaves

Phytochemical composition	References
Acetylated triterpene glycosides	
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of 23-hydroxybetulinic acid	[94]
28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of 23-hydroxybetulinic acid	[94]
28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	[94]
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	[94]
3-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	[94]
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	[94]
3-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of ursolic acid	[94]
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of ursolic acid	[94]
3-O-α-L-arabinopyranosyl-28-O-(4-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	[94]
2-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	[94]
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of hederagenin	[94]
3-O-β-D-glucopyranosyl-(1→2)-O-α-L-arabinopyranosyl-28-O-(2-O-acetyl-α-L-rhamnopyranosyl)-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	[94]
3-O-acetyl-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanic acid	[94]
Unacetylated triterpene glycosides	
28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranoside of 23-hydroxyursolic acid	[93]
3-O-β-D-glucopyranoside of β-sitosterol	[93]
3-O-α-L-arabinopyranosides of oleanolic acid	[93]
3-O-α-L-arabinopyranosides of ursolic acid	[93]
3-O-α-L-arabinopyranosides of hederagenin	[93]
3-O-β-D-glucopyranosyl-(1→2)-α-L-arabinopyranoside of oleanolic acid	[93]
3-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of oleanolic acid	[93]
3-O-α-L-arabinopyranosyl-28-O-α-L-rhamnopyranosyl-(1→4)-O-β-D-glucopyranosyl-(1→6)-O-β-D-glucopyranosides of ursolic acid	[93]
Flavonoid	
Rutin	[76]
Steroidal saponin	
Pseudoprostodioscin	[76]
Triterpenoid saponin	
Clethroidoside B	[76]
Spinasaponin A	[76]

(0.01 mg/mL) as a positive control. Only methanol extract exhibited activities with MIC value of 1.0 mg/mL and 1.3 mg/mL against *C. paniculata* subsp. *paniculata* and *C. paniculata* subsp. *sinuata* extracts, respectively, and these values were higher than 0.001 mg/mL exhibited by the control [104].

A β 42 protein reduction activities

Thakur *et al.* [76] evaluated the A β 42 protein reduction activities of dichloromethane: methanol (1:1) leaf and stem extracts of *C. paniculata* using ELISA – sAPP α , sAPP β , and A β peptide assays. The extract reduced the secreted level of A β 42 in a dose-dependent manner compared to the control by 57.5%. The extract also decreased the levels of A β 40, sAPP β -sw, and sAPP α in a dose-dependent manner [76].

Cytotoxicity activities

De Villiers *et al.* [104] evaluated cytotoxicity activities of aqueous and methanol leaf extracts of *C. paniculata* subsp. *paniculata* and *C. paniculata* subsp. *sinuata* against the human T-cell leukemia (Jurkat) cell line using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide calorimetric assay with (S)-(+)-camptothecin as a positive control. The extracts exhibited moderate cytotoxicity activities with IC₅₀ values ranging from 26.5 mg/mL to >50.0 mg/mL [104].

Toxicity activities

Adedapo *et al.* [95] evaluated acute toxicity activities of aqueous extract of the stem bark of *C. paniculata* by oral administration of graded doses of the extract of 200 mg/kg, 400 mg/kg, 800 mg/kg, 1600 mg/kg, and 3200 mg/kg body weight in Wistar male rats. All the rats were allowed free access to food and water and observed over a period of 48 h for signs of acute toxicity and deaths within this period. Acute toxicity test showed that the extract caused 80% mortality in rats, and hence, *C. paniculata* can be regarded as toxic [95].

CONCLUSION

The diverse medicinal uses of *C. paniculata* documented in southern Africa, and the scientific evidence of its phytochemistry and biological activities indicates its potential as herbal medicine. However, there is a need for detailed phytochemical and pharmacological studies aimed at correlating its documented ethnomedicinal uses with the phytochemical and pharmacological properties of the species. There is a need for clinical and toxicological evaluations since preliminary acute toxicity studies by Adebapo *et al.* [95] indicated that aqueous extract of the stem bark of *C. paniculata* contains potentially toxic compounds. Therefore, future research should focus on the identification of toxic compounds, the possible side effects caused by taking *C. paniculata* as herbal medicine, and mechanisms of how potential toxic components of the species can be managed when the species is used as herbal medicine.

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AUTHORS' CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICTS OF INTEREST

The author declares that he has no conflict of interest.

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