

## CUSSONIA SPICATA THUNB. IN TROPICAL AFRICA: PHYTOCHEMISTRY, PHARMACOLOGY, AND MEDICINAL POTENTIAL

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**ABSTRACT**

*Cussonia spicata* is an evergreen tree widely used as herbal medicine throughout its distributional range in tropical Africa. The current study is aimed at providing a critical review of the phytochemistry, pharmacology, and evaluation of the medicinal potential of *C. spicata*. Documented information on the phytochemistry, pharmacology, and medicinal applications of *C. spicata* 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 phytochemistry, pharmacology, and medicinal applications of *C. spicata* 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, flowers, flower stalks, fruits, leaves, roots, root bark, and stems of *C. spicata* are used as antifebrile and emetic and herbal medicine for fever, nausea, vomiting, gonorrhoea, venereal diseases, malaria, and mental illness. Phytochemical compounds identified from the leaves, root bark, stems, and stem bark of *C. spicata* include alkaloids, anthocyanins, anthracene glycosides, botulin, condensed tannins, free gallic acid, gallotannins, iridoids, pentacyclic triterpenoids, saponins, steroids, tannins, flavonoids, phenolics, triterpenoids, and volatile oils. Pharmacological research revealed that *C. spicata* crude extracts and compounds have acetylcholinesterase, antibacterial, antiviral, anti-inflammatory, antileishmanial, antiplasmodial, antiprotozoan, antioxidant, larvicidal, molluscicidal, spermicidal, and cytotoxicity activities. Future research should focus on evaluating the phytochemical, pharmacological, and toxicological properties of *C. spicata* crude extracts as well as compounds isolated from the species.

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

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**INTRODUCTION**

*Cussonia spicata* Thunb. is a member of the Araliaceae or ginseng family. Ginseng is a common name for species such as *Panax bipinnatifidus* Seem., *P. ginseng* C.A. Meyer, *P. japonicus* (T. Nees) C.A. Meyer, *P. notoginseng* (Burkill) F. H. Chen, *P. quinquefolius* L., *P. stiphuleanatus* H.T. Tsai and K. M. Feng, and *P. vietnamensis* Ha and Grushv. that are widely used as herbal medicines throughout the world [1-17]. These species are associated with several pharmacological properties which include anti-aging, antiapoptotic, anticancer, antidiabetic, anti-inflammatory, antiobesity, antioxidant, antiviral, immunomodulatory, immunostimulant, and neuroprotective [2,6,11,13,18,19]. 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 [20-26]. *Cussonia spicata* is widely used as herbal medicine in tropical Africa [27-31]. *Cussonia spicata* is also domesticated in home gardens in South Africa and Tanzania as a medicinal plant, shade, ornamental, and used for boundary and grave marking [32-35]. The thick tuberous roots of *C. spicata* are peeled and eaten raw as emergency food, as a source of water and snack in South Africa, Swaziland, and Tanzania [34,36-41]. The bark, leaves, roots, and stems of *C. spicata* are sold as herbal medicines in the informal herbal medicine markets in Kenya and South Africa in the Eastern Cape, Gauteng and Western Cape Provinces [42-44]. Therefore, *C. spicata* is an important medicinal plant widely used in the region. It is against this background that this study was undertaken aimed at providing a critical review of the phytochemistry, pharmacology, and evaluation of the medicinal potential of *C. spicata*.

**BOTANICAL DESCRIPTION OF CUSSONIA SPICATA**

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

in the plant group Umbrelliferae [45,46]. The specific name "*spicata*" is derived from the Latin word "*spica*" in reference to the species' erect and "spike-like" floral arrangement [46,47]. The English common name of *C. spicata* is "cabbage tree" or "common cabbage tree," mainly because the thick, often blue-green leaves resemble those of cabbage (*Brassica oleracea* L.) [32]. Synonyms associated with the name *C. spicata* include *C. boivinii* Drake, *C. calophylla* Miq., *C. kraussii* Hochst., *C. quercifolia* Colla, and *C. triptera* Colla [48-52]. *C. spicata* is an evergreen tree which grows up to 17 m in height [37,51,53]. The roots of the species may be large, swollen, and succulent. The trunk of *C. spicata* is unbranched, light brown in color, with a corky, grooved, rough, thick bark, marked with leaf scars, up to 46 cm or more in diameter [32]. The leaves are evergreen or deciduous, crowded together at the ends of the trunk or branches, green, blue-green or gray-green in color. The leaves are large, divided into lance-shaped leaflets, which taper to the pointed tips and which radiate from the swollen ends of the long sturdy leaf stalks [32]. The leaflets are usually deeply lobed, have toothed or untoothed margins and a prominent midrib. The flowers are small, stalkless, greenish in color with a pronounced calyx. The flowers are borne on densely packed, erect, candle-like spikes on long stalks. The fruits are small fleshy berries, round to almost angular in shape, pale green to brown-black at maturity and closely packed along with the spikes. *C. spicata* has been recorded in Botswana, Comoros, the Democratic Republic of Congo, Kenya, Malawi, Mozambique, South Africa, South Sudan, Sudan, Swaziland, Tanzania, Uganda, and Zambia and Zimbabwe [32,47,49-54]. The species has been recorded in the upland rainforest, upland dry evergreen forest, forest margins, wooded grassland, montane grassland, Bushveld, on rocky, stony and wooded hillsides and mountains at an altitude ranging from 5 m to 2600 m above the sea level [32,37,51,53].

**MEDICINAL USES OF CUSSONIA SPICATA**

The bark, flowers, flower stalks, fruits, leaves, roots, root bark, roots, and stems of *C. spicata* are used as herbal medicines against 43 human

diseases and also as ethnoveterinary medicine (Table 1). Medicinal applications of *C. spicata* recorded in at least three countries include antifebrile, fever, emetic, nausea, vomiting, gonorrhoea, venereal diseases, malaria, and mental illness (Fig. 1). Other major applications of the species recorded in at least two countries include abdominal pain, amenorrhoea, dysmenorrhoea, biliousness, constipation, indigestion, stomach complaints, convulsions, epilepsy, measles, pimples, shingles, skin irritation, muscular spasm, camps, painful legs, and uterine pain (Table 1).

#### PHYTOCHEMISTRY OF *CUSSONIA SPICATA*

Several compounds which include alkaloids, anthocyanins, anthracene glycosides, botulin, condensed tannins, free gallic acid, gallotannins, iridoids, pentacyclic triterpenoids, saponins, steroids, tannins, total

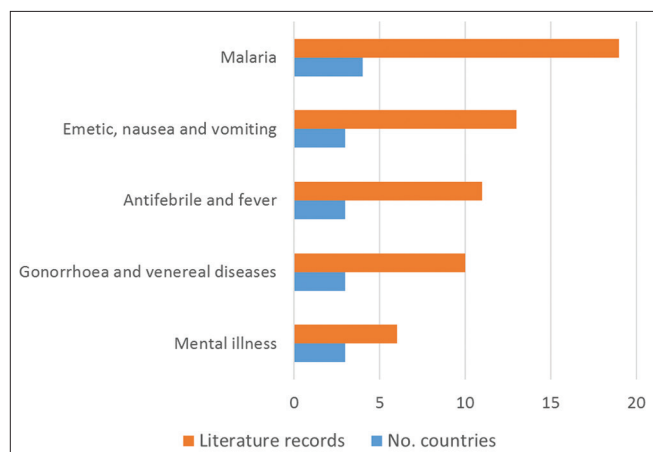
flavonoids, total phenolics, triterpenoids, and volatile oils (Table 2) have been identified from the leaves, root bark, stems, and stem bark of *C. spicata* [28,60,99,100]. Some of the pharmacological activities associated with the species which include antioxidant activities can be attributed to flavonoids and phenolics which have been identified from the leaves of the species [98].

#### BIOLOGICAL ACTIVITIES OF *CUSSONIA SPICATA*

Biological activities of *C. spicata* extracts and compounds isolated from the species include acetylcholinesterase [100], antibacterial [57,58,77,101,102], antiviral [101,103], anti-inflammatory [57,58], antileishmanial [104], antiplasmodial [57,58,63,64,102,105-107], antiprotozoan [102], antioxidant [100], larvicidal [108,109], molluscicidal [60,110,111], spermicidal [112], and cytotoxicity [63,64,102-104] activities.

Table 1: Medicinal uses of *Cussonia spicata*

| Medicinal use   | Parts used   | Country   | References  |
|---|--|---|---|
| Abdominal pain  | Bark and roots   | Kenya and South Africa                          | [55,56]   |
| Amenorrhoea and dysmenorrhoea                           | Roots and stems  | South Africa and Zimbabwe                       | [30,57,58]  |
| Antifebrile and fever                                   | Leaves, root bark, and roots   | Kenya, South Africa, and Tanzania               | [27-29,31,55,59-64]                               |
| Anthelmintic  | Leaves   | Tanzania  | [65]  |
| Appetite  | Roots  | South Africa                                    | [66]  |
| Biliousness   | Flowers, flower stalks, and roots  | South Africa and Tanzania                       | [28,29,32,58,67]                                  |
| Constipation, indigestion, and stomach complaints       | Flowers, fruits, leaves, roots, and stems  | South Africa and Tanzania                       | [28,29,31,34,37,58,61,68-72]                      |
| Convulsions and epilepsy                                | Leaves   | Tanzania and Zimbabwe                           | [30,72,74]  |
| Diabetes mellitus                                       | Roots  | South Africa                                    | [75]  |
| Diuretic  | Roots  | South Africa                                    | [31,61,76]  |
| Emetic, nausea and vomiting                             | Fruits, roots, and stems   | South Africa, Swaziland, and Tanzania           | [27-29,31,38,55,58,59,61,63-65,77]                |
| Gonorrhoea and venereal diseases                        | Bark, flowers, fruits, roots, and stems  | Lesotho, South Africa, and Tanzania             | [27-29,31,32,37,55,58,61,68,70]                   |
| Headache  | Roots  | Tanzania  | [78]  |
| Heart problems  |  | Zimbabwe  | [30]  |
| Human immunodeficiency virus (HIV)                      | Flowers, fruits, roots, and stems  | South Africa                                    | [68,70]   |
| Immune booster  | Flowers, fruits, leaves, roots, and stems  | South Africa                                    | [68,70-72]  |
| Inflammation  | Root   | South Africa                                    | [67]  |
| Laxative and purgative                                  | Flowers, fruits, roots, and stems  | South Africa                                    | [31,61,68,70,76]                                  |
| Magical purposes  | Bark   | South Africa                                    | [31,79,80]  |
| Malaria   | Bark, flowers, fruits, roots, and stems  | South Africa, Tanzania, Swaziland, and Zimbabwe | [27-29,31,32,34,37,38,57,58,60,61,68,70,79,81-84] |
| Measles, pimples, shingles, and skin irritation         | Flowers, fruits, leaves, roots, and stems  | South Africa and Tanzania                       | [27-29,31,60,65,68,70,71]                         |
| Mental illness  | Bark and root bark   | South Africa, Tanzania, and Zimbabwe            | [28,29,30,31,80,85]                               |
| Muscular spasm, camps, and painful legs                 | Bark   | South Africa and Zimbabwe                       | [30,58,81,84,86]                                  |
| Snakebite   | Leaves   | Tanzania  | [34]  |
| Spinal cord problems                                    | Leaves   | Kenya   | [62]  |
| Stomach ulcers  | Bark   | South Africa                                    | [31,58,61,79]                                     |
| Teething  | Leaves   | Kenya   | [62]  |
| Tonic   | Flowers, fruits, roots, and stems  | South Africa                                    | [67,68,70,71]                                     |
| Tuberculosis  | Roots  | Tanzania  | [65]  |
| Uterine pain  | Roots  | South Africa and Zimbabwe                       | [30,31,55,61]                                     |
| Wounds  | Bark, leaves, and roots  | South Africa                                    | [87]  |
| Ethnoveterinary medicine                                |  |   |   |
| Anthelmintics   | Bark   | South Africa                                    | [88-90]   |
| Bloody urine after calving, endometriosis and vaginitis | Leaves mixed with those of <i>Olea europaea</i> L. subsp. <i>africana</i> (Mill.) P.S. Green | South Africa                                    | [91,92]   |
| Gallsickness  | Bark and leaves  | South Africa                                    | [91,92-95]  |
| Heartwater  | Bark   | South Africa                                    | [96,97]   |
| Paralyzed goats   | Leaves   | South Africa                                    | [31,32,92]  |
| Redwater  | Bark and leaves  | South Africa                                    | [95,96]   |
| Retained placenta                                       | Bark   | South Africa                                    | [91,92,98]  |



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

**Acetylcholinesterase inhibitory**

Amoo *et al.* [100] evaluated acetylcholinesterase inhibitory properties of aqueous leaf extract of *C. spicata* using colorimetric assay with galanthamine at 20 µM as a positive control. Acetylcholinesterase inhibition (%) at 1.0 mg/ml was 72.1%–86.5%. These results suggest that *C. spicata* extracts deserve further investigation as they may provide secondary metabolites which can act as natural acetylcholinesterase inhibitors required for the treatment of neurodegenerative disorders.

**Antibacterial activities**

McGaw *et al.* [77] evaluated the antibacterial activities of aqueous, ethanol, and hexane leaf extracts of *C. spicata* 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 all tested pathogens with minimum inhibitory concentration (MIC) values ranging from 3.1 mg/ml to 12.5 mg/ml [77]. Tetyana [57] and Tetyana *et al.* [58] evaluated antibacterial activities of bark and root ethanolic, ethyl acetate and water extracts of *C. spicata* against *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Micrococcus luteus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Staphylococcus epidermidis* using disc diffusion assay with neomycin as a positive control. The extracts exhibited activities against all tested pathogens with the ratio of the inhibition zone (mm) produced around the extract to the inhibition zone around the control ranging from 0.02 to 0.5 [57,58]. McGaw *et al.* [101] evaluated the antibacterial activities of aqueous, methanol, and hexane root extracts of *C. spicata* against *Enterococcus faecalis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus* using the serial microplate dilution method with neomycin as the positive control. The extracts exhibited activities with MIC values ranging from 6.3 mg/ml to >12.5 mg/ml [101]. Similarly, De Villiers *et al.* [102] evaluated antibacterial activities of aqueous and methanol leaf extracts of *C. spicata* 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 values ranging from 0.3 mg/mL to 16.0 mg/mL [102].

**Antiviral activities**

McGaw *et al.* [101,103] evaluated antiviral activities of acetone extracts of the leaves of *C. spicata* using antiviral assay against the sensitive feline herpesvirus type 1. The extract exhibited activities causing a 2 log reduction in viral growth of 12.5% [101,103].

**Anti-inflammatory activities**

Tetyana [57] and Tetyana *et al.* [58] evaluated anti-inflammatory activities of bark, leaves, roots, and stems ethanolic, ethyl acetate and water extracts of *C. spicata* using the cyclooxygenase (COX-1) assay. The

**Table 2: Phytochemical composition of *Cussonia spicata***

| Phytochemical composition   | Values      | Plant parts      | References |
|---|-------------|------------------|------------|
| Alkaloids   | -           | Root bark        | [28]       |
| Anthocyanins  | -           | Root bark        | [28]       |
| Anthracene glycosides   | -           | Root bark        | [28]       |
| Botulin   | -           | Leaves and stems | [99]       |
| Condensed tannins (% in dry matter)   | 0.01        | Leaves           | [100]      |
| Free gallic acid (µg gallic acid equivalents/g dry weight)  | 12.8–138.2  | Leaves           | [100]      |
| Gallotannins (µg gallic acid equivalents/g dry weight)  | 397.4–468.8 | Leaves           | [100]      |
| Iridoids (µg harpagoside equivalents/g dry weight)  | 38.8–82.8   | Leaves           | [100]      |
| Pentacyclic triterpenoids   | -           | Leaves and stems | [99]       |
| α-amyrin  | -           | Leaves and stems | [99]       |
| β-amyrin  | -           | Leaves and stems | [99]       |
| Lupeol  | -           | Leaves and stems | [99]       |
| Saponins  | -           | Stem bark        | [60]       |
| [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid                             | -           | Stem bark        | [60]       |
| [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)]-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid | -           | Root bark        | [28]       |
| Steroids  | -           | Root bark        | [28]       |
| Tannins   | 3.4–9.1     | Leaves           | [100]      |
| Total flavonoids (mg catechin equivalents/g dry weight)   | 7.6–11.4    | Leaves           | [100]      |
| Total phenolics (mg gallic acid equivalents/g dry weight)   | -           | Root bark        | [28]       |
| Triterpenoids   | -           | Root bark        | [28]       |
| Volatile oils   | -           | Root bark        | [28]       |

extracts inhibited cyclooxygenase in the cyclooxygenase-1 assay, with 56.0% being the highest inhibition [57,58].

#### Antileishmanial activities

Bapela *et al.* [104] evaluated antileishmanial activities of dichloromethane and 50% methanol root bark extracts of *C. spicata* against *Leishmania donovani*. The dichloromethane extracts displayed inhibitory effects on the growth of amastigote forms of *Leishmania donovani* with half-maximal inhibitory concentration (IC<sub>50</sub>) values of 8.2 µg/mL [104]. Bapela *et al.* [63] demonstrated that most of the non-polar extracts of medicinal plants used in the treatment of malaria also possess significant antiplasmodial activities, and therefore, likely to have antileishmanicidal properties as both malaria and leishmaniasis are protozoal infections sharing several unique metabolic pathways. Therefore, findings of this research imply that *C. spicata* extracts may have potential as antileishmanial agents.

#### Antiplasmodial activities

Tetyana [57] and Tetyana *et al.* [58] evaluated antiplasmodial activities of bark ethanolic, ethyl acetate, and water extracts of *C. spicata* against *Plasmodium falciparum* in an *in vitro* assay, a slightly modified version of the parasite lactate dehydrogenase assay with chloroquine as a positive control. Weak inhibitory activities of 20% and 35% against water and ethanol extracts, respectively, at a concentration of 200 mg/ml were observed [57,58]. Kraft *et al.* [105] evaluated the *in vitro* antiplasmodial activities of petrol ether: ethylacetate (1:1) bark and leaf extracts of *C. spicata* using the [<sup>3</sup>H] hypoxanthine incorporation assay using the chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*. The leaf extract exhibited weak activities with IC<sub>50</sub> values of 45.1 µg/mL and 47.5 µg/ml against chloroquine-sensitive and chloroquine-resistant strains of *Plasmodium falciparum*, respectively [105]. Clarkson *et al.* [106] evaluated antiplasmodial activities of *C. spicata* aqueous, dichloromethane, dichloromethane-methanol (1:1) fruit, and leaf extracts against *Plasmodium falciparum* using the parasite lactate dehydrogenase assay. Both the fruit and leaf dichloromethane-methanol (1:1) extracts showed weak activities with IC<sub>50</sub> values of 14 µg/mL and 13 µg/mL, respectively [106]. De Villiers *et al.* [102] evaluated antiplasmodial activities of aqueous and methanol leaf extracts of *C. spicata* using the [<sup>3</sup>H] hypoxanthine incorporation assay using chloroquine-sensitive (3D7) strain of *Plasmodium falciparum* as the test organism. The extracts exhibited moderate antiplasmodial activities with IC<sub>50</sub> values ranging from 20.2 mg/mL to >50.0 mg/mL [102]. Bapela *et al.* [63], Bapela [64], and Bapela *et al.* [107] evaluated antiplasmodial activities of dichloromethane and 50% methanol root bark extract of *C. spicata* using the [<sup>3</sup>H]-hypoxanthine incorporation assay using chloroquine-sensitive (NF54) strain of *Plasmodium falciparum* as the test organism with chloroquine as a positive control. The dichloromethane extract exhibited pronounced activities with IC<sub>50</sub> value of 3.3 µg/ml [63,64,107].

#### Antiprotozoal activities

De Villiers *et al.* [102] evaluated antiprotozoal activities of aqueous and methanol leaf extracts of *C. spicata* against protozoan pathogen associated with urogenital or sexually transmitted infections, *Trichomonas vaginalis* using the microplate bioassay with ciprofloxacin (0.01 mg/mL) as a positive control. The extracts exhibited activities with MIC values ranging from 0.3 mg/mL to 13.3 mg/mL which were higher than 0.001 mg/mL exhibited by the control [102].

#### Antioxidant activities

Amoo *et al.* [100] evaluated the antioxidant activities of aqueous leaf extract of *C. spicata* using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging and β-carotene linoleic acid model assays after long-term storage in comparison with freshly collected materials. The DPPH results showed half-maximal effective concentration (EC<sub>50</sub>) values of 14.3 µg/ml–43.6 µg/ml while the antioxidant activity of 41.8%–55.7% at 200 µg/ml was exhibited using the β-carotene linoleic acid model assay [100].

#### Larvicidal activities

Maharaj *et al.* [108] evaluated larvicidal activities of aqueous, dichloromethane, dichloromethane: methanol (1:1), and methanol fruit extracts of *C. spicata* against the 3<sup>rd</sup> instar larvae of *Anopheles arabiensis* using Temephos (Mostop; Agrivo) as a positive control. The extract exhibited mortality between 40% and 59%, demonstrating limited toxicity against the target species [108]. Similarly, Maharaj *et al.* [109] evaluated larvicidal activities of aqueous, dichloromethane, dichloromethane: methanol (1:1), and methanol fruit extracts of *C. spicata* against the 3<sup>rd</sup> instar larvae of *Anopheles arabiensis* with mortality evaluated relative to the positive control Temephos (Mostop; Agrivo). The third stage of larvae was used to determine if the extracts had induced any growth inhibition or abnormalities in ecdysis to 4<sup>th</sup> instar and pupation. The dichloromethane extract caused 100% mortality after 72 h [109].

#### Molluscicidal activities

Marston and Hostettmann [110] and Msonthi *et al.* [111] evaluated the molluscicidal activities of the water extract of *C. spicata* stem bark using bioassays that were made with *Biomphalaria glabrata* snails, the intermediate host of *Schistosoma mansoni*. The extract showed activities of 400 ppm within 24 h against *Biomphalaria glabrata* snails [110,111]. Similarly, Gunzinger *et al.* [60] evaluated the molluscicidal activities of the compounds [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid and [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)]-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid isolated from *C. spicata* stem bark using bioassays that were made with *Biomphalaria glabrata* snails. The compound [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 12.5 mg/l while [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)]-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 100 mg/l [60].

#### Spermicidal activities

Hostettmann *et al.* [112] evaluated the spermicidal activities of the compounds [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid and [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid against human spermatozooids using a modified version of the protocol originally described by Sander and Cramer [113]. Compound [α-L-arabinofuranosyl-(1→4)-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 1 mg/l and compound [α-L-arabinofuranosyl-(1→4)-β-D-galactopyranosyl-(1→2)]-β-D-glucuronopyranosyl-(1→3)]-3β-hydroxyolean-12-en-28-oic acid was active at 3 mg/l, within 3 min [112].

#### Cytotoxicity activities

De Villiers *et al.* [102] evaluated cytotoxicity activities of aqueous and methanol leaf extracts of *C. spicata* against the human T-cell leukemia (Jurkat) cell line using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) calorimetric assay with (S)-(+)-camptothecin as a positive control. The extracts exhibited moderate cytotoxicity activities with IC<sub>50</sub> values ranging from 23.9 mg/mL to >50.0 mg/mL [102]. Bapela [64] and Bapela *et al.* [63,104,107] evaluated cytotoxicity activities of dichloromethane and 50% methanol root bark extracts of *C. spicata* against mammalian L-6 rat skeletal myoblast cells with podophyllotoxin as a control. The dichloromethane extract demonstrated IC<sub>50</sub> value of 47.8 µg/ml and selectivity index value of 15 and 50% methanol extract exhibited IC<sub>50</sub> value of 69.1 µg/ml which was considered to be non-toxic to rat skeletal myoblast L6 cells [63,104,107].

#### Toxicity activities

McGaw *et al.* [114] evaluated toxicity activities of aqueous, methanol, and hexane root extracts of *C. spicata* using the brine shrimp lethality mortality assay against the larvae of *Artemia salina* with podophyllotoxin as a positive control. The only aqueous extract showed activities with median lethal concentration (LC<sub>50</sub>) value of 2.6 µg/mL which was

comparable to LC<sub>50</sub> value of 7 µg/mL exhibited by the control [114].

## CONCLUSION

This study showed that the medicinal applications of *C. spicata* are quite broad, ranging from infections and pain to complex medical conditions such as heart problems, amenorrhea, and dysmenorrhea. However, the research carried out so far on phytochemical and pharmacological effects of the crude extracts and compounds isolated from *C. spicata* are limited. The preliminary scientific evidence of its phytochemistry and biological activities indicates its potential as herbal medicine. Therefore, 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 the species is suspected of causing poisoning in cattle [27,114]. Therefore, future research should focus on identification of toxic compounds, the possible side effects caused by taking *C. spicata* 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 they have no conflicts of interest.

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