Cissampelos torulosa (Menispermaceae): a synthesis and review of its botany, medicinal uses and biological activities

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Abstract
Cissampelos torulosa is a slender climber widely used as herbal medicine in southern Africa. The current study critically reviewed the botany, medicinal uses and biological activities of C. torulosa. Literature on botany, medicinal uses and biological activities of C. torulosa was collected from multiple internet sources including Elsevier, Google Scholar, SciFinder, Web of Science, Pubmed, BMC, Science Direct and Scopus. Complementary information was gathered from pre-electronic sources such as books, book chapters, theses, scientific reports and journal articles obtained from the University library. This study revealed that the species is used to induce labour, for hallucinations and ritual purification, and herbal medicine for kidney problems, swellings, hematemesis, syphilis, gastro-intestinal problems, respiratory problems and toothache. Ethnopharmacological research showed that the crude extracts of the species have anti-amoebic, antibacterial, antifungal activities. Cissampelos torulosa should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological activities.

Keywords: Cissampelos torulosa, herbal medicine, indigenous knowledge, Menispermaceae, southern Africa

INTRODUCTION
Cissampelos torulosa E. Mey. ex Harv. is a slender climber belonging to the Menispermaceae or moonseed family. The family Menispermaceae consists of approximately 70 genera and 450 species distributed throughout the tropics.1-6 The family Menispermaceae contains a wide range of biologically active bisbenzylisoquinoline alkaloids and therefore, used in traditional medicines in the tropics.7-10 The family is also characterized by various pharmacological activities which include anthelmintic, antibacterial, antifungal, antivirus, antiparasitic, cytotoxic, analgesic, anti-inflammatory, anti-allergic, bronchodilator, immunomodulatory, memory-enhancing, antidepressant, histamine release inhibition, neuroprotective, antimalarial, immunomodulatory, anti-inflammatory, hepatoprotective, antidiabetic, anti-diarrhoeal, acetylcholinesterase (ACH) inhibitory, antifertility and antiviral.11-13 The genus Cissampelos L. consists of mainly climbers or rarely erect shrubs or perennial herbs of approximately 20 species in north and south America, Africa and Asia.1 The species belonging to the genus Cissampelos have a long history of traditional use as herbal medicines throughout the distributional range of the genus.14 The species are used for a wide range of therapeutic applications which include asthma, cough, fever, arthritis, obesity, dysentery, snakebite, jaundice and heart, blood pressure and skin-related problems.14 In southern Africa, four closely related Cissampelos species, C. capensis L.F., C. hirta Klotzsch, C. mucronata A.Rich. and C. torulosa are widely used as traditional medicines.15-18 The leaves and stems of C. torulosa are sold as herbal medicines in informal herbal medicine markets in Gauteng and KwaZulu Natal provinces in South Africa.19-22 The leaves of C. torulosa are collected from the wild and used as leafy vegetables in the Limpopo province in South Africa.30-32 Cissampelos torulosa appears to be an important food plant and source of traditional medicines within its distributional range in southern Africa, and therefore, there is need for formal documentation and systematic research which is beneficial to indigenous and traditional systems of herbal medicine. It is within this context that this review was undertaken aimed at reviewing the botany, medicinal uses and biological activities of C. torulosa so as to provide baseline data required in evaluating the therapeutic potential of the species.

Botanical profile of Cissampelos torulosa
The genus name Cissampelos is derived from the Greek words “kissos” meaning “ivy” and “ampelos” meaning “vine” or “climber” in reference to the species of genus Cissampelos being confused with species of the genus ivy (Hedera L., family Araliaceae) as both plant groups are climbers or creepers.33-34 The specific epithet “torulosa” is derived from the Latin word “torulus” meaning little bumps in reference to small swellings associated with the species.35 The English common name of the species is “kidney-leaf” in reference to kidney-shaped leaves. Synonyms associated with the name C. torulosa include Menispernum capense Thunb., C. torulosa E.Mey., C. torulosa E.Mey. ex Harv. & Sond., C. truncata Engl., C. truncatus Engl. and C. wildeumanniana Van de Bossche ex De Wild.36-40 Cissampelos torulosa is a perennial, dioecious, sparsely hairy to glabrescent vine, reaching 15 m in length.36-39 Cissampelos torulosa is a slender climber with a woody rootstock. The leaves are simple, broadly to very broadly ovate and shallowly to deeply cordate at the base, often broader than long, obtuse or rounded at the apex, discolorous, slightly pubescent or glabrescent on
both sides with yellowish hairs at the base of nerves. The leaves of *C. torulosa* are kidney-shaped with three to five veins from the base of the leaf.\(^3^5\) The flowers are green in colour, supra-auxillary above a hairy gland, male inflorescence is an auxiliary cyme, solitary or two together while the female inflorescence is a cyme of one to four cymes.\(^3^6,3^7,4^1\) The fruit is an ovate-compressed drupe which is yellowish in colour. *Cissampelos torulosa* has been recorded in Malawi, Mozambique, South Africa, Swaziland, Tanzania, Zambia and Zimbabwe.\(^3^3,3^5-3^9,4^1-5^1\)

**Medicinal uses of *Cissampelos torulosa***

The bark, leaves, roots, stems and whole plant parts of *C. torulosa* are used to induce labour, for hallucinations and ritual purification, and herbal medicine for kidney problems, swellings, hematemesis, syphilis, gastrointestinal problems, respiratory problems and toothache (Table 1, Figure 1). The leaves of *C. torulosa* are mixed with those of *Knowltonia bracteata* Harv. ex Zahlbr. as herbal medicine for itching skin.\(^8\)

**Phytochemistry of *Cissampelos torulosa***

Watt and Breyer-Brandwijk\(^5^7\) argued that the chemical constituents of *C. torulosa* include pelosine. The leaves and stems of *C. torulosa* contain alkaloids such as bulbocapnine, cissacapine, cycleine, dencitrene, insulanolene, lauroscholtzine, pronuciferine, reticuline and salutaridine.\(^2^2\)

**Biological activities of *Cissampelos torulosa***

The following biological activities have been reported from the leaves and whole plant extracts of *C. torulosa*: anti-amoebic,\(^5^5\) antibacterial,\(^5^4,5^5,6^4,6^5\) antifungal,\(^6^4,6^5\) cytotoxicity and toxicity\(^5^5,6^4,6^5,6^6,6^7,6^8\) activities.

**Anti-amoebic activities**

Samie et al.\(^5^5\) evaluated anti-amoebic activities of methanol whole plant extracts of *C. torulosa* against *Entamoeba histolytica* with metronidazole (0.01 μg/ml to 2 μg/ml) as a positive control. The extract exhibited activities with the same 50% inhibitory concentration (IC\(_{50}\)) and 90% (IC\(_{90}\)) value of > 10.0 mg/ml which was higher than 0.05 μg/ml to 0.1 μg/ml exhibited by the positive control.\(^5^5\)

**Table 1: Medicinal uses of *Cissampelos torulosa* in South Africa and Swaziland**

<table>
<thead>
<tr>
<th>Medicinal use</th>
<th>Parts used</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Roots</td>
<td>Hulley and Van Wyk(^5^2)</td>
</tr>
<tr>
<td>Backache</td>
<td>Roots</td>
<td>Hulley and Van Wyk(^5^2)</td>
</tr>
<tr>
<td>Candidal infections</td>
<td>Bark</td>
<td>Masevhe et al.(^3^3)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Roots</td>
<td>Hulley and Van Wyk(^5^2)</td>
</tr>
<tr>
<td>Gastro-intestinal problems (diarrhoea, dysentery and stomach problems)</td>
<td>Leaves and stems</td>
<td>De Wet and Van Wyk(^8); Oyen(^2^2); Mabogo(^3^0); Constant and Tshisikhawe(^3^1); Samie et al.(^5^4); Samie et al.(^5^5); Stark et al.(^5^6)</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>Leaves</td>
<td>De Wet and Van Wyk(^8); Van Wyk and Gericie(^5^9); Oyen(^2^2); Watt and Breyer-Brandwijk(^5^7); Hutchings et al.(^5^8); Sobiecki(^5^9); Long(^6^0)</td>
</tr>
<tr>
<td>Hematemesis</td>
<td>Leaves</td>
<td>De Wet and Van Wyk(^8); Oyen(^2^2); Watt and Breyer-Brandwijk(^5^7); Hutchings et al.(^5^8)</td>
</tr>
<tr>
<td>Induce labour</td>
<td>Leaves</td>
<td>De Wet and Van Wyk(^8); Hutchings et al.(^5^8)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>Roots</td>
<td>Hulley and Van Wyk(^5^2)</td>
</tr>
<tr>
<td>Itching skin</td>
<td>Leaves mixed with those of <em>Knowltonia bracteata</em> Harv. ex Zahlbr.</td>
<td>De Wet and Van Wyk(^8)</td>
</tr>
<tr>
<td>Kidney problems</td>
<td>Roots</td>
<td>De Wet and Van Wyk(^8); Oyen(^2^2)</td>
</tr>
<tr>
<td>Respiratory problems (flu, scrofula and sore throat)</td>
<td>Leaves and stems</td>
<td>De Wet and Van Wyk(^8); Mabogo(^3^0); Constant and Tshisikhawe(^3^1); Samie et al.(^5^4); Samie et al.(^5^5); Watt and Breyer-Brandwijk(^5^7); Bryant(^4^1)</td>
</tr>
<tr>
<td>Ritual purification</td>
<td>Whole plant</td>
<td>De Wet and Van Wyk(^8); Mabogo(^3^0); Constant and Tshisikhawe(^3^1)</td>
</tr>
<tr>
<td>Swellings</td>
<td>Leaves</td>
<td>Oyen(^2^2); Hutchings et al.(^5^8); Bryant(^6^1)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Leaves and roots</td>
<td>De Wet and Van Wyk(^8); Oyen(^2^2); Masevhe et al.(^7^7); Watt and Breyer-Brandwijk(^5^7); Hutchings et al.(^5^8)</td>
</tr>
<tr>
<td>Toothache</td>
<td>Bark and roots</td>
<td>De Wet and Van Wyk(^8); Masevhe et al.(^3^3); Watt and Breyer-Brandwijk(^5^7); Hutchings et al.(^5^8); Mayr(^6^2); Hutchings(^6^3); Akhalwaya(^6^4); Akhalwaya et al.(^5^3); Sagbo and Mbeng(^6^6)</td>
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Antibacterial activities
Samie et al.54 evaluated the antibacterial activities of acetone, hexane and methanol leaf extracts of *C. torulosa* against *Aeromonas hydrophila, Bacillus cereus, Bacillus pumilus, Bacillus subtilis, Enterobacter cloacae, Enterococcus fecalis, Escherichia coli, Klebsiella pneumoniae, Pantoea agglomerans, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella cholerae-suis, Serratia marcescens, Staphylococcus aureus* and *Shigella flexneri* using the disc diffusion and the micro-dilution methods with gentamicin as a positive control. The methanol extract exhibited activities against most of the pathogens with the exception of *Bacillus subtilis, Klebsiella pneumoniae, Pseudomonas aeruginosa, Salmonella cholerae-suis* and *Serratia marcescens* with diameter of zone of inhibition ranging from 8 mm to 18 mm which was much lower than 18 mm to 30 mm exhibited by the positive control. The hexane extract exhibited activities against *Bacillus cereus, Bacillus subtilis* and *Proteus mirabilis* with zone of inhibition ranging from 8 mm to 9 mm. The minimal inhibitory concentration (MIC) values of methanol, acetone and hexane extracts against the tested bacteria ranged from 3.0 mg/ml to >12.0 mg/ml which was much higher than MIC value of 0.01 mg/ml to 0.02 mg/ml exhibited by the control54. Samie et al.55 evaluated antibacterial activities of methanol leaf extracts of *C. torulosa* against *Campylobacter* isolates using a microdilution method with gentamicin (0.25 μg/ml to 32.0 μg/ml) as a positive control. At a concentration of 6.0 mg/ml, the extract exhibited weak activities, suppressing 38% of the *Campylobacter* isolates.55 Akhalwaya64 and Akhalwaya et al.65 evaluated antibacterial activities of aqueous and dichloromethane : methanol (1 : 1) leaf and stem extracts of *C. torulosa* against *Streptococcus mutans, Streptococcus sanguis, Lactobacillus acidophilus, Lactobacillus casei, Porphyromonas gingivalis* and *Fusobacterium nucleatum* using the microtiter plate dilution assay with ciprofloxacin (0.1 mg/mL) as a positive control. The extracts exhibited activities with MIC values ranging from 0.05 mg/mL to >8.0 mg/mL.64,65

Antifungal activities
Akhalwaya64 and Akhalwaya et al.65 evaluated antifungal activities of aqueous and dichloromethane : methanol (1 : 1) leaf and stem extracts of *C. torulosa* against *Candida albicans, Candida glabrata* and *Candida krusei* using the microtiter plate dilution assay with amphotericin B (0.01 mg/mL) as a positive control. The extracts exhibited activities with MIC values ranging from 1.3 mg/mL to >8.0 mg/mL.64,65

Cytotoxicity and toxicity activities
Samie et al.55 evaluated cytotoxicity activities of methanol leaf extracts of *C. torulosa* using Vero cell cultures. The extract exhibited activities with the IC50 value of 206.4 μg/ml.35 Van Zyl et al.67 evaluated the cytotoxicity activities of methanol rhizome extracts of *C. torulosa* using the tetrazolium cell proliferation assay against human kidney epithelial cells. The extract exhibited activities with IC50 value which was <25.0 μg/mL.67 De Wet et al.68 evaluated cytotoxicity activities of crude alkaloidal extracts isolated from the rhizome of *C. torulosa* using MCF7 (breast), UACC62 (melanoma) and
TK10 (renal) cancer cell lines with adriamycin and 5-fluorouracil as positive controls. The crude extract exhibited weak activities with total growth inhibition (TGI) values ranging from 28.0 μg/mL to 50.0 μg/mL. The GI50 (concentration required for 50% inhibition of cell growth) values ranged from 9.0 μg/mL to 12.5 μg/mL. Akhalwaya64 and Akhalwaya et al.65 evaluated toxicity activities of aqueous stem extracts of C. torulosa using the brine shrimp lethality assay with potassium dichromate (1.6 mg/mL) as a positive control. The extract exhibited 100% mortality in brine shrimp assay after 24 hours of exposure. The median lethal concentration (LC50) value after 24 hours and 48 hours was 135.0 μg/mL and 129.0 μg/mL, respectively which was comparable to LC50 value of 100.0 μg/mL exhibited by the positive control.54,66

CONCLUSION

The present review summarizes the ethnomedicinal uses and ethnopharmacological properties of C. torulosa. A few ethnopharmacological studies have focused on evaluating anti-amoebic, antibacterial, antifungal, cytotoxicity and toxicity activities of the different extracts of the species. 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. torulosa contain potentially toxic compounds, future studies should include the identification of toxic compounds, possible side effects caused by taking C. torulosa as herbal medicine, and mechanisms of how potential toxic components of the species can be managed.

Conflict of interest

The author declares that he has no conflict of interest.

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REFERENCES