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Cussonia natalensis Sond. and *C. zuluensis* Strey (Araliaceae): A comparative analysis of their medicinal uses and pharmacological properties

Alfred Maroyi*

Department of Botany, University of Fort Hare, Private Bag X1314, Alice 5700, South Africa

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Abstract

Cussonia natalensis Sond. and *C. zuluensis* Strey have a long history of medicinal use in southern Africa. The aim of this study was to review the medicinal uses and pharmacological properties of the two species. Results of this study are based on data derived from several online databases such as Scopus, Google Scholar, PubMed and Science Direct, and pre-electronic sources such as scientific publications, books, dissertations, book chapters and journal articles. The bark, fruits and roots of *C. natalensis* and *C. zuluensis* are used as emetic, purgative and protective charm, and traditional medicine for diarrhoea, fever, stomach ache and swellings. This study showed that pentacyclic triterpene acids, cardiac glycosides, flavonoids, polyphenols, saponins and steroids have been identified from the leaves, roots and twigs of the species. The leaf extracts and compounds isolated from *C. natalensis* and *C. zuluensis* exhibited antibacterial, antifungal, antimalarial, antiprotozoal and cytotoxicity activities. Documentation of the medicinal uses, phytochemistry and pharmacological properties of *C. natalensis* and *C. zuluensis* is important as this information provides baseline data required for future research and development of health-promoting and pharmaceutical products. There is need for extensive phytochemical, pharmacological and toxicological studies of crude extracts of *C. natalensis* and *C. zuluensis* to establish the safety profiles of different preparations of the two species.

*Corresponding Author

Name: Alfred Maroyi
Phone: +27406022322
Email: amaroyi@ufh.ac.za

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INTRODUCTION

The genus *Cussonia* Thunb. is one of the most important sources of herbal medicines among the Araliaceae genera. The Araliaceae family consists of approximately 55 genera and 1500 species, which are mainly woody plants with a few herbaceous plants (Frodin *et al.*, 2004; Kim *et al.*, 2017). Research by (Brussell, 2004) revealed that many Araliaceae species such as *Acanthopanax sciadophylloide* Franch. & Sav., *A. seiboldianum* Makino, *Acer mono* Maxim., *Aralia cordata* Thunb., *A. elata* (Miq.) Seem., *A. spinosa* L., *Eleutherococcus spinosus* (L. f.) S.Y. Hu, *Fatsia japonica* (Thunb.) Decne. & Planch., *Gamblea innovans* (Siebold & Zucc.) C.B. Shang, Lowry & Frodin, *Hedera helix* L., *H. rhombea* (Miq.) Siebold ex Bean, *Oplopanax japonicus* Nakai, *Panax ginseng* C.A. Mey., *P. japonicus* (T. Nees) C.A. Mey. and *Schefflera heptaphylla* (L.) Frodin are noteworthy culinary and medicinal plants. Some members of the Araliaceae family have demonstrated pharmacological properties such as neuroprotective, anti-aging, immunostimulant, antiapoptotic,

immunomodulatory, anticancer, antiviral, antidiabetic, antibacterial, antidiabetes, antipsoriasis, antiarthritis, antifungal, anticonvulsant, antioxidant, antiobesity and anti-inflammatory (Kim *et al.*, 2016). Phytochemical studies on species belonging to the Araliaceae family revealed the presence of flavonoids, triterpenes, volatile oils, triterpenoid glycosides, saponins and tannins (Kim *et al.*, 2016)

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 (Reyneke, 1984; de Villiers *et al.*, 2009). *Cussonia natalensis* Sond. and *C. zuluensis* Strey are among the species widely used as herbal medicines in southern Africa. Other *Cussonia* species regarded as important medicinal plants in tropical Africa include *C. arborea* Hochst. ex A. Rich., *C. bancoensis* Aubrév. & Pellegr., *C. holstii* Harms ex Engl., *C. nicholsonii* Strey, *C. ostinii* Chiov., *C. paniculata* Eckl. & Zeyh., *S. spicata* Thunb., *C. transvaalensis* Reyneke and *C. zimmermannii* Harms (Watt and Breyer-Brandwijk, 1962; Kokwaro, 2009). Apart from used as herbal medicines for similar medicinal conditions, *C. natalensis* and *C. zuluensis* have been recorded in overlapping geographical areas in southern Africa (Figure 1). It is therefore, within this context that the current review was undertaken aimed at providing a comparative analysis of the botanical, medicinal, chemical and biological activities of *C. natalensis* and *C. zuluensis*.

MATERIALS AND METHODS

Results of the current study are based on literature search on the botanical, medicinal, chemical and biological activities of *C. natalensis* and *C. zuluensis* using information derived from several internet databases. The databases included Scopus, Google Scholar, PubMed and Science Direct. Other sources of information used included pre-electronic sources such as journal articles, theses, books, book chapters and other scientific articles obtained from the University library.

RESULTS AND DISCUSSION

Botanical description of *Cussonia natalensis* and *C. zuluensis*

The genus name "*Cussonia*" is in honour of Pierre Cusson (1727-1783), a French Professor of botany at the University of Montpellier who specialized in Apiaceae family (Palmer and Pitman, 1972). The specific name "*natalensis*" means "of Natal", part of KwaZulu-Natal province in South Africa where the type specimen of the species was collected (Bayton, 2019). *Cussonia natalensis* is commonly referred to as "rock cabbage tree", "simple-leaved cabbage tree" and "Natal cabbage tree". *Cussonia natalensis* is a sturdy, small to medium-sized deciduous tree with a rounded crown which can grow up to a height of 11 metres (Schmidt *et al.*, 2017). The bark of *C. natalensis* is dark grey to brown in colour, deeply rectangularly fissured and corky. The leaves of *C. natalensis* are simple, deeply lobed, leathery, glossy green, hairless, apex tapering to a point, base lobed with bluntly toothed leaf margins. The flowers are greenish yellow in colour, occurring in terminal heads of radiating cylindrical spikes. The fruit is a cone-shaped drupe, fleshy and purple in colour when ripe and closely crowded along the spikes. *Cussonia natalensis* has been recorded in Eswatini, South Africa and Zimbabwe at an altitude ranging from 100 m to 1640 m above sea level (Germishuizen and Meyer, 2003). *Cussonia natalensis* has been recorded in bushveld, usually in rocky places, hills, hillsides and mountain sides.

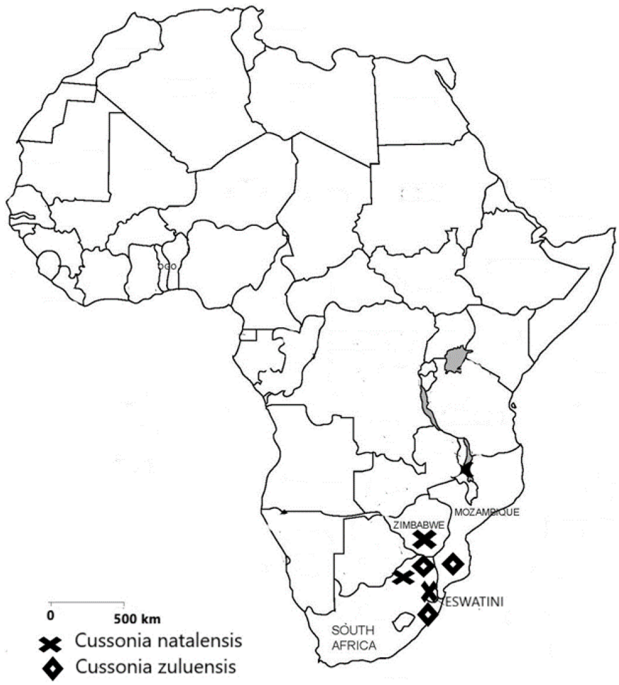

Figure 1: Geographical distribution of *Cussonia natalensis* and *C. zuluensis*

The specific name "*zuluensis*" refers to Zululand (part of KwaZulu-Natal province in South Africa) from where the type specimen of the species was collected (Glen, 2004). *Cussonia zuluensis* is commonly referred to as "Zulu cabbage tree". *Cussonia zuluensis* is a small, multi-stemmed, sparsely branched tree with a spindly shape, growing to a height of six metres (Germishuizen and Meyer,

Table 1: Medicinal uses of Cussonia natalensis and C. zuluensis

Medicinal uses	Parts used	Country	Reference
Cussonia natalensis			
Diarrhoea	Root decoction taken orally	Zimbabwe	(Mukanganyama *et al.*, 2012)
Emetic	Root decoction taken orally	Eswatini	(Amusan *et al.*, 2002; Long, 2005)
Gastro-intestinal problems	Stem bark mixed with that of Gardenia volkensii K. Schum. subsp. spatulifolia (Stapf. & Hutch.) Verdc.	Eswatini	(Amusan, 2010)
Protective charm	Bark, fruits and roots	Eswatini	(Long, 2005)
Purgative	Bark decoction taken orally	Eswatini	(Amusan *et al.*, 2002)
Stomach ache	Bark and root decoction taken orally	Eswatini	(Amusan *et al.*, 2002; Amusan, 2010)
Cussonia zuluensis			
Emetic	Root infusion taken orally	Eswatini	(Long, 2005; Amusan *et al.*, 2007)
Fever	Root decoction taken orally	Eswatini	(Amusan *et al.*, 2007)
Purgative	Root infusion taken orally	South Africa	(Corrigan *et al.*, 2011)
Swellings	Root infusion applied topically	South Africa	(Corrigan *et al.*, 2011)

2003). The bark is grey-green in colour, smooth to flaking. The leaves of *C. zuluensis* are multi-digitate, clustered near ends of branches or arranged spirally at the ends of branches. The leaves are leathery, glossy dark green above, dull green below, apex tapering with a hair-like tip, base tapering with sparsely to distinctly toothed leaf margins. Flowers occur in terminal simple umbels and are greenish yellow in colour. The fruit is a goblet-shaped drupe, fleshy and mauve in colour when ripe and closely crowded along the axes. *Cussonia zuluensis* has been recorded in Eswatini, Mozambique and South Africa at an altitude ranging from 10 m to 1000 m above sea level (Germishuizen and Meyer, 2003). *Cussonia zuluensis* has been recorded in sandy soils and river valleys in bushveld, dry coastal scrub and forest.

Medicinal uses of *Cussonia natalensis* and *C. zuluensis*

In Eswatini and Zimbabwe, the bark, fruits and roots of *C. natalensis* are used as emetic, purgative and protective charm, and traditional medicine against diarrhoea and stomach ache (Table 1). In Eswatini, the stem bark of *C. natalensis* is mixed with that of *Gardenia volkensii* K. Schum. subsp. *spatulifolia* (Stapf. & Hutch.) Verdc. as herbal medicine for gastro-intestinal problems (Amusan, 2010). In Eswatini and South Africa, the root infusion of *C. zuluensis* is used as emetic and purgative, and herbal medicine for fever and swellings (Long, 2005; Amusan *et al.*, 2007).

Phytochemical and biological activities of *Cussonia natalensis* and *C. zuluensis*

There is very little information available concerning the phytochemistry of the crude extracts of *C. natalensis* and *C. zuluensis*. However, Fourie *et al.* (1989) identified pentacyclic triterpene acids, 23-hydroxy-3-oxo-urs-12-en-28-oic acid and oleanolic acid from the leaves and twigs of *C. natalensis*. Preliminary research by Fourie *et al.* (1989) showed that the triterpene acid, 23-hydroxy-3-oxo-urs-12-en-28-oic acid isolated from the leaves and twigs of *C. natalensis* has anti-ulcer properties. Similarly, Amusan *et al.* (2007) identified cardiac glycosides, flavonoids, polyphenols, saponins and steroids from the roots of *C. zuluensis*. Some of these chemical compounds may be responsible for the pharmacological properties of the species. The phytochemical compounds like triterpenes are associated with antioxidant, antimicrobial, antimalarial, anti-inflammatory, anticancer, α-glucosidase inhibitors and antidia-

betic properties (Tan *et al.*, 2008; Zhang *et al.*, 2016). Many flavonoids, polyphenols, saponins and steroids have anti-inflammatory, anticancer, antioxidant, antiparasitic, antiphlogistic, antiallergic, immunomodulating, antihepatotoxic, antiviral, hypoglycemic, antifungal and molluscicidal activities (Rasouli *et al.*, 2017; Sülsen *et al.*, 2017).

De Villiers *et al.* (2010) evaluated the antibacterial activities of methanol and water extracts of *C. natalensis* leaves against *Pseudomonas aeruginosa, Neisseria gonorrhoeae, Enterococcus faecalis, Staphylococcus aureus* and *Escherichia coli* using the microdilution method with ciprofloxacin (0.01 mg/mL) as positive control. Both extracts exhibited activities against all the tested pathogens with the minimum inhibitory concentrations (MIC) values ranging from 0.3 mg/mL to 8.0 mg/mL. Similarly, De Villiers *et al.* (2010) evaluated the antibacterial activities of methanol and water extracts of *C. zuluensis* leaves against *Pseudomonas aeruginosa, Neisseria gonorrhoeae, Enterococcus faecalis, Staphylococcus aureus* and *Escherichia coli* using the microdilution method with ciprofloxacin (0.01 mg/mL) as positive control. Both extracts exhibited activities against all the tested pathogens with the MIC values ranging from 0.2 mg/mL to 9.3 mg/mL (De Villiers *et al.*, 2010). Shai (2007); Shai *et al.* (2008) evaluated the antibacterial activities of acetone, dichloromethane and n-hexane extracts of *C. zuluensis* leaves against *Enterococcus faecalis, Pseudomonas aeruginosa, Escherichia coli* and *Staphylococcus aureus* using the microdilution method with gentamicin as a positive control. The extracts exhibited activities against the tested pathogens with MIC values ranging from 0.3 mg/ml to 2.5 mg/ml and total activity ranging from 8.0 ml to 267.0 ml (Shai, 2007; Shai *et al.*, 2008).

Mangoyi and Mukanganyama (2011) evaluated the antifungal activities of ethanol extracts of *C. natalensis* leaves against *Candida krusei* and *Candida albicans* using the agar disc diffusion and broth dilution methods with miconazole as positive control. The extract exhibited activities against *Candida albicans* with zone of inhibition value of 16.0 mm, MIC and minimum fungicidal concentration (MFC) values of 0.3 mg/ml and 1.3 mg/ml, respectively. The zone of inhibition exhibited by miconazole, the control ranged from 20.0 mm to 22.6 mm, and the MIC and MFC values ranged from 0.3 mg/ml to 0.6 mg/ml (Mangoyi and Mukanganyama, 2011). Shai (2007); Shai *et al.* (2008) evaluated the antifungal activities of acetone, dichloromethane and n-hexane extracts of *C. zuluensis* leaves against *Cryptococcus neoformans, Aspergillus fumigatus, Candida albicans, Micrococcus canis* and *Sporothrix schenckii* using the microdilution method with amphotericin B as positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.06 mg/ml to 2.5 mg/ml and total activity ranging from 8.0 ml to 133.0 ml (Shai, 2007; Shai *et al.*, 2008). Mokoka (2007); Mokoka *et al.* (2010) evaluated the antifungal activities of hexane, dichloromethane, acetone and methanol leaf extracts of *C. zuluensis* against *Cryptococcus neoformans* using the two-fold serial dilution microplate and microdilution methods. The extracts exhibited activities against the tested pathogen with MIC values ranging from 0.02 mg/mL to 0.6 mg/mL and total activity ranging from 9.0 mL/g to 496.0 mL/g (Mokoka, 2007; Mokoka *et al.*, 2010).

De Villiers *et al.* (2010) evaluated the antiprotozoal activities of methanol and water extracts of *C. natalensis* against the protozoan pathogen associated with urogenital or sexually transmitted infections, *Trichomonas vaginalis* using the microdilution method with ciprofloxacin (0.01 mg/mL) as positive control. The methanol extract exhibited activities against the tested pathogen with MIC value of 1.0 mg/mL which was higher than the MIC value of 0.001 mg/mL exhibited by the positive control. De Villiers *et al.* (2010) evaluated the antiprotozoal activities of methanol and water extracts of *C. zuluensis* leaves against the protozoan pathogen associated with urogenital or sexually transmitted infections, *Trichomonas vaginalis* using the microdilution method with ciprofloxacin (0.01 mg/mL) as positive control. The methanol extract exhibited activities against the tested pathogen with MIC value of 0.8 mg/mL which was higher than the MIC value of 0.001 mg/mL exhibited by the positive control (De Villiers *et al.*, 2010).

De Villiers *et al.* (2010) evaluated the antimalarial activities of methanol and water extracts of *C. natalensis* leaves using the [G-^{3}H] hypoxanthine incorporation assay using chloroquine-sensitive (3D7) strain of Plasmodium falciparum as the test organism. The extracts exhibited weak activities with half maximal inhibitory concentration (IC_{50}) values >50.0 μg/mL. (De Villiers *et al.*, 2010) also evaluated the antimalarial activities of methanol and water extracts of *C. zuluensis* leaves using the [G-^{3}H] hypoxanthine incorporation assay using chloroquine-sensitive (3D7) strain of *Plasmodium falciparum* as the test organism. The extracts exhibited weak activities with IC_{50} values >50.0 μg/mL (De Villiers *et al.*, 2010).

De Villiers *et al.* (2010) evaluated the cytotoxicity activities of methanol and water extracts of *C. natalensis* 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 weak cytotoxicity activities with IC_{50} values >50.0 μg/mL in comparison to IC_{50} value of 0.07 μg/mL exhibited by the positive control. Corrigan *et al.* (2011) also evaluated the cytotoxicity activities of methanol and water extracts of *C. zuluensis* leaves against the human T-cell leukemia (Jurkat) cell line using the MTT calorimetric assay with (S)-(+)- camptothecin as a positive control. The methanol and water extracts exhibited moderate cytotoxicity activities with IC_{50} values of 37.0 μg/mL and >50.0 μg/mL, respectively in comparison to IC_{50} value of 0.07 μg/mL exhibited by the positive control (de Villiers *et al.*, 2009).

CONCLUSIONS

The present review summarizes the botanical, medicinal, chemical and biological activities of *C. natalensis* and *C. zuluensis*. Based on the presented information, these two species are closely related and deemed as potent traditional medicines for treating and managing fever, heart problems, headache, earache, skin disorders, fatigue and respiratory problems. *Cussonia natalensis* and *C. zuluensis* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating their medicinal uses with their phytochemistry and pharmacological properties.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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