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

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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 diarrhea, 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.

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

| Medicinal uses          | Parts used                                      | Country       | Reference                                                                 |
|-------------------------|------------------------------------------------|---------------|---------------------------------------------------------------------------|
| Cussonia natalensis     | Root decoction taken orally                     | Zimbabwe      | (Mukanganyama et al., 2012)                                               |
| Diarrhoea               | Root decoction taken orally                     | Eswatini      | (Amusan et al., 2002; Long, 2005)                                         |
| Emetic                  | Root decoction taken orally                     | Eswatini      | (Amusan, 2010)                                                            |
| Gastro-intestinal       | Stem bark mixed with that of Gardenia volkensii K. Schum. subsp. spatulifolia (Stapf. & Hutch.) Verdc. | Eswatini      | (Amusan et al., 2010)                                                     |
| problems                |                                                |               |                                                                           |
| Protective charm        | Bark, fruits and roots                          | Eswatini      | (Amusan et al., 2010)                                                     |
| 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      | Root infusion taken orally                      | Eswatini      | (Long, 2005; Amusan et al., 2007)                                         |
| Emetic                  | Root decoction taken orally                     | Eswatini      | (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)                                                   |

(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. arboarea Hochst. ex A. Rich., C. bancoensis Aubrèv. & Pellegr., C. holstii Harms ex Engl., C. nicholsonii Strey, C. ostinii Chiov., C. paniculata Eckl. & Zeyh., S. spicata Thunb., C. transvaalensis Reynke 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 tapering 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 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 antidiabetic properties (Tan et al., 2008; Zhang et al., 2016). Many flavonoids, polyphenols, saponins and steroids have anti-inflammatory, anticancer,
antioxidant, antiparasitic, antiphlogistic, antiallergic, immunomodulating, antihypertoxic, antiviral, hypoglycemic, antifungal and molluscicidal activities (Rasouli et al., 2017; Sülsen et al., 2017).

(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, (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 (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).

(Mangoyo 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 (Mangoyo 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).

(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. (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 (Villiers et al., 2010).

(Villiers et al., 2010) evaluated the antimalarial activities of methanol and water extracts of C. natalensis leaves using the [G-14H] 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 (IC50) values >50.0 µg/mL. (Villiers et al., 2010) also evaluated the antimalarial activities of methanol and water extracts of C. zuluensis leaves using the [G-14H] hypoxanthine incorporation assay using chloroquine-sensitive (3D7) strain of Plasmodium falciparum as the test organism. The extracts exhibited weak activities with IC50 values >50.0 µg/mL (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 con-
The extracts exhibited weak cytotoxicity activities with IC50 values >50.0 μg/mL in comparison to IC50 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 colorimetric assay with (S)-(+) camptothecin as a positive control. The methanol and water extracts exhibited moderate cytotoxicity activities with IC50 values of 37.0 μg/mL and >50.0 μg/mL, respectively in comparison to IC50 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
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