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A synthesis and review of medicinal uses, phytochemistry and pharmacological properties of *Schefflera umbellifera* (Sond.) Baill. (Ar aliaceae)

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ABSTRACT

Schefflera umbellifera (Sond.) Baill. is an evergreen tree widely used as traditional medicine throughout its distributional range in southern Africa. *Schefflera umbellifera* is indigenous to Eswatini, Malawi, Mozambique, South Africa and Zimbabwe. This study was aimed at providing a critical review of medicinal uses, phytochemical and pharmacological properties of *S. umbellifera*. Documented information on medicinal uses, phytochemical and pharmacological properties of *S. umbellifera* was collected from several online sources such as Scopus, Google Scholar, PubMed, Francis and Taylor and Science Direct, and pre-electronic sources such as book chapters, books, journal articles and scientific publications obtained from the University library. This study revealed that the bark, leaf and root decoction or infusion of *S. umbellifera* are mainly used as diuretic, laxative, colic and protective charm, and traditional medicine for stomach ulcers, weaning infants, insanity, inflammation, rheumatism and malaria. Phytochemical compounds identified from the species include 3-hydroxy-20(29)-lupen-28-ol, 7-hydroxy-6-methoxycoumarin, betulin, ent-kaur-16-en-19-oic acid and oleanolic acid. Pharmacological research revealed that *S. umbellifera* extracts and compounds isolated from the species have antibacterial, anti-HIV, anti-inflammatory, antimalarial, antiprotozoal, larvicidal and cytotoxicity activities. *Schefflera umbellifera* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological activities.

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INTRODUCTION

Schefflera umbellifera (Sond.) Baill. is an evergreen tree belonging to the Araliaceae family. The Araliaceae family consists of approximately 55 genera and 1500 species, which are mainly woody plants with a few herbaceous plants (Kim *et al.*, 2017). The genus name *Schefflera* J.R. Forst. & G. Forst. is in honour of Johann Peter Ernst Von Scheffler, an 18^{th} century German physician and botanist (Palmer and Pitman, 1972). *Schefflera* is a genus of between 600 to 900 species, mainly trees, shrubs and lianas with several species grown as garden ornamental and house plants (Plunkett *et al.*, 2005; Fiaschi and Plunkett, 2011). The specific name "*umbellifera*" refers to the umbellate arrangement of the

flowers in which the flower stalks spring from the same point like the ribs of an umbrella (Palmer and Pitman, 1972). The English common name of *S. umbellifera* is "false-cabbage tree" and "forest cabbage tree". The synonyms associated with the name *S. umbellifera* include *Cussonia chartacea* Schinz, *C. umbellifera* Sond. and *Neocussonia umbellifera* (Sond.) Hutch (Strey, 1973). *Schefflera umbellifera* is a medium to large evergreen tree with a tall trunk and much-branched and rounded crown, reaching a height of 20 metres (Strey, 1973; Venter and Venter, 2015). The bark on young stems is smooth with raised cork dots, resinous and rough to longitudinally fissured on older branches and stems. The leaves of *S. umbellifera* are clustered at ends of branches, alternate, compound and hand-shaped. The leaves are glossy dark green above, paler below with toothed and waxy margins in the upper half of the leaf. The flowers are large, branched and terminal and pale yellow to white in colour. The fruit is a cone-shaped drupe, fleshy and dark red in colour when ripe. *Schefflera umbellifera* is widely distributed in Eswatini, Malawi, Mozambique and Zimbabwe as well as in South Africa at an altitude ranging from 60 m to 1980 m above sea level (Strey, 1973; Venter and Venter, 2015). *Schefflera umbellifera* has been recorded in well-drained and humus-rich soil in coastal forest, evergreen forest, afromontane forest and forest margins. *Schefflera umbellifera* is widely used as traditional medicine throughout its distributional range in southern Africa (Watt and Breyer-Brandwijk, 1962; Long, 2005). It is therefore, within this context that this review was undertaken aimed at reviewing the medicinal uses, phytochemical and pharmacological properties of *S. umbellifera* so as to provide baseline data required in evaluating the therapeutic potential of the species.

MATERIALS AND METHODS

Results of the current study are based on literature search on the phytochemistry, pharmacological properties and medicinal uses of *S. umbellifera* 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

Medicinal uses of *Schefflera umbellifera*

The bark, leaf and root decoction or infusion of *S. umbellifera* are mainly used as diuretic, laxative, colic and protective charm, and traditional medicine for stomach ulcers, weaning infants, insanity, inflammation, rheumatism and malaria (Table 1; Figure 1). Other medicinal applications of *S. umbellifera* supported by at least two literature records include the use of the leaf and root decoction or infusion of the species as traditional medicine for nausea, stomach ache and venereal diseases (Palmer and Pitman, 1972; Mthembu *et al.*, 2010).

Phytochemistry of *Schefflera umbellifera*

Mthembu (2007) and Mthembu *et al.* (2010) isolated coumarin, kraurane diterpene and triterpenes compounds such as 3-hydroxy-20(29)-lupen-28-ol, 7-hydroxy-6-methoxycoumarin, betulin, ent-kaur-16-en-19-oic acid and oleanolic acid (Figure 2) from the leaves of *S. umbellifera*. The coumarin compounds are characterized by pharmacological properties such as antioxidant, anti-depressant, anti-convulsant, anti-coagulant, anti-inflammatory, antimicrobial and anticancer properties (Riveiro *et al.*, 2010; Stefanachi *et al.*, 2018). Similarly, diterpenes are associated with antitumor, antitubercular, antimicrobial, anti-peptic ulcer, antiplasmodial, anti-inflammatory, antiadipogenic, hypoglycemic, antihypertensive, neuroprotective and anti-thrombin inhibitory activities (Li *et al.*, 2016; Roncero *et al.*, 2018). The triterpenes compounds are also associated with antioxidant, antimicrobial, antimalarial, anti-inflammatory, anticancer, α-glucosidase inhibitors and antidiabetic properties (Tan *et al.*, 2008; Zhang *et al.*, 2016). Some of these phytochemical compounds may be responsible for the pharmacological properties of the species.

Pharmacological properties of *Schefflera umbellifera*

The following pharmacological activities have been documented from the bark, leaves, roots, stems and twigs of *S. umbellifera* and compounds isolated from the species: antibacterial, anti-HIV, anti-inflammatory, antimalarial, antiprotozoal, larvicidal and cytotoxicity activities.

Antibacterial activities

Similarly, De Villiers *et al.* (2010) evaluated the antibacterial activities of methanol and water extracts of *S. umbellifera* 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. The methanol extract exhibited activities against all the tested pathogens with the exception of *Enterococcus fae-*

Table 1: Medicinal uses of *Schefflera umbellifera*

Medicinal use	Part used	Country	Reference
Colic	Leaf decoction or infusion taken orally	South Africa	Hutchings *et al.* (1996); Tetyana *et al.* (2002)
Diuretic	Root infusion taken orally	South Africa	Shai (2007); Mthembu *et al.* (2010)
Inflammation	Bark, leaf and root infusion applied topically	South Africa	Jäger and van Staden (2005); Venter and Venter (2015)
Inflammation of navel	Roof infusion applied topically	Zimbabwe	Gelfand *et al.* (1985); Hutchings *et al.* (1996)
Insanity	Leaf decoction or infusion taken orally	South Africa	Palmer and Pitman (1972); Van Wyk and Gericke (2018)
Laxative	Root infusion taken orally	South Africa	Shai (2007); Mthembu *et al.* (2010)
Malaria	Bark and leaf decoction or infusion taken orally	Eswatini, South Africa and Zimbabwe	Gelfand *et al.* (1985); Netshiluvhi (1996)
Nausea	Root infusion taken orally	South Africa	Mthembu (2007); Mthembu *et al.* (2010)
Protective charm (good luck and magical)	Bark	Eswatini and South Africa	Watt and Breyer-Brandwijk (1962); Long (2005)
Rheumatism	Leaf decoction or infusion taken orally	Eswatini and South Africa	Long (2005); Venter and Venter (2015)
Stomach ache	Leaf infusion taken orally	South Africa	Palmer and Pitman (1972); Mbambezeli *et al.* (2006)
Stomach ulcers	Bark decoction or infusion taken orally	South Africa	Watt and Breyer-Brandwijk (1962); Mthembu *et al.* (2010)
Venereal diseases	Root infusion taken orally	South Africa	Mthembu (2007); Mthembu *et al.* (2010)
Weaning infants	Root infusion applied topically	South Africa	Shai (2007); Mthembu *et al.* (2010)

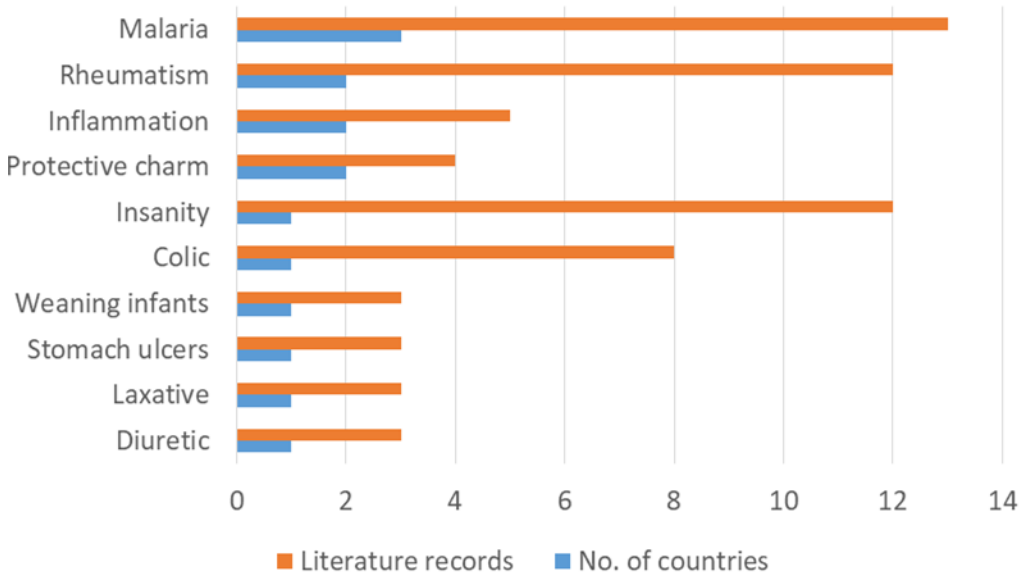

Figure 1: Medicinal applications of *Schefflera umbellifera* derived from literature records

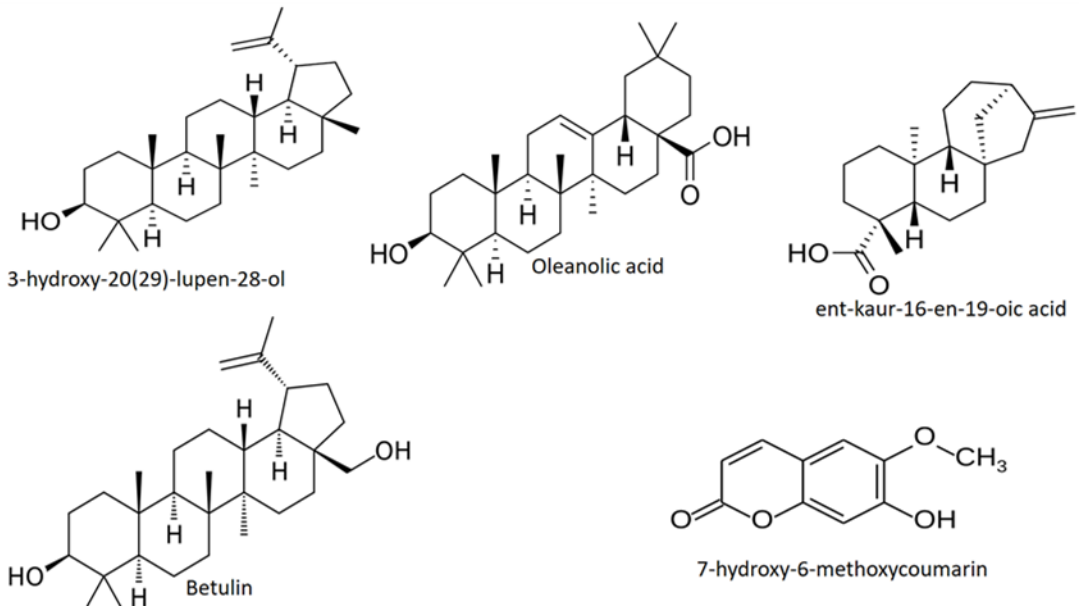

Figure 2: Chemical structures of coumarin, kraurane diterpene and triterpenes isolated from the leaves of *Schefflera umbellifera*

calis with the minimum inhibitory concentrations (MIC) values ranging from 1.5 mg/mL to 6.7 mg/mL while both extracts exhibited activities against *Neisseria gonorrhoeae* with MIC values ranging from 0.2 mg/mL to 6.7 mg/mL (Villiers *et al.*, 2010).

Anti-HIV activities

Nthambeleni *et al.* (2010) evaluated the anti-HIV activities of aqueous extract of *S. umbellifera* leaves using EMF and InPheno bioassay screening against the cellular co-receptor types for human immunodeficiency virus (HIV), CCR5 and CXCR4 viruses. The extract exhibited moderate activities shown by inhibition of 50% viral replication (IC_{50}) and concentration of extract provoking 50% of cell death after a 4-day time-window (CD_{50}) (Nthambeleni *et al.*, 2010).

Anti-inflammatory activities

Tetyana (2000) and Tetyana *et al.* (2002) evaluated the anti-inflammatory activities of the ethyl acetate, ethanol and aqueous extracts of *S. umbellifera* bark using the cyclooxygenase (COX-1) assay. The ethyl acetate and ethanol extracts inhibited cyclooxygenase in the cyclooxygenase-1 assay with inhibition percentage ranging between 80.0% and 93.0% (Tetyana, 2000; Tetyana *et al.*, 2002).

Antimalarial activities

Tetyana (2000) and Tetyana *et al.* (2002) evaluated the antimalarial activities of the ethyl acetate, ethanol and aqueous extracts of *S. umbellifera* bark against *Plasmodium falciparum* (PfUP1) isolate using a parasite lactate dehydrogenase (pLDH) assay with chloroquine as positive control. The ethyl acetate and ethanol extracts exhibited 100% inhibitory activities against the pathogen at a concentration of 200.0 μg/ml (Tetyana, 2000; Tetyana *et al.*, 2002). Clarkson *et al.* (2004) evaluated the antimalarial activities of aqueous, dichloromethane, dichloromethane : methanol (1:1) and methanol extracts of *S. umbellifera* leaves, roots, stems and twigs against *Plasmodium falciparum* using a parasite lactate dehydrogenase (pLDH) assay. The extracts exhibited activities with half maximal inhibitory concentration (IC_{50}) values ranging from 3.7 μg/ml to >100.0 μg/ml (Clarkson *et al.*, 2004). De Villiers *et al.* (2010) evaluated antimalarial activities of methanol and water extracts of *S. umbellifera* 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 (Villiers *et al.*, 2010). Mthembu (2007) and Mthembu *et al.* (2010) evaluated the antimalarial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of leaves of *S. umbellifera* and the compounds 7-hydroxy-6-methoxycoumarin, botulin and ent-kaur16-en-19-oic acid isolated from the species against the chloroquine-susceptible *Plasmodium falciparum* D10 using a parasite lactate dehydrogenase (pLDH) assay with chloroquine used as a reference drug. The dichloromethane and dichloromethane: methanol (1:1) extracts and the compound betulin exhibited activities with IC_{50} values ranging from 3.2 μg/ml to 5.0 μg/ml in comparison to IC_{50} value of 27.2 ng/ml exhibited by the reference compound (Mthembu, 2007; Mthembu *et al.*, 2010). Mokoka (2013) and Mokoka *et al.* (2011) evalu-

ated the antimalarial activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *S. umbellifera* roots against *Plasmodium falciparum* with benznidazole chloroquine (IC_{50} = 0.05 μM) as a positive control using the [G-^{3}H]-hypoxanthine incorporation assay. The dichloromethane and dichloromethane: methanol (1:1) extracts exhibited weak activities with IC_{50} values of 2.7 μg/mL and 7.7 μg/mL, respectively (Mokoka, 2013; Mokoka *et al.*, 2011).

Antiprotozoal activities

De Villiers *et al.* (2010) evaluated the antiprotozoal activities of methanol and water extracts of *S. umbellifera* 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 and water extracts exhibited activities with MIC values of 1.5 mg/mL and 4.5 mg/mL, respectively which were higher than the MIC value of 0.001 mg/mL exhibited by the positive control (Villiers *et al.*, 2010). Mokoka (2013) and Mokoka *et al.* (2011) evaluated the antiprotozoal activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *S. umbellifera* roots against *Trypanosoma cruzi, Trypanosoma brucei rhodesiense* and *Leishmania donovani* with benznidazole (IC_{50} = 0.5 μg/mL), melarsoprol (IC_{50} = 0.03 μM) and miltfosine (IC_{50} = 0.2 μg/mL) as reference drugs. Determination of the activities of the extracts against these pathogens was done using Almar Blue and resazurin assays. The extracts exhibited activities with IC_{50} values ranging from 5.0 μg/mL to 99.5 μg/mL (Mokoka, 2013; Mokoka *et al.*, 2011).

Larvicidal activities

Maharaj *et al.* (2006) evaluated the larvicidal activities of water, dichloromethane, methanol and dichloromethane: methanol (1:1) extracts of *S. umbellifera* leaves against the 3rd instar larvae of *Anopheles arabiensis* using Temephos (Mostop; Agrivo) as positive control. The extract exhibited mortality between 40.0% and 59.0%, indicating limited toxicity (Maharaj *et al.*, 2006).

Cytotoxicity activities

De Villiers *et al.* (2010) evaluated the cytotoxicity activities of methanol and water extracts of *S. umbellifera* leaves 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 (Villiers *et al.*, 2010). Mokoka (2013) and Mokoka *et al.* (2011) evaluated the cytotoxicity activities of dichloromethane and dichloromethane: methanol (1:1) extracts of *S. umbellifera* roots against the rat myoblast L6 cells with podophyllotoxin (IC_{50} = 0.05 μM) as a reference drug. The dichloromethane and dichloromethane: methanol (1:1) extracts exhibited activities with IC_{50} values of 13.9 μg/mL and 48.3 μg/mL, respectively (Mokoka, 2013; Mokoka *et al.*, 2011) .

CONCLUSIONS

The present review summarizes the medicinal uses, phytochemistry and pharmacological properties of *S. umbellifera*. Detailed studies on the pharmacokinetics, *in vivo* and clinical research involving both extracts and compounds isolated from the species are required. Therefore, future research should focus on the molecular modes or mechanisms of action, pharmacokinetics and physiological pathways for specific extracts of the species including identification of the bioactive compounds of the species and their associated pharmacological activities.

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Conflict of Interest

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

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