Gardenia volkensii K. Schum. (Rubiaceae): Review of Medicinal uses, Phytochemistry and Biological Activities

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Abstract: *Gardenia volkensii* K. Schum. is a shrub or small tree widely used as traditional medicine throughout its distributional range in tropical Africa. This study is aimed at providing a critical review of the medicinal uses, phytochemistry and biological activities of *G. volkensii*. Documented information on the medicinal uses, phytochemistry and biological activities of *G. volkensii* was collected from several online sources, which included Scopus, Google Scholar, PubMed and Science Direct. Additional information was gathered from pre-electronic sources such as book chapters, books, journal articles and scientific publications sourced from the university library. The articles published between 1972 and 2020 were used in this study. This study showed that the species is widely used as emetic and protective charm, and as traditional medicine for infertility, sore eyes, sexually transmitted infections, headache, gastro-intestinal infections, earache, convulsions, epilepsy and respiratory infections. Phytochemical compounds identified from the species include aldehydes, benzenoids, cinnamates, coumarins, essential oils, fatty acids, flavonoids, iridoids, phenolics, phytosterols and triterpenoids. Pharmacological research revealed that *G. volkensii* extracts and compounds isolated from the species have antibacterial, antifungal, antioxidant, mutagenic and antimutagenic and cytotoxicity activities. Future research on *G. volkensii* should focus on detailed phytochemical evaluations including toxicological, *in vivo* and clinical studies to corroborate the traditional medical applications of the species.

Keywords: *Gardenia volkensii*, ethnopharmacology, herbal medicine, indigenous pharmacopeia, Rubiaceae.

INTRODUCTION

Gardenia volkensii K. Schum. is a shrub or small tree belonging to Rubiaceae family, commonly known as coffee family. The genus *Gardenia* J. Ellis comprises of approximately 140 species of shrubs and trees found in tropical and warm temperate regions of Africa, Madagascar, East and Southeast Asia, western Pacific and Hawaiian islands [1,2]. The genus name is in the honour of Alexander Garden (1730-1791), a Scottish physician, botanist and zoologist who lived in Charleston, South Carolina and was a correspondent of Carl Linnaeus [3]. The species name "*volkensii*" is in the honour of Georg Ludwig August Volkens (1855-1917), a German botanist and plant collector on Mount Kilimanjaro in Tanzania from 1892 to 1894 [4]. The synonyms associated with the name *G. volkensii* include *G. somalensis* Fiori ex Chiov., *G. spatulifolia* Stapf & Hutch., *G. saundersiae* N.E.Br., *G. volkensii* K. Schum. var. *somalensis* (Fiori ex Chiov.) Cufod. [5-7]. Three infraspecific taxa of *G. volkensii* are recognized and these include *G. volkensii* subsp. *spatulifolia* (Stapf & Hutch.) Verdc. (recorded in southern Africa), a widespread *G. volkensii* subsp. *volkensii* recorded in eastern to central and southern Africa and *G. volkensii* subsp. *volkensii* var. *saundersiae* (N.E.Br.) Verdc. confined to southern Mozambique and KwaZulu-Natal province in South Africa [5-7]. The English common names of *G. volkensii* include bushveld gardenia, common gardenia, sandveld gardenia, savanna gardenia, Transvaal gardenia, wild gardenia and woodland gardenia. In ethnobotanical literature, the infraspecific taxa of *G. volkensii* are rarely mentioned, therefore, in this study *G. volkensii sensu lato* is used throughout the manuscript.

Gardenia volkensii is a shrub or small sturdy tree with short, rigid branches and often multi-stemmed with dense crown, growing to a height of eight metres [8]. The bark is pale grey to reddish-brown in colour, smooth or slightly rough, flaking in thicker and older trees. The leaves of *G. volkensii* are usually whorled, or opposite, clustered at the ends of short lateral twigs, obovate in shape, hairless, and rarely with rough hairs above and below. The flowers are axillary, solitary, large and showy, white in colour and fading to cream with age. The fruits are oval to roundish in shape, grey in colour with longitudinal ribs, and have a rich winey smell when ripe. *Gardenia volkensii* has been recorded in Angola, Botswana, Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Namibia, Tanzania, Uganda, Somalia, South Africa, Zambia and Zimbabwe [9-19]. *Gardenia volkensii* has been recorded in sandy, clay and rocky well-drained soils, edges of floodplains, coastal and lakeside areas, open woodlands, bushlands, riverine woodlands and coastal thickets at altitudes ranging from sea level to 1750 m above sea level [20]. *Gardenia volkensii* is widely planted as an

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ornamental tree and garden plant throughout the tropics [20]. The leaves of *G. volkensii* are browsed by game and livestock [3,21-24] while fruits are eaten by humans in Ethiopia [25,26] and Mozambique [27]. The roots of *G. volkensii* are sold as traditional medicines in informal herbal medicine markets of Gauteng and KwaZulu-Natal provinces in South Africa [28,29]. It is, therefore, within this context that the current study was undertaken aimed at documenting the pharmacological properties, phytochemistry and medicinal uses of *G. volkensii.*

Medicinal uses

The medicinal uses of *G. volkensii* have been recorded in Angola, Botswana, Eswatini, Ethiopia, Kenya, Malawi, Mozambique, Namibia, South Africa, Zambia and Zimbabwe, representing 71.4% of the countries where the species is indigenous. Major medicinal applications of *G. volkensii* that have been recorded in two countries and supported by at least three literature records, including the use of the species as emetic and protective charm, and as traditional

Table 1: Medicinal uses of *Gardenia volkensii*

Medicinal use	Part used	Country	Reference
Analgesic	Root infusion taken orally	Eswatini	[21]
Anthelmintic	Fruit and root infusion taken orally	Eswatini and South Africa	[21,30]
Antivenom	Leaves mixed with those of *Euclea divinorum* Hiern and *Plectranthus barbatus* Andrews, and applied topically	Kenya	[35]
Breast, skin and uterine cancer	Bark infusion taken orally	Kenya	[36]
Convulsions and epilepsy	Bark and root decoction or infusion taken orally	Botswana, Eswatini, Kenya, South Africa and Zimbabwe	[24,32,37-40]
Cosmetic	Flower infusion applied topically	South Africa	[41]
Diabetes mellitus	Fruit infusion taken orally	Eswatini	[40]
Earache	Fruit decoction or infusion applied topically	Eswatini, Kenya, South Africa and Zimbabwe	[24,30,37,39,40,42,43]
Emetic	Fruit and root decoction or infusion taken orally	Botswana, Eswatini, Kenya and South Africa	[3,21,22,31,39,42-47]
Erectile dysfunction	Leaf infusion taken orally	Angola and Zambia	[33,34]
Gastro-intestinal problems (diarrhoea, dysentery and stomach ache)	Fruit and leaf decoction of infusion taken orally	Eswatini, Mozambique and Namibia	[27,40,48-50]
Headache	Fruit, leaf and root decoction or infusion taken orally	Eswatini, Kenya and Zimbabwe	[24,30,37,39,40,42,43]
Infertility	Root and root bark infusion taken orally	Kenya and Zimbabwe	[37,39,51]
Madness	Root decoction taken orally	Malawi	[37,39]
Malaria	Fruit infusion taken orally	Kenya	[31,43]
Menstrual problems	Root decoction taken orally	Zimbabwe	[37,39]
Protective charm (evil spirits, lightning and witchcraft)	Leaves, roots and twigs	Botswana, Eswatini, Kenya, Mozambique, South Africa and Zimbabwe	[4,21,22,27,30,37,39,51,52]
Purgative	Bark and root infusion taken orally	Botswana and Kenya	[31,32]
Respiratory infections (asthma, chest complaints, colds and pneumonia, sore throat and tuberculosis)	Root and stem bark infusion taken orally	Botswana, Eswatini, Namibia and South Africa and Zimbabwe	[24,30,37,39,40,53-55]
Sexually transmitted infections (gonorrhoea, syphilis and venereal diseases)	Bark, leaf and root decoction or infusion taken orally	Botswana, Kenya and Zambia	[32,34,56,57]
Sore eyes	Root infusion applied topically	Zimbabwe and South Africa	[24,37,39]
Vomiting	Fruit and root decoction or infusion taken orally	Eswatini, Ethiopia, Kenya and South Africa	[20,30,40,48,58]
Weaning of babies	Leaf and root infusion applied topically	South Africa	[39,59]

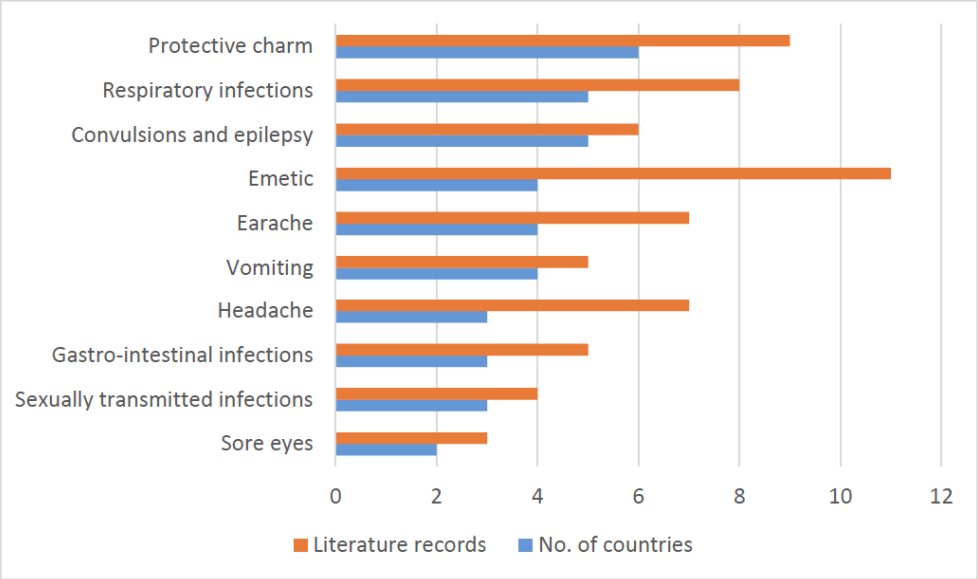

Figure 1: Medicinal applications of *Gardenia volkensii* derived from literature records.

medicine for infertility, sore eyes, sexually transmitted infections, headache, gastro-intestinal infections, earache, convulsions, epilepsy and respiratory infections (Table **1**; Figure **1**). Other medicinal applications of *G. volkensii* recorded in at least two countries include the use of the species as an anthelmintic [21,30] and purgative [31,32] and traditional medicine for erectile dysfunction [33,34].

Phytochemistry

Peter [60], Juma and Majinda [61], Sibandze [40], Kinuthia *et al.* [42] and Suwannakud *et al.* [62] identified aldehydes, benzenoids, cinnamates, coumarins, essential oils, fatty acids, flavonoids, iridoids, phenolics, phytosterols and triterpenoids from the fruit pulp, fruits, leaves and seeds of *G. volkensii* (Table **2**). Some of these phytochemical compounds may be responsible for the pharmacological properties exhibited by the species.

Biological Activities of *Gardenia volkensii*

Pharmacological research revealed that different extracts of *G. volkensii* and compounds isolated from the species have various biological activities such as antibacterial, antifungal, antioxidant, mutagenic and antimutagenic and cytotoxicity activities.

Antibacterial Activities

Mutta [63] evaluated the antibacterial activities of methanol extracts of G. volkensii roots against Staphylococcus aureus, Bacillus subtilis, Mycobacterium phlei, Streptococcus faecalis, Escherichia coli, Salmonella typhimurium and Pseudomonas aeruginosa using the agar diffusion method with gentiamycin and 8-methoxypsoralen as positive controls. The extracts exhibited activities against the tested pathogens with the exception of Pseudomonas aeruginosa and Streptococcus faecalis with the inhibition zone ranging from 7.0 mm to 10.0 mm in comparison to 13.0 mm to 26.0 mm exhibited by the positive control [63]. Kinuthia et al. [43] evaluated the antibacterial activities of ethyl acetate, dichloromethane and hexane extracts of G. volkensii fruit pulp, leaves, seeds and stem bark, and the compound modified iridoid (GV2) against Escherichia coli, Salmonella typhimurium, Staphylococcus aureus and Bacillus subtilis using serial dilution assay with doxycycline® as positive control. The extracts and compounds exhibited activities against Escherichia coli, Staphylococcus aureus and Bacillus subtilis with minimum inhibitory concentration (MIC) values ranging from 0.2 mg/mL to >0.4 mg/mL [43]. Sibandze [40] evaluated the antibacterial activities of acetone extracts of G. volkensii fruits and leaves against Escherichia coli, Staphylococcus epidermis, Staphylococcus aureus and Klebsiella pneumoniae using the microplate dilution method with ciprofloxacin (0.01 mg/ml) as positive control. The extracts exhibited activities against the tested pathogens with the MIC values ranging from 1.3 mg/ml to 12.0 mg/ml [40].

Antifungal Activities

Sibandze [40] evaluated the antifungal activities of acetone extracts of *G. volkensii* fruits and leaves against *Candida albicans* using the microplate dilution

Table 2: Phytochemical Compounds Identified from *Gardenia volkensii*

Compound	Plant part	Reference
3,3',4',5,7-pentamethoxyflavone	Fruit pulp and seeds	[61]
3,4-dihydroxybenzoic acid	Fruit pulp and seeds	[61]
3-oxo-22α-hydroxy-olean-12-en-28-oic acid	Seeds	[42]
4-(2N-gardenamyl)n-butanoic acid	Fruit pulp and seeds	[61]
4-hydroxybenzoic acid	Fruit pulp and seeds	[61]
4-hydroxy-2,5-dimethyl-3-methoxybenzoic acid	Fruit pulp and seeds	[61]
4-hydroxy-3-methoxy-2,5-dimethylbenzoic acid	Fruit pulp and seeds	[61]
4-hydroxy-3-methoxybenzoic acid	Fruit pulp and seeds	[60,61]
5-hydroxy-3,3',4',5,7-tetramethoxyflavone	Fruit pulp and seeds	[60,61]
10-hydroxy-1-oxo-7-iriden-11-oic acid methyl ester	Seeds	[42]
Asculetin	Fruit pulp and seeds	[61]
Benzoic acid	Fruit pulp and seeds	[61]
Cinnamic acid	Fruit pulp and seeds	[61]
Coniferaldehyde	Fruit pulp and seeds	[61]
Flavonoid phenolic	Fruits and leaves	[40]
Genipin	Fruit pulp and seeds	[61]
Genipin gentiobioside	Fruit pulp and seeds	[61]
Linolenyl alcohol	Leaves	[62]
Medicarpin	Fruit pulp and seeds	[61]
Methyl 2-(2,5-dihydroxyphenyl) acetate	Fruit pulp and seeds	[61]
Neophytadiene	Leaves	[62]
Oleanolic acid	Seeds	[42]
Palmitic acid	Leaves	[62]
p-coumaric acid	Fruit pulp and seeds	[61]
Pterocarpan	Fruit pulp and seeds	[61]
Scopoletin	Fruit pulp and seeds	[61]
Squalene	Leaves	[62]
Stigmasterol	Fruit pulp and seeds	[61]
stigmasterol-3-O-β-D-glucopyranoside	Fruit pulp and seeds	[61]
Total phenolic content	Fruits and leaves	[40]
Vanillin	Fruit pulp and seeds	[61]

method with amphotericin B (0.01 mg/ml) as positive control. The leaf and fruit extracts exhibited activities against *Candida albicans* with the MIC values of 0.4 mg/ml and 12.0 mg/ml, respectively [40].

Antioxidant Activities

Juma and Majinda [61] evaluated the antioxidant activities of chloroform and methanol extracts of *G. volkensii* fruits and the compounds 3,4-dihydroxybenzoic acid, 4-(2N-gardenamyl)n-butanoic acid, 4-hydroxybenzoic acid, 4-hydroxy-2,5-dimethyl-3-methoxybenzoic acid, asculetin, benzoic acid, cinnamic acid, genipin gentiobioside, medicarpin, p-coumaric acid, scopoletin, stigmasterol and stigmasterol-3-O-β-D-glucopyranoside, which were isolated from the fruit pulp and seeds of the species using 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay with ascorbic acid (0.05 µg) as positive control. The chloroform and methanol extracts, and the compounds genipin and medicarpin exhibited weak activities [61]. Sibandze [40] evaluated the antioxidant activities of acetone extracts of *G. volkensii* fruits and leaves using the DPPH free radical scavenging assay, metal

chelating assay and inhibition of lipid peroxidation method with ascorbic acid and trolox as positive controls. The leaf extract exhibited the best activities demonstrated by half maximal inhibitory concentration (IC_{50}) value of 21.6 µg/ml in DPPH, >100.0 µg/ml in metal chelation and 77.6% inhibition of lipid peroxidation at a concentration of 100.0 µg/ml [40].

Mutagenic and Antimutagenic Activities

Elgorashi *et al.* [64] evaluated the mutagenic activities of dichloromethane and 90% methanol extracts of *G. volkensii* bark, leaf and twigs using the Ames test performed on *Salmonella typhimurium* strain TA98, micronucleus test, comet assay and VITOTOX® test. The extracts exhibited activities in micronucleus test and comet assay [64]. Similarly, Taylor *et al.* [65] evaluated the mutagenic activities of dichloromethane and 90% methanol extracts of the bark, leaves and twigs of *G. volkensii* using the Ames test performed on *Salmonella typhimurium* strains TA98 and TA100, micronucleus test, comet assay and VITOTOX® test. The extracts exhibited activities in comet assay [65]. Verschaeve *et al.* [66] evaluated the mutagenic and antimutagenic activities of dichloromethane extract of *G. volkensii* bark and twigs using the Ames test performed on *Salmonella typhimurium* strain TA98 and the micronucleus test. The extracts were genotoxic in the micronucleus test at a concentration of 100.0 µg/ml [66].

Cytotoxicity Activities

Sibandze [40] evaluated the cytotoxicity activities of acetone extracts of *G. volkensii* fruits and leaves against human kidney epithelial (Graham) cells using the 3-(4,5-dimethyl-2-thiazolyl)-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay. The fruit and leaf extracts exhibited activities with IC_{50} values of 21.3 µg/ml and 89.5 µg/ml, respectively [40].

Toxicity Activities

Juma and Majinda [61] evaluated the toxicity activities of chloroform and methanol extracts of *G. volkensii* fruits using the brine shrimp lethality test with potassium dichromate and bufadienolide scillaren A as positive controls. The chloroform and methanol extracts exhibited activities with half maximal lethal dose (LD_{50}) value of 47.9 ppm and 22.9 ppm, respectively, which were comparable to LD_{50} values of 25.4 ppm and 190.9 ppm exhibited by potassium dichromate and bufadienolide scillaren A, respectively [61].

CONCLUSION

Palmer and Pitman [3] argued that the fruits of *G. volkensii* could be poisonous and, therefore, there is need for detailed clinical and toxicological evaluations of crude extracts and compounds isolated from the species. The widespread use of *G. volkensii* as food plant and source of traditional medicines throughout its distributional range in tropical Africa suggest that the species is not taken at toxic dosages. But use of *G. volkensii* as food and for the treatment of human diseases and ailments should be treated with caution, and rigorous toxicological and clinical studies of the bark, fruits, leaves, roots and seeds, and compounds isolated from the species are necessary.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

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