Review of Pharmacological Properties, Phytochemistry and Medicinal uses of *Volkameria glabra*

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Abstract: *Volkameria glabra* (E. Mey.) Mabb. & Y.W. Yuan is a deciduous shrub or a small tree widely used as traditional medicine throughout its distributional range in tropical Africa. This study is aimed at providing a critical review of pharmacological properties, phytochemistry, and medicinal uses of *V. glabra*. Documented information on pharmacological properties, phytochemistry and medicinal uses of *V. glabra* was collected from several online sources such as Scopus, Google Scholar, PubMed 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 infusion and/or decoction of *V. glabra* are mainly used as immune booster, protective charm, anthelmintic and ethnoveterinary medicine, and traditional medicine for convulsions, fractured bones, fever, wounds, gastro-intestinal problems, snake bite and respiratory diseases. Phytochemical compounds identified from the species include aliphatic glycosides, anthraquinones, cardiac glycosides, flavonoids, iridoid, phenols, saponins, steroids, tannins and triterpenoids. The *V. glabra* and compounds isolated from the species exhibited acaricidal, anthelmintic, antibacterial, antifungal, antimycobacterial, anti-collagenase, antidiabetic, anti-elastase, anti-inflammatory, antileishmanial, antioxidant, antiplasmodial, antipyretic, cholinesterase enzyme inhibition, immune-stimulant and cytotoxicity activities. *Volkameria glabra* should be subjected to detailed phytochemical, pharmacological and toxicological evaluations aimed at correlating its medicinal uses with its phytochemistry and pharmacological activities.

Keywords: *Clerodendrum glabrum*, ethnopharmacology, indigenous knowledge, Labiatae, Lamiaceae, traditional medicine, *Volkameria glabra.*

INTRODUCTION

Volkameria glabra (E. Mey.) Mabb. & Y.W. Yuan is a member of the Lamiaceae, Labiatae, mint or sage family. The genus name *Volkameria* L. is in honour of a German botanist Johann Georg Volckamer or Volcamer (1662–1744) [1]. The species name "*glabra*" is a Latin word meaning "hairless", "bald" or "smooth", in reference to the leaves that are mostly without hairs [2]. The genus *Volkameria* (including genus *Huxleya* Ewart) was recently revived by Yuan *et al*. [3] following phylogenetic studies, which employed chloroplast DNA regions such as trnT-L, trnL-F, trnD-T and trnS-fM aimed at clarifying the generic boundaries of the genus *Clerodendrum* L. and its relationship to allied genera. As such, *V. glabra* has been treated as *Clerodendrum glabrum* E. Mey in the past and also in several recent publications [4-11]. Furthermore, *V. glabra* is wrongly referred to as *Rotheca glabrum* by Mawela *et al*. [12]. These observed taxonomic problems corroborate observations made by other researchers that erroneous nomenclature has a negative effect on ethnopharmacological research, threaten conservation initiatives and usage of plant genetic resources [13-17].

Volkameria glabra is a shrub or small to medium-sized deciduous tree growing up to 10 metres in height with branches growing upwards to form a V-shaped canopy [4]. The bark of *V. glabra* is grey-brown in colour, roughly fissured or flaking with pale lenticels. The leaves are whorled or opposite, often drooping with soft hairs below and with a pungent foul smell when crushed. Flowers of *V. glabra* are white to pink in colour, foul or sweet-scented and occur in dense and rounded terminal heads. The fruits are fleshy, round, yellowish-white in colour, and surrounded by withered persistent cup-like calyx. *Volkameria glabra* has been recorded in the bushveld, riverine thickets, rocky hillsides, coastal dunes, forest margins, and evergreen coastal thickets. *Volkameria glabra* has been recorded in Angola, Botswana, the Democratic Republic of Congo (DRC), Eswatini, Kenya, Mozambique, Namibia, Somalia, South Africa, Tanzania, Seychelles and Comoros at an altitude ranging from sea level to 1600 m above sea level [3,5,6,8,18-27]. Synonyms associated with the name *V. glabra* include *C. glabrum*, *C. capense* D. Don ex Steud., *C. capense* Eckl. & Zeyh. ex Schauer, *C. glabratum* Gürke, *C. glabrum* var. *minutiflorum* (Baker) Fosberg, *C. glabrum* f. *pubescens* R. Fern., *C. minutiflorum* Baker, *C. ovale* Klotzsch, *C. ovalifolium* Engl., *C. rehmannii* Gürke, *C. somalense* Chiov., *Premna suaveolens* Chiov. and *Siphonanthus glaber* (E. Mey.) Hiern. [3,5,8,19,25]. *Volkameria glabra* is widely used as traditional medicine in southern

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Table 1: Medicinal uses of *Volkameria glabra*

Medicinal use	Part used	Country	Reference
Anal prolapse	Leaves	Eswatini and South Africa	[37,38]
Angina pain	Leaves	South Africa	[39,40]
Anthelmintic	Bark, leaves and roots	Eswatini, South Africa and Tanzania	[2,11,37,41,42]
Anthelmintic	Leaves mixed with those of *Brachylaena discolor* DC., *Ekebergia capensis* Sparrm., *Clausena anisata* (Willd.) Hook. f. ex Benth., *Zanthoxylum capense* (Thunb.) Harv. and roots of *Cymbopogon marginatus* (Steud.) Stapf ex Burtt-Davy, *Erythrophleum lasianthum* Corbishley, *Margaritaria discoidea* (Baill.) Webster and *Hypoxis* spp.	South Africa	[32,33]
Aphonia	Leaves	South Africa	[40,43]
Candidal infections	Bark and roots	South Africa	[44]
Colic	Leaves	Eswatini	[37]
Convulsions	Leaves	South Africa	[11,33,41]
Dropsy	Roots mixed with those of *Tetradenia riparia* (Hochst.) Codd	South Africa	[33]
Energy booster	Roots mixed with those of *Polianthes tuberosa* L., *Rotheca myricoides* (Hochst.) Steane & Mabb. and *Senna occidentalis* L.	South Africa	[28]
Fever	Leaves and roots	DRC and South Africa	[33,41,45,46]
Fever	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[31]
Fractured bones	Root bark	South Africa	[33,47,48]
Gastro-intestinal problems (bloody stool and stomachache)	Leaves	Eswatini and South Africa	[34,49,50]
Diarrhoea and bloody stool	Leaves mixed with bark of *Protorhus longifolia* (Bernh.) Engl. and *Psidium guajava* L.	South Africa	34,35]
Gastro-intestinal problems	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[31]
Immune booster	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[28-31]
Inflammation	Roots	South Africa	[51]
Loss of appetite and weight	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[31]
Mouth ulcers	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[31]
Protective charm (against bad luck, spirits and witchcraft)	Leaves	South Africa and Zimbabwe	[2,33,38,48,52]
Rash	Leaves	Zimbabwe	[52]
Respiratory diseases (asthma, chest infections, colds, coughs, sinusitis, sore throat and tuberculosis)	Leaves and roots	DRC, Eswatini and South Africa	[2,11,33,34,37-41,45,48,53-55]
Cough	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[31]
Rheumatism	Leaves	South Africa	[41]
Rheumatism	Roots mixed with those of *Tetradenia riparia*	South Africa	[33]
Sexual dysfunction	Roots	Tanzania	[42]

(Table 1). Continued.

Medicinal use	Part used	Country	Reference
Snake bite	Leaves and roots	DRC, Eswatini and South Africa	[2,33,37,38,41,56]
Toothache	Leaves	Zimbabwe	[52]
Wasting conditions	Roots mixed with those of *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis*	South Africa	[28]
Wounds	Leaves	Eswatini and South Africa	[37,38,41]
Ethnoveterinary medicine (anthelmintics, diarrhoea, purgative, wounds, tick and insect-repellent)	Leaves	DRC and South Africa	[2,12,33,38,41,55,57,58]
Infertility	Leaves mixed with those of *Sansevieria pearsonii* N.E.Br.	Zimbabwe	[36]

Africa, and the species is an ingredient of some formulas, prescriptions or herbal concoctions (Table **1**). In the last 20 years, several researchers conducted ethnopharmacological research on a herbal concoction known as "phela" consisting of *V. glabra* mixed with *Polianthes tuberosa* L. (family Asparagaceae), *Rotheca myricoides* (Hochst.) Steane & Mabb. (family Lamiaceae) and *Senna occidentalis* L. (family Fabaceae) [28-31]. Thus, the aim of this review is to provide an integrated and detailed appraisal of the existing knowledge on the pharmacological properties, phytochemistry, and ethnomedicinal uses of *V. glabra* in an attempt to unravel and explore the therapeutic potential of this species.

Medicinal uses

The bark, leaf and root infusion and/or decoction of *V. glabra* are mainly used as an immune booster, protective charm, anthelmintic and ethnoveterinary medicine, and traditional medicine for convulsions, fractured bones, fever, wounds, gastro-intestinal problems, snake bite and respiratory diseases (Table **1**; Figure **1**). The leaves of *V. glabra* are mixed with those of *Brachylaena discolor* DC., *Ekebergia capensis* Sparrm., *Clausena anisata* (Willd.) Hook. f. ex Benth., *Zanthoxylum capense* (Thunb.) Harv. and roots of *Cymbopogon marginatus* (Steud.) Stapf ex Burtt-Davy, *Erythrophleum lasianthum* Corbishley, *Margaritaria discoidea* (Baill.) Webster and *Hypoxis* spp. and used as anthelmintic [32,33]. The roots of *V. glabra* are mixed with those of *Tetradenia riparia* (Hochst.) Codd and used as traditional medicine against dropsy [33] or mixed with roots of *Polianthes tuberosa* L., *Rotheca myricoides* (Hochst.) Steane & Mabb. and *Senna occidentalis* L. and used as an energy booster, immune booster, and a traditional medicine for gastro-intestinal

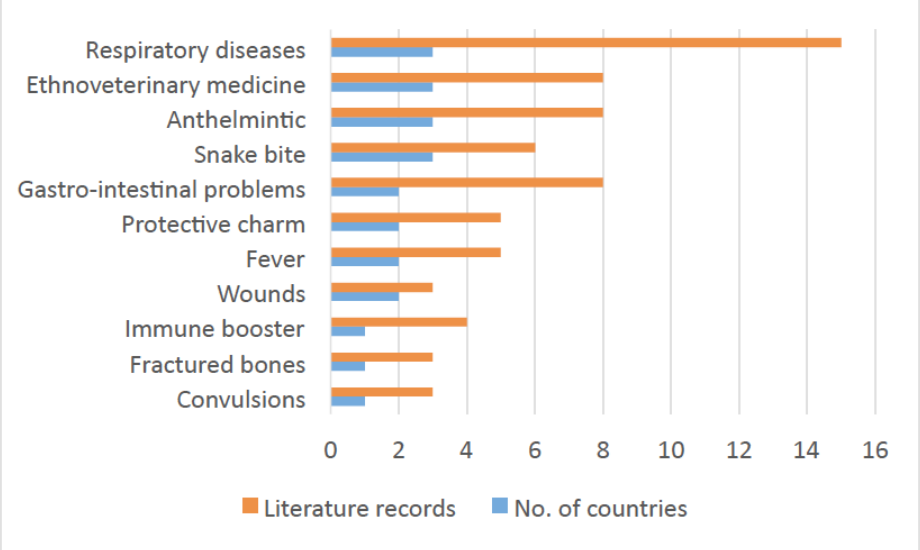

Figure 1: Medicinal applications of *Volkameria glabra* derived from literature records.

problems, cough, mouth ulcers, wasting conditions, loss of appetite and weight [28-31]. The leaves of *V. glabra* are mixed with bark of *Protorhus longifolia* (Bernh.) Engl. and *Psidium guajava* L. as traditional medicine for diarrhoea and bloody stool [34,35]. The roots of *V. glabra* are mixed with those of *Tetradenia riparia* (Hochst.) Codd as a traditional medicine for rheumatism [33] and the leaves are mixed with those of *Sansevieria pearsonii* N.E.Br. as ethnoveterinary for infertility [36].

Nutritional and Phytochemical Composition

Wilson and Downs [59] investigated the nutritional properties of *V. glabra* fruits (Table **2**). Amusan *et al*. [49] and Ogundajo and Ashafa [60] identified anthraquinones, cardiac glycosides, flavonoids, phenols, polyphenols, saponins, steroids, tannins and terpenoids from the leaves of *V. glabra*. From an extract of the leaves and stem bark of *V. glabra*, Fouad *et al.* [61], Masevhe *et al.* [62], Wanas *et al.* [63] and Teclegeorgish [64] isolated aliphatic glycosides, iridoid, phenolics, phytosterol and triterpenoids (Table **2**). Some of these chemical compounds may be responsible for the biological activities of the species.

Pharmacological Properties of *Volkameria glabra*

The following pharmacological activities have been documented from the bark, fruits, leaves, roots and stems, and the compounds isolated from *V. glabra*:

Table 2: Nutritional and Phytochemical Composition of *Volkameria glabra*

Phytochemical compound	Value	Plant part	Reference
Nutritional components			
Glucose (mg/g)	55.0	Fruits	[59]
Fructose (mg/g)	36.5	Fruits	[59]
Lipid content (%)	3.5	Fruits	[59]
Protein content (%)	8.4	Fruits	[59]
Sucrose (mg/g)	9.8	Fruits	[59]
Water content (%)	81.3	Fruits	[59]
Aliphatic glycosides			
N-butyl-β-D-fructofuranoside	-	Leaves	[61,63]
N-butyl-β-D-fructopyranoside	-	Leaves	[61,63]
N-butyl-α-D-fructofuranoside	-	Leaves	[61,63]
Iridoid			
2'-**O**-(β-D-apiofuranosyl)-mussaenosidic acid	-	Leaves	[61,63]
Phenolics			
3,5-Dimethoxy-benzoic acid	-	Leaves	[61,63]
3-(4-Hydroxy-3-methoxy-phenyl)-acrylic acid	-	Leaves	[63]
Ferulic acid	-	Leaves	[61]
Phytosterol			
Stigmasta-5-22-dien-3β-ol	-	Leaves and stem bark	[64]
Triterpenoids			
3β-Olean-12-en3-yl palmitate	-	Leaves and stem bark	[64]
3β-hydroxy-5-glutinene	-	Leaves and stem bark	[64]
3β-lup-20(29)-en3-ol	-	Leaves and stem bark	[64]
Clerodendrumic acid	-	Leaves	[62]
Heptadecanoic acid	-	Leaves	[62]
Other phytochemical compounds			
Total flavonoid (mg quercetin/g)	22.6 – 47.0	Leaves	[60]
Total flavanol (mg rutin/g)	17.9 – 173.7	Leaves	[60]
Total phenol (mg gallic acid/g)	61.5 – 66.0	Leaves	[60]

acaricidal, anthelmintic, antibacterial, antifungal, antimycobacterial, anti-collagenase, antidiabetic, anti-elastase, anti-inflammatory, antileishmanial, antioxidant, antiplasmodial, antipyretic, cholinesterase enzyme inhibition, immune-stimulant and cytotoxicity activities.

Acaricidal Activities

Mawela *et al.* [12] evaluated the acaricidal activities of methanol, acetone, dichloromethane, soap-water and water-based extracts of *V. glabra* leaves against the adult stage of the livestock tick *Rhipicephalus appendiculatus* with Amitix and Bayticol as positive controls. The hexane fraction from acetone extract exhibited a higher tick repellent activity than the positive controls at the same concentrations [12].

Anthelmintic Activities

McGaw *et al.* [65] evaluated the anthelmintic activities of hexane, ethanol and water extracts of *V. glabra* leaves on the mortality and reproductive ability of the free-living nematode *Caenorhabditis elegans* in two different assays. Ethanol and water extracts exhibited activities at a concentration of 1.0 mg/ml and 2.0 mg/ml after the two and seven days incubation period [65]. Adamu *et al.* [66] evaluated the anthelmintic activities of the acetone extract of *V. glabra* using the egg hatch assay and the larval development tests using *Haemonchus contortus* with albendazole as positive control. The extract exhibited activities with half maximal effective concentration (EC_{50}) values of 1.5 mg/ml and 13.0 mg/ml for the egg hatch and the larval development assays, respectively [66].

Antibacterial Activities

Adamu *et al.* [67] evaluated the antibacterial activities of acetone extracts of *V. glabra* leaves against *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Enterococcus faecalis* using a serial microdilution method with gentamicin as a positive control. The extract exhibited activities with minimum inhibitory concentration (MIC) values ranging from 0.3 mg/ml to 1.3 mg/ml in comparison to a MIC value of <0.02 mg/ml exhibited by the positive control [67]. Masevhe *et al.* [62] evaluated the antibacterial activities of fractions of the hexane extract of *V. glabra* leaves and the compounds clerodendrumic acid and heptadecanoic acid isolated from the species against *Staphylococcus aureus, Pseudomonas aeruginosa, Enterococcus faecalis* and *Escherichia coli* using twofold serial microdilution method with gentamicin as a positive control. Both the fractions and compounds exhibited activities with the MIC values ranging from 0.2 mg/ml to 1.3 mg/ml and 125.0 µg/ml to 188.0 µg/ml, respectively [62].

Antifungal Activities

Adamu *et al.* [68] evaluated the antifungal activities of acetone extract of *V. glabra* leaves against *Aspergillus fumigatus, Cryptococcus neoformans* and *Candida albicans* using serial microdilution method. The extract exhibited activities with MIC values ranging from 0.04 mg/mL to 0.6 mg/mL [68]. Fouad *et al.* [61] evaluated the antifungal activities of the compounds n-butyl-β-D-fructofuranoside, n-butyl-β-D-fructopyranoside, n-butyl-α-D-fructofuranoside, 2'-O-(β-D-apiofuranosyl)-mussaenosidic acid, ferulic acid and 3,5 dimethoxy benzoic acid isolated from the leaves of *V. glabra* against *Mucor racemosus* using the broth microdilution method with amphotericin B as a positive control. Only compound 2'-O-(β-D-apiofuranosyl)-mussaenosidic acid exhibited activities with half-maximal inhibitory concentration (IC_{50}) value of 5.5 µg/ml in comparison to an IC_{50} value of 0.4 µg/ml exhibited by the positive control [61]. Masevhe *et al.* [62] evaluated the antifungal activities of fractions of the hexane extract of *V. glabra* leaves and the compounds clerodendrumic acid and heptadecanoic acid isolated from the species against *Candida albicans, Cryptococcus neoformans* and *Aspergillus niger* using twofold serial microdilution method with amphotericin B as positive control. Both the fractions and the compounds exhibited activities with the MIC values ranging from 0.1 mg/ml to 0.6 mg/ml and 125.0 µg/ml to 188.0 µg/ml, respectively [62].

Antimycobacterial Activities

Dzoyem *et al.* [69] evaluated the antimycobacterial activities of acetone leaf extracts of *V. glabra* against *Mycobacterium smegmatis, Mycobacterium aurum and Mycobacterium fortuitum* and *Mycobacterium tuberculosis* using the broth microdilution method with isoniazid and rifampicin as positive controls. The extract exhibited activities against tested pathogens with the MIC values ranging from 0.2 mg/mL to 0.6 mg/mL and total activity ranging from 7.3 mL/g to 29.2 mL/g [69].

Anti-Collagenase Activities

Ndlovu *et al.* [70] evaluated the anti-collagenase activities of methanol and ethyl acetate extracts of

bark, fruits, roots and stems of *V. glabra* by assessing the anti-collagenase assay using the spectro-photometric methods with ethylenediaminetetraacetic acid (EDTA) as positive control. The ethyl acetate extract of the bark and stems inhibited collagenase activity by more than 80.0%, which was comparable to an activity of 83.8% exhibited by the control [70].

Antidiabetic Activities

Ogundajo and Ashafa [60] evaluated the antidiabetic activities of aqueous, hexane, ethyl acetate and methanol extracts of *V. glabra* leaves using the α-amylase inhibitory and α-glucosidase inhibitory assays with acarbose as a positive control. The extracts exhibited activities against α-amylase and α-glucosidase with IC_{50} values ranging from 0.7 mg/mL to 2.5 mg/mL and 0.2 mg/mL to 2.8 mg/mL, respectively [60].

Anti-Elastase Activities

Ndlovu *et al.* [70] evaluated the anti-elastase activities of methanol and ethyl acetate extracts of bark, fruits, roots and stems of *V. glabra* by assessing the anti-elastase assay using the spectrophotometric methods with N-Methoxysuccinyl-Ala-Ala-Pro-Chloro (10.0 µg/ml) as positive control. The ethyl acetate extract of the bark, fruits and stems inhibited elastase activity by more than 81.5% to 89.4%, which was comparable to an activity of 91.5% exhibited by the control [70].

Anti-Inflammatory Activities

Jäger *et al.* [51] evaluated the anti-inflammatory activities of aqueous and ethanolic extracts of *V. glabra* roots in an *in vitro* assay for cyclooxygenase (COX) inhibitors with indomethacin (0.5 µg) as a positive control. The ethanolic extract exhibited an inhibition of 88.0% which was higher than 66.5% inhibition exhibited by the indomethacin control [51]. Wahba *et al.* [71] evaluated the anti-inflammatory activities of the methanol and chloroform extracts of *V. glabra* leaves using the carrageenan-induced rat paw edema assay. The rat groups that received the methanol extract at an oral dose of 100.0 mg/kg body weight exhibited activities of about 56.0% to 63.0% of indomethacin after 4 hours [71].

Antileishmanial Activities

Bapela *et al.* [72] evaluated antileishmanial activities of dichloromethane and 50% methanol extracts of *V. glabra* leaves against axenically grown amastigote forms of *Leishmania donovani* following the resazurin assay protocol with miltefosine as a positive control. The dichloromethane extracts exhibited weak activities with an IC_{50} value of 13.4 µg/ml in comparison to an IC_{50} value of 0.2 µg/ml exhibited by the positive control [72].

Antioxidant Activities

Ndlovu *et al.* [70] evaluated the antioxidant activities of methanol and ethyl acetate extracts of the bark, fruits, roots and stems of *V. glabra* using the sodium aurothiomalate, 2,2'-azinobis-3-ethyl benzothiazoline 6-sulfonic acid (ABTS) radical scavenging assay with trolox as positive control. The extract exhibited activities with an IC_{50} values ranging from 10.0 µg/mL to 63.9 µg/mL in comparison to an IC_{50} value of 2.8 µg/mL exhibited by the positive control [70]. Ogundajo and Ashafa [60] evaluated the antioxidant activities of aqueous, hexane, ethyl acetate and methanol extracts of *V. glabra* leaves using ABTS, 1,1-Diphenyl-2-picrylhydrazyl (DPPH) radical scavenging, metal chelation, superoxide anion scavenging capability, hydroxyl radical scavenging and ferric ions reducing power (FRAP) assays with gallic acid and silymarin as positive controls. The extracts exhibited activities in all assays with an IC_{50} values ranging from 0.05 mg/mL to 69.1 mg/mL in comparison to an IC_{50} of 0.03 mg/mL to 29.6 mg/mL exhibited by the positive control [60]. Das *et al.* [31] evaluated the antioxidant activities of a herbal concoction of *V. glabra* mixed with *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis* using the DPPH free radical scavenging and hydroxyl radical scavenging assays with ascorbic acid as positive control. In DPPH, the concoction exhibited an IC_{50} value of 105.9 µg/ml in comparison to an IC_{50} value of 93.2 µg/ml exhibited by the positive control. In hydroxyl radical scavenging assay, the concoction exhibited an IC_{50} value of 108.0 µg/ml in comparison to an IC_{50} value of 98.7 µg/ml exhibited by the positive control [31].

Antiplasmodial Activities

Clarkson *et al.* [73] evaluated antiplasmodial activities of aqueous and dichloromethane : methanol (1:1) extracts of *V. glabra* twigs against *Plasmodium falciparum* using the parasite lactate dehydrogenase assay. The dichloromethane: methanol (1:1) extract exhibited weak activities with IC_{50} values of 19.0 µg/ml [73]. Bapela *et al.* [74,75] evaluated the antiplasmodial activities of dichloromethane and 50% methanol extracts of *V. glabra* using the [^{3}H]-hypoxanthine

incorporation assay using chloroquine-sensitive (NF54) strain of Plasmodium falciparum as the test organism with chloroquine as positive control. The dichloromethane extract exhibited weak activities with an IC_{50} value of 8.9 µg/ml in comparison to an IC_{50} value of 0.003 µg/ml exhibited by the positive control [74,75].

Antipyretic Activities

Wahba *et al.* [71] evaluated the antipyretic activities of the methanol and chloroform extracts of *V. glabra* leaves using the yeast-induced hyperthermia method on female Albino rats of Sprague-Dawley strain with paracetamol as the standard drug. The rat group that received methanol extract at an oral dose of 100.0 mg/kg body weight exhibited activities of about 57.0% of paracetamol after 1 hour and about 55.0% of paracetamol activity after 2 hours [71].

Cholinesterase Enzyme Inhibition Activities

Das *et al.* [31] evaluated the cholinesterase enzyme inhibition activities of a herbal concoction of *V. glabra* mixed with *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis* using a 96-well micro plate method based on Ellman's colorimetric assay with galantamine as a positive control. The concoction exhibited activities with IC_{50} value of 257.9 µg/ml in comparison to IC_{50} value of 20.2 µg/ml exhibited by the positive control [31].

Immune-Stimulant Activities

Lekhooa *et al.* [28] evaluated the immune-stimulant activities of a herbal concoction of *V. glabra* mixed with *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis* by assessing the subclinical changes in Th1 cytokines (IL-2, IFN-γ and TNF-α) and Th2 cytokines (IL-4 and IL-10) in Sprague Dawley rats. The rats were treated daily and separately with normal-saline, cyclosporine-A, extract only and extract + cyclosporine-A, and after 7 and 14 days of treatment, the serum Th1 cytokines and Th2 cytokines were measured by ELISA. The extract did not stimulate Th1 cytokines of a normal immune system but stimulated them when the immune system was suppressed by cyclosporine-A [28]. Lekhooa *et al.* [30] evaluated the immune-stimulant activities of a herbal concoction of *V. glabra* mixed with *Polianthes tuberosa, Rotheca myricoides* and *Senna occidentalis* by assessing the effect of the extract on cyclosporine A, cyclophosphamide and dexamethasone induced immunosuppression in Sprague Dawley rats. The effective dose of the extract was determined to be 15.4 mg/kg/day, which led to a moderate increase in the immune parameters in the normal rats [30].

Cytotoxicity Activities

Adamu *et al.* [66] evaluated the cytotoxicity activities of acetone extract of *V. glabra* against African Green Monkey kidney (Vero) cells using the tetrazolium-based colorimetric MTT (3-5-dimethyl thiazol-2-yl-2, 5-diphenyl tetrazolium bromide) assay. The extract exhibited activities with half maximal lethal concentration (LC_{50}) value of 0.04 mg/ml [66]. Adamu *et al.* [68] evaluated the cytotoxicity activities of acetone extracts of *V. glabra* leaves against Vero monkey kidney cells using the tetrazolium-based colorimetric MTT assay. The extract exhibited activities with half maximal lethal dose (LD_{50}) value of 0.2 mg/mL [68]. Fouad *et al.* [61] evaluated the cytotoxicity activities of the compounds n-butyl-β-D-fructofuranoside, n-butyl-β-D-fructopyranoside, n-butyl-α-D-fructofuranoside, 2'-O-(β-D-apiofuranosyl)-mussaenosidic acid, ferulic acid and 3,5 dimethoxy benzoic acid isolated from the leaves of *V. glabra* against the human lung cancer cell line A549 using the MTT assay. Only compound 2'-O-(β-D-apiofuranosyl)-mussaenosidic acid exhibited activities with an IC_{50} value of 51.1 µg/ml [61]. Bapela *et al.* [72,74,75] evaluated the cytotoxicity activities of dichloromethane and 50% methanol extract of *V. glabra* leaves against mammalian L-6 rat skeletal myoblast cells with podophyllotoxin as positive control. The dichloromethane and 50% methanol extracts exhibited IC_{50} values of 62.2 µg/ml and 72.7 µg/ml, respectively, which were considered to be non-toxic to rat skeletal myoblast L6 cells [72,74,75]. Dzoyem *et al.* [69] evaluated the cytotoxicity activities of acetone leaf extracts of *V. glabra* against Vero cells using the MTT assay with doxorubicin as a positive control. The extract exhibited the LC_{50} value of 357.1 µg/mL in comparison to the LC_{50} value of 4.5 µg/mL exhibited by the positive control, implying that the plant extracts screened could be considered as relatively safe [69]. Mehrbod *et al.* [76] evaluated the cytotoxicity activities of methanol extracts of *V. glabra* leaves against MDCK cells using the MTT assay. The extract exhibited activities with half maximal cytotoxic concentration (CC_{50}) value of 221.0 µg/ ml [76]. Ogundajo and Ashafa [60] evaluated the cytotoxicity activities of aqueous, hexane, ethyl acetate and methanol extracts of *V. glabra* leaves against the Vero monkey kidney cells using the tetrazolium-based colorimetric assay (MTT assay). The extracts exhibited activities with the LC_{50} values ranging from 0.1 mg/mL to 0.5 mg/mL [60].

CONCLUSION

Research on *V. glabra* over the past decades showed that the species is an important traditional medicine in east, central and southern Africa. The species is also an ingredient of some formulas, prescriptions or herbal concoctions. Therefore, future research should also evaluate the combinational, additive, and synergetic effects associated with complex herbal concoctions that have *V. glabra* as an ingredient. These evaluations should aim at correlating the medicinal uses of the species with its phytochemistry and pharmacological activities.

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