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Phytochemical and ethnopharmacological review of *Elephantorrhiza goetzei* (Harms) Harms

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ABSTRACT

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Keywords: Africa Anthelmintic Antimicrobial Antioxidant Elephantorrhiza goetzei Primary healthcare Elephantorrhiza goetzei (E. goetzei) commonly known as Goetze's elephantorrhiza, is traditionally used as a decoction in the treatment of a variety of conditions such as pain, sores, sexually transmitted infections (STIs), gastro-intestinal disorders, microbial infections and genito-urinary system disorders. On the basis of its wide distribution in south central Africa, E. goetzei has a long history of applications among the different ethnic groups. A total of 23 ethnomedicinal uses of E. goetzei are documented in this study from 62.5% of the countries where the species is indigenous. Multiple classes of phytochemicals including phenolic compounds, coumarins, flavonoids, saponins, stilbenoids, tannins and triterpenoids have been identified from E. goetzei bark, leaves and roots in different investigations. Scientific validation of its diverse uses in traditional medicine has been demonstrated through antibacterial, antifungal, antiviral, anthelmintic, antioxidant and cytotoxicity assays of crude extracts as well as isolated compounds from the species. E. goetzei has been widely used as a source of herbal medicine for several years without any adverse effects. In light of its long traditional use and the modern phytochemical and pharmacological evaluations summarized in this study, E. goetzei has been demonstrated to show a strong potential for therapeutic and health-maintaining uses. However, there is need for additional studies on the isolated compounds to validate the traditional uses in human models as well as evaluating the possible mechanisms of action. The present review focussing on the biology, traditional uses, phytochemistry and pharmacological properties of E. goetzei has provided preliminary information for further studies on the species.

1. Introduction

Traditional medicines play an important role in primary health care of both rural and urban communities as well as the development of pharmaceutical drugs and health products. About 80% of people in rural communities in developing countries rely on traditional medicines [1] as an integral part of their culture and also because traditional medicines are affordable and easily accessible. The world market for herbal medicines including herbal products and raw materials is estimated to be growing at a rate of 15% per annum with large multinational companies interested in commercializing herbal drugs [2]. Pharmaceutical drugs and health products derived from plants are gaining popularity and use worldwide as complementary and alternative health products [1] as well as

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nutraceuticals and cosmeceuticals. According to van Wyk et al. [3] natural products and their derivatives represent more than 50% of all drugs in clinical use in the world and wellknown examples of such plant-derived medicines include quinine, morphine, codeine, aspirin, atropine, reserpine and cocaine. There is a growing realization worldwide that traditional medicines based on indigenous medical systems such as African Traditional Medicine, Ayurveda, Native American Medicine, Traditional Chinese Medicine and Unani are potential sources of natural products that can be developed into pharmaceutical drugs and products. Therefore, the traditional knowledge-inspired natural product drug discovery is reemerging as an attractive option. But Mukherjee et al. [2] argued that the major challenge for the development and promotion of traditional medicine include the chemoprofiling, safety evaluations, quality control and effective regulatory guidelines for traditional medicines. It is within this context that the ethnomedicinal uses of Elephantorrhiza goetzei (E. goetzei) (Harms) Harms of the Fabaceae family were



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evaluated throughout its distributional range as well as ethnopharmacological evaluations done so far, emphasizing the correlations between the ethnomedicinal uses of the species and its phytochemistry and pharmacological properties.

2. Methodology of the review

The literature search was performed from March to December 2016 using electronic search engines such as Google, Google scholar, publishing sites such as Elsevier, scienceDirect, BioMed Central (BMC) and PubMed. The databases and literature sources were chosen based on the topic covered (i.e., ethnobotany, ethnomedicinal uses, ethnopharmacology, pharmacology, phytochemistry and therapeutic value) and geographical coverage (i.e., Africa). The following keywords were used to search literature sources: Elephantorrhiza goetzei, Elephantorrhiza elongata, Elephantorrhiza rubescens, Piptadenia goetzei, long-pod cassia, narrow-rod elephant root, Goetze's elephantorrhiza, narrow-pod elephant-root and false sumach bean. Other literature sources included papers published in international journals, reports from international, regional and national organizations, conference papers, books, theses, websites and other grey literature. References were also identified by searching the library collections of the National Herbarium and Botanic Gardens (SRGH), Harare, Zimbabwe and the University of Fort Hare, South Africa.

3. Species description

E. goetzei, commonly known as Goetze's elephantorrhiza is a small, deciduous tree or shrub growing in Botswana, Malawi, Mozambique, Namibia, South Africa, Tanzania, Zambia and Zimbabwe. Synonyms of E. goetzei include Elephantorrhiza elongata Burtt Davy, Elephantorrhiza rubescens Gibbs and Piptadenia goetzei Harms. The generic name 'Elephantorrhiza' means 'elephant root' in reference to large underground stem common to some members of this genus [4]. The specific name 'goetzei' honours Walter Goetze (1872-1899), a German naturalist, explorer, photographer and collector of botanical and zoological specimens in East Africa who died there in 1899 [4]. E. goetzei is multi-stemmed with brown or reddish bark and smooth dark twigs with conspicuous lenticels. The annual stems of nearly one metre in height grow from an enormous underground rhizome of up to seven metres long [5]. The finely divided leaves have numerous small, narrow leaflets with clusters of small, cream-coloured flowers produced along the lower half of the aerial stem [4]. The characteristic pods are up to 30 cm long, with the inner parts breaking free and peeling off from the persistent margins [5]. The species is divided into two subspecies based on distribution and leaf characteristics. E. goetzei subsp. goetzei is the most widespread species recorded from Tanzania to South Africa and has 14-41 pairs of pinnae, each bearing 20-48 pairs of leaflets measuring up to 1.2 cm long [5]. E. goetzei subsp. lata Brenan & Brummit has been recorded in the north and west of Zimbabwe, is characterized by 4-15 pairs of pinnae, each bearing 9-28 pairs of leaflets of up to 2.2 cm long [5]. Most published literature, ethnobotany researchers, traditional healers and local communities do not separate E. goetzei into subspecies, but rather to E. goetzei sensu lato, and the same approach has been adopted in this study. E. goetzei is recorded in the

Red Data List of Namibia as data deficient by Craven and Loots [6] and Klaassen, and Kwembeya [7] because there is inadequate information to make a direct or indirect assessment of its risk of extinction based on its distribution and/or population status. These authors argued that listing of *E. goetzei* in this category in Namibia indicates that more information is required and acknowledges the possibility that future research will show that threatened classification is appropriate.

4. Vernacular names and ethnomedicinal uses of *E. goetzei*

E. goetzei is known by several vernacular names in its geographical areas of occurrence (Table 1). Literature survey showed no fewer than 17 common or vernacular names for E. goetzei (Table 1). Zimbabwe has the highest number of common or vernacular names (eight in total) followed by Botswana with seven and South Africa with three names, and the rest of the countries have either one or two names (Table 1). A vernacular name often describes the history, some characteristic feature of the plant species or the plant parts, for example 'Goetze's elephantorrhiza', 'narrow-pod elephant-root', 'narrow-rod elephant root', 'bastard sumach bean' or 'false sumach bean' (Table 1). This English name 'Goetze's elephantorrhiza' is in honour of Walter Goetze, a German plant collector who first collected this species on his journey from Dar es Salaam in Tanzania to Lake Malawi where he died of blackwater fever [18]. The other English common names, 'narrow-pod elephant-root' and 'narrow-rod elephant root' are in reference to long and flat pods, sometimes measuring 30 cm long and up to 4 cm broad and also large and long roots up to 8 m long [4]. The common names 'bastard sumach bean' and 'false sumach bean' translate into 'false sumach bean', because E. goetzei superficially resembles a closely related species 'sumach bean' (Elephantorrhiza burkei Benth.). The common Afrikaans names 'basterbasboontjie' and 'smalpeulbasboontjie' are based on the use of this species in tanning [4]. E. goetzei roots are traded in informal medicinal markets in Zimbabwe [19]. More research needs to be carried out in Tanzania, where documentation of vernacular names and ethnomedicinal uses of E. goetzei are missing.

Table 1

Vernacular names of Elephantorrhiza goetzei.

Vernacular (ethnic group or geographical region)	Country	Refs
Bastard sumach bean, large bean elephant root (English), mereko, mosidi, mosidigodimo, mositsane, mudamba (Setswana)	Botswana	[8,9]
Chiteta (Ngoni), thetha (Sena)	Malawi	[10,11]
Churai, mussambanhanga	Mozambique	[12]
(ChiTewe/chiNdau)		
Basterbasboontjie (Afrikaans),	Namibia	[13]
narrow-pod elephant-root (English)		
Smalpeulbasboontjie (Afrikaans), Goetze's	South Africa	[4,5]
elephantorrhiza, narrow-pod elephant-root,		
false sumach bean (English)		
Long-pod cassia, narrow-rod elephant root	Zimbabwe	[14–17]
(English), ililamba, intolwane (Ndebele),		
chiurayi, mugudzuru, muzezepasi, ntorani		
(Shona)		

The underground rhizomes of E. goetzei, commonly referred to as roots and bark are reported to possess diverse medicinal properties and used to treat or manage various human ailments and diseases throughout its distributional range (Table 2). A total of 23 ethnomedicinal uses of E. goetzei are documented in literature (Table 2) from five countries in southern Africa, representing 62.5% of the countries where the species is indigenous. The country with the highest number of ethnomedicinal uses is Zimbabwe [13] based on seven literature records, followed by Mozambique with eight uses and two literature records, Malawi with five uses and three literature record, Botswana and South Africa with four uses and two literature records each. E. goetzei is mainly used to treat pain and sores (eight citations in three countries), followed by sexually transmitted infections (eight citations in three countries), gastro-intestinal disorders (seven citations in three countries), infections (four citations in two countries) and genitourinary system disorders (three citations in two countries) (Table 2). These records show high degree of consensus for the major diseases and ailments (Table 2) and imply high cross-cultural agreement among ethnomedicinal uses of E. goetzei throughout its distributional range.

Table 2						
Traditional	uses	of	Elepl	hantor	rrhiza	goetzei

Use	Plant part(s) used and preparation	Country	Refs
Abdominal pain	Root powder taken orally or taken in porridge	Malawi, Mozambique, Zimbabwe	[14,15,20,21]
Anthelmintic	Root infusion taken orally	Zimbabwe	[14]
Aphrodisiac	Part of herbal mixture including roots of <i>Albizia antunesiana</i> Harms, bark of <i>Mondia whitei</i> (Hook.f.) Skeels, stem bark of <i>Ozoroa insignis</i> Delile, <i>Pouzolzia mixta</i> Solms and <i>Senna</i> <i>singueana</i> (Delile) Lock)	Zimbabwe	[22]
Backache	Bark or root decoction taken orally	Mozambique, Zimbabwe	[12,20]
Bilharzia	Root decoction taken orally or mixed with root of <i>Piliostigma</i> <i>thonningii</i> (Schumach.) Milne-Rehd. and infusion taken orally	Malawi, Zimbabwe	[10,15,20,23]
Bloody vomit	Bark or root decoction taken orally	Mozambique	[12]
Boils	Root macerate taken orally	Malawi	[11]
Cleanser and purifier	Powdered root mixed with powdered seed of <i>Citrullus</i> <i>lanatus</i> (Thunb.) Mastum. & Nakai and powdered <i>Mylabris</i> <i>oculata</i> Thunb. taken orally	South Africa	[4]
Constipation	Root infusion taken orally	Zimbabwe	[20]
Cough	Bark or root decoction taken orally	Mozambique	[12]
Depressed fontanelle	Root infusion taken orally	Zimbabwe	[14,20]
Diarrhoea	Bark or root decoction, infusion or macerate taken orally	Malawi, Mozambique, Zimbabwe	[11,12,14,15,20,21]
Fever	Root infusion taken orally and patient sits naked in a dish of the infusion	Zimbabwe	[20]
General weakness	Bark or root cooked as food and taken orally	Mozambique	[12]
Gonorrhoea	Root infusion taken mixed with roots of <i>Annona stenophylla</i> Engl. & Diels and <i>Securidaca longepedunculata</i> Fresen. taken orally	South Africa	[24]
Gonorrhoea	Root decoction or infusion taken orally	Zimbabwe	[15,20]
Heart pains	Root infusion taken orally	Zimbabwe	[20]
High blood pressure	Root decoction taken orally	Botswana	[9]
Malaria	Root infusion taken orally	Zimbabwe	[16]
Menstruation problems	Root decoction taken orally mixed with milk	Botswana	[25]
Painful uterus	Root infusion taken orally	Zimbabwe	[20]
Sores of the penis and vulva	Root decoction taken orally	Botswana	[25]
Stomachache	Root macerate taken orally or bark or roots cooked as food and taken orally	Malawi, Mozambique	[11,12]
Syphilis	Root infusion taken mixed with roots of Annona stenophylla	South Africa	[24]
Syphilis	Root infusion taken orally or mixed with roots of <i>Annona</i> stenophylla	Zimbabwe	[14,18]
To increase blood	Root infusion taken orally	Zimbabwe	[14,20]
Venereal diseases	Bark or roots decoction taken orally	Mozambique, Zimbabwe	[12,14]
Womb problems	Root decoction taken orally mixed with milk	Botswana	[25]

The root powder of E. goetzei is taken orally in porridge as remedy for abdominal pains in Malawi, Mozambique and Zimbabwe [20]. Root infusion of E. goetzei is taken orally as an anthelmintic and remedy for depressed fontenelle in Zimbabwe [14]. In Zimbabwe, root infusion is taken as remedy for backache [20], while in Mozambique, bark and root decoction of E. goetzei is taken orally for backache [12]. In Malawi and Zimbabwe, root decoction is taken orally as remedy for bilharzia [10,23], while in some cases in Zimbabwe, the roots of E. goetzei are mixed with roots of Piliostigma thonningii (Schumach.) Milne-Rehd. into an infusion which is taken orally [15,20]. Research by Bruschi et al. [12] showed that either the bark or root decoction of E. goetzei is taken orally in Mozambique as remedy for bloody vomit, cough and general body weakness. In Zimbabwe, the root infusion of E. goetzei is taken orally as remedy for fever and malaria [16,20] or the patient is made to sit naked in a dish with root infusion as treatment for fever [20]. In Zimbabwe, the root infusion of E. goetzei is taken orally as remedy for heart pains, painful uterus to increase blood in the body [20]. In Malawi, root macerate of E. goetzei is taken orally for boils [11], while in Botswana, the root decoction is taken orally as

remedy for high blood pressure [9], sores of the penis and vulva [25] or root decoction is sometimes taken orally mixed with milk for womb and menstruation problems [25].

Research by Hostettmann et al. [22] showed that the roots of E. goetzei mixed with other plant species to form a herbal concoction which is used as aphrodisiac in Zimbabwe. Other ingredients of this herbal concoction include roots of Albizia antunesiana Harms, bark of Mondia whitei (Hook.f.) Skeels, stem bark of Ozoroa insignis Delile, stem bark of Pouzolzia mixta Solms and stem bark of Senna singueana (Delile) Lock [22]. Root decoction, infusion or macerate of E. goetzei is taken orally as remedy for diarrhoea in Malawi, Mozambique and Zimbabwe [11,12,14,15,20]. In Malawi, root macerate of E. goetzei is taken orally as remedy for stomachache [11], while in Mozambique, bark or roots are cooked as food and taken orally for stomachache [12]. Root decoction or infusion of E. goetzei is taken orally as remedy for sexually transmitted infections such as gonorrhoea, syphilis and venereal diseases in Mozambique and Zimbabwe [12,14,15,20]. Research by Scmidt et al. [18] showed that in Zimbabwe, roots of E. goetzei; are sometimes mixed with those of Annona stenophylla Engl. & Diels as remedy for syphilis. In South Africa, a root infusion of Annona stenophylla mixed with roots of E. goetzei is used to treat syphilis, while roots of E. goetzei mixed with Annona stenophylla and Securidaca longepedunculata Fresen. are taken orally as remedy for gonorrhoea [24]. In South Africa, powdered root of E. goetzei mixed with powdered seed of Citrullus lanatus (Thunb.) Mastum. & Nakai and powdered Mylabris oculata Thunb. is taken as body system cleanser and purifier [4].

5. Phytochemistry

Based on literature records documenting traditional and potential medicinal uses of E. goetzei, many researchers have also investigated its phytochemical and pharmacological properties aimed at identifying the compounds responsible for its wide use as herbal medicine. Multiple classes of phytochemicals including phenolic compounds, coumarins, flavonoids, saponins, stilbenoids, tannins and triterpenoids have been identified in E. goetzei bark, leaves and roots in different investigations [26-31]. Research by Ganduri et al. [31] revealed that bark, leaves and roots of E. goetzei are widely used in Zimbabwe as an important traditional source of tannin to generate black or brown dye. Tannins are known antidiarrhoeals and antiseptics, effective in the treatment of infectious diarrhoeal disease [32]. Viol et al. [30] determined the total phenolic content (TPC) of E. goetzei root extracts by the Folin Ciocalteu reagent using gallic acid (GAE) as reference. E. goetzei showed TPC of (0.339 ± 0.084) mg/mg GAE which correlated with the antiradical activity of the species [30], confirming that the phenolics are the likely cause of the radical scavenging activity of the species. Phytochemical screening of E. goetzei roots demonstrated the presence of phenolic compounds, flavan-3-ols, stilbenoids and triterpenoids as shown in Table 3. Four compounds, 3,3',4',5,6,7,8-heptahydroxyflavan, (±)-catechin, 2-(3',4'-dihydroxyphenyl)ethanol and methyl gallate were isolated from the roots of E. goetzei by Moyo et al. [26]. Wanjala and Majinda [28] isolated 5-methoxy-(E)-resveratrol

3-O-rutinoside, 4'-methoxy-(E)-resveratrol 3-O-rutinoside, 4',5dimethoxy-(E)-resveratrol 3-O-rutinoside, gallic acid, (E)resveratrol, (E)-resveratrol 3-O-rutinoside, (\pm) -gallocatechin, arjungenin, belliricoside and sericoside from the root bark of *E. goetzei*.

Table 3

Phenolic compounds, flavan-3-ol, stilbenoid and triterpenoids isolated from *Elephantorrhiza goetzei*.

Compound		Refs
Phenolic compounds	2-(3',4'-Dihydroxyphenyl)ethanol	[26]
*	Methyl gallate	[26]
	Gallic acid	[28]
	Flavan-3-ol	
	3,3',4',5,6,7,8-Heptahydroxyflavan	[26]
	(±)-Catechin	[26]
	(±)-Gallocatechin	[28]
	Epigacatechin	[27]
Stilbenoid	5-Methoxy-(E)-resveratrol 3-O-	[28]
	rutinoside	
	(E)-Resveratrol	[28]
	(E)-Resveratrol 3-O-rutinoside	[28]
	4',5-Dimethoxy-(E)-resveratrol 3-	[28]
	O-rutinoside	
	4'-Methoxy-(E)-resveratrol 3-O-	[28]
	rutinoside	
Triterpenoids	Arjungenin	[28]
	Belliricoside	[28]
	Sericoside	[28]

6. Pharmacological activities

6.1. Antimicrobial

Moyo et al. [26] evaluated antibacterial and antifungal activities of the crude, ethyl acetate, nu-butanol, dichloromethane and aqueous extracts of E. goetzei roots against Grampositive bacteria (Bacillus subtilis, Staphylococcus aureus), Gram-negative bacteria (Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa), fungus (Candida mycoderma) and methyl gallate using the thin-layer chromatography (TLC) bioautography technique with chloramphenicol and miconazole as controls (Table 4). The investigated extractives showed weak to moderate activity against the microbes and methyl gallate [26]. Viol et al. [29] evaluated antibacterial activity of E. goetzei roots using the agar well diffusion assay method by measuring the zone of inhibition. The root extract of E. goetzei (10 mg/ mL) was active inhibiting the growth of Staphylococcus aureus (4.00 \pm 0.00) mm compared with reference amoxicillin $(10 \ \mu g) \ (9.00 \ \pm \ 0.41) \ mm \ and \ (4.50 \ \pm \ 0.58) \ mm \ against$ Staphylococcus group A compared with reference gentamicin (10 μ g) (9.25 ± 0.65) mm. Similarly, 5-methoxy-(E)-resveratrol 3-O-rutinoside and arjungenin showed weak to moderate activity against Gram-positive bacteria and fungi, while gallic acid and methyl gallate were also weakly active against Grampositive bacteria [27]. These positive antimicrobial activities somehow confirm the species' potential and usefulness in the treatment and management of bacterial infections such as diarrhoea, boils, sexually transmitted infections (STIs) and sores that have been recorded throughout the distributional range of E. goetzei.

Table 4 Summary of pharmacological activities of the extracts isolated from different parts of *Elephantorrhiza goetzei*.

Activity tested	Extract	Plant parts	Model	Effect	Refs
Antibacterial Crude,	Crude, ethyl acetate, water	Roots	TLC bioautography	All extracts showed activity at a loading of 100 µg against <i>Bacillus subtilis</i>	[26]
	Methyl gallate			Showed activity at a loading of 72 µg against Bacillus subtilis	[26]
	3,3',4',5,6,7,8-Heptahydroxyflavan			Showed activity at a loading of 15 µg against Bacillus subtilis	[26]
	Crude, water			All extracts showed activity at a loading of 100 µg against Escherichia coli	[26]
	Methyl acetate			Showed activity at a loading of 72 μ g against <i>Escherichia coli</i>	[26]
	3,3',4',5,6,7,8-Heptahydroxyflavan			Showed activity at a loading of 50 μ g against <i>Escherichia coli</i>	[26]
	Crude, water			All extracts showed activity at a loading of 100 µg against Proteus mirabilis	[26]
	Methyl gallate			Showed activity at a loading of 72 μ g against <i>Proteus mirabilis</i>	[26]
	3,3',4',5,6,7,8-Heptahydroxyflavan			Showed activity at a loading of 25 µg against Proteus mirabilis	[26]
	Crude, water			All extracts showed activity at a loading of 100 µg against <i>Pseudomonas aeruginosa</i>	[26]
	Methyl gallate			Showed activity at a loading of 70 µg against Pseudomonas aeruginosa	[26]
	3,3',4',5,6,7,8-Heptahydroxyflavan			Showed activity at a loading of 15 μ g against <i>Pseudomonas aeruginosa</i>	[26]
	Crude, water			All extracts showed activity at a loading of 100 µg against Staphylococcus aureus	[26]
	Methyl gallate			Showed activity at a loading of 70 μ g against <i>Staphylococcus aureus</i>	[26]
	3,3',4',5,6,7,8-Heptahydroxyflavan			Showed activity at a loading of 15 μ g against <i>Staphylococcus aureus</i>	[26]
Antifungal	Crude; water; 3,3',4',5,6,7,8-heptahydroxyflavan	Roots	TLC bioautography	All extracts showed activity at a loading of 100 μ g against <i>Candida mycoderma</i>	[26]
	Methyl gallate			Showed activity at a loading of 72 μ g against <i>Candida mycoderma</i>	[26]
Anthelmintic	Water	Fruits	_	Lethal concentration of 12.1 mg/mL after 1 h and 1.6 mg/mL after	[33]
		Tuno		24 h against Hymenolepis diminuta	
		Leaves, stem		Lethal concentration of 42.2 mg/mL after 1 and 24 h against <i>Hymenolepis diminuta</i>	[33]
		Roots		Lethal concentration of 17.4 mg/mL after 1 h and 0.5 mg/mL after	[33]
		Roots		24 h against Hymenolepis diminuta	[]
		Stem bark		Lethal concentration of 4.2 mg/mL after 1 h and 0.5 mg/mL after	[33]
		Stelli bark		24 h against Hymenolepis diminuta	[00]
		Fruits		Lethal concentration of 0.75 mg/mL against <i>Schistosoma mansoni</i>	[33]
		Leaves, stems		Lethal concentration of 0.25 mg/mL against Schistosoma mansoni	[33]
		Roots		Lethal concentration of 0.5 mg/mL against Schistosoma mansoni	[33]
		Stem bark		Lethal concentration of 0.25 mg/mL against <i>Schistosoma mansoni</i>	[33]
Cytotoxicity	Ethyl acetate-methanol	Root bark	Brine shrimp	LC_{50} value of 10.8 ppm	[28]
Cytotoxicity	(±)-Catechin	KOOL DAIK	brine similip	LC_{50} value of 25.3 ppm	[28]
	(±)-Gallocatechin			LC_{50} value of 20.3 ppm	[28]
	(E)-Resveratrol			LC_{50} value of 56.8 ppm	[28]
	(E)-Resveratrol 3-O-rutinoside			LC_{50} value of 398.7 ppm	[28]
	5-Methoxy-(E)-resveratrol 3-O-rutinoside,			All compounds showed LC_{50} value of >10 ⁷ ppm	[28]
	4'-methoxy-(E)-resveratrol			An compounds showed LC ₅₀ value of >10 ppm	[20]
	3- O -rutinoside, 4',5-dimethoxy-(E)-resveratrol				
	3-O-rutinoside				
	Sericoside			LC ₅₀ value of 126.3 ppm	[28]
	Bellericoside			LC_{50} value of 213.2 ppm	[28]
	Arjungenin			LC_{50} value of 245.5 ppm	[28]

Viol *et al.* ^[34] evaluated the antiviral activity of *E. goetzei* against Herpes Simplex Virus-2 (HSV-2) by the End Point Titration Technique (EPTT) and Neutralisation Test (NT) on VERO cells. Results from the Neutralisation Test showed effect with ID_{50} value of 83.33 µg/mL. The antiviral End Point Titration Technique reduction factor was 10^2 . The activity of the plant parts lend support to its traditional uses as the species is traditionally used to treat and manage human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDs) opportunistic infections such as diarrhoea and sexually transmitted infections (STIs).

6.2. Anthelmintic

Mølgaard et al. [33] evaluated the anthelmintic effects of E. goetzei fruit, leaf, root, stem and stem bark extracts against schistosomules of the trematode Schistosoma mansoni and cysticercoids of the cestode Hymenolepis diminuta. The extracts killed the newly excysted cysticercoids within an hour, when incubated in a culture medium. The lethal concentrations of E. goetzei extracts varied from 0.5 to 42.2 mg/mL after 24 h [33]. The best results against Hymenolepis diminuta were obtained with stem bark extracts (see Table 4). E. goetzei extracts showed activity against Schistosoma mansoni with lethal concentrations varying from 0.25 to 0.75 mg/mL [33]. The best results against Schistosoma mansoni were obtained with leaves and stem as well as stem bark (Table 4). E. goetzei stem bark extract was also tested against schistosomules showing activity with lethal concentrations of 0.8 mg/mL [33]. These pharmacological evaluations are of importance in the traditional use of E. goetzei as an anthelmintic [14] and as herbal medicine against bilharzia [10,15,20,23] and future research focussing on control and management of schistosomiasis in sub-Saharan Africa.

6.3. Antioxidant

Viol *et al.* [30] screened *E. goetzei* for phytochemical composition, antioxidant activity by reducing 2,2-diphenyl-picrylhydrazyl (DPPH) free radical with β -carotene as reference and through total phenolic content (TPC) by Folin-Ciocalteu reagent using gallic acid as reference. Methanolic extract of *E. goetzei* exhibited strong antioxidant activity of 85.69% \pm 0.03% compared to reference β -carotene (99%) [30]. The antioxidant activities of *E. goetzei* are probably due to the documented flavonoids, phenolic compounds and tannins [26.29,30]. Research by Bhandare *et al.* [35] showed that polyphenols such as flavonoids, tannins and phenolic acids possess an ideal structural chemistry for free radical scavenging activity.

6.4. Cytotoxicity

Wanjala and Majinda [28] evaluated the cytotoxicity of *E. goetzei* using the brine shrimp (*Artemia salina*) lethality test on the combined ethyl acetate-methanol root bark extract, (\pm) -catechin, (\pm) -gallocatechin, (E)-resveratrol, (*E*)-resveratrol 3-*O*-rutinoside, 5-methoxy-(E)-resveratrol 3-*O*-rutinoside, 4', methoxy-(E)-resveratrol 3-*O*-rutinoside, arjungenin, bellericoside and sericoside (Table 4). Research by Wanjala and Majinda [28]

revealed that the combined ethyl acetate-methanol extract exhibited high no lethality against brine shrimp larvae with LD₅₀ value of 10.8 ppm when compared with other isolates, some of which were not active (Table 4). Similarly, Viol *et al.* [34] investigated the cytotoxicity of methanolic root extract of *E. goetzei* using the brine shrimp lethality test and 50% cytopathic effect on VERO cultured cells. Results from the brine shrimp lethality test showed effect of (356.55 ± 24.55) μ g/mL, which suggest that caution is necessary when using roots for medicinal purposes. Results from the 50% cytopathic effect of 156.25 μ g/mL [34]. These research findings calls for rigorous toxicological tests for *E. goetzei* considering its widespread use as herbal medicine with the possibility that it may contain useful cytotoxic compounds which have not been reported.

7. Conclusions

The traditional usage of E. goetzei was shown to be quite broad ranging from infections and pain to complex medical conditions like high blood pressure and menstruation problems. The chemical constituents of E. goetzei were shown to be phenolic compounds, flavonoids, stilbenoids, tannins and triterpenoids, and many of these compounds have proven pharmacological properties. However, the research carried out so far on the species' phytochemical and pharmacological effects are limited. There is need for further research on chemical profiling using modern chromatographic techniques such as high performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometry (LC-MS) to obtain the chromatographic profile of the chemical composition of the extracts. In addition to this, there has been an increased research interest in the phytochemistry and pharmacological properties of the species in the last 20 years, it is still noteworthy that several gaps in our understanding of its application still exist. An increasing number of studies have revealed that some crude extracts of E. goetzei as well as pure chemicals or compounds showed promising antimicrobial, anthelmintic and antioxidant activities. These and additional biological activities need to be further proved through additional animal experiments. Biological activities also need to be complemented with research into clinical applications. This study also revealed that E. goetzei is used in combination with other plant species, therefore, there is need to investigate the possible mechanism of action of the species involved as well as potential synergistic or antagonistic effects of such mixtures. Although no serious side effects or marked toxicity of E. goetzei have been reported, further toxicity and safety evaluation of the crude extracts and chemical compounds isolated from the species should be carried out.

Conflict of interest statement

The author declares that he has no conflict of interest.

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