



MINI REVIEW ARTICLE

A systematic review on biological and medicinal properties of Ehretia rigida (Thunb.) Druce (Ehretiaceae) in Southern Africa

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Abstract

Wild plants are widely utilized as important sources of traditional medicines and food. Ehretia rigida (Thunb.) Druce is one such plant species that occurs naturally in southern Africa and different parts of the plant have nutritional, cultural, and pharmaceutical importance. The current study is aimed at providing information on the medicinal and biological properties of E. rigida. The current review assessed the existing literature on the biological properties and medicinal uses of the plant. The study revealed that the leaves, twigs, stems, bark and roots of the plant are mainly used for ritual purposes, as traditional medicines for infertility, headache, abdominal pains, chest pains, pain, skin cuts, sprained joints, newborn baby infections, a good-luck charm, fire-making and rain-making ceremonies, warding-off enemies and dangerous animals and as ethnoveterinary medicine. The phytochemical evaluation of the species showed that it is characterized by allantoin, α -amyrin, β -amyrin, flavonoids, phenolics, saponins, tannins, β sitosterol and 1-triacontanol. The pharmacological properties of different crude extracts demonstrated anticholinesterase inhibition, antifungal, antibacterial, antidiabetic, anti-inflammatory, and antioxidant properties. This review highlights the pharmaceutical and health benefits of *E. rigida* in different countries of southern Africa. Therefore, detailed ethnopharmacological evaluations of the species focusing on phytochemistry, pharmacological properties, toxicological evaluations, and in vivo and clinical research investigations are recommended.

Keywords

Boraginaceae; Ehretia rigida; Ehretiaceae; indigenous pharmacopeia; toxicological evaluations; traditional medicine

Introduction

The genus name Ehretia P.Browne is honoring a German, Georg Dionysius Ehret born on 30 January 1708 and died on 9 September 1770, an entomologist and botanist well-known for his botanical illustrations (1). The specific epithet rigida means rigid or stiff branches (2, 3). Synonyms of E. rigida include Capraria rigida Thunb., E. eckloniana H. Buek ex Harv., E. hottentotica Burch., E. violacea Kunth, E. zeyheriana Buek. ex Harv., Pittosporum commutatum Krauss and Freylinia rigida (Thunb.) G.Don. (4-7). The English common names of E. rigida include "Cape lilac", "forest puzzle bush", "puzzle bush" and "stamper wood" (2, 8). E. rigida (Thunb.) Druce (Fig. 1) naturally occurs in southern Africa in Botswana, Lesotho, Mozambique, Eswatini, Namibia, Zimbabwe, and South Africa (Fig. 2) (4-6, 9-11). Local people in

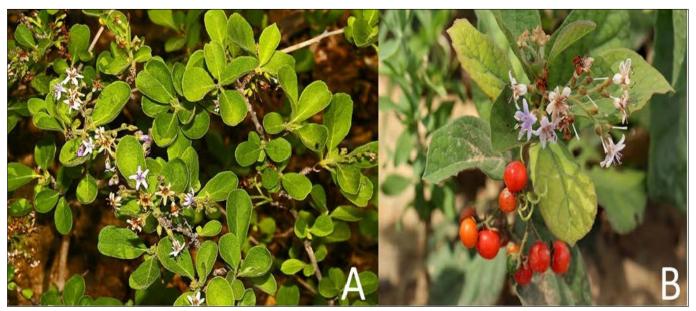
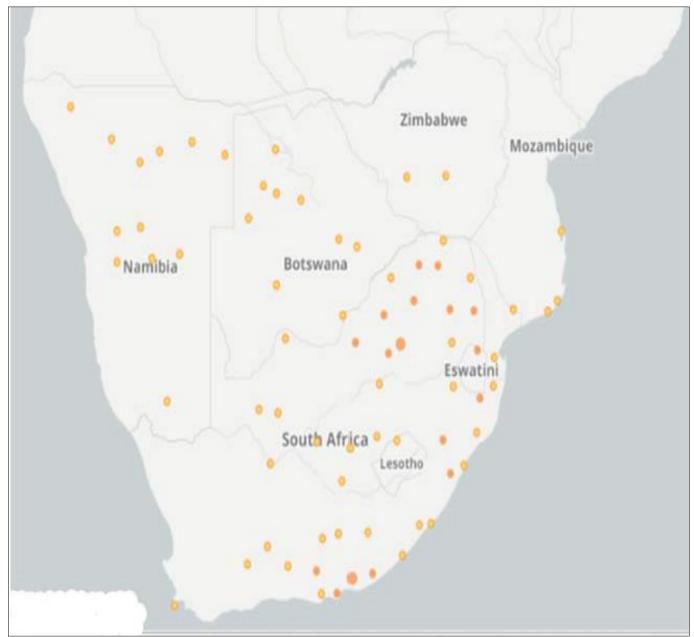


Fig. 1. Ehretia rigida A: branch showing leaves and flowers, and B: branch showing flowers and fruits (Photos: MC Palgrave and B Wursten)



 $\textbf{Fig. 2.} \ \textbf{Distribution of} \ \textit{Ehretia rigida} \ \textbf{in southern Africa} \)$

people in southern Africa have developed indigenous knowledge and skills necessary to provide locally appropriate solutions to local problems, particularly the exploitation of medicinal plants including E. rigida. The use of medicinal plants, crude plant extracts, and their active ingredients, or phytochemicals plays an important role in the primary health care needs of local communities in southern Africa. Medicinal plants are an important aspect of the daily lives of many people and an important part of the Southern African cultural heritage (12). Therefore, understanding the phytochemicals associated with E. rigida is important as these active ingredients act directly or indirectly to prevent or treat diseases and also maintain health. Due to its ability to withstand drought, E. rigida has been identified as an important local species in southern Africa that can be easily integrated into home gardens as an ornamental or hedge plant (2). Therefore, the objective of this review was to collect and summarize information about the medicinal uses, phytochemistry, and biological properties of *E. rigida*.

Methodology

The literature review of the medicinal and biological properties of *E. rigida* within its geographical ranges in southern Africa was conducted using online databases such as JSTOR, Scopus, PubMed, Science Direct, and Google Scholar. In addition to this, pre-electronic literature sources used which included journal articles, books, theses, dissertations, book chapters, and other scientific articles were obtained from the University of Fort Hare library. Keywords such as *Ehretia rigida*, biological activities, pharmacological properties, ethnobotany, medicinal uses, phytochemistry, and traditional uses of *Ehretia rigida* were used to search for relevant articles as shown in the flow diagram (Fig. 3). Literature sources excluded from this re-

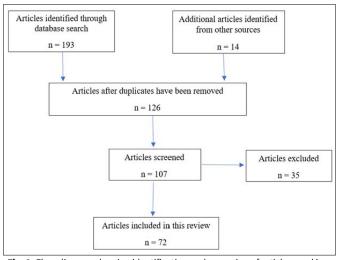


Fig. 3. Flow diagram showing identification and screening of articles used in this review

view are those articles that are partially accessed, that is, accessed as abstracts only, and also published or unpublished ethnopharmacological surveys lacking information on the medicinal uses, phytochemistry, pharmacological or biological activities of *E. rigida*. The chemical structures of phytochemical compounds isolated from *E. rigida* have been drawn using the program ChemSketch.

Results

Morphological description and taxonomy of the species

The genus Ehretia consists of about 40 tree and shrub species belonging to the family Ehretiaceae (13). The Ehretia genus has been recorded in the New and Old World tropics with its center of diversity in East Asia and Africa (13). The family Ehretiaceae has been segregated from Boraginaceae sensu lato based on molecular and phylogenetic studies focusing on plastid loci (trnL-trnF, rps16, and trnStrnG) and nuclear (ITS) (13-16). E. rigida is a highly branched shrub or multi-stemmed tree, deciduous, reaching up to 12 meters in height (5). The stems, usually several to many, are often low branching and crooked with grey to pale brown bark with prominent lenticels (4). The inner bark is soft, white, spotted with orange-brown, and turning brown upon exposure (1). The leaves are simple and alternate but often clustered on reduced shoots; obovate, dark green or grey-green above, hairless with prominent venation on lower surfaces (4). The leaf stalks may be absent, short, or sometimes pronounced (1). The flowers are bisexual, regular, pale mauve to dark purple, usually on branched terminal heads, densely congested with peduncles and pedicels (8). The fruit is a berry, subglobose, spherical in shape, yellow to bright orange-red when riped (3, 17). E. rigida is divided into three subspecies distinguished by vegetative and reproductive characteristics, and geographical distribution. E. rigida subsp. rigida is a stunted tree or shrub of up to four meters in height with terminal inflorescences, thick peduncles, and pedicels, and confined to the Albany Centre of Endemism in South Africa (5). Ehretia rigida subsp. silvatica Retief and A.E. Van Wyk and E. rigida subsp. nervifolia Retief and A.E. Van Wyk are widespread with heights, exceeding five metres (8).

Distribution and growing condition

E. rigida has been recorded in coastal areas, forests, thickets, woodland, and bushland biomes (1). E. rigida naturally occurs in valleys, open flats, stony slopes, granite hills, dunes, Kalahari sand areas and termite mounds at an altitude ranging from sea level to 1700 m above sea level (4, 6-8, 11). In the forest biome, the species loses the shrub characteristic habit and grows upwards to about 12 meters in height with a small tangled crown (1). E. rigida is usually in flower from March to December, and fruits are often produced from October to May (3, 4, 8). E. rigida is drought and frost-resistant, easily grown from seeds and cuttings, characterized by fast growth rate of about 600 mm to 700 mm per annum (2, 18). E. rigida can be planted in a garden to attract birds and insects, and also the lilac-to-mauve flowers and orange-to-red fruits make the plant species an interesting and decorative shrub in the garden (2). Subspecies rigida is the most widespread taxon, recorded in Botswana, Mozambique, South Africa, and Zimbabwe (6-11). Subspecies nervifolia has been recorded in Botswana, Eswatini, Lesotho, the Free State, Gauteng, KwaZulu Natal, Limpopo, Mpumalanga, and North-West provinces in South Africa while subspecies sylvatica is confined to the Eastern Cape and KwaZulu Natal provinces in South Africa (6, 8).

Ethnomedicinal significance

In South Africa, *E. rigida* roots are traded as sources of traditional medicines in rural, peri-urban and urban markets in the Gauteng province (19). The fruits are eaten as snacks (1, 18, 20-26), as vegetables and to make non-alcoholic beverages (3). In South Africa, the leaves and twigs are used as cattle feed and eaten by birds and wild animals such as bushbuck (*Tragelaphus scriptus*), grey duiker (*Sylvicapra grimmia*), impala (*Aepyceros melampus petersi*), kudu (*Tragelaphus strepsiceros*), monkey (*Cercopithecus aethiops*) and nyala (*Tragelaphus angasii*) (1, 2, 23). In southern Africa, the herbal concoctions pre-

pared from leaves, bark, roots and twigs are used to treat several animal and human ailments including infertility, headache, abdominal pains, chest pains, pain, skin cuts, sprained joints, newborn baby infections, a good-luck charm, fire-making and rain-making ceremonies, warding off enemies and dangerous animals and as ethnoveterinary medicine (Table 1). In South Africa, the root powder of *E. rigida* is often mixed with the root powder of *Zanthoxylum davyi* (I.Verd.) P.G.Waterman and the bark of *Maerua angolensis* DC. as a remedy against diabetes (27), while the root paste is topically applied with the root paste of *Asparagus falcatus* L. for sprained joints (20, 27).

Table 1. Traditional and ethnomedicinal uses of Ehretia rigida

Plant part Region used		Mode of preparation	Traditional/ethnomedicinal uses	Reference
South Africa	Roots	Root decoction is taken orally	Abdominal pains	(8, 18, 28, 29)
South Africa	Leaves	Leaf paste topically applied	Burns	(30)
South Africa	Leaves	Leaf paste topically applied	Candidiasis	(31)
Botswana	Whole plant	The tree is used for rain-making ceremonies with the cloud of smoke from twigs being symbolic of rain clouds	Rain-making ceremonies	(1)
Lesotho	Twigs	Hunters smear themselves with the decoction of the twigs	Charm for success when hunting	(32-34)
South Africa	Stems and twigs	People smear themselves with the decoction of stems and twigs	Good luck, hunting and protective charm, warding-off enemies and dangerous animals	(1, 18, 20, 22, 2 29)
South Africa	Roots	Root powder decoction is taken orally	Chest pains	(8, 3, 18, 28, 29)
South Africa	Roots	Root powder mixed with root powder of <i>Zanthoxylum davyi</i> (I.Verd.) P.G.Waterman and the bark of <i>Maerua angolensis</i> DC.	Diabetes	(27)
South Africa	Roots	Root powder infusion is taken orally	Emetic	(35)
South Africa	Roots	Root powder infusion is taken orally	General childhood infections	(36)
South Africa	Roots	Root powder decoction is taken orally	Headache	(27, 37-39)
South Africa	Roots	Root powder decoction is taken orally	Infertility	(20, 27, 40)
South Africa	Roots	Root powder decoction is taken orally	Newborn infections	(27, 41)
Eswatini	Roots	Root powder decoction is taken orally	Pain	(42)
Namibia	Roots	Root powder decoction is taken orally	Pain	(43)
South Africa	Roots	Root powder decoction is taken orally	Pain	(44)
South Africa	Roots	Root powder infusion is taken orally	Respiratory infections	(45)
Eswatini	Roots	Root powder decoction topically applied	Skin cuts	(42)
South Africa	Roots	Root powder decoction topically applied	Skin cuts	(8, 18)
South Africa	Roots	Root paste topically applied and mixed with root paste Asparagus falcatus L	Sprained joints	(20, 27)
South Africa	Roots	Root powder infusion is taken orally	Stomach pains	(3)
South Africa	Roots	Root powder infusion is taken orally	Tonic	(46)
Eswatini	Roots	Root maceration topically applied	Toothache	(42)
South Africa	Leaves	The leaf powder was topically applied	Wounds	(30)
Ethnoveterinary	medicine			
South Africa	Roots	Root powder decoction used	Eating problems in cattle	(47, 48)
South Africa	Roots	Root paste topically applied	Fractures	(48, 49)
South Africa	Roots	Root powder decoction used	Gall sickness in cattle	(2, 8, 18, 29)

Nutritional composition

Various scientists identified elementary, nutritional and chemical compounds from the fruits, bark, roots and leaves of *E. rigida* (Table 2).

Table 2. Nutritional composition of Ehretia rigida .

Nutritional components	Value	Plant part	References
Ash (g/100g)	1.3	Fruits	(50, 51)
Calcium (mg/100g)	30.5	Fruits	(50, 51)
Carbohydrates (g/100g)	10.4	Fruits	(50, 51)
Copper (mg/100g)	0.2	Fruits	(50, 51)
Crude fiber (g/100g)	0.7	Fruits	(50, 51)
Energy (KJ/100g)	215	Fruits	(50, 51)
Fat (g/100g)	0.3	Fruits	(50, 51)
Iron (mg/100g)	0.9	Fruits	(50, 51)
Magnesium (mg/100g)	27.8	Fruits	(50, 51)
Moisture (g/100g)	85.6	Fruits	(50, 51)
Potassium (mg/100g)	547.0	Fruits	(50, 51)
Protein (g/100g)	1.7	Fruits	(50, 51)
Sodium (mg/100g)	2.5	Fruits	(50, 51)
Vitamin C (mg/100g)	6.9	Fruits	(50, 51)
Zinc (mg/100g)	0.2	Fruits	(50, 51)

Phytochemistry

Various researchers identified chemical compounds from the bark, leaves and roots of *E. rigida* (Fig. 4; Table 3). The chemical compounds identified from *E. rigida* include allantoin, α -amyrin, β -amyrin, β -sitosterol, 1-triacontanol, flavonoids, phenolics, saponins and tannins (52-55).

Pharmacological properties

Anticholinesterase inhibition activity

The anticholinesterase inhibition properties of acetone leaf extracts were assessed using an acetylcholinesterase inhibition assay, with eserine as a positive control (54). At a determined concentration of 500.0 μ g/mL, the acetone extracts showed the anticholinesterase inhibitory activity of 50.0% and a dose-dependent half maximum inhibitory concentrations (IC₅₀) average value of 487.4 μ g/mL. The positive control, eserine exhibited anticholinesterase inhibitory activity of 60.0% and an IC₅₀ value of 4.9 μ g/mL (54).

Antimicrobial property

The antibacterial properties of hexane, diethyl ether, chloroform and ethyl acetate leaf extracts were evaluated at 50.0 mg/ml concentration against bacterial pathogens viz. Agrobacterium tumefaciens, Erwinia carotovora subsp. carotovora, Clavibacter michiganense, Xanthomonas campestris and Pseudomonas solanacearum, through an agar diffusion assay using dimethyl dodecyl ammonium chloride (DDAC) as a positive or standard control (56). Ethyl acetate extract demonstrated antibacterial properties against Erwinia carotovora subsp. carotovora exhibiting inhibition of 7.0 mm in comparison with inhibition of 13.0 mm demonstrated by the positive or standard control (56). Similarly, the antibacterial properties of dichloromethane, methanol and ethyl-acetate bark, root and leaf extracts were evaluated against Escherichia coli, Staphylococcus aureus, Micrococcus luteus and Klebsiella pneumoniae through a microdilution assay with neomycin as a positive control (55). The dichloromethane, methanol and ethylacetate extracts demonstrated antibacterial properties against the tested bacterial pathogens with minimum in-

Fig. 4. Chemical structures of allantoin, α -amyrin, β -amyrin, β -sitosterol and 1-triacontanol isolated from *Ehretia rigida*

Table 3. Phytochemical composition of Ehretia rigida

Type of compound	Name of the compound	Plant part from where extracted/ identified/documented	Process of detection/ isolation/ extraction	References
Glyoxylic acid	Allantoin	Bark	¹ H and ¹³ C NMR	(52)
Triterpene	α-amyrin	Bark	GC	(52)
Triterpene	β-amyrin	Bark	GC	(52)
<u>Phytosterol</u>	β-sitosterol	Bark	¹ H and ¹³ C NMR	(52)
Fatty alcohol	1-triacontanol	Bark	¹ H and ¹³ C NMR	(52)
Flavonoids	-	Bark, leaves, and roots	Calorimetric assay	(54, 55)
Phenolics	-	Bark, leaves, and roots	Folin-Ciocalteau	(53-55)
Saponins	-	Bark, leaves, and roots	Froth test	(55)
Tannins	-	Bark, leaves, and roots	Butanol-HCL assay	(55)

hibitory concentration (MIC) values within the range from 0.78 to >6.25 mg/ml which were higher than the MIC values ranging from 0.01 mg/ml to 0.05 mg/ml demonstrated by the positive control (55).

The antifungal properties of water and acetone leaf extracts were evaluated against Candida parapsilosis, C. albicans, Cryptococcus neoformans, C. glabrata, C. tropicalis and C. krusei, through microdilution method, with clotrimazole as a positive control (30). The plant extracts demonstrated weak antifungal activity in comparison to the positive control with MIC values ranging between 0.04 mg/ml - 0.08 mg/ml (30). The antifungal properties of acetone leaf, root and bark extracts were assessed against C. albicans, Aspergillus fumigatus and Cryptococcus neoformans using a microdilution assay (57). The extracts demonstrated moderate activity with MIC values of 0.02 mg/ml to 0.08 mg/ml (57). Further, the antifungal properties of dichloromethane, methanol and ethyl-acetate plant bark, leaf and root extracts were evaluated against C. albicans through microdilution assay, with an amphotericin B as a positive control (55). The extracts demonstrated considerably significant antifungal activity against C. albicans with MIC values ranging from 0.78 mg/ml to >6.25 mg/ml compared to a positive control (MIC: 0.01 to 0.08 mg/ml (55).

Antidiabetic activity

The antidiabetic properties of leaf, bark and root extracts were evaluated using a microplate serial dilution assay to determine the inhibition of α -glucosidase (55). The α -glucosidase inhibitory activities exhibited by the extracts were dose-dependent ranging from 16.0% to 23.0% at 125.0 μ g/ml, 40.0% to 44.0% at 250.0 μ g/ml and 59.0% to 65.0% at 500.0 μ g/ml (55).

Anti-inflammatory activity

The anti-inflammatory properties of acetone extracts of leaves were assessed using soybean lipoxygenase inhibition, nitric oxide production and the viability of LPS-activated RAW 264.7 macrophage assay, using indomethacin and quercetin as positive controls (54). The acetone extracts demonstrated properties with anti-lipoxygenase activities showing 50.0% inhibition and an IC50 value of 63.0 μ g/mL at 100.0 μ g/mL. Effective dose-dependent inhibition reactions of nitric oxide production (rate of inhibi-

tion: 86.3% to 92.6%; cell viability: 34.3% to 63.9%) were exhibited by acetone extract at 6.3 μ g/mL, 12.5 μ g/mL, 25.0 μ g/mL, and 50.0 μ g/mL concentrations (54).

Antioxidant activities

The antioxidant properties of water extracts of leaves were evaluated against 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2-azinobis (3-ethyl benzothiazolium-6-sulfonic acid (ABTS), and ferric reducing antioxidant potential (FRAP) methods (53). The extract showed activities against DPPH radicals only, exhibiting 94.9% inhibition (53). The antioxidant properties of the acetone extracts of E. rigida leaf were assessed using the DPPH, ABTS, and FRAP methods with ascorbic acid and trolox as positive controls (54). The extracts demonstrated significant antioxidant properties with IC₅₀ values of 171.8 μg/mL for DPPH, 94.1 μg/mL for FRAP, and 234.8 µg/mL for ABTS (54). The antioxidant properties of acetone and water extracts of leaves were evaluated against DPPH free radicals (30). Both acetone and water extracts exhibited activities with IC50 values ranging from 62.0 μg/ml to 131.0 μg/ml (30). The antioxidant properties of methanol, dichloromethane, and ethylacetate extracts of roots, bark, and leaves were assessed using DPPH free radical scavenging assay with ascorbic acid as a positive control (55). The extracts demonstrated significant dose-dependent antioxidant properties (55).

Discussion

The current review attempted to provide information available on the medicinal uses, phytochemistry and biological activities of *E. rigida* covering literature from 1962 to 2023, a very long period to capture all the relevant research on the ethnopharmacological properties of the species. This species belongs to the Ehretia genus which is widely used as a source of herbal medicines in tropical Africa (58, 59). Some of the species belonging to the Ehretia genus used as sources of traditional medicines in tropical Africa include E. amoena Klotzsch, E. cymosa Thonn., E. obtusifolia Hochst. ex DC., E. rigida, and E. trachyphylla C.H. Wright (58-67). The value and importance of E. rigida as traditional medicine is demonstrated by the inclusion of the species in the monograph Medicinal and magical plants of Southern Africa: An Annotated Checklist (62) and also its trade as a source of traditional medicines in both informal and formal herbal medicine markets in South Africa (19). Research findings in this review show how indigenous people in southern Africa have adapted and become familiar with the diverse medicinal uses and properties of *E. rigida*. The dependence of rural households on *E. rigida* for non-medicinal and miscellaneous uses for their livelihood needs is also well recognized in southern Africa.

Different classes of phytochemicals of E. rigida including flavonoids, phenolics, saponins, and tannins, have been quantified using different methods (53-55) but several factors such as plant part, season, and environmental factors influence such phytochemical synthesis and quantities (68). Some of these classes of secondary phytochemical constituents may be responsible for the documented biological activities of *E. rigida*. For example, the chemical compound allantoin identified from E. rigida is known to enhance the smoothness of the skin by stimulating the healing of wounds and soothing irritated skin (69). The chemical compounds α - and β -amyrin identified from E. rigida are characterized by analgesic, anti-inflammatory, anticonvulsant, anti-depressive, gastroprotective, hepatoprotective, anti-pancreatitis, anticholytic, antihyperglycemic and hypolipidemic activities (70). Similarly, the phytosterol, β-sitosterol identified from *E. rigida* is known to have antimicrobial, anti-inflammatory, anticancer, antifertility, angiogenic, antioxidant, immunomodulatory, antidiabetic, and antinociceptive activities (71). This background information highlights the need for detailed phytochemical evaluation of various E. rigida extracts aimed at isolating, purifying, and characterizing phytochemical compounds of this species. Therefore, the little data on the phytochemical compounds of the species highlights a research gap requiring attention from researchers. There is growing interest in phytochemical constituents of plant species in a quest to discover new remedies or to explain the modes of action of these medicinal plants (72).

E. rigida has been subjected to a series of anticholinesterase inhibition, antibacterial, antifungal, antidiabetic, anti-inflammatory, and antioxidant assays as the species is widely used as traditional medicine for abdominal pains, burns, candidiasis, chest pains, childhood infections, diabetes, headache, infertility, pain, respiratory infections, skin cuts, sprained joints, stomach pains, toothache and wounds in humans, eating problems, fractures and gall sickness in cattle (Table 1). The antimicrobial and antioxidant activities exhibited by the crude extracts of E. rigida are directly or indirectly involved in protection against free radicals and the growth of undesirable microbes. There is a need for detailed ethnopharmacological studies focusing on their potential in vitro and in vivo conditions as there is a need to assess the clinical relevance of these different extracts of the species. Therefore, knowledge about the resultant pharmacological and toxicological properties of both crude extracts and the phytochemical constituents isolated from E. rigida should be subjected to controlled clinical trials to determine if such crude extracts and phytochemical compounds are characterized by sufficient therapeutic properties and can be linked to a particular disease or indication associated with the species. Till now, limited ethnopharmacological research has been made in the pharmacokinetics studies related to the mechanism of action of the individual isolated phytochemical compound under *in vivo* conditions. Also, ethnopharmacological research should focus on toxicity, preclinical, and clinical trials aimed at accounting for the safety, effectiveness, and side effects of the phytochemical compounds in the formulation of *E. rigida* as a source of traditional medicines.

Conclusion

The current study provides a summary of the medicinal, phytochemical and biological activities of E. rigida. Such evaluations are important considering that E. rigida is widely used in southern Africa as a food plant and also as an important source of traditional medicines. E. rigida is among the indigenous fruit trees with high medicinal and therapeutic potential that is not fully researched, and have fragmented information in the literature. The presence of carbohydrates, fats, fiber, proteins, vitamins, minerals and biologically active phytochemicals such as flavonoids and phenolic acids makes E. rigida suitable for day-to-day activities as a source of food and medicines. However, there is a lack of alignment between food and ethnomedicinal uses, and existing phytochemical and biological screenings of the species, indicating the need for further ethnopharmacological evaluations. Although the existing research efforts are laudable, several areas of research on E. rigida have been neglected. It is expected that the identified research gaps will serve as a guide for future holistic research focusing on E. rigida. Therefore, detailed ethnopharmacological evaluations of the species focusing on phytochemistry, pharmacological properties, and toxicological evaluations as well as in vivo and clinical research aimed at corroborating the traditional medical and food applications of the species are recommended. The outcomes of such research have the potential to accelerate the commercialization of E. rigida health and pharmaceutical products.

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Compliance with ethical standards

Conflict of interest: The author declares no conflict of interest.

Ethical issues: None.

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