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Review Article

REVIEW OF MEDICINAL USES, PHYTOCHEMISTRY, AND PHARMACOLOGICAL PROPERTIES OF *DRIMIA ELATA*

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ABSTRACT

Drimia elata is an important and well-known medicinal plant in tropical Africa. This study critically reviewed the medicinal applications, phytochemistry, and pharmacological activities of *D. elata*. Literature on medicinal applications, phytochemical, and pharmacological activities of *D. elata* was collected from multiple internet sources including Elsevier, Google Scholar, SciFinder, Web of Science, PubMed, BMC, ScienceDirect, and Scopus. Complementary information was gathered from pre-electronic sources such as books, book chapters, theses, scientific reports, and journal articles obtained from the university library. This study showed that *D. elata* is used for treating several medical conditions, particularly general ailments, blood and cardiovascular system, reproductive system and sexual health, urinary system, infections and infestations, digestive system, respiratory system, and muscular-skeletal system disorders. Phytochemical compounds identified from the species include bufadienolides, alkaloids, aromatic acids, flavonoids, phlobatannins, saponins, steroids, tannins, and terpenoids. Ethnopharmacological research revealed that *D. elata* extracts have acetylcholinesterase enzyme inhibitory, antibacterial, antifungal, antimycobaceterial, anticancer, anti-inflammatory, antioxidant, hemagglutinating, and cytotoxicity activities. *D. elata* should be subjected to extensive *in vivo* experiments and also future studies should focus on how potential toxic components of the species can be managed when it is used as herbal medicine.

Keywords: Asparagaceae, *Drimia elata*, Herbal medicine, Tropical africa.

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INTRODUCTION

Drimia elata Jacq. is an important and well-known medicinal plant in South Africa. Van *et al*.[1] provide an excellent introduction to the ethnopharmacological properties of *D. elata* and several other important medicinal plants in South Africa. *D. elata* is an ingredient of at least two traditional herbal concoctions in South Africa, known as "*imbizae phuzwato*" and "*intelezi*" that are sold commercially in the country. A herbal tonic, *imbizae phuzwato* is made from a mixture of roots, bulbs, rhizomes, and leaves of *Acokanthera oppositifolia* (Lam.) Codd, *Aster bakeranus* Burtt Davy ex C.A. Sim., *Corchorus asplenifolius* Burch., *Cyrtanthus obliquus* (L.f.) Aiton, *Fusifilum physodes* (Jacq.) Raf. ex Speta, *Eriosema cordatum* E.Mey., *Gnidia kraussiana* Meisn. var. *kraussiana, Gomphocarpus fruticosus* (L.) W.T. Aiton, *Gunnera perpensa* L., *Hypericum aethiopicum* Thunb., *Ledebouria* spp., *Lycopodium clavatum* L., *Momordica balsamina* L., *Rubia cordifolia* L., *Scadoxus puniceus* (L.) Friis and Nordal, *Stephania abyssinica* (Quart.-Dill. and A. Rich.) Walp., *Tetradenia riparia* (Hochst.) Codd, *Vitellariopsis marginata* (N.E.Br.) Aubrév, *Watsonia densiflora* Bak., and *Zanthoxylum capense* (Thunb.) Harv. [2,3]. The concoction is used as an energizing and detoxifying tonic used against general body pains, stress, constipation, arthritis, kidney problems, high blood pressure, and to increase sexual prowess [2,3]. *D. elata* is also an ingredient of "*intelezi*," whose plant species composition varies from region to region of South Africa. *Intelezi* is used to protect households from evil spirits and lightning, and also to chase away, ward off or root out evil spirits [4].

D. elata is the third most popular bulbous medicinal plant used in South African traditional therapy [5] and is one of the topmost wild-harvested species sold in the informal economy trade in the Eastern Cape [6,7], Gauteng [8-10], KwaZulu-Natal [8,11], Limpopo [12], and the Western Cape [7,13,14] provinces in South Africa. Research by Ndawonde *et al*. [15] showed that *D. elata* bulb was sold by >50.0% of the traders in KwaZulu-Natal Province, while Philander *et al*. [14] revealed that bulbs of the species were sold by 35% of the traders in the Western Cape province, with 60.48 kg of the bulb fetching US$26.21. Earlier research by Dold and Cocks [6] revealed that *D. elata* is among the most frequently traded species in the Eastern Cape Province with 113.9 kg as the mean quantity traded per trader per annun with a kilogram of the bulb fetching US$3.36. Marshall [16] argued that *D. elata* is scarce and heavily traded in South Africa, characterized by a high monetary value in the country. Due to increasing demand for the species, *D. elata* is managed in herbal medicine home gardens in the Eastern Cape [17], Limpopo [18-20], and the Western Cape [14] provinces. Research by Wiersum *et al*. [17] revealed that *D. elata* is among the ten most frequently cultivated herbal medicines in medicinal home gardens in the Eastern Cape Province. It is, therefore, within this context that the current study was undertaken aimed at summarizing the medicinal uses, phytochemical, and ethnopharmacological properties of *D. elata* so as to evaluate its therapeutic importance throughout its distributional range.

BOTANICAL PROFILE AND DESCRIPTION OF *D. ELATA*

The genus *Drimia* Jacq. is a large group of deciduous geophytes belonging to the family Asparagaceae, previously included in the Hyacinthaceae family. The family of Hyacinthaceae is divided into four monophyletic subfamilies, namely Hyacinthoideae, Ornithogaloideae, Oziroeoideae, and Urginoideae [21]. At present, this family is considered as a subfamily Scilloideae in the expanded Asparagaceae sensu [22,23]. The species in each subfamily synthesize specialized secondary metabolites with Hyacinthoideae synthesizing homoisoflavanones and triterpenoids, Ornithogaloideae (cardenolides and steroidal glycosides), and Urgineoideae synthesizing bufadienolides [21]. The subfamily Urgineoideae has flat or winged seeds characterized by brittle, loosely adhering test a comprising genera *Bowiea* Harv. ex Hook. f. and *Drimia* [24].The genus *Drimia* is described by Manning *et al*. [24,25] in an inclusive and broad sense, including genera such as *Litanthus* Harv., *Mucinea* M. Pinter *et al*., *Rhadamanthus* Salisb., *Rhodocodon* Baker, *Sagittanthera* Mart-Azorín *et al*., *Thuranthos* C. H. Wright, *Tenicroa* Raf., and *Urginea* Steinh. The taxonomy of genus *Drimia* has always been difficult with several species treated under genus *Urginea* until Jessop [26] reduced *Urginea* to a synonym of *Drimia*. The genus consists of about 100 bulbous species distributed in Southern Africa through tropical Africa to the Mediterranean, Asia, and Madagascar [24]. Synonyms of *D. elata* include *D. alta* R.A. Dyer, *D. ciliaris* Jacq. ex Willd., *D. purpurascens* J. Jacq., *D. robusta* Baker, *D. villosa* (Lindl.) Kunth, *D. zombensis* Baker, *Idotheaelata* Kunth, *I. ciliaris* (Jacq. ex Willd.) Kunth, *I. purpurascens* (J. Jacq.) Kunth, *I. robusta* (Baker) Kuntze, and *I. villosa* (Lindl.) Kunth [1,27-31].

D. elata is a geophyte with large underground bulb, strap-shaped leaves and long, slender flowering stalk which grows up 1.8 m in height [1,27-29,31]. The flowers are tubular, whitish to purple in color with the tips of the petals characteristically reflexed and the stamens fused into a narrow tube [1]. *D. elata* has been recorded in grassland, often among rocks at an altitude ranging from 15 m to 1650 m above sea level [29]. The species has been recorded in Botswana, Angola, Malawi, Kenya, South Africa, Swaziland, Zambia, South Sudan, Tanzania, Sudan, Uganda, Zimbabwe, and Mozambique [1,27-31](Fig. 1).

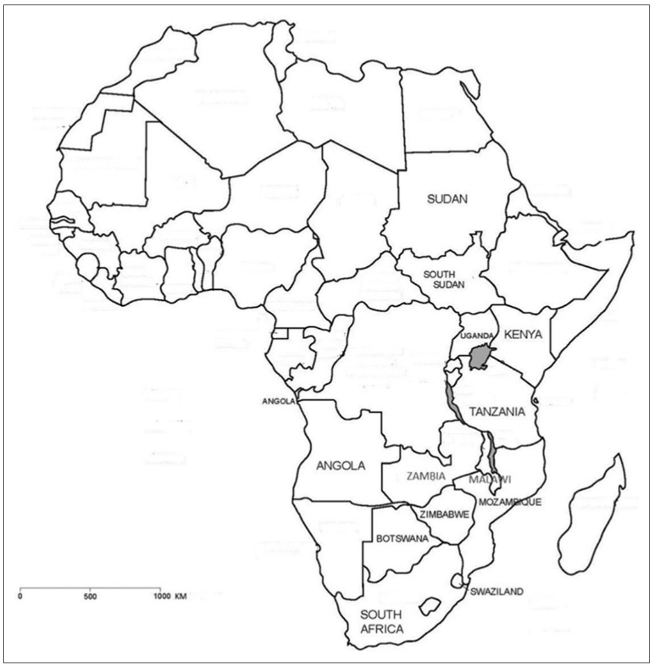

Fig. 1: Distribution of *Drimia elata* in tropical Africa

MEDICINAL USES OF *D. ELATA*

The medicinal applications recorded from literature were classified into ten medical categories following the Economic Botany Data Collection Standard [32] with some changes proposed by Macía *et al*. [33] and Gruca *et al*. [34]. This review showed that *D. elata* is used for treating several medicinal conditions, particularly general ailments, blood and cardiovascular system, reproductive system and sexual health, urinary system, infections and infestations, digestive system, respiratory system, and muscular-skeletal system disorders (Fig. 2). *D. elata* is used as herbal medicine against three out of five diseases categorized by the World Health Organization (WHO) as the top five killer diseases in sub-Saharan Africa in 2012. These diseases include human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS), lower respiratory tract infections, and diarrheal diseases [35]. Most medicinal uses are linked to the bulb and leaf or the entire plant in ritual or magical uses, and the species is also used mixed with other plant species (Table 1). Research by Gurib-Fakim [36] and Maroyi [37,38] revealed that traditional medicines are often prepared by combining several different plant species to effect synergistic properties or to initiate an interaction with a relevant molecular target.

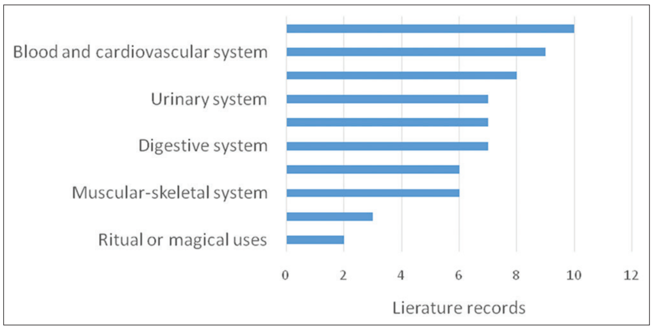

Fig. 2: Number of literature records per medicinal category of *Drimia elata* following the economic botany data collection standard [32]

PHYTOCHEMICAL CONSTITUENTS OF *D. ELATA*

D. elata is characterized by cardiac glycosides, particularly bufadienolides. All the bufadienolides that have been isolated from *D. elata* are collated in Table 2. Kellerman *et al*. [59,60] argued that bufadienolide containing plants are toxic to livestock with an estimated 33% of plant-related mortality in cattle in South Africa attributed to this compound. Van *et al*. [61] argued that there is a danger of accidental poisoning or that people may be harmed if bulbs of *D. elata* are used indiscriminately as rubbing the bulb scales or leaves on bare skin produces a stinging and irritating effect and a skin rash is produced. However, bufadienolides are known to have a wide range of biological activities including anti-tumor, antiproliferative, and cytotoxic activities [62-68].

Koorbanally *et al*. [69] identified aromatic acids, 4-hydroxy-3-methoxybenzoic acid, 3,4-dihydroxybenzoic acid, and trans-3-(4'-hydroxyphenyl)-2-propenoic acid from the ethyl acetate bulb extract of *D. elata*. Matotoka and Masoko [70] identified flavonoids, phlobatannins, saponins, tannins, and terpenoids from the *D. elata* bulb (Table 3). Similarly, Matotoka and Masoko [41] identified alkaloids, flavonoids, saponins, steroids, tannins, and terpenoids from a herbal mixture of *D. elata* bulb mixed with leaves of *Monsonia angustifolia, Sarcostemma viminale* and *Vahlia capensis*, *Kirkia wilmsii* (leaves, roots, and twigs), and *Hypoxis hemerocallidea* (corm).

Okem *et al*. [71] argued that *D. elata* bulbs obtained from the herbal medicine informal markets in Pietermaritzburg, KwaZulu-Natal Province in South Africa contained high levels of heavy metals, with aluminum, cadmium, manganese, and chromium being above the WHO recommended safety levels (Table 3). Quantities of mineral elements and phytochemical compounds isolated from *D. elata* are listed in Table 3.

PHARMACOLOGICAL PROPERTIES OF *D. ELATA*

Pharmacological studies on *D. elata* bulb and leaf extracts exhibited potent *in vitro* pharmacological activities including acetylcholinesterase enzyme inhibitory [2], antibacterial [2,43,50,70-80], antifungal [2,76], antimycobacterial [50], anticancer [81], anti-inflammatory [2,72,82,83], antioxidant [43,70], hemagglutinating [84], and cytotoxicity [43] activities.

Acetylcholinesterase enzyme inhibitory activities

Ndhlala *et al*. [2] investigated the acetylcholinesterase enzyme inhibitory activities of aqueous bulb extracts of *D. elata* using the enzyme isolated from electric eels with galanthamine as the positive control. The extract showed moderate AChE inhibitory activity of 50.0% with half maximal inhibitory concentration (IC_{50}) value of 487.4±8.0 μg/mL [2]. The ability of *D. elata* bulb extracts to inhibit acetylcholinesterase shows potential therapeutic potential of the species in the management of memory loss and neurodegenerative disorders.

Antibacterial activities

Luyt *et al*. [72] evaluated antibacterial activities of aqueous, ethyl acetate, and ethanol bulb and leaf extracts of *D. elata* against *Bacillus*

Table 1: Medicinal uses of *D. elata*

Medicinal use	Parts of the plant used	References
Blood and cardiovascular system		
Blood purification	Bulbs or *imbizae phuzwata* concoction	[2,3,39-42]
Blood purification	Bulbs mixed with leaves, roots, and twigs of *Kirkia wilmsii* Engl., *Hypoxis hemerocallidea* Fisch., C. A. Mey. and Avé-Lall. (corms), *Monsonia angustifolia* E. Mey. ex A. Rich. (leaves), and leaves of *Sarcostem maviminale* (L.) Br. and *Vahlia capensis* (L. f.) Thunb.	[43]
Hypertension	Bulbs	[2,3,19,44]
Digestive system		
Antidiarrheal	Bulbs mixed with leaves, roots, and twigs of *Kirkia wilmsii, Hypoxishem erocallidea* (corms), *Monsonia angustifolia* (leaves), and leaves of *Sarcostem maviminale,* and *Vahlia capensis*	[43]
Constipation	*Imbizae phuzwata* concoction	[2,3]
Emetic	Bulbs	[37,45-47]
General ailments		
Angina pain	Bulbs	[48]
Body pains	*Imbizae phuzwata* concoction	[2,3]
Energizing tonic	*Imbizae phuzwata* concoction	[2,3]
Fever	Bulbs and leaves or bulbs mixed with roots of *Artemisia afra* Jacq. ex Willd., *Siphonochilus aethiopicus* (Schweinf.) B. L. Burtt and *Erythrina caffra* Thunb.	[45,49,50]
Headache	Bulbs	[1]
Heart tonic	Bulbs	[47]
Internal sores	Bulbs	[41]
Sores	Bulbs and leaves	[51]
Stress	*Imbizae phuzwata* concoctions	[2,3]
Infections and infestations		
Gonorrhea	Bulbs	[19,52,53]
HIV/AIDS opportunistic infections	Bulbs or bulbs mixed with twigs of *Sarcostemm aviminale* (L.) R. Br. and roots of *Elaeodendron transvaalense* (Burtt Davy) R. H. Archer, *Elephantor rhizaelephantina* (Burch.) Skeels and *Zanthoxylumcapense* (Thunb.) Harv. and bark of *Sclero caryabirrea* (A. Rich.) Hochst.	[19,53,54]
STIs	Bulbs mixed with roots of *Elaeodendron transvaalense*, *Elephantor rhizaelephantina* (roots), *Sarcostemm aviminale* (twigs), *Scleroc aryabirrea* (bark), and *Zantho xylumcapense* (root)	[55]
Tuberculosis	Bulbs or bulbs mixed with roots of *Callilep islaureola* DC, *Croton menyharthii* Pax, *Senna italica* Mill. and bulb of *Siphonochilus aethiopicus* (Schweinf.) B. L. Burtt or bulbs mixed with the bark of *Warburgi asalutaris* (G. Bertol.) Chiov. or bulbs mixed with leaves of *Ricinus communis* L. or bulbs mixed with roots of *Dicoma anomala* Sond. and bulb of *Eucomis autumnalis* (Mill.) Chitt.	[48,50]
Muscular-skeletal system		
Arthritis	Bulbs and *imbizae phuzwata* concoction	[2,3,39]
Back pain	Bulbs	[41]
Edema	Bulbs	[1]
Inflammation	Bulbs and leaves	[51]
Muscle pain	Bulbs	[41]
Swelling	Bulbs	[39]
Pain		
Pain	Bulbs and leaves or bulb mixed with leaves, roots, and twigs of *Kirkia wilmsii, Hypoxis hemerocallidea* (corm), *Monsonia angustifolia* (leaves), and leaves of *Sarcostemma viminale* and *Vahlia capensis*	[43,46,51]
Reproductive system and sexual health		
Aphrodisiac	*Imbizae phuzwata* concoction or bulbs mixed with leaves, roots, and twigs of *Kirkia wilmsii, Hypoxis hemerocallidea* (corm), *Monsonia angustifolia* (leaves), and leaves of *Sarcostemma viminale* and *Vahlia capensis*	[2,3,43]
Erectile dysfunction	Bulbs	[56]
Impotence	Bulbs	[19,57]
Infertility	Bulbs	[1,18,19,57]
Respiratory system		

(Contd...)

Table 1: *(Continued)*

Medicinal use	Parts of the plant used	References
Blocked nose	Bulbs or bulbs mixed with roots of *Artemisia afra*, *Siphonochilus aethiopicus,* and *Erythrina caffra*	[50]
Chest pains	Bulbs and leaves or bulbs mixed with leaves of *Lippia javanica* (Burm. f.) Spreng. or bulbs mixed with roots of *Artemisia afra, Siphonochilus aethiopicus,* and *Erythrina caffra* or bulbs mixed with roots of *Elaeodendron transvaalense* (Burtt Davy) R. H. Archer	[48-50]
Colds	Bulbs and leaves	[45,46,49]
Cough	Bulbs mixed with leaves of *Lippia javanica*	[50]
Expectorant	Bulbs	[45,47]
Runny nose	Bulbs mixed with leaves of *Lippia javanica*	[50]
Ritual or magical uses		
Protect households from evil spirits and lightning, and also to chase away, ward off or root out evil spirits	*Intelezi* herbal concoction	[4,45]
Urinary system		
Bladder complaints	Leaves	[1,15,58]
Diuretic	Leaves	[1,39,47,58]
Kidney problems	*Imbizae phuzwata* concoction	[2,3]
Uterus problems	Bulbs and leaves	[1,15,58]

HIV: Human immunodeficiency virus, AIDS: Acquired immune deficiency syndrome, STIs: Sexually transmitted infections

Table 2: Bufadienolides isolated from *D. elata* bulb using NMR spectroscopy

Bufadienolides	Extract	References
Proscillaridin A	Chloroform: isopropanol	[72,73]
Scilliroside	Chloroform or chloroform-n-butanol	[74]
12β-hydroxyscillirosidin	Chloroform or chloroform-n-butanol	[74]
12β-hydroxyscilliroside	Chloroform or chloroform-n-butanol	[74]
Hellebrigenin-3-0-β-glucoside	Chloroform or chloroform-n-butanol	[74]
16β-hydroxyhellebrigenin	Chloroform or chloroform-n-butanol	[74]
16β-hydroxyhellebrigenin-3-0-β-glucoside	Chloroform or chloroform-n-butanol	[74]
5β,16β-dihydroxybufalin-3-O-β-glucoside	Chloroform or chloroform-n-butanol	[74]
6β-acetoxy-3β,8β,12β,14β-tetrahydroxybufa-4,20,22-trienolide (12β-hydroxyscillirosidin)	Dichloromethane	[75]
14β-hydroxybufa-4,20,22-trienolide 3β-O-{α-ʟ-rhamnopyranosyl-[(1→4)-β-D-glucopyranosyl]-(1→3)-α-ʟ-rhamnopyranoside} (urginin)	Dichloromethane	[75]
6β-acetoxy-3β,8β,14β-trihydroxy-12-oxobufa-4,20,22-trienolide	Dichloromethane	[69]
6β-acetoxy-3β,8β,12β,14β-tetrahydroxybufa-4,20,22-trienolide (12β-hydroxyscillirosidin)	Dichloromethane	[69]

NMR: Nuclear magnetic resonance

subtlis, Escherichia coli, Klebsiella pneumoniae, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus aureus, and *Staphylococcus epidermis* using disk-diffusion assay with neomycin (2 μg/ml) as the positive control. Only ethyl acetate bulb extract was active against *B. subtlis, K. pneumoniae, M. luteus, P. aeruginosa,* and *S. aureus* with inhibition ratios ranging from 0.1 to 0.63 [72]. Ncube *et al*. [76] evaluated antibacterial activities of aqueous, dichloromethane, ethanol, and petroleum ether extracts of bulb and leaves of *D. elata* between spring, summer, autumn, and winter seasons against *Bacillus subtilis, S. aureus, E. coli,* and *K. pneumoniae* using the microdilution bioassay with neomycin (μg/ml) as the positive control. The extracts were active in all seasons except for winter when the leaves are not available showing minimum inhibitory concentration (MIC) values ranging from 0.8 mg/ml to >12.5 mg/ml [76]. Ndhlala *et al*. [2] evaluated the antibacterial activities of aqueous, petroleum ether, dichloromethane, and ethanol bulb extracts of *D. elata* against *Bacillus subtilis, E. coli, K. pneumoniae,* and *S. aureus* using the microdilution bioassay with neomycin as the positive control. The extracts showed activities with MIC values ranging from 0.8 to >12.5mg/mL [2]. Baskaran *et al*. [77] evaluated the antibacterial activities of ethanol bulb, leaf, shoots, and plantlet extracts of *in vitro* and *ex vitro* regenerated *D. elata* in comparison to naturally-grown plants against *S. aureus, Enterococcus faecalis, E. coli,* and *P. aeruginosa* using the microdilution method with neomycin (100 μl) as the positive control. All extracts exhibited activities with MIC values ranging from 0.2 mg/ml to 12.5 mg/ml [77]. Okem *et al*. [71] evaluated antibacterial activities of ethanol stem bulb extracts of *D. elata* against *E. coli* and *S. aureus* using microdilution assay with neomycin (2 μg/ml) as the positive control. The extracts exhibited activities with MIC values ranging from 6.3 mg/mL to 12.5 mg/mL [71]. Okem *et al*. [78] evaluated the effects of cadmium and aluminum accumulation on antibacterial activities of ethanol stem bulb extracts of *D. elata* against *E. coli* and *S. aureus* using microdilution assay with neomycin (2 μg/ml) as the positive control. The control extracts exhibited MIC values of 0.4 mg/ml and 0.8 mg/ml against *S. aureus* and *E. coli*, respectively, while antibacterial activities decreased in extracts exposed to increasing heavy metal stress with MIC values ranging from 0.8 mg/ml to 12.5 mg/ml [78]. Madisha [50] evaluated the antibacterial activities of ethanol, methanol, hydroethanol, and dichloromethane bulb extracts of *D. elata* against *Bacillus cereus*, *E. faecalis*, *E. coli*, *Neisseria gonorrhoeae*, *Proteus vulgaris, P. aeruginosa, Shigella flexneri, S. aureus, Staphylococcus epidermidis,* and *Vibrio parahaemolyticus* using agar well dilution method and streak plate disc diffusion assays. The extracts revealed varying degrees of activities with the zone of inhibition values ranging from 8.0 mm to 19.0 mm and MIC values ranging from 0.1 mg/mL to 12.5 mg/mL [50]. Madisha [50] also evaluated the antibacterial activities of ethanol and hydroethanol bulb extracts of *D. elata* mixed with roots of *Elephantorrhiza elephantina* and leaves of *Aloe marlothii* and *Maurea angolensis* against *B. cereus*, *E. faecalis*, *E. coli*, *N. gonorrhea*, *P. vulgaris*, *P. aeruginosa*, *S. flexneri*, *S. aureus*, *S. epidermidis,* and *V. parahaemolyticus* using agar well dilution method and streak plate disk diffusion assays. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.4 mg/mL to 1.6 mg/mL [50]. Matotoka and Masoko [70] evaluated antibacterial activities of acetone and hexane extracts of *D. elata* bulb against *S. aureus, E. faecalis, E. coli,* and *P. aeruginosa* using the broth

Table 3: Mineral and phytochemical composition of *D. elata*

Mineral and phytochemical composition	Values	Plant parts	References
Aluminum (mg/kg dry weight)	559.8–1595.0	Bulbs	[70,71]
Arsenic (mg/kg dry weight)	1.8	Bulbs	[71]
Boron (mg/L)	3.0	Bulbs	[70]
Cadmium (mg/kg dry weight)	0.01–0.06	Bulbs	[71]
Calcium (mg/L)	19.0	Bulbs	[70]
Cobalt (mg/L)	0.04	Bulbs	[70]
Copper (mg/kg dry weight)	5.6–11.3	Bulbs	[71]
Chromium (mg/kg dry weight)	7.8–12.0	Bulbs	[71]
Flavonoid (mg of quercetin equivalent/g extract)	0.54–15.0	Bulbs and leaves	[43,71,76]
Gallotannin (µg gallic acid equivalent/g dry weight)	4.0–7.0	Bulbs and leaves	[76]
Iron (mg/L)	0.15	Bulbs	[70]
Iron (mg/kg dry weight)	593.0–1634.0	Bulbs	[71]
Lead (mg/kg dry weight)	0.2–1.2	Bulbs	[71]
Magnesium (mg/L)	28.0	Bulbs	[70]
Manganese (mg/kg dry weight)	60.7–145.8	Bulbs	[70,71]
Mercury (mg/kg dry weight)	0.04–0.8	Bulbs	[71]
Molybdenum (mg/L)	0.02	Bulbs	[70]
Nickel (mg/kg dry weight)	4.2–10.0	Bulbs	[71]
Phosphorus (mg/L)	24.0	Bulbs	[70]
Potassium (mg/L)	53.0	Bulbs	[70]
Silicon (mg/L)	4.0	Bulbs	[70]
Sodium (mg/L)	56.0	Bulbs	[70]
Sulfur (mg/L)	7.0	Bulbs	[70]
Tannin (mg of gallic acid equivalent/g extract)	4.5–9.6	Bulbs and leaves	[43,76]
Tin (mg/kg dry weight)	31.4–79.8	Bulbs	[71]
Total phenolics (mg gallic acid equivalent/g dry weight)	0.05–2.5	Bulbs and leaves	[43,71,76]
Total saponins (mg diosgenin equivalent/g dry weight)	5.0–17.0	Bulbs and leaves	[76]
Total steroidal saponin (mg diosgenin equivalent/g dry weight)	1.0–4.5	Bulbs and leaves	[76]
Zinc (mg/L)	0.1	Bulbs	[70]
Zinc (mg/kg dry weight)	34.1–102.6	Bulbs	[71]

microdilution assay. The extracts exhibited activities against *E. faecalis* and *P. aeruginosa* with MIC values ranging from 0.6 mg/mL to 2.5 mg/mL and total activities ranging from 3.3 mL/g to 13.3 mL/g [70]. Baskaran *et al*. [79] evaluated antibacterial activities of the aqueous bulb and root extracts of *ex vitro* grown *D. elata* derived from somatic embryogenesis against *Bacillus subtilis*, *E. faecalis*, *M. luteus*, *S. aureus*, *E. coli*, *K. pneumonia,* and *P. aeruginosa* using microtiter bioassay with neomycin (µg/ml) as a positive control. The extracts exhibited activities with MIC values ranging from 0.4 mg/ml to 6.3 mg/ml [79]. Kandari [80] evaluated antibacterial activities of aqueous, dichloromethane, and ethanol bulb extracts of *D. elata* subjected to vermicompost leachate at different concentrations against Bacillus subtilis, *S. aureus*, and *E. coli* using microdilution assay. The extracts exhibited activities with MIC values ranging from 0.4 mg/ml to 6.3 mg/ml [80]. Matotoka and Masoko [43] evaluated antibacterial activities of an herbal mixture of *D. elata* bulb together with leaves of *M. angustifolia*, *S. viminale* and Vahlia capensis, *Kirkia wilmsii* (leaves, roots, and twigs), and *Hypoxis hemerocallidea* (corm) against *Bacillus subtilis, Citrobacter braakii, Enterobacter aerogenes, Enterobacter cloacae, E. faecalis, E. coli, K. pneumoniae, Leclercia adecarboxylata, Pantoea agglomerans, P. aeruginosa,* and *S. aureus* using broth microdilution assay with ampicillin (µg/mL) as a positive control. The herbal mixture exhibited activities with MIC values ranging from 0.3 mg/mL to >2.5 mg/mL [43]. The documented antibacterial activities exhibited by extracts of *D. elata* corroborate the traditional application of the species as herbal medicine against bacterial infections causing diarrhea [43], gonorrhea [19,52,53], sexually transmitted infections [55], and sores [51].

Antifungal activities

Ncube *et al*. [76] evaluated antifungal activities of aqueous, dichloromethane, ethanol, and petroleum ether extracts of bulb and leaf extracts of *D. elata* between spring, summer, autumn, and winter seasons against *Candida albicans* using the microdilution bioassay with amphotericin B (µg/ml) as the positive control. The extracts were active in all seasons except for winter when the leaves are not available showing MIC and MFC values ranging from 0.4 mg/ml to >12.5 mg/ml [76]. Ndhlala *et al*. [2] investigated the antifungal activity of aqueous, petroleum ether, dichloromethane, and ethanol bulb extracts of *D. elata* against *C. albicans* using the microdilution assay with amphotericin B as the positive control. The extracts exhibited activities with MIC and MFC values ranging from 3.1 to 6.3 mg/mL and 6.3 mg/mL to 12.5 mg/mL [2].

Antimycobacterial activities

Madisha [50] evaluated the antimycobaceterial activities of ethanol, methanol, hydroethanol, and dichloromethane bulb extracts of *D. elata* against *Mycobacterium tuberculosis, Mycobacterium smegmatis, Mycobacterium peregrinum,* and *Mycobacterium haemophilus* using agar well dilution method and streak plate disc diffusion assays. The extracts revealed varying degrees of activities with the zone of inhibition values ranging from 9.0 mm to 21.0 mm and MIC values ranging from 0.1 mg/mL to 12.5 mg/mL [50]. Madisha [50] also evaluated the antimycobacterial activities of ethanol and hydroethanol bulb extracts of *D. elata* mixed with roots of *Elephantor rhizaelephantina* and leaves of *A. marlothii* and *M. angolensis* against *M. tuberculosis, M. smegmatis, M. peregrinum,* and *M. haemophilus* using agar well dilution method and streak plate disc diffusion assays. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.1 mg/mL to 1.6 mg/mL [50]. These findings show the potential of *D. elata* in the treatment and management of respiratory problems such as blocked nose [48], chest pains [46-48], colds [43,44,47], cough [48], and runny nose [50].

Anticancer activities

Fouche *et al*. [81] evaluated *in vitro* anticancer activities of dichloromethane:methane (1:1) of the whole plant of *D. elata* against a panel of three human cell lines (breast MCF7, renal TK10, and melanoma UACC62). The extract exhibited total growth inhibition values ranging from 6.3 µg/ml to 29.6 µg/ml. The extracts were screened against 60 human cancer cell lines organized into sub-panels representing leukemia, melanoma, cancer of the lung, colon, kidney, ovary, central nervous system, breast, and prostate. The extract exhibited total growth inhibition values of 1.1 μg/ml against ovarian (OVCAR-3), 1.4 μg/ml against central nervous system cancer, CNSC SF-539 and 1.4 μg/ml against non-small cell lung cancer, NSCLC A549/ATCC [81]. The documented anticancer activities may be attributed to bufadienolides as these compounds are known to have anticancer activities [62-68].

Anti-inflammatory activities

Luyt *et al*. [72] evaluated anti-inflammatory activities of aqueous, ethyl acetate, and ethanol bulb and leaf extracts of *D. elata* using the cyclooxygenase assay with indomethacin as the positive control. The bulb extracts inhibited cyclooxygenase with inhibition ranging from 69.0% to 98.0% which was comparable to 94% exhibited by indomethacin, the positive control [72]. Stafford *et al*. [82] evaluated anti-inflammatory activities of aqueous, ethanol, and hexane bulb extracts of fresh and stored material of *D. elata* by assessing their ability to inhibit cyclooxygenase (COX)-1 enzymes. The ethanol extract showed high inhibition level of 96.0% which decreased to 76.0% of the COX-1 enzyme after 90 days of storage while aqueous extract showed 61.0% inhibition which decreased to 0% of the COX-1 enzyme after 90 days of storage [82]. Ndhlala *et al*. [2] investigated the anti-inflammatory effects of aqueous, dichloromethane, ethanol, and petroleum ether bulb extracts of *D. elata* using COX-1 and COX-2 inhibitory bioassays. The aqueous and ethanol extracts showed percentage inhibition of over 80.0% and 48.0%, respectively, for COX-1 while only the aqueous extract showed moderate inhibition of over 55.0% for COX-2 enzyme [2]. Ncube *et al*. [83] evaluated the anti-inflammatory activities of aqueous, dichloromethane, ethanol, and petroleum ether bulb and leaf extracts of *D. elata* collected in spring, summer, autumn, and winter seasons by assessing their ability to inhibit COX-1 and COX-2 enzymes. The dichloromethane and petroleum ether bulb and leaf extracts in all seasons except for winter when the leaves are not available showed moderate to high inhibition levels ranging from 58.0% to 94.1% of the COX-1 enzyme. A similar trend was observed for COX-2 enzyme with inhibition levels ranging from 52.8% to 91.2% [83]. These findings support the traditional use of *D. elata* as herbal medicine for back pain [39], body pains [2,3],inflammation [51], muscle pain [41], pain [43,46,51], and swelling [39].

Antioxidant activities

Matotoka and Masoko [70] evaluated antioxidant activities of acetone and hexane extracts of *D. elata* bulb using 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging assay. The hexane extracts exhibited antioxidant activities [70]. Matotoka and Masoko [43] evaluated antioxidant activities of an herbal mixture of *D. elata* bulb together with leaves of *M. angustifolia, S. viminale* and *Vahlia capensis, Kirkia wilmsii* (leaves, roots, and twigs), and *Hypoxis hemerocallidea* (corm) using the DPPH free radical scavenging assay and ferric reducing power with L-ascorbic acid as the positive control. The free radical scavenging activity showed that the herbal concoction exhibited moderate antioxidant activities. The ferric reducing power measuring the reduction of Fe3+ to Fe2+ revealed that the herbal concoction exhibited good reducing activity compared to L-ascorbic acid, the positive control [43]. The documented antioxidant activities of the bulb extracts of *D. elata* are probably due to flavonoids, gallotannins, phenolics, saponins, and tannins which have been isolated from the species [43,71,76].

Hemagglutinating activities

Gaidamashvili and Van Staden [84] evaluated hemagglutinating activities of aqueous bulb extracts of *D. elata* toward fresh and glutaraldehyde-treated rabbit erythrocytes using the hemagglutination and hapten inhibition assays. The extracts yielded hemagglutinating activity which was detected in the crude protein extracts at the minimal concentrations of 19.9 mg/ml. The was inhibited by 200 mM lactose along with major inhibition by D(+) trehalose, >DL arabinose, and D fructose [84]. The documented information on hemagglutinating activities and the identification of proteins from *D. elata* may be useful for future characterization of the species extracts in developing pharmaceutical products.

Cytotoxicity activities

Matotoka and Masoko [43] evaluated cytotoxicity activities of an herbal mixture of *D. elata* bulb together with leaves of *M. angustifolia, S. viminale* and *Vahlia capensis, Kirkia wilmsii* (leaves, roots, and twigs), and *Hypoxis hemerocallidea* (corm) using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide calorimetric assay with actinomycin D as the negative control. The cytotoxic concentration (CC_{50}) values of all the concoctions were above the highest concentration used (1000 μg/mL) and Actinomycin D; the negative control exhibited CC_{50} value of 0.6 μg/mL [43]. The documented cytotoxicity activities exhibited by *D. elata* extracts may be attributed to bufadienolides as these compounds are known to have cytotoxicity activities [64,65].

CONCLUSION

Based on information about *D. elata* that has been documented in this review, there appear to be research gaps on ethnopharmacological evaluation and clinical research on the species. No *in vivo* evaluations nor an assessment of target-organ toxicity have been carried out using the extracts from the species. Since *D. elata* is widely used in combination with other plant species in various herbal concoctions, there is a need for extensive research to evaluate synergistic effects of the different extracts and also to evaluate their ability to enhance the efficiency of the additive mixtures. Future research should also focus on aerial parts of the species to ensure full utilization of the possible medicinal potential of the species. Literature studies show that the major phytochemical compounds isolated from *D. elata* so far are mainly bufadienolides but very little attempt has been made to correlate the activities of these compounds with the ethnomedicinal uses of the species. Therefore, detailed phytochemical studies of *D. elata* and its pharmacological properties, especially the mechanism of action of its bioactive constituents to illustrate the correlation between its ethnomedicinal uses and pharmacological activities should be the focus of future research studies. Extensive *in vivo* experiments are required to validate the existing pharmacological activities. Since *D. elata* contain potentially toxic compounds, future studies should research on how potential toxic components of the species can be managed.

AUTHOR'S CONTRIBUTIONS

The author declares that this work was done by the author named in this article.

CONFLICTS OF INTEREST

The author declares that there are no conflicts of interest regarding the publication of this paper.

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