Review Of Medicinal Uses, Phytochemistry And Biological Activities Of Brunsvigia Grandiflora Lindl. And B. Radulosa Herb. (Amaryllidaceae)

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Abstract: Brunsvigia grandiflora Lindl. and B. radulosa Herb. are perennial herbs with a long history of medicinal use in southern Africa. The aim of this study was to review the medicinal uses, phytochemistry and biological activities of B. grandiflora and B. radulosa. A systematic review of the literature was carried out to document the medicinal uses, phytochemistry and biological activities of B. grandiflora and B. radulosa. The results of this study are based on data obtained from electronic databases such as Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis, and pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. This study revealed that B. grandiflora and B. radulosa are mainly used to facilitate easy birth and traditional medicines for circumcision wounds, colds, cough, infertility in women, liver and renal complaints. Pharmacological research identified phytochemical compounds such as 11-hydroxyvittatine, 1-o-acetyl-lycorine, 1-o-acetylnorpluviine, 1-epideacetylbowdensine, anhydrolycorin-6-one, anhydrolycorinium chloride, apohaemanthamine, brunsvigine, crinamine, crinine, galantamine, hamayne, lycorine and sternbergine. The crude extracts of B. grandiflora and B. radulosa and phytochemical compounds isolated from the species exhibited antibacterial, antimycobacterial, anticonvulsant, anti-inflammatory, neurological, antiplasmodial, antitumour and cytotoxicity activities. There is need for extensive phytochemical, pharmacological and toxicological studies of crude extracts of B. grandiflora and B. radulosa and phytochemical compounds isolated from the species.

Keywords: Alkaloids, Amaryllidaceae, Brunsvigia grandiflora, Brunsvigia radulosa, indigenous knowledge, southern Africa, traditional medicine

1 INTRODUCTION

The genus Brunsvigia Heist. consists of perennial, deciduous, temperate and bulbous herbal plants with annual leaves belonging to the Amaryllidaceae or amaryllis family [1]. Similarly, species of the family Amaryllidaceae are mostly bulbous perennials or biennial plants that are distributed in the tropics and the warm parts of the temperate regions of the world [2]. The family Amaryllidaceae comprises about 1000 species belonging to 60 genera of which an estimated 300 species in 20 genera are of African origin [2]. Several species belonging to the family Amaryllidaceae are widely used as sources of traditional medicines throughout the world to cure diseases and ailments such as ophthalmological, odontological, musculoskeletal system, injuries, gynaecological, fever, fainting, fits, ear, dermatological, antidote, gastro-intestinal disorders, urinary problems, sexually transmitted infections, sexual dysfunction, respiratory infections, and gynaecological problems [3-9]. Species widely used as sources of traditional medicines include Amaryllis belladonna L., Boophone disticha (L.f.) Herb., Clivia miniata (Lindl.) Regel, Crinum bulbispermum (Brum. f.) Milne-Redh. & Schweick., Crinum macowanii Bak., Crinum moorei Hook. f., Cyrtanthus falcatus R.A. Dyer, Galanthus nivalis L., Gethyllis ciliaris (Thunb.) Thunb., Gethyllis multifolia L. Bolus, Gethyllis villosa (Thunb.) Thunb., Haemanthus albiflos Jacq., Haemanthus deformis Hook. f. and Scadoxus puniceus (L.) Friis & Nordal [5,10-12]. Some of these species exhibited analgesic, anti-inflammatory, anticholinergic, antitumour, antiviral, antioxidant, antiparasitic, nervous system effects, antifertility, antibacterial, antifungal, anxiolytic, antimalarial, immunostimulatory, antidepressive, cardiovascular, uterotonic, hypotensive and acetylcholinesterase activities.

Some of these pharmacological properties could be attributed to the alkaloids such as buphanidrin, undulatin, buphanisine, nerbowdine, lycorine, clivacetine, galanthamine, clivonine, crinamine, cliviasine, pratorimine, clividine, pratorinine, crinine, powelline, macowine, hamayne, cherylline and bulbispermine isolated from the species [10]. Similarly, Ding et al. [13] argued that the medicinal value of the Amaryllidaceae species is attributed to the presence of tyrosine-derived alkaloids. Previous research revealed that the Amaryllidaceae family is one of the 20 most important alkaloid-containing plant families [13]. The genus has approximately 20 species confined to southeastern and southern Africa, from Tanzania to South Africa [14,15]. The genus name Brunsvigia is in honour of Duke of Brunswick of the House of Braunschweig Brunswick-Lüneburg who promoted the study of vascular plants, including B. orientalis (L.) Aiton ex Eckl. [15]. The specific epithet grandiflora is derived from two Latin words “grandis” and “flora”, meaning “large” and “flower”, respectively, in reference to the large flowers that are characteristic of B. grandiflora. Hence, B. grandiflora is often referred to as “giant candelabra flower” or “giant candellabria”. The specific epithet radulosa is in reference to the roughness of the leaf surface of B. radulosa [16]. The synonyms of B. grandiflora include Amaryllis banksiana Lindl., A. slateriana Lindl., Ammocharis slateriana (Lindl.) Kunth, Brunsvigia banksiana (Lindl.) T. Durand & Schinz, B. slateriana (Lindl.) Benth. & Hook. f. ex Tavel and B. sphaerocarpa Baker [17]. The synonyms associated with the name B. radulosa include B. burchelliana Herb. and B. cooperi Baker [17]. Brunsvigia grandiflora has been recorded in South Africa while B. radulosa has been recorded in Botswana, Eswatini, Lesotho and South Africa (Fig. 1).

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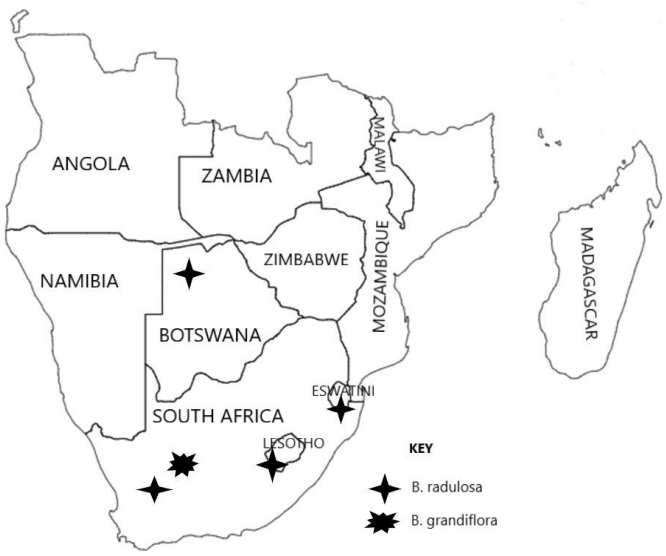

***Fig. 1**: Geographical distribution of Brunsvigia grandiflora and B. radulosa*

Research by Watt and Breyer-Brandwijk [3] and Hutchings et al. [4] showed that bulb decoctions of several Brunsvigia species are used as traditional medicines for colds, cough and administered as enemas for liver and renal complaints. The Brunsvigia species widely used as sources of traditional medicines include B. grandiflora, B. josephinae (Redouté) Ker Gawl., B. natalensis Baker, B. radulosa and B. undulata F.M. Leight. [18-29]. The dry bulb tunics of B. josephinae are used to compress pain and inflammation, wound dressing and plasters after male circumcision [29,30]. The bulbs of B. natalensis are used as traditional medicines to straighten bones in children [23,29,31]. The bulbs of Brunsvigia species are sold as sources of traditional medicines in informal herbal medicine markets of Gauteng province in South Africa [32]. Brunsvigia litoralis is categorized as Endangered using the IUCN Red List Categories and Criteria version 3.1 of threatened species (http://www.iucnredlist.org). The population size of the species is small, severely fragmented and restricted to the coastal flats of the Great Brak River in the Western Cape to Port Elizabeth in the Eastern Cape of South Africa. The infrastructural developments in the coastal areas and invasive alien plant species appear to be threats throughout the distributional range of the species [33-38]. It is therefore, within this context that this study was undertaken aimed at reviewing the medicinal uses, phytochemistry and pharmacological properties of B. grandiflora and B. radulosa.

2. Materials and Methods

Several electronic databases searched for the medicinal uses, phytochemistry and pharmacological properties of B. grandiflora and B. radulosa included Web of Science, Elsevier, Pubmed, Google scholar, Springer, Science Direct, Scopus, Taylor and Francis. Additional information was obtained from pre-electronic sources such as books, book chapters, scientific journals and other grey literature obtained from the University library. The relevant terms included Brunsvigia grandiflora and B. radulosa, which were paired with keywords such as "medicinal uses of Brunsvigia grandiflora or B. radulosa", "phytochemicals of Brunsvigia grandiflora or B. radulosa", "biological activities of Brunsvigia grandiflora and B. radulosa", "pharmacological properties of Brunsvigia grandiflora and B. radulosa", "ethnobotany of Brunsvigia grandiflora and B. radulosa", and various other synonyms and common names of the plant species. The ultimate goal of this search was to explore articles that investigated the medicinal uses, phytochemical and pharmacological properties of Brunsvigia grandiflora and B. radulosa. A total of 74 articles published between 1950 and 2021 matched the inclusion criteria and were included in this review (Fig. 2).

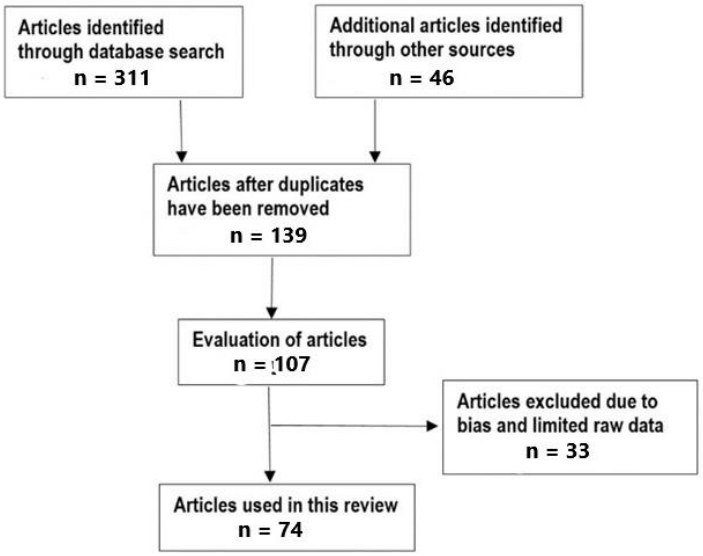

***Fig.** 2. Flow chart showing the number of research publications used in this study*

3. Results and Discussion

3.1 Botanical description of Brunsvigia grandiflora and B. radulosa

Brunsvigia grandiflora is a bulbous perennial herb which can grow up to 60.0 cm in height [39-41]. Brunsvigia grandiflora has a large perennial bulb that can reach up to 20 cm in diameter, covered with tan coloured and brittle tunics [41]. The leaves of B. grandiflora appear at flowering, are grey-green in colour, upright, spiralled, usually 10 to 15, oblong in shape with waxy margins and more or less erect in a fan. The flowers of B. grandiflora occur in a rounded terminal cluster on long pedicels and joined together on a thick stem. The flowers are star shaped, 40.0 mm in diameter, and deep pink in colour. When the seeds are dry, the main stem dries and the head falls off, the seeds are blown away by the wind, and scattered across the veld. Brunsvigia grandiflora has been recorded in the grasslands of the Mpumalanga, Eastern Cape, KwaZulu-Natal and Free State provinces of South Africa (Fig. 1) at an altitude ranging from 300 m to 2200 m above sea level [17]. Brunsvigia radulosa is a deciduous, bulbous perennial herb which can grow up to 80.0 cm in height [17]. Brunsvigia radulosa has a large perennial bulb averaging 100.0 mm in diameter [16]. The bulb has a short neck covered by hard, brown coloured and brittle tunics. The leaves of B. radulosa appear at flowering, are usually 4 to 6 leaves, below the flowers, spreading flat on the ground with thick, tough and rough surfaces and margins. The inflorescence of B. radulosa consist of several flowers, individually pedicelled, forming a large umbel. The dead umbels break away from the stem,

tumble around the veld, and the seeds are blown away by the wind, and scattered across the veld. Brunsvigia radulosa has been recorded in the grasslands and open woodland in Botswana, Eswatini, Lesotho and South Africa (Fig. 1) at an altitude ranging from 1000 m to 1500 m above sea level [17].

3.2 Medicinal uses of Brunsvigia grandiflora and B. radulosa

Medicinal uses of Brunsvigia grandiflora and B. radulosa

The bulbs of B. grandiflora are used as decoctions and the outer skin of the bulb is used as a circumcision wound dressing (Table 1, Fig. 3). The major medicinal applications of the bulbs of B. grandiflora include their use as traditional medicines against colds, cough, liver and renal complaints. The bulb decoction of B. radulosa are used as traditional medicines to facilitate easy birth and infertility in women (Table 1). Other medicinal applications of the two species supported by at least two literature sources include the use of the bulbs of radulosa in Eswatini and South Africa to straighten bones of children [42,43], while bulbs of B. grandiflora are used in South Africa as traditional medicines against diarrhoea and stomach complaints [44-46] and tuberculosis [46-48].

TABLE 1

MEDICINAL USES OF BRUNSVIGIA GRANDIFLORA AND B. RADULOSA IN SOUTHERN AFRICA

Medicinal uses	Part used	Country	Reference
B. grandiflora			
Circumcision wounds	Bulb	South Africa	[4,19,41,42,46,49,50]
Colds	Bulb	South Africa	[3,4,42,46,47,50-55]
Convulsions and epilepsy	Bulb	South Africa	[56]
Cough	Bulb	South Africa	[3,4,42,46,47,50-55,57,58]
Diarrhoea and stomach complaints	Bulb	South Africa	[45,46,52]
Liver complaints	Bulb	South Africa	[3,4,42,50,52]
Renal complaints	Bulb	South Africa	[3,4,42,50,52]
Tuberculosis	Bulb	South Africa	[46-48]
Wounds	Bulb	South Africa	[52]
B. ragulosa			
Boosts immune system	Bulbs	Lesotho	[59]
Facilitate easy birth	Bulbs	South Africa	[24,31,42,60-62]
Infertility in women	Bulbs	Lesotho and South Africa	[3,24,42,43,60-65]
Straighten bones of children	Bulbs	Eswatini and South Africa	[42,43]

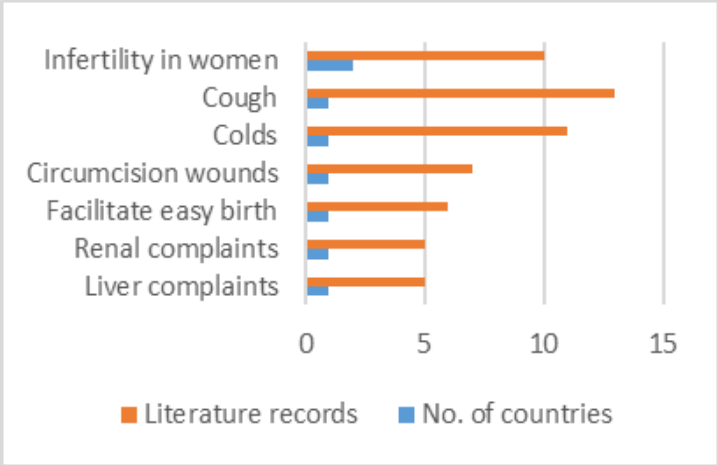

***Fig. 3**: Medicinal uses of Brunsvigia grandiflora and B. radulosa in southern Africa*

3.3 Phytochemistry of Brunsvigia grandiflora and B. radulosa

Numerous alkaloids have been isolated from the bulbs of B. grandiflora and B. radulosa, including 11-hydroxyvittatine, 1-o-acetyl-lycorine, 1-o-acetylnorpluviine, 1-epideacetylbowdensine, anhydrolycorin-6-one, anhydrolycorinium chloride, apohaemanthamine, brunsvigine, crinamine, crinine, galantamine, hamayne, lycorine and sternbergine (Table 2; Fig. 4). Masi et al. [66] identified the alkaloids 11-hydroxyvittatine and crinamine from the bulbs of B. grandiflora while the rest of the alkaloids were identified from the bulbs of B. radulosa [42,60,67-71]. Some of the pharmacological effects exhibited by B. grandiflora and B. radulosa maybe attributed to some of the alkaloids as the alkaloid crinamine is a known respiratory depressant and transient hypotensive agent [6].

TABLE 2

ALKALOIDS ISOLATED FROM THE BULBS OF BRUNSVIGIA GRANDIFLORA AND B. RADULOSA

Alkaloid	Reference
B. grandiflora	
11-hydroxyvittatine	[66]
Crinamine	[66]
B. radulosa	
1-O-acetyl-lycorine	[42]
1-O-acetylnorpluviine	[60,71]
1-epideacetylbowdensine	[60,71]
Anhydrolycorin-6-one	[60,71]
Anhydrolycorinium chloride	[42]
Apohaemanthamine	[71]
Brunsvigine	[60,67-69]
Crinamine	[42,60,67,71]
Crinine	[42,60,71]
Galantamine	[70]
Hamayne	[42,60,71]
Lycorine	[42,60,67,68,71]
Sternbergine	[60,71]

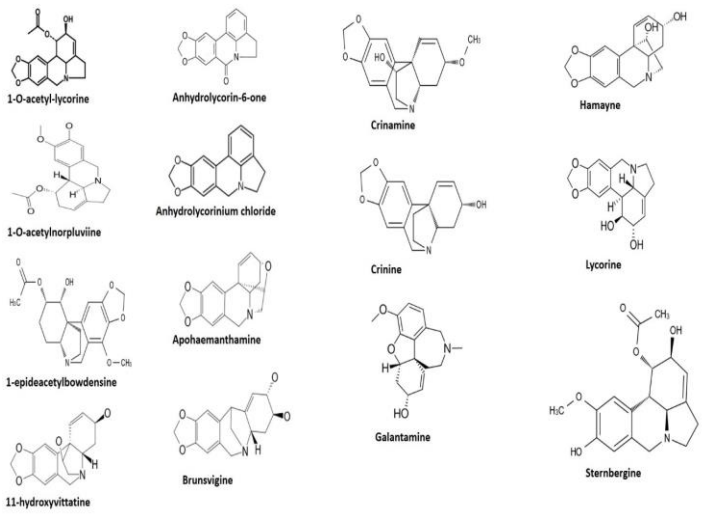

***Fig. 4**: Chemical structures of alkaloids isolated from the bulbs of Brunsvigia grandiflora and B. radulosa*

3.4 Pharmacological properties of Brunsvigia grandiflora and B. radulosa

The following biological activities have been reported from the bulbs of B. grandiflora and B. radulosa and alkaloids isolated from the species: antibacterial [47,53], antimycobacterial [48,53], anticonvulsant [56], anti-inflammatory [48,53], neurological [72], antiplasmodial [71], antitumour [73] and cytotoxicity [71,74] activities.

3.4.1 Antibacterial activities

Madikizela [53] and Madikizela et al. [47] evaluated the antibacterial activities of aqueous, dichloromethane, 80% ethanol and petroleum ether extracts of B. grandiflora bulb against Klebsiella pneumoniae, Staphylococcus aureus and Mycobacterium aurum using the microdilution assay with neomycin and streptomycin as the positive controls. The extracts exhibited activities against tested pathogens with MIC values ranging from 3.1 mg/ml to 12.5 mg/ml [47,53].

3.4.2 Antimycobacterial activities

Madikizela [53] and Madikizela et al. [48] evaluated the antimycobacterial activities of aqueous, dichloromethane, 80% ethanol and petroleum ether extracts of B. grandiflora bulb using the resazurin microplate assay against Mycobacterium tuberculosis H37Ra with rifampicin as a positive control. The extracts exhibited activities against the tested pathogen with MIC values ranging from 6.3 mg/ml to 12.5 mg/ml which were higher than 0.02 mg/ml exhibited by the positive control [48,53].

3.4.3 Anticonvulsant activity

Risa et al. [56] evaluated the anticonvulsant activities of the aqueous and ethanol extracts of of B. grandiflora leaves using the $GABA_A$-benzodiazepine receptor binding assay. The ethanol extract exhibited dose-dependent activities [56].

3.4.4 Anti-inflammatory activities

Madikizela [53] and Madikizela et al. [48] evaluated the anti-inflammatory activities of aqueous, dichloromethane, 80% ethanol and petroleum ether extracts of B. grandiflora bulb using the cyclooxygenase-2 (COX2) inhibition assay with indomethacin as a positive control. The petroleum ether and dichloromethane extracts exhibited weak and moderate activities with percentage inhibition of 23.4% and 42.5%, respectively [48,53].

3.4.5 Neurological activities

Nielsen et al. [72] evaluated the neurological activities of aqueous and 70.0% ethanolic extracts of B. grandiflora bulbs and leaves using an in vitro serotonin reuptake transport protein binding assay. The extracts exhibited activities characterized by more than 50.0% inhibition at 5.0 mg/ml, 1.0 mg/ml, 0.01 mg/ml and 0.001 mg/ml [72].

3.4.6 Antiplasmodial activities

Campbell et al. [71] evaluated the in vitro antiplasmodial activities of the phytochemical compounds 1-O-acetylnorpluviine, apohaemanthamine, 1-epideacetylbowdensine, crinamine, hamayne, lycorine, anhydrolycorin-6-one and sternbergine isolated from the bulbs of B. radulosa against chloroquine-sensitive (D10) and chloroquine-resistant (FAC8) strains of Plasmodium falciparum with chloroquine as a positive control. The compounds exhibited activities against the tested strains with IC50 values ranging from 0.6 µg/ml to >50.0 µg/ml [71].

3.4.7 Antitumour activities

Charlson [73] evaluated the antitumour activities of 50% ethanol and n-butanol extracts of B. radulosa leaves and bulbs against the P-388 lymphocytic leukemic mice. The extracts exhibited activities against the P-388 lymphocytic leukemia [73].

3.4.8 Cytotoxicity activities

Campbell et al. [71] evaluated the cytotoxicity activities of the alkaloids 1-O-acetylnorpluviine, apohaemanthamine, 1-epideacetylbowdensine, crinamine, hamayne, lycorine, anhydrolycorin-6-one and sternbergine isolated from the bulbs of B. radulosa on B16-F10-BL-6 mouse melanoma cells in culture daunomycin as a positive control. The alkaloids exhibited activities with IC50 values ranging from 1.6 µg/ml to >100.0 µg/ml [71]. Nair et al. [74] evaluated the cytotoxicity activities of the alkaloids crinine and crinamine isolated from B. radulosa against the human cervical adenocarcinoma cell line using the calcein AM assay with galanthamine as a positive control. The alkaloids crinine and crinamine exhibited activities with IC50 values of >50.0 µM and 5.8 µM, respectively [74].

4. CONCLUSION

Brunsvigia grandiflora and B. radulosa have been used in southern Africa as traditional medicines for many centuries. Utilization of B. grandiflora and B. radulosa because of their medicinal properties forms the basis of the current demand for the plant species in southern Africa. Research on B. grandiflora and B. radulosa over the past decade on health promoting properties has greatly contributed to the increased consumption of the species as herbal medicine. The focus of this research has been on phytochemical compounds, particularly 11-hydroxyvittatine, 1-o-acetyl-lycorine, 1-o-acetylnorpluviine, 1-epideacetylbowdensine, anhydrolycorin-6-one, anhydrolycorinium chloride, apohaemanthamine, brunsvigine, crinamine, crinine, galantamine, hamayne, lycorine and sternbergine. More research in this regard is required and future research should focus on more

comprehensive chemical characterization of both crude and pure extracts and evaluate potential for development of health products based on traditional uses of B. grandiflora and B. radulosa. Most of the pharmacological researches conducted on B. grandiflora and B. radulosa so far have focused on the phytochemistry and biological properties of bulbs, and little or no research has been done on leaves and other plant parts. Therefore, future research on the species should focus on other plant parts, for example, aerial parts, flowers, leaves and stems, as well as organ-to-organ, age, and seasonal variation evaluations in the phytochemical content and pharmacological activities of the species. The recent increase in the demand for B. grandiflora and B. radulosa products may partly be ascribed to growing body of scientific evidence indicating important health benefits. Brunsvigia grandiflora and B. radulosa are widely sold as traditional medicines in South Africa. For local people who rely on herbal medicines as part of their primary healthcare as well as cultural beliefs, they prefer B. grandiflora and B. radulosa harvested from the wild and unprocessed plant parts sold in informal herbal medicine markets. In the past, there were no records of overexploitation of B. grandiflora and B. radulosa wild populations in southern Africa, resulting in Raimondo et al. [38] listing the species as Least Concern (LC) under the IUCN Red List Categories and Criteria version 3.1 of threatened species (http://www.iucnredlist.org). Recently, signs of local overharvesting have been noted, where local people or plant traders have uprooted whole plants to supply informal medicine markets or use the plants as herbal medicines. Therefore, large-scale commercial utilization of B. grandiflora and B. radulosa is not sustainable if the species are harvested from the wild. Cultivation of B. grandiflora and B. radulosa is therefore, a solution to the sustainability problems associated with harvesting of the species from the wild, and this option is also necessary for establishing commercial scale medicinal production and processing and trade enterprises. The success of commercial cultivation of B. grandiflora and B. radulosa will depend on how the species are marketed as herbal medicines. Significant research has been made in the past 60 years into the chemistry and pharmacology of B. grandiflora and B. radulosa. These studies have shown B. grandiflora and B. radulosa to display various chemical and different biological activities some of which justify their ethnopharmacological utilization in a variety of cultures. Detailed phytochemical studies of B. grandiflora and B. radulosa and their phytochemical properties, especially the mechanisms of action of their bioactive constituents aimed at correlating ethnomedicinal uses with pharmacological activities, should be the focus of further research on the species. There is need for extensive in vivo and clinical experiments to validate the existing pharmacological activities. However, because B. grandiflora and B. radulosa contain potentially toxic compounds, their toxicological properties need to be properly established through proper quality control of product development to ensure that potentially toxic components are kept below tolerance levels.

CONFLICT OF INTEREST

No conflict of interest is associated with this work.

REFERENCES

[1] Du Plessis N and Duncan G. Bulbous plants of southern Africa. Tafelberg, Cape Town; 1989.

[2] Elgorashi EE. Phytochemistry and pharmacology of the family Amaryllidaceae: An overview of research at RCPGD. Natural Product Communications. 2019; 14: 1–11.

[3] Watt JM and Breyer-Brandwijk MG. The medicinal and poisonous plants of southern and eastern Africa. 2nd ed. Livingstone, London; 1962.

[4] Hutchings A, Scott AH, Lewis G and Cunningham A. Zulu medicinal plants: An inventory. University of Natal Press, Pietermaritzburg; 1996.

[5] Fennell CW and Van Staden J. Crinum species in traditional and modern medicine. Journal of Ethnopharmacology. 2001; 78: 15-26.

[6] Van Wyk B-E, Van Oudtshoorn B and Gericke N. Medicinal plants of South Africa. Briza Publications, Pretoria, South Africa; 2013

[7] Maroyi A. A review of ethnobotany, therapeutic value, phytochemistry and pharmacology of Crinum macowanii Baker: A highly traded bulbous plant in southern Africa. Journal of Ethnopharmacology. 2016; 194: 595-608.

[8] Maroyi A. Ethnobotanical, phytochemical and pharmacological properties of Crinum bulbispermum (Burm. f.) Milne-Redh. & Schweick. (Amaryllidaceae). Tropical Journal of Pharmaceutical Research. 2016; 15: 2497-2506.

[9] Van Wyk B-E and Wink M. Medicinal plants of the world. Briza Publications, Pretoria; 2017.

[10] Mason LH, Puschett ER and Wildman WC. Alkaloids of the Amaryllidaceae. Part IV: Crystalline alkaloids of Ammocharis coranica (Ker-Gawl.) Herb., Brunsvigia rosea (Lam.) Hannibal and two Crinum species. Journal of the American Chemical Society. 1955; 77: 1253-1256.

[11] Nair JJ and Van Staden J. Traditional usage, phytochemistry and pharmacology of the South African medicinal plant Boophone disticha (L.f.) Herb. (Amaryllidaceae). Journal of Ethnopharmacology. 2014; 151: 12–26.

[12] Mhlongo LS and Van Wyk B-E. Zulu medicinal ethnobotany: New records from the Amandawe area of KwaZulu-Natal, South Africa. South African Journal of Botany. 2019; 122: 266–290.

[13] Ding Y, Qu D, Zhang K-M, Cang X-X, Kou Z-N, Xiao W and Zhu J-B. Phytochemical and biological investigations of Amaryllidaceae alkaloids: A review, Journal of Asian Natural Products Research. 2017; 19: 53-100,

[14] Snijman DA. A revision of the Brunsvigia radula-group (Amaryllidaceae: Amaryllideae) of species in South Africa, including the description of Brunsvigia gariepensis a new species from Bushmanland in Northern Cape. South African Journal of Botany. 2012; 79: 106–116,

[15] Van Jaarsveld E. Brunsvigia Amaryllidaceae. In: Eggli U and Nyffeler R (Eds.), Illustrated handbook of succulent plants: Monocotyledons. Springer-Verlag GmbH; 2020, pp. 433-434.

[16] Archer RH and Archer C. Brunsvigia radulosa Herb.; 2005. Available at: http://pza.sanbi.org/brunsvigia-radulosa, accessed on 14 March 2021.

[17] Germishuizen G and Meyer NL. Plants of southern Africa: An annotated checklist. Strelitzia 14, National Botanical Institute, Pretoria, South Africa; 2003.
[18] Hutchings A. A survey and analysis of traditional medicinal plants as used by the Zulu, Xhosa and Sotho. Bothalia. 1989; 19: 111-123.
[19] Hutchings A. Some observations on plant usage in Xhosa and Zulu medicine. Bothalia. 1989; 19: 225-235.
[20] Hutchings A and Terblanche SE. Observations on the use of some known and suspected toxic Liliiflorae in Zulu and Xhosa medicine. South African Medical Journal. 1989; 75: 62–69.
[21] Dlisani PB and Bhat RB. Traditional health practices in Transkei with special emphasis on maternal and child health. Pharmaceutical Biology. 1999; 37: 32-36,
[22] Louw CAM, Regnier TJC and Korsten L. Medicinal bulbous plants of South Africa and their traditional relevance in the control of infectious diseases. Journal of Ethnopharmacology. 2002; 82: 147–154.
[23] Moodley N. The chemical investigation of the Amaryllidaceae and Hyacinthaceae. PhD Thesis, University of KwaZulu-Natal, Durban; 2004.
[24] Rice LJ. Micropropagation of Brunsvigia undulata F.M. Leight. MSc Dissertation, University of KwaZulu-Natal, Pietermaritzburg; 2009.
[25] Rice LJ, Finnie JF and Van Staden J. In vitro bulblet production of Brunsvigia undulata from twin-scales. South African Journal of Botany. 2011; 77: 305–312.
[26] Nair JJ and Van Staden J. Pharmacological and toxicological insights to the South African Amaryllidaceae. Food Chemistry and Toxicology. 2013; 62: 262-275.
[27] Torras-Claveria L, Tallini L, Viladomat F and Bastida J. Research in natural products: Amaryllidaceae ornamental plants as sources of bioactive compounds. In: Munoz-Torrero D and Feliu C (Eds.), Recent advances in pharmaceutical Sciences. Transworld Research Network, Trivandrum, Kerala, India; 2017, pp. 69–82.
[28] Hulley IM and Van Wyk B-E. Quantitative medicinal ethnobotany of Kannaland (western Little Karoo, South Africa): Non-homogeneity amongst villages. South African Journal of Botany. 2019; 122: 225–265.
[29] Moodley N, Crouch NR, Bastida J and Mulholland DA. Novel alkaloids and a ceramide from Brunsvigia natalensis (Amaryllidaceae) and their anti-neoplastic activity. South African Journal of Botany. 2021; 136: 40−44.
[30] Voigt W. Brunsvigia josephinae (Redouté) Ker Gawl.; 2004. Available at: http://pza.sanbi.org/brunsvigia-josephinae, accessed on 21 April 2021.
[31] Pooley E. A field guide to wild flowers of KwaZulu-Natal and the eastern region. Natal Flora Publications Trust, Durban; 1998.
[32] Williams VL, Balkwill K and Witkowski ET. A lexicon of plants traded in the Witwatersrand umuthi shops, South Africa. Bothalia. 2001; 31: 71-98.
[33] Hall AV, De Winter M, De Winter B and Van Oosterhout SAM. Threatened plants of southern Africa. South African National Scientific Programmes Report 45. CSIR, Pretoria; 1980.
[34] Hilton-Taylor C. Red data list of southern African plants. Strelitzia 4. South African National Botanical Institute, Pretoria; 1996.
[35] Goldblatt P and Manning JC. Cape plants: A conspectus of the Cape Flora of South Africa. Strelitzia 9. National Botanical Institute, Cape Town; 2000.
[36] Victor JE. South Africa. In: Golding JS (Ed.), Southern African plant Red Data Lists. Southern African Botanical Diversity Network Report 14, SABONET, Pretoria; 2002, pp. 93-120.
[37] Victor JE and Dold AP. Threatened plants of the Albany Centre of Floristic Endemism, South Africa. South African Journal of Science. 2003; 99: 437-446.
[38] Raimondo D, Von Staden L, Foden W, Victor JE, Helme NA, Turner RC, Kamundi DA and Manyama PA. Red List of South African Plants. Strelitzia 25, South African National Biodiversity Institute, Pretoria; 2009.
[39] Dyer RA. A review of the genus Brunsvigia. Plant Life. 1950; 6: 63-83.
[40] Dyer RA. A review of the genus Brunsvigia Heist. Plant Life. 1951; 7: 45-64.
[41] Manning J. Photo guide to the wildflowers of South Africa. Briza Publications, Pretoria; 2012.
[42] Chetty J. Extractives from the Amaryllidaceae: Brunsvigia radulosa and Cyrtanthus breviflorus. MSc Dissertation, University of Natal, Durban; 2001.
[43] Long C. Swaziland's Flora: siSwati names and uses. Swaziland National Trust Commission; 2005. Available at: http://www.sntc.org.sz/index.asp, accessed on 16 April 2021.
[44] Verschaeve L and Van Staden J. Mutagenic and antimutagenic properties of extracts from South African traditional medicinal plants. Journal of Ethnopharmacology. 2008; 119: 575–587.
[45] Madikizela B, Ndhlala AR, Finnie JF and Van Staden J. 2012. Ethnopharmacological study of plants from Pondoland used against diarrhoea. Journal of Ethnopharmacology. 2012; 141: 61–71.
[46] Nair JJ, Van Staden J, Bonnet SL and Wilhelm A. Distribution and diversity of usage of the Amaryllidaceae in the traditional remediation of infectious diseases. Natural Product Communications. 2017; 12: 635-639.
[47] Madikizela B, Ndhlala AR, Finnie JF and Van Staden J. 2013. In vitro antimicrobial activity of extracts from plants used traditionally in South Africa to treat tuberculosis and related symptoms. Evidence-Based Complementary and Alternative Medicine. 2013, volume 2013, article ID 840719.
[48] Madikizela B, Ndhlala AR, Finnie JF and Van Staden J. Antimycobacterial, anti-inflammatory and genotoxicity evaluation of plants used for the treatment of tuberculosis and related symptoms in South Africa. Journal of Ethnopharmacology. 2014; 153: 386–391.
[49] Bhat RB and Jacobs TV. Traditional herbal medicine in Transkei. Journal of Ethnopharmacology. 1995; 48: 7-12.
[50] Nombewu N. The impacts of harvesting circumcision amaryllids from the Eastern Cape province, South Africa. MSc Dissertation. Nelson Mandela Metropolitan University, Port Elizabeth; 2014.
[51] Viladomat F, Bastida J, Codina C, Nair JJ and Campbell WE. Alkaloids of the South African Amaryllidaceae. In:

Pandalai SG (Ed.), Recent research developments in phytochemistry, vol. 1. Research Signpost, Trivandrum; 1997, pp. 131–71.

[52] Van Wyk B-E, Van Oudtshoorn B and Gericke N. Medicinal plants of South Africa. Briza Publications, Pretoria, South Africa; 2009

[53] Madikizela B. Pharmacological evaluation of South African medicinal plants used for treating tuberculosis and related symptoms. PhD Thesis. University of KwaZulu-Natal, Pietermaritzburg; 2014.

[54] Cock IE and Van Vuuren SF. The traditional use of southern African medicinal plants in the treatment of viral respiratory diseases: A review of the ethnobotany and scientific evaluations. Journal of Ethnopharmacology. 2020; 262: 113194.

[55] Sharifi-Rad J, Salehi B, Stojanović-Radić ZZ, Fokou PVT, Sharifi-Rad M, Mahady GB, Sharifi-Rad M, Masjedi M-R, Lawal TO, Ayatollahi SA, Masjedi J, Sharifi-Rad R, Setzer WN, Sharifi-Rad M, Kobarfard F, Rahman A, Choudhary MI, Ata A and Iriti M. Medicinal plants used in the treatment of tuberculosis: Ethnobotanical and ethnopharmacological approaches. Biotechnology Advances. 2020; 44: 107629.

[56] Risa J, Risa A, Adsersen A, Gauguin B, Stafford GI, Van Staden J and Jäger AK. Screening of plants used in southern Africa for epilepsy and convulsions in the GABAA-benzodiazepine receptor assay. Journal of Ethnopharmacology. 2004; 93: 177–182.

[57] McGaw LJ, Lall N, Meyer JJM and Eloff JN. The potential of South African plants against Mycobacterium infections. Journal of Ethnopharmacology. 2008; 119: 482–500.

[58] Chingwaru W, Vidmar J and Kapewangolo PT. The potential of sub-Saharan African plants in the management of human immunodeficiency virus infections: A review. Phytotherapy Research. 2015; 29: 1452–1487.

[59] Mugomeri E, Chatanga P, Raditladi T, Makara M and Tarirai C. Ethnobotanical study and conservation status of local medicinal plants: Towards a repository and monograph of herbal medicines in Lesotho. African Journal of Traditional, Complementary, and Alternative Medicines. 2016; 13: 143–156.

[60] Crouch NR, Chetty J, Mulholland DA and Ndlovu E. Bulb alkaloids of the reputedly psychoactive Brunsvigia radulosa (Amaryllidaceae). South African Journal of Botany. 2002; 68: 86-89.

[61] Moffett RO. Sesotho plant and animal names and plants used by the Basotho. Sun Press, Stellenbosch; 2010.

[62] Nair JJ, Bastida J, Codina C, Viladomat F and Van Staden J. Alkaloids of the South African Amaryllidaceae: A review. Natural Product Communications. 2013; 8: 1335-1350.

[63] Jacot Guillarmod A. Flora of Lesotho. Cramer, Lehre, Germany; 1971.

[64] Moteetee A and Van Wyk B-E. The medical ethnobotany of Lesotho: A review. Bothalia. 2011; 41: 209–228.

[65] Moteetee A and Kose LS. Medicinal plants used in Lesotho for treatment of reproductive and post reproductive problems. Journal of Ethnopharmacology. 2016; 194: 827–849.

[66] Masi M, Mubaiwa B, Mabank T, Karakoyun Ç, Cimmino A, Van Otterlo WAL, Green IR and Evidente A. Alkaloids isolated from indigenous South African Amaryllidaceae: Crinum buphanoides (Welw. ex Baker), Crinum graminicola (I. Verd.), Cyrtanthus mackenii (Hook. f) and Brunsvigia grandiflora (Lindl). South African Journal of Botany. 2018; 118: 188–191.

[67] Dry LJ, Poynton M, Thompson ME and Warren FL. The alkaloids of the Amaryllidaceae. Part IV. The alkaloids of Brunsvigia cooperi Baker. Journal of the Chemical Society. 1958; 4701–4704.

[68] Inubushi Y, Fales HM, Warnhoff EW and Wildman WC. Structures of montanine, coccinine, and manthine. The Journal of Organic Chemistry. 1960; 25: 2153–2164.

[69] Laing M and Clark RC. The crystal and molecular structure of the O,O1-di-para-bromobenzoate of brunsvigine, an Amaryllidaceae alkaloid from Brunsvigia cooperii. Tetrahedron Letters. 1974; 7: 583–584.

[70] Tanahashi T, Poulev A and Zenk MH. Radio immunoasay for the quantitative determination of galanthamine. Planta Medica. 1990; 56: 77–81.

[71] Campbell WE, Nair JJ, Gammon DW, Codina C, Bastida J, Vildomat F, Smith P and Albrecht CF. Bioactive alkaloids from Brunsvigia radulosa. Phytochemistry. 2000; 53: 587–591

[72] Nielsen ND, Sandager M, Stafford GI, Van Staden J and Jäger AK. Screening of indigenous plants from South Africa for affinity to the serotonin reuptake transport protein. Journal of Ethnopharmacology. 2004; 94: 159–163.

[73] Charlson AJ. Antineoplastic constituents of some southern African plants. Journal of Ethnopharmacology. 1980; 2: 323–335.

[74] Nair JJ, Rárová L, Strnad M, Bastida J, Cheesman L and Van Staden J. Crinane alkaloids of the Amaryllidaceae with cytotoxic effects in human cervical adenocarcinoma (HeLa) cells. Natural Product Communications. 2014; 9: 461-466.