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Review of phytochemistry, biological activities and therapeutic potential of *Brachylaena discolor*

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Abstract

Brachylaena discolor DC. is a shrub or tree widely used as herbal medicine in southern Africa. *Brachylaena discolor* is indigenous to Botswana, Eswatini, Mozambique, South Africa, Zambia and Zimbabwe. This study was aimed at reviewing the phytochemistry, biological activities and therapeutic potential of *B. discolor*. Information on phytochemistry, biological activities and therapeutic potential of *B. discolor* was collected from online sources such as Google Scholar, PubMed and Science Direct, and pre-electronic sources such as books, book chapters, theses and journal articles obtained from the University library. This investigation revealed that the bark, leaf, root, stem and twig infusion or decoction of *B. discolor* are mainly used for magical purposes and as anthelmintic and tonic, and traditional medicine for female infertility, skin infections, renal problems, diabetes, gastro-intestinal problems and respiratory infections. Chemical compounds identified from *B. discolor* include alkaloids, flavonoids, phenolics, phlobatannins, saponins, sesquiterpene lactones, steroids, tannins and terpenoids. Ethnopharmacological review showed that *B. discolor* and phytochemical compounds identified from the species have anticancer, anthelmintic, anti-hyperglycaemic, antibacterial, cytotoxicity, antifungal, antidiabetic, antioxidant and leishmanicidal activities. Advanced ethnopharmacological research on *B. discolor* should focus on the possible biochemical mechanisms of both the crude extracts and identified phytochemical compounds including toxicological, *in vivo* and clinical studies to corroborate the traditional medicinal applications of the species.

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INTRODUCTION

Brachylaena discolor DC. is a shrub or tree belonging to Compositae or Asteraceae family which is commonly referred to as sunflower, aster or daisy family. The genus name *Brachylaena* R. Br. is a contraction of two Greek words "*brachus*" meaning "short" and "*klaina*" meaning "cloak", in reference to the florests which are longer than the bracts surrounding the flower head (Venter and Venter, 2015). The specific name "*discolor*" which translates to "two-coloured" refers to the leaves, the upper surface of which is darker than the lower (Palmer and Pitman, 1972). The common name of the species "coastal silver-oak", mostly refer to the silver-grey under-surface of the leaves which often gives the tree a silvery appearance (Palmer and Pitman, 1972). *Brachylaena discolor* is distinguished into three infraspecific taxa, namely var. *discolor*, var. *rotundata* (S. Moore) Beentje and var. *transvaalensis* (E. Phillips & Beentje) Beentje. *Brachylaena discolor* is an ever-

green or deciduous shrub or tree growing up to 30 m in height (Beentje, 2000); (Germishuizen and Meyer, 2003). The bark of *B. discolor* is rough, light black to reddish-brown in colour with lenticellate branches. The leaves of *B. discolor* are lanceolate to ovate in shape, dull green above and light green to whitish below. The leaf margins of *B. discolor* are entire or are slightly serrated. The flower heads of *B. discolor* are grouped into axillate panicles with creamy-white coloured flowers. The fruits of *B. discolor* are small achenes characterized by apical tuft of creamy brown bristles (Palgrave and Keith, 2002); (Van Wyk and Van Wyk, 2013). *Brachylaena discolor* is indigenous to Zimbabwe, Botswana, Eswatini, Zambia, South Africa and Mozambique (Beentje, 2000). The species is found on termite mounds, sandy soils, secondary bushland, evergreen, dune, kloof, gully forests, forest margins, deciduous woodland, rocky outcrops and hillsides at sea level up to 1900 m above sea level (Germishuizen and Meyer, 2003); (Schmidt *et al.*, 2017). *Brachylaena discolor* is a valuable medicinal plant species in tropical Africa as the roots and leaves of the species are traded in informal herbal medicine markets in KwaZulu-Natal and Gauteng provinces of South Africa (Cunningham, 1993); (Williams *et al.*, 2001). Thus, the aim of this review is to summarize the phytochemistry, biological activities and therapeutic potential of *B. discolor*.

Medicinal uses of *Brachylaena discolor*

The twig, stem, bark, root and leaf infusion or decoction of *B. discolor* are mainly used for magical purposes and as anthelmintic and tonic, and traditional medicine for female infertility, skin infections, renal problems, diabetes, gastro-intestinal problems and respiratory infections (Table 1, Figure 1). The leaves of *B. discolor* are mixed with those of *Ekebergia capensis* Sparrm., *Clausena anisata* (Willd.) Hook. f. ex Benth., *Volkameria glabra* (E. Mey.) Mabb. & Y.W. Yuan, *Zanthoxylum capense* (Thunb.) Harv. and roots of *Cymbopogon marginatus* (Steud.) Stapf. ex Burtt-Davy, *Erythrophleum lasianthum* Corbishley, *Margaritaria discoidea* (Baill.) Webster and *Hypoxis* spp. and used as anthelmintic (Bryant, 1966); (Hutchings *et al.*, 1996). The twigs of *B. discolor* are mixed with stems of *Euphorbia tirucalli* L., *Hypoxis hemerocallidea* Fisch., C.A. Mey. & Avé-Lall. (corm), *Ozoroa engleri* R. Fern. & A. Fern. (bark) and *Senecio serratuloides* DC. (leaves) and applied topically on sores (De Wet *et al.*, 2013).

Phytochemistry of *Brachylaena discolor*

Several researchers investigated the phytochemical properties of *B. discolor* aerial parts and leaves (Table 2). Phytochemical compounds such as alkaloids, flavonoids, phenolics, phlobatannins, saponins, sesquiterpene lactones, steroids, tannins and terpenoids have been identified from *B. discolor*. Some of the documented chemical compounds could be responsible for the pharmacological properties associated with the species.

Pharmacological properties of *Brachylaena discolor*

The following pharmacological activities have been documented from the aerial parts and leaf extracts of *B. discolor* and compounds isolated from the species: anthelmintic, antibacterial, antifungal, anticancer, antidiabetic, antioxidant, anti-hyperglycaemic, leishmanicidal and cytotoxicity activities.

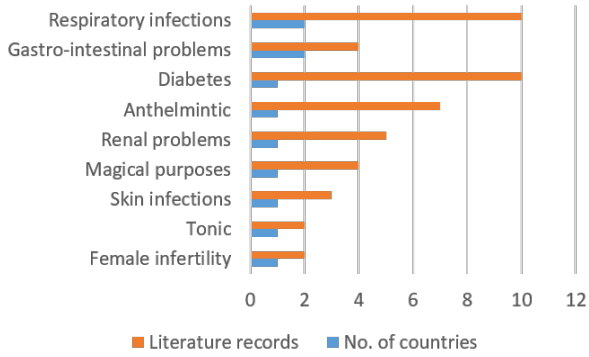

Figure 1: Medicinal uses of Brachylaena discolor derived from literature records

Anthelmintic activities

(Mcgaw *et al.*, 2000) evaluated the anthelmintic activities of hexane, ethanol and water extracts of *B. discolor* leaves on the mortality and reproductive ability of the free-living nematode *Caenorhabditis elegans* in two different assays. All extracts exhibited activities at a concentration of 1.0 mg/ml and 2.0 mg/ml after the two and seven days incubation period (Mcgaw *et al.*, 2000). (Adamu *et al.*, 2013) evaluated the anthelmintic activities of the acetone extract of *B. discolor* leaves using the egg hatch assay and the larval development tests using *Haemonchus contortus* with albendazole as positive control. The extract exhibited activities with half maximal effective concentration (EC_{50}) values of 3.6 mg/ml and 17.2 mg/ml for the egg hatch and the larval development assays, respectively (Adamu *et al.*, 2013).

Antibacterial activities

(Adamu *et al.*, 2014) evaluated the antibacterial activities of acetone extract of *B. discolor* leaves against *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Enterococcus faecalis* using a serial microdilution method with gentamicin as

Table 1: Medicinal uses of Brachylaena discolor

Medicinal use	Part used	Reference
Abdominal pains	Root decoction taken orally	(Gelfand *et al.*, 1985)
Anthelmintic	Leaf and root infusion or decoction taken orally	(Thomas and Grant, 2013); (Constant and Tshisikhawe, 2018)
Anthelmintic	Leaves mixed with those of Ekebergia capensis Sparrm., Clausena anisata (Willd.) Hook. f. ex Benth., Volkameria glabra (E. Mey.) Mabb. & Y.W. Yuan, Zanthoxylum capense (Thunb.) Harv. and roots of Cymbopogon marginatus (Steud.) Stapf. ex Burtt-Davy, Erythrophleum lasianthum Corbishley, Margaritaria discoidea (Baill.) Webster and Hypoxis spp.	(Bryant, 1966); (Hutchings *et al.*, 1996)
Diabetes	Leaf and root infusion and decoction taken orally	(Watt and Breyer-Brandwijk, 1962); (Erasto *et al.*, 2005)
Dysmenorrhoea	Root decoction taken orally	(Gelfand *et al.*, 1985)
Female infertility and prevent miscarriage	Bark and root decoction taken orally	(Semenya *et al.*, 2013); (Mhlongo and Wyk, 2019)
Fever	Leaf infusion taken orally	(Pujol and Naturafrica, 1990)
Gastro-intestinal problems (diarrhoea and stomach ache)	Leaf and bark infusion taken orally or anally	(de Wet *et al.*, 2010); (Monjane *et al.*, 2018)
Haemorrhoids	Root infusion applied topically	(Palmer and Pitman, 1972)
Magical purposes	Leaves, roots and stems	(Cunningham, 1988); (Cunningham and Zondi, 1991)
Nervous system	Leaf infusion taken orally	(Hutchings, 1989)
Renal problems	Leaf infusion or decoction taken orally	(Mellem, 2013), (Mellem *et al.*, 2015)
Respiratory infections (chest pains, cough, sore throat and tuberculosis)	Leaf and root decoction or infusion taken orally	(York *et al.*, 2011); (Semenya and Maroyi, 2018)
Skin infections (burns, cleaning facial skin and sores)	Leaf and twig infusion applied topically	(Afolayan *et al.*, 2014); (Nciki *et al.*, 2016)
Sores	Twigs mixed with Euphorbia tirucalli L. (stems), Hypoxis hemerocallidea Fisch., C.A. Mey. & Avé-Lall. (corm), Ozoroa engelri R. Fern. & A. Fern. (bark) and Senecio serratuloides DC. (leaves)	(De Wet *et al.*, 2013)
Syphilis	Root decoction taken orally	(Gelfand *et al.*, 1985)
Tonic	Leaf decoction taken orally	(Palmer and Pitman, 1972); (Hutchings, 1989)
Ulcers	Leaf infusion taken orally	(Chigora *et al.*, 2007)
Wounds	Leaf infusion applied topically	(Afolayan *et al.*, 2014)
Ethnoveterinary medicine (anthelmintic)	Leaf infusion	(Hutchings *et al.*, 1996)

Table 2: Phytochemical composition of Brachylaena discolor

Phytochemical compound	Plant part	Reference
3'-hydroxygenkwanin	Leaves	(Monjane *et al.*, 2018)
3 -acetoxy-12-lupene	Aerial parts and leaves	(Bohlmann and Zdero, 1982); (Adam, 2017)
4β,15-Dihydrodehydrozaluzanin C	Aerial parts	(Bohlmann and Zdero, 1982)
6"-O-acetyl homoplantaginin	Leaves	(Monjane *et al.*, 2018)
11β,13-Dihydrotubiferin	Aerial parts	(Bohlmann and Zdero, 1982)
11β,13-Dihydrozaluzanin C	Aerial parts	(Bohlmann and Zdero, 1982)
Brachylaenolide	Aerial parts	(Bohlmann and Zdero, 1982)
Costunolide	Aerial parts	(Bohlmann and Zdero, 1982)
α-D-Glucopyranose	Leaves	(Adam, 2017)
β-D-Glucopyranose	Leaves	(Adam, 2017)
Dehydrobrachylaenolide	Aerial parts	(Bohlmann and Zdero, 1982)
Dehydrocostuslactone	Aerial parts	(Bohlmann and Zdero, 1982)
Dehydrozaluzanin C	Aerial parts	(Bohlmann and Zdero, 1982)
Dihydroxysinapic acid	Leaves	(Monjane *et al.*, 2018)
Dihydrodehydrocostuslactone	Aerial parts	(Bohlmann and Zdero, 1982)
Eupafolin	Leaves	(Monjane *et al.*, 2018)
Furanoheliangolide	Aerial parts	(Bohlmann and Zdero, 1982)
Germacranolide	Aerial parts	(Bohlmann and Zdero, 1982)
Germacrene D	Aerial parts	(Bohlmann and Zdero, 1982)
Genkwanin5-O-β-Dglucopyranoside	Leaves	(Adam, 2017)
Germacronolide epoxide	Leaves	(Monjane *et al.*, 2018)
Hydroxytyrosol	Leaves	(Monjane *et al.*, 2018)
Linoleic acid	Aerial parts	(Bohlmann and Zdero, 1982)
Linolenic acid	Aerial parts	(Bohlmann and Zdero, 1982)
Lupeol acetate	Aerial parts and leaves	(Bohlmann and Zdero, 1982); (Zdero and Bohlmann, 1987)
Luteolin	Leaves	(Monjane *et al.*, 2018)
Onopordopicrin	Aerial parts and leaves	(Bohlmann and Zdero, 1982); (Zdero and Bohlmann, 1987)
Onoporidin	Leaves	(Monjane *et al.*, 2018)
9-oxo-nerolidol	Aerial parts	(Bohlmann and Zdero, 1982)
Quercetin3-Oglucoside-7,3',4'-trimethyl ether	Leaves	(Monjane *et al.*, 2018)
Quercetin-3-O-β-D-galactopyranoside	Leaves	(Monjane *et al.*, 2018)
Quercetin-7-galactopyranoside	Leaves	(Monjane *et al.*, 2018)
Salonitenolide	Aerial parts	(Bohlmann and Zdero, 1982)
Salonitenolide-8-O-2,3-epoxy isobutyrate	Aerial parts	(Bohlmann and Zdero, 1982)
β-sitosteryl linelonate	Leaves	(Adam, 2017)
Tetrahydrodehydrozaluzanin C	Aerial parts	(Bohlmann and Zdero, 1982)
α-tocopherol	Leaves	(Adam, 2017)
Tubiferin	Aerial parts	(Bohlmann and Zdero, 1982)
Zaluzanin C	Aerial parts	(Bohlmann and Zdero, 1982)

positive control. The extract exhibited activities

with minimum inhibitory concentration (MIC) values ranging from 0.2 mg/ml to 1.3 mg/ml in comparison to MIC value of <0.02 mg/ml exhibited by the positive control, and total activity ranging from 52.8 ml/g to 412.5 ml/g (Adamu *et al.*, 2014). (van Vuuren *et al.*, 2015) evaluated the antibacterial activities of dichloromethane : methanol (1:1) and aqueous extracts of *B. discolor* var. *transvaalensis* leaves against *Staphylococcus aureus, Enterococcus faecalis, Proteus vulgaris, Bacillus cereus, Shigella flexneri, Salmonella typhimurium* and *Escherichia coli* with ciprofloxacin as positive control. The aqueous extract exhibited activities against all tested pathogens with MIC values ranging from 0.3 mg/mL to 2.0 mg/mL while the organic extract exhibited weak activities against *Shigella flexneri* with MIC value of 4.0 mg/mL. The antibacterial interaction of *B. discolor* var. *transvaalensis* used in combination with *Psidium guajava* L. and *Sclerocarya birrea* (A. Rich.) Hochst. subsp. *caffra* (Sond.) Kokwaro was evaluated by calculating the sum of the fractional inhibitory concentrations (∑FIC) against *Staphylococcus aureus, Enterococcus faecalis, Proteus vulgaris, Bacillus cereus, Shigella flexneri, Salmonella typhimurium* and *Escherichia coli* with ciprofloxacin as positive control. The extracts exhibited activities against tested pathogens with MIC values ranging from 0.02 mg/mL to 12.0 mg/mL while the combination of *B. discolor* var. transvaalensis with other species resulted in synergistic to additive effects (van Vuuren *et al.*, 2015). (Nciki *et al.*, 2016) evaluated the antibacterial activities of aqueous and dichloromethane : methanol (1:1) extracts of *B. discolor* twigs against *Escherichia coli, Staphylococcus epidermidis, Brevibacterium agri, Pseudomonas aeruginosa, Brevibacterium linens, Propionibacterium acnes* and *Staphylococcus aureus* using the micro-titer plate dilution assay with ciprofloxacin as positive control. The antibacterial interaction of *B. discolor* used in combination with *Euphorbia tirucalli, Hypoxis hemerocallidea, Ozoroa engleri* and *Senecio serratuloides* was evaluated by calculating ∑FIC against *Pseudomonas aeruginosa, Staphylococcus epidermidis* and *Staphylococcus aureus*. The extracts showed activities with MIC values ranging from 190.0 μg/mL to > 8000.0 μg/mL which was much higher than MIC values of 0.1 μg/mL to 1.25 μg/mL showed by ciprofloxacin, the positive the control. The combination of B. discolor with other species resulted in synergistic to additive effects (Nciki *et al.*, 2016).

Antifungal activities

(Adamu *et al.*, 2012) evaluated the antifungal activities of acetone extract of *B. discolor* leaves against *Aspergillus fumigatus, Cryptococcus neoformans* and *Candida albicans* using serial microdilution method. The extract exhibited activities with MIC values ranging from 0.08 mg/mL to 0.6 mg/mL and total activity values ranging from 108.0 mL/g to 825.0 mL/g (Adamu *et al.*, 2012). (Nciki *et al.*, 2016) evaluated the antifungal activities of aqueous and dichloromethane : methanol (1:1) extracts of *B. discolor* twigs against *Microsporum canis, Candida albicans* and *Trichophyton mentagrophytes* using the micro-titer plate dilution assay with amphotericin B as positive control. The extracts exhibited weak activities with MIC values ranging from 250.0 μg/mL to > 8000.0 μg/mL which was much higher than MIC values of 0.01 μg/mL to 0.1 μg/mL showed by the positive control (Nciki *et al.*, 2016). (Dikhoba *et al.*, 2019) evaluated the antifungal activities of acetone extract of *B. discolor* leaves against *Fusarium verticillioides, Aspergillus flavus* and *Aspergillus ochraceous* using the microplate dilution method with amphotericin B as positive control. The extract exhibited weak activities against tested pathogens exhibiting MIC values ranging from 0.2 mg/ml to 2.5 mg/ml and total activity of 17.0 ml/g to 271.0 ml/g at both 24 hour and 48 hour incubation periods (Dikhoba *et al.*, 2019).

Anticancer activities

(Fouche *et al.*, 2008) evaluated the anticancer activities of dichloromethane extracts of *B. discolor* var. *rotundata* leaves against melanoma UACC62, renal TK10 and breast MCF7. The extracts exhibited activities against melanoma UACC62, renal TK10 and breast MCF7 with total growth inhibition (TGI) values of 13.1 μg/ml, 15.0 μg/ml and 26.0 μg/ml, respectively. The authors also evaluated the anticancer activities of dichloromethane extracts of *B. discolor* var. *rotundata* leaves against leukaemia SR, ovarian OVCAR-5 and colon HT 29. The extracts exhibited activities against leukaemia SR, ovarian OVCAR-5 and colon HT 29 with TGI values of 12.3 μg/ml, 20.0 μg/ml and 24.6 μg/ml, respectively (Fouche *et al.*, 2008).

Antidiabetic activities

(De *et al.*, 2008) evaluated the antidiabetic activities of organic and aqueous extracts of *B. discolor* leaves, roots and stems against 3T3-L1 adipose, C2C12 muscle and Chang liver cells using a glucose utilisation assay with 1.0 μM metformin for Chang liver cells, 1.0 μM insulin for C2C12 and 3T3-L1 cells as positive controls. The extracts demonstrated activities (De *et al.*, 2008). (Mellem *et al.*, 2015) evaluated the antidiabetic activities of the aqueous and methanol extracts of *B. discolor* leaves

by using the α-amylase inhibition and a-glucosidase inhibition assays with acarbose as positive control. The extracts exhibited activities on a-amylase and a-glucosidase with half maximal inhibitory concentration (IC_{50}) values ranging from 1.8 mg/ml to 11.0 mg/ml in comparison to IC_{50} values of 0.03 mg/ml to 1.2 mg/ml exhibited by the positive control (Mellem *et al.*, 2015).

Antioxidant activities

(Adamu *et al.*, 2014) evaluated the antioxidant activities of acetone extract of *B. discolor* leaves using 2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid (ABTS) and 1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging assays. The extracts exhibited activities with a trolox equivalent a*ntioxidant c*apacity (TEAC) value of 0.2 and an EC_{50} value of 2.6, using ABTS and DPPH, respectively (Adamu *et al.*, 2014). (Mellem *et al.*, 2015) evaluated the antioxidant activities of the crude extracts of *B. discolor* leaves by using the DPPH free radical scavenging assay with rutin as positive control. The methanol and aqueous extracts exhibited activities with IC_{50} values of 92.3 μg/ml and 82.8 μg/ml, respectively (Mellem *et al.*, 2015). (Dikhoba *et al.*, 2019) evaluated the antioxidant activities of acetone extract of *B. discolor* leaves using the ABTS and DPPH free radical scavenging assays with ascorbic acid (0.5 mg/ml) as positive control. The extract exhibited activities with IC_{50} values of 0.03 mg/ml and 0.2 mg/ml against ABTS and DPPH, respectively (Dikhoba *et al.*, 2019).

Anti-hyperglycaemic activities

(Mellem, 2013) evaluated the anti-hyperglycaemic activities of the methanol extract of B. discolor leaves using a streptozotocin-induced diabetic rat model. The doses of 50.0 mg/ml and 150.0 mg/ml) were administered daily to both streptozotocin-induced and control rats and the biochemical profile of the rats assessed over 28 days. The extract at both doses caused a significant reduction in the blood glucose levels, and other observed changes included total bilirubin, creatinine, alkaline phosphatase and body weight (Mellem, 2013).

Leishmanicidal activities

(Monjane *et al.*, 2018) evaluated the leishmanicidal activities of the compounds onopordopicrin and germacronolide epoxide isolated from the leaves of *B. discolor* against *Leishmania amazonensis* and *Leishmania braziliensis* using the colorimetric method-XXT with miltefone as positive control. The compound onopordopicrin exhibited activities with IC_{50} values of 39.6 μM and 27.9 μM against *Leishmania amazonensis* and *Leishmania braziliensis*, respectively compared to IC_{50} values of 12.5 μM and 12.0 μM exhibited by the positive control (Monjane *et al.*, 2018).

Cytotoxicity, toxicity and mutagenicity activities

(Adamu *et al.*, 2012) evaluated the cytotoxicity activities of acetone extracts of *B. discolor* leaves against Vero monkey kidney cells using the tetrazolium-based colorimetric 3-5-dimethyl thiazol-2-yl-2, 5-diphenyl tetrazolium bromide (MTT) assay. The extract exhibited activities with half maximal lethal dose (LD_{50}) value of 0.004 mg/mL (Adamu *et al.*, 2012). (Adamu *et al.*, 2013) evaluated the cytotoxicity activities of acetone extract of *B. discolor* against African Green Monkey kidney (Vero) cells using the tetrazolium-based colorimetric MTT assay. The extract exhibited activities with half maximal lethal concentration (LC_{50}) value of 0.008 mg/ml (Adamu *et al.*, 2013). (Mellem *et al.*, 2015) evaluated the cytotoxicity activities of the crude extracts of *B. discolor* leaves against the HeLa cell line using the colorimetric MTT assay. Both extracts stimulated the growth of the HeLa cell line with an increase in cell viability in a concentration dependent manner implying that the extracts are safe for use (Mellem *et al.*, 2015) (Mellem *et al.,* 2015).

(Mellem *et al.*, 2015) Mellem *et al.* (2015) evaluated the mutagenicity activities of aqueous and methanol extract of *B. discolor* leaves using the *Salmonella typhimurium* TA 100 and TA 98 strains mutagenicity assay. Both extracts exhibited no mutagenic activities up to the highest concentration tested which was 1000.0 μg/ml (Mellem *et al.*, 2015). (Mellem *et al.*, 2015) evaluated the toxicity activities of aqueous and methanol extracts of *B. discolor* leaves using the brine shrimp assay with organophosphate as positive control. Both extracts showed 100% shrimp survival at the highest concentration tested which was 1000.0 μg/ml while the positive control showed 100 % mortality (Mellem *et al.*, 2015).

CONCLUSIONS

The present review summarizes the phytochemistry, biological activities and therapeutic potential of *B. discolor*. *Brachylaena discolor* is a variable species, distinguished into three varieties, var. *discolor*, var. *rotundata* and var. *transvaalensis* which are deemed as highly potent traditional medicines for various human diseases and ailments. These three varieties have overlapping distributional range in southern Africa and are quite similar in appearance and often confused when growing together. There are similarities and overlaps in terms of ethnomedicinal uses, phytochemistry

and biological activities. From a phytochemical and pharmacological point of view, no chemical variation studies have been conducted on these three varieties. Future studies should try to establish whether there are phytochemical compounds and pharmacological properties that could be used to distinguish these three varieties as this information will complement the taxonomical characters used to distinguish the three varieties.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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