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A review of botany, medicinal uses and biological activities of *Berkheya setifera* DC. (Asteraceae)

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Abstract

Berkheya setifera is a well-known plant species in southern Africa in traditional and folk medicine. This study is aimed at providing a critical review of the botany, biological activities and medicinal uses of *B. setifera*. Documented information on botany, biological activities and medicinal uses of *B. setifera* was collected from several online sources which included BMC, Scopus, SciFinder, Google Scholar, Science Direct, Elsevier, Pubmed and Web of Science. Additional information on the botany, biological activities and medicinal uses of *B. setifera* was sourced from book chapters, books, journal articles, theses and scientific publications sourced from the University of Fort Hare library. The current study showed that the leaves and roots of *B. setifera* are traditionally used in 60% of the countries where the species is indigenous. *Berkheya setifera* is used as herbal medicine for 28 human diseases which include abdominal pains, arthritis, blood circulatory problems, colds, coughs, itching skin and rash, jaundice, kidney problems, magical uses, stomach complaints, sterility and uterine disorders. Pharmacological research revealed that *B. setifera* extracts have antibacterial, antimalarial, anti-inflammatory, antioxidant, haemolysis, antifungal and cytotoxicity properties. Future studies should concentrate on assessing the phytochemical, pharmacological and toxicological activities of *B. setifera* crude extracts as well as chemical ingredients isolated from the species.

Keywords: *Berkheya setifera*, Compositae, herbal medicine, indigenous pharmacopeia, pharmacology, phytochemistry

INTRODUCTION

Berkheya setifera DC. is a perennial herbaceous plant belonging to Compositae or the Asteraceae family. *Berkheya setifera* together with other related species such as *B. echinacea* (Harv.) O.Hoffm. and Burtt-Davy subsp. *echinacea*, *B. rhapontica* (DC.) Hutch. ex Burtt-Davy subsp. *aristosa* (DC.) Roessler var. *aristosa*, *B. multijuga* (DC.) Roessler, *B. seminivea* Harv. & Sond., *B. speciosa* (DC.) Hoffm., *B. subulata* Harv., *B. umbellata* DC. and *B. zeyheri* (Sond. & Harv.) Oliv. Hiern are widely used as herbal medicines in south-central Africa.[1-4] The different parts of *B. setifera* are applied in indigenous herbal practices against fever, malaria, skin diseases, sexually-transmitted infections, gastro-intestinal disorders, inflammatory, respiratory and reproductive problems.[1-4] Traditional medicines are regarded as an important source of natural products required for pharmaceutical drugs and other health promoting products.[5-7] Several pharmaceutical drugs and their derivatives that are in current use today are plant-derived and traditional medicines have historically proven to be invaluable sources of phytochemical molecules with the necessary therapeutic potential.[6,7] Such well-known examples of plant-derived medicines include aspirin, atropine, cocaine, codeine, morphine, quinine and reserpine.[5] But there is lack of detailed information on the botany, medicinal uses and active ingredients of plants that are used as herbal medicines. For medicinal plants that have been incorporated into traditional *materia medica* to be appreciated and understood by the wider scientific community, there is need for formal documentation of such species given the fragility of oral-tradition knowledge associated with herbal medicines. It is against this background that this study was undertaken aimed at appraising the botany, medicinal uses and biological activities of *B. setifera*.

Taxonomy and botanical description of *Berkheya setifera*

Research by Phaliso et al.[8] revealed that genus *Berkheya* Ehrhart consisting of about 80 species is paraphyletic with the related genera *Cullumia* R.Br. ex Aiton (15 species), *Cuspidia* Gaertner (one species), *Didelta* L'Héritier de Brutelle (two species) and *Heterorhachis* Walpers (two species) embedded within a broad and large taxonomic clade referred to as the '*Berkheya* clade'. This group of plants require some taxonomic revision aimed at merging these different genera as supported by both molecular and morphological studies. The genus name "*Berkheya*" is in honour of a Dutch naturalist, biologist, painter and poet Johannes Le Francq Van Berkhey (1729 - 1812).[9] Synonyms associated with *B. setifera* include *B. setifera* (DC.) L. var. *tropica* S.Moore, *Crocodilodes harveyanum* Kuntze and *C. setiferum* (DC.) Kuntze.[10-12] The English common names of the species are buffalo-tongue berkheya, buffalo-tongue thistle and ox tongue. The other vernacular names include rasperdissel and rasperdisseldoring (Afrikaans), lelelemla-khomo and ntsoantsane (Southern Sotho), indlebe-lenkomo and umhlondlo (Xhosa), ikhakhasi, ulimi-iwenkomo and ulimi-iwenyathi (Zulu).[12-15]

Berkheya setifera is a perennial herb which grows up to a height of 60 cm to 120 cm.[11] The erect, single, annual, glabrous or thinly hairy stems, branching in the upper part arise from a stout woody rootstock. The leaves are oblanceolate to obovate in shape and mostly basal with some smaller leaves along the stem.[10] Both the upper and lower leaf surfaces have straw-coloured spiny and coarse bristles. The leaf margins are entire or slightly lobed and lamina base clasping the stems. The flowers are solitary on the stems and branches or rarely several more or less clustered and bright yellow in colour. *Berkheya setifera*

has been recorded in Zimbabwe, Lesotho, Swaziland, South Africa and Mozambique.[10] The species has been recorded in sub-montane grassland, bracken scrubland and along road sides at an altitude which range from 460 m to 2135 m above the sea level.[10]

Medicinal uses of *Berkheya setifera*

The leaves and roots of *B. setifera* are utilized as herbal medicines in 60% of the countries where the taxon is indigenous (Table 1). *Berkheya setifera* is used as herbal medicines for 28 human diseases (Table 1). The major diseases recorded in a minimum of two countries include abdominal pains, arthritis, blood circulatory problems, colds, coughs, itching skin and rash, jaundice, kidney problems, magical uses, stomach complaints, sterility and uterine disorders (Table 1). In Lesotho, the roots of *B. setifera* are mixed with those of *Dicoma anomala* Sond. as remedy for biliousness and jaundice[16] while leaves and roots are combined with roots of *Rumex lanceolatus* Thunb. as remedy for female sterility.[17,18] Previous research findings by Dzerefos et al.[19] showed that *B. setifera* is among the top 20 ranking medicinal plants in the Limpopo province of South Africa and unfortunately, the taxon is now difficult to find in the province. Research by Fox and Norwood[20] and Welcome and Van Wyk[21] showed that the leaves of *B. setifera* are cooked as leafy vegetables in South Africa.

Table 1: Medicinal uses of *Berkheya setifera*

Medicinal use	Parts of the plant used	Country	References
Abdominal pains	Leaves and roots	Lesotho and South Africa	Watt and Breyer-Brandwijk[1]; Kose et al.[15]; Pooley[22]
Arthritis	Leaves and roots	Lesotho and South Africa	Watt and Breyer-Brandwijk[1]; Kose et al.[15]; Schmitz[23]
Biliousness	Roots mixed *Dicoma anomala* Sond.	Lesotho	Moffett[12]; Maroyi[16]
Blood circulatory problems	Roots	Lesotho and South Africa	Moffett[12]; Moteetee and Van Wyk[14]
Blood detoxification	Roots	South Africa	Zukulu et al.[24]
Boils	Roots	Swaziland	Sibandze[25]
Burns	Roots	Swaziland	Sibandze[25]
Cleanses blood	Leaves and roots	Lesotho	Moteetee and Van Wyk[14]
Colds	Leaves and roots	Lesotho and South Africa	Watt and Breyer-Brandwijk[1]; Moteetee and Van Wyk[14]
Coughs	Leaves and roots	Lesotho and South Africa	Watt and Breyer-Brandwijk[1]; Moteetee and Van Wyk[14]; Maliehe[26]
Herpes	Leaves and roots	Lesotho	Watt and Breyer-Brandwijk[1]; Kose et al.[15]
Itching skin and rash	Leaves and roots	Lesotho and Swaziland	Sibandze[25]; Mugomeri et al.[27]
Jaundice	Roots mixed *Dicoma anomala* Sond.	Lesotho	Moffett[12]; Maroyi[16]
Jaundice	Leaves and roots	Lesotho and South Africa	Watt and Breyer-Brandwijk[1]; Kose et al.[15]
Kidney problems	Leaves and roots	Lesotho and Swaziland	Watt and Breyer-Brandwijk[1]; Kose et al.[15]
Lymphatic filariasis	Roots	South Africa	Komoreng et al.[28]
Magical uses (good luck charm)	Roots	Lesotho and South Africa	Moteetee et al.[29]
Menstrual pains	Roots	South Africa	Zukulu et al.[24]
Otitis media	Roots	Swaziland	Sibandze[25]
Pregnancy complications	Leaves and roots	Lesotho	Kose et al.[15]; Moteetee and Kose[18]
Reduces mother-child HIV transmission	Leaves and roots	Lesotho	Kose et al.[15]; Kose et al.[30]
Respiratory infections	Leaves and roots	Lesotho	Moteetee and Van Wyk[14]
Sores	Leaves and roots	Lesotho	Moteetee and Van Wyk[14]
Stomach complaints	Leaves and roots	Lesotho, South Africa and Swaziland	Watt and Breyer-Brandwijk[1]; Long[13]; Moteetee and Van Wyk[14]; Dlamini[31]; Amusan[32]
Sterility	Leaves and roots	Lesotho, South Africa and Swaziland	Watt and Breyer-Brandwijk[1]; Moteetee and Van Wyk[14]; Amusan et al.[33]
Sterility	Leaves and roots mixed with *Rumex lanceolatus* Thunb.	Lesotho	Watt and Brandwijk[17]; Moteetee and Kose[18]
Toothache	Leaves and roots	Swaziland	Sibandze[25]; Amusan et al.[34]
Ulcers	Leaves and roots	Lesotho	Moteetee and Van Wyk[14]
Uterine disorders	Leaves and roots	Lesotho and Swaziland	Kose et al.[15]; Sibandze[25]

Phytochemistry of *Berkheya setifera*

Bohlmann et al.[35] identified terpenoids and thiophene acetylenes such as (-)-β-isocomere, isocomere and modhepene from the roots of *B. setifera*. Amusan et al.[33] identified cardenolides, polyphenols and terpenoids from roots of *B. setifera*. Muleya[36] identified reducing sugars, phenolics, saponins, glycosides, alkaloids and terpenoids from roots of *B. setifera*. Mtunzi et al.[37] quantified heavy metals in *B. setifera* roots, with manganese showing the highest concentration of 5.7 ppm, followed by copper (0.6 ppm), nickel and zinc (0.2 ppm each) and iron (0.03 ppm). The manganese concentration was above the permissible FAO/WHO limit of manganese in edible plants of 2.0 ppm.[38] The concentrations of the remainder of trace elements in *B. setifera* roots were below the permissible limits set by Codex Alimentarious Commission[38] and, therefore, Mtunzi et al.[37] concluded that the species extracts used as herbal medicines may not result in heavy metal toxicity when used as herbal medicine or leafy vegetable.

Biological activities of of *Berkheya setifera*

The following biological activities (Table 2) have been reported from the flower, leaf, root and stem extracts of *B. setifera*: antibacterial,[25,30,36,39-41] antifungal,[25,30,36,39-41] anti-inflammatory,[36,39,41] antimalarial,[25,42] antioxidant,[36,39,41,43] haemolysis[25] and cytotoxicity[30] activities.

Antibacterial activities

Sibandze[25] assessed the antibacterial properties (Table 2) of flowers, leaves, roots and stems acetone extracts of *B. setifera* against *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Escherichia coli* using the serial dilution technique with ciprofloxacin as a positive control. The extracts demonstrated activities with minimum inhibitory concentration (MIC) values within the range of 1.3 mg/ml to 8.0 mg/ml.[25] Muleya[36], Muleya et al.[39] and Mtunzi et al.[41] assessed the antibacterial properties of crude, acetone, dichloromethane, ethyl acetate, hexane and methanol root extract of *B. setifera* against *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Enterococcus faecalis* using the twofold serial dilution with gentamicin as a positive control. The extract exhibited properties with MIC values within the range of 20.0 μg/ml to 625.0 μg/ml against MIC value of 4.0 μg/ml exhibited by the positive control.[36,39,41] Kose[40] and Kose et al.[30] assessed the antibacterial properties of aqueous and organic leaf and root extracts of *B. setifera* against *Oligella ureolytica*, *Neisseria gonorrhoeae* and *Gardnerella vaginalis* using micro-dillution technique using ciprofloxacin (0.01 mg/ml) as a positive control. The extracts showed activities with MIC values within the range of 0.8 mg/ml to >8.0 mg/ml.[30,40] Kose[40] assessed the antibacterial properties of aqueous and organic leaf and root extracts of *B. setifera* against *Citrobacter freundii*, *Enterobacter homaendis*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Mycobacterium fortuitum*, *Mycobacterium smegmatis* and *Staphylococcus aureus* using micro-dilution technique using ciprofloxacin (0.01 mg/ml) as positive control. The extracts showed activities against all tested microrganisms with the exception of *Mycobacterium fortuitum* and *Mycobacterium smegmatis*, exhibiting MIC values within the range of 0.3 mg/ml to >8.0 mg/ml.[40]

Antifungal activities

Sibandze[25] assessed the antifungal properties (Table 2) of acetone flowers, leaves, roots and stems extract of *B. setifera* against *Candida albicans* using the serial dilution technique with amphotericin B as positive control. The extracts showed properties with MIC values within the range of 0.7 mg/ml to 2.0 mg/ml.[25] Muleya[36], Muleya et al.[39] and Mtunzi et al.[41] assessed the antifungal properties of crude, acetone, dichloromethane, ethyl acetate, hexane and methanol root extract of *B. setifera* against *Aspergillus fumigatus* and *Candida albicans* using the twofold serial dilution with amphotericin B as positive control. The extracts exhibited properties with MIC values within the range of 20.0 μg/ml to 1250.0 μg/ml against MIC value of 0.6 μg/ml to 13.0 μg/ml demonstrated by the positive control.[36,39,41] Kose[40] and Kose et al.[30] assessed the antifungal properties of aqueous and organic leaf and root extracts of *B. setifera* against *Candida albicans* using micro-dilution assay using amphotericin B (0.1 mg/ml) as a positive control. The extracts showed activities with MIC values within the range of 1.7 mg/ml to >8.0 mg/ml.[30,40]

Anti-inflammatory activities

Muleya[36], Muleya et al.[39] and Mtunzi et al.[41] assessed the anti-inflammatory (Table 2) properties of crude root extracts of *B. setifera* against 15-soybean lipoxygenase (15-LOX) enzyme. The crude extract exhibited anti-inflammatory activities with 80% in total 15-LOX inhibition at 25 μg/ml with half maximal effective concentration (EC_{50}) value of 11.9 μg/ml.[36,39,41]

Antimalarial activities

Sibandze and Van Zyl[42] and Sibandze[25] evaluated antimalarial activities (Table 2) of dichloromethane:methanol (1:1) leaf, flower, root and stem extract of *B. setifera* using the [$G^{-3}H$] hypoxanthine incorporation assay using chloroquine sensitive and resistant strains of *Plasmodium falciparum* as the test organism. The extracts showed properties with half maximal inhibitory concentration (IC_{50}) values within the range of 15.1 μg/ml to 66.4 μg/ml.[25,42] Sibandze[25] evaluated the pharmacological interactive antimalarial relationship of adding quinine to the *B. setifera* extracts. The root and stem extracts with quinine exhibited antagonistic activities with ∑FIC value of 5.5.[25]

Antioxidant activities

Magama et al.[43] assessed the antioxidant properties (Table 2) of crude root extract of *B. setifera* using reducing power, 1,1-diphenyl-2- picrylhydrazyl (DPPH) free radical, hydrogen peroxide scavenging assays and total phenolics with L-ascorbic acid as positive control. The extract demonstrated that the extracts scavenged DPPH radicals, reduced Fe^{3+} to Fe^{2+}, scavenged hydrogen

peroxide and were characterized by phenolics. A direct correlation between total phenolics of 66.0 mg GAE/g dry extract and antioxidant activities was observed. The extract exhibited 58% inhibition of DPPH and IC_{50} value of 2335 μg/mL while the positive control exhibited 86% inhibition of DPPH and IC_{50} value of 750 μg/mL. The extracts showed hydrogen peroxide scavenging activities in a concentration dependent manner and reduced Fe^{3+} to Fe^{2+}.[43] Muleya[36], Muleya et al.[39] and Mtunzi et al.[41] assessed the antioxidant properties of crude, dichloromethane, acetone, ethyl acetate, hexane and methanol root extract of *B. setifera* using 2, 2-azinobis (3-ethylbenzothiazoline)-6-sulfonic acid (ABTS) and 2, 2-di (4-*tert*octylphenyl)-1-picrylhydrazyl (DPPH) free radical scavenging assays with trolox (25-0.5 g/mL) as positive control. The extracts showed properties with EC_{50} values within the range of 1.0 μg/ml to 157.8 μg/ml against DPPH and EC_{50} values of 1.4 μg/ml to 577.1 μg/ml against ABTS.[36,39,41]

Haemolysis activities

Sibandze[25] evaluated haemolysis activities (Table 2) of dichloromethane:methanol (1:1) root, flower, leaf and stem extract of *B. setifera* using the red blood cells haemolytic *in vitro* assay. The extracts showed properties with IC_{50} values within the range of >100.0 μg/ml to 178.4 μg/ml.[25]

Cytotoxicity activities

Kose et al.[30] assessed the cytotoxicity properties (Table 2) of organic and aqueous leaf and root extracts of *B. setifera* using the brine shrimp, *Artemia franciscana* lethality technique using potassium dichromate as positive control. The aqueous and organic leaf extracts showed properties with percentage mortalities of 88.2 and 89.3, respectively.[30]

Table 2: Summary of biological activities of *Berkheya setifera* crude extracts

Activity tested	Extract	Plant part	Model	Effect	Reference
Antibacterial	Acetone	Flowers	Serial dilution	Exhibited activities against *Escherichia coli* with MIC value of 3.0 mg/ml, *Klebsiella pneumoniae* (3.3 mg/ml), and 4.0 mg/ml against *Staphylococcus aureus* and *S. epidermidis*	Sibandze[25]
Antibacterial	Acetone	Leaves	Serial dilution	Exhibited activities against *K. pneumoniae* with MIC value of 1.3 mg/ml, *S. epidermidis* (1.7 mg/ml), *S. aureus* (3.3 mg/ml) and *E. coli* (5.3 mg/ml)	Sibandze[25]
Antibacterial	Acetone	Roots and stems	Serial dilution	Exhibited activities against *K. pneumoniae* with MIC value of 1.3 mg/ml, *E. coli* (2.0 mg/ml), *S. aureus* (4.0 mg/ml) and *S. epidermidis* (8.0 mg/ml)	Sibandze[25]
Antibacterial	Crude	Roots	Serial dilution	Exhibited activities against *E. coli* with MIC value of >20.0 μg/ml, *P. aeruginosa* (160.0 μg/ml), *E. faecalis* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Acetone	Roots	Serial dilution	Exhibited activities against *E. faecalis* and *P. aeruginosa* with MIC value of 160.0 μg/ml, and *E. coli* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Dichloromethane	Roots	Serial dilution	Exhibited activities against *P. aeruginosa* with MIC value of 160.0 μg/ml, and *E. faecalis*, *E. coli* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Ethyl acetate	Roots	Serial dilution	Exhibited activities against and *E. coli* with MIC value of 160.0 μg/ml, and *P. aeruginosa* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Hexane	Roots	Serial dilution	Exhibited activities against *E. coli* with MIC value of >20.0 μg/ml, *P. aeruginosa* (160.0 μg/ml), *E. faecalis* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Methanol	Roots	Serial dilution	Exhibited activities against *P. aeruginosa* with MIC value of 160.0 μg/ml, *E. coli*, *E. faecalis* and *S. aureus* (320.0 μg/ml)	Muleya[36]
Antibacterial	Crude	Roots	Serial dilution	Exhibited activities against *E. faecalis* and *P. aeruginosa* with MIC value of 160.0 μg/ml, *E. coli* and *S. aureus* (320.0 μg/ml)	Muleya et al.[39]
Antibacterial	Acetone	Roots	Serial dilution	Exhibited activities against *E. faecalis*, *E. coli*, *P. aeruginosa* and *S. aureus* with MIC value of 320.0 μg/ml	Muleya et al.[39]
Antibacterial	Dichloromethane	Roots	Serial dilution	Exhibited activities against *E. faecalis*, *P. aeruginosa* and *S. aureus* with MIC value of 160.0 μg/ml and *E. coli* (320.0 μg/ml)	Muleya et al.[39]

Activity tested	Extract	Plant part	Model	Effect	Reference
Antibacterial	Ethyl acetate	Roots	Serial dilution	Exhibited activities against *E. coli*, *P. aeruginosa* and *S. aureus* with MIC value of 160.0 μg/ml and *E. faecalis* (625.0 μg/ml)	Muleya et al.[39]
Antibacterial	Hexane	Roots	Serial dilution	Exhibited activities against *P. aeruginosa* and *S. aureus* with MIC value of 80.0 μg/ml, *E. faecalis* (160.0 μg/ml) and *E. coli* (320.0 μg/ml)	Muleya et al.[39]
Antibacterial	Methanol	Roots	Serial dilution	Exhibited activities against *E. faecalis* and *E. coli* with MIC value of 160.0 μg/ml, *P. aeruginosa* and *S. aureus* (320.0 μg/ml)	Muleya et al.[39]
Antibacterial	Aqueous	Leaves	Micro-dilution	Exhibited activities against *Gardnerella vaginalis*, *Neisseria gonorrhoeae* and *Oligella ureolytica* with MIC value of >8.0 mg/ml	Kose et al.[30]; Kose[40]
Antibacterial	Organic	Leaves	Micro-dilution	Exhibited activities against *N. gonorrhoeae* with MIC value of 0.8 mg/ml, *O. ureolytica* (2.5 mg/ml) and *G. vaginalis* (5.0 mg/ml)	Kose et al.[30]; Kose[40]
Antibacterial	Aqueous	Roots	Micro-dilution	Exhibited activities against *G. vaginalis*, *N. gonorrhoeae* and *Oligella ureolytica* with MIC value of >8.0 mg/ml	Kose et al.[30]; Kose[40]
Antibacterial	Organic	Roots	Micro-dilution	Exhibited activities against *N. gonorrhoeae* with MIC value of 0.8 mg/ml, *O. ureolytica* and *G. vaginalis* (4.0 mg/ml)	Kose et al.[30]; Kose[40]
Antifungal	Acetone	Flowers	Serial dilution	Exhibited activities against *Candida albicans* with MIC value of 2.0 mg/ml	Sibandze[25]
Antifungal	Acetone	Leaves	Serial dilution	Exhibited activities against *C. albicans* with MIC value of 1.3 mg/ml	Sibandze[25]
Antifungal	Acetone	Roots and stems	Serial dilution	Exhibited activities against *C. albicans* with MIC value of 0.7 mg/ml	Sibandze[25]
Antifungal	Crude	Roots	Serial dilution	Exhibited activities against *C. albicans* and *Aspergillus fumigatus* with MIC values of 160.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Acetone	Roots	Serial dilution	Exhibited activities against *C. albicans* and *A. fumigatus* with MIC values of 320.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Dichloromethane	Roots	Serial dilution	Exhibited activities against *C. albicans* and *A. fumigatus* with MIC values of 160.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Ethyl acetate	Roots	Serial dilution	Exhibited activities against *C. albicans* and *A. fumigatus* with MIC values of 160.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Hexane	Roots	Serial dilution	Exhibited activities against *C. albicans* and *A. fumigatus* with MIC values of 160.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Hexane	Roots	Serial dilution	Exhibited activities against *C. albicans* and *A. fumigatus* with MIC values of 320.0 μg/ml and 625.0 μg/ml, respectively	Muleya[36]
Antifungal	Aqueous	Leaves	Micro-dilution	Exhibited activities against *C. albicans* with MIC value of 4.0 mg/ml	Kose et al.[30]; Kose[40]
Antifungal	Organic	Leaves	Micro-dilution	Exhibited activities against *C. albicans* with MIC value of 1.7 mg/ml	Kose et al.[30]; Kose[40]
Antifungal	Aqueous	Roots	Micro-dilution	Exhibited activities against *C. albicans* with MIC value of >8.0 mg/ml	Kose et al.[30]; Kose[40]
Antifungal	Organic	Roots	Micro-dilution	Exhibited activities against *C. albicans* with MIC value of 3.2 mg/ml	Kose et al.[30]; Kose[40]
Anti-inflammatory	Crude	Roots	15-soybean lipoxygenase (15-LOX) enzyme	Exhibited activities with EC_{50} value of 11.9 μg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antimalarial	Dichloromethane:methanol (1:1)	Flowers	[$G^{-3}H$] hypoxanthine incorporation assay	Extract exhibited activities with IC_{50} value of 32.3 μg/ml	Sibandze[25]; Sibandze and Van Zyl[42]
Antimalarial	Dichloromethane:methanol (1:1)	Leaves	[$G^{-3}H$] hypoxanthine incorporation assay	Extract exhibited activities with IC_{50} value of 66.4 μg/ml	Sibandze[25]; Sibandze and Van Zyl[42]
Antimalarial	Dichloromethane:methanol (1:1)	Roots and stems	[$G^{-3}H$] hypoxanthine incorporation assay	Extract exhibited activities with IC_{50} value of 15.1 μg/ml	Sibandze[25]; Sibandze and Van Zyl[42]

Activity tested	Extract	Plant part	Model	Effect	Reference
Antioxidant	Crude	Roots	1,1-diphenyl-2-picrylhydrazyl (DPPH) free radical scavenging	Exhibited 58% inhibition of DPPH and IC_{50} value of 2335 µg/mL	Magama et al.[43]
Antioxidant	Crude	Roots	Reducing power assay	Extracts reduced Fe^{3+} to Fe^{2+}	Magama et al.[43]
Antioxidant	Crude	Roots	Hydrogen peroxide scavenging assay	Extract demonstrated hydrogen peroxide scavenging activities in a concentration dependent manner	Magama et al.[43]
Antioxidant	Crude	Roots	2, 2-azinobis (3-ethylbenzothiazoline)-6-sulfonic acid (ABTS) assay	Exhibited activities with EC_{50} value of 2.0 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Acetone	Roots	ABTS assay	Exhibited activities with EC_{50} value of 73.0 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Dichloromethane	Roots	ABTS assay	Exhibited activities with EC_{50} value of 158.1 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Ethyl acetate	Roots	ABTS assay	Exhibited activities with EC_{50} value of 57.2 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Hexane	Roots	ABTS assay	Exhibited activities with EC_{50} value of 577.1 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Methanol	Roots	ABTS assay	Exhibited activities with EC_{50} value of 1.5 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Crude	Roots	DPPH assay	Exhibited activities with EC_{50} value of 2.5 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Acetone	Roots	DPPH assay	Exhibited activities with EC_{50} value of 2.0 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Dichloromethane	Roots	DPPH assay	Exhibited activities with EC_{50} value of 55.3 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Ethyl acetate	Roots	DPPH assay	Exhibited activities with EC_{50} value of 38.1 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Hexane	Roots	DPPH assay	Exhibited activities with EC_{50} value of 157.1 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Antioxidant	Methanol	Roots	DPPH assay	Exhibited activities with EC_{50} value of 1.0 µg/ml	Muleya[36]; Muleya et al.[39]; Mtunzi et al.[41]
Haemolysis	Dichloromethane : methanol (1:1)	Flowers	Haemolytic in vitro assay	Extracts exhibited activities with IC_{50} values of >100.0 µg/ml	Sibandze[25]
Haemolysis	Dichloromethane:methanol (1:1)	Leaves	Haemolytic in vitro assay	Extracts exhibited activities with IC_{50} values of >100.0 µg/ml	Sibandze[25]
Haemolysis	Dichloromethane : methanol (1:1)	Roots and stems	Haemolytic in vitro assay	Extracts exhibited activities with IC_{50} values of 178.0 µg/ml	Sibandze[25]
Cytotoxicity	Aqueous	Leaves	Brine shrimp lethality assay	Exhibited activities with percentage mortalities of 89.3	Kose et al.[30]
Cytotoxicity	Organic	Leaves	Brine shrimp lethality assay	Exhibited activities with percentage mortalities of 88.2	Kose et al.[30]

CONCLUSION

Berkheya setifera is a well-known plant species in southern Africa in traditional and folk medicine which is an important part of indigenous culture in the region. In many cases, different plant parts such as leaves and roots are used to manage and treat several human diseases. Detailed phytochemical evaluations are lacking although terpenoids, thiophene acetylenes, cardenolides, polyphenols, reducing sugars, saponins, glycosides and alkaloids have been identified from the roots of the species. The studies focusing on biological activities of *B. setifera* crude extracts have been conducted in *in vitro*. Not much data are available on biological activities of compounds isolated from the species and toxicity of *B. setifera* crude extracts and chemical ingredients isolated from the species. Therefore, there is need for further studies focusing on the phytochemistry, pharmacological, toxicological and *in vivo* studies involving the crude extracts and chemical ingredients isolated from the species.

Conflict of interest

The author declares that he has no conflict of interest.

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