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Helichrysum caespititium (DC.) Harv.: Review of its medicinal uses, phytochemistry and biological activities

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ABSTRACT

Helichrysum caespititium is a valuable and well-known medicinal plant in south and central Africa. The current study examined ethnomedicinal uses, chemical and biological properties of *H. caespititium*. Information on medicinal uses, phytochemistry, and biological activities of *H. caespititium* were assembled from several internet sources which included Scopus, Google Scholar, Elsevier, Science Direct, Web of Science, Pubmed, SciFinder, and BMC. Additional information was sourced from journal articles, scientific reports, theses, books, and book chapters gathered from the University library. The current study showed that *H. caespititium* is used for treating several medical conditions, particularly respiratory infections, sexually transmitted infections, nausea, headache, wounds, ulceration, and used as an aphrodisiac. The pharmacological research showed that *H. caespititium* extracts and compounds isolated from the species have antibacterial, antigonorrhea, antimycobacterial, antifungal, antioxidant, and cytotoxicity activities. This research showed that *H. caespititium* is an integral part of indigenous pharmacopeia in southern Africa, but there is lack of alignment between the ethnomedicinal uses and existing biological screening. Therefore, future research should focus on evaluation of the chemical and pharmacological properties of *H. caespititium* extracts and compounds isolated from the species.

INTRODUCTION

Helichrysum caespititium (DC.) Harv. is a perennial creeping herb (Fig. 1) which belongs to the Asteraceae or Compositae family. The species has been recorded in Lesotho, South Africa, Swaziland, and Zimbabwe (Fabian and Germishuizen, 1997; Germishuizen and Meyer, 2003; Hilliard, 1977; 1983; Hyde *et al*., 2019). *Helichrysum caespititium* is known by several vernacular names in southern Africa which include the following: golden everlasting (English), sewejaartjies and speelwonderboom (Afrikaans), phate-ea-naha, boriba, moriri-oa-lefatse, lelula-phooko, and botsiki-nyane (southern Sotho), mabjana, matšana, and mmetse (northern Sotho) (Erasmus *et al*., 2012; Hutchings and Van Staden, 1994; Pooley, 1998; 2003). A single synonym, "*Helichrysum lineare* DC. var. *caespititium* DC.," was found in the literature (Fabian and Germishuizen, 1997; Germishuizen and Meyer, 2003; Hilliard, 1983; Hyde *et al*., 2019). The species name *caespititium* was derived from the Latin word "caespitose" which means very much tufted and matted, in reference to the cushion-forming or mat-forming growth habit of the species (Hyde *et al*., 2019). The height of *H. caespititium* ranges from 10 to 20 cm has been recorded in open spaces in the grassland and savanna biomes, particularly disturbed areas at an average altitude range of 650–2,440 m above the sea level (Fabian and Germishuizen, 1997 ; Germishuizen and Meyer, 2003; Hilliard, 1983; Hyde *et al*., 2019). The leaves are linear, clasping at the base and hairy on both sides (Fig. 1). The leaves are orange gland-dotted with margin rolled under and densely crowded along the stems (Hilliard, 1983; Hyde *et al*., 2019). The flowers of *H. caespititium* are white to yellow in color and pale furry underneath (Hilliard, 1983; Hyde *et al*., 2019).

Helichrysum caespititium is a popular herbal medicine throughout its geographical distributional range in Lesotho, South Africa, Swaziland, and Zimbabwe (Arnold *et al*., 2002; Gelfand *et al*., 1985; Long, 2005; Moteetee and Van Wyk, 2011). Therefore, *H. caespititium* is regarded as an integral part of traditional pharmacopoeia in southern Africa, with species tolerated and

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Figure 1. *Helichrysum caespititium*, (A) a photograph showing an entire plant, the leaves and inflorescence (photo: F Lagarde) and (B) photograph of a herbarium specimen housed in the National Herbarium of Zimbabwe (photo: B Wursten).

managed in domestic home gardens of the North West province of South Africa as herbal medicine (Molebatsi, 2011). *Helichrysum caespititium* makes an enormous contribution to basic primary healthcare of local people in southern Africa. Therefore, this is the rationale behind the review of ethnopharmacological properties of *H. caespititium*. The current study is aimed at appraising the existing ethnomedicinal value, phytochemistry, and biological activities of the compounds isolated from the species, including *H. caespititium* crude extracts as well as exploring the potential of the species as herbal medicine.

MATERIALS AND METHODS

Relevant information on medicinal applications, chemistry, phytochemistry, and biological activities of *H. caespititium* were assembled from the several sources which included Scopus, Google Scholar, Elsevier, Science Direct, Web of Science, Pubmed, SciFinder, and BMC. Additional information was sourced from journal articles, scientific reports, theses, books, and book chapters gathered from the University library. The search for this information was carried out between September 2018 and February 2019. The key words used in the search included "ethnobotany," "ethnomedicinal uses," "medicinal uses," "phytochemistry," "biological activities," "pharmacological properties," "toxicological properties," "*Helichrysum caespititium*," the synonym of the species, "*Helichrysum lineare* DC. var. *caespititium* DC." and the English common name "golden everlasting."

RESULTS AND DISCUSSION

Medicinal uses

The leaves, roots, and the whole plant of *H. caespititium* are widely used as the herbal medicines for 29 human diseases in south and central Africa (Table 1). Following medical categorization of human diseases and ailments proposed by Cook (1995), Gruca *et al.* (2014), Macía *et al.* (2011), and Staub *et al.* (2015), *H. caespititium* is mainly used as the herbal medicine against respiratory infections in all the countries where the taxon is indigenous (Fig. 2). Other important medicinal applications include sexually transmitted infections, nausea, aphrodisiac, headache, wounds, and ulceration (Fig. 2). In South Africa, the whole plant of *H. caespititium* is mixed with roots of *Callilepis laureola* DC. and *Osyris lanceolata* Hochst. & Steud., leaves of *Lippia javanica* (Burm. f.) Spreng., and *Tragia dioica* Sond. as remedy for fatigue (Semenya and Maroyi, 2018; 2019a). Similarly, the whole plant parts of *H. caespititium* is mixed with bark of *Sclerocarya birrea* (A.Rich.) Hochst., entire plant parts of *Enicostema axillare* (Lam.) A. Raynal, and roots of *Callilepis laureola* as the herbal medicine for pneumonia (Semenya and Maroyi, 2018c; 2019a). In Lesotho, the whole plant of *H. caespititium* is mixed with roots of *Dicoma anomala* Sond., *Scabiosa columbaria* L., and *Zantedeschia albomaculata* (Hook.) Baill. as the herbal medicine for venereal diseases (Maliehe, 1997; Maroyi, 2018; Moteetee and Van Wyk, 2011; Watt and Brandwijk, 1927; Watt and Breyer-Brandwijk, 1962).

Phytochemistry

Dekker *et al.* (1983) isolated the phloroglucinol compound, caespitin [2 (4-methylpentanoyl)-4-(3-methylbuten-2-yl) phloroglucinol] from whole plant of *H. caespititium* (Fig. 3A). Similarly, Mathekga *et al.* (2000) isolated a phloroglucinol compound caespitate, often referred to as 2-methyl 4-[2′,4′,6′ trihydroxy-3′ (2-methylpropanoyl) phenyl]but-2-enyl acetate from the aerial parts of *H. caespititium* (Fig. 3B). Based on pharmacological evaluations done so far, both caespitin and caespitate have antibacterial and antifungal activities (Dekker *et al.*, 1983; Mathekga, 2001; Mathekga *et al.*, 2000; Van Der Schyf *et al.*, 1986), while caespitate also exhibited antituberculosis activities (Meyer *et al.*, 2002). Documentation of phloroglucinol compounds only highlights an existing gap requiring attention from researchers and future research should focus on the identification and isolation of phytochemical compounds in the utilized parts, particularly aerials parts, stems, and roots.

Biological activities

The following biological activities have been reported from *H. caespititium* crude extracts and compounds isolated from

Table 1. Medicinal uses of *Helichrysum caespititium*.

Disease	Parts used	Country	References
Anti-emetic	Whole plant	Lesotho	Jacot Guillarmod, 1971; Schmitz, 1982
Aphrodisiac	Roots and whole plant	Lesotho and South Africa	Ajao *et al*., 2018; Jacot Guillarmod, 1971; Lourens *et al*., 2008; Maliehe, 1997; Moffett, 2010; Moteetee *et al*., 2018; Moteetee and Seleteng-Kose, 2016; Schmitz, 1982; Seleteng-Kose *et al*., 2015; Watt and Breyer-Brandwijk, 1962
Boost immunity	Whole plant	Lesotho	Mugomeri *et al*., 2016a
Burnt as incense	Whole plant	Lesotho	Moteetee *et al*., 2018
Depressed fontanelle	Whole plant	Zimbabwe	Gelfand *et al*., 1985
Diabetes mellitus	Whole plant	South Africa	Adebayo and Masoko, 2017; Chinsembu, 2018; Semenya *et al*., 2012
Fatigue	Whole plant mixed with roots of *Callilepis laureola* DC. and *Osyris lanceolata* Hochst. & Steud., leaves of *Lippia javanica* (Burm. f.) Spreng. and *Tragia dioica* Sond.	South Africa	Semenya and Maroyi, 2018; 2019a
Fumigant	Whole plant	Lesotho	Moteetee *et al*., 2018
Gastro-intestinal tract problems and diarrhea	Whole plant	South Africa	Mamabolo *et al*., 2018; Semenya and Maroyi, 2012
Headache	Whole plant	South Africa and Zimbabwe	Hutchings and Van Staden, 1994; Hutchings *et al*., 1996; Meyer *et al*., 2002; Reddy, 2007; Watt and Breyer-Brandwijk, 1962
Hypertension	Whole plant	South Africa	Semenya and Wadesango, 2018
Intestinal worms	Whole plant	Lesotho	Seleteng-Kose *et al*., 2015; Watt and Breyer-Brandwijk, 1962
Liver problems	Whole plant	Lesotho	Seleteng-Kose *et al*., 2015
Nausea	Whole plant	Lesotho, South Africa and Swaziland	Long, 2005; Lourens *et al*., 2008; Seleteng-Kose *et al*., 2015; Watt and Breyer-Brandwijk, 1962
Respiratory infections (chest pains, colds, cough, flu, pneumonia, sinuses and tuberculosis)	Leaves, roots and whole plant	Lesotho, South Africa, Swaziland and Zimbabwe	Dekker *et al*., 1983; Jacot Guillarmod, 1971; Gelfand *et al*., 1985; Hutchings and Van Staden, 1994; Hutchings *et al*., 1996; Maliehe, 1997; Mamabolo *et al*., 2017; 2018; Mammino and Kabanda, 2007; 2012; Mathekga, 2001; Mathekga *et al*., 2000; Meyer *et al*., 2002; Mugomeri *et al*., 2016a; 2016b; Long, 2005; Reddy, 2007; Moteetee and Van Wyk, 2011; Schmitz, 1982; Seleteng-Kose *et al*., 2015; Semenya and Maroyi, 2018b; 2019b; Watt and Breyer-Brandwijk, 1962
Pneumonia	Whole plant mixed with bark of *Sclerocarya birrea* (A.Rich.) Hochst., entire plant of *Enicostema axillare* (Lam.) A. Raynal and root of *Callilepis laureola*	South Africa	Semenya and Maroyi, 2018c; 2019a
Sexually transmitted diseases and gonorrhoea	Whole plant	Lesotho, South Africa and Zimbabwe	Erasmus *et al*., 2012; Gelfand *et al*., 1985; Mathekga, 2001; Mamabolo *et al*., 2017; Mammino and Kabanda, 2007,2012; Seleteng-Kose *et al*., 2015; Seleteng-Kose *et al*., 2019; Semenya *et al*., 2013; Watt and Breyer-Brandwijk, 1962
Venereal diseases	Whole plant mixed with roots of *Dicoma anomala* Sond., *Scabiosa columbaria* L. and *Zantedeschia albomaculata* (Hook.) Baill.	Lesotho	Maliehe, 1997; Maroyi, 2018; Moteetee and Van Wyk, 2011; Watt and Brandwijk, 1927; Watt and Breyer-Brandwijk, 1962
Skin infections	Whole plant	South Africa	Mamabolo *et al*., 2018
Ulceration	Whole plant	South Africa and Zimbabwe	Gelfand *et al*., 1985; Mammino and Kabanda, 2007; Mathekga, 2001; Watt and Breyer-Brandwijk, 1962
Wounds	Whole plant	Lesotho and South Africa	Mamabolo *et al*., 2017; Mammino and Kabanda, 2012; Mathekga, 2001; Watt and Breyer-Brandwijk, 1962

the species (Table 2): antibacterial (Dekker *et al*., 1983; Mamabolo *et al*., 2017; Mathekga, 2001; Mathekga *et al*., 2000; Seleteng-Kose *et al*., 2019; Van der Schyf *et al*., 1986), antigonorrhea (Mamabolo *et al*., 2018), antimycobacterial (Meyer *et al*., 2002), antifungal (Dekker *et al*., 1983; Mathekga, 2001; Mathekga *et al*., 2000; Seleteng-Kose *et al*., 2019; Van der Schyf *et al*., 1986), antioxidant (Mamabolo *et al*., 2017), and cytotoxicity (Mamabolo *et al*., 2018) activities.

Antibacterial activities

Preliminary evaluation of antibacterial activities of the compound caespitin isolated from *H. caespititium* by Dekker *et al*. (1983) showed that the compound exhibited significant antibacterial activities against *Streptococcus pyogenes* and *Staphylococcus aureus*; however, the screening method used or the activity level are not indicated in the paper. Similarly, Van der Schyf (1986) assessed antibacterial properties of caespitin identified from *H. caespititium* against *S. pyogenes, Proteus mirabilis*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *S. aureus* using a serial dilution method. The compound exhibited activities against *S. pyogenes* and *S. aureus* with the minimum inhibitory concentration (MIC) value of 8.0 µg/ml and the minimum bactericidal concentration (MBC) value of 16.0 µg/ml (Van der Schyf, 1986). Mathekga (2001) and Mathekga *et al*. (2000) evaluated the antibacterial

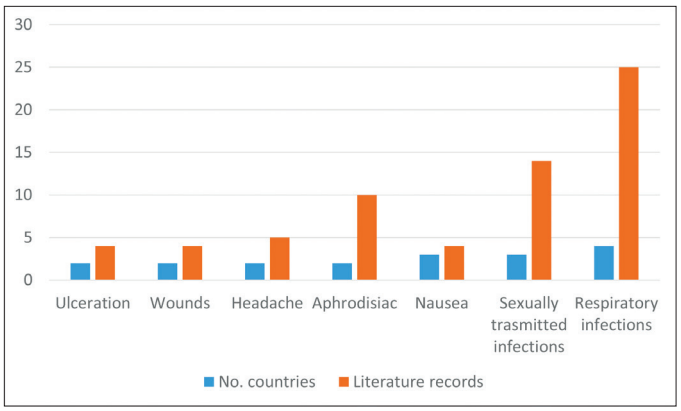

Figure 2. Diseases and ailments treated by *Helichrysum caespititium* in southern Africa.

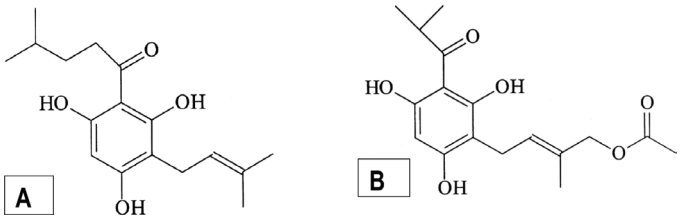

Figure 3. Chemical structures of phloroglucinol compounds, caespitin (A) and caespitate (B) isolated from *Helichrysum caespititium*.

activities of acetone extracts of aerial parts of *H. caespititium* against *Bacillus subtilis*, *Enterobacter cloacae*, *Bacillus cereus*, *P. aeruginosa*, *Bacillus pumilus*, *Micrococcus kristinae*, *S. aureus*, *E. coli*, *Serratia marcescens*, and *Klebsiella pneumoniae* using the agar dilution technique. The extract exhibited activities against all the tested pathogens, except *S. marcescens* and *K. pneumoniae* with MIC value of 1.0 mg/ml (Mathekga, 2001; Mathekga *et al*., 2000). Mathekga *et al*. (2000) assessed the antibacterial properties of the compounds caespitin and caespitate against *E. cloacae*, *B. pumilus*, *M. kristinae*, *E. coli*, *B. subtilis*, *S. aureus*, *S. marcescens*, *K. pneumoniae*, *B. cereus*, and *P. aeruginosa* using agar dilution method. Both compounds, caespitin and caespitate were active against *B. subtilis*, *M. kristinae*, *B. pumilus*, *S. aureus*, and *B. cereus* with the MIC value range of 0.5 to 1.0 µg/ml (Mathekga, *et al*. 2000). Mathekga (2001) also evaluated the synergistic antibacterial activities of the compounds caespitate and caespitin isolated from *H. caespititium* against *B. subtilis*, *K. pneumoniae*, *M. kristinae*, *E. cloacae*, *B. pumilus*, *S. marcescens*, *S. aureus*, *B. cereus*, *E. coli*, and *P. aeruginosa* using agar dilution method. Caespitate and caespitin exhibited antibacterial activities against *S. aureus*, *B. cereus*, *M. kristinae*, *B. subtilis*, and *B. pumilus* with MIC values ranging from 0.5 to 1.0 µg/ml. The combination of caespitin and caespitate maintained their original antibacterial activities against all the tested pathogens except *S. marcescens* and also enhanced their synergistic effects with MIC values within the range of 0.05–0.1 µg/ml (Mathekga, 2001). Mamabolo *et al*. (2017) assessed antibacterial properties of n-hexane, dichloromethane, acetone, methanol and aqueous extracts of whole plant of *H. caespititium* against *Klebsiella oxytoca*, *B. cereus*, *Enterococcus faecalis*, *B. subtilis*, *E. cloacae*, *Mycobaterium smegmatis*, *E. coli*, *K. pneumoniae*, *Proteus vulgaris*, *Staphylococcus epidermidis*, *P. aeruginosa*, *P. mirabilis*, *S. aureus*, and *Enterobacter aerogenes* using the microdilution technique with streptomycin and nalidixic acid as positive drugs. The extracts showed antibacterial activities against all the tested pathogens with the MIC values within the range of 0.01–0.4 mg/ml (Mamabolo *et al*., 2017). Seleteng-Kose *et al*. (2019) assessed the properties of organic and water extracts of whole plant parts of *H. caespititium* against *Neisseria gonorrhoeae*, *Gardnerella vaginalis*, and *Oligella ureolytica* using the micro-dilution technique with ciprofloxacin (0.01 mg/ml) as the positive drug. The organic extracts showed moderate properties against *G. vaginalis* and *N. gonorrhoeae* with the MIC value of 0.1 and 0.06 mg/ml. The MIC value of organic extract against *O. ureolytica* was 7.2 mg/ml, while aqueous extract showed the MIC values of >8.0 mg/ml against all the tested pathogens (Seleteng-Kose *et al*., 2019).

Antigonorrhea activities

Mamabolo *et al*. (2018) assessed the antigonorrhea properties of n-hexane, dichloromethane, methanol and aqueous extracts of whole plant of *H. caespititium* against strains F, N, O, and G of *N. gonorrhoeae* using micro-dilution technique with gentamicin and amoxicillin as positive drugs. The extracts showed properties with the MIC values within the range of 0.04 to >0.3 mg/ml which were within the same range of MIC values of 0.2–0.3 mg/ml exhibited by the controls (Mamabolo *et al*., 2018).

Antimycobacterial activities

Meyer *et al*. (2002) evaluated the antimycobacterial properties of acetone and aqueous leaf extract of *H. caespititium* against a drug-sensitive strain of *Mycobacterium tuberculosis* using the agar plate technique. Meyer *et al*. (2002) also evaluated the antimycobacterial activities of the phloroglucinol compound, caespitate isolated from *H. caespititium* against drug-resistant and drug sensitive strains of *M. tuberculosis*. The acetone extract showed activities against the tested pathogens at a concentration of 0.5 mg/ml whereas, *M. tuberculosis* was susceptible to the aqueous extract at 5.0 mg/ml. The activities exhibited by the acetone extract against *M. tuberculosis* were corroborated by the use of the rapid radiometric method and the MIC value was found to be 0.1 mg/ml. The MIC value of caespitate was determined to be 0.1 mg/ml for the *M. tuberculosis* strains (Meyer *et al*., 2002).

Antifungal activities

Preliminary evaluation of antifungal activities of the compound caespitin isolated from *H. caespititium* by Dekker *et al*. (1983) showed that the compound exhibited significant antifungal activities against *Trichophyton mentagrophytes*, *Trichophyton rubrum*, *Microsporum canis*, and *Cryptococcus neoformans*; however, the screening method used or the activity level are not indicated in the paper. Van der Schyf *et al*. (1986) evaluated antifungal activities of the compound caespitin isolated from *H. caespititium* against *Candida albicans*, *Candida tropicalis*, *Absidia corymbifera*, *Aspergillus fumigatus*, *Sporotrichum schenkii*, *T. rubrum*, *M. canis*, and *T. mentagrophytes* using a serial dilution technique and nystatin as the positive drug. The compound exhibited best activities against *T. rubrum*, *M. canis*, and *T. mentagrophytes* with MIC and the minimum fungicidal concentration (MFC) values within the range of 6.0–13.0 µg/ml, while MIC and MFC

Table 2. Summary of biological activities of *Helichrysum caespititium* crude extracts and compounds isolated from the species.

Activity tested	Extract	Plant part/ compound	Model	Effect	Reference
Antibacterial	Not applicable	Caespitin	Not mentioned	Exhibited significant antibacterial activities against *S. aureus* and *S. pyogenes* (level of activity not indicated)	Dekker *et al*., 1983
Antibacterial	Not applicable	Caespitin	Serial dilution method	Exhibited activities against *S. pyogenes* and *S. aureus* with minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) values of 8.0 and 16.0 µg/ml, respectively	Van der Schyf *et al*., 1986
Antibacterial	Acetone	Aerial parts	Agar dilution method	Exhibited activities against *P. aeruginosa, B. cereus, M. kristinae, B. pumilus, E. cloacae, B. subtilis, E. coli*, and *S. aureus* with MIC value of 1.0 mg/ml	Mathekga *et al*., 2000
Antibacterial	Acetone	Aerial parts	Agar dilution method	Exhibited activities against *S. aureus*, *B. cereus, E. coli, B. subtilis, M. kristinae, B. pumilus, E. cloacae*, and *P. aeruginosa* with MIC value of 1.0 mg/ml	Mathekga, 2001
Antibacterial	Not applicable	Caespitin	Agar dilution method	Exhibited activities against *S. aureus*, *B. cereus, B. subtilis, B. pumilus*, and *M. kristinae* with MIC value of 1.0 µg/ml	Mathekga *et al*., 2000
Antibacterial	Not applicable	Caespitate	Agar dilution method	Exhibited activities against *M. kristinae*, *B. cereus, B. subtilis, S. aureus*, and *B. pumilus* with MIC value of 0.5 µg/ml	Mathekga *et al*., 2000
Antibacterial	Not applicable	Caespitate and caespitin	Agar dilution method	Exhibited activities with MIC value of 0.05 µg/ml against *K. pneumoniae, B. cereus, B. subtilis, S. aureus, M. kristinae*, and *B. pumilus*, and MIC value of 0.01 µg/ml against *E. cloacae* and *E. coli*	Mathekga, 2001
Antibacterial	Acetone	Whole plant	Microdilution method	Exhibited activities with MIC values of 0.01 mg/ml against *P. vulgaris; S. epidermidis* (0.02 mg/ml); *E. coli*, *E. aerogenes, B. subtilis, E. faecalis*, and *E. cloacae,* and (0.2 mg/ml); *B. cereus, K. oxytoca, K. pneumoniae, M. smegmatis, P. vulgaris, P. aeruginosa, P. mirabilis*, and *S. aureus* (0.4 mg/ml)	Mamabolo *et al*., 2017
Antibacterial	Aqueous	Whole plant	Microdilution method	Exhibited activities with MIC values of 0.01 mg/ml against *K. oxytoca* and *S. epidermidis; E. faecalis*, and *P. vulgaris* (0.02 mg/ml); *K. pneumoniae, B. cereus, E. aerogenes, E. coli, M. smegmatis, P. aeruginosa, E. cloacae, P. mirabilis, S. aureus*, and *B. subtilis,* (0.4 mg/ml)	Mamabolo *et al*., 2017
Antibacterial	Dichloromethane	Whole plant	Microdilution method	Exhibited activities with MIC values of 0.01 mg/ml against *E. faecalis, E. coli*, and *P. vulgaris; K. pneumoniae* (0.02 mg/ml); *B. cereus, E. aerogenes, B. subtilis, E. cloacae, K. oxytoca, P. mirabilis, S. aureus*, *P. aeruginosa*, and *S. epidermidis* (0.2 mg/ml), and *M. smegmatis* (0.4 mg/ml)	Mamabolo *et al*., 2017
Antibacterial	n-hexane	Whole plant	Microdilution method	Exhibited activities with MIC values of 0.01 mg/ml against *S. epidermidis; E. faecalis*, and *P. vulgaris* (0.02 mg/ml); *B. subtilis, K. oxytoca, K. pneumoniae, M. smegmatis*, and *S. aureus* (0.1 mg/ml); *B. cereus, E. aerogenes, E. coli, P. mirabilis* and *P. aeruginosa* (0.2 mg/ml), and *E. cloacae* (0.4 mg/ml).	Mamabolo *et al*., 2017
Antibacterial	Methanol	Whole plant	Microdilution method	Exhibited activities with MIC value of 0.02 mg/ml against *E. coli, K. pneumoniae*, and *P. vulgaris* (0.05 mg/ml); *S. aureus*, and *S. epidermidis* (0.1 mg/ml); *B. cereus, B. subtilis, E. aerogenes, E. cloacae, E. faecalis, K. oxytoca, M. smegmatis, P. mirabilis*, and *P. aeruginosa* (0.2 mg/ml)	Mamabolo *et al*., 2017
Antibacterial	Aqueous	Whole plant	Micro-dilution assay	Exhibited activities against *N. gonorrhoeae, G. vaginalis*, and *O. ureolytica* with MIC values >8.0 mg/ml	Seleteng-Kose *et al*., 2019
Antibacterial	Organic	Whole plant	Micro-dilution assay	Exhibited activities with MIC value of 0.1 mg/ml against *G. vaginalis, N. gonorrhoeae* (0.06 mg/ml), and *O. ureolytica* (7.2 mg/ml)	Seleteng-Kose *et al*., 2019
Antigonorrhea	Aqueous	Whole plant	Micro-dilution assay	Exhibited activities against *N. gonorrhoeae* with MIC value of >0.3 mg/ml	Mamabolo *et al*., 2018
Antigonorrhea	Dichloromethane	Whole plant	Micro-dilution assay	Exhibited activities against *N. gonorrhoeae* with MIC value of >0.3 mg/ml	Mamabolo *et al*., 2018
Antigonorrhea	n-hexane	Whole plant	Micro-dilution assay	Exhibited activities against *N. gonorrhoeae* with MIC values ranging from 0.04 mg/ml to 0.3 mg/ml	Mamabolo *et al*., 2018
Antigonorrhea	Methanol	Whole plant	Micro-dilution assay	Exhibited activities against *N. gonorrhoeae* with MIC value of >0.3 mg/ml	Mamabolo *et al*., 2018
Antimycobacterial	Acetone	Leaves	Agar plate method	Exhibited activities with MIC value of 0.1 mg/ml against *M. tuberculosis*	Meyer *et al*., 2002
Antimycobacterial	Not applicable	Caespitate	Agar plate method	Exhibited activities with MIC value of 0.1 mg/ml against *M. tuberculosis*	Meyer *et al*., 2002

continued

Activity tested	Extract	Plant part/ compound	Model	Effect	Reference
Antifungal	Not applicable	Caespitin	Not mentioned	Exhibited significant antifungal activities against *M. canis, C. neoformans, T. mentagrophytes*, and *T. rubrum* (level of activity not indicated)	Dekker *et al*., 1983
Antifungal	Not applicable	Caespitin	Serial dilution method	Exhibited activities against tested pathogens with MIC and minimum fungicidal concentration (MFC) values of 25.0 µg/ml and 100.0 µg/ml against *C. albicans, C. tropicalis* (50.0 µg/ml, 100.0 µg/ml), *A. corymbifera* (100.0 µg/ml, >100.0 µg/ml), *A. fumigatus* (100.0 µg/ml, 100.0 µg/ml), *S. schenkii* (25.0 µg/ml, 50.0 µg/ml), *T. rubrum* (6.0 µg/ml, 6.0 µg/ml), *T. mentagrophytes* (6.0 µg/ml, 13.0 µg/ml), and *M. canis* (6.0 µg/ml, 13.0 µg/ml)	Van der Schyf *et al*., 1986
Antifungal	Acetone	Aerial parts	Agar dilution method	Exhibited activities with MIC value of 0.01 mg/ml against *A. niger, C. sphaerospermum, C. cucumerinum,* and *C. cladosporioides*, and MIC value of 1.0 mg/ml against *A. flavus* and *P. capsici*	Mathekga *et al*., 2000
Antifungal	Acetone	Caespitate	Agar dilution method	Exhibited activities with MIC value of 0.5 mg/ml against *C. cucumerinum* and *C. sphaerospermum*, MIC value of 1.0 mg/ml against *A. flavus, A. niger*, and *P. capsici*, and MIC value of 5.0 mg/ml against *C. cladosporioides*	Mathekga *et al*., 2000
Antifungal	Aqueous	Whole plant	Micro-dilution assay	Exhibited activities against *C. albicans* with MIC value of >8.0 mg/ml	Seleteng-Kose *et al*., 2019
Antifungal	Organic	Whole plant	Micro-dilution assay	Exhibited activities against *C. albicans* with MIC value of 0.02 mg/ml	Seleteng-Kose *et al*., 2019
Antioxidant	Acetone	Whole plant	2,2-dipheny-l-picrylhydrazyl (DPPH) free radical scavenging assay	Exhibited activities with IC_{50} value of 0.06 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Aqueous	Whole plant	DPPH free radical scavenging assay	Exhibited activities with IC_{50} value of 0.05 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Dichloromethane	Whole plant	DPPH free radical scavenging assay	Exhibited activities with IC_{50} value of 0.06 mg/ml	Mamabolo *et al*., 2017
Antioxidant	n-hexane	Whole plant	DPPH free radical scavenging assay	Exhibited activities with IC_{50} value of 0.06 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Methanol	Whole plant	DPPH free radical scavenging assay	Exhibited activities with IC_{50} value of 0.05 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Acetone	Whole plant	Hydrogen peroxide scavenging assay	Exhibited activities with IC_{50} value of 0.3 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Aqueous	Whole plant	Hydrogen peroxide scavenging assay	Exhibited activities with IC_{50} value of 0.08 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Dichloromethane	Whole plant	Hydrogen peroxide scavenging assay	Exhibited activities with IC_{50} value of 0.4 mg/ml	Mamabolo *et al*., 2017
Antioxidant	n-hexane	Whole plant	Hydrogen peroxide scavenging assay	Exhibited activities with IC_{50} value of 0.2 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Methanol	Whole plant	Hydrogen peroxide scavenging assay	Exhibited activities with IC_{50} value of 0.2 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Acetone	Whole plant	Reducing power assay	Exhibited activities with IC_{50} value of 0.3 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Aqueous	Whole plant	Reducing power assay	Exhibited activities with IC_{50} value of >0.5 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Dichloromethane	Whole plant	Reducing power assay	Exhibited activities with IC_{50} value of >0.5 mg/ml	Mamabolo *et al*., 2017
Antioxidant	n-hexane	Whole plant	Reducing power assay	Exhibited activities with IC_{50} value of 0.09 mg/ml	Mamabolo *et al*., 2017
Antioxidant	Methanol	Whole plant	Reducing power assay	Exhibited activities with IC_{50} value of 0.4 mg/ml	Mamabolo *et al*., 2017
Cytotoxicity	Dichloromethane	Whole plant	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) calorimetric assay in H411E rat hepatoma (liver) cell lines	Exhibited weak activities with the median lethal concentration (LC_{50}) value of 82.9 µg/ml which was higher than LC_{50} value of 10.8 µg/ml exhibited by the control	Mamabolo *et al*., 2018

values for *C. albicans*, *C. tropicalis*, *A. corymbifera*, *A. fumigatus*, and *S. schenkii* were within the range of 25.0 to >100.0 µg/ml. These results were within the same range as MIC and MFC values exhibited by nystatin, the positive drug which exhibited 2.0 to >100.0 µg/ml (Van der Schyf *et al*., 1986). Mathekga (2001) and Mathekga *et al*. (2000) evaluated the antifungal activities of acetone extracts of aerial parts of *H. caespititium* against *M. canis*, *Aspergillus niger*, *Aspergillus flavus*, *Cladosporium sphaerospermum*, *Cladosporium cladosporioides*, *M. canis*, and *Cladosporium cucumerinum* using agar dilution method. The extract showed properties against all the tested pathogens with the MIC values within the range of 0.01–1.0 mg/ml (Mathekga, 2001;

Mathekga *et al*., 2000). Mathekga *et al*. (2000) also evaluated the antifungal activities of the compound caespitate isolated from *H. caespititium* against *C. sphaerospermum*, *Phytophthora capsici*, *A. niger*, *C. cucumerinum*, *A. flavus*, and *C. cladosporioides* using agar dilution method. The compound was active against all tested pathogens with the MIC values within the range of 0.5–5.0 µg/ml (Mathekga *et al*., 2000). Seleteng-Kose *et al*. (2019) assessed the antifungal properties of water and organic extracts of whole plant parts of *H. caespititium* against *C. albicans* using the micro-dilution assay with amphotericin B (0.1 mg/ml) as the positive drug. The organic extracts showed moderate properties with the MIC values of 0.02 mg/ml, while the MIC value exhibited by aqueous extract was >8.0 mg/ml (Seleteng-Kose *et al*., 2019).

Antioxidant activities

Mamabolo *et al*. (2017) assessed the antioxidant activities of dichloromethane, n-hexane, acetone, methanol, and aqueous extracts of whole plant parts of *H. caespititium* using hydrogen peroxide scavenging, 2,2-diphenyl-1-picrylhydrazyl (DPPH) free radical scavenging and reducing power assays with ascorbic acid and butylated hydroxytoluene (BHT) as positive controls. The extracts exhibited properties with half maximal inhibitory concentration (IC_{50}) values within the range of 0.05–0.6 mg/ml which were within the (IC_{50}) values of 0.04 to >0.5 mg/ml exhibited by the positive drugs (Mamabolo *et al*., 2017).

Cytotoxicity activities

Mathekga (2001) evaluated the cytotoxicity activities of the compound caespitate isolated from *H. caespititium* on vervet monkey kidney cells using the 3-(4,5 dimethylthiazol-2-yl) 2,5-diphenyl tetrazolium bromide (MTT) technique. The maximum non-toxic concentration of the bioactive compound on the vervet kidney monkey cell cultures was 50 mg/ml and at this level the cells did not show any morphological alterations or any signs of growth indicating some cytotoxic effects (Mathekga, 2001). Mamabolo *et al*. (2018) assessed cytotoxicity properties of n-hexane, dichloromethane, methanol, and aqueous extracts of whole plant parts of *H. caespititium* in H411E rat hepatoma (liver) cell lines using the MTT technique with doxorubicin as the positive control. The extracts exhibited weak activities with the median lethal concentration (LC_{50}) values ranging from 82.9–428.8 µg/ml which were much higher than LC_{50} value of 10.8 µg/ml showed by the positive control (Mamabolo *et al*., 2018). These results suggest that the plant extract can safely be used without any worries of being toxic to the cells. Seleteng-Kose *et al*. (2019) assessed cytotoxicity properties of water and organic extracts of whole plant parts of *H. caespititium* using the brine shrimp (*Artemia franciscana*) lethality assay with potassium dichromate as a positive drug. The extracts appear to be non-toxic as aqueous and organic extracts caused 3.3% and 40.7% mortality of *A. franciscana* after 24 hours in comparison to 98% and 100% mortality displayed by the positive control, potassium dichromate (Seleteng-Kose *et al*., 2019). Based on these evaluations done so far, there is a need for more research in order to establish the safety of extracts and isolated (bioactive) compounds from *H. caespititium*.

CONCLUSION

The diverse medicinal uses of *H. caespititium* and the scientific evidence of its biological activities indicate its potential as the herbal medicine. Its diverse pharmacological activities are directly or indirectly involved associated with a wide range of physiological processes which offers protection against growth of undesirable microbes and free radicals. There is a need for evaluation of the clinical significance of the antioxidant properties, cytotoxicity, and toxicity using *in vivo* models. Future research should also focus on assessing the classes of phytochemical compounds associated with the species. The biological potency of such phytochemicals needs to be evaluated aimed at exploring their potential.

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CONFLICT OF INTEREST

The author declares that he has no conflict of interest.

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