A review of the traditional use of southern African medicinal plants for the treatment of fungal skin infections

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ABSTRACT

Ethnopharmacological relevance: Human dermatophyte infections are one of the most common classes of infection globally, with an estimated 1.7 billion people contracting at least one infection annually. Southern African ethnic groups used multiple plants to treat dermatophytosis and to alleviate the symptoms, yet the anti-dermatophyte properties of most species remain poorly explored.

Aim of the study: Our study aimed to critically review the literature to document southern African plant species used to treat one or more dermatophytic infections, and to summarise scientific evaluations of these and other plant species. Our study aims to stimulate and focus future studies in this field.

Materials and methods: A thorough review of the ethnobotanical books, reviews and primary scientific studies were undertaken to identify southern African plants used traditionally to treat dermatophytosis, thereby identifying gaps in the research requiring further study.

Results: Eighty-nine southern African plant species are recorded as traditional therapies for dermatophytosis. Scientific evaluations of 140 plant species were identified, although most of the species in those studies were selected for reasons apart from their traditional uses. None of those studies examined the mechanism of action of the plant species, and only a single study screened the extracts for toxicity.

Conclusions: Despite southern Africa having some of the longest continuous human civilisations globally, as well as unique and diverse flora, and good ethnobotanical records, the anti-dermatophyte properties of southern African medicinal plants remains relatively poorly explored. The efficacy of the majority of plants used traditionally to treat fungal skin disease are yet to be verified and substantial further research is required in this field.

Keywords

Ringworm, tinea pedis, onychomycosis, dermatophytosis, *Candida albicans*, traditional medicine, South African medicinal plants

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Abbreviations: CDC, Centre for Disease Control; MIC, minimum inhibitory concentration; TCM, traditional Chinese medicine; SI, selectivity index; WHO, World Health Organisation

1. Introduction

Superficial fungal skin infections in humans are common globally, although there is a substantially higher incidence in developing countries, rural communities, and amongst socio-

economically disadvantaged groups. Whilst fungal pathogens may affect all people, they are opportunistic and are especially common as secondary infections and in immunocompromised individuals (Köhler et al., 2015). It has been estimated that more than 1.7 billion people globally (~25 % of the world's population) contract at least one fungal skin infection each year (Havlickova et al., 2008). Whilst approximately 40 fungal pathogens can infect human skin, nearly all fungal skin infections in humans are caused by closely related dermatophytes of three genre, namely the *Epidermophyton*, *Microsporum* and *Trichophyton* spp.

Most of the dermatophytes are similar and induce similar symptoms. For this reason, dermatophytic infections in humans are generally classified with regard to the part of the body that they affect, rather than on the basis of the fungal species causing the infection. Whilst dermatophytes may infect almost any exterior body surface, they thrive in warm, moist environments and are most frequent in areas with high perspiration, and in skin folds. Individual dermatophytic infections can be caused by multiple fungal pathogens. For example, tinea capitis (ringworm of the scalp) may be caused by multiple fungal pathogens, although it is primarily caused by several *Microsporum* and *Trichophyton* spp. The severity of each individual dermatophytic infection depends on several factors, including the infecting dermatophyte species, the site of infection, if the affected individual has co-infections, the host's general health and the extent of their immune response.

1.1. Human dermaphytosis

Of the human dermatophytic infections, tinea pedis (athlete's foot) is particularly common. Indeed, it has been estimated that it affects approximately 15% of the world's population at any time (Brown et al., 2012). Tinea pedis infections induce itching and cause scaling, cracking, redness and inflammation of the feet. Any part of the foot may be affected,

although the warm, moist environment between the toes and on the soles of the foot are best suited to fungal growth and are most commonly affected. Tinea pedis may be caused by numerous *Epidermophyton*, *Microsporum* and *Trichophyton* species via contact with the skin of other infected individuals, or via contact with environmental fungal sources (e.g. soil, infected clothing and bedding, household surfaces etc).

Tinea cruris (often referred to as jock itch) is also common and often occurs concurrently with tinea pedis. This infection occurs most frequently in males and may be caused by transfer of dermatophytes from the feet to the groin region whilst dressing. Tinea cruris is most commonly caused by *Trichophyton rubrum*, although it may also be caused by *Trichophyton mentagrophytes* and *Epidermophyton floccosum*.

Notably, *Candida albicans* infections also frequently cause tinea cruris. *C. albicans* is not generally classified as a dermatophytic disease and instead is better known for oral, throat, infant nappy rash and vulvovaginal infections. However, in humid tropical environments, it can also cause fungal skin infections, with identical symptoms to dermatophytosis. Therefore, despite it not generally being regarded as a dermatophyte, we have included *C. albicans* in this study.

Tinea corporis (ringworm of the body) is also common and may affect the arms, legs and trunk/body regions. It manifests as a scaly, red, itchy circular rash. This dermatophytosis is particularly versatile and can be caused by nearly 40 fungal pathogens, with *Epidermophyton*, *Microsporum* and *Trichophyton* species accounting for most infections. When these dermatophytes infect other regions of the body, similar symptoms may occur. Ring-shaped dermatophytic infections caused by the same fungal pathogens may also occur on the hands (tinea manuum), face (tinea faciei), or scalp (tinea capitis). As well as causing superficial skin infections, the same fungal pathogens may also infect the nails.

Onychomycosis (tinea unguium) are fungal infections which may affect either the fingernails or toenails. However, onychomycosis of the toenails are far more frequent, perhaps because the feet provide a warmer, moister environment conducive to fungal growth. Multiple fungal pathogens can cause onychomycosis, although *Epidermophyton*, *Microsporum* and *Trichophyton* and *Fusarium* spp., are the main causative dermatophytes in temperate regions. In contrast, in humid tropical regions, *Candida* spp. (particularly *C. albicans*) are the most common causes of onychomycosis.

Whilst generally not classified as dermatophytosis (and are therefore not the focus of this study), fungal infections of mucosal tissues, especially of the oral and urogenital tracts, are also common. Oral and vulvovaginal candidiasis (commonly known as thrush) are caused by *Candida* spp., particularly, *C. albicans*. Vaginal thrush is particularly prevalent and it has been estimated that approximately 75 % of adult women will suffer from at least one vaginal thrush infection annually (Sobel, 2007).

1.2. Zoonotic dermatophytosis: animals as sources of fungal pathogens

Many of the same fungal pathogens that affect humans also affect other mammals, where wild and domestic animals constitute a major reservoir of dermatophytes. Of the three main genera responsible for human dermatophytosis, *Trichophyton* and *Microsporum* are also widespread in animals. Indeed, a study examined ten domestic and farm animals for the presence of human-infective dermatophytes and reported the presence of at least one dermatophyte species in all of the animal species tested (Nweze, 2011). Domestic dogs and cats were both main reservoirs of dermatophytes, with four and six dermatophyte species isolated from each respectively. Furthermore, 52% of dogs and 47% of cats tested were infected with at least one dermatophyte in that study. Farm animals also provided a substantial reservoir for dermatophytes, with 27%

of cows, 15% of sheep, 17% of goats, 22% of pigs, 11% of horses and 6% of rabbits tested also infected with at least one dermatophyte species. Notably cows, pigs and horses each harboured six different dermatophyte species. Whilst less prevalent in domestic fowl, ducks and chickens tested in that study also harboured at least one dermatophyte species. *Microsporum canis* and *T. mentagrophytes* were generally the most common dermatophyte across species, being present in approximately 37% and 23% of all dermatophyte positive samples respectively (Nweze, 2011) .

While that study tested domestic animals in Nigeria, very little could be found on similar studies screening South African domestic animals for dermatophytes so the prevalence may differ between these regions. Interestingly, there has been a South African study on an animal vector (cat) and the not so common Chromoblastomycosis (an emerging fungal tropical disease transmitted to humans in mostly farming communities) (Zambelli and Griffiths, 2015). These studies demonstrate the importance of domestic animals as dermatophyte reservoirs. Interestingly, whilst those studies did not detect *Epidermophyton* spp. in the animals that they tested, other studies have reported *Epidermophyton* spp. dermatophytes in domestic animals (Efuntoye and Fashanu, 2002). The dermatophytes in domestic animals may cross species and ultimately infect humans. Thus, prevention of human dermatophytosis should also consider animal reservoirs to inhibit reinfection. As this review focuses specifically on the treatment of dermatophytosis in humans we have excluded any studies that exclusively discuss the use of southern African plants to treat these infections in domestic animals and livestock, rather than in humans.

2. Current treatment options for fungal skin infections and antibiotic drug resistance

Several effective therapeutic options are available for the treatment of dermatophytic infections in humans, with the treatment regimen dependent on the region of the body affected and the severity of the infection. Generally, for most superficial skin infections, over the counter antifungal creams, lotions or powders are effective against most fungal strains (Brown et al., 2012). Some of the most common therapies include:

- Clotrimazole may be used as a monotherapy to treat oral, vulvovaginal and skin *Candida* spp. infections. It functions by altering the permeability of the fungal cell membrane by inhibiting fungal ergosterol synthesis (Crowley and Gallagher, 2014) Clotrimazole may also be combined with glucocorticoids (e.g. betamethasone) to produce creams to treat tinea pedis, tinea cruris and tinea corporis. Whilst these treatments are generally effective, they are not preferred treatments for longer-term antifungal therapy due to the side-effects associated with the glucocorticoid component. Furthermore, fungal resistance to clotrimazole is increasingly being reported and the expression of clotrimazole efflux pumps is now relatively common, especially in *Candida* spp. (Crowley and Gallagher, 2014). Further resistance mechanisms, including modification of the lanosterol-14- α -demethylase target have also been reported (Mishra et al., 2007). The development of resistance to clotrimazole by fungal skin pathogens is worrisome due to our previous reliance on this drug due to its safety and efficacy. Effective new therapies are urgently needed.

- Miconazole is also effective for the treatment of tinea pedis, tinea cruris, tinea corporis and vulvovaginal *Candida* spp. infections. It functions via the same mechanism as clotrimazole and causes many of the same side effects and drug interactions. Furthermore, miconazole resistant fungal strains have recently been reported (Krishnasamy et al., 2018).

- Ketokonazole is another azole antifungal drug that functions via similar mechanisms as clotrimazole and miconazole, as well as inducing similar side effects and having similar

resistance patterns (Ghannoum et al., 2016). It is expected that it will also have reduced efficacy against many dermatophytic strains in the future.

- Terbinafine is a different class of drug to the previous three azole drugs. However, it also works by blocking fungal sterol synthesis, thereby decreasing the permeability of the fungal cell membrane. The drug is quite safe when used topically. However, when ingested, numerous side effects and adverse reactions have been reported (George et al., 2015). Furthermore, resistance to terbinafine is now relatively common in *Trichophyton* spp. via alterations in fungal squalene epoxidase (Yamada et al., 2017) and salicylate 1-monooxygenase genes (Santos et al., 2017). Recently, terbinafine resistant *Microsporum canis* (Hsiao et al., 2018) and *C. albicans* strains have also been reported (Hu et al., 2017) and it is expected that the prevalence of terbinafine resistant dermatophytic strains will increase further in the future.

For more severe infections, the oral medications fluconazole, griseofulvin and itraconazole may be used and are generally effective. However, as for the topical therapies, antibiotic failures are increasingly being reported due to the development of fungal resistance mechanisms. Indeed, the overuse of fluconazole has resulted in rapid increases in fluconazole-resistant fungal strains in recent years (Berkhow and Lockhart, 2017). Thus, medical science is faced with a diminishing arsenal of effective treatments to treat human fungal skin diseases and new therapies are urgently needed. However, the development of new dermatophytosis therapies tends to be a relatively neglected field compared to the development of new therapies targeting other infectious diseases. Whilst dermatophytosis induces discomfort, it is limited to superficial skin infections and generally does not cause mortality or morbidity. Furthermore, dermatophytic infections are usually transient and are often self-resolved by the host's immune system (Brown et al., 2012). However, timely treatment of these infections is recommended as there is a risk of re-infection or transfer to other individuals if untreated.

Plant-based and traditional medicines are also used to treat and control fungal skin infections, especially in developing countries. Consultation with traditional healers for fungal skin infections is particularly prevalent among rural patients (Dlova and Ollengo, 2018). Furthermore, allopathic drugs are relatively expensive compared to traditional medicines and are not affordable to some low-income groups in rural areas. Inhabitants in isolated rural regions may also not have regular access to Westernised medical practitioners and conventional medicines may not always be readily available. An examination of the antifungal properties of traditional medicines against dermatophytes may detect new and effective therapies and may highlight future leads for antifungal drug discovery.

3. An overview of fungal skin disease in South Africa

Dermatophytosis is common worldwide and nearly all 40 fungal dermatophytes that cause these infections in humans are present and cause skin infections in southern Africa. However, the causative species and infection severity may vary widely across regions. Several dermatophyte species are common globally (*T. rubrum*, *T. mentagrophytes*, *M. canis* and *E. floccosum*). These species are also prevalent in southern Africa and account for a substantial amount of the fungal skin infections across the region. Indeed, *T. rubrum* is a major cause of tinea cruris and tinea unguium in developed urban regions of South Africa (Ameen, 2010). However, the major causative species for dermatophyte infections are variable in southern Africa, with strong geographic and cultural correlations.

Tinea capitis accounts for the highest number of reported cases of dermatophytosis in southern Africa and is particularly high amongst children (Coulibaly et al., 2018). Unlike other regions of the world, *Microsporum audouinii* and *Trichophyton violaceum* are the most prevalent dermatophytes responsible for tinea capitis in much of southern Africa. Indeed, one study in KwaZulu-Natal province tested individuals with tinea capitis and identified *T.*

violaceum in 90% of cases (Morar et al., 2004). An earlier study in the Cape Peninsula and Western Cape coast regions of South Africa reported similar results, with *T. violaceum* reported in 91% of cases of tinea capitis (Neil et al., 1987). Those studies concluded that *T. violaceum* is the major cause of tinea capitis in South Africa. However, in the neighbouring country of Mozambique, *M. audouinii* has been reported to be responsible for 88% of the cases of tinea capitis (Sidat et al., 2006). It is interesting that the causative dermatophytes of tinea capitis in southern Africa are different to the other regions of the developed world, where *M. canis*, *T. rubrum*, *T. mentagrophytes* and *Trichophyton tonsurans* are the main causative species (Ameen, 2010). Thus, screening southern African plants against those fungal species may not be the most relevant model in a southern African context and studies should also test against the most prevalent southern Africa dermatophyte species.

The classes of dermatophytosis also vary widely in South Africa and often correlated with specific cultural groupings. Interestingly, tinea pedis and tinea unguium (particularly of the toenails) are relatively rare in rural regions of southern Africa, but are common in urban environments (Havlickova et al., 2008). This may be because much of the population in rural areas do not wear shoes and thus do not provide an environment conducive to feet and toenail dermatophytosis. Globally, *T. rubrum*, *T. mentagrophytes* and *E. floccosum* are the main species responsible for tinea pedis and tinea unguium (Ameen, 2010). As tinea pedis dermatophytes may be readily transferred from the feet to the groin region whilst dressing, these are also the main causes of tinea cruris. These dermatophyte species are also major causes of tinea pedis, tinea unguium and tinea cruris in southern Africa. However, *T. violaceum* and *M. audouinii* (to a lesser extent) also cause a large proportion of these infections in southern Africa (Coulibaly et al., 2018; Ameen, 2010). In tropical regions of southern Africa, *C. albicans* also has a greater contribution to these infections. Similar trends have also been reported for tinea corporis (Coulibaly et al., 2018).

Rural areas and lower socio-economic communities often have higher incidences of dermatophytic infections than other regions. Dermatophytes are zoonotic, and may infect domestic animals and livestock, as well as humans. People living in rural areas often have close contact with animals, providing an extra avenue for infection. Similarly, high density living in some urban areas also increases the likelihood of person to person dermatophyte transfer. Rural and the lower socio-economic urban communities also share attributes that increase the spread of dermatophytes:

- Residents of these communities may have limited access to clinical care due to their isolation, and availability of medical personnel.
- Even where medical care is available, individuals may not be able to afford those services. Instead, residents of these communities may rely on traditional healers. Alternatively, given the lower concern regarding dermatophytes compared to other infectious diseases, they may forgo medical treatment and instead allow dermatophyte infections to clear up on their own. Indeed, it has been proposed that the relatively low reported levels of tinea pedis in southern Africa (compared to other regions of the world) may be partly due to individuals with this condition not seeking medical assistance (Ameen, 2010; Coulibaly et al., 2018;).
- Socioeconomically disadvantaged individuals and rural residents may also have less access to education than people in urban areas and therefore have less understanding of preventative methods to limit the spread of dermatophytes.

Notably, the incidences of dermatophytic infections and most notably, the fungi that cause them, are changing in southern Africa. Whilst *T. violaceum* and *M. audouinii* are still the most prevalent dermatophytes in most regions of southern Africa, in recent years there has been a substantial increase in dermatophytes that are more frequently found in infections from Europe and the United States. In particular, substantial increases in the prevalence of *T. rubrum*, *T. mentagrophytes* and *E. floccosum* have been noted in recent years (Zhan and Liu,

2017; Coulibaly et al., 2018; Nweze and Eke, 2018). Increased globalisation and more frequent travel have introduced fungal species to regions that they were previously not prevalent. Furthermore, increasing resistance to clinical antifungal agents have allowed resistance strains to out-compete non-resistant dermatophyte species, thereby changing the epidemiology of dermatophytosis in southern Africa.

4. Materials and methods

The aim of this was to identify southern African plants traditionally used for the treatment of fungal skin diseases in humans. The information presented herein was sourced from several ethnobotanical books (Smith, 1888; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Von Koenen, 2001; Moffett, 2010; Ngwenya et al., 2003; Van Wyk et al., 2009) and variety of ethnobotanical reviews (Thring and Weitz, 2006; Van Wyk, 2008; de Beer and Van Wyk, 2011; Nortje and Van Wyk, 2011; Philander, 2011; De Wet et al., 2013; Afolayan et al., 2014; Hulley and Van Wyk 2017; Asong et al., 2019). Google-Scholar, PubMed, Scopus and Science-Direct electronic databases were also used to identify original scientific research papers. The following terms were used as filters and were searched both alone and as combinations: “South African”, “medicinal plant”, “traditional medicine”, “ethnobotany”, “fungal skin infection” “dermatophyte”, “dermatophytosis”, “ringworm”, “tinea”, “*Epidermophyton*”, “*Microsporum*”, “*Trichophyton*”, “*Candida*”, “antifungal”. Our study was non-biased and was without taxonomic preference. We did not only include plants native to southern Africa, but also included other introduced plant species if they were extensively documented in traditional southern African healing systems. The initial aim was to document the usage of all plant species used therapeutically for fungal skin diseases in southern Africa. A thorough literature search identified eighty-nine plant species as traditional remedies in

southern Africa for fungal skin infections. The majority of these species are native southern African plants. However, several introduced species that have either been naturalised or are widely cultivated were included where they have been incorporated into the pharmacopoea of at least one southern African ethnic group. Subsequently, a further literature review was then undertaken on each of the plant species identified as therapies for fungal skin disease to identify the extent of scientific research previously reported on each of the identified species.

Specific criteria to filter studies for inclusion in review included ethnomedicine, South African medicinal plants and other key words related to dermatophytic infections. We did not prioritise the need for scientific evidence to support the traditional use of plants in our initial ethnobotanical literature search. However, further searches were undertaken on all plants identified as being used to treat fungal skin diseases to determine whether the traditional usage had been validated via rigorous scientific studies. Despite domestic animals forming readily available reservoirs of fungal skin pathogens, ethnobotanical veterinary studies were excluded from this review and only the use of plants to treat human fungal infections have been included. Our study aimed to summarise the published traditional South African ethnopharmacological knowledge and discuss the plant species traditionally used to treat fungal skin infections, with the hopes of highlighting plant species for future testing and to foster future research in this field.

5. South African medicinal plants used traditionally to treat fungal skin disease

An extensive search of ethnobotanical books and reviews, and from primary research studies, was used to identify the plant species used to treat fungal skin diseases presented herein. Traditional medicines are often used to target multiple diseases and infections presenting with similar symptoms. Medicinal plant species are often described as being used for skin complaints, or for skin infections. However, skin complaints may include rashes, sores,

boils, cuts and abrasions, as well as skin infections (Mabona and Van Vuuren, 2013). Even if skin infections are specified, they may be due to pathogen classes other than fungi such as bacterial pathogens, including *Streptococcus pyogenes* (which causes impetigo), *Cutibacterium acnes* (which causes acne) or *Trepanoma palladium* (which causes syphilis and its associated sores). Similarly, several viral pathogens including measles virus cause skin rashes, as do some protozoal pathogens including *Leishmania* spp. (which can cause cutaneous leishmaniasis). Many of these other diseases produce rashes and flaking inflamed skin, similar to some dermatophytic fungal infections which can lead to an ambiguous diagnosis.

Herein we list eighty-nine South African plants which are used in at least one southern African traditional healing system to treat fungal skin infections (Table 1). Given the prevalence of these infections, this number may seem relatively low. However, where ambiguity exists as to the nature of the infection that the southern African plants were used to treat, the plant species were excluded from this record. It is therefore likely that this review has underestimated the number of species used for this purpose. For example, Hutchings (1996) lists multiple plant species including *Crinum bulbispermum* (Burm.f) Milne-Redh. & Schweick, *Crinum moorei* (Hook.f.) Stapf, *Haemanthus coccineus* L., *Stylochiton natalensis* Schott, *Gloriosa superba* L. and numerous other species as being used to treat various skin complaints. However, that text does not specify the type of complaint(s) treated by these species. Due to the constraints we have applied to this study, plant species were only included where their usage to treat fungal skin diseases is specific. It is therefore likely that future studies may identify substantially more plants used for this purpose. Indeed, a number of plant species have been identified in recent botanical studies that have not previously been reported to treat fungal skin disease. For example, a recent report by Hulley and Van Wyk (2017) was the first to thoroughly examine the ethnobotany of the Kannaland region of western Little Karoo. The study identified a number of plant species as being used to treat ringworm. Even though a

number of these species had already been identified for the treatment of ringworm (and other fungal skin diseases), 12 plant species (*Asclepias crispa* P.J.Bergius, *Elytropappus rhinocerotis* (L.f) Less., *Euphorbia mauritanica* L., *Galium tomentosum* Thunb., *Hermannia cuneifolia* Jacq., *Osteospermum calendulaceum* L.f., *Ricinus communis* L., *Rosmarinus officianalis* L., *Salvia microphylla* Kunth., *Salvia runcinata* L.f., *Solanum tomentosum* L., *Urtica urens* L.) were identified as new reports for the treatment of ringworm. It is likely that future ethnobotanical studies will identify substantially more species for this purpose, especially if specific questions to address dermatophytic diseases are targeted. Ethnobotanical studies such as these are valuable for evaluating the therapeutic potential of a medicinal plant preparation. Application of traditional plant preparation that produce notable effects on skin infections are relatively trustworthy indication of efficacy.

Table 1: South African plants used traditionally to treat fungal skin conditions

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Acacia burkei</i> Benth	Fabaceae	Black monkey thorn (English), swartapiesdoring (Afrikaans), umkhaya wehlatalathi, umbabampala (Zulu). Mokgwa, mokoba (Tswana),	Bark	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018; et al.
<i>Acacia karoo</i> Hayne	Fabaceae	Sweet thorn (English), soetdoring (Afrikaans), mooka (Tswana), umuNga (Zulu, Xhosa)	Bark	A decoction is applied topically to treat ringworm infections	Afolayan et al., 2014; Maroyi, 2017; et al.
<i>Aloe ferox</i> Miller	Asphodelaceae	Cape aloe (English), Bitteraalwyn, Winkelaalwyn (Afrikaans), iKhala (Xhosa), iNhlabha (Zulu)	Leaves	Applied topically to treat ringworm	De Wet et al., 2013; Dlova and Ollengo, 2018; et al.
<i>Aloe maculata</i> All.	Asphodelaceae	Soap aloe (English), bontaalwyn (Afrikaans), lekhala (southern Sotho)	Leaves	Applied topically to treat ringworm	Smith, 1888; Watt and Breyer-Brandwijk, 1962; Hutchings, 1996
<i>Aloe microstigma</i> Salm-Dyck subsp. <i>microstigma</i>	Asphodelaceae	Bitteraalwyn, aalwyn, veldaalwyn, kamiesberg (Afrikaans)	Leaves	Applied topically to treat ringworm	Nortje and Van Wyk, 2015
<i>Aloe vera</i> (L.) Burm.f	Asphodelaceae	Burn aloe, True aloe, Indian aloe, Barbados aloe (English)	Leaves	Applied topically to treat ringworm	Asong et al., 2019

<i>Aptosimum procumbens</i> (Lehm.) Steud.	Scrophulariaceae	Veld violet, violet of the karoo, wild violet, karoo carpet flower (English), brandblare, brandbossie, karooviooltjie (Afrikaans)	Not specified	A decoction is applied topically to treat ringworm infections	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996;
<i>Arctotis arctoides</i> (L.F.) O.Hoffm.	Asteraceae	Botterblom (Afrikaans), ubushwa (Xhosa)	Leaves, juice	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018; et al.
<i>Asclepias crispera</i> P.J.Bergius	Apocynaceae	Bitterwortel, witvergeet, kattedoring (Afrikaans)	Leaves	An infusion is applied topically to treat ringworm infections	Hulley and Van Wyk, 2017
<i>Blumea lacera</i> (Burm.f.) DC.	Asteraceae	Unknown	Unspecified	Useful in the treatment of tinea. Preparation and application are not specified	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996;
<i>Bulbine asphodeloides</i> R. & S.	Asphodelaceae	Snake flower, copaiva (English), balsamkopieva, geelkatstert (Afrikaans), ibhucu, inthethe elimpofu (Zulu), intelezi, itswelemyoka (Xhosa), pekane, moetsa-mollo Sotho)	Leaves	The leaf juice is applied directly to ringworm infections	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996
<i>Bulbine frutescens</i> (L.) Willd	Asphodelaceae	Burn jelly plant, cat's tail, snake flower (English), balsem kopieva, geelkatstert (Afrikaans)	Leaves	Applied topically to treat ringworm	Mabona and Van Vuuren, 2013

<i>Bulbine narcissifolia</i> Salm Dyck.	Asphodelaceae	Strap-leaved bulbine, snake flower (English), lintblaar bulbine, geelslangkop, wildekopieva (Afrikaans), khomo-ea-balisa, serelelile (Sotho)	Leaves	The leaf juice is applied directly to ringworm infections	Watt and Breyer- Brandwijk, 1962
<i>Buxus natalensis</i> (Oliv.) Hitch.	Buxaceae	Large leaved box, Natal box, box wattle (English), grootblaarbuksboom, Natalebuksboom (Afrikaans), umgalagala, isixesa, umngquzu, isixhaza (Xhosa), igudlangulubi, umgalagala, umhlulambazo (Zulu)	Leaves, juice	A decoction is applied topically to treat ringworm infections	Afolayan et al., 2014
<i>Canthium inerme</i> (L.f.) Kuntze	Rubiaceae	Turkey berry, Cape date (English). Gewone bokdrol, doringels (Afrikaans), umvuthwamini (Xhosa, Zulu), isipintigo (Xhosa), isotobe (Zulu), muvhivvela-shadani (Venda)	Leaves	A decoction is applied topically to treat ringworm infections	Afolayan et al., 2014
<i>Carpobrotus edulis</i> (L.) L. Bolus	Aizoaceae	Sour fig, Cape fig, Hottentot's fig (English), vyerank, ghaukum,ghoenavy, hotnotsvye, Kaapvy, perdevy, rankvy (Afrikaans), ikhambi- lamabulawo, umgongozi (Zulu)	Leaves	Juice from squeezed leaves is applied topically to treat ringworm	Watt and Breyer- Brandwijk, 1962; Hutchings, 1996; Thring and Weitz, 2006

<i>Carpobrotus acinaciformis</i> (L.) L. Bolus	Aizoaceae	Hottentot fig	Leaves	Juice from squeezed leaves is applied topically to treat ringworm	Thring and Weitz, 2006
<i>Carpobrotus murii</i> (L.) L. Bolus	Aizoaceae	Dwarf sour fig (English), Dwerg Suurvy (Afrikaans)	Leaves	Juice from squeezed leaves is applied topically to treat ringworm.	Thring and Weitz, 2006
<i>Cassytha ciliolate</i> Nees	Lauriaceae	False Dodder, devils tresses (English), bobbejaantou, nooienshar (Afrikaans)	Leaves	A decoction is applied topically to treat ringworm infections	Nortje and Van Wyk, 2015
<i>Citrus limon</i> L.	Rutaceae	Lemon (English)	Fruit peel, juice	Diluted fruit juice is applied directly to ringworm infections. A fruit peel decoction was applied topically to treat skin <i>Candida</i> infections	Watt and Breyer-Brandwijk, 1962; Otang and Afolayan, 2016
<i>Conyza bonariensis</i> (L.) Cronquist	Asteraceae	Horseweed, asthmaweed, Candian fleabane, coltstail, maretail, butterweed (English)	Unspecified	Used to treat ringworm. Preparation and usage not specified.	Moffett, 2010
<i>Cordia myxa</i> L.	Boraginaceae	Assyrian plum	Bark	Powdered bark is applied directly to ringworm infections.	Watt and Breyer-Brandwijk, 1962

<i>Cirsium vulgare</i> Airy-Shaw	Asteraceae	Scottish thistle, spear thistle (English), skotse dissel (Afrikaans), hlaba (Sotho)	Unspecified	A brandy tincture is applied directly to ringworm infections.	Watt and Breyer- Brandwijk, 1962
<i>Cissampelos</i> <i>capensis</i> L.f.	Menispermaceae	Dawidjies, fynblaarklimop (Afrikaans)	Leaves	The leaf juice is applied directly to ringworm infections	De Wet and Van Wyk, 2008
<i>Dichapetalum</i> <i>cymosum</i> (Hook.) Engl. & Prantl.	Dichapetalaceae	Poison leaf (English), gifblaar (Afrikaans)	Leaves	A leaf decoction is applied directly to ringworm infections	Von Koenen, 2001
<i>Dicoma anomala</i> Sond.	Asteraceae	Fever bush, stomach bush (English), maagbitterwortel, kalwerbossie, koorsbossie, gryshout, maagbossie (Afrikaans), inyongana (Xhosa), isihlabamakhondlwane, umuna (Zulu)	Charred roots, stems, leaves	A paste is prepared and applied topically to ringworm infections	Watt and Breyer- Brandwijk, 1962; Hutchings, 1996; Mabona and Van Vuuren, 2013
<i>Diospyros austro-</i> <i>africana</i> De Winter	Ebenaceae	Fire sticks, star-apple (English), kritikom, jakkalsbos, vuurmaakbossie (Afrikaans), umbhongisa (Xhosa)	Leaves	An infusion is applied topically to treat ringworm infections	Van Wyk et al., 2008

<i>Diospyros mespiliformis</i> Hochst. Ex A.D.C.	Ebenaceae	African ebony, jackal berry (English), jakkalbessie (Afrikaans), mgula (Tsonga)	Roots, leaves	A decoction is applied topically to treat ringworm infections	Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001; Mabona and Van Vuuren, 2013
<i>Dodonaea viscosa</i> Jacq var. <i>agustifolia</i> L.f. benth	Sapindaceae	Sand olive (English), sandolien, ysterbos (Afrikaans), mutata-vhana (Venda)	Leaves, twigs	A decoction is applied topically to treat ringworm infections	Mabona and Van Vuuren, 2013
<i>Drimea sanguinea</i> (Schinz) Jessop	Asparagaceae	rooislangkop (Afrikaans), sekaname (Tswana)	Bulb	A decoction is applied topically to treat skin <i>Candida</i> infections	Asong et al., 2019
<i>Elytropappus rhinocerotis</i> (L.f) Less.	Asteraceae	Rhinoceros bush (English)	Unspecified	Preparation and application methods are not specified.	Hulley and VanWyk, 2017
<i>Erigeron canadense</i> L.	Asteraceae	Horseweed, coltstail, marestail, butterweed (English)	Leaf	Ringworm infected areas are washed with a leaf decoction.	Watt and Breyer-Brandwijk, 1962
<i>Eriocephalus punctalatis</i> DC	Asteraceae	Wild rosemary, Cape snowbush (English), kapokbos (Afrikaans)	Leaf	A leaf decoction is applied directly to treat ringworm on the scalp.	Nortje and Van Wyk, 2015

<i>Eucalyptus gummifera</i> Hochr.	Myrtaceae	Red bloodwood (English)	Sap/gum	A decoction of the gum is applied directly to ringworm infections.	Watt and Breyer-Brandwijk, 1962
<i>Euphorbia mauritanica</i> L.	Euphorbiaceae	Yellow milk bush, golden spurge (English), geelmelkbos, beesmelkbos, gifmelkbos, kleinmelkbos (Afrikaans)	Stem latex	Milky latex is applied directly to ringworm infections.	Hulley and VanWyk, 2017
<i>Euphorbia prostrata</i> Aiton	Asparagaceae	Prostrate spurge, prostrate sandmat (English), letsletwane (Tswana)	Roots	A decoction is applied topically to treat skin Candida infections	Asong et al., 2019
<i>Euphorbia serpens</i> Kunth	Asparagaceae	Matted sandmat (English), lwetsane (Tswana)	Roots, leaves	Decocotions used to treat tinea pedis and ringworm.	Asong et al., 2019
<i>Ficus exasperata</i> Vahl.	Moraceae	White fig, sandpaper tree (English)	Leaf	Fresh leaves are applied as plasters to ringworm infections.	Watt and Breyer-Brandwijk, 1962
<i>Galenia africana</i> L.	Aizoaceae	Yellow bush (English), brakkraalbossie, geelbos, kraalbos, muisbos, muisgeelbossie, perdebos (Afrikaans), iqina (Xhosa)	Leaves and twigs	An infusion is applied topically to treat ringworm.	Nortje and Van Wyk, 2015; Hulley and Van Wyk, 2017 Van
<i>Galium tomentosum</i> Thunb.	Rubiaceae	Old man's beard (English), kleefgras, rooivergeet (Afrikaans)	Roots	Root infusions are applied topically to ringworm infections.	Hulley and Van Wyk, 2017

<i>Gasteria croucheri</i> (Hook.f.) Baker	Asphodelaceae	Forest gasteria forest ox-tongue, Natal gasteria (English), bosaalwee, oukossies (Afrikaans), impundu, iqhomololo (Zulu)	Whole plant	Decocotions used to treat ringworm infections.	Philander, 2011
<i>Hawthoria fasciata</i> (Willd.) Haw.	Asphodelaceae	Zebra plant (English)	Whole plant	Decocotions used to treat ringworm infections.	Philander, 2011
<i>Helichrysum paronychioides</i> DC Humbert	Asteraceae	Phate-ya-ngaka (Tswana)	Whole plant	Decocotions used to treat ringworm and Candida skin infections.	Asong et al., 2019
<i>Hermannia cuneifolia</i> Jacq.	Malvaceae	Agtdaegeneesbos, broodbos, geneesbossie, pleisterbos (Afrikaans)	Unspecified	Used as an ointment to treat ringworm.	Hulley and Van Wyk, 2017
<i>Heteromorpha arborescens</i> Cham. & Schlect.	Apiaceae	Parsley tree (English), wildepietersielie (Afrikaans)	Leaves	Leaf decoctions are applied directly to ringworm infections.	Watt and Breyer- Brandwijk, 1962
<i>Hypoxis argentea</i> Harv.ex Baker	Malvaceae	Small silver star-flower (English), inongwe (Xhosa and Zulu), isinana (Zulu), ixalanxa (Xhosa)	Corms	A decoction is applied topically to treat ringworm infections	Afolayan et al., 2014

<i>Hypoxis hemerocallidea</i> Fisch. C.A. Mey & Ave	Malvaceae	Yellow star, star lily, star flower (English), sterblom, geelsterretjie, gifbol (Afrikaans), moli kharatsa, lotsane (southern Sotho); inkomfe, inkomfe enkulu (Zulu), inongwe, ilabatheka, ixhalanxa, ikhubalo lezithunzela (Xhosa), tshuka (Tswana)	Corms	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018 et al.
<i>Jatropha zeyheri</i> Sond.	Euphorbiaceae	Verfbol (Afrikaans), sefapabadia (Sotho), ugodide (Zulu)	Unspecified	A decoction is applied topically to treat ringworm infections	Watt and Breyer-Brandwijk, 1962
<i>Kigellia africana</i> (Lam.) Benth.	Bignoniaceae	Sausage tree (English), worsboom (Afrikaans), umVunguta, umFongothi (Zulu), muvevha (Venda)	Bark, fruit	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018; et al.
<i>Lantana angolensis</i> Moldenke	Verbenaceae	Selaole (Tswana)	Roots	A decoction is applied topically to treat ringworm infections	Asong et al., 2019
<i>Lobostemon fruticosus</i> (Linné)Buek	Boraginaceae	Agdaegeneesbos, douwurmbos (Afrikaans)	Leaves	Leaves were ground into a paste and applied directly to ringworm infections.	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996; VanVan Wyk et al.,

2009; Hulley
and Van Wyk,
2017

<i>Maceia lanceolata</i> Forssk.	Primulaceae	False assegai (English), isidenda, umaguqu (Zulu)	Fruit	Fruit are ground into milk and consumed to treat ringworm.	Ngwenya et al., 2003
<i>Maerua edulis</i> (Gilg. & Gilg-Ben.) DeWolf	Capparaceae	Blue bush cherry (English)	Roots	A decoction is applied topically to treat unspecified fungal skin infections	Samie et al., 2010
<i>Melianthus comosus</i> Vahl.	Francoaceae	Honey flower (Eng); kruidjie- roer-my-nie (Afr.)	Leaves	An infusion is applied topically to treat ringworm.	Thring and Weitz, 2006; Van Wyk et al., 2009; Mabona, 2013; Vanet al.
<i>Melianthus major</i> L.	Francoaceae	Giant honey flower, kruidjie- roer-my-nie (Afrikaans)	Leaves	An infusion is applied topically to treat ringworm. Also useful for the treatment of tinea	Watt and Breyer- Brandwijk, 1962
<i>Myrsine africana</i> L.	Primulaceae	Cape myrtle, African boxwood (English), vlieebos, mirting (Afrikaans), moroko-pheleu, samapo, thakisa (Sotho)	Fruit	Preparation and application methods are not specified.	Watt and Breyer- Brandwijk, 1962

<i>Nicotiana tabacum</i> L.	Solonaceae	Tobacco (English)	Leaves	A decoction is applied topically to treat ringworm.	Watt and Breyer-Brandwijk, 1962
<i>Oesteospermum calendulaceum</i> L.f.	Asteraceae	Geneesbos, bietou (Afrikaans)	Not specified	Infusions are applied topically to treat ringworm.	Hulley and Van Wyk, 2017
<i>Pappea capensis</i> E. & Z. var. <i>radlkoferi</i> Schinz.	Sapindaceae	Jacket plum, indaba tree, bushveld cherry (English), doppruim (Afrikaans), umqhokwane, umvuna, indaba (Zulu), ilitye, umgqalutye (Xhosa)	Seed kernal oil	Applied topically to treat ringworm. Also useful in the treatment of tinea capitis	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996; Von Koenen, 2001;
<i>Phyllanthus maderaspatensis</i> L.	Phyllanthaceae	Leestane (Tswana)	Leaves	A decoction is applied topically to treat ringworm infections and exzema.	Asong et al., 2019
<i>Pterocarpus angolensis</i> DC.	Fabaceae	kiaat, bloodwood, paddle-wood, sealing-wax tree, wild teak, Transvaal teak (English), bloedhout, dolfhout, greinhout, kajatenhout, wilde-kiaat (Afrikaans), moroto (Northern Sotho), umvangazi, umbilo (Zulu)	Sap	The red sap from under the bark is applied directly to ringworm infections.	Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001;

<i>Rawsonia lucida</i> Harv. & Sond.	Archariaceae	Forest peach(English),bosperske (Afrikaans), iTambo (Zulu), umLongo (Xhosa)	Leaves	A decoction is applied topically to treat ringworm infections	Amoo et al., 2014Dlova and Ollengo, 2018; et al.
<i>Ricinus communis</i> L.	Euphorbiaceae	Castor bean, castor oil plant (English)	Leaves	Fresh leaves are used as a compress to treat ringworm infections on the head.	Hulley and Van Wyk, 2017
<i>Rosmarinus officianalis</i> L.	Lamiaceae	Rosemary (English), makroosmaryn (Afrikaans)	Leaves	Used as an ointment to treat ringworm.	Hulley and Van Wyk, 2017
<i>Rumex crispus</i> L.	Polygonaceae	Yellow dock (English)	Used to treat ringworm. Preparation and application methods are not specified.	Preparation and application methods are not specified.	Watt and Breyer- Brandwijk, 1962
<i>Salvia microphylla</i> Kunth.	Lamiaceae	Rooiblomsalie, rooisalie (Afrikaans)	Not specified	Used to treat ringworm. Preparation and application methods are not specified.	Hulley and Van Wyk, 2017
<i>Salvia runcinata</i> L.f.	Lamiaceae	Sage (English), hardie salie (Afrikaans)	Not specified	A compress is applied to treat ringworm on the head.	Hulley and Van Wyk, 2017

<i>Samolus valerandi</i> L.	Primulaceae	Brookweed, seaside brookweed, water cabbage, water rose (English)	Not specified	Used to treat ringworm. Preparation and application methods are not specified.	Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001
<i>Scilla nervosa</i> (Burch) Jessop	Asparagaceae	Isiphingo (Xhosa)	Leaves	A paste is prepared and applied topically to ringworm infections.	Afolayan et al., 2014
<i>Senecio longifolia</i> (DC) Sch.Bip	Asteraceae	Mosiama (Tswana)	Whole plant	A decoction is applied topically to treat tinea pedis	Asong et al., 2019
<i>Senecio scapiflorus</i> (L'Hér.) C.A.Sm.	Asteraceae	Unknown	Leaves	An infusion is applied topically to treat ringworm.	Nortje and Van Wyk, 2015
<i>Senna alata</i> (L.) Roxb.	Fabaceae	Candle bush, emperor's candlesticks, candelabra bush, ringworm shrub (English)	Bark, leaves and flowers	Ringworm infected areas are bathed in a decoction prepared from bark, leaves and flowers.	Watt and Breyer-Brandwijk, 1962
<i>Solanum acanthoideum</i> Drège ex Dun.	Solanaceae	Unknown	Fruit	Juice from the fruit is applied directly to ringworm infections.	Watt and Breyer-Brandwijk, 1962

<i>Solanum aculeastrum</i> Dun.	Solonaceae	Goat bitter apple, bitter apple, goat apple, poison apple (English), bok-bitterappel, bitterappel, gifappel (Afrikaans), murulwa (Venda), umthuma, itunga (Xhosa), mtuma (Zulu)	Fruit	Juice from the fruit is applied directly to ringworm infections	Watt and Breyer-Brandwijk, 1962
<i>Solanum capense</i> L.	Solonaceae	Nightshade (English)	Berries	Berries are squashed and applied directly to ringworm infections	Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001; Mabona and Van Vuuren, 2013; Von
<i>Solanum incanum</i> L.	Solonaceae	Bark weed, bitter apple, thorn apple (English)	Roots and leaves	A decoction is applied topically to treat ringworm infections	Watt and Breyer-Brandwijk, 1962; Van; Von Koenen, 2001; Mabona and Van Vuuren, 2013
<i>Solanum indicum</i> L.	Solonaceae	Indian nightshade (English)	Roots	Preparation and application methods are not specified.	Watt and Breyer-Brandwijk, 1962

<i>Solanum lichensteinii</i> Willd.	Solonaceae	Kgaba (Tswana)	Roots	A decoction is applied topically to treat ringworm infections	Asong et al., 2019
<i>Solanum linnaeanum</i> Hepper & P.-M.L.Jaeger	Solonaceae	Devil's apple, apple of Sodom (English)	Fruit	Preparation and application methods are not specified.	Watt and Breyer-Brandwijk, 1962
<i>Solanum nigrum</i> L.	Solonaceae	Black nightshade (English)	Whole plant	A decoction is applied topically to treat ringworm infections	Watt and Breyer-Brandwijk, 1962;; Von Koenen, 2001; Mabona and Van Vuuren, 2013VanVon
<i>Solanum panduraeforme</i> Drège ex Dun.	Solonaceae	Bitter apple, apple of Sodom (English), bitterappel, geelappel (Afrikaans), intuma-omncane, intumemncane (Zulu), moralane (Northern Sotho)	Fruit	Preparation and application methods are not specified.	Watt and Breyer-Brandwijk, 1962; Hutchings, 1996
<i>Solanum tomentosum</i> L.	Solonaceae	Slangappel, slangappelbos (Afrikaans)	Not specified	Applied topically for the treatment of ringworm.	Hulley and Van Wyk, 2017

<i>Strychnos madagascariensis</i> Poir	Strychnaceae	Black monkey orange (English), swartklapper, botterklapper (Afrikaans), nkwaka (Tsonga), mukwakwa(Venda), umGluguza, umKwakwa (Zulu)	Bark and leaves	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018 et al.
<i>Salvia disermas</i> L.	Lamiaceae	Wild giant sage, Transvaal sage (English), grootsalie, teesalie (Afrikaans), mogasane (Tswana)	Leaf	A decoction is applied topically to treat ringworm infections	De Beer and Van Wyk, 2011
<i>Tabernaemontana elgans</i> Stapf.	Apocynaceae	Toad tree (English), laeveldse paddaboom (Afrikaans), umKhahlwana, umKhadu (Zulu)	Fruit and laeves	A decoction is applied topically to treat ringworm infections	De Wet et al., 2013; Dlova and Ollengo, 2018et al.
<i>Urtica urens</i> L.	Urticaceae	Annual nettle, burning nettle, sting nettle bush, dwarf stinging nettle (English), brandnekel (Afrikaans)	Bark	Bark infusions are applied topically to treat ringworm.	Hulley and Van Wyk, 2017
<i>Withania somnifera</i> (L.) Dunal	Solonaceae	Indian ginseng, poison gooseberry, winter cherry (English), bitterappelliefie, koorshout (Afrikaans), ubuvuma (Xhosa), ubuvimbha (Zulu)	Berries	The green berries are crushed and applied topically to treat ringworm.	Smith, 1888; Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001;

<i>Ximenia caffra</i> Sond.	Olacaceae	Large sourplum (English), groot suurpruim (Afrikaans), unThunduluka-obmvu (Zulu)	Bark and root	Pulversised bark and roots are applied directly to ringworm infections.	Watt and Breyer- Brandwijk, 1962; Hutchings, 1996
<i>Ximenia americana</i> L.	Olacaceae	Tallow wood, yellow plum, sea lemon (English)	Bark and root	Pulversised bark and roots are applied directly to ringworm infections.	Watt and Breyer- Brandwijk, 1962; Von Koenen, 2001;

The plant species (Table 1) come from a wide range of families including Asioaceae, Asparagaceae, Asphodelaceae, Asteraceae, Euphorbiaceae, Fabaceae, Lamiaceae, Malvaceae, Primulaceae and Solonaceae (Figure 1). Some of these species have already had their anti-dermatophytic activity validated through *in vitro* testing (Table 2). In contrast, others species have only had their medicinal uses documented in various ethnobotanical studies and studies are required to validate their traditional use to treat fungal skin infections (de Beer and Van Wyk, 2011; Van Wyk, 2011; Hulley and Van Wyk, 2017). The Asteraceae, Solonaceae and Asphodelaceae families were particularly well represented for the treatment of fungal skin infections, with 12, 11 and 9 species identified from each of these families respectively (Figure 1). Whilst the high representation of plants of these families may indicate that they have better efficacies against fungal skin pathogens, it may also be because of the greater amount of attention that they have received in the ethnopharmacological and laboratory based research in comparison to many of the other plant families (Jaiswal, 2012; Achika et al., 2014; Bessada et al., 2015; Cock, 2015;). Furthermore, these are large families, with species widely spread globally. Asteraceae is a particularly large family with nearly 33,000 species and a wide global distribution (Bremer *et al.*, 1992). Four members of both Fabaceae and Asparagaceae were also identified, as well as three members each of Asioaceae, Euphorbaceae, Lamiaceae, Malvaceae and Primulaceae.

The most frequently used plant part to treat fungal skin infections in traditional southern African healing systems was the leaves (Figure 2). Interestingly, many other studies have also reported leaves as being the most frequently used plant part to treat a variety of pathogenic conditions (Afolayan et al., 2014; Asong et al., 2019; Cock et al., 2018; Cock et al., 2019; de Beer and Van Wyk, 2011; Hulley and Van Wyk, 2017; Nortje and Van Wyk, 2011; Philander, 2011). The roots/bulbs/corms, bark, fruit/berries/juice and the whole plant are also commonly

used to treat dermatophytosis. However, bark should only be used sparingly as its removal by wild harvest practices can damage and possibly even kill the plant if careless or incorrect harvesting practices are employed. Decoctions and infusions were most frequently used traditionally for the treatment of fungal skin diseases (for 51 plant species). The plant material was applied directly to the affected area for 18 species, whereas juice/sap/latex was applied for 11 species. The preparation and usage was not specified for the remaining plant species. It is also noteworthy from Table 1 that many of the plant species used to treat fungal skin infections are herbaceous. These species generally grow rapidly and therefore the usage of these species are likely to be more sustainable than the use of bark or roots harvested from trees. As many medicinal plants are endangered, the use of species and the harvesting of plant parts that does not cause extensive damage the plant is preferred. For some of the plants species mentioned, the specific plant part was not specified and further comparative research is required to investigate whether the efficacy between different plant parts varies.

Figure 1: The number of plant species per families related to medicinal plants for the treatment of fungal infections.

Figure 2: Plant parts and frequency mentioned to dermatological infections.

6. Scientific studies into the growth inhibitory activity of fungal skin pathogens by South African plants

Previous studies have screened southern African plants for the ability to inhibit the growth of fungal skin infections (Table 2). Overwhelmingly, these investigations have screened using *in vitro* methods and very few studies have examined the efficacy *in vivo*.

6.1. Antifungal activity of plant monotherapies

Of the 89 plant species that have been identified as being used to treat fungal skin infections, 19 of these (*Acacia burkei*, *Aloe ferox*, *Bulbine frutescens*, *Canthium inerme*, *Carpobrotus edulis*, *Citrus limon*, *Cissampelos capensis*, *Dicoma anomala*, *Diospyros mespiliformis*, *Hypoxis hemerocallidea*, *Kigellia africana*, *Melianthus comosus*, *Melianthus major*, *Solanum incanum*, *Solanum panduraeforme*, *Strychnos madagascariensis*, *Tabernaemontana elegans*, *Withania somnifera*, *Ximenia caffra*) were tested against dermatophytes. Nearly all of these plants strongly inhibited the growth of several dermatophytes, with several species displaying potent activity. The exception was *C. edulis*, for which only low activity was noted. *T. mentagrophytes* was the most susceptible dermatophyte to the plant extracts. Indeed, *D. anomala* (MIC 30 µg/mL), *D. mespiliformis* (MIC 100 µg/mL), *K. africana* (MIC 60 µg/mL), *M. comosus* (MIC 50 µg/mL) and *M. major* (MIC 50 µg/mL) were particularly good inhibitors of that dermatophyte. Also worth mentioning were *A. burkei*, *A. ferox*, *C. inerme*, *H. harmerocallidea*, *S. panduriforme*, *S. madagascariensis*, *T. elegans*, *W. somnifera* and *X. caffra* which were also strong inhibitors of *T. mentagrophytes* growth, each with MIC values ≤500 µg/mL. Both, *M. comosus* (MIC 50 µg/mL) and *M. major* (MIC 50 µg/mL) were also strong inhibitors of *M. canis*. Several other of the traditionally used plant extracts were also good inhibitors of *M. canis*, albeit with MIC values substantially higher than those recorded against *T. mentagrophytes*. In contrast, *C. albicans* was more resistant to these plant extracts, with MIC values >1000 µg/mL. One exception was *C. limon*, with an MIC value of 10 µg/mL reported against *C. albicans*. Studies are still required to test the other seventy species traditionally used to treat fungal skin infections.

Table 2: Scientific evaluations of the inhibitory activity of South African plants against fungal skin pathogens.

Plant Species	Common Name	Family	Plant Part Used	Formulation	Results	Reference
<i>Acacia burkei</i> Benth	Black monkey thorn (English), swartapiesdoring (Afrikaans), umkhaya wehlatalathi, umbabampala (Zulu). Mokgwa, mokoba (Tswana)	Fabaceae	Bark	Aqueous and methanolic extracts were tested.	MICs of 250, 130, 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Acacia erioloba</i> E.mey.	Camel thorn, giraffe thorn (English), kameeldoring (Afrikaans)	Fabaceae	Bark and leaves	Extracted with multiple solvents of varying polarity	MICs of 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i>	Mabona et al., 2013
<i>Acokanthera oppositifolia</i> (Lam.) Codd.	Bushman's poison (English), boesmansgif (Afrikaans), inHlungunyembe (Zulu), inlungunyembe (Xhosa)	Apocynaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 2000 µgmL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i>	Mabona et al., 2013
<i>Albizia adianthifolia</i> (Schumac.) W. Wight	Flat crown albizia, rough barkflat-crown (English), platkroon (Afrikaans), umgadankawu, iGowane, uSolu (Zulu), umHlandlothi (Xhosa)	Faceaceae	Bark	Aqueous and methanolic extracts were tested	MICs of 60, 130, 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively.	Nciki et al., 2016

<i>Albizia vesicolor</i> Welw. ex Oliv	Poison-podalbizia, large-leaved false-thorn (English), grootblaarvals-doring (Afrikaans), umvangazi, umphizo, umbhangazi (Zulu)	Faceaceae	Bark	Aqueous and methanolic extracts were tested	MICs of 250, 2000, 750 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Allium sativum</i> L.	Garlic (English)	Amaryllidaceae	Bulb	Extracted with multiple solvents of varying polarity	MICs as low as 560 µg/mL against <i>C. albicans</i>	Motsei et al., 2003
<i>Aloe arborescens</i> Mill.	Krantz aloe (English), kransaalwyn (Afrikaans), ikalene (Xhosa), inkalane, umhlabana (Zulu)	Asphodelaceae	Leaf	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. Mabona et al., 2013 report an MIC of 250 µg/mL against <i>T. mentagrophytes</i> , but ineffective against <i>M. canis</i> and <i>C. albicans</i> . In contrast, Ghuman et al. 2016 report stronger activity against most fungi (MICs of 630 µg/mL against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i>).	Mabona et al., 2013; Ghuman et al., 2016.
<i>Aloe excelsa</i> Berger	Zimbabwe aloe (English)	Asphodelaceae	Leaf	Aqueous and ethanolic extracts	MICs of 200 µg/mL against	Naidoo and Coopooosamy, 2011

					<i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> .	
<i>Aloe ferox</i> Miller	Cape aloe (English), Bitteraalwyn, Winkelaalwyn (Afrikaans), iKhala (Xhosa), iNhlaba (Zulu)	Asphodelaceae	Leaf	Aqueous and ethanolic extracts	MICs of 310-630 µg/mL against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> .	Ghuman et al., 2016
<i>Aloidendron barbarae</i> (Dyer) Klopper & Gideon F.Sm.	Tree aloe (English)	Asphodelaceae	Leaf and root	Sequential extraction in solvents of different polarity	MICs as low as 800 µg/mL against <i>C. albicans</i>	Ndhlala et al., 2009
<i>Annona senegalensis</i> Oers.	African custard apple, wild custard apple, wild soup (English), wildesuikerappel (Afrikaans), muembe (Venda), umhlalajuba, umphofu (Zulu)	Annonaceae	Roots	Aqueous and methanolic extracts were tested.	MICs of 130, 60, 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Athrixia phylicoides</i> DC	Bushman's tea (English), ishayelo, iphephetha (Zulu), icholocholo (Xhosa), sephomolo (Sotho)	Asteraceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Aristea ecklonni</i> Baker	Blue stars (English), blousterre (Afrikaans), umhushuza (Zulu)	Iridaceae	Root and leaves	Extracted with multiple solvents of varying polarity	MICs of 50, 30 and 50 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and	Mabona et al., 2013

<i>Bauhinia macranthera</i> Benth. ex Hemsl.	Chihuahuan orchid tree (English)	Fabaceae	Leaf	Extracted with multiple solvents of varying polarity	<i>C. albicans</i> respectively MICs of 1000, 2000 and 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Bidens pilosa</i> L.	Black jack, beggars' ticks, cobblers pegs, sticky beaks (English)	Asteraceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Boophane distichya</i> L.f.	Bushman's poison bulb (English), gifbol (Afrikaans), leshoma (Sotho, Tswana), incwadi (Xhosa), incotha (Zulu)	Amaryllidaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 2000 and 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Brachylaena discolor</i> DC.	Coastal silver oak (English), kusvaalbos (Afrikaans), phahla (Zulu), umphahla (Xhosa)	Asteraceae	Roots	Aqueous and methanolic extracts were tested.	MICs of 250, 2000, 750 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Brachylaena hullensis</i> O.Hoffm.	Silver oak (English)	Asteraceae	Leaves	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003

<i>Bridelia micrantha</i> (Hochst.) Baill.	Mitseeri, bruin stinkhout (Afrikaans), motsere (Sotho), ndzerhe (Tswana)	Phyllanthaceae	Leaves	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Bulbine frutescens</i> (L.) Willd	Burn jelly plant, cat's tail, snake flower (English), balsem kopieva, geelkatstert (Afrikaans)	Asphodelaceae	Leaves	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. Inactive (MIC >10 000 µg/mL for all extracts) reported by Motsei et al. 2003. MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 630-1250 µg/mL reported by Ghuman et al., 2016.	Motsei et al., 2003; Ghuman et al., 2016.
<i>Bulbine natalensis</i> Baker	Rooiwortel (Afrikaans), ibhucu (Zulu)	Asphodelaceae	Leaves	Extracted with multiple solvents of varying polarity	MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 630-2500 µg/mL	Ghuman et al., 2016

<i>Canthium inerme</i> (L.f.) Kuntze	Turkey berry, Cape date (English), gewone bokdrol, doringels (Afrikaans), umvuthwamini (Xhosa, Zulu), umnyushulube (Xhosa), isitobe (Zulu)muhibvela-shadani (Venda)	Rubiaceae	Twigs	Aqueous and methanolic extracts were tested.	MICs of 250, 2000, 750 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Carpobrotus edulis</i> (L.) L. Bolus	Sour fig, Cape fig, Hottentot's fig (English), vyerank, ghaukum,ghoenavy, hotnotsveye, Kaapvy, perdevy, rankvy (Afrikaans), ikhambi- lamabulawo, umgongozi (Zulu)	Aizoaceae	Leaves	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Chenopodium ambrosioides</i> Bert. ex Steud.	Wormseed, Jesuit's tea (English)	Amaranthaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 250, 2000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Cissampeios capensis</i> Thumb.	Dawidjies, dawidjiewortel (Afrikaans)	Menispermaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 500, 1000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Citrus limon</i> L.	Lemon (English)	Rutaceae	Fruit peel	Extracted with acetone and ethanol	MIC <10 µg/ml against <i>Candida</i> spp.	Otang and Afolayan, 2016
<i>Combretum acuminatum</i> Roxb.	Rooiboswilg (Afrikaans), umbondwe (Zulu), mohwidiri (Tswana), imbondvo (Swazi)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 20 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum albopunctatum</i> Suesseng	Unknown	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 320 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum apiculatum</i> Sond.	Redbushwillow (English), rooiboswilg (Afrikaans), umbondwe (Zulu), mohwidiri (Tswana), mohwelere (Pedi), ndhuva (Tsonga)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 320 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum bracteosum</i> (Hoscht)	Hiccup nut (English), hikklimop (Afrikaans), uQotha (Xhosa)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 80 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum caffrum</i> (Eckl. & Zeyh) Kuntze	Cape bushwillow (English), rooiblaar, rooiblad, vaderlandwilgerbool (Afrikaans), umdubu (Zulu),	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007

<i>Combretum celestroides</i> Welw. ex Laws subsp. <i>celestroides</i>	Cape bushwillow(English), rooiblaar, rooiblad, vaderlandwilgerbool (Afrikaans), umdubu (Zulu),	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum celestroides</i> Welw. ex Laws subsp. <i>orientale</i>	Jesse bush bushwillow, trailing bushwillow (English), umlalanyathi (Ndebele)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum collinum</i> Fresen subsp. <i>suluense</i>	Weeping bushwillow, bicoloured bushwillow, variable bushwillow (English), vaiërende boswilg (Afrikaans)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 80 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum collinum</i> Fresen subsp. <i>taborense</i>	Weeping bushwillow, bicoloured bushwillow, variable bushwillow (English), vaiërende boswilg (Afrikaans)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 640 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum edwardsii</i> Excell.	Natal combretum, forest climbing bushwillow (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 40 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007

<i>Combretum erythophyllum</i> (Burch.) Sond.	River bushwillow (English), riviervaderlandswilg, rooiblaar, rooiblad (Afrikaans), umbondwe, umdubu-wehlandze, umhlalavane (Zulu), miavana, modubo (Sotho), mugavhi, muvuvhu (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 640 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum hereroense</i> Schinz	Russet bushwillow, mouse-eared combretum (English), kieriessler (Afrikaans), umhlalavane (Zulu), mokabi (Northern Sotho), mugavhi (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against <i>M. canis</i> and <i>C. albicans</i>	Masoko et al., 2007
<i>Combretum imberbe</i> Wawra	Leadwood (English), hardekool (Afrikaans), motswiri (Pedi), ummono (Sotho), mondzo (Tsonga), motswere (Tswana), umbondwe omnyama (Zulu), muhiri (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 40 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum kraussii</i> Hochst	Forest bushwillow (English), bosvaderlandswilg (Afrikaans), uhwabhu, umdubuwelathi (Zulu), ulandile (Xhosa), modlubu (Northern Sotho), muvuvhu (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 80 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007

<i>Combretum microphyllum</i> Klotzsch	Flame creeper (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against <i>M. canis</i> and <i>C. albicans</i>	Masoko et al., 2007
<i>Combretum miossambicense</i> (Klotzsch)	Knobbly creeper (English), knoppiesklomp (Afrikaans)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 40 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum moggii</i> Excell.	Unknown	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 20 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum molle</i> R. Br.	Velvet bushwillow, velvet leaf willow (English), fluweelboswilg, basterrooibos (Afrikaans), umBondwe-omhlope (Zulu), mokgwethe (Northern Sotho), mugwiti (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against <i>M. canis</i> and <i>C. albicans</i>	Masoko et al., 2007
<i>Combretum nelsonii</i> Duemmer	Waterberg bushwillow (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 40 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum padoides</i> Eng. & Diels	Thicket bushwillow (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 80 and 320 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007

<i>Combretum paniculatum</i> Vent.	Forest flame creeper, burning bush (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against <i>M. canis</i> and <i>C. albicans</i>	Masoko et al., 2007
<i>Combretum petrophilum</i> Retief	Unknown	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against <i>M. canis</i> and <i>C. albicans</i>	Masoko et al., 2007
<i>Combretum woodii</i> Duemmer	large leaved forest bushwillow (English), grootblaarvaderlandwilg (Afrikaans), iWaphu (Zulu), mbondvo sehlati (Swazi)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 80 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Combretum zeyheri</i> Sond.	Large-fruited bushwillow, Zeyhers bushwillow (English), raasblaar, fluisterboom (Afrikaans), moduba-tshipi (Pedi), umbondwe wasembudwini (Zulu)mufhatelathundu (Venda)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 80 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Masoko et al., 2007
<i>Cotyledon orbiculata</i> Forssk.	Pig's ear (English), plakkie, kouterie (Afrikaans), impbewula (Xhosa), seredile (Sotho, Tswana)	Crassulaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 500, 1000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Curtisa dentata</i> (Burm.f) C.A. Sm.	Cape lancewood, assegai tree (English), assegaai (Afrikaans), umgxina (Xhosa), umagunda (Zulu)	Comaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 470 and 360 µgmL against <i>M. canis</i> and <i>C. albicans</i> respectively	Shai et al.,2008
<i>Cussonia zuluensis</i> Strey	Zulu cabbage tree (English), bergkiepersol (Afrikaans), umsenge (Xhosa), umsengembuzi (Zulu)	Araliaceae	Leaf	Extracted with multiple solvents of varying polarity	MIC of 880 µg/mL against <i>C. albicans</i> . Inactive against <i>M. canis</i>	Shai et al.,2008
<i>Dicoma anomala</i> Sond.	Fever bush, stomach bush (English), maagbitterwortel, kalwerbossie, koorsbossie, gryshout, maagbossie (Afrikaans), inyongana (Xhosa), isihlabamakhondlwane, umuna (Zulu)	Asteraceae	Tuber	Extracted with multiple solvents of varying polarity	MICs of 30, 4000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Dialium schlechteri</i> Harms.	Sherbet tree, zulu pod berry (English), zoeloepeulbessie (Afrikaans), umthiba (Zulu)	Fabaceae	Bark	Aqueous and methanolic extracts were tested.	MICs of 130, 190, 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Dioscorea dregeana</i> T. Durand & Schinz.	Wild yam (English), wildejam (Afrikaans), isidakwa, udakwa (Zulu)	Dioscoreaceae	Tuber	Extracted with multiple solvents of varying polarity	MICs of 2000, 4000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Diospyros mespiliformis</i> Hochst. Ex A.D.C.	African ebony, jackal berry (English), jakkalbessie (Afrikaans), mgula (Tsonga)	Ebenaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 100, 500 and 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Dichrostachys cinerea</i> (L.) Wight & Arn.	Sickle bush (English), sekelbos (Afrikaans), ugagane (Zulu)	Fabaceae	Twigs	Aqueous and methanolic extracts were tested.	MICs of 500, 250, 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Dodonaea augustifolia</i> L.f.	Sand olive (English), sandolien, ysterbos (Afrikaans), mutata-vhana (Venda)	Sapindaceae	Leaves	Extracted with multiple solvents of varying polarity	Low activity. MIC >10,000 µg/mL for all extracts	Motsei et al., 2003
<i>Dolbergia obovata</i> E. Mey.	Climbing flat bean (English, bobbejaankoudoring, rankplatboontjie (Afrikaans), udukuduku, isibandhlube, uphandlazi (Zulu), umzungu (Xhosa)	Fabaceae	Leaves	Aqueous and methanolic extracts were tested.	MICs of 340, 1000, 750 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Ekebergia capenses</i> Sparm.	Cape ash (English), essenhout (Afrikaans), mmidibidibi (Northern Sotho), umnyamathi (Zulu)	Meliaceae	Bark	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Elephantorrhiza elephantina</i> (Burch.) Skeels	Elandsbean (English), elandsboontjie (Afrikaans), mositsane (Sotho, Tswana), intolwane (Xhosa, Zulu)	Fabaceae	Leaf, rhizome	Extracted with multiple solvents of varying polarity	MICs of 250, 500 and 1000 µg/mL for leaf extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively. Rhizome extracts are stronger	Mabona et al., 2013; Nciki et al., 2016.
<i>Embelia ruminata</i> (E. Mey ex A.DC) Mez	Ibhinini (Zulu)	Myrsinaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 4000, 2000 and 200 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Erythina lysistemom</i> Hutch.	Common coral tree, lucky bean tree (English), gewone, koraalboom, kanniedood (Afrikaans), umsintsi (Xhosa), muvhale (Venda), mophete (Tswana), umsinsi (Zulu)	Fabaceae	Bark	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003; Mabona et al., 2013 et al.
<i>Eucalyptus camaldulensis</i> Dehnh.	Red rivergum (English)	Myrtaceae	Bark	Extracted with multiple solvents of varying polarity	MICs of 1000, 2000 and 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Euphorbia tirucalli</i> L.	Pencil plant, rubber hedge euphorbia (English), kraalmelkbos (Afrikaans)	Euphorbiaceae	Stems	Aqueous and methanolic extracts were tested.	MICs of 500, 4000, 1500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Eucomis autumnalis</i> (Mill.) Chitt.	Autumn pineapple lily, pineapple flower (English), wildepynappel, krulkoppie (Afrikaans), ubuhlungu becanti, isithithibala esimathunzi (Xhosa), umathunga, ukhokho, umakhandakantsele (Zulu)	Asparagaceae	Bulb	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 1250 µg/mL reported by Ghuman et al., 2016. Inactive (MIC >10,000 µg/mL for all extracts) reported by Motsei et al., 2003.	Ghuman et al., 2016; Motsei et al., 2003
<i>Ficus natalensis</i> Forssk.	Natal fig (English), mutuba (Zulu)	Moraceae	Bark	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Garcinia livingstonei</i> T. Anderson	African mangosteen (English), Afrika-geelmelkhout (Afrikaans), uGobandlovu (Zulu), mmimbi (Tsonga), mokongono (Pedi)	Clusiaceae	Bark	Aqueous and methanolic extracts were tested.	MICs of 130, 130, 250 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016

<i>Glycyrrhiza glabra</i> L.	Liquorice, licorice (English)	Fabaceae	Rhizome	Extracted with multiple solvents of varying polarity	Moderate activity. MIC 1560 µg/mL	Motsei et al., 2003
<i>Gumnera purpensa</i> L.	River pumpkin (English), rivierpampoen, wilde ramenas (Afrikaans), qobo (Sotho), rambola-vhadzimu(Venda), iphuzilomlambo (Xhosa), ugobho (Zulu)	Gunneraceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 250, 1000 and 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Haemanthus albiflos</i> Jacq.	Paintbrush (English), poeierkwas (Afrikaans)	Amaryllidaceae	Leaves and bulbs	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Hallaria lucida</i> L.	Tree fuchsia, white olive (English), notsung, witolienhout, witolyfhout (Afrikaans), umbinza, (Xhosa), indomela, umbinza (Zulu)	Stilbaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 2000, 2000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Harpephyllum caffrum</i> Bernh. ex Krauss	Wildplum (English), wildepruim (Afrikaans), mothekele (Northern Sotho), umgwenya (Xhosa, Zulu)	Anacardiaceae	Bark	Extracted with multiple solvents of varying polarity	MICs of 500, 1000 and 250 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Haworthiopsis limifolia</i> (Marloth.) G.D.Rowley	Fairy washboard (English)	Asphodelaceae	Leaf	Aqueous and ethanolic extracts	MICs of 200-2500 µg/mL against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i>	Naidoo and Coopooosamy, 2011; Ghuman et al., 2016
<i>Hewittia malabarica</i> L. (Suresh.)	Ihlanzandulo (Zulu)	Convolvulaceae	Leaf	Aqueous and methanolic extracts were tested.	MICs of 500, 750, 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Hibiscus surattensis</i> L.	Wild sour shrub (English)	Malvaceae	Leaf	Aqueous and methanolic extracts were tested.	MICs of 500, 750, 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Hypericum aethiopicum</i> Thunb.	Unknown	Asphodelaceae	Leaf	Chloroform extract	MICs of 630 µg/mL against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i>	Ghuman et al., 2016
<i>Hypericum perforatum</i> L.	Saint John's wort (English), Johanneskruid (Afrikaans)	Hypericaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Hypoxis hemerocallidea</i> Fisch. C.A. Mey & Ave	Yellow star, star lily, star flower (English), sterblom, geelsterretjie, gifbol (Afrikaans), moli kharatsa, lotsane (southern Sotho); inkomfe, inkomfe enkulu (Zulu), inongwe, ilabatheka, ixhalanxa, ikhubalo lezithunzela (Xhosa), tshuka (Tswana)	Malvaceae	Corms	Aqueous and methanolic extracts	MICs of 130, 1000, 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Ilex mitis</i> Radlk.	Cape holly, African holly, water tree (English), waterboom, waterhout (Afrikaans), nonaname (Northern Sotho), ipuphuma (Zulu), unduma (Xhosa), phukgu, phukgile (Sotho), mutanzwa-khameol (Venda)	Aquifoliaceae	Bark	Extracted with multiple solvents of varying polarity	MICs of 2000, 1000 and 4000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Jatropha curcas</i> L.	Physicnut, poison nut, bubble nut, purging nut (English)	Euphorbiaceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Kigelia africana</i> (Lam) Benth	Sausage tree (English), worsboom (Afrikaans), umVunguta, umFongothi (Zulu), muvevha (Venda)	Bignoniaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 60 µg/mL against <i>T. mentagrophytes</i> , <i>T. rubrum</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Shai et al., 2008; Mabona et al., 2013; Arkhipov et al., 2014; Nciki et al., 2016; et al.et al.et al.

<i>Lannea discolor</i> Engl.	Live-long, tree grape (English), morulamopsane, mokgokgothwane (Pedi), muvhumbu (Venda)	Anacardiaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 4000, 2000 and 200 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Lantana rugosa</i> Thunb.	Bird's beer, bird's brandy (English), voelbrandewyn, wildesalie (Afrikaans), utyani-bentaka (Xhosa), impema, ubukhwebezane, uguguvama (Zulu)	Verbenaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 50, 2000 and 3000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Leonitis leonoris</i> (L.) R.Br.	Wild dagga (English), wildedagga, duiwelstabak (Afrikaans), mvovo (Xhosa), uyshwala- bezinyoni (Zulu)	Lamiaceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Lipia jaVanica</i> (Burm F.) Spreng	Fever tea, lemon bush (English), koorbossie, beukesbossie, lemoenbossie (Afrikaans), inzinzinba (Xhosa), umsuzwane, umswazi (Zulu)	Verbenaceae	Twigs	Aqueous and methanolic extracts were tested.	MICs of 130, 130, 250 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Malva parviflora</i> L.	Small mallow, bread-and- butter, cheeseweed mallow (English), brood-en-botter, kiesieblaar (Afrikaans)	Malvaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 50 µg/mL against <i>T. mentagrophytes</i> . Inactive against <i>M. canis</i> and <i>C. albicans</i>	Mabona et al., 2013

<i>Melianthus comosus</i> Vahl.	Honey flower (Eng); kruidjie-roer-my-nie (Afr.)	Francoaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 50, 50 and 250 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Melianthus major</i> L.	Giant honey flower, kruidjie-roer-my-nie (Afrikaans)	Francoaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 50, 50 and 25 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Mentha longifolia</i> Huds.	Wild mint (English), kruisement, balderjan (Afrikaans), koena-ya- thabo (Sotho), inixina, inzinziniba (Xhosa), ufuthana, lomhlanga (Zulu)	Lamiaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 800, 1000 and 200 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Merwilia plumbea</i> (Lindl.) Speta	Wild squill, blue squill, blue yacinth (English), blouberglelie, blouslangkop (Afrikaans), inguduza (Zulu)	Asparagaceae	Leaves, bulbs, roots	Extracted with multiple solvents of varying polarity	MICs 310-1250 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i>	Ghuman et al., 2016
<i>Momordica balsamina</i> L.	Balsam pear (English), laloentjie (Afrikaans), mohodo (Sotho), intshungu (Zulu)	Curcubitaceae	Leaves	Aqueous and methanolic extracts	MICs of 190, 500, 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016

<i>Opuntia ficus-indica</i> Mill.	Sweet prickly pear (English)	Cactaceae	Leaf	Extracted with multiple solvents of varying polarity	MIC of 2000 µg/mL against <i>T. mentagrophytes</i>	Mabona et al., 2013
<i>Ozoroa engleri</i> R.Fern & A.Fern	Unknown	Anacardiaceae	Bark and leaves	Aqueous and methanolic extracts	MICs of 890, 190, 500 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Parinari capensis</i> Harv. subsp. <i>capensis</i>	Sand apple, dwarf mobola plum (English), bosappel, gruisappeltjie (Arikaans)	Chrysobalanaceae	Roots	Aqueous and methanolic extracts	MICs of 660, 60, 380 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Pellaea calomelanos</i> Link.	Hard fern (English), lehorometso (Sotho), inkomankoma (Zulu)	Adiantaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 2000 and 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Pentanasia pruinelloides</i> Walp.	Wild verbena (English), sooibrandbossie (Afrikaans), setimamollo (Sotho), icimamlilo (Zulu)	Rubiaceae	Rhizomes, root bark	Extracted with multiple solvents of varying polarity	MICs of 2000 µg/mL against both <i>T. mentagrophytes</i> and <i>M. canis</i>	Mabona et al., 2013

<i>Pittosporum viridiflorum</i> Sm.	Cheesewood (English), kasuur (Afrikaans), kgalagangwe (Northern Sotho), umkhwenkwe (Xhosa, Zulu), umfusamvu (Zulu)	Pittosporaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 500, 1000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Polygala myrtifolia</i> L.	September bush (English), septemberbossie, blouertjie, langelede (Afrikaans), ulopesi, umabalabala (Xhosa), uchwasha (Zulu)	Polygalaceae	Leaf	Extracted with multiple solvents of varying polarity	Moderate activity MIC 1560 µg/mL	Motsei et al., 2003
<i>Portulacaria afra</i> Jacq.	Elephant bush, dwarf jade plant, porkbush (English), spekboom (Afrikaans), isicococo (Zulu), iGqwanitsha (Xhosa)	Portulacaceae	Leaf	Aqueous and methanolic extracts	MICs of 1940, 250, 190 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Plumbago auriculata</i> Lam.	Cape leadwort, plumbago (English), blousysebos (Afrikaans), umabophe (Xhosa, Zulu), umasheleshele (Zulu)	Plumbaginaceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Ranunculus multifidus</i> Forssk.	Common buttercup (English), botterblom (Afrikaans), hlapi (Sotho), isijokazane, uxhaphozi (Zulu)	Ranunculaceae	Whole plant	Aqueous and methanolic extracts	MICs of 1710, 130, 250 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively.	Nciki et al., 2016

<i>Rauvolfia caffra</i> Sond.	Quinine tree (English), kinaboom (Afrikaans), umhlambamase (Xhosa), umhlambamanzi (Zulu)	Apocynaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 2000, 1000 and 4000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Rothmannia capensis</i> Thunb.	Wild gardenia, common rothmannia (English), wildekatjiekiering (Afrikaans), modulatshwene (Northern Sotho), mukubudu (Venda), umPhazane- mkhlu (Zulu), ibolo (Xhosa)	Rubiaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 2000, 4000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Rubus rigidus</i> Sm.	Wild bramble, white bramble (English), braambos, braambossie (Afrikaans), ijingijolo, igagane (Zulu)	Rosaceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Scadoxus puniceus</i> Friis & Nordal	Unknown	Amaryllidaceae	Roots and rhizomes	Extracted with multiple solvents of varying polarity	MICs of 4000 and 3000 µg/mL against <i>T. mentagrophytes</i> and <i>C. albicans</i> respectively.	Mabona et al., 2013
<i>Schotia brachypetala</i> Sond.	Weeping boer bean, tree fuchsia, African walnut (English), hullboerboon (Afrikaans), umfofofo, umgxam (Xhosa), ihluze, umgxamu, uvovovo (Zulu)	Fabaceae	Bark	Aqueous and methanolic extracts	MICs of 650, 600, 2000 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and	Nciki et al., 2016

C. albicans
respectively

<i>Sclerocarya birrea</i> (A. Rich.) Hotsch.	Marula (English), morula (Northern Sotho)	Anacardiaceae	Bark	Aqueous and methanolic extracts	MICs of 370, 380, 190 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Senecio serratuloides</i> DC.	Two-day cure (English), ichazampukane, insukumbili (Zulu)	Asteraceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1280, 380 and 1000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Siphonocilus aethiopicus</i> (Schweif.) B.L. Burt	Natal ginger, wild ginger (English), wildegemmer (Afrikaans), indungulo, isiphephetho (Zulu)	Zingiberaceae	Bulb	Extracted with multiple solvents of varying polarity	Low activity. MIC >10 000 µg/mL for all extracts	Motsei et al., 2003
<i>Solanun incanum</i> L.	Bark weed, bitter apple, thorn apple (English)	Solonaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 2000 and 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013

<i>Solanum panduriforme</i> E. Mey.	Apple of Sodom, bitter apple, poison apple (English), bitterappel, geelappel, gifappel (Afrikaans), intuma, intumemncane (Zulu)	Solanaceae	Fruit	Aqueous and methanolic extracts	MICs of 500 and 1000 µg/mL against <i>T. mentagrophytes</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Solanum rigescens</i> Jacq.	Unknown	Solanaceae	Fruit	Aqueous and methanolic extracts	MICs of 130, 190, 130 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Strychnos madagascariensis</i> Poir	Black monkey orange (English), swartklapper, botterklapper (Afrikaans), nkwaka (Tsonga), mukwakwa (Venda), umGluguza, umKwakwa (Zulu)	Strychnaceae	Bark and leaves	Aqueous and methanolic extracts were tested.	MICs of 130, 1000, 250 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Strychnos spinosa</i> Lam.	Unknown	Strychnaceae	Fruit	Aqueous and methanolic extracts were tested.	MICs of 250, 500, 500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Syzygium cordatum</i> Hochst. ex C. Krauss	Waterberry (English), waterbessie, waterboom, waterhout (Afrikaans), umdoni (Zulu), umswi, umjomi (Xhosa), mawthoo (Sotho), mutu (Venda)	Myrtaceae	Bark	Aqueous and methanolic extracts	MICs of 370, 380, 190 µg/mL for the bark extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016

<i>Tabernaemontana elgans</i> Stapf.	Toad tree (English), laeveldse paddaboom (Afrikaans), umKhahlwana, umKhadu (Zulu)	Apocynaceae	Fruit and leaves	Aqueous and methanolic extracts	MICs of 130, 130, 750 µg/mL for the leaf extracts against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Tagetes minuta</i> L.	Wildmarigold, stinking roger, tall khaki weed, khaki bush (English), kakiebos, Lang kakiebos, stinkbos (Afrikaans)	Asteraceae	Leaf	Extracted with multiple solvents of varying polarity	Low activity. MIC >10000 µg/mL for all extracts	Motsei et al., 2003
<i>Terminalia brachystema</i> Exell.	Unknown	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Mosoko et al., 2005
<i>Terminalia gazensis</i> Baker f.	Fringe-leaved cluster leaf, fringe-leaved terminalia (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Mosoko et al., 2005
<i>Terminalia mollis</i> M.A. Lawson	Large-leaved terminalia (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Mosoko et al., 2005
<i>Terminalia phanerophlebia</i> Engl. & Diels	Lebombo cluster-leaf (English), lebombotrosblaar (Afrikaans), amaNgwe-	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 880 and 490 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Shai et al., 2008

amnyama, amaNgwe-
omphofu (Zulu)

<i>Terminalia pruinoides</i> M.A.Lawson	Purple pod terminalia (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 20 and 160 µg/mL against <i>M. canis</i> and <i>C. albicans</i> respectively	Mosoko et al., 2005
<i>Terminalia sambesiaca</i> Engl. & Diels	River cluster-leaf, river terminalia (English)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	Inactive against both fungal species	Masoko et al., 2005; Shai et al.,2008.
<i>Terminalia sericea</i> Burch. ex DC	Silver terminalia, silver cluster-leaf, (English), vaalboom (Afrikaans), mususu (Venda), mogonono (Tswana), amangwe (Zulu)	Combretaceae	Leaf	Extracted with multiple solvents of varying polarity	MICs as low as 40, 130, 130 and 160 µg/mL against <i>M. canis</i> , <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> respectively	Nciki et al., 2016; Mabona et al., 2013; Mosoko et al., 2005
<i>Tetradenia riparia</i> (Hochst.) Codd.	Misty plume bush, ginger bush (English), gemmerbos, watersalie (Afrikaans), iboza, ibozane (Zulu)	Lamiaceae	Stems, leaves	Extracted with multiple solvents of varying polarity	MICs 310-2500 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i>	Ghuman et al., 2016
<i>Trichilia emetica</i> Vahl	Natal mahogany (English), rooissenhout (Afrikaans), mamba (Northern Sotho), umkhuhlu (Xhosa),	Meliaceae	Leaf	Extracted with multiple solvents of varying polarity	MIC of 880 µg/mL against <i>C. albicans</i> . Inactive against <i>M. cani</i> .	Mabona et al., 2013; Shai et al.,2008

umathunzini (Zulu),
mutuhu (Venda)

<i>Tulbaghia violaceae</i> Harv.	Wild garlic, society garlic (English), wildeknoffel, wildeknofflok (Afrikaans), utswelane (Xhosa), isihaqa, incisini (Zulu)	Alliaceae	Leaf	Extracted with multiple solvents of varying polarity	Moderate to poor activity. MIC 3250 µg/mL	Motsei et al., 2003
<i>Vepris reflexa</i> I. Verd	Unknown	Rutaceae	Leaf	Extracted with multiple solvents of varying polarity	MIC of 880 µg/mL against <i>C. albicans</i> . Inactive against <i>M. canis</i>	Shai et al., 2008
<i>Vernonia natalensis</i> Sch. Bip. ex Walp.	Silver vernonia (English), ihlambihloshana, ileleva (Zulu)	Asteraceae	Leaf	Extracted with multiple solvents of varying polarity	MICs of 1000, 4000 and 4000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
<i>Vertiveria zizanioides</i> (Linn) Nash	Vertiver grass (English)	Poaceae	Leaf	Extracted with multiple solvents of varying polarity	Moderate activity. MIC 3250 µg/mL	Motsei et al., 2003
<i>Viscum capense</i> L.f.	Cape mistletoe (English), lidliestee, voelent (Afrikaans)	Santalaceae	Roots and leaves	Extracted with multiple solvents of varying polarity	MICs of 1000, 1000 and 4000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and	Mabona et al., 2013

C. albicans
respectively

<i>Waltheria indica</i> L.	Meidebossie (Afrikaans), mokhuteseia (Pedi)	Malvaceae	Roots	Aqueous and methanolic extracts	MICs of 250 µg/mL against <i>T. mentagrophyte</i> .	Nciki et al., 2016
<i>Warbargia salutaris</i> (Bertol.) Chlov	Pepper-bark tree (English), peperbasboom (Afrikaans), isibhaha (Zulu), manaka (Venda), shibaha (Tsonga)	Canellaceae	Bark and leaves	Extracted with multiple solvents of varying polarity	Low activity. MIC 6250 µg/mL for the bark extracts, >10 000 µg/mL for the leaf extracts	Mabona et al., 2013; Motsei et al., 2003
<i>Withania somnifera</i> (L.) Dunal	Indian ginseng, poison gooseberry, winter cherry (English), bitterappelliefie, koorshout (Afrikaans), ubuvuma (Xhosa), ubuvimbha (Zulu)	Solonaceae	Roots	Aqueous and methanolic extracts	MICs of 250, 500, 2000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016
<i>Ximenia caffra</i> Sond.	Large sourplum (English), groot suurpruim (Afrikaans), unThunduluka-obmvu (Zulu)	Olacaceae	Twigs	Aqueous and methanolic extracts	MICs of 130, 750, 500µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Nciki et al., 2016

<i>Zantedeschia aethiopica</i> (L.) Spreng.	Whitecommon arum lily (English), wit varkoor (Afrikaans), intebe (Xhosa), ihlukwe (Zulu)	Araceae	Leaf	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 630-1250 µg/mL reported by Ghuman et al., 2016. Low activity reported in the Mabona et al., 2013 and Motsei et al., 2003 studies (MIC >10 000 µg/mL for all extracts)	Ghuman et al., 2016; Mabona et al., 2013; Motsei et al., 2003
<i>Zanthoxylum capense</i> (Thunb.) Harv.	Small knob-wood, lemon thorn, wild cardamon (English), kleinperdepram, parapis, prambos, knopdoring (Afrikaans), amaBelentombi, umNungumabele (Zulu), umLungumabele(Xhosa)	Rutaceae	Bark	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 130-500 µg/mL reported by Nciki et al., 2016. Low activity reported in the Mabona et al., 2013 and Motsei et al., 2003 studies (MIC >10000 µg/mL for all extracts)	Motsei et al., 2003

<i>Ziziphus murconata</i> Willd.	Buffalo-thorn (English), blinkblaar-wag-n-bietjie (Afrikaans), mokgalo (Northern Sotho, Tswana), umphafa (Xhosa, Zulu), umlahlankosi (Zulu)	Rhamnaceae	Leaf	Extracted with multiple solvents of varying polarity	Conflicting reports of efficacy. MICs against <i>T. mentagrophytes</i> , <i>T. rubrum</i> and <i>C. albicans</i> of 130-500 µg/mL reported by Nciki et al., 2016. MIC's of 2 000, 2 000 and 4 000 µg/mL against <i>T. mentagrophytes</i> , <i>M. canis</i> and <i>C. albicans</i> respectively	Mabona et al., 2013
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There are no records of therapeutic use to treat dermatophytosis for the other 121 plant species that have been screened for anti-dermatophytic activity. Plant species were additionally screened based on alternative criteria other than ethnobotanical, including their genus/family. For example, twenty-four *Combretum* species (Masoko et al., 2007) and seven *Terminalia* species (Masoko et al., 2005) were screened in two separate studies by the same group. The selection of these species coincides with that group's interest in plants of the family Combretaceae, rather than on their traditional use to treat fungal skin diseases. However, *Combretum* (de Morais Lima et al., 2012) and *Terminalia* (Cock, 2015b) species from other global regions have good antifungal activity and therefore these species are good candidates for further testing. Regardless of the reason for selecting those species, their inclusion in those studies was fortuitous as most of the species were potent inhibitors of *M. canis* and *C. albicans*. Indeed, MIC values of 20-80 µg/mL were achieved by various *Combretum* and *Terminalia* spp. against *M. canis*. Extracts prepared from the same species were also good inhibitors of *C. albicans* growth, albeit generally with MIC values an order of magnitude higher than noted against *M. canis* (Masoko et al., 2005). With the exception of *T. sericea* (MIC 130 µg/mL), these plants were not tested against *T. mentagrophytes* and further testing is required to test the efficacy of these extracts against this pathogen.

Four *Aloe* species (*A. ferox*, *A. maculata*, *A. microstigma*, *A. vera*) are used traditionally to treat fungal skin infections. *A. ferox* has been screened for inhibitory activity against *T. mentagrophytes*, *T. rubrum* and *C. albicans* (MIC 310-630 µg/mL against all fungi) (Ghuman et al., 2016). *Aloe vera*, has only had some international recognition with respect to antifungal activity. A recent study has been undertaken on *C. albicans* biofilms (Nazar and Meidyawati, 2019) but until recently more attention has been given to other fungal pathogens not related to human skin dermatophytes (Rosca-Casian et al., 2007). *Aloe maculata* has been neglected

completely. Further studies are required to test the other three traditionally used *Aloe* species against these fungi. Interestingly, three other *Aloe* species (*A. arborescens*, *A. excels*, *A. barbata*) have been screened against the dermatophytes and have displayed good inhibition (MICs 200-800 µg/mL) (Ndhlala et al., 2009; Ghuman et al., 2016; Mabona et al., 2013; Naidoo and Coopooosamy, 2011). Presumably these species were also selected for screening on the basis of their taxonomic relationship to the traditionally used *Aloe* species. Whilst it is unclear why the other plant species were selected for screening against the dermatophytes, it is likely that many were randomly selected. Table 2 summarises studies that have screened on southern African plant species against fungal skin pathogens.

The following introduced plant species were good inhibitors of dermatophyte growth: *Allium sativum* (MIC value 560 µg/mL against *C. albicans*), *Citrus limon* (MIC value <10 µg/mL against *C. albicans*) and *Withania somnifera* (MIC values of 250, 500 and 2000 µg/mL against *T. mentagrophytes*, *M. canis* and *C. albicans* respectively). *Eucalyptus camaldulensis* (MIC values of 1000, 2000 and 500 µg/mL against *T. mentagrophytes*, *M. canis* and *C. albicans* respectively) and *Glycyrrhiza glabra* (MIC values of 1560 µg/mL) also had moderate inhibitory activity against those dermatophytes.

6.2. Synergistic antifungal activity of plant combinations

Traditional plant-based healing systems frequently use combinations of plants to provide effective therapies. This is particularly evident for traditional Asian therapeutic systems, including Indian Ayurveda and traditional Chinese medicine (TCM). Whilst plant monotherapies are more frequently used in most southern African traditional medicine systems, combinations of plants may be used for some disorders to increase the efficacy of the therapy. As well as containing therapeutic compounds, plants may also contain compounds that

potentiate the effects of the therapy (Cheesman et al., 2017). For example, studies comparing the efficacy of the antimalarial drug artemisinin with *Artemisia annua* extracts (from which artemisinin is derived) highlights this point. Substantially lower doses of *Artemisia annua* extracts are required to inhibit *Plasmodium falciparum* growth compared to an equivalent amount of pure artemisinin (as reviewed by Cock, 2018). Indeed, *A. annua* extracts contain approximately 20% of the artemisinin required to produce the same effects, indicating that other extract components may potentiate the activity of artemisinin in the extract. Notably, several *A. annua* flavonoids have been reported to potentiate the activity of artemisinin, despite being inactive alone (Deharo and Ginsburg 2011). It is surprising that studies examining the effects of combinations of plant extracts, or combinations of extracts and conventional drugs remain under-represented in antifungal drug discovery research and far more combinational studies are required.

Few studies (Mabona et al., 2013; Naidoo et al., 2013) have examined the effects of combinations of southern African medicinal plants against fungal skin pathogens. Those studies screened nearly 65 different plant species traditionally used to treat skin disorders for the ability to inhibit the growth of dermatophytes and *C. albicans*. The majority of the plant species displayed moderate to promising antifungal activity. Three species (*D. anolala*, *E. elephantina*, *P. pruinelloides*) were selected for further combinational studies based on their strong antimicrobial activity and reports of their traditional use as combinations to treat fungal skin infections (Watt and Breyer-Brandwijk, 1962; Hutchings, 1996; Von Koenen, 2001; Van Wyk, 2009). Whilst the majority of the combinations produced no notable benefit over plant monotherapy alone, the combination of *D. anolala* and *P. pruinelloides* extracts was substantially more potent than either therapy alone against *C. albicans*. Unfortunately, the effects of combinations of the extracts were not tested against *T. mentagrophytes* or *M. canis* in that study so it is uncertain whether this (or other combinations) have similar synergistic

effects against these dermatophytes. Further studies are required to evaluate combinations of these plants (and the other plants screened in that study) against these, and other dermatophytes. Furthermore, the toxicity of the extracts (and the combinations) was not examined in that study, so it is not possible to calculate selectivity indices (SI) and further research is required to evaluate the potential of these plant extracts and their combinations therapeutically. However, whilst combinational therapy studies against skin fungi are still in their infancy, the Mabona et al. (2013), study highlights the potential of combinational therapies. Far more studies are needed to test extract/extract combinations, as well as combinations of conventional antifungal drugs with plant extracts. A study on a selection of medicinal plants with commercial potential, in combination with nystatin and amphotericin B, has shown various effective interactions against *C. albicans* (Hübsch et al., 2014). Synergy was observed for the combination of *Lippia javanica* with nystatin. Synergy was also noted for the combination of *Salvia frutescens* with amphotericin B. What should also be considered is antagonism, and many more combinations in that study demonstrated antagonistic interactions. It is possible that not only may new antifungal combination therapies be discovered, but strategies to counteract fungal antibiotic resistance mechanisms may also be developed, thereby extending the effective life of current antibiotics, and even repurposing some drugs that are no longer effective alone. The author Jin, 2019 has made a significant contribution in the review of natural antifungal flavonoids and their derivatives with special emphasis on synergistic interactions. Works such as that pave the way for future studies to develop.

7. Discussion and conclusions

Fungal skin infections are one of the most widespread classes of infectious diseases globally, yet development of new therapies to treat these infections remains relatively

neglected. Whilst dermatophyte infections cause discomfort, they rarely cause mortality or serious morbidity except in immune-compromised individuals. It is likely that the relative lack of severity of these infections may contribute to the low number of studies into the effects of southern African plants on dermatophytes. Indeed, a large portion of these studies have occurred in the most recent 15-year period. Interestingly, the increase in research in this field coincides with increases in the incidence in these infections, not only in southern Africa, but globally. The global increase in dermatophytosis further correlates with the development of dermatophyte resistance to the commonly used antifungal drugs. Prior to 2000, antibiotic-resistant dermatophyte strains were rare. However, more recently, resistance to many human-infective dermatophytes are evident (Khurana et al., 2019) and new antifungal agents are urgently needed.

Whilst this review focused on dermatophytes such as the *Epidermophyton*, *Microsporum* and *Trichophyton* spp., it must be noted that emerging fungal skin infections caused by other species such as *Histoplasma capsulatum*, *Blastomyces dermatitidis*, *Cladosporium carrionii*, *Fonsecaea pedrosoi*, *Fonsecaea compacta*, *Phialophora verrucosa* and *Coccidioides* spp. are becoming more prevalent (Zambelli and Griffiths, 2015; Lockhart and Guarner, 2019) and attention should be given to these species as well.

Several studies have already screened some southern African plants for dermatophyte inhibitory activity. Indeed, Table 2 summarises studies screening 140 plant species. Surprisingly, of those 140 species, only 19 species were selected for study on the basis of their traditional usage, despite 89 species being recorded as being used traditionally to treat dermatophytosis. Looking at the low correlation (13%) between recorded traditional knowledge (Table 1) and what research has been done (Table 2), there are many good candidates that are used as therapies for dermatophytosis and are yet to be screened against these pathogens. It seems that much of the existing antifungal data is based on plant availability

rather than ethnobotanical leads. This is particularly evident when looking at the Combretaceae family as there is no traditional link with use for infectious dermatitis. Another aspect that requires attention is the correlation to the plant part tested. In some cases the plant part tested correlates with traditional use. However, in some instances for example with *K. africana*, the leaf material was tested, yet traditionally the bark and fruit is used. While it is understandable to forego testing on bark and roots for sustainability reasons, the fruit is readily available and should have been tested. Another example in this respect is *C. inerme* where twigs were tested yet traditionally the leaves are used. Also, with *D. anomala*, the tuber was tested, yet the stems and leaves are used traditionally. Researchers need to take cognisance that the chemistry between different plant parts is variable and thus might yield completely different biological activity.

It is likely that substantially more species are also used to treat dermatophytosis, although many of the older records are not definitive and often refer to the usage of the plants in generic terms. For example, several books and reviews refer to the use of some plant species to treat skin disorders. Whilst this may indicate that they were used for skin infections, or for some other type of skin condition. Skin infections may encompass dermatophytosis, although it could also refer to bacterial or viral infections. Furthermore, ethnobotanical surveys may reveal more specific roles for some of these plant species and may thereby provide further plant targets for anti-dermatophyte screening in the future.

Even those studies that have screened southern African plants against skin-infective fungi generally did not screen against the most relevant model organisms for a southern African context. *Tinea capitis* is substantially more prevalent in southern Africa than all other forms of dermatophytosis combined (Coulibaly et al., 2018). Whilst *tinea capitis* is caused by *M. canis*, *T. rubrum*, *T. mentagrophytes* and *Trichophyton tonsurans* in most regions of the world (Ameen, 2010), *T. violaceum* and *M. audouinii* are the main causative dermatophytes in

southern Africa (Neil et al., 1987; Morar et al., 2004). Despite this, we were unable to find any studies that screened southern African plants against these dermatophytes. Instead, all of the previous studies have screened against dermatophytes which are more relevant to northern hemisphere regions. Screening the plants against *M. canis*, *T. rubrum*, *T. mentagrophytes* is still relevant as these species contribute to the dermatophytosis load in southern Africa. However, susceptibility of these fungi to southern African plant extracts does not necessarily indicate that the plants will also be effective against the dominant southern African dermatophyte species, as different dermatophytes may have substantially different susceptibilities. Future studies are needed to confirm efficacy against *T. violaceum* and *M. audouinii*. Additionally, all of the previous studies have screened against dermatophytes that are susceptible to conventional therapies. Screening against resistant strains has been neglected. As there have been substantial increases in reports of dermatophyte strains that are resistant to conventional therapies in recent years, it is important that southern African plants are also screened against resistant dermatophyte strains.

Almost without exception, the plants species screened for anti-dermatophyte activity were also not tested for toxicity. Perhaps this is because these plants have been used for hundreds of years and are assumed to be safe. However, often the plant is prepared by different methods for bioactivity screening than was employed by traditional medicine practitioners. Different preparation methods will alter the phytochemical profile of the preparations and could thereby also alter their toxicity profiles. Indeed, some studies have reported toxic, carcinogenic and mutagenic effects for extracts prepared from multiple plants traditionally used as medicines (Fennell et al., 2004). Several other studies have also investigated the toxicity of several of the plant species highlighted herein. However, the focus of those studies was solely on evaluation of toxicity of the extracts, or on investigating the safety of the extracts in conjunction with other bioactivities (Fennell et al., 2004; Mapunya et al., 2006; Steenkamp and

Gouws 2006; Versaevé and Van Staden, 2008). Toxicity evaluations should be run concurrently with anti-dermatophyte studies to allow the safety/selectivity indices to be calculated. This is imperative as the chemotherapeutic value of a plant preparation will be limited if it has substantial toxicity. Of the studies we identified of southern African plants for anti-dermatophyte activity, only a single study (Ghuman et al., 2016) also screened the extracts for toxicity in parallel with the bioactivity screening, and toxicity evaluations of all other plant species are required. Ideally, toxicity screening should incorporate more than one assay to allow for comparisons between studies.

Ethnobotanical records have already identified a number of promising plant species used traditionally for the treatment of dermatophytosis and several of those species (as well as multiple species for which a traditional use against dermatophytes was not recorded) have already been tested against one or more pathogen. Further research is required to screen all identified species (including previously tested species) against *T. violaceum* and *M. audouinii* (which are particularly relevant in a southern African context), and against resistant dermatophyte strains.

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