A review of the traditional use of southern African medicinal plants for the treatment of selected parasite infections affecting humans

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ABSTRACT

Ethnopharmacological relevance:

Worldwide, more than three billion cases of parasitic disease are reported yearly and it is likely that this figure is substantially under-estimated. Approximately one in six people globally are estimated to be infected with at least one parasite species annually. In South

Africa, the prevalence of *Schistosoma haematobium* (bilharzia) and intestinal worms and helminths are particularly high, especially in children and in crowded or poorer rural communities with inadequate sanitation and nutritional status. Despite alarmingly high estimates, medical research into parasitic diseases remains neglected and only malaria receives significant attention and funding. Traditional medicines have been used for centuries in Africa by multiple ethnic groups and many people rely on these healing systems as their primary healthcare modality. The traditional use of South African medicinal plants to treat parasite infestations is relatively well documented, and it is important to link these traditional uses to scientific evidence validating efficacy.

Aim of the study:

To document the medicinal plants used for parasitic infections and critically review the literature on the anti-parasitic properties of South African plants against some neglected parasitic diseases.

Materials and methods:

A review of the literature (ethnobotanical books and publications documenting traditional plant use) was undertaken related to specific medicinal use for parasitic infections in Southern Africa. Inclusion criteria focused on human use. Exclusion criteria included veterinary use and Malaria due to the extensive nature of these subject matters. An in-depth analysis of previous studies was undertaken and future perspectives are considered.

Results: In particular, bilharzia, gastrointestinal worms and helminths, ectoparasites, trichomoniasis, leishmaniasis and trypanosomiasis are reviewed with special emphasis on the gaps in research.

Conclusions:

Despite the availability of relatively extensive ethnobotanical records on the anti-parasitic properties of southern African medicinal plants, the antiparasitic properties of many plants

have been poorly examined. There was in many instances a lack of evidence to support traditional use of many species towards some parasites and research is urgently needed in this area.

Graphical abstract:

Abbreviations

CDC, Centre for Disease Control; HIV, Human immunodeficiency virus; Σ FIC, Fractional inhibitory concentrations; WHO, World Health Organisation.

Keywords

Ascaris lumbricoides, Bilharzia, Ectoparasites, *Entamoeba histolytica*, Gastrointestinal parasites, *Giardia duodenalis*, Medicinal plants, *Schistosoma* spp., Southern African, *Taenia* spp., *Trichomonas vaginalis*.

1. Introduction

Parasitic diseases inflict significant global suffering and place enormous pressure on medical resources. Recent statistics from the American Centre for Disease Control (CDC) estimate that approximately three billion cases of parasitic diseases were reported in the 2012-2013 period alone (Centre for Disease Control and Prevention, 2017). However, it is likely that this figure is vastly underestimated as many incidences of parasitic infection are

unreported and less serious parasitic diseases are often left to run their natural course. Furthermore, due to both economic considerations and a lack of therapeutic options in developing regions, parasitic diseases are often treated with traditional remedies and their incidence remains unreported. The prevalence of ascariasis globally was estimated in the CDC report at nearly one billion cases per year. Infection with the parasitic roundworm *Ascariasis lumbricoides* which inflicts this disease causes no obvious symptoms in nearly 85% of infected individuals. Even when symptoms are apparent, they often only present as shortness of breath and mild fever, and thus may be overlooked. The disease is often only diagnosed when severe abdominal swelling, pain and diarrhoea become apparent. Thus, whilst the reported cases of ascariasis are alarmingly high, the incidence may actually be substantially higher. The incidence of trichuriasis (caused by whipworms of the genus *Trichuris*) is estimated in the same report to be nearly half a billion cases a year globally. Many infected individuals display only mild transient symptoms and it is likely that the actual number of infected people is substantially higher. The incidence of hookworm infection is similarly high although it is also believed to be significantly underestimated. Whilst ascariasis, trichuriasis and hookworm infections may cause considerable discomfort and loss of productivity for infected individuals, they are rarely fatal. Indeed, individually these diseases are estimated to cause less than 1000 deaths globally per year. Perhaps for these reasons, these parasitic diseases are neglected yet further research should be considered for humanitarian reasons.

In contrast, some other parasitic diseases are of considerably greater concern and may result in high levels of mortality if not promptly treated. Indeed, the same CDC study reported that parasitic disease caused over 800,000 deaths in the 2012-2013 period. Malaria was responsible for nearly 600,000 of these deaths, whilst cryptosporidiosis, leishmaniasis, amebiasis and schistosomiasis each also causes significant loss of life annually. It is perhaps

surprising that despite the high incidence of parasitic disease globally and the significant level of suffering that these parasites cause, most are considered neglected diseases. Only the treatment and prevention of malaria receives significant funding and much work is required to alleviate the suffering of the large populations of people affected by other parasitic diseases. Indeed, with approximately one in six people globally estimated to be infected with at least one species of parasite annually, it is surprising that there is no vaccine yet clinically available for any parasitic pathogen. Similarly, drug discovery efforts for parasitic diseases are lacking, with only about 1% of new drugs in the last 40 years targeting parasitic disease despite parasitic diseases being responsible for >10% of the global disease burden (Centre for Disease Control and Prevention, 2017).

From previous experience, with the treatment and prevention of malaria, it is apparent that parasitic diseases can be controlled and elimination may even be possible in many cases. Such programs would involve a significant increase in medical research, strong public health programs, proper sanitation, vector control and widespread drug distribution. However, such concerted efforts are expensive and put considerable financial burdens on regions where they are instigated. Furthermore, as these diseases are often most prevalent in poorer socio-economic regions, westernised models for controlling parasitic disease may not be realistic. Instead, there is a need to develop new cost effective therapies to control human parasitic disease. One approach is to reinvestigate traditional medicines. This review focuses on parasitic diseases infecting humans and the traditional southern African medicinal plants which have therapeutic or reported relevance in treating such diseases.

2. Materials and methods

The aim of the review was to identify the Southern African medicinal plants used *in situ* for human parasitic infections and then analyse the available published literature to determine what scientific evidence is available to support traditional use. The information presented in this review was obtained from a variety of ethnobotanical books (Smith, 1895; Watt and Breyer-Brandwijk, 1962; Bryant, 1966; Hutchings et al., 1996; Von Koenen, 1996; Felhaber 1997; Van Wyk et al., 2009) and ethnobotanical reviews (Chinsamy et al., 2011; Philander, 2011; Corrigan et al., 2011; Nortje and Van Wyk, 2015) where the traditional use was recorded. The analysed scientific papers were selected from three different electronic databases: PubMed, ScienceDirect, and Scopus, and the filters used included either/or and a combination of “parasite”, “bilharzia”, or “aromatherapy”, “worms “helminths”, “protozoa”, amoebiasis”, “giardiasis”, “ectoparasite”, “trichomoniasis”, “leishmaniasis”, “trypanosomiasis” with the scientific name for each medicinal plant identified traditionally to treat parasitic infections (Tables 1-4). Over 120 different southern African plant species were identified as a traditional remedy to treat various parasitic infections in humans. The initial focus was to document traditional use of all plants used in Southern Africa, with no specific emphasis on endemic or taxonomic preference. Thereafter, based on medicinal plant identified, a thorough review was undertaken on each specified plant species to identify any research pertaining to parasites for that species.

Inclusion criteria included human use, medicinal plants of southern African, bilharzia, gastrointestinal parasites, ectoparasites, giardia, trichomoniasis and other key words related to commonly occurring parasitic infections. Scientific evidence to support traditional use was included, but only if relevant to the treatment of human parasites.

Although animal vectors are important in parasitic diseases, ethnobotanical veterinary uses have been excluded as the subject matter is vast and has been covered in other publications such as the excellent review on ticks by Adenubi et al., 2016. Several recent

studies have already adequately reviewed malaria and its traditional treatment with botanical drugs (Batista et al., 2009; Clarkson et al., 2004; Willcox and Bodeker, 2004). Therefore, traditional South African treatments of malaria are not reported in this review.

Instead, this report summarises traditional southern African ethnopharmacological knowledge for the treatment of other parasitic diseases, with the hopes of highlighting plant species for future testing against parasitic diseases and to foster future research in this area.

3. An overview of parasitic infections in southern Africa

In South Africa, a wide variety of parasites affect humans, livestock, pets, wildlife and crops (Horak et al., 1988; Junker and Boomker, 2007; Van der Merwe et al., 2012; Tsoka-Gwegweni and Ntombela, 2014). As many parasitic diseases are spread via contaminated food and water, these diseases are often most prevalent in areas of South Africa with less effective sanitation systems. Thus, rural areas and lower socio-economic communities often have higher incidences of parasitic diseases than other areas. Other factors may also further facilitate parasite spread in rural areas. Many parasites are zoonotic, with a single species of parasite often infecting human hosts as well as domestic and wild animals, as well as livestock. Thus, when considering treatment and prevention strategies for parasitic diseases, it is often necessary to also consider eradication of the parasite in animal hosts. A high density of people living in many urban areas of South Africa (e.g. poorer inner city communities) also provide an increased likelihood of person to person transfer of parasites and thus a higher incidence of parasitic disease may also occur in these communities. Ectoparasites in particular, spread more rapidly in high density populations.

Rural and the lower socio-economic urban communities in South Africa share attributes which also increase the incidence and severity of parasitic infections. Individuals in

these communities often have limited access to effective medical care. This may be due to their isolation and the lack of adequately trained medical personnel in some remote rural communities. Alternatively, poorer individuals in these communities may be unable to afford effective medical services. Often these people instead rely entirely on traditional healers, or even go without any medical treatment for these conditions. Furthermore, often these communities have lower levels of education than more affluent urban areas. Thus, there may be less understanding of simple methods of preventing the spread of parasitic diseases, or of recognising them when they occur and taking the appropriate action.

The most prevalent human parasites in southern Africa include the intestinal parasites, *Schistosoma* spp., *Plasmodium* spp., *Toxoplasma* spp. and parasites that cause diseases of the reproductive system (Tsoka-Gwegweni and Ntombela, 2014). Not surprisingly, the prevalence of many of these parasitic infestations is directly related to sanitation and socio-economic status, with significantly higher rates of infection in poor and rural areas (Nxasana et al., 2015). Improvement of water sanitation in these communities has been shown to decrease the levels of parasitic infestations (Hugo and Malan, 2010).

Intestinal parasites are most prevalent in children of school-going age, pregnant women and immune-compromised individuals (Tsoka-Gwegweni and Ntombela, 2014). Indeed, it has been estimated that between 70% and 100% of children of school-going age in South Africa are infected with intestinal parasites at any time (Nxasana et al., 2015). This figure is alarmingly high, and is particularly worrisome as parasitic infections often have pronounced effects on growth and development. Children with parasite infections may suffer from a wide variety of symptoms including anaemia as well as a myriad of mental and physical problems (Tsoka-Gwegweni and Ntombela, 2014). As intestinal parasites survive by removing important nutrition from their human host, children infected with gastrointestinal parasites may have decreased mental and physical development. Thus the parasitic disease

may have far greater effects than are immediately apparent and may decrease the learning ability and productivity of infected children.

Intestinal parasite infestation in pregnant women is also of particular concern. It may result in anaemia, a weakened immune system and a resulting susceptibility to infections, all of which may affect foetal survival and development (Tsoka-Gwegweni and Ntombela, 2014). Maternal intestinal parasite infestation may result in low birth-weight infants who are also susceptible to infections and have developmental problems. Even postnatal, maternal infestation may cause lethargy and malaise which may adversely affect the mothers' ability to provide adequate care for the infant. Of further concern, some parasitic diseases may accelerate the progression of the human immunodeficiency virus (HIV) infections in pregnant women to the end stage of the disease (Adeleke et al., 2015). Whilst this is not only a concern for pregnant HIV sufferers, the affects may be more evident due to alterations in the maternal immune responses that occur during pregnancy. However, the progression of all HIV positive individuals with intestinal parasites may also be more rapid if not adequately treated.

The most common human intestinal parasites in South Africa are *Ascaris lumbricoides* (giant roundworm), *Giardia duodenalis* (causing giardiasis), *Entamoeba histolytica* (causing amoebiasis), *Taenia solium* and *Taenia saginata* (tapeworm) (Coral-Almeida and Gabriël, 2015). *Taenia solium* can be transmitted by eating poorly cooked infected pork (Coral-Almeida and Gabriël, 2015). If *T. solium* cysts lodge in the brain, they may cause epilepsy or other similar clinical conditions, with the severity of the disease dependent upon in which tissue they lodge (Coral-Almeida and Gabriël, 2015). *Taenia saginata* follows a similar pattern, but is relatively rare in South Africa. It is usually transmitted by eating poorly cooked infected beef (Gbueloh, 2015). *Schistosoma* species can cause urinary bladder bilharzia (*Schistosoma haematobium*), intestinal bilharzia (*Schistosoma mansoni*, *Schistosoma japonicum*, *Schistosoma mekongi* and *Schistosoma guineensis*) and

female genital schistosomiasis (*Schistosoma haematobium*) (World Health Organization, 2015; 2017). Schistosomiasis is most prevalent in communities living close to rivers and dams, and accounts for 40% of tropical diseases worldwide (excluding malaria) (Adenowo et al., 2015).

Several common reproductive system parasites also affect significant proportions of the South African population. *Trichomonas vaginalis* causes urethritis with a purulent discharge and is also linked to other morbidities of the reproductive tract in both males and females. In endemic areas, community studies indicate that between 33% and 75% of females are infected with *Schistosoma haematobium* in their genital tracts (Magaisa et al., 2015). These infections may cause chronic inflammation of the urogenital tract, resulting in infertility. *Entamoeba histolytica* can also infest the female urogenital tract and cause foul-smelling and bloody vaginal discharge, genital ulcers and abdominal pain (Siteti and Injete, 2015).

Zoonotic helminths affect some of the South African wildlife and these may therefore constitute a readily assessable reservoir of parasites. Many species of wild animal are known to harbour human infective pathogens, included impalas, kudus, wildebeests, gemsboks, warthogs and bush pigs (Van Wyk and Boomker, 2011). Parasites are stressful to the animals, and high parasite loads might even kill animals that would otherwise survive under normal conditions (Van Wyk and Boomker, 2011). The parasites in these wild animals may cross species into farm livestock or domestic animals and ultimately infect humans. Alternatively, close contact with wild animals or the consumption of infected bush meat may result in a direct infection of human hosts. Similarly, close contact with farm livestock (particularly in rural areas) may also result in cross species parasitic infections. Domestic animals can also serve as a reservoir for some parasites. *Toxoplasma gondii* infects dogs and cats in southern Africa and can be transmitted via their faeces. *Toxoplasma gondii* is thought to infect 25% of

the human population globally (Hammond-Aryee et al., 2014), and it is likely that the infection rate is similar in South Africa. Toxoplasmosis can have severe consequences in immuno-compromised individuals and pregnant women where it poses a major health risk to the foetus (Hammond-Aryee et al., 2014). Thus, regimes for the treatment and prevention of parasites need to consider animal reservoirs of parasites and limit cross species infection.

4. Southern African medicinal plants used traditionally to treat parasitic infections

The traditional models of parasitic infections and the non-scientific diagnostic methods used amongst traditional healthcare practitioners makes it difficult to pinpoint exactly which plants are used to treat specific parasites. Furthermore, traditional medicines are often used to target disease symptoms and therefore it is often difficult to discern between treatments for diseases with similar symptoms. For example, ethnobotanical records may record a traditional medicine as being useful for the treatment of diarrhoea. However, diarrhoea may be caused by a wide variety of parasites, as well as by many bacterial and viral pathogens. Thus, it is often difficult to adequately discern the specific agent that a treatment is effective against by just consulting the traditional medicine records. By necessity, plant selection for herbal medicine research is often based on the symptoms instead of the disease. There are some reports that are not specific in their medicinal plant treatment against parasites. For example, *Abrus precatorius* L. subsp. *africanus* Verdc., *Gloriosa superba* L. are *Helichrysum odoratissimum* (L.) Sweet are indicated for a general use against parasitic infections (Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk and Gericke, 2000). Other instances resort to the treatment of selected plant species such as *Phytolacca heptandra* Retz. and *Cussonia paniculata* Eckl. & Zeyh. subsp. *sinuate* (Reyneke&Kok)DeWinter for the expelling of parasites inflicted by witchcraft (Watt and

Breyer-Brandwijk 1962; Moteetee and van Wyk, 2011). The medicinal plants are discussed according to common parasitic infections they are used to treat. The most common parasitic infections excluding Malaria in South Africa are;

- Bilharzia.
- Intestinal parasitic worms and helminths.
- Giardiasis and amoebiasis.
- Zoonotic parasites.
- Trichomoniasis
- Leishmaniasis and African trypanosomiasis.

5. Bilharzia (*Schistosoma haematobium*)

5.1. Epidemiology of bilharzia in South Africa

Bilharzia is caused by helminthic parasites of the genus *Schistosoma*. In South Africa, the most common cause of bilharzia is *Schistosoma haematobium*. In a comprehensive cohort study, the prevalence of bilharzia in a KwaZulu-Natal primary school (children aged between 13 and 15 years old) was between 60% and 90% (Saathof et al., 2004). As bilharzia can cause growth and development retardation, the high incidence in South African children is particularly troubling. It is likely that whilst many symptoms are immediately apparent, affected children may suffer from prolonged effects of this disease later in their lives. The disease may also induce a wide variety of other chronic symptoms and complications including ulcers of the urinary tract, cancer of the urinary bladder, nutrient deficiencies and renal failure.

Schistosoma haematobium needs two types of hosts to survive: a snail intermediate host and ultimately a human host. The *S. haematobium* eggs may enter drinking water sources when an infected human host urinates or defecates near a watercourse. After hatching, the miracidia stage locates and penetrates specific snail hosts where it develops into the cercaria life stage. These are released from the snail and the cercaria penetrates the skin of a human host. In the human body, the cercaria shed their forked tail and develops into the schistosomulae stage. These migrate throughout the body and lodge in the venous plexus of the bladder where they develop into the adult *S. haematobium*, causing irritation and ulceration of the bladder, often evident as bloody urine (Levinson, 2015). Strategies for the treatment of bilharzia involve killing the worms in infected people and a number of plants have been traditionally used for this purpose. Additionally, the disease may be prevented prior to infestation by elimination of the snail hosts that are required to maintain the parasite's life cycle.

5.2. Southern African medicinal plants traditionally used to treat bilharzia

Twenty six species of southern African medicinal plants have been reported in a variety of ethnobotanical texts to be used to treat bilharzia (Table 1). Follow up investigations to determine efficacy of the plant species include a study where the schistosomules life stages of *S. haematobium* was exposed to a standard concentration of each plant extract. Assessments were done on the specimens after one and 24 hours to determine the effects of the extracts (Mølgaard et al., 2000). The study did not test against the adult stage of the parasite. Whilst this study provides information about the protective potential of these plants against infestation, it may misrepresent the therapeutic potential against bilharzia as most chemotherapeutic bilharzia treatments require delaying treatment for several days post-

infection to target the adult life stage of the parasite. Surprisingly, only one of the plant species examined in that study, *Abrus precatorius*, was confirmed as having anti-schistosomal activity (Mølgaard et al., 2000). That study investigated a panel of medicinal plant species harvested from Zimbabwe (most of which are also available and used in South Africa) against *S. haematobium*. No data is available on the anti-schistosomal activities of medical plants obtained from South Africa. As the bioactivity properties of plant species may vary substantially, dependent upon harvest location, plants harvested in Zimbabwe may have different therapeutic indications compared to those harvested in South Africa. Any possible differences may be due to the dependence of medicinal plant chemistry on factors such as climatic conditions and soil composition (Builders, 2015). In addition, four other plant species native to South Africa which are not recorded as being traditionally used to treat bilharzia were also identified as having anti-schistosomal activities in that study. These plants include *Acacia karroo*, *Maytenus senegalensis*, *Peltophorum africanum* and *Ziziphus mucronata*.

Whilst interesting, the Mølgaard et al. (2000) study only tested a single aqueous solvent for the extraction process. Water only extracts compounds of a limited range of polarity and therefore many potentially anti-parasitic compounds would have been neglected in that study. Other solvents with wider extractability ranges (e.g. ethanol, methanol, etc.) were not used. It has been suggested that for a particular medicinal plant, there may be a relationship between the type of extraction solvent used and the efficiency of the extraction process, as well as the level of biological activity of the extracts (Melariri et al., 2012). The use of the single extraction solvent may have underestimated or misrepresented inhibitory activities of the plant extracts against *S. haematobium* (Mølgaard et al., 2000). Toxicity studies were also not reported in that study. A subsequent study by a different group was undertaken to determine the safety of these plants through evaluation of their toxicity (Aremu

et al., 2012). Whilst that study provides crucial information about the toxicity of these plants, the effective extract concentrations of the plant extracts was not examined in comparison to the toxic concentrations. It is therefore not possible to compare therapeutic and toxic doses.

6. Intestinal parasitic infections

6.1. Worms and helminths

A number of common intestinal worms which affect humans are prevalent in southern Africa. These include *Ascaris lumbricoides*, *Taenia solium* and *Taenia saginata* (Coral-Almeida and Gabril, 2015). These diseases are most common in rural areas and are particularly prevalent in children. Indeed, a recent study estimated that between 70% and 100% of children of school-going age in rural Kwa-Zulu-Natal, South Africa are infested with intestinal worms (Nxasana et al., 2015). The infested children are likely to suffer from anaemia, as well as mental and physical problems (Tsoka-Gwegweni and Ntombela, 2014). In pregnant women, intestinal parasites may also cause lethargy, anaemia, a weakened immune system and a resulting susceptibility to infections (Tsoka-Gwegweni and Ntombela, 2014). The maternal problems

Table 1 Southern African plants used traditionally to treat bilharzia.

Plant species	Common name(s)	Fa mil y	Tradi tional uses	Plant part used	Re fer enc e
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Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Abrus precatorius</i> L. subsp. <i>africanus</i> Verdc.	Bead vine, coral bean, crabs eye, licorice vine, red bean vine, weather vine (English), amabope (Ndebele), nsimani (Shangaan), umkhokha (Zulu)	Leguminosae	Bilharzia and intestinal worms	Roots and seeds	Hutchings et al., 1996
<i>Afzelia quanzensis</i> Welw.	Pod mahogany, lucky bean tree (English), peulmahonie (Afrikaans), iNkehli (Zulu)	Leguminosae	Bilharzia	Roots	Hutchings et al., 1996
<i>Antidesma venosum</i> E.Mey. ex Tul.	Tasselberry (English), voëlsitboom (Afrikaans), modulane (Sotho), isiBangamlotha	Euphorbiaceae	Bilharzia and malaria	Roots and leaves	Hutchings et al., 1996
<i>Boswellia carteri</i> Birdw.	Frankincense (English), olibanum	Burseraceae	Bilharzia and stomach ache	Resin	Watt and Breyer - Brand

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					wijk, 1962
<i>Berkheya speciosa</i> (DC.) O.Hoffm.	Unknown	Asteraceae	Bilharzia	Root	Hutchings et al., 1996
<i>Cassia abbreviata</i> Oliver subsp. <i>Beareana</i> (Holmes) Brenan	Long-tailed cassia (English), sambokpeul (Afrikaans)	Leguminosae	Bilharzia and black water fever	Roots	Von Koenen, 1996
<i>Cissampelos murconata</i> A. Rich.	Hairy heartleaf, heart-leaved vine (English), Davidjies, Davidjieswortel (Afrikaans), umbombo (Zulu), nyakuta, ruzambu (Shona)	Menispermaceae	Bilharzia, malaria and scabies	Rhizomes and roots	Hutchings et al., 1996
<i>Euclea divinorum</i> Hiern.	Magic guarri (English), towerghwarrie (Afrikaans), Mohlakola (Sotho), umhlangula, ubophanyamazane, umncafuzana (Zulu), umdlelanyamatane (Swati),	Ebenaceae	Bilharzia	Roots and bark	Hutchings

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
	nhlangula (Tsonga), Mutangule (Venda)	e			s et al., 1996
<i>Euclea natalensis</i> A. DC.	Natal gaurri, Natal ebony, large leaved gaurri (English), Natalghwarrie, berggwarrie, swartbasboom (Afrikaans), umTshekisani, umKhasa (Xhosa), iDungamuzi, iChitamuzi, umZimane, umTshikisane, inKunzane, (Zulu), umHlangula (Tsonga)	Ebenaceae	Bilharzia	Roots and bark	Hutchings et al., 1996
<i>Faurea saligna</i> Harv.	Willow beechwood, African beech (English), Bosvelsboekenhout (Afrikaans), iSefu, umCalathole (Zulu), isiDwadwa, umOnyeli (Ndebele), mohlako, mongena (Sotho), muTango (Venda)	Proteaceae	Bilharzia	Leaves	Manganyi and Mukanganayama, 2011; Hutchings et al., 1996

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Macaranga kilimandscharica</i> Pax.	Unknown	Euphorbiaceae	Bilharzia	Root	Watt and Breyer - Brandwijk, 1962
<i>Maytenus senegalensis</i> (Lam.) Excell.	Confetti tree, red spike-thorn (English), isihlangu (Ndebele), chivhunabadza, chizhuzhu, mugaranjiva, mukokoba, musosaguva, mutotova (Shona), ubuhlangwe, isihlangu, isihlangwane (Zulu)	Celastraceae	Bilharzia	Roots and leaves	Dasilva et al., 2011; Hutchings et al., 1996
<i>Mondia whitei</i> Skeels	White's ginger, tonic root (English), umondi, mundi, mindi (Zulu)	Asclepiaceae	Bilharzia	Roots	Hutchings

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		dac eae			s et al., 19 96
<i>Ocimum americanum</i> L.	Basil (English)	La mi ace ae	Bilhar zia	Leaf	Wa tt and Bre yer - Bra nd wij k, 19 62
<i>Ocimum canum</i> Sims	Wild basil (English)	La mi ace ae	Bilhar zia	Leav es and flowe rs	Vo n Ko ene n, 19 96
<i>Ormocar pum trichoca rpum</i> (Taub.) Engl.	caterpillar-pod (English) Mupotanzou (Shona)	Le gu mi nos ae	Bilhar zia	Pod	Wa tt and Bre yer -

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Brandwijk, 1962
<i>Pterocarpus angolensis</i> DC.	Bloodwood, wild teak, Transvaal teak (English), kiaat, bloedhout, grienhout (Afrikaans), morôtô (Sotho), mokwa, morotômadi (Tswana), umVangazi, umbilo (Zulu)	Leguminosae	Bilharzia	Bark	Hutchings et al., 1996
<i>Protaspargus buchanaanii</i> (Baker) Oberm.	Wild asparagus (English), Iufhaladzmakole (Venda)	Asparagaceae	Bilharzia	Roots and leaves	Von Koenen, 1996
<i>Rhus gueinzii</i> Sond	Thorny Karee (English)	Anacardiaceae	Bilharzia	Roots	Watt and Breyer-Brandwijk

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					k, 1962
<i>Rumex lanceolatus</i> Thunb.	Common dock (English), idolo lenkonyane (Zulu), idolonyana (Xhosa), khamane, kxanane, molokoli (Sotho)	Pol yg onacea	Bilharzia, internal parasites and intestinal worms	Roots (mainly) and leaves	Von Koenen, 1996
<i>Rumex nepalensis</i> Spreng.	Nepal Dock (English)	Pol yg onacea	Bilharzia	Leaf	Watt and Breyer - Brandwijk, 1962
<i>Sclerocarya birrea</i>	Marula (English), morula (Sotho), mufula (Venda), ukanyi (Tsonga)	Anacardi	Bilharzia and	Root and bark	Hutchings

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
(A.Rich.) Hochst. subsp. <i>caffra</i>		aceae	malari		s et al., 1996; Von Koenen, 1996
<i>Tephrosia macropoda</i> Harv.	Fish bean, fish-poison bean (English), visbbontjie, visboontjebossie, visboontjehout, vishoutbossie (Afrikaans), ilozana, ugwengu, (Zulu), Intozane (Xhosa)	Leguminosae	Direct treatment of bilharzia as well as control of snail populations (and thus prevention of the diseases	Roots	Watt and Breyer - Brandwijk, 1962

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
			e). Also used as a general parasiticide		
<i>Terminalia phanero- phlebia</i> Engl. & Diels	Lebombo cluster-leaf (English), lebombotrosblaar (Afrikaans), amaNgwe-amnyama, amaNgwe-omphofu (Zulu), mambonjwane (Swati)	Combretaceae	Bilharzia	Powdered roots mixed with <i>Mylabris</i> beetle	Hutchings et al., 1996
<i>Ximenia americana</i> L. var. <i>americana</i>	Hog plum, wild plum, false sandalwood, seaside plum, small sour plum (English), kleinsuurpruim (Afrikaans)	Oleaceae	Bilharzia and trypanosomiasis	Roots and leaves	Hutchings et al., 1996

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Ximenia caffra</i> Sond.	Large sourplum (English), grootsuurpruim (Afrikaans), unThunduluka-obmvu (Zulu), morokologa (Sotho)	Oleaceae	Bilharzia	Roots and leaves	Hutchings et al., 1996

may result in low birth weight infants, who are also susceptible to infections and have developmental problems (Tsoka-Gwegweni and Ntombela, 2014). *Taenia solium* can be transmitted by eating poorly cooked infected pork (Coral-Almeida and Gabriël, 2015). The cysts can lodge in the brain, or elsewhere, and cause epilepsy or other clinical conditions, whose severity will depend on the location (Coral-Almeida and Gabriël, 2015). *Taenia saginata* follows a similar pattern, but is relatively rare in South Africa and is transmitted by eating poorly cooked infected beef (Gbueloh, 2015). *Ascaris lumbricoides*, *Giardia duodenalis* and *Entamoeba histolytica* cysts can be transmitted by contaminated fruit, vegetable, drinking water, or any other oral-faecal means (World Health Organisation, 2010).

6.1.1. Southern African plants traditionally used to treat intestinal worms and helminth in humans

More than 80 plant species have been described as being used to treat general helminthiasis. *Clerodendrum glabrum* E. Mey. (Lamiaceae) is the only medicinal plant recorded as a specific treatment against *Enterobius vermicularis* (pinworm/threadworm) infections.

Despite the number of plants with recorded ethnobotanical uses against gastrointestinal worms and helminths, no rigorous studies have yet evaluated the activity of South African medicinal plants against specific human intestinal worms. Instead, previous research has relied on the use of model organisms as a substitute for these parasites. Most studies have used the free living (non-parasitic) nematode *Caenorhabditis elegans* as a helminth model to represent human intestinal worms. *Acorus calamus*, *Cotyledon orbiculata* var. *orbiculata*, *Cyathea dregei*, *Melia azedarach* and *Tulbaghia violacea* have all been reported to have activity against *C. elegans* (Aremu et al., 2012). Whilst *C. elegans* represents a wide variety of helminths and is preferred by many researchers, its susceptibilities are not entirely consistent with human parasitic helminths and this model system has not previously been very successful in discovering new treatments (Aremu, 2009; Aremu et al., 2012;). Those authors defined a minimum lethal concentration (MLC) of <16.67 mg/mL against *Caenorhabditis elegans* as indicative of anthelmintic activity. They did not specify minimum toxicity requirements for the criteria in those studies, so the suitability of the plant extracts for human treatment is not clear. *Acorus calamus* and *Hypoxis colchicifolia* have been reported to have high anthelmintic activities (McGaw et al., 2000; Aremu, 2009). Lower levels of anthelmintic activity were reported for *Aloe marlothii*, *Artemisia afra*, *Brachylaena discolor*, *Ricinus communis*, *Trema orientalis* and *Tulbaghia violacea* (McGaw et al., 2000). The type of extraction solvent was also found to influence the level of anthelmintic activity of plant extracts. Water extracts were more active than ethanol extracts, while hexane extracts were the least active.

When considering regimens for treatment and eradication of gastrointestinal parasite infections in humans, it is necessary to consider that many of these parasites are zoonotic, often with a portion of their lifecycle in one or more intermediate hosts, as well as the manifestations in the human host. Whilst the life stages may differ between species, all helminths have three main life cycle stages: egg, larvae and adult. Adult worms infect definitive hosts, although many are zoonotic and can infect multiple hosts. Thus, even when a parasite no longer infects a human population, it may remain as a ready reservoir in other animal populations. The larval stage may be free living for some helminths, but they often parasitise other intermediate hosts. Eggs may be produced within one host, released and infect a host of a different species. Therefore, when considering treatment and eradication programs for intestinal worms and helminths, it is important to consider treatment in domestic animals, livestock and wild animal populations. Veterinary deworming programs are recommended to help prevent human infestations.

Table 2 Southern African plants used traditionally to treat intestinal worm and helminth infections.

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Acacia sieberiana</i> DC. var. <i>woodii</i> (Burt Davy) Keay & Brenan	Paperbark thorn (English), papierbasdoring (Afrikaans), mphoka (Sotho), umNganduzi (Swati), mokha, morumosetlha (Tswana), musaunga (Venda), umKhamba (Zulu), nkowankowa (Tsonga)	Leguminosae	General vermifuge and taenifuge	Leaves	Hutchings et al., 1996
<i>Acokanthera oblongifolia</i>	Dune poison bush (English), duinegifboom, kaffergifboom	Apocynaceae	Anthelmintic	Leaves, roots and	Hutchings

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
(Hochst.) Codd	(Afrikaans), umhlagashiso, inHlungunyembe (Zulu), iNxinebe, iNtlungunyembe (Xhosa)	cy na ce ae		twigs	ing s et al., 19 96
<i>Acokanthera oppositifolia</i> (Lam.) Codd	Bushman's poison (English), boesmansgif (Afrikaans), inHlungunyembe (Zulu), iNtlungunyembe (Xhosa)	A po cy na ce ae	Tapeworm	Leaves, roots and twigs	Hu tch ing s et al., 19 96
<i>Acorus calamus</i> L.	Sweet flag (English), makkalmoes (Afrikaans), iKakamuzi (Zulu)	Ac or ac ea e	Anthelminti c	Rhizomes	Hu tch ing s et al., 19 96
<i>Acrotome inflata</i> Benth.	Unknown	La mi ac ea e	Anthelminti c	Whole plant	Vo n Ko en en, 19 96

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Agrimonia bracteata</i> E. Mey. ex C.A.Mey	Agrimony (English), misinoana (Sotho)	Rosaceae	Tapeworm	Leaves	Hutchings et al., 1996; Felhaber 1997
<i>Agrimonia eupatoria</i> L.	In- Nyinga	Rosaceae	Tapeworm	Leaves or roots	Smith, 1895
<i>Albizia adianthifolia</i> W.	Flat-crown albizia (English), platkroon (Afrikaans), umgadankawu, iGowane, umNalahanga, umNebelele, uSotho (Zulu), umHlandlothi (Xhosa)	Leguminosae	General use against internal worms	Bark	Hutchings et al., 1996; Wattan

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Br ey er- Br an dw ijk, 19 62
<i>Albizia anthelmintica</i> Brongn.	Worm-cure albizia (English), munanzwa (Shona)	Leguminosae	General anthelmintic with documented success against tapeworm in humans	Bark	Hutchings et al., 1996; Von Koenen, 1996; Watt and

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Br ey er- Br an dw ijk, 19 62
<i>Albizia lebbeck</i> (L.) Benth.	Lebbeck tree (English), Lebbeckboom (Afrikaans)	Legu mi no sa e	Roundworm	Bark	Hu tch ing s et al., 19 96; Vo n Ko en en, 19 96; W att an d Br

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					ey er- Br an dw ijk, 19 62
<i>Albizia veriscolor</i> Welw. ex Oliv.	Poison-pod albizia, large leaved false thorn (English)	Leguminosae	Anthelmintic	Roots and bark	Von Ko en en, 19 96
<i>Aloe tenuior</i> Haw.	i-kalana	Alloaceae	Tapeworm	Root	Smith, 18 95
<i>Amaranthus thunbergii</i> Moq.	Thepe-ea-Lesotho (Sesotho)	Amaranthaceae	Vermifuge	Leaves	Mote ete e an d Van W

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Yk, 2011
<i>Artemisia afra</i> Jacq. ex Willd	Lengana (Sesotho)	Asteraceae	Intestinal worms	Leaves	Moteete and Van Wyk, 2011
<i>Aster bakeranus</i> Burt Davy ex C. A. Sm	Phoa (Sotho), unozixekana (Xhosa), udlutshana (Zulu), Phoa (Sesotho)	Asteraceae	Intestinal worms	Roots	Watt and Breyer-Brandwijk, 1962; Van

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					n W yk et al., 20 09; Sel ete ng Ko se et al., 20 15
<i>Aster erigeroides</i> Harv.	White heath aster, white aster (English)	As ter ac ea e	General use against intestinal worms.	Leaves	W att an d Br ey er- Br an dw ijk, 19 62

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Bauhinia galpinii</i> N.E.Br.	Mutswiriri	Leguminosae	Roots are boiled and the mixture drank for treating stomach worms	Roots	Mahwa et al., 2013
<i>Brachylaena discolor</i> DC.	Coastal silver oak (English), kusvaalbos (Afrikaans), phahla (Zulu), mphahla (Sotho), umPhahla (Xhosa)	Asteraceae	Roundworm	Leaves	Hutchings et al., 1996; Bryant, 1966
<i>Bridelia ferruginea</i> Benth	South African names unknown	Euphorbiaceae	Roundworm	Bark	Hutchings et al., 19

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					96
<i>Bridelia micrantha</i> Baill.	Mitseeri, bruin stinkhout (Afrikaans), ndzerhe (Tswana), motsere (Sotho)	Euphorbiaceae	Tapeworm	Bark (mainly) and root	Hutchings et al., 1996
<i>Callilepis laureola</i> DC.	Ox-eye daisy (English), wildemargriet (Afrikaans), amafuthomhlaba, ihlamvu, implia (Zulu)	Asteraceae	Tapeworm	Roots	Hutchings et al., 1996
<i>Capsicum annum</i> L.	Ikhanakhana (Xhosa), Pelepele (Xhosa), chilli pepper (English)	Solanaceae	Deworming	Fruits	Asowata - Ayodele et al., 2016

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Celosia trigyna</i> L.	Silver spinach (English)	Amaranthaceae	Roundworm and tapeworm	Leaves	Hutchings et al., 1996
<i>Cheilanthes hirta</i> Sw.	Lip fern (English)	Adiantaceae	Tapeworm	Rhizomes	Hutchings et al., 1996; Von Koenen, 1996
<i>Chenopodium album</i> Bathua	Lambsquarters, white goosefoot, fat hen, pig weed (English)	Adiantaceae	Removal of sandworms	Whole plant	Hutchings et al.,

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					1996
<i>Chenopodium ambrosioides</i> Hance	Wormseed, Jesuit's tea (English)	Chenopodiaceae	Tapeworm and hookworm	Whole plant	Hutchings et al., 1996; Von Koenen, 1996
<i>Clausena anisata</i> (Willd.) Hook. F.	Horsewood (English), perdepis (Afrikaans)	Rutaceae	Tapeworm	Roots and leaves	Hutchings et al., 1996
<i>Clematis brachiata</i> Thunb.	Travellers joy, old man's beard, wild clematis (English), klimop, lemoenbloeisels (Afrikaans), ityolo	Ranunculaceae	Roundworm	Leaves, roots and stems,	Von Koenen

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
	(Xhosa), mogau Tswana), morara (Sotho), umDlonzo (Zulu), morara- oa-thaba (Sesotho)	ul ar ac ea e		vermifuge	en en, 19 96; M ote ete e an d Va n W yk, 20 11
<i>Clerodendrum glabrum</i> E.Mey.	Tinderwood (English), tontelhout (Afrikaans), moswaapeba (Sotho), munukha-tshilongwe (Venda), umqwaqwanam (Xhosa), umQoqonga (Zulu), xinhunwelanbeva (Tswana)	La mi ac ea e	General use against intestinal parasites, particularly roundworm and tapeworm. Used to repel parasites from wounds	Leaves	W att an d Br ey er- Br an dw ijk, 19 62;

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Von Koenen, 1996
<i>Combretum molle</i> R. Br. ex G. Don	Velvet bush willow, velvet leaf willow (English), fluweelboswilg, basterrooibos (Afrikaans), mokgwethe (Sotho), xikhukhutsane (Tsonga), modubatshipi, moduba (Tswana), mugwiti (Venda), umBondwe-omhlope (Zulu)	Combretaceae	Hookworm	Root infusions (mainly) and leaves	Hutchings et al., 1996; Corrigan et al., 2011
<i>Cotyledon orbiculata</i> L.	Plakkie (Afrikaans), pigs ears (English), imphewula (Xhosa), seredile (Sotho)	Crasulaceae	Used as a vermifuge	Leaf	Van Wyk et al.,

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					2009
<i>Crassula peplodes</i> Harv.	Mo-ora-metsi (Sesotho)	Crassulaceae	Vermifuge	Roots	Moteete and Van Wyk, 2011
<i>Cussonia paniculata</i> Eyckl. & Zuyh.	Mountain cabbage tree (English), bergkiepersol (Afrikaans), umsenge (Xhosa), umsengembuzi (Zulu)	Araliaceae	General use against internal parasites	Root, stem and fruit	Watt and Brandwijk, 1962
<i>Cymbopogon marginatus</i>	Lemon scented grass (English)	Poaceae	General use against	Roots	Hutch

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
Stapf ex Burt Davy		ea e	internal parasites		ing s et al., 19 96
<i>Cystopteris fragilis</i> Bernh.	lehōrōmetso	W oo dsi ea ce ae	De- worming (mixed with other plants)	Rhizomes	M ote ete e an d Va n W yk, 20 11
<i>Dialium schlechteri</i> Harms	Sherbet tree (English), zulu podberry (English), zoeloepeulbessie (Afrikaans), umThiba (Zulu), ensiba (Tsonga)	Fa ba ce ae	Ingested to stop anus from itching (possible de- wormer?)	Roots	Co rri ga n et al., 20 11
<i>Dicoma anomala</i> Sond. subsp.	Hloenya (Sesotho)	As ter ac	Intestinal worms	Roots and leaves	W att an

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
anomala		ee			d Br ey er- Br an dw ijk, 19 62; M ote ete e an d Va n W yk, 20 11
<i>Diospyros austro-africana</i> De Winter	Jakkalsbos (Afrikaans)	Ebenaceae	Ringworm	Leaves	Va n W yk et al., 20

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					08
<i>Diospyros villosa</i> (L.) de Winter var. <i>parvifolia</i> (De Winter) De Winter	Inyamyempunzi (Zulu)	Ebenaceae	Treats gastrointestinal complaints, worms, and flatulence	Roots	Philaender, 2011
<i>Ekebergia capensis</i> Sparrm.	Cape ash dogplum (English), essenhout (Afrikaans), mmidibidi (Sotho), umNyamatsi (Swati), nyamaru (Tswana)	Meliaceae	Purgative parasiticide	Leaves and bark	Hutchings et al., 1996
<i>Embelia ruminata</i> (E.Mey.ex A. DC.) Mez	False black pepper (English), white-flowered Embelia (English)	Primulaceae	Tapeworm	Leaves	Hutchings et al., 1996; Van Wyk

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					et al., 2009
<i>Ethulia conyzoides</i> L.F.	Carter's curse (English)	Asteraceae	Roundworm	Aerial parts	Hutchings et al., 1996; Von Koenen, 1996; Watt and Breyer-Brandw

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					ijk, 1962
<i>Eulophia welwitschii</i> (Rchb.f.) Rolfe	Makhōlela (Sesotho)	Orchidaceae	Vermifuge	Not provided	Moteete and Van Wyk, 2011
<i>Fagara capensis</i> Thunb.	Small knobwood (English), umhungwane, umnungumabele (Ndebele), chikafusi, mudzanganyia, muritsa (Shona), umLumamabele (Zulu)	Rutaceae	General use against intestinal worms	Bark and leaves	Watt and Breyer-Brandwijk, 1962
<i>Gerbera</i>	Gerbera (English), botterblom,	As	Tapeworm,	Leaves or	Hu

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>ambigua</i> Sch. Bip.	griekwateebossie (Afrikaans), moarubetso (Sotho), ucabazane (Zulu)	teracaeae	vermifuge	whole plant	Hutchings et al., 1996; Motete et al. and Van Wyk, 2011
<i>Gerbera piloselloides</i> Cass.	Cobweb Afrodaisy (English), swartee, swartteebossie (Afrikaans), moarubetso, mothuntsetso (Sotho), ubulawu (Xhosa), indlebeyempithi, uhlango olimpofu, umoya-wezwe (Zulu)	Asteraceae	Tapeworm	Leaves	Hutchings et al., 1996
<i>Gunnera perpensa</i> L.	Qobo (Sesotho)	Gun	Vermifuge	Not specified	Mote

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		neraceae			ete e an d Va n W yk, 20 11
<i>Helichrysum caespititium</i> (DC.) Harv.	Phateeangaka (Sesotho)	Asteraceae	Cleanses intestines of worms	Whole plant	W att an d Br ey er- Br an dw ijk, 19 62; Sel ete ng Ko se et

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					al., 20 15
<i>Heteromorph a arborescens</i> Cham. & Schltdl. var. <i>abyssinica</i> (A.Rich.) H.Wolff	Monkhoane (Sesotho)	A pi ac ea e	Intestinal worms in children	Leaves	M ote ete e an d Va n W yk, 20 11
<i>Hibiscus trionum</i> L.	Bladderweed, flower of an hour (English)	M al va ce ae	Roundworm	Aerial parts	Vo n Ko en en, 19 96
<i>Indigofera frutescens</i> L.F.	River indigo (English), kouebos, ertjiesbos (Afrikaans)	Le gu mi no sa e	Roundworm	Leaves	Hu tch ing s et al., 19

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					96
<i>Kalanchoe thyrsiflora</i> Harv.	Serelile (Sesotho)	Crassulaceae	Intestinal worms and as a vermifuge	Roots	Moteete and Van Wyk, 2011
<i>Leucosidea sericea</i> Eckl. & Zeyh.	Oldwood (English), ouhout (Afrikaans), umTshitshi (Zulu), umTyityi (Xhosa), Mošino (Northern Sotho), Munyonga-tshifumbu (Venda)	Rosaceae	Expelling parasitic worms and as a vermifuge	Leaves and stem	Mafole et al., 2017
<i>Leonotis leonurus</i> (L.) R. Br.	Wild dagga, lions ear (English), wildedagga, duiwelstabak (Afrikaans), imvovo, utywala-bengcungcu, umfincafincane, umunyamunya (Xhosa), umfincafincane, umcwili, imunyane, utshwala-bezinyoni (Zulu)	Lamiaceae	Tapeworm	Leaves and Flowers	Smith, 1895; Hutchings

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					et al., 1996
<i>Lonchocarpus capassa</i> Rolfe	Apple-leaf (English), Appelblaar (Afrikaans), umBhandu, umPhanda, isiHomohomo (Zulu)	Leguminosae	Hookworm	Root	Hutchings et al., 1996
<i>Malva parviflora</i> L.	Cheeseweed, marshmallow, small mallow, bread-and-cheese (English), kasieblaar, brood-en-botter, kasies (Afrikaans)	Malvaceae	Tapeworm	Roots and leaves	Von Koenen, 1996
<i>Melhania acuminata</i> Masters var. <i>acuminata</i>	Bushy honeycup (English), mokhana, murupe (Tswana)	Steruliaceae	General use against intestinal worms	Aerial parts	Von Koenen, 1996
<i>Melia azedarach</i> L.	Persian lily, bead tree, Cape lilac, China berry, white cedar (English), maksering, sering, bessieboom	Meliaceae	Roundworm	Drupes and bark	Wattan

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
	(Afrikaans), umsilinga (Zulu)	ea e			d Br ey er- Br an dw ijk, 19 62
<i>Myrsine africana</i> L.	Moroka-pheleu (Sesotho)	M yr sin ac ea e	Anthelminti c, ringworm	Branches	W att an d Br ey er- Br an dw ijk, 19 62; Sel ete ng Ko se et

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					al., 2015
<i>Oxalis smithii</i> Sond.	Um-Muncwane	Oxalidaceae	Tapeworm	Bulb	Smith, 1895
<i>Pelargonium sidoides</i> DC.	Khoara (Sesotho)	Geraniaceae	Worms	Roots	Watt and Breyer-Brandwijk, 1962; Seling Koese et al.,

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					2015
<i>Phytolacca dodecandra</i> L'Herit	Soap berry, endod, gopo berry (English)	Phytolaccaceae	Tapeworm	Fruit and roots	Hutchings et al., 1996
<i>Polystichum pungens</i> (Kaulf.) C.Presl	Lehōrōmetso (Sesotho)	Dryopteridaceae	Vermifuge	Rhizomes	Moteete and Van Wyk, 2011
<i>Pterocarpus angolensis</i> DC.	Bloodwood, wild teak, Transvaal teak (English), kiaat, bloedhout, grienhout (Afrikaans), morôtô (Sotho), mokwa, morotômadi (Tswana), umVangazi, umbilo (Zulu)	Leguminosae	General use against intestinal worms	Bark	Watt and Breyer-

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Brandwijk, 1962
<i>Pittosporum viridiflorum</i> Sims	Cheesewood (English)	Pittosporaceae	Worms	Bark	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Madi

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					kizela and McGaw, 2017
<i>Punica granatum</i> L.	granaat (Afrikaans), pomegranate (English)	Lythraceae	Tapeworm	Root bark and in combination sometimes with stem bark and leaves	Van Wyk et al., 2009
<i>Rumex eckloni</i> Meisn.	i-dolo lenkonyana, calfs knee (English)	Polygonaceae	Tapeworm	Root	Smith, 1895
<i>Rumex lanceolatus</i> Thunb.	Common dock (English), idolo lenkonyane (Zulu), idolonyana (Xhosa), khamane, kxanane, molokoli (Sotho)	Polygonaceae	General use against intestinal worms.	Root	Von Koenen,

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		ae			1996
<i>Rumex nepalensis</i> Spreng.	Nepal dock, sorrel (English)	Polygonaceae	General use against intestinal worms.	Root and leaves	Watt and Breyer-Brandwijk, 1962
<i>Ruta graveolens</i> L.	Wynruit (Afrikaans), wynruik (Afrikaans),	Rutaceae	General use against intestinal worms.	Leaf	Nortje and Van Wyk, 2015
<i>Sansevieria aethiopica</i> Thunb	Aambeiwortel (Afrikaans), ghaiwortel (Khoi)	Asparagus	Decoction for intestinal	Rhizomes	Van W

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		garceae	worms		Yk, 2008
<i>Sansevieria hyacinthoides</i>	Aambeiwortel (Afrikaans), ghaiwortel (Khoi), piles root (English), isikholokotho (Zulu)	Asparagaceae	Intestinal worms	Not specified	Van Wyk et al., 2009
<i>Sansevieria thyrsiflora</i> Thunb.	Isi-kolokoto	Asparagaceae	Tapeworm	Root	Smith, 1895
<i>Salvadora persica</i> L.	Mustard tree, South African toothbrush tree	Salvadoraceae	Hookworm	Root	Von Koenen, 1996
<i>Satyrium bracteatum</i> (L.f.) Thunb	ubani lwenkangala	Orchidaceae	Intestinal worms	Information not provided	Chinsamy et

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		e			al., 2011
<i>Securidaca longepedunculata</i> Fresen.	Violet tree (English), krinkhout (Afrikaans), mpesu (Venda), mamba (Tswana)	Polycogonaceae	Tapeworm	Roots and bark	Von Koenen, 1996
<i>Strychnos henningsii</i> Gilg.	Natal teak, coffee-bean strychnos, walking stick (English), koffiehardepeer (Afrikaans), umqalothi, umnono, umdunye (Zulu)	Loganiaceae	Tapeworm	Roots (mainly), bark and fruit	Hutchings et al., 1996; Bryant, 1966.
<i>Suregada zanzibariensis</i> Baill.	Sand canary-berry (English), Sand-kanariebessie (Afrikaans), ikhushwane elikhulu, umdlankawu (Zulu)	Euphorbiaceae	Hookworm	Roots and bark	Hutchings et al.,

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
		e			1996
<i>Teclea natalensis</i> (Sond.) Engl.	UmOzane	Rutaceae	To kill worms in the baby's teeth	Fruit	Corriگان et al., 2011
<i>Tulbaghia alliacea</i> L.f.	Wilde knoflook (Afrikaans)	Alliaceae	Infusion used to treat intestinal worms	Root bulb	Van Wyk, 2008; Philander, 2011
<i>Trema orientalis</i> Linn. Blume	Trema, pigeon wood (English), hophout (Afrikaans), umVumvu, umVangazi, uPhakane (Xhosa), makuru-kuru (Venda), modutu (Sotho), umSekeseke, umBhangabhanga, ifamu, iphubane, ubathini, umVangazi (Zulu)	Ulmaceae	Roundworm and hookworm	Root bulb	Hutchings et al., 19

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					96
<i>Urginea macrocentra</i> Baker (also known as <i>Drimia macrocentra</i> (Baker))	Poison snakehead (English), Natal slangkop (Afrikaans), injoba (Xhosa), isiklenama (Zulu)	Hyacinthaceae	Roundworm and tapeworm	Root bulb	Hutchings et al., 1996
<i>Vangueria infausta</i> Burch. subsp. <i>infausta</i>	Wild medlar (English), wilde mispel (Afrikaans), mmilo (Sotho), muzwilu, mavelo (Venda), unVilo (Xhosa), umbizio, umViyo (Ndebele), mmilo, mothwanye (Tswana), unViyo, umTulwa (Zulu)	Rubiaceae	Roundworm	Roots and leaves	Von Koenen, 1996
<i>Withania somnifera</i> (L.) Dunal	Mofera-ngope (Sesotho)	Solanaceae	Ringworm, worms introduced into the body by witchcraft	Roots, bark, leaves	Watt and Breyer-Brandwijk, 1962;

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					Van Wyk et al., 2009, Motete et al. and Van Wyk, 2011
<i>Ximenia caffra</i> Sond.	Sour plum, Wild plum (English)	Ximeniaceae	Intestinal worms	Leaves, roots	Marozi, 2016

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Xysmalobium parviflorum</i> Harv. ex Scott-Elliot	leoto-la-khoho (Sesotho)	Apocynaceae	Vermifuge in children, intestinal worms	Roots	Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 2009, Motete et al. and Van

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
					W yk, 20 11
<i>Zanthoxylum capense</i> (Thunb.) Harv	amaBelentombi; Umnungu mabele (Sotho)	Rutaceae	Used as an ingredient in purgative parasiticides and stomach complaints	Leaves	Br ya nt, 19 66

6.2. Gastrointestinal protozoal parasites

Human gastrointestinal protozoal parasites are generally classified within four general groups: Sarcodina (e.g. *Entamoeba* spp.), Mastigophora (e.g. *Giardia* spp), Sporozoa (e.g. *Cryptosporidium* spp.) and Ciliophora (e.g. *Balantidium* spp.). As all of these parasites are generally associated with the consumption of contaminated food and water, communities without access to effective sanitation are at the greatest risk. Of these parasites, *Giardia duodenalis* (the pathogen which causes giardiasis in humans) and *Entamoeba histolytica* (the cause of amoebiasis) have the greatest impact on human health in South Africa (Coral-Almeida and Gabriël, 2015). Giardiasis and amoebiasis can be difficult to diagnose as the symptoms of both diseases are similar to those of a number of bacterial, viral and other protozoal illnesses. Both pathogens cause diarrhoea and may be mistaken for other illnesses.

Thus, it is difficult to obtain definitive information about traditional medicines used to treat these illnesses. Instead, most records document treatments for the symptom, diarrhoea.

As for bilharzia and gastrointestinal worms, the *E. histolytica* and *G. duodenalis* parasites are zoonotic. Thus, whilst both allopathic and traditional medicines may be effective for the treatment of these diseases, any prevention and/or eradication strategy should also consider eradication in intermediate animal hosts. If only the human hosts suffering from the disease are considered, it is likely that reinfection will occur from intermediate animal hosts, continuing the infection cycle.

6.2.1. Amoebiasis (*Entamoeba histolytica*)

This disease is prevalent globally and in southern Africa. The World Health Organisation (WHO) has estimated that there are over 500 million *E. histolytica* carriers worldwide and annual mortalities are in the tens of thousands (World Health Organisation, 2010). The disease is usually self-limiting and sufferers often do not seek medical assistance, instead opting to let the disease run its course. For this reason, regional incidence statistics are difficult to compile (World Health Organisation, 2010). In most cases, *E. histolytica* infection is confined to the gastrointestinal tract and causes amoebic dysentery. However, in some individuals, the parasite may breach the lining of the gastrointestinal tract and contaminate the blood stream. When systemic infection occurs, the parasite may form abscesses in several tissues including the lungs, liver and brain. Such extra-gastrointestinal manifestations are most common in malnourished and immunocompromised individuals, as well as in pregnant women (World Health Organisation, 2010).

Most plant species used to treat gastrointestinal disorders have been reported based on their usage to treat diarrhoea and dysentery, rather than as treatments for specific pathogens.

Only four South African plant species have been definitively identified as traditional treatments for amoebiasis (Table 3). *Gymnosporia buxifolia* Szysz., *Gymnosporia heterophylla* Eckl. & Zeyh. Robson, *Lablab purpureus* L. and *Uapaca kirkiana* Milli Arg are recorded as treatments for amoebic dysentery in humans, although the ethnobotanical records are incomplete and in most cases, the plant part use is not known (Watt and Breyer-Brandwijk, 1962; Von Koenen, 1996).

It is likely that other plant species described as therapies for diarrhoea and dysentery may also have been used as treatments for amoebiasis and several studies have reported the activity of South African plants traditionally used to treat diarrhoea against *E. histolytica*. One study reported that the ethanol extracts had greater activity against the parasite than the water extracts (McGaw et al., 2007). The authors of that study did not define the criteria that need to be met for plant extracts to be classified as anti-*E. histolytica* drug leads. However, they concluded that extracts prepared from *Acorus calamus* L., *Albizia adianthifolia* (Schumach.) W.F.Wight, *Deinbollia oblongifolia* (E.May. ex. Am.) Radlk. and *Sclerocarya birrea* (A.Rich.) Hochst. were good inhibitors of *E. histolytica* (McGaw et al., 2007). Unfortunately, toxicology evaluations were not undertaken in that study, making it difficult to determine the safety of these extracts at their effective doses and further research is required in this field. Many other plant species which were used to treat diarrhoea are yet to be tested against *E. histolytica* and still much work is required. A number of comprehensive studies record South African plant species used to treat diarrhoea (Samie et al., 2009; Madikizela et al., 2012; Okem et al., 2012; Ahmed et al., 2012; Van Vuuren et al, 2015) and these may form useful starting points for future anti-*E. histolytica* studies.

Table 3 Southern African plants used traditionally to treat amoebiasis.

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Gymnosporia buxifolia</i> Szysz	Gifdoring, Lemoendoring, (Afrikaans), iligqwangane (Zulu), rnopasu (Northern Sotho), n1utotova (Shona), umhlangwe (Xhosa)	Celastraceae	amoebic dysentery	Not given	Watt and Breyer-Brandwijk, 1962
<i>Gymnosporia heterophylla</i> (Eckl. & Zeyh.) Robson	Common spike-thorn (English)	Celastraceae	amoebic dysentery	Not given	Von Koenen, 1996
<i>Lablab purpureus</i> L.	hyacinth bean	Fabaceae	amoebic dysentery	Root	Von Koenen, 1996
<i>Uapaca kirkiana</i> Milli Arg	Wild loquat (English), ilihobohobo (Ndebele), mujanJe (Shona)	Phyllanthaceae	amoebiasis	Not given	Watt and Breyer-Brandwijk, 1962

6.2.2. Giardiasis

Giardiasis is a debilitating gastrointestinal disease caused by the protozoan parasite *Giardia duodenalis* (also known as *Giardia lamblia* and *Giardia intestinalis*). This disease is prevalent globally and in South Africa. It was estimated in 2002 that over 280 million people per year are diagnosed with giardiasis globally (Lane and Lloyd, 2002). In South Africa, giardiasis is most common in poorer rural communities with untreated water, inadequate sanitation and poor dietary status. Indeed, one survey reported that the *Giardia* parasite was

common in South African surface water, as well as in treated effluent and drinking water in many rural communities (Kfir et al., 1995). Furthermore, a more recent study showed that whilst wastewater treatment can dramatically decrease the presence of Giardial cysts in treated water, the current treatment regimens (even in more affluent urbanised areas) are not completely effective (Dungeni and Momba, 2010). Indeed, that study reported substantial levels of cysts in treated water from all treatment facilities tested in Gauteng province of South Africa.

This prevalence of *G. duodenalis* is particularly concerning given the relative lack of effective treatment options. Metronidazole is currently the ‘gold standard’ drug of choice for the treatment of giardiasis, although it is only effective against the trophozoite stage of the parasites life cycle. Furthermore, this drug is not completely effective and often produces unpleasant side effects including nausea, vertigo, anorexia, vomiting, diarrhoea, and hallucinations (Upcroft and Upcroft, 2001; Upcroft et al., 2006). Drug toxicity with metronidazole therapy has also been widely reported (Harris et al., 2001; Granados et al., 2012). There have also been increasing reports of treatment failure and drug resistance by the organism is a major concern (Harris et al., 2001; Upcroft et al., 2006).

Whilst many studies have investigated the usage of traditional South African diarrhoeal therapies for antibacterial activity, studies examining their anti-Giardial properties are scarce and much more research is required in this field. Indeed, we were only able to find a single study which examined the ability of a South African plant (*Kigelia africana*) used to treat diarrhoea for the ability to inhibit *G. duodenalis* growth (Arkhipov et al., 2014). That study reported good activity against the trophozoid stage of the protozoal life cycle. However, the effects against the cyst were not examined so it is possible that the treated individual may still be able to pass the disease on and further work is required to test this. Many other plant species should also be tested for the ability to inhibit *G. duodenalis* growth.

Due to the lack of records of specific use against giardiasis, perhaps a study targeting plant species traditionally used in the treatment of diarrhoeal diseases may be the best option for a targeted approach. The same panel of plants previously tested against amoebiasis (McGaw et al., 2007) or general diarrhoea (Samie et al., 2009; Madikizela et al., 2012; Ahmed et al., 2012; Okem et al., 2012; Van Vuuren et al., 2015) may also prove to be a good starting point in screening South African medicinal plants against *G. duodenalis*.

7. Southern African plants traditionally used to treat ectoparasitic infestations

A total of 31 South African medicinal plants are recorded in various ethnobotanical texts as being used to combat ectoparasites. Of these, 31 plant species, the anti-ectoparasitic activities have only yet been confirmed for *Calpurnia aurea*, *Nicotiana tabacum*, *Ptaeroxylon obliquum*, *Strychnos spinosa* and *Tagetes minuta* (Nchu et al., 2012; Nyahangare et al., 2015). These species are active against ectoparasites including ticks and fleas that may spread parasites such as malaria, leishmaniasis and helminthiasis, as well as other pathogens. Ticks are important vectors for transmitting disease in both humans and animals in South Africa (Soneshine, 1991) although only three southern African plant species are recorded as being traditionally used to repel them in humans (Table 4). The diseases transmitted by ticks include heartwater, gallsickness and redwater. Ticks may also cause loss in milk production, weight loss, damage to hides and anaemia in livestock (Rajput et al., 2006). Several scientific studies have also screened other plant species against ticks. *Ptaeroxylon obliquum*, *Nicotiana tabacum*, *Eucalyptus globoides* and *Tagetes minuta* essential oils were reported to repel ticks in laboratory tests (Nchu et al., 2012; Nyahangare et al., 2015). Furthermore, *Tagetes minuta* essential oils also delayed the moulting of engorged nymphs by 60% after 25 days (Nchu et

al., 2012). Aqueous *Solanum incanum* and *Strychnos spinosa* extracts (5%) were reported to be highly lethal to ticks following a 48 hour treatment (Madzimore et al., 2013).

Fleas have pronounced effects on chickens and infestations can also cross species and infect humans. They may cause soft tissue ulcers, anaemia, transmit infections and predispose the infested individuals to skin infections and helminthiasis (Philips, 2005; Moyo and Masika, 2013). Several South African medicinal plants have been shown to reduce the number of fleas in chickens (Moyo and Masika, 2013). *Clutia pulchella* and *Calpurnia aurea* extracts are effective at significantly reducing the number of fleas on infested chickens for a 24 hour period (Moyo and Masika, 2013). However, as the toxicity of these plant extracts were not determined, it is not possible to determine their safety in humans. Further investigation into the activity of southern African medicinal plants against ectoparasites is required.

8. Trichomoniasis

Trichomoniasis is the most common non-viral sexually transmitted infection in humans globally (Mavedzeng et al., 2010). It is caused by the protozoan parasite *Trichomonas vaginalis*. In one rural South African study, 58% of women accessing family planning services at clinics were infected with this parasite (Naidoo and Wand, 2013). If left untreated, the infection can result in cancer of the cervix, complicated pregnancy and chronic vaginosis in

Table 4 Southern African plants used to treat ectoparasite infestations.

Plant species	Common name(s)	Family	Traditional uses	Plant part used	Reference
<i>Gloriosa superba</i> L.	Flame lily, climbing lily, glory lily (English), vlamlelie, boslelie, geelboslelie, rooiboslelie (Afrikaans), ihlamvu, nentombazana, isimiselo (Zulu)	Colchicaceae	Ticks, maggots or worms	Root	Von Koenen, 1996
<i>Nicotiana glauca</i> L.	Tobacco (English)	Solanaceae	To rid the skin of ticks	Leaf	Watt and Breyer-Brandwijk, 1962
<i>Sclerocarya birrea</i> (A.Rich.) Hochst	marula (Eng.); morula (Northern Sotho); mufula (Tshivenda); ukanyi (Tsonga)	Anacardiaceae	Expel ticks	Fruit	Watt and Breyer-Brandwijk, 1962

women. In both men and women, it can cause infertility and it increases the risk of contracting HIV. However, this disease may be difficult to diagnose as more than half of the

infected individuals may remain asymptomatic. Four South African medicinal plants (*Maesa lanceolata*, *Myrica kandtiana*, *Polygala luteo-viridis* and *Vernonia amygdalina*) are recorded as traditional treatments against trichomoniasis (Hutchings et al., 1996). However, none of these plants have yet been scientifically validated against this disease. Instead, most research into the therapeutic potential of South African plants for the treatment of trichomoniasis has focussed on other plant species. Studies have identified 15 South African plants which are active against *T. vaginalis*. In these studies, extracts were considered to have some antimicrobial activity against *T. vaginalis* if they have a minimum inhibitory concentration (MIC) <8 mg/ml (Fabry et al., 1998). One study reported that *Albizia adianthifolia*, *Aloe marlothii*, *Bidens pilosa*, *Carica papaya*, *Clematis brachiata*, *Euphorbia hypericifolia*, *Hypoxis hemerocallidea*, *Ozoroa engleri*, *Peltophorum africanum*, *Ranunculus multifidus*, *Sarcophyte sanguinea*, *Senecio serratuloides*, *Trichilia dregeana* and *Ximenia caffra* were effective inhibitors of *T. vaginalis* (Naidoo et al., 2013). That study also reported that these plant species were also non-toxic to human kidney epithelial line cells, further indicating their benefit in the treatment of *T. vaginalis*. More recent criteria for considering antimicrobial activity shows that activities <1 mg/mL should be considered as active (Van Vuuren and Holl, 2017), hence some of the plant species reported as active in Naidoo et al. (2013), may not necessarily be considered as effective anti-trichomonas treatments.

Some studies have also examined the effects of combinations of plant extracts against *T. vaginalis* and determined the class of interaction based on the fractional inhibitory concentrations (Σ FIC) analysis. Whilst none of the investigated combinations showed synergy against *T. vaginalis*, several combinations displayed additive effects (Naidoo et al., 2013). In particular, combinations of *Kigelia africana* with *Hypoxis hemerocallidea*; *Cassipourea mollosana* with *Hypoxis hemerocallidea*, and *Musa acuminata* with *Senecio*

serratuloides and *Hypoxis hemerocallidea* all had greater inhibitory activity than the sum of the individual components when tested alone (Naidoo et al., 2013).

9. Leishmaniasis and Tripanosomiasis

The protozoal parasite diseases leishmaniasis and trypanosomiasis have received limited attention globally and are classified as neglected tropical diseases. Neglected tropical diseases affect over a billion people globally and may be life-threatening (Schmidt et al., 2012). In sub-Saharan Africa, human sleeping sickness (trypanosomiasis) is endemic and is transmitted by the tsetse fly. Trypanosomiasis causes an inflammation of the nervous system and is often fatal (World Health Organisation, 2010). Chronic trypanosomiasis is most commonly caused by *Trypanosoma brucei gambiense* in sub-Saharan Africa, whilst *Trypanosoma brucei rhodesiense* most commonly causes acute trypanosomiasis in East Africa (Franco et al., 2014). Leishmaniasis occurs mostly in developing countries worldwide and is caused by protozoans of the *Leishmania* species (World Health Organisation, 2010). Leishmaniasis can manifest cutaneously, mucocutaneously or viscerally. Cutaneous and mucocutaneous leishmaniasis results in the formation of superficial lesions. Visceral leishmaniasis is a substantially more serious disease. In this form of the disease, the parasite invades the host's bone marrow and internal organs and may often be fatal (González et al., 2009).

Very little has been published regarding the potential of Southern African plants to treat leishmaniasis and trypanosomiasis. The majority of the research has been studied by Mokoka and co-authors (2013). They defined plant extracts which inhibited *Trypanosoma brucei rhodesiense* and *Leishmania donovani* with IC₅₀ values of 5.0 µg/mL or less against the pathogens as being effective. Toxicity was assessed in that study using L-6 myoblast cells

and quantified as LC₅₀ values. Selectivity Index (SI) values were then calculated as $SI = (LC_{50} \text{ value for L-6 myoblast cells}) / (IC_{50} \text{ value for parasite})$. Several plant extracts were active against *Trypanosoma brucei rhodesiense*. These included *Abrus precatorius*, *Ekebergia capensis*, *Psoralea pinnata*, *Schkuhria pinnata* and *Vernonia mespilifolia*, with selective indices ranging from 8.6 to 97.3. The most effective species were *Psoralea pinnata*, *Vernonia mespilifolia* and *Abrus precatorius*. *Psoralea pinnata* was the least toxic to the L6 myoblast cells, with a selectivity index of 97.3 (Mokoka et al., 2013). Only two plant species (*Oedera genistifolia* and *Vernonia mespilifolia*) met the criteria defined by that study for classification as targets for drug discovery as anti-*Leishmania donovani* therapies. Of these, *O. genistifolia* (SI = 28.60) was less toxic to L-6 myoblast cells than was *V. mespilifolia* (SI = 5.97 (Mokoka et al., 2013)).

10. Mode of action studies

Where anti-parasitic activity has been demonstrated for South African plants, examination of the mode of action has generally been neglected. Instead, the majority of studies have focused on the efficacy of the traditional medicines and on their phytochemistry. These studies are useful and informative for validating the efficacy of the traditional medicine, and in highlighting which species should be prioritized for further study. However, for potential future clinical usage of these medicines, a thorough examination of their mode of action is imperative. This was further confirmed in a recent review on helminth parasites where no mode of action studies were recorded but recognised as important for further study (van der Ree and Mutapi, 2015). It appears that mode of action studies are complex when studying the different parasites as each parasite has a complex life cycle and the mode of action would need to be studied at every stage within that life cycle in order to get a bigger picture.

Metabolomics has been used to dissect host–parasite interactions but such approaches to gain mechanism of action information are infrequent as indicated in the review by Kloehn and co-workers (2016). The most frequently encountered mode of action studies have been towards plasmodium parasite studies, but some investigative work has been undertaken on the anti-trypanosomal activities where the major target is the inhibition of enzymes responsible for the conversion of glucose to 3-phosphoglycerate and glycerol. Other natural product mode of action studies on trypanosomes and schistosomiasis have also been conducted (Morello et al., 1995; Doenhoff et al., 2008; Sülsen et al., 2016), which provide a good reference point with which to perform further studies on Southern African plants.

11. Discussion and conclusions

Parasitic infections and infestations are prevalent in countries with developing economies such as South Africa, particularly in areas where health care resources are scarce. In these countries, there is a high demand for treatment drugs and related therapies. However, the supply of effective treatments is often too little or may not be available at all (Mokoka et al., 2013). Through scientific research of the anti-parasitic activities of traditionally used medicinal plants, potent, less toxic and more cost effective therapies may be realised (Refaat et al., 2012). Unfortunately, this line of research is often hampered by a lack of interest from multinational pharmaceutical companies, particularly for diseases which are often only prevalent in poorer, developing countries (Ahmed et al., 2013). Whilst ‘Big Pharma’ do not always see the potential health and economic benefits from this kind of research, the benefits to local communities, as well as local farming and wildlife industries are often substantial.

To date, the number of studies examining the anti-parasitic activities of southern African medicinal plants were found to be limited. This is perhaps not surprising as parasitic

diseases (with the exception of malaria) are relatively neglected globally, with only about 1% of new drugs in the last 40 years targeting parasitic disease despite parasitic diseases being responsible for >10% of the global disease burden (Centre for Disease Control and Prevention, 2017). South Africa has well developed and documented traditional medicine systems. Coupled with one of the most diverse floras globally, it is well positioned for the discovery of new drugs. Indeed, over 30,000 plant species have been recorded in South Africa, with 3000 species used therapeutically (Van Wyk, 2011). However, species selection for screening against some parasites may be ambiguous. For example, ethnobotanical records list numerous South African plants used for the treatment of diarrhoea (Hutchings et al., 1996; Von Koenen, 1996; Watt and Breyer-Brandwijk, 1962). However, not only is diarrhoea a symptom for the parasitic diseases amoebiasis and giardiasis, but it may also be caused by multiple bacterial and viral pathogens. Thus, it may not be possible to discern whether a plant was used against *Amoeba* or *Giardia* parasites which cause those diseases, or if they are effective against bacteria or viruses instead. In fact, many medicinal plant antidiarrheal studies (for example Samie et al., 2009; Madikizela et al., 2012; Ahmed et al., 2012; Okem et al., 2012; Van Vuuren et al., 2015) have focused on bacterial or fungal sources, but avoiding testing against parasites causing diarrhoea is a definite shortcoming.

Other challenges in anti-parasitic medicinal plant research include finding the most appropriate extraction technique for a particular medicinal plant in order to get optimum activity against a particular parasite. In most traditional healing systems, decoctions and infusions are generally the most common preparation methods. Aqueous extracts are often limited to extraction of the higher polarity compounds, although this is not always the case. The presence of tensio-active or dispersing agents in the extracts may result in non-polar compounds in forming emulsions or dispersions. Furthermore, decoctions may also present an oily layer that can be part of the remedy. Thus, decoctions and infusions often lack mid-

low polarity compounds. Whilst this may be desirable under Lipinski's rules of 5 (Lipinski, 2004), it may not be optimal for gastrointestinal worms and helminths. When compounds in an extract are mid-highly polar, they will be readily absorbed through the gut lumen. However, as parasites such as *E. histolytica*, *G. duodenalis* and the intestinal worms live in the digestive system, a less polar drug may be beneficial as it would be absorbed less rapidly and therefore be exposed to the parasite for a longer time.

Relevant test models are required for some diseases. Currently, *C. elegans* is used to study the anthelmintic activity of plant extracts. Whilst this test provides a more rapid assay of screening for general helminth inhibition than *in vivo* assays, it is not specific for individual helminths, nor is activity towards *C. elegans* entirely consistent with medically relevant human or livestock parasites. Thus, when a drug candidate is highlighted by this assay, substantial further research is needed to test the plant species against these parasites. Despite some promising plant species being highlighted using the *C. elegans* bioassay (McGaw et al., 2000; Aremu, 2009), these species are yet to be followed up against specific helminths, or in relevant *in vivo* models.

Furthermore, even if the parasite of interest (or a good model organism) is examined, most preparations are generally only tested against a single phase of that organism's life cycle. For example, nearly all studies examining new treatments for giardiasis examine the trophozoite phase (Leboho et al., 2015; Rayan et al., 2015). Very rarely is the cyst considered. However, the parasite transitions between phases as it moves through the gastrointestinal tract (Gillin et al., 1989). In the acidic environment of the stomach and the upper reaches of the small intestine, the parasite exists as trophozoites. As it moves into the more alkaline regions of the lower small intestine and the large intestine, the parasite exists almost exclusively as cysts. These are subsequently released and infect the next host. As the cyst phase is substantially more resilient than the trophozoite phase, a treatment which kills the

trophozoites may not completely eradicate the parasite. Similarly, most drugs used to eradicate *S. haematobium* (the causative agent for bilharzia) target the adult life phase of the parasite. Praziquantel (the current 'gold standard' drug for the treatment of bilharzia) is completely ineffective against developing schistosomula (Doenhoff et al., 2008). However, nearly all studies screening therapies for anti-bilharzia properties screen against the larval stage. Whilst the schistosomula are no doubt easier to handle and screen in a laboratory situation, screening only against this life stage would result in overlooking many promising therapies. Thus, it is recommended that extracts be screened against several parasitic life phases.

Parasites of medical relevance to humans are often zoonotic. Thus, eradication of a parasite from an infected individual may be only a temporary measure unless the parasite is also removed from other animal hosts, or alternatively interaction between humans and the animal hosts are minimised. It is important that anti-parasitic drugs also be validated in other animal species. Furthermore, many parasites require an intermediate host (e.g. water snails for *S. haematobium*). Thus eradication of the intermediate host will block the transfer of the pathogen. Similarly, many insects and other ectoparasites are required to spread a parasite to a new host. More studies are required to develop treatments that will eradicate these intermediate hosts and vectors as a means of preventing the disease.

Furthermore, toxicity studies should be run in parallel with studies investigating the anti-parasitic activity of medicinal plant extracts. Variability in medicinal plant composition between different studies makes it difficult to link toxicology and activity results if they were reported in different studies. Furthermore, there should be uniformity in the definition of toxicity between studies. There is also a need for uniformity in conducting toxicology and activity investigations, and in expressing the results obtained. Employment of uniform

research methods and result presentation will help avoid unnecessary duplication of research, resulting in more efficient use of the scarce resources allocated for research.

Despite the availability of relatively extensive ethnobotanical records on the anti-parasitic properties of South African medicinal plants, the antiparasitic properties of many plants have been poorly examined. There was a complete lack of validation of the usage of many species towards some parasites and research is urgently needed in this area. In particular, research is needed to examine;

- The activities of southern African medicinal plants harvested in South Africa against *S. haematobium* and *S. mansoni* (bilharzia).
- *In vivo* and *in vitro* bioactivities of southern African medicinal plants against *T. saginata* and *T. solium* (tapeworm), *A. lumbricoides* (roundworm), *Ancylostoma doudenale* (hookworm) and *Enterobius vermicularis* (pinworm/threadworm).
- The inhibitory activity of southern African medicinal plants against *G. duodenalis* and *E. histolytica*. Giardiasis and amoebiasis are very common diseases and are prevalent in rural and poor communities of southern Africa. However, the selection of species to study is hampered by ethnobotanical usage records often being unable to distinguish between bacterial, viral and parasitic causes of diarrhoea.
- *In vivo* and *in vitro* investigations of southern African medicinal plants activities against toxoplasmosis and filariasis pathogens.
- *In vivo* and *in vitro* investigations of South African medicinal plants against insect and arachnid vectors including mosquitos, lice, mites, scabies and maggots.
- Mode of action studies.

In conclusion, there is still a plethora of possible investigative options to study parasitic diseases of Africa and researchers with access to veterinary sources may be in the

prime position to take this further. As parasites may be of zoonotic origin, medicinal plants recommended for parasite treatment in animals should also be considered for human use. Furthermore, a greener approach in combating less life threatening diseases will enable man kind to conserve conventional antimicrobials for more serious life threatening diseases.

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I.E. Cock: Researched, contributed to writing and approved final edited manuscript.

M.I. Selesho: Researched, contributed to writing and approved final edited manuscript.

S.F. van Vuuren: Conceptualized study, researched, contributed to writing and submitted final edited manuscript.

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