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The traditional use of Southern African medicinal plants to alleviate fever and their antipyretic activities

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ABSTRACT

Ethnopharmacological relevance: Multiple plant species are used traditionally in southern Africa to treat fever. This review summarises the traditional use, highlights promising plant species and focuses on validation studies to highlight future areas of research.

Aim of the study: This study aimed to critically review the use of southern African plants to alleviate fever. Additionally, an examination of research into those plants was undertaken to highlight gaps in the literature with the aim of stimulating further research in this field.

Materials and methods: Ethnobotanical books, reviews and primary research studies were searched to identify plant species traditionally used to treat fever in southern Africa and to summarise the current knowledge and identify areas requiring further research. This study was non-biased and did not have any taxonomic preferences, nor did it favour any southern African healing systems over the others.

Results: The traditional therapeutic uses of 203 southern African plant species to alleviate fever were recorded. Leaves and roots/bulbs/rhizomes were the most commonly used plant part, and they were most commonly prepared as decoctions or infusions and consumed orally. Notably, only twenty-two species (~11% of the identified species) have been scientifically evaluated for antipyretic properties, with substantially fewer mechanistic studies evident.

Conclusions: Despite the availability of ethnobotanical records, the antipyretic properties of southern African medicinal plants are poorly reported. Indeed, the efficacy of most plants is yet to be verified and very few mechanistic studies are available.

1. Introduction

Fever is characterised as a rise in body temperature above the normal range and is a normal response of the body to microbial infection (Anochie, 2013). Mild fevers ($\leq$39 ^{o}C) are generally beneficial to the immune system and aid in overcoming the infection, whilst mild fever generally self-resolves within a couple of days. Prolonged and/or severe fever can be life-threatening. In addition to the elevation of core body temperature, fever may also induce alterations to the endocrine, immunological, and neurological systems, as well as result in behavioural changes. Fever (and the microbial infections that induce it) may induce increased production of pyrogenic cytokines (Ogoina, 2011). Additionally, fever-inducing microbial pathogens may also cause nonspecific systemic symptoms including headaches, malaise, somnolence and anorexia. Fever (particularly prolonged or recurring) may also induce further serious symptoms including stupor, thrombocytopenia, delirium, apathy, dizziness, seizures, and myocarditis (Barbour, 2020).

1.1. Etiology of fever

The establishment of fever involves complex mechanisms and can be initiated by numerous exogenous or endogenous substances called pyrogens (Anochie, 2013; Dinarello and Porat, 2018). Additionally, fever etiology and progression mechanisms can be regulated by cryogens, which are anti-pyretic substances that can prevent excessive body temperature elevation (Ogoina, 2011). The balance between pyrogenic and cryogenic substances in an individual determines the establishment and progression of fever mechanisms.

1.2. Pyrogens and cryogens

Exogenous pyrogens include (but are not limited to) whole microorganism or parts thereof, and the toxins produced by microorganisms. Gram-negative bacteria and their pyrogenic endotoxic cell wall component lipopolysaccharide (LPS) are the most potent exogenous pyrogens (Plaisance and Mackowiak, 2000; Anochie, 2013;

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Abbreviations

AVP	arginine vasopressin
CNS	central nervous system
CNTF	ciliary neurotropic factor
COX-2	cyclooxygenase 2
CRH	corticotrophin releasing hormone
CYP450	cytochrome-P450
HIV	human immunodeficiency virus
IDSA	Infectious Disease Society of America
IL	nterleukin
INF-γ	interferon gamma
LPS	lipopolysaccharide
MIP-1	macrophage inflammatory protein 1
NF-κB	nuclear factor κB
NSAIDs	Nonsteroidal anti-inflammatory drugs
NST	nucleus of tractus solitaris
OVLT	organum vasculosum of the lamina terminalis
PFPF	preformed pyrogenic factors
PG	prostaglandin
PGE2	prostaglandin E2
POAH	preoptic region of the anterior hypothalamus
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
Tbs	tablespoon
TLR-4	Toll-like receptors 4
TNF-α	tumour necrosis factor alpha
Tsp	teaspoon
WHO	World Health Organisation
α-MSH	alpha-melanocyte-stimulating-hormone

Dinarello and Porat, 2018; El-Radhi, 2019). The exogenous pyrogens may act directly on the organum vasculosum of the lamina terminalis (OVLT), or they may act indirectly by stimulating the production of endogenous pyrogenic cytokines, which subsequently act on the OVLT (Walter et al., 2016). Endogenous pyrogens are produced by immune mediatory cells (particularly macrophages) in response to exogenous pyrogenic invasion (Walter et al., 2016; Plaisance and Mackowiak, 2000; Ma et al., 2021). Exogenous pyrogens direct the host's cells to produce endogenous pyrogens, which have multiple biological functions that modulate immunological mechanisms (El-Radhi, 2019). Notable endogenous pyrogens include (but are not limited to) the pyrogenic cytokines interleukin (IL)-1, IL-6, interferon gamma (INF-γ), tumour necrosis factor alpha (TNF-α) and ciliary neurotropic factor (CNTF) (Kluger, 1991; Zampronio et al., 2015; Dinarello and Porat, 2018; Marik, 2000; Wrotek et al., 2020).

Exogenous pyrogenic invasion also triggers the production and release of cryogens (Kluger, 1991), which down-regulate the production of pyrogenic cytokines, block cytokine receptors and increase the firing of warm sensitive neurons, thereby increasing the body's heat loss mechanisms and alleviating fever (Ogoina, 2011).

1.3. Fever development pathways

Humoral pathways for fever development are initiated by pyrogenic molecules, which bind cell surface toll-like receptors 4 (TLR-4) on macrophages, microglia, Kupffer cells and adipocytes (Zampronio et al., 2015). This binding triggers a cascade of intracellular events, eventually resulting in fever. Intracellular nuclear factor κB (NF-κB) is activated, which upregulates the synthesis and release of endogenous pyrogens (Wrotek et al., 2020). These pyrogens stimulate the release of membrane arachidonic acid and activate the enzyme cyclooxegenase-2 (COX-2), which subsequently increases production of the pro-inflammatory mediator PGE_2, which directs the POAH to reset the set-point temperature to a higher range than normal (Ogoina, 2011; Dinarello and Porat, 2018). Notably, corticotrophin-releasing hormone, IL-6, nitric oxide, bradykinin, IL-8, substance P, endothelin-1, preformed pyrogenic factors (PFPF), and macrophage inflammatory protein 1 (MIP-1) have similar fever mediating effects (Ogoina, 2011; Wrotek et al., 2020).

Stimulation of localised PGE_2 production at sites of inflammation also contributes to the development of fever through the stimulation of cold sensitive cutaneous neurons, which transmit fever signals to the CNS (Ma et al., 2021), and stimulate the production of further pyrogenic cytokines, thereby amplifying the fever pathways (Ogoina, 2011; Walter et al., 2016). These cytokines activate the hepatic branch of the vagus nerve, which then transmits fever signals to the nucleus of tractus solitaris (NST), resulting in intrapreoptic norepinephrine release (Ogoina, 2011). The increased levels of norepinephrine subsequently induce increases in the set-point temperature, resulting in fever (Ogoina, 2011).

1.4. Current antipyretic therapeutic options

Most antipyretic chemotherapies target intermediates in the arachidonic acid cascade to alleviate the symptoms of fever (Anochie, 2013). Antipyretic drugs including salicylates (e.g., aspirin) and Nonsteroidal anti-inflammatory drug (NSAIDs) (e.g., ibuprofen) target the cytokine-induced rise in the set-point temperature by binding and inhibiting the COX-2 enzyme (Anochie, 2013). This subsequently inhibits the biosynthesis of PGE_2 from arachidonic acid (Plaisance and Mackowiak, 2000), thereby down-regulating neural signals to the thermoregulating area in the hypothalamus, decreasing the set-point temperature and alleviating fever (Zampronio et al., 2015). Corticosteriods such as prednisone inhibit the enzyme phopholipase A2 and block arachidonic acid release and the prostaglandin cascade (Dinarello and Porat, 2018). They also downregulate the transcription of pyrogenic cytokines. Anti-cytokine immune- and anti-inflammatory therapies may also be used, although they are generally regarded as unreliable as multiple cytokines may be blocked, including those that both induce and reduce fever (Dinarello and Porat, 2018).

Undesirable effects of antipyretic therapy include renal dysfunction, gastro-intestinal irritation from NSAIDs, and Reye's syndrome in children under the age of sixteen to whom aspirin is administered (SAMF, 2020). Paracetamol is generally the preferred therapy to alleviate fever as it has a narrower range of side effects compared with steroidal or other NSAIDs (Dinarello and Porat, 2018). Whilst conventional chemotherapy is generally effective in alleviating fever, it is also associated with multiple negative side-effect profiles. Additionally, affordability and poor accessibility of some antipyretic therapies has prompted the use of alternative therapies including medicinal plants (Welz et al., 2018).

1.5. The use of medicinal plants to treat fever

Many southern African people (particularly in rural regions) lack access to conventional medicine (Hubsch, 2014). Even where available, allopathic healthcare may be beyond the financial reach of some people. Therefore, the use of medicinal plants may be the only healthcare option for a large proportion of the southern African population (Maoela, 2005; Chinyama and Thesis, 2009). Additionally, tradition and cultural values also contribute to the reliance on traditional therapies in rural areas. Furthermore, the close proximity of Muthi markets within the urban cities of South Africa make access to plant material easy and affordable (Mander, 1998; Mothibe and Sibanda, 2019; Otshudi et al., 2000; Haynes et al., 2002).

1.6. An overview of fever in southern Africa

Fever is one of the most common symptoms experienced by people living in sub-Saharan Africa (Maze et al., 2018). Notably, the WHO lists some of the main causes of death in southern Africa as human immunodeficiency virus (HIV), influenza, pneumonia, tuberculosis, malaria, and the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Each of these diseases present with fever, either as an early, persistent, predominant, minor, or late symptom (De Munter et al., 2012; Colley et al., 2014; Cavallazzi and Ramirez, 2018; Collazos et al., 2000; Zhang et al., 2020; Cock et al., 2020). Therefore, treating the fever symptoms of these diseases may be effective in reducing mortality rates and suffering of individuals with these diseases.

It is estimated that 12–15 million southern Africans relied on and consumed traditional medicines between 1995 and 1996. Approximately 700 indigenous plant species have been documented for the treatment of ailments as diverse as HIV, pain, inflammation and asthma (Brandt et al., 1995; Meyer et al., 1996; Khumalo et al., 2022). The number of southern Africans using traditional medicines increased further to approximately 27 million in 1998 (Mander, 1998). Whilst the WHO statistics are not specific to southern Africa, they do indicate a global trend towards greater adoption of traditional medicines. There is also increasing usage of both conventional and traditional medicines concurrently to combat numerous diseases in southern Africa (commonly termed medical pluralism) (Moshabela et al., 2016).

In southern Africa, the usage of traditional medicines is particularly prevalent in black African populations. Indeed, it has been estimated that approximately 72% of the black African population of southern African either consult traditional healers before consulting western healthcare practitioners or consult both physicians and traditional healers and combine both types of therapy, often without informing either practitioner (Hubsch, 2014; Moshabela et al., 2016; Mothibe and Sibanda, 2019). Interestingly, despite substantial advances in allopathic medicine in recent years, there has been a substantial increase in the number of traditional healers in southern Africa, with current estimates that there are approximately 500 traditional healers for every 100,000 people in southern Africa, compared to 77 allopathic healthcare practitioners for the same population size (Mothibe and Sibanda, 2019). This trend is not only evident in rural areas but is also apparent in urban populations and clearly demonstrates an increased acceptance in traditional healthcare and a corresponding increase in demand for traditional herbal medicines in southern Africa.

There is a need to develop effective and inexpensive antipyretic therapies that are available to the majority of southern Africans. A promising approach is to reinvestigate traditional medicines and assess their potential as new antipyretic therapies. This study aimed to document the plant species used traditionally by southern Africans to treat fever, thereby providing a resource to assist with plant selection for future studies. As the plant part used, the method of preparation, and the way the therapy was used impact on the efficacy of a therapy, these details were also included. Additionally, we have summarised the previous studies examining the antipyretic activities of southern African plants, with the goal of highlighting gaps in the literature and focussing future studies.

2. Materials and methods

This study documents the current knowledge on southern African medicinal plants that are used in traditional medicine to alleviate fever. The information presented herein was obtained from ethnobotanical books (including Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk and Gericke, 2000), as well as multiple peer-reviewed journal articles. Multiple online databases (Google Scholar, PubMed, Scopus and ScienceDirect) were searched to identify relevant original scientific research publications and ahead-of-publication manuscripts. The following terms were used as keywords to filter the online databases: “South Africa”, “southern Africa”, Namibia”, ‘’Lesotho’’, “Swaziland”, “Botswana”, “Zimbabwe”, “Mozambique”, “traditional medicinal plant”, “ethnobotany”, “fever”, “herbal medicine”, “natural medicine”, “antipyretic”, and “traditional healer.” All terms were searched both alone and as combinations. Initial literature searches aimed to identify and document the traditional uses of all plant species used to alleviate fever in southern Africa. Following the initial literature search, a further review was undertaken on the traditionally used plant species to identify any studies examining the antipyretic properties of the traditionally used species.

2.1. Eligibility criteria

Following the electronic database searches, the identified peer reviewed journal articles were further filtered using specific key words related to fever and antipyretic activity. The abstracts of relevant manuscripts were initially read thoroughly to ensure that the eligibility criteria were met, and if relevant further analysed.

2.2. Inclusion criteria

For inclusion in this study, all identified publications were required to meet the following criteria:

- Only English language manuscripts published prior to July 2022 were used in this review.
- This study is non-biased and has no taxonomic preferences, nor is it biased towards the ethnobotanical usage of any ethnic group.
- Plant species were specifically recorded as being used to alleviate fever. Taxonomically related species are not included unless their use is also documented for fever.
- The ethnobotanical studies included herein included studies of plants that occur in any (or all) of the following regions: Botswana, Lesotho, Mozambique, Namibia, South Africa, Eswatini (formerly called Swaziland) and Zimbabwe.

2.3. Exclusion criteria

The following criteria were used to exclude studies deemed not be relevant to this review:

- Where the usage of any plant species to treat fever was not specifically stated.
- Introduced and exotic species were only included when they were extensively (documented for one or more southern African ethnic group) used in traditional southern African medicine.

2.4. Data collection

A thorough publication search of the traditional usage of southern African plants to alleviate fever was used to identify relavant plant species for inclusion in this study. Additionally, studies documenting the biological screening of southern African medicinal plants to alleviate fever were included, regardless of the study origin. The following data was collected:

- Plant species and family names for each recorded species were checked and updated using The World Flora Online (http://www.worldfloraonline.org/) and SANBI (http://www.sanbi.org) website.
- Common names and vernacular names used by different ethnic groups groups were obtained from individual publications and from the SANBI red list website.
- Relevant information on how the medicine is used, including the part used, the method of preparation, and mode of administration were recorded (where available). Microsoft Excel was used for statistical data analysis.

3. Results

3.1. South African medicial plants used to treat fever

A thorough examination of southern African ethnobotanical studies and historical records identified a total of 203 medicinal plant species with traditional uses to treat fever (Table 1). *Adansonia digitata* L., *Artemisia afra* Jacq. ex Willd., *Ballota africana* Benth., *Conyza scabrida* DC., *Dodonaea viscosa* Jacq., *Elephantorrhiza elephantine* (Burch.) Skeels, *Eucalyptus globulus* Labill., *Eucomis autumnalis* (Mill.) Chitt., *Lippia javanica* Spreng., *Mentha longifolia* (L.) L., *Pentanisia prunelloides* (Klotzsch) Walp., *Pittosporum viridiflorum* Sims, *Ruta graveolens* L., *Salix mucronata* Thunb., *Tetradenia riparia* (Hochst.) Codd. and *Tulbaghia alliacea* L.f. were the most frequently cited as traditionally used to alleviate fever, each having ≥5 ethnobotanical records, with *A. afra* being the most cited plant for this purpose. Notably, *A. afra* is one of the most widely distributed medicinal plants in southern Africa, which may contribute to its widespread usage (Liu et al., 2009). In some cases (*Conium sphaerocarpum* Hilliard & B.L. Burtt., *Croton gratissimus Burch, Croton sylvaticus* Hochst. *Lippia javanica* Spreng., *Tabernaemontana ventricose* Hochst. Ex A.D.C. and *Warburgia salutaris* G. Bertol. Chiov.), the common name includes the word "fever" alluding to the medicinal use of having pyretic properties.

The southern African plant species traditionally used to treat fever are from a wide range of floral families (Supplementary Fig. 1). Indeed, a total of 60 families were recorded, with Compositae being the most frequently cited family used to treat fever, with 42 species recorded to be used for that purpose. This is perhaps not surprising as a recent study listed Compositae as one of the top families represented in African traditional medicine for most therapeutic purposes (Van Wyk, 2020). Plants from the Compositae family were mentioned substantially more than any other family, followed by Lamiaceae and Leguminonesae (13 species each). Rutaceae (eight species), as well as Amaranthaceae, Apiaceae, Euphorbiaceae, Geraniaceae, Myrtaceae and Verbenaceae (six species each) were also well represented. Additionally, Amarylidaceae, Anarcardiaceae, Salicaceae, Scrophulariaceae were each represented by five species, whilst Crassulaceae, Rubiaceae, Solanaceae, Thymelaeceae, Vitaceae and Xanthorrhoeaceae were each represented by four species. Three or less species were recorded for the remaining 41 families.

Leaves, as well as roots/bulbs and rhizomes were the most frequently used traditionally to treat fever, each accounting for 26.4% of the plant parts used for this purpose (Fig. 1). Bark was also relatively commonly used, accounting for 10.4% of the total usage as antipyretic traditional southern African medicines. In contrast, fruit (5%), resin (1.8%), stem (1.1%) and whole plant (2.1%) were used substantially less frequently. The plant part used traditionally to treat fever was not specified for a high proportion (25%) of the antipyretic plants. It is noteworthy that much of the ethnobotanical data presented herein (and in other similar studies) is related to Zulu traditional plant usage, because of the greater number of studies into the ethnobotany of that culture. Further studies into the traditional use and practices of other southern African cultural groups may reveal more information on the plant part used, the preparation of each medicine, and their application(s).

Various methods of preparation and treatment were used to administer the medicinal plants to treat fever (Fig. 2.). Besides oral consumption of decoctions, infusions and tinctures (37% of the total administration methods), as well as the usage of enemas to treat fever was also surprisingly common (13%), which may be due to the rapid absorption of medicinal compounds into the bloodstream via that route (Shitut et al., 2021). Inhalation of traditional medicines as steam, or smoke from burned plant material, or through the use of snuff (7.5%) was also relatively common. Only a relatively small percentage of medicinal plants were directly eaten (2.4%) and this generally relates to the medicinal use of edible fruits or berries. In most cases, when different dosages and methods of use are listed for children, half the adult dose is generally recommended. Furthermore, when steaming is listed as the method of administration, it is not recommended for children, or was recommended that they use the steam for substantially shorter time, and only under adult supervision.

3.2. The traditional use of mixtures of southern african plants to treat fever

Southern African plants are most frequently used as single plant medicines. However, for some tharapies, traditional healers mix plant species in an attempt to reduce the toxic effects, or to elicit synergistic effects (Eliopoulos and Moellering, 1996; Cheesman et al., 2017). An examination of the ethnobotanical literature identified a total of 19 mixtures of plants used to treat fever (Table 2). All of these mixtures contained medicinal plants identified in Table 1.

Eucalyptus grandis (a component of seven combination therapies), *A. afra* (a component of three combination therapies), *A. calamus* (a component of two combination therapies) and *L. javanica* were relative common components in therapeutic mixtures. Notably, most of these plant species were amongst the most cited in the ethnobotanical literature as antipyretic therapies and were frequently listed as single component therapies for this purpose.

As noted for the single component plant therapies, leaves, bark and roots/bulbs/rhizomes were most commonly used in the plant mixtures. Interestingly, ethnobotanical records of plant mixture usage often provided substantially greater clarity and greater detail about the preparation of the mixed plant therapy and the dosage. Most mixtures required the plant parts to be crushed and boiled in water for specific periods. The mixed therapies may then be drunk as a warm beverage, or in several cases the published method stated that the medicine should be strained and allowed to cool for later consumption. Steaming, (often listed as "futha" in the ethnobotanical literature), oral consumption and topical application were some of the other recommended routes of administration. Recommended doses for children were generally substantially lower than for adults, and children either were not recommended to use steam, or the recommended period or frequency of steam administration was substantially less than for adults.

3.3. Scientific studies into the anti-pyretic activity of southern African plants

Twenty-two studies were identified having reported antipyretic activities of southern African medicinal plants with reported ethnobotanical uses to treat fever (Table 3). The majority of those studies screened the plant-based prepartions using *in vivo* assays. Indeed, thirteen studies (59% of the total studies) screened the plant extracts using *in vivo* rodent models. Rats were most frequently used, although mice were also screened in a limited number of studies. Notably, none of those studies examined the antipyretic mechanisms of the plant extracts. Instead, the antipyretic activity of the extracts were usually just validated by measuring decreases in rectal temperatures following treatment and the results were compared to the temperatures of control animals. Substantial decreases in body temperature (up to 1.3 °C) were reported for aqueous *A. digitata* extracts (800 mg/kg) within 4 h of treatment (Ramadan et al., 1994).

Several other studies also reported substantial decreases in body temperature following treatment, many using substantially lower doses of extracts, including aqueous *E. africanus* (100 mg/kg) (Amabeoku et al., 2000), dichloromethane *E. globus* leaf (250 mg/kg) (Mworia et al., 2019), aqueous *M. longifolia* leaf (~38 mg/kg) (Amabeoku et al., 2009), methanolic *R. graveolens* leaf (400 mg/kg) (Loonat and Amabeoku, 2014), methanolic *T. capensis* leaf (100 mg/kg) (Saini and Singha, 2012) and methanol *V. glabrum* leaf extracts (100 mg/kg) (Wahba et al., 2010).

Pelargonium sidoides is the only plant preparation that has undergone human trials. A recent study screened the effects of a *P. sidoides* extract fraction in children with acute tonsillophrayngitis and reported substantial decreases in fever and accelerated recovery following theapy

Table 1
Southern African plants used traditionally to alleviate fever.

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Acanthospermum glabratum (DC.) Wild.	Compositae	Isihlazaa, nkunzana, inkonzana, isibambaphansi, isichathabantwana (Zulu)	Whole plant	The whole plant is crushed and mixed with warm water. The decoction is then filtered and used as an enema once daily. Alternatively, 1 Tbs is taken orally three times a day.	York et al., 2011
Achyropsis avicularis (E. Mey.ex Moq.) Benth. & Hook.f ex B.D.Jacks.	Amaranthaceae	Ibohlololo, isinama senyonga (Zulu)	Roots	Unspecified.	Hutchings et al., 1996
Achyropsis leptostachya (E.Mey.) Benth. & Hook.f. ex B.D. Jacks.	Amaranthaceae	Isinama senyonga (Zulu)	Unspecified	Taken orally as an emetic.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Acorus calamus L.	Acoraceae	Kalmoes (Afrikaans); ikalamuzi (Zulu)	Unspecified	Infusions are used to treat fever. Application method was not specified.	Hulley and Van Wyk, 2019
Adansonia digitata L.	Malvaceae	Kremetartboom (Afrikaans), baobab (English), shimuwu (Tsonga), movana (Tswana), muvhuyu (Venda)	Leaves, fruit pulp, bark, resin	Taken orally. The yellow/whitish fruit pulp is mixed with water to produce a pleasant-tasting drink. Alternatively, the boiled, edible fruit is eaten to reduce fever.	Watt and Breyer-Brandwijk, 1962; von Koenen, 1996; Van Wyk et al., 2009; Mokganya and Tshisikhawe, 2019
Adenia gummifera Harms.	Passifloraceae	umPhindamshaya; imFule; imFulwa; imPinda (Zulu)	Roots	The root is used to make a tonic and is taken orally for febrile conditions that are known as *umkhuhlane*.	Bryant and Struik, 1966; Corrigan et al., 2011
Agathosma betulina (P.J. Bergius) Pillans	Rutaceae	Boegoe, winkelboegoe (Afrikaans); buchu	Leaves	Decoctions are used. Application was not specified.	Thring and Weitz, 2006; Nortje and Van Wyk, 2015
Agathosma puberula (Steud.) Fourc.	Rutaceae	Boegoe, winkelboegoe (Afrikaans); buchu	Leaves	Decoctions of the leaf is used to reduce fever. Application was not specified.	Watt and Breyer-Brandwijk, 1962
Albertisia delagoensis (N. E.Br.) Forman.	Menispemaceae	Umgandaganda, umqhumane, ungandingandi (Zulu)	Roots	Aqueous root extract is drunk to alleviate fever.	De Wet and Van Wyk, 2008
Albizia suluensis Gerstner.	Leguminosae	Zoeloevalsdoring (Afrikaans); Zulu albizia (English); ingweb'enkulu, ingwebo omkhulu, ingwebunkulu, unyazangoma (Zulu)	Unspecified	An aqueous macerate is administered as an enema. Caution is urged and no more than a cupful is recommended as it is very potent.	Gerstner, 1941; Hutchings et al., 1996
Alepidea amatymbica Eckl. and Zeyh.	Apiaceae	Iqwili (Xhosa)	Roots	Unspecified.	Maroyi, 2017a; Semenya and Maroyi, 2020
***Allium sativum* L.**	Amaryllidaceae	Knoffel (Afrikaans); garlic (English)	Clove	Cloves are eaten raw.	Thring and Weitz, 2006; Van Wyk, 2011
Aloe marlothii A. Berger.	Xanthorrhoeaceae	Inhlaba, umhlaba (Afrikaans)	Leaves	Unspecified.	York et al., 2011
Aloe maculata All.	Xanthorrhoeaceae	Bontaalwyn, seepaalwyn (Afrikaans); soap aloe, white spotted aloe (English); icena (Zulu)	Flowers	Powdered dried flowers are steeped in water and given to children orally, or as an enema.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Amoo et al., 2014; Ndhlovu et al. 2021
Alysicarpus rugosus (Willd.) DC.	Leguminosae	Red moneywort (English); inkonazana (Zulu)	Roots	Hot water infusions of pounded roots are taken as emetics for febrile complaints.	Bryant and Struik, 1966; Hutchings et al., 1996
Annona senegalensis Pers.	Annonaceae	Wild custard apple (English)	Roots	Roots are boiled and the mixture is drunk to relieve fever.	Mahwasane et al., 2013
Aptosimum procumbens (Lehm.) Steud.	Scrophulariaceae	Unknown	Leaves and stem	A cold infusion of the leaf and stem taken orally.	Watt and Breyer-Brandwijk, 1962
Aristea ecklonii Baker.	Iridaceae	Nlue stars, blue flies, blue-eyed iris, blue corn-lily (English); ikhambi eliluhlaza, umafosi, umhushuza (Zulu)	Leaves	Leaf infusions are administered as enemas to relieve *umkhuhlane* (any sickness accompanied by fever or coughing).	Hutchings et al., 1996
***Artemisia absinthium* L.**	Compositae	Groenamara (Afrikaans)	Leaves	Leaves can be chewed or infused for the treatment of fever.	Hulley and Van Wyk, 2019

(*continued on next page*)

Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Artemisia afra Jacq. ex Willd.	Compositae	Als, alsem, wildeals (Afrikaans), African wormwood (English), lengana (Sotho, Tswana), umhlonyane (Xhosa, Zulu); umhlonyane omcane (Zulu)	Roots and leaves	An infusion or decoction is generally used and is often made syrupy with the addition of honey or sugar to mask the natural bitter taste. Leaves may also be made into a poultice with brandy or vinegar and wrapped around the stomach. Alternatively, leaves are crushed into a powder and added to boiling water and the steam is inhaled several times a day.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; von Koenen, 1996; Felhaber and Mayeng, 1997; Thring and Weitz, 2006; Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Seleteng Kose et al. 2015; Davids et al., 2016; Van Wyk and Gorelik, 2017; Hulley and Van Wyk, 2019; Semenya and Maroyi, 2020
***Artemisia vulgaris* L.**	Compositae	Wonderkroon (Afrikaans)	Leaves	Unspecified.	Nortje and Van Wyk, 2015
Aspilia natalensis (Sond.) Wild.	Compositae	Kleinperdepram, kardamon (Afrikaans); small knobwood, cardamon (English); monokwane (Sotho); umlungumabele (Xhosa); ikhambi-lenyongo, ingcolozi, ubuhlungwana, uhlungwana, umphamaphuce (Zulu)	Fruit, bark, roots and leaves	Infusions or decoctions of the fruits or leaves are used as a carminative.	Hutchings et al., 1996; Dugmore and Van Wyk, 2008; Van Wyk et al., 2009; Philander, 2011
Aster bakeranus Burtt Davy ex C.A.Sm.	Compositae	Idlutshane, udhlatshana, uhloshana, umaqhunsula, umhludwana (Zulu)	Whole plant	The whole plant is powdered and used to treat febrile conditions. Application is not specified.	Hutchings et al. 1996
Baccharoides adoensis (Sch. Bip. ex Walp.) H. Rob.	Compositae	Innyathelo, inyathelo, uhlonyane (Zulu)	Leaves	Leaf infusions are taken orally or administered as enemas for febrile complaints.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Bryant and Struik, 1966;
Ballota africana Benth.	Lamiaceae	Kattekruid, kattekruie (Afrikaans)	Leaves and fruit pulp	The leaves are steeped in hot water for 10 min and taken as a tea to treat fever. A syrup can be made from the fruit pulp with boiling water and sugar.	Van Wyk and Gericke, 2000; Thring and Weitz, 2006; Van Wyk et al., 2009; Philander, 2011; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Davids et al., 2016; Van Wyk and Gorelik, 2017; Hulley and Van Wyk, 2019
Berkheya onopordifolia (DC.) Burtt Davy.	Compositae	Unknown	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962
Bersama tysoniana Oliv.	Mellianthaceae	Gewone witessenhout (Afrikaans); common white ash (English); isindiyandiya, undiyaza (Zulu)	Bark	Unspecified.	Hutchings et al., 1996; Watt and Breyer-Brandwijk, 1962
***Bidens pilosa* L.**	Compositae	Gewone knapsekerel (Afrikaans); blackjack (English); ucadolo, uqadolo (Zulu)	Unspecified	Used for fever in paediatrics. Usage method is not specified.	Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021
Brachylaena spp. (specific species was not specified)	Compositae	Iphahla (Zulu)	Leaves	Unspecified.	York et al., 2011
Bulbine foleyi E.Phillips.	Xanthorrhoeaceae	Bulbine (English)	Leaves	Unspecified.	Philander, 2011
Bulbine frutescens (L.) Willd.	Xanthorrhoeaceae	Burn jelly plants, cat's tail, rankkopieva, yellow and orange garlic (English); ibhucu, ithethe elimpofu (Zulu)	Roots	Root decoctions are administered as enemas to reduce fever.	Hutchings et al., 1996
Bulbine lydenburgensis Poelln. (synonym *B. capitata*)	Xanthorrhoeaceae	Unspecified.	Leaves and roots	Unspecified.	Bodede and Prinsloo, 2020
Callilepis laureola DC.	Compositae	Ox-eye daisy (English)	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Callilepis leptophylla Harv.	Compositae	Ox-eye daisy (English); bergbitterbossie (Afrikaans)	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962; Van Vuuren and Frank, 2020
***Capsicum annuum* L.**	Solanaceae	Itshilisi (Xhosa)	Fruit	Unspecified.	Maroyi, 2017a
Carpobrotus edulis (L.) N. E.Br.	Aizoaceae	Hotnotsvye, vyerank (Afrikaans)	Leaves	Leaf decoctions are consumed for fever.	Nortje and Van Wyk, 2015
Cassine transvaalensis (Burtt Davy) Codd	Celastraceae	Lepelhout, oupitjie, Transvaal saffraan (Afrikaans); Transvaal saffron wood (English); ingwavuma, umgugudo, umqotha (Zulu)	Bark	Bark infusions are taken orally as emetics or administered as enemas.	Gerstner 1941; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk and Gericke, 2000
Cassytha ciliolate Nees.	Lauraceae	Bobbejaantou, jakkalsgare (Afrikaans)	Unspecified	Infusions are consumed.	Nortje and Van Wyk, 2015
Catunaregam spinosa (Thunb.) Tirveng.	Rubiaceae	Doringbeenappel (Afrikaans); thorny bone-apple (English); isibihla, isbibihli, isigongongo, isikwakwane, umaqhatini, umkhwakhwane (Zulu)	Roots and other unspecified parts.	Unspecified parts are administered as emetics for fever and roots are reported to have anti-febrile properties.	Gerstner, 1941; Hutchings et al., 1996
Cavacoa aurea (Cavaco.) J.Leonard.	Euphorbiaceae	Natalokkerneut (Afrikaans); Natal hickory (English); umbhuku, umbuku (Zulu)	Roots	Root infusions are taken orally.	Palmer and Pitman, 1972; Hutchings et al., 1996

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Cephalanthus natalensis Oliv.	Rubiaceae	Witaarbeibos (Afrikaans); quinine berry, strawberry bush, tree strawberry (English); isamfomfo, umfimfi, umfomfo, umkhumbe (Zulu)	Fruit	Three to four fruits a day are consumed to treat fever (particularly associated with malaria).	Watt and Breyer-Brandwijk, 1962; Pooley, 1993; Hutchings et al., 1996; Cock et al., 2019
Chironia baccifera L.	Gentianaceae	Bitterbos, skilpadbossie, sesparella, aambeibos (Afrikaans); Christmas berry (English)	Leaves	Leaf infusions are consumed.	Hulley and Van Wyk, 2019; Ndhlovu et al., 2021
Chrysanthemoides monilifera (L.) Norl.	Compositae	Bietou, boetabessie (Afrikaans); brother berry (English); inkhupuyana, itholonja, umtholombi (Zulu)	Leaves	Infusions from the leaves are administered as enemas for feverish conditions.	Palmer and Pitman, 1972; Hutchings et al., 1996; Van Vuuren and Frank, 2020
Chrysocoma ciliata L.	Compositae	Bitterbos (Afrikaans)	Leaves and roots	A decoction of the leaves and roots is consumed.	Davids et al. 2016; Hulley and Van Wyk, 2019
***Cinnamonum camphora* (L.) J.Presl.**	Lauraceae	Kanferboom (Afrikaans); camphor tree (English); urosalina (Zulu)	Bark	Unspecified.	Van Wyk et al., 2009; Philander, 2011; Reid et al., 2018
Cissampelos capensis L.f.	Menispemaceae	Dawidjie (Afrikaans)	Roots	Unspecified.	Van Wyk et al., 2009; Semenya and Maroyi, 2020
Cissampelos mucronata A.Rich.	Menispemaceae	Dawidjies (Afrikaans); umbombo (Zulu)	Roots	A root decoction is drunk to alleviate fever.	Van Wyk and Gericke, 2000; De Wet and Van Wyk, 2008
Clausena anisata (Willd.) Hook.f. ex Benth	Rutaceae	Basternieshout, perdeboom, perdepis (boom/bos) (Afrikaans); horsewood (English); isifudu, isifuthu, umnukambhiba, umnukelambiba, umsanka (Zulu)	Leaves and roots	Steam from leaf decoctions is inhaled to treat fever. Roots are also used orally for pyrexia in children, as an enema or a bathing lotion for minor ailments.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; York et al., 2011; Van Vuuren and Frank, 2020
Clematis brachiata Thunb.	Ranunculaceae	Lemoenbioesels (Afrikaans); traveller's joy (English); ikhambi lesiduli, ihlozi, Ihluzi, umdlonzo (Zulu); ityolo (Xhosa); morara (Sesotho); mogau (Tsonga)	Leaves and other unspecified parts	Leaf macerations are used to treat fevers in paediatrics.	Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021
Coddia rudis (E.Mey. ex Harv.) Verdc.	Rubiaceae	Kleinbeenappel (Afrikaans); small bone-apple, small gardenia (English); isibihla, isibihli, isikwakwane, umdondwane, umgogwane, umkwakwane omncane, umsilinjane (Zulu)	Unspecified	Unspecified.	Gerstner, 1941; Hutchings et al., 1996
Coleonema album (Thunb.) Bartl. & H.L. Wendl.	Rutaceae	Aasbossie (Afrikaans); confetti bush (English)	Leaves	Unspecified.	Philander, 2011
Combretum molle R.Br. ex G.Don.	Combretaceae	Basterrooibos, hardekool (Afrikaans); rooibos, velvet bushwillow (English); umdubu wehlathi, umBondwe; umBondwe-omhlope; umBondo (Zulu)	Leaves	Unspecified.	Hutchings et al., 1996; Pooley, 1993; Corrigan et al., 2011; York et al., 2011
Commiphora africana (A. Rich.) Engl.	Burseraceae	Harige kanniedood (Afrikaans); african corkwood, hairy corkwood (English); ozidlaxo, uminyela (Zulu)	Gum and resin	Unspecified.	Watt and Breyer-Brandwijk, 1962; Pooley, 1993; Hutchings et al., 1996
Conium chaerophylloides Eckl. & Zeyh.	Apiaceae	Lefokololi (Sesotho)	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962; Moteetee et al., 2019
Conium sphaerocarpum Hilliard & B.L.Burtt.	Apiaceae	Fever root (English)	Leaves and roots	Unspecified.	Philander, 2011
Conyza obscura DC.	Compositae	Unknown	Roots	Unspecified.	Watt and Breyer-Brandwijk, 1962
Conyza podocephala DC.	Compositae	Isitshotshokazane (Zulu); manku-e-moholo (Sesotho)	Roots	Root decoctions are consumed.	Hutchings et al., 1996; Moteetee et al., 2019
Conyza scabrida DC.	Compositae	Bakbesembossie, galsiektebossie, kouebos, bakbos (Afrikaans); oven bush, albany gall-sick bush (English), uhlabo, umanzimnyama (Zulu)	Leaves	Use as a compress to relieve fever. Leaf infusions and decoctions are also consumed.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; von Koenen, 1996; Philander, 2011; Nortje and Van Wyk, 2015; Hulley and Van Wyk, 2019
Crassula alba Forssk.	Crassulaceae	Isidwe, isikelekhehlane, isikhelekhehlane (Zulu)	Sap	The sap is mixed with water and used as a nasal douche.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Crassula ericoides Haw.	Crassulaceae	Large whipcord (English)	Unspecified	Unspecified.	Van Wyk et al., 2009; Van Wyk and Gorelik, 2017
Crassula mucosa L.	Crassulaceae	Akkedisbos, skilpadbos, kleinkoorsbos (Afrikaans)	Leaves	The leaves are boiled in water and used to treat fever.	Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Davids et al., 2016; Van Wyk and Gorelik, 2017
Crassula peploides Harv.	Crassulaceae	Uknown	Roots	A lotion made from the root is applied to treat fever.	Watt and Breyer-Brandwijk, 1962
Croton gratissimus Burch.	Euphorbiaceae	Bergboegoe, laventelkoorsbessie, leventelbos, rekstokbos stinkhout (Arikaans); lavender croton, Kalahari buku, lavender fever berry (English); maquassie (San); umahlabekufeni, ihubeshane-elikhulu, ilabele, ilethi, intumbanhlosi, uhubeshane, umhluka, umhuluga (Zulu)	Bark and leaves	Leaves are used in steam baths and the steam is inhaled.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 2009; Moremi et al., 2021

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Croton sylvaticus Hochst.	Euphorbiaceae	Forest fever-berry (English); amahlabakufeni, indumbahlozi, ugibeleweni, umgeleweni, umhlalajuba, umhloshazane, uminya, ummbila, umzilanyoni (Zulu)	Bark and roots	Enemas made from the bark and roots are administered for febrile conditions.	Gerstner, 1941; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Moremi et al., 2021
Cryptocarya transvaalensis Burtt Davy.	Lauraceae	Unknown	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Cussonia spicata Thunb.	Araliaceae	Waaiboom, smabreelboom, oumeidhout, kiepersol (Afrikaans); cabbage tree, Krauss' cabbage tree (English); umsenge (Zulu)	Roots	Root infusions are taken as emetics for fever.	Hutchings et al., 1996
***Cymbopogon nardus* (L.) Rendle**	Poaceae	Citronella grass, lemongrass (English); tamboekiegras (Afrikaans); isicunge, isiqunga (Zulu)	Unspecified	Unspecified parts are used as a vermifuge.	Philander, 2011; Hutchings et al., 1996
Cyperus sexangularis Nees.	Cyperaceae	Biesiegras (Afrikaans)	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Cyphostemma hypoleucum (Harv.) Desc. ex Wild & R.B. Drumm.	Vitaceae	Udekane (Zulu)	Unspecified	Unspecified parts are administered as enemas for febrile conditions.	Gerstner, 1941; Hutchings et al., 1996
Dicerothamnus rhinocerotis (L.f.) Koek.	Compositae	Anosterbos, renosterbos, platanosterbos (Afrikaans)	Leaves	Tea is made from leaves and is drunk to alleviate fever.	Watt and Breyer-Brandwijk, 1962; Thring and Weitz, 2006; Hulley and Van Wyk, 2019
Dicoma anomala Sond.	Compositae	Fever bush (English), maagbitterwortel, kalwerbossie, koorbossie, gryshout (Afrikaans); isihlabamakhondlwane, umuna (Zulu)	Roots	A decoction of the root is mixed with "melkbos" for fever.	Watt and Breyer-Brandwijk, 1962
Dicoma capensis Less.	Compositae	Wilde karmedik, koorsbossie (Afrikaans)	Roots, leaves and twigs	An infusion/decoction of the leaves is used.	Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015
Drimia elata Jacq.	Asparagaceae	Brandui (Afrikaans); indongana-zibomvana, isiklenama, umqumba (Zulu)	Bulb and leaves	Hot water infusions of the pounded bulbs and leaves are used as enemas to alleviate fevers.	Hutchings et al., 1996; Thring and Weitz, 2006
Dodonaea viscosa Jacq.	Sapindaceae	Sandolien, ysterhouttoppe (Afrikaans); sand olive (English); mutepipuma (Shona); mutata-vhana (Venda)	Leaves and fruit pulp	Fresh leaves are boiled in water, steeped and then filtered. Infusions are used for the treatment of fever.	Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Van Wyk and Gorelik, 2017; Hulley and Van Wyk, 2019
***Dysphania ambrosioides* (L.) Mosyakin & Clemants.**	Amaranthaceae	galsiektebos (Afrikaans); amerrican goosefoot, worm weed (English); usukumbili (Zulu); umbikicane (Xhosa)	Leaves	An ointment prepared from the leaves is rubbed on the body of an infant for the treatment of high fever.	Hulley and Van Wyk, 2019; Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021
Elephantorrhiza elephantina (Burch.) Skeels	Leguminosae	Baswortel, elandsboontjie (Afrikaans); eland's bean, elephant's foot (English); intolwana enkulu, intolwane, ugweje, umdabu (Zulu)	Roots and tuber	After scraping off the tuber's outer sheath, it is chopped, and a water extract is made, which is used as an enema or drunk for febrile conditions.	Gerstner, 1941; Hutchings et al., 1996; von Koenen, 1996; Seleteng Kose et al., 2015; Moteetee et al., 2019; Van Vuuren and Frank, 2020
Eriocephalus africanus L.	Compositae	Kapokbos, skaapkarroo, sneeubos, hartbossie (Afrikaans); infection bush (English)	Unspecified	Unspecified.	Philander, 2011; Nortje and Van Wyk, 2015; Hulley and Van Wyk, 2019
Eriocephalus punctulatus DC.	Compositae	Kapokbos (Afrikaans); Cape chamomile (English)	Leaves	Unspecified.	Philander, 2011; Nortje and Van Wyk, 2015; Hulley and Van Wyk, 2019
Erythrina caffra Thunb.	Leguminosae	Umsinsi (Zulu)	Roots	Unspecified.	York et al., 2011
***Eucalyptus absita* Grayling & Brooker.**	Myrtaceae	Gumtree (English)	Leaves and roots	Infusions of the leaves and roots are used for fever. Leaves are crushed into a bowl and covered in boiling water and the fumes are inhaled.	Thring and Weitz, 2006; Ndhlovu et al., 2021
***Eucalyptus globulus* Labill.**	Myrtaceae	Blougom, bloekom (Afrikaans); eucalyptus (English)	Leaves	Fresh or dried leaves are crushed into a bowl and covered in boiling water. The fumes are inhaled.	Felhaber and Mayeng, 1997; Thring and Weitz, 2006; Van Wyk et al., 2009; Philander, 2011; Van Wyk and Gorelik, 2017
***Eucalyptus grandis* W. Hill ex Maiden.**	Myrtaceae	Gumtree, gumbush (English), impiskayihlangulwa, umdlavusa umdlebe (Zulu)	Leaves	Fresh or dried leaves are crushed into a bowl and covered in boiling water. The fumes are inhaled.	York et al., 2011
***Eucalyptus sideroxylon* A.Cunn. Ex Woolls**	Myrtaceae	Bloekom (Afrikaans)	Leaves	Decoctions and infusions prepared using leaves are used for the treatment of fever. The leaves are crushed and covered in boiling water and the fumes are inhaled.	Thring and Weitz, 2006; Nortje and Van Wyk, 2015

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Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Eucomis autumnalis (Mill.) Chitt.	Asparagaceae	Gifbolaandblom, wildepynappel (Afrikaans); pineapple flower/plant (English); ukhokho, umakhandakantsele, umathunga, amathunga (Zulu)	Bulb	Bulbs are used in decoctions and administered in small quantities as enemas for fever.	Hutchings et al., 1996; Van Wyk and Gericke, 2000; Dugmore and Van Wyk, 2008; Seleteng Kose et al., 2015; Mugomeri et al., 2016
Eucomis bicolor Baker.	Asparagaceae	Imbola (Xhosa)	Bulb and roots	Bulb and root shavings are boiled in water or milk and used as ingredients in infusions.	Komoreng et al., 2017
Exomis microphylla (Thunb.) Aellen	Amaranthaceae	Hondepisbos, hondebossie (Afrikaans)	Leaves	Infusions or compresses of leaves are used.	Hulley and Van Wyk, 2019
***Foeniculum vulgare* Mill.**	Apiaceae	Vinkel (Afrikaans); fennel (English)	Leaves	An infusion made from the leaves is drunk.	Thring and Weitz, 2006
Gardenia thunbergia Thunb.	Rubiaceae	Buffelsbal, kannetjieboom, swartbas, wildekatjiepiering, witkatjiepiering (Afrikaans), white gardenia (English); umavalasangwane, umkangaze, umkhangazo, umkhwakhwane, umkwakwane omkhulu, umvalasangweni wehlathi (Zulu)	Roots	Roots are used to prepaere emetics.	Gerstner, 1941; Hutchings et al., 1996
Garuleum bipinnatum (Thunb.) Less.	Compositae	Slanghoutjie (Afrikaans)	Unspecified	Unspecified.	Van Wyk et al., 2009
Geranium canescens L'Her.	Geraniaceae	Forest/tree/white/wild gardenia (English)	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962
Geranium incanum Burm. f.	Geraniaceae	Vrouebossie, amaramarabossie (Afrikaans)	Leaves	Unspecified.	Philander, 2011
Gladiolus aurantiacus Klatt.	Iridaceae	Isihlazi (Zulu)	Unspecified	Unspecified.	Hutchings et al., 1996
Gnidia anthylloides Gilg.	Thymelaeaceae	Brandbossie (Afrikaans); indolo, intozwane, isidikili esikhulu (Zulu)	Whole plant	Smoke from burning the plant is used as an inhalant.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Gnidia burchellii Gilg.	Thymelaeaceae	Harpuisbossie, repuis (Afrikaans); Burchell's yellow-head (English); isidikili (Zulu)	Roots	Roots are used in enemas.	Gerstner, 1941; Bryant and Struik, 1966; Hutchings et al., 1996
Gnidia cuneata Meisn.	Thymelaeaceae	Koorssbossie (Afrikaans), idikili (Zulu)	Roots	Roots are used in enemas.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Vuuren and Frank, 2020
Gnidia deserticola Gilg.	Thymelaeaceae	Saffraan, saffraanbos (Afrikaans); saffron curry flower (English); impevu (Zulu)	Unspecified	Unspecified.	Ndhlovu, 2021
Gunnera perpensa L.	Gunneraceae	River pumpkin (English); ubhoqo, ughobo (Xhosa, Zulu)	Rhizome	Bark decoctions are used to treat fever. Application is not specified.	Philander, 2011; Komoreng et al., 2017
Gymnanthemum mespilifolia (Less.) H. Rob.	Compositae	Inyathelo, usikisiki (Zulu)	Unspecified	Unspecified.	Hutchings et al., 1996
Helichrysum nudifolium (L.) Less.	Compositae	Hottentotseenbossie, kooigoed (Afrikaans); everlastings (English); isicwe, indlebe zebhokwe, undleni (Xhosa); icholocholo, imphepho, isidwaba-somkhovu (Zulu)	Leaves	Leaves are boilied in milk and consumed to reduce fever. Alternatively, a steam bath is made by pouring an infusion on hot stones and the steam is inhaled.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 2009
Helichrysum odoratissimum (L.) Sweet.	Compositae	Kooigoed, hotnotskooigoed, slangbos (Afrikaans); everlastings (English); imphepho (Xhosa, Zulu)	Leaves	An infusion is prepared from the leaves and is drunk to reduce fever.	Dugmore and Van Wyk, 2008; Van Wyk et al., 2009; Nortje and Van Wyk, 2015
Helichrysum patulum (L.) D.Don.	Compositae	Kooigoed (Afrikaans)	Leaves	An infusion is prepared using dried leaves and consumed.	Thring and Weitz, 2006
Hermbstaedtia glauca Rchb. ex Steud.	Amaranthaceae	Bokhoutjie (Afrikaans)	Unspecified	Unspecified.	Nortje and Van Wyk, 2015
Hilliardiella aristata, DC.) H.Rob.	Compositae	Silver vernonia (English)	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Hoodia gordonii (Masson) Sweet ex Decne	Apocynaceae	Hoodia, ghaap, kakimas (Afrikaans); bushman's hat (English)	Stem	Unspecified.	Philander, 2011
Ilex mitis (L.) Radlk.	Aquifoliaceae	Waterboom (Afrikaans); African/Cape holly (English); iphuphuma, isidumo, umdumo, umdumowazo (Zulu)	Bark	Bark infusions are used as emetics.	Hutchings et al., 1996; Philander (2011
***Ipomoea cairica*, L.) Sweet.**	Convolvulaceae	Ihlambe, ijalambu, umaholwana (Zulu)	Leaves	Leaf infusions are consumed to relieve febrile rashes.	Bryant and Struik, 1966; Hutchings et al., 1996
Jatropha hirsuta Hochst.	Euphorbiaceae	Ugodide (Zulu)	Unspecified	Unspecified parts are used in enemas.	Gerstner, 1941; Hutchings et al., 1996
Lantana rugosa Thunb.	Verbenaceae	Wildesalie (Afrikaans); Bird's beer, bird's brandy (English); sekwebetane (Ndebele); utyanibentaka (Xhosa); impema, ubukhwebezane (Zulu); tshidzimbavhalesa (Venda)	Roots	Roots are boiled and the infusion is drunk to reduce fever.	Mahwasane et al., 2013; Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Laphangium luteoalbum (L.) Tzvelev	Compositae	Vaalbossie, roerkruid (Afrikaans); jersey cudweed (English); umgilane (Zulu)	Whole plant	The plant is burnt in the hut of a feverish child.	Moteetee et al., 2019; Ndhlovu et al., 2021; Watt and Breyer-Brandwijk, 1962
Ledebouria spp. (species was not specified)	Asparagaceae	Umathunga (Zulu)	Bulb	Decoction of the bulb are taken orally for fever.	Komoreng et al., 2017
Leonotis leonurus (L.) R. Br.	Lamiaceae	Duiwelstabak, koppiesdagga, rooidagga, wildedagga (Afrikaans); Cape hemp, lion's ear, minaret flower, wild dagga (English); imunyamunya, umunyane omcane (Zulu)	Leaves	Cold water infusions of pounded leaves are drawn into the nostrils to relieve feverish headaches.	Bryant and Struik, 1966; Hutchings et al., 1996
Lessertia frutescens (L.) Goldblatt & J.C. Manning. (synonym *Sutherlandia frutescens* (L.) R.Br.)	Leguminosae	Keurtjie, keurtjiebos, kankerbos (Afrikaans)	Roots and leaves	Leaf infusions or decoctions are used.	Hulley and Van Wyk, 2019
***Leucas lavandulifolia* Sm.**	Lamiaceae	Umagumede (Zulu)	Unspecified	Unspecified.	Mhlongo and Van Wyk, 2019
Leucas martinicensis (Jacq.) R.Br.	Lamiaceae	Kruisement, tolbossie (Afrikaans); tumbleweed (English); amandetshi (Zulu)	Unspecified	Mostly used to alleviate fever in children.	Gerstner, 1941; Hutchings et al., 1996
Lichtensteinia interrupta E.Mey.	Apiaceae	Imbozisa, inhlashane-emhlope, inhlashane-encane, intlashane, umkhapalanga (Zulu)	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Lichtensteinia lacera Cham. & Schltdl.	Apiaceae	Ikathazo (Zulu)	Roots	Unspecified.	Philander, 2011
Lippia javanica Spreng.	Verbenaceae	Koorsbossie (Afrikaans); fever tea (English); mumara (Shona); musukudu, selaole bokhukwane (Tswana); inzinziniba (Xhosa); umsuzwane (Zulu)	Leaves and twigs	Hot leaf infusions or decoctions (usually with water, but sometimes with milk) are taken orally. The leaves are boiled in water and the whole body is covered over the steam to cure fever.	Van Wyk and Gericke, 2000; Van Wyk et al., 2009; Corrigan et al., 2011, York et al., 2011; Asowata-Ayodele et al., 2016; Asong et al., 2019; Semenya and Maroyi, 2020
Litogyne gariepina (DC.) Anderb. Steetz.	Compositae	Isitabuka (Zulu)	Unspecified	Unspecified.	Hutchings et al., 1996
Lotononis mucronata Conrath.	Leguminosae	Semanamana (Sesotho)	Unspecified	Unspecified.	Ndhlovu, 2021
***Mentha longifolia* (L.) L.**	Lamiaceae	Ballerja, kruisement (Afrikaans); wild mint (English); koena-ya-thaba (Sotho); inixina (Xhosa); ufuthane lomhlange (Zulu)	Leaves (most frequently), stems and rhizomes	Infusions or decoctions of a handful of the leaves are made into a tea and drunk. Alternatively, can be used for steam inhalation.	Felhaber and Mayeng, 1997; Van Wyk and Gericke, 2000; Thring and Weitz, 2006; Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Seleteng Kose et al., 2015; Reid et al., 2018; Hulley and Van Wyk, 2019
Microglossa mespilifolia B.L.Rob.	Compositae	Ikhambi-lentwala, indhlondhlo, umdlonzo, Ikhambi lesduli, Ikhambi elimhlophe, Umazambezi (Zulu)	Leaves and stem	Infusions prepared from leaves and stems are consumed.	Watt and Breyer-Brandwijk, 1962; Semenya and Maroyi, 2020
Mimulus gracilis R. Br.	Phrymaceae	Monkey flower (English)	Leaves	A lotion made from leaves used for feverish patients.	Watt and Breyer-Brandwijk, 1962
Momordica balsamina L.	Cucurbitaceae	Unknown	Roots	Used in combination with other medicinal plants to treat fever. Preparation and application are not specified	Van Wyk et al., 2009
Momordica foetida Schumach.	Cucurbitaceae	Nngu (Venda)	Leaves	A decoction of the leaves is taken orally for fever.	Mokganya and Tshisikhawe, 2019
***Nepeta cataria* L.**	Lamiaceae	Kattekruid (Afrikaans); catnip (English)	Leaves	Unspecified.	Philander, 2011
Nidorella resedifolia DC.	Compositae	Stinkkruid (Afrikaans); pverty (English); mokotelio-mosehla (Sesotho)	Unspecified	The plant is burned to fumigate a hut when a child is feverish.	Watt and Breyer-Brandwijk, 1962; Ndhlovu et al., 2021
Oncosiphon piluliferum (L.f.) Källersjö	Compositae	Stinkkruid (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Oncosiphon suffruticosus (L.) Källersjö	Compositae	Stinkkruid (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Osmitopsis asteriscoides (L.) Less.	Compositae	Bels, belskruie (Afrikaans)	Leaves and foliage	A brandy tincture of the leaves is consumed.	Van Wyk et al., 2009; Philander, 2011
Osteospermum imbricatum L.	Compositae	Bergbietou (Afrikaans); umasigcolo nkonekazi (Zulu)	Leaves and stem	Leaves and stems are used as emetics for febrile complaints.	Hutchings et al., 1996
Pelargonium alchemilloides (L.) Aiton	Geraniaceae	Uknown	Roots	A decoction of the root is used to wash a feverish patient.	Watt and Breyer-Brandwijk, 1962
Pelargonium luridum (Andrews) Sweet.	Geraniaceae	Wild geranium (English); inyonkulu, isandhla sonwabu, ishaqa, ishwaqa, uvendle (Zulu)	Leaves, stem, and roots	Unspecified.	Watt and Breyer-Brandwijk, 1962; Roberts, 1990; Hutchings et al., 1996; Thring and Weitz, 2006

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Pelargonium reniforme Curtis.	Geraniaceae	Rabas, rooirabas (Afrikaans)	Tuberous root	Unspecified.	Thring and Weitz, 2006; Van Wyk et al., 2009; Van Wyk and Gorelik, 2017
Pelargonium sidoides DC.	Geraniaceae	Rabas, rooirabas (Afrikaans)	Tuberous root	Unspecified.	Thring and Weitz, 2006; Van Wyk et al., 2009
Peliostomum calcycinum N.E.Br.	Scrophulariaceae	Karooviolets (English); isindwana (Zulu)	Leaves and stem	Cold infusions of leaves and stems are consumed to treat fever.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Ndhlovu et al., 2021
Peltophorum africanum Sond.	Leguminosae	Unkown	Bark	Unspecified.	Mulaudzi et al., 2011
Pentanisia prunelloides (Klotzsch) Walp.	Rubiaceae	Sooibrandbossie (Afrikaans); wild verbena (English); icimamilo, icishamililo-elincane, umakuphole (Zulu)	Leaves and roots	Leaf poultices or hot root decoctions are used to treat fever. Lotions are prepared and administered to febrile patients.	Gerstner, 1941; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Philander, 2011; Seleteng Kose et al., 2015; Mugomeri et al., 2016 Van Vuuren and Frank, 2020
Plumbago zeylanica L.	Plumbaginaceae	Doctor bush (English)	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Phytolacca dodecandra L'Her.	Phytolaccaceae	Ingubivumile, umahedeni (Zulu)	Unspecified	Unspecified parts are used as antifebrile emetics.	Bryant and Struik, 1966; Hutchings et al., 1996
Pittosporum viridiflorum Sims.	Pittosporaceae	Kaarsuur, bosbeukenhout, bosboekenhout (Afrikaans); cheesewood (English); umfusamvu, umkhwenkhwe, umkwenkwe (Xhosa); umvusamu (Zulu)	Bark, leaves and roots	Bark decoctions are consumed to treat febrile complaints. Leaf infusions are consumed.	Bryant and Struik, 1966; Hutchings et al., 1996; Philander, 2011; Asowata-Ayodele et al., 2016; Maroyi, 2017a; Van Vuuren and Frank, 2020
Plectranthus ambiguus (Bolus) Codd.	Lamiaceae	Iboza, Iboza elincane, Ibozane, Imbatatane (Zulu)	Unspecified	Unspecified.	Mhlongo and Van Wyk, 2019
Plectranthus laxiflorus Benth.	Lamiaceae	Ubebebe wehlathi, ufuthane, umadolwane, umsuthuza (Zulu)	Leaves	Powdered leaves are used as enemas.	Gerstner, 1941; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Polygala leptophylla Burch.	Polygalaceae	Skaap-ertjie (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Portulaca oleracea L.	Portulacaceae	Misbredie, oumisbredie (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Portulacaria afra Jacq.	Didiereaceae	Spekbossie, spekboom (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Pouzolzia mixta Solms.	Urticaceae	Seepnetel, wildebraam (Afrikaans); soap nettle (English); udekane (Zulu)	Unspecified	Unspecified parts are used in enemas and administered for feverish conditions.	Gerstner, 1941; Hutchings et al., 1996
Prunus africana (Hook.f.) Kalkman.	Rosaceae	Red stinkwood (English); inyazangoma elimnyana (Zulu); umkakase (Xhosa)	Bark	Unspecified.	Dugmore and Van Wyk, 2008
Psiadia punctulata (DC.) Vatke.	Compositae	Unknown	Unspecified	Unspecified.	Semenya and Maroyi, 2020
Pseudobersama- mossam bicensis (Sim) Verdc	Meliaceae	False white ash, mock white ash (English), umopho (Zulu), vals-witessenhout (Afrikaans)	Root	Unspecified.	Oyedeji-Amusa et al., 2021
***Psidium guajava* L.**	Myrtaceae	Uknown	Leaves	Leaf infusions are prepared by boiling the leaves in water and consumed.	York et al., 2011
Ptaeroxylon obliquum (Thunb.) Radlk.	Rutaceae	Nieshout (Afrikaans); sneezewood (English); umthathe (Xhosa, Zulu)	Wood or bark	Wood or bark is used as an infusion or snuff for fever.	Hutchings et al., 1996; Van Vuuren and Frank, 2020
Pupalia lappacea (L.) Juss.	Amaranthaceae	Bosklits, klits (Afrikaans); sweethearts (English); isinama esibomvu (Zulu)	Roots	Infusions of roots are taken as emetics for fever.	Hutchings et al., 1996
Ranunculus multifidus Forssk.	Ranunculaceae	African buttercup (English)	Whole plant	The plant is burned, and the ash is mixed with beef or mutton fat and is applied to the fontanelle of a baby suffering from fever.	Watt and Breyer-Brandwijk, 1962
Rapanea melanophloeos Mez.	Primulaceae	Kaapse boekenhout, rooiboekenhout, swartbas (Afrikaans); Cape beech (English); ikhubalwane, inhluthe, isicalabi, isiqalaba-sehlati, umaphipha-khubalo, umhluti-wentaba (Zulu)	Bark	Unspecified.	Gerstner, 1941; Hutchings et al., 1996
Rauvolfia caffra Sond.	Apocynaceae	Kinaboom, koorsboom (Afrikaans); quinine tree (English); umhlambamase (Xhosa); umhlambamanzi, umhlabamasi, umjele, umkhabamasi (Zulu)	Bark or root bark	Decoctions of the bark are consumed as emetics for fever.	Hutchings et al., 1996; Van Wyk et al., 2009; Van Vuuren and Frank, 2020
Ricinus communis L.	Euphorbiaceae	Olieboom, kasterolie (Afrikaans); uhlakuva, umhlakuva (Zulu)	Leaves and seeds	Infusions of leaves and seeds are consumed to treat fever in children.	Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Rumex sagittatus Thunb.	Polygonaceae	(klim/rank/rooi) suuring (Afrikaans); umdende (Zulu)	Roots	Powdered root is used for febrile conditions. Preparation and application was not specified.	Hutchings et al., 1996;
***Ruta graveolens* L.**	Rutaceae	Wynruit, wynruik (Afrikaans)	Leaves	Leaf infusions and poultices are used to reduce fever.	Watt and Breyer-Brandwijk, 1962; Thring and Weitz, 2006; Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Philander, 2011; Nortje and Van Wyk, 2015; Van Wyk and Gorelik, 2017; Hulley and Van Wyk, 2019
Salix mucronata Thunb.	Salicaceae	Wilde wilger, rivierwilger (Afrikaans); wild willow (English)	Branch tips and leaves	Decoctions or infusions of the bark and leaves are used for fever.	Van Wyk et al., 2009; De Beer and Van Wyk, 2011; Philander, 2011; Van Wyk and Gorelik, 2017; Hulley and Van Wyk, 2019
***Salix babylonica* L.**	Salicaceae	Wilgeboom bas (Afrikaans)	Bark	An infusion of the bark is drunk to treaty fever.	Van Wyk et al., 2009
Salvia chamelaeagnea Berg.	Lamiaceae	Bloublom (metjie)salie, afrikaanse salie, bloublomsalie (Afrikaans)	Flowers	Infusions prepared using the flowering tops of the plant are used consumed to treat fever.	Van Wyk and Gorelik, 2017
Salvia dentata Aiton.	Lamiaceae	Bloublomsalie, bergsalie (Afrikaans)	Leaves	Leaf infusions are consumed to treat fever.	Nortje and Van Wyk, 2015
***Salvia microphylla* Kunth.**	Lamiaceae	Rooiblomsalie, rooisalie (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Scadoxus puniceus (L.) Friis & Nordal	Amaryllidaceae	Idumbelikahloyile, (isangoma), uhloyileumphompo (Zulu)	Unspecified	Unspecified.	Mhlongo and Van Wyk, 2019; Van Vuuren and Frank, 2020
***Schinus molle* L.**	Anacardiaceae	Peperboom (Afrikaans); Peruvian pepper (English)	Leaves	Leaf compresses are placed on the head to reduce fever. Infusions are consumed	Van Wyk et al., 2009; Nortje and Van Wyk, 2015; Hulley and Van Wyk, 2019
Sceletium tortuosum (L.) N.E. Br.	Aizoaceae	Kougoed (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
***Schkuhria pinnata* (Lam.) Kuntze ex Thell.**	Compositae	Kleinkakiebos (Afrikaans); dwarf marigold (English); unsakansakane, umanxiweni (Zulu)	Unspecified	Mostly used in paediatrics. Preparation and application was not specified.	Mhlongo and Van Wyk, 2019; Ndhlovu et al., 2021
Sclerocarya birrea (A. Rich.) Hochst.	Anacardiaceae	Maroela (Afrikaans); cider tree, marula (English); umganu (Zulu, Tsonga); morula (Tswana)	Bark	Decoctions are made from the bark and consumed to reduce fever.	Gerstner, 1941; Hutchings et al., 1996; Van Wyk and Gericke, 2000
Searsia burchellii (Sond. ex Engl.) Moffett	Anacardiaceae	Taaibos (Afrikaans)	Unspecified	Unspecified.	Nortje and Van Wyk, 2015
Searsia lancea (L.f.) F.A. Barkley	Anacardiaceae	Karee (English)	Leaves	Unspecified.	Mulaudzi et al., 2012
Senecio cinerascens Aiton.	Compositae	Vieroulap, oulap (Afrikaans)	Leaves	Leaf infusions are consumed to treat fever.	Nortje and Van Wyk, 2015
Senecio oxyriifolius DC.	Compositae	Old-man-in-the-spring (English); idinjana, idumbe, idumbe les endhle, ihlula (Zulu)	Roots	Root decoctions are consumed to alleviate shivering during fever.	Hutchings et al., 1996; Watt and Breyer-Brandwijk, 1962
Senecio serratuloides DC.	Compositae	Ichazampukane, insukumbili, intsukumbili-umahanya, umaphozisa, umkutelo (Zulu)	Leaves	Leaf decoctions and infusions are consumed to treat fever.	York et al., 2011
Silene undulata Aiton.	Caryophyllaceae	Gunpowder plant (English)	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962
***Solanum americanum* Mill.**	Solanaceae	Blackberry nightshade, English)	Berries	The berry is consumed as a tonic to relieve fever.	Watt and Breyer-Brandwijk, 1962
Solanum incanum L.	Solanaceae	Intuma, intuma encane, umagangeni (Zulu)	Unspecified	Unspecified.	Mhlongo and Van Wyk, 2019
Spirostachys africanus Sond.	Euphorbiaceae	Tambootie (English)	Bark	Unspecified.	Mulaudzi et al., 2012
Stachys aethiopica L.	Lamiaceae	Teebossie (Afrikaans)	Unspecified	Unspecified.	Hulley and Van Wyk, 2019
Stachys rugosa Aiton.	Lamiaceae	Koorsbos, bergsalie, stinkkoorsbos, stinkbos (Afrikaans)	Leaves	Leaf decoctions and infusions are consumed to treat fever.	Nortje and Van Wyk, 2015
Strychnos spinosa Lam.	Loganiaceae	Bobbejaanklapaper, groenklapper, wildekalabasboom (Afrikaans); green monkey orange, monkey apple/orange (English); ihlala, umhla, umhlahlakolotsho, umhlahlawehlathi (Zulu)	Roots and green fruit	Unspecified.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Corrigan et al., 2011
Sutera spp. (species was not specified)	Scrophulariaceae	Umahokwe (Zulu)	Leaves and stem	Infusions from leaves and stems are taken orally or administered as enemas for fever.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Sutherlandia microphylla Burch. ex DC.	Leguminosae	Unknown	Unspecified	Unspecified.	Watt and Breyer-Brandwijk, 1962
Syzygium cordatum Hochst.	Myrtaceae	Waterbessie (Afrikaans)	Bark	Unspecified.	Mulaudzi et al., 2011

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Tabernaemontana ventricosa Hochst. Ex A.DC.	Apocynaceae	Bospaddaboom (Afrikaans); fever tree, forest toad tree (English), umkhamamasane (Zulu)	Bark	Unspecified.	Hutchings et al., 1996
Tecoma capensis (Thunb.) Lindl.	Bignoniaceae	Kaapse kamperfoelie (Afrikaans); Cape honeysuckle (English); lungana, uthswala benyonuchahacha, umunyane (Zulu)	Bark	Dried powdered bark infusions are consumed.	Watt and Breyer-Brandwijk, 1962; Roberts, 1990; Hutchings et al., 1996; Mhlongo and Van Wyk, 2019
Tetradenia riparia (Hochst.) Codd.	Lamiaceae	Watersalie (Afrikaans); ginger bush (English); iboza, ibozane (Zulu)	Leaves	A leaf infusion is prepared and used for steam inhalation. Alternatively, a leaf decoction is drunk to reduce fever.	Hutchings et al., 1996; Felhaber and Mayeng, 1997; Van Wyk et al., 2009; York et al., 2011; Mhlongo and Van Wyk, 2019
Teucrium africanum Thunb.	Lamiaceae	Aambeibossie (Afrikaans)	Whole plant	A decoction of the whole plant is used for the treatment of fever.	Watt and Breyer-Brandwijk, 1962
Thalictrum minus L.	Ranunculaceae	Lesser meadow-rue (English)	Leaves and roots	An infusion of the leaf or a decoction of the root is used.	Watt and Breyer-Brandwijk, 1962
Trichilia dregeana Sond.	Meliaceae	Bos Rooi-essenhout, bosrooiessenhout (Afrikaans); cape mahogany, forest mahogany, forest natal mahogany, white mahogany (English); mutshikili, mutuhu, muuhu (Venda); umhlakele, umkhuhlu, umkhuhlwa (Xhoza), ixolo, umathunzi, umathunzini, umkhuhlu (Zulu)	Root	Unspecified	Oyedeji-Amusa et al., 2021
Trichilia emetica Vahl	Meliaceae	Natal mahogany (English); rooiessenhout (Afrikaans); mamba (Northern Sotho); umathunzini (Zulu); umkhuhlu (Xhosa); mutuhu (Venda)	Root, bark	Decoction or infusion.	Oyedeji-Amusa et al., 2021
Tulbaghia alliacea L.f.	Amaryllidaceae	Wildeknofflok (Afrikaans); wild garlic (English); ishaladi-lezinyoka, isikhwa, umwelela (Zulu)	Leaves	A milk infusion of the leaves is used.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 2009; Nortje and Van Wyk, 2015; Van Wyk and Gorelik, 2017
Tulbaghia capensis L.	Amaryllidaceae	Wilde knoffel (Afrikaans); wild garlic (English)	Bulb	Unspecified.	Philander, 2011
Tulbaghia violacea Harv.	Amaryllidaceae	Wilde knoffel (Afrikaans); wild garlic (English); isihaqa (Zulu)	Bulb	The freshly harvested bulbs are boiled in water and are administered as enemas. For fever, a tea is made from bulbs and is consumed three times daily.	Hutchings et al., 1996; Thring and Weitz, 2006; Van Wyk et al., 2009; Davids et al., 2016
Vigna luteola (Jacq.) Benth.	Leguminosae	Isikhwali (Zulu)	Unspecified	Emetics made from unspecified parts of the plant are taken.	Gerstner, 1941; Hutchings et al., 1996
Vigna unguiculata (L.) Walp.	Leguminosae	Koertjie (Afrikaans); cow pea (English); isikhwali (Zulu)	Unspecified	Emetics made from unspecified parts of the plant are taken.	Gerstner, 1941; Hutchings et al., 1996; von Koenen, 1996
Vigna vexillata (L.) A. Rich.	Leguminosae	Isikhwali (Zulu)	Unspecified	Emetics made from unspecified parts of the plant are taken.	Gerstner, 1941; Hutchings et al., 1996
Viscum capense L.f.	Santalaceae	Voelent (Afrikaans)	Whole plant	Whole plant pieces are placed in brandy and taken to relieve fever.	Thring and Weitz, 2006
Volkameria glabrum (E. Mey.) Mabb. & Y.W. Tuan	Verbenaceae	Bitterblaar, bontelhout, harpuisblaar, huilboom, stinkboom (Afrikaans); tinderwood, verbena tree, white cat's whiskers (English), ifamu, umnukalembeba, umnukambiba, umqangazane, umqaqongo, umnqoqongo, umqwaqwane, uphehlacwathi (Zulu)	Leaves	Unspecified.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Warburgia salutaris (G. Bertol.) Chiov.	Canellaceae	Koorsboom, peperbasboom (Afrikaans); pepper-bark tree, fever tree (English); isibaha, isibhaha, amazwecehlabayo (Zulu)	Bark	Bark (crushed into a powder) is consumed.	Hutchings et al., 1996; Van Wyk et al., 2009
***Withania somnifera* (L.) Dun.**	Solanaceae	Bitterappelliefie, geneesblaarbossie, spanjoolbossie, stuipebossie, vernietbossie, vuilsiektebossie, (Afrikaans); poisinous gooseberry, winter cherry (English); ibuvimba, ubuvimbha, ubuvimbo, umaqhunsula (Zulu)	Roots	Enemas made from roots are administered to infants for fever. A decoction of the roots is used to treat fever.	Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Van Wyk et al., 2009; Seleteng Kose et al., 2015
Ximenia caffra Sond.	Olacaceae	Sourplum (English); umthunduluka (Ndebele)	Fruit, bark, and leaves	Unspecified.	Chingwaru et al., 2019

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Table 1 (*continued*)

Plant species	Family	Common names	Plant part used medicinally	Traditional preparation or application	Reference
Zanthoxylum capense Harv.	Rutaceae	Kleinperdepram, kardamon (Afrikaans); small knobwood, cardamon (English); monokwane (Sotho); umlungumabele (Xhosa); umnungamabele (Zulu)	Fruit, bark, and leaves	Infusions or decoctions of the fruits or leaves are used as a carminative to treat fever.	Dugmore and Van Wyk, 2008; Van Wyk et al., 2009; Philander, 2011
Ziziphus mucronata Willd.	Rhamnaceae	Buffalo thorn (English); blinkblaar-wag-'n-bietjie (Afrikaans); mokgalo (Tswana); mutshetshete (Venda); umPhafa (Xhosa); unPhafa, umLahlankosi, isiLahla (Zulu)	Leaves	A cold-water extract of leaves is given to children with fever.	Cock et al., 2019

Introduced and/or widely used alien species are indicated in **bold text**; Tbs = tablespoon.

(Seifert et al., 2021). Whilst studies such as these are important to verify the antipyretic activity of the plant medicines, they provide no information on the antipyretic mechanisms of the plant preparations. Two other studies screened pure components of plants used to alleviate fever. One study tested the compound roemrefidine, which is present in substantial levels in aqueous *A. delagoensis* leaf extracts and reported that it had noteworthy antipyretic activity *in vivo* (Hawkes et al., 2011). More recently, viscosine was identified in substantial levels in aqueous *D. viscosa* leaf extracts (as reviewed in Al-Snafi, 2017). Notably, anti-inflammatory activity has been reported for this compound via the inhibition of the enzyme liopoxygenase (Khan et al., 2013). On the basis of these findings, pure vincosine was tested for antipyretic activity in an *in vivo* rat model and substantial decreases in body temperature were reported (Amabeoku et al., 2001; Muhammad et al., 2019). Whilst these studies indicate that crude *D. viscosa* extracts may also have noteworthy antipyretic activity, this has yet to be confirmed and further studies are required to validate the use of this plant to treat fever.

Several studies also examined the ability of the plant extracts to inhibit specific components of fever. Most of those studies screened the ability of the traditional medicines to block PGE2 production as it is a major inflammatory mediator of fever development. Indeed, the majority of the current range of conventional antipyretic treatments (including the NSAID ibuprofen) inhibit the COX-2 enzyme, decreasing PGE2 production and thereby alleviating fever (Zampronio et al., 2015). Several studies have screened southern African plants for COX inhibitory activity. A recent study screened an ethanol *C. sylvaticus* bark extract for COX-2 inhibitory activity and reported that it inhibited the enzyme by approximately 60%, which was similar to the level of inhibition seen for indomethacin (Maroyi, 2017a). Similarly, an ethanolic *S. africanus* bark extract inhibited both COX-1 and COX-2 activities (Mulaudzi et al., 2012), whilst ethanol bulb extracts of both *E. autumnalis* and *E. bicolor* both inhibited COX-1 activity significantly (Taylor and Van Staden, 2001). Noteworthy COX inhibitory activity was also reported for an ethanolic *H. nudifolium* leaf extract, although that study did not differentiate between COX-1 and COX-2 inhibitory activity. In contrast, *C. molle* lacked COX-2 inhibitory activity (Schultz et al., 2021). This was perhaps surprising as several related *Combretum* spp. (Cock et al., 2022) and *Terminalia* spp. (Cock, 2015) have noteworthy COX inhibitory activity. Notably, the Schultz et al. study (2021) only screened the extracts against COX-2 and did not screen against COX-1. Further studies are required to test the potential of this plant against that ezyme to more fully examine its potential to decrease prostaglandin production.

The effects of southern African plants on other pyrogenic mediators have been even less studied. Indeed, we were only able to find two studies that examined southern African plants (or compounds derived from them) for their effects on cytokine release. A hydro-alcoholic *P. oleraceae* extract significantly decreased the levels of the endogenous pyrogens TNF-α and IL-6 in LPS-stimulated peripheral blood mononuclear cells (PMBCs), thereby alleviating fever (Allahmoradi et al., 2017). Another study screened the scalarane sesterterpenoid taraxerone for cytokine inhibitory activity on the basis of that compound being identified in substantial quantities in *L. lavandulifolia* extracts (Jayaraman and Variyar, 2021). Notably, that study reported that treatment with taraxerone substantially decreased the production of IL-4 and IL-6 pyrogens. We were unable to find studies examining the effects of the other southern African plants against these or other pyrogenic mediators and substantially more work is required in this area.

4. Discussion

Plants play an important role in southern Africa medicine and they

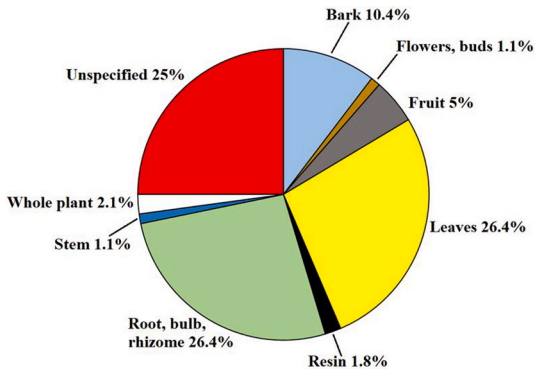

Fig. 1. The relative proportion that individual plant parts were used to treat fever, expressed as a % of the overall usage. For several plant species, more than one part was used therapeutically to treat fever. Those species are included in all of the plant part categories in which they are listed.

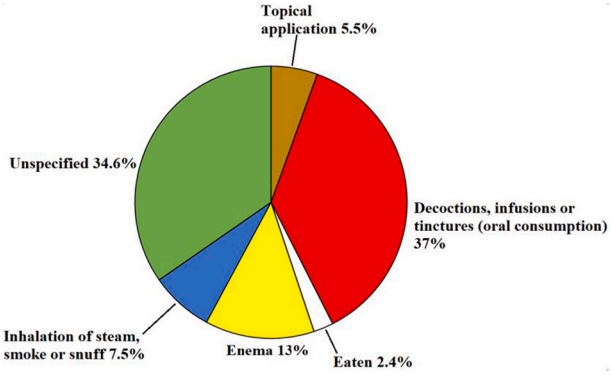

Fig. 2. The methods of administration and preparation of southern African plants to treat fever, expressed as a % of the overall administration methods. Several plant species were administered by more than one method traditionally. Those species are included in all of the administration categories in which they are listed.

Table 2
Southern African medicinal plants used as mixtures to reduce fever.

Plant species	Plant part used medicinally	Plant species combined with	Part of second plant used medicinally	Traditional method of usage	Reference
Acorus calamus	Rhizome	*Artemisia afra*	Leaves	The powdered herbs are bolied in 1.5 L of water for half an hour. The mixture is strained, cooled and half a cup is drunk four times a day.	Felhaber and Mayeng, 1997
		Warburgia salutaris (	Bark	Half a litre of boiling water is poured onto the mixture of powdered herbs and allowed to stand for 10 min, strained and bottled. Half a cup is drunk three times a day to relieve fever.	
Artemisia afra	Leaves	*Alepidea amatymbica*	Root	The mixture is bolied in 1 L of water for 5 min. When cool, half a cup is drunk three times a day until finished.	Felhaber and Mayeng, 1997
		Warburgia salutaris	Bark	Half a litre of boiling water is poured over the plant material and allowed to stand for half an hour. The liquid is then strained and a quarter cup is consumed three times a day.	
		Lippia javanica	Leaves and stem	Preparation and application unspecified.	Smith, 1895; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996
Eucalyptus grandis	Leaves	*Lippia javanica*	Leaves	A mixture of *E. grandis* and *L. javanica* leaves is mixed with water and allowed to stand. The decoction (1 Tbs) is consumed three times a day. The steam may also be inhaled. Children may also drink the decoction but at half dosages used for adults.	York et al., 2011
		Clausena anisata. combined with	Leaves	A mixture of *E. grandis, C. anisata* and *L. javanica* leaves are boiled in water for 40 min. Once cool, 1 Tbs of the decoction is consumed twice a day to treat fever. Children take 1 Tsp three times a day.	York et al., 2011
		Lippia javanica	Leaves		
		Combretum molle combined with	Leaves	A mixture of *E. grandis, C. molle* and *L. javanica* leaves are boiled with 1.5 L of water until 0.5 L has evaporated. Half a cup is consumed three times a day to treat fever. Children take 1 Tbs three times a day.	York et al., 2011
		Lippia javanica	Leaves		
		Brachylaena dicolor (DC.) combined with	Leaves	A mixture of *E. grandis, B. discolor* and *L. javanica* leaves are boiled in water. One cup is consumed three times a day. Children take one Tsp of this decoction three times a day.	York et al., 2011
		Lippia javanica	Leaves		
		Ozoroa obovata (Oliv.) R.Fern. & A. Fern.	Leaves	A mixture of *E. grandis* and *O. obovata* leaves are boiled in water and the steam is inhaled daily to treat fever.	York et al., 2011
		Lippia javanica combined with	Leaves	A mixture of *E. grandis, L. javanica, P. guajava* and *S. serratuloides* leaves is boiled in water and the steam is inhaled twice a day to treat fever.	York et al., 2011
		Psidium guajava and	Leaves		
		Senecio serratuloides	Leaves		
		Lippia javanica combined with	Leaves	A handful of leaves of *E. grandis, L. javanica* and *T. riparia* leaves are boiled in water. A half cup is drunk three times a day to treat fever.	York et al., 2011
		Tetradenia riparia	Leaves		
Hypoxis spp. (species not specified)	Bulb	*Aloe marlothii* combined with	Leaves	One *Hypoxis* spp. bulb is combined with a chopped *A. marlothii* leaf and chopped *S. puniceus* and *E. caffra* roots. Boiling water is added, and a half cup is drunk daily.	York et al., 2011
		Scadoxus puniceus and	Roots		
		Erythrina caffra	Roots		
Lippia javanica	Leaves	*Trichilia emetica*	Leaves	Dried L. *javanica* and *T. emetica* leaves are boiled in water and the steam is inhaled twice a day. Not recommended to be used by children.	York et al., 2011
		Tetradenia riparia	Leaves	Dried L. *javanica* and *T. riparia* leaves are added to a cup of warm water. Two Tbs is consumed as required.	
Sclerocarya birrea	Bark	*Syzygium cordatum*	Bark	The barks of *S. birrea* and *S. cordatum* are boiled in water and drunk (2 Tbs/day) to treat fever. Children only take one Tsp twice a day.	York et al., 2011
Senecio deltoideus Less.	Leaves	*Senecio serratuloides*	Leaves	A mixture of *S. deltoideus* and *S. serratuloides* leaves are boiled in water. Half a cup is drunk twice a day to treat fever. Children only take 1 Tbs twice a day.	York et al., 2011
Tulbaghia alliacea	Bulb	*Artemisia afra*	Leaves	A poultice of *T. alliaceae* and *A. afra* leaves are applied to children's chests until the fever abates.	York et al., 2011
Withania somnifera	Root	*Xysmalobium undulatum* (L.) W.T. Aiton	Unspecified	Roots of *W. somnifera* are mixed with unspecified *X. undulatum* plant parts and used to treat fever. Preparation and application were not specified.	York et al., 2011

Tbs = tablespoon; Tsp = teaspoon.

Table 3
Scientific evaluations of antipyretic-related activities of southern African medicinal plants.

Plant species	Plant part used medicinally	Type of extract used	Outcome of study	Reference
Adansonia digitata	Leaves, fruit pulp, bark, resin	Water	An average reduction in body temperature of 1.3 °C was recorded in a rat model 4 h after treatment with aqueous *A. digitata* extract (800 mg/kg).	Ramadan et al., 1994
Albertisia delagoensis	Leaves	Aqueous	Aqueous *A. delagoensis* extract contains roemrefidine, which has antipyretic activity.	Hawkes et al., 2011
Clematis brachiata	Leaves	Aqueous	A significant decrease in pyrexia was observed following *C. brachiata* treatment in a rodent brewer's yeast-induced pyrexia model.	Mostafa et al., 2010
Combretum molle	Leaves	Ethanol	Despite other *Combretum* spp. extracts displaying COX-2 inhibitory activity, *C. molle* extracts lacked inhibitory activity.	Schultz et al., 2021
Croton sylvaticus	Bark	Ethanol	An ethanolic *C. sylvaticus* extract inhibited COX-2 by 59% (compared with 66.5% inhibition by an indomethacin control) providing it with antipyretic activity.	Maroyi, 2017b
Dodonaea viscosa	Leaves (mainly), or pale yellow/whitish fruit pulp	Water	Viscosine is present in substantial levels in aqueous *D. viscosa* extracts. Viscosine treatment resulted in significantly reduced body temperatures in test animals following viscosine treatment in a yeast-induced pyrexia model, with a higher antipyretic potential compared to aspirin during later stages of fever progression.	Muhammad et al., 2019; Amabeoku et al., 2001
Eriocephalus africanus	Unspecified	Water	A significant reduction in body temperature was observed following administration of aqueous *E. africanus* extract (100–200 mg/kg). Peak therapeutic activity was noted at 2 h.	Amabeoku et al., 2000
Eucalyptus globulus	Leaves and foliage	Dichloromethane	A dichloromethane *E. globulus* extract (250 mg/kg) displayed antipyretic activity *in vivo* at comparable doses to the reference drug aspirin in a rat model. The anti-pyretic mechanism of the extract is thought to be due to terpinolene, alpha-pinene, borneol, globulol and terpineols in the extract.	Mworia et al., 2019
Eucomis autumnalis	Bulb	Ethanol	Substantial COX-1 inhibitory activity was observed for an ethanolic bulb extract	Taylor and Van Staden, 2001
Eucomis bicolor	Bulb and roots	Ethanol	Ethanol extract of the bulb and root have substantial COX-1 inhibitory activity.	Taylor and Van Staden, 2001
Foeniculum vulgare	Leaves	Aqueous	Aqueous *F. vulgare* leaf extract had substantial antipyretic activity *in vivo*.	Khan et al., 2017
Helichrysum nudifolium	Leaves	Ethanol	COX activity was inhibited by an ethanolic *H. nudifolium* extract by 96%.	Maroyi, 2019
Leucas lavandulifolia	Unspecified	Methanol	Taraxerone has been identified in substantial quantities in *L. lavandulifolia* extracts. Production of IL-4 and IL-6 pyrogens is suppressed by taraxerone (25 μg/mL) treatment.	Jayaraman and Variyar, 2021
Mentha longifolia	Leaves	Aqueous	Administration of aqueous *M. longifolia* leaf extract (37.5–150 mg/kg) significantly reduces LPS-induced pyrexia in rats.	Amabeoku et al., 2009
Pelargonium sidoides	Tuberous root	Aqueous fraction	Children suffering from acute tonsillopharyngitis received comedication of EPs 7630, an active ingredient of *P. sidoides* during a meta-analysis. The results showed accelerated recovery from fever and a reduction in the need for comedication with paracetamol.	Seifert et al., 2021
Portulaca oleracea	Aerial parts (stems and leaves)	Hydro-alcohol	A significant decrease in the concentration of the pyrogenic cytokines TNF-α and IL-6 was observed in LPS-stimulated peripheral blood mononuclear cells (PMBC's) following treatment with *P. oleraceae* extract.	Allahmoradi et al., 2017
Pupalia lappacea	Aerial parts (stems and leaves)	Hydro-alcohol	There was a significant reduction in the rat body temperature following *P. lappacea* extract treatment in a yeast-induced pyrexia model.	Neeharika et al., 2013
Ruta graveolens	Leaves	Methanol	There was a significant delay in the onset of thermally stimulated pyrexia in mice following *R. graveolens* (400 mg/kg) treatment.	Loonat and Amabeoku, 2014
Solanum nigrum L.	Leaves	Aqueous	Significant antipyretic activity was observed in response to *S. nigrum* treatment in a brewer's yeast-induced pyrexia model.	Zakaria et al., 2009
Spirostachys africanus	Bark	Ethanol	COX-1 and COX-2 activities were inhibited by an ethanolic *S. africana* bark extract.	Khumalo et al., 2022; Mulaudzi et al., 2012
Tecoma capensis	Leaves	Methanol	A significant reduction in body temperature was observed following oral treatment with *T. capensis* methanol leaf extract (100–500 mg/kg) in an induced fever rat model.	Saini and Singha, 2012
Volkameria glabrum	Leaves	Methanol	Significant antipyretic activity was observed for methanol *C. glabrum* leaf extract (100 mg/kg) following oral administration in a rat model. The antipyretic activity was approximately half as potent as paracetamol.	Wahba et al., 2010

are often the first-choice treatment for many rural and urban populations (Mmushi et al., 2009). It is widely believed by much of the southern African population (often erroneously) that medicines of plant origin are safe. This review highlights the paucity of information into the effectiveness of southern African medicinal plants used traditionally to alleviate fever. Currently, there is little information on the dosages, therapeutic forms, and dosage intervals for many of these plants. This information is necessary to ensure that the plants are used in safe and effective ways. Further in-depth ethnobotanical studies would provide the basis for these studies and would provide a platform for researchers to select the most appropriate plant, plant parts and treatment methods for examination, and to provide the best chances of developing effective and novel antipyretic therapies.

Notably only ~11% of the 203 plants identified from ethnobotanical records and studies have been screened to validate their efficacy. Fewer of those studies also reported the toxicology profiles of the extracts in the same study. Furthermore, of the plants that have been scientifically examined, most have only been examined *in vivo*, and only a single clinical evaluation was noted in the literature for a *P. sidoides* fraction (Seifert et al., 2021). Whilst *in vivo* and clinical evaluations are important to evaluate the effectiveness of the medicine in complex multicellular systems, they do not provide information about the mechanism of action of the intended medicinal plant. Furthermore, the paucity of information on the preparation of the medicine, its dosage and method of administration complicates ongoing studies and may provide misleading and fallacious information about the effectiveness of some therapies.

The antipyretic mechanism(s) of most the southern African plants traditionally used to treat fever have not yet been rigorously examined. Of the mechanistic studies, COX inhibitory activity has been most extensively studied. This is perhaps not surprising as PGE2 (a product of COX enzymatic activity) is a major mediator of fever. Inhibition of PGE2 release via COX inhibition is therefore a valid antipyrogenis target. However, despite COX inhibition being the most studied antipyrogenic mechanism of southern African plants, only five species have been tested to date for that activity and similar studies are required for all of the southern African plants used traditionally to treat fever. Of further note, none of the studies reported herein quantified the levels of PGE2 produced. Whilst the enzymatic assays show the inhibition of existing enzyme, they do not examine COX production following pyrogen stimulus. If COX production is increased during fever (as is expected), the increased levels may still allow for significantly elevated PGE2 levels (despite inhibition of some of the enzyme molecules), which may still result in fever. Future studies quantifying the production of COX enzymes, as well as the levels of PGE2 are required.

Few studies tested the effects of the southern African plants against other pyrogenic mediators. Indeed, we only found two studies that examined the effects of the extracts on TNF-α, IL-4 and IL-6 levels (Allahmoradi et al., 2017; Jayaraman and Variyar, 2021). The effects of the plant extracts on other pro- and anti-inflammatory mediators have been completely neglected. Substantially more research is needed to evaluate the effects of the traditionally used southern African plants against the pyrogenic and cryogenic mediators. Furthermore, to the best of our knowledge, no studies have evaluated the effects of southern African plants on the production of endogenous cryogens such as IL-10. Additionally, the following effects relevant to fever etiology and progression have been completely ignored to date and further studies are required to evaluate;

- The presence and levels of cryogenic compounds in the extracts.
- Whether the plant extracts can induce production of cryogens in fever models.
- Whether the plant extracts can down-regulate the firing of cold sensitive neurons and thereby prevent elevation of the core body temperature.
- Whether plant extracts or compounds can bind to pyrogenic cytokines and inhibit the activation of arachidonic acid/prostaglandin production pathways.
- Whether plant extract components can inhibit TLR-4 receptors on the surface of cells, thereby inactivating NF-κB, which would subsequently down-regulate endogenous pyrogen formation.
- Whether plant extract components inhibit NF-κB activation of endogenous pyrogens by other mechanisms, thereby blocking the production of endogenous pyrogens.
- Whether the plant preparations that are yet to be tested can inhibit COX activity (both COX-1 and COX-2), and therefore inhibit PGE2 synthesis.
- Whether the plant extracts can inhibit the synthesis of PGE2 peripherally in the lungs, liver and at the site of inflammation.
- Whether the plant extracts can directly inhibit the effects of PGE2.
- Whether the plant extracts can block vagal nerve stimulation and the humoral pathway leading to the onset of fever.

A further consideration for future studies is the selection of the appropriate solvent to prepare the extracts. Aqueous decoctions and infusions are the most common traditional preparation method. Despite this, more than half of the studies highlighted in this review used methanolic or ethanolic extracts to screen for antipyretic bio-activities. As aqueous preparations are the most common form used traditionally, future studies should test aqueous extracts to validate traditional usage. However, the screening of alcoholic extracts in the previous studies may have been fortuitous as aqueous extracts are limited to extracting higher polarity compounds and mid-low polarity compounds may be overlooked in aqueous extracts. In contrast, alcoholic extracts have substantially wider extractant ranges and can extract mid-low polarity compounds, in addition to higher polarity compounds. What further needs be investigated is the adverse effects of these alcoholic extracts in the animal model.

Because fever is a host defence mechanism against foreign invasion of pathogenic species, amongst others, the antimicrobial link to antipyretic properties requires further attention. It would be interesting to investigate if those plants in the *in vivo* model having superior antipyretic activity can inhibit pathogens commonly associated with inducing a fever. Furthermore, the link between anti-inflammatory activity and fever should be further expolored.

5. Conclusion

This study identified plant species used in southern African traditional medicine to alleviate fever and cross-referenced those species with studies undertaken on antipyretic activities. Ethnobotanical records identified 203 plant species that are used in southern African traditional medicine to treat fever. When examining other ethnobotanical leads into Southern African plants, it is apparent that there are some plant species mentioned herein, that clearly overlap with those mentioned for more specific diseases (such as malaria, bacterial and viral infections) inducing fever. Approximately 11% of all the plant species ethnobotanically recorded herein have been studied scientifically for antipyretic properties. Additionally, where plant preparations have been tested for antipyretic activities, the studies have generally only confirmed the ability of the plant medicines to decrease body temperature, without consideration of the antipyretic mechanism(s). Substantially more work is required to further investigate this. There exists a wealth of potential into the exploratory research of antipyretic effects of southern African plants and this review should provide a number of promising leads.

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CRediT authorship contribution statement

I.E. Cock: Wrote, Conceptualization. **N. Luwaca:** Original data collection, Wrote initial drafts. **S.F. Van Vuuren:** Conceptualization, Wrote, Edited and Submitted final submission.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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