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The traditional use of southern African medicinal plants in the treatment of viral respiratory diseases: A review of the ethnobotany and scientific evaluations

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ARTICLE INFO

Keywords:

South African plants
Traditional medicine
Influenza
Rhinovirus
Parainfluenza
Bronchitis

ABSTRACT

Ethnopharmacological relevance: Viral respiratory infections are amongst the most common infections globally, with most of the world's population contracting at least one infection annually. Numerous plant species are used in traditional southern African healing systems to treat these diseases and to alleviate the symptoms. Despite this, the therapeutic potential of these plants against viral respiratory diseases remains poorly explored.

Aim of the study: The aim of this study was to document the southern African plant species used in traditional medicine to treat viral respiratory infections. We also examined the extent of scientific evaluations of southern African plant species against the respiratory-infective viruses, with the aim of stimulating interest in this area and focusing on future studies.

Materials and methods: We undertook an extensive review of ethnobotanical books, reviews and primary scientific studies to identify southern African plants which are used in traditional southern African medicine to treat viral respiratory diseases. This information was used to identify gaps in the current research that require further study.

Results: Two hundred and fifty-seven southern African plant species were identified as traditional therapies for viral respiratory diseases. Surprisingly, only one of those species (as well as twenty-one other species not recorded for these purposes) has been evaluated for the ability to block respiratory virus production. Furthermore, most of these studies screened against a single viral strain and none of those studies examined the mechanism of action of the plant preparations.

Conclusions: Despite well documented records of the use of southern African plants to treat respiratory viral diseases, the field is poorly explored. Nearly all of the plant species used in traditional healing systems to treat these diseases are yet to be tested. Substantial further work is required to verify the efficacy of these traditional medicines.

1. Introduction

Respiratory diseases are amongst the most prevalent diseases globally and impose an immense burden on the healthcare system. Several of these diseases are common causes of severe illness and mortality (Wang et al., 2015). The greatest burden of respiratory diseases is due to pathogenic infections. Acute lower respiratory tract infections are one of the top causes of mortality and disability globally, causing approximately four million deaths annually (Unicef et al., 2006). These conditions are particularly concerning in children and are the leading cause of mortality in children under five years of age. Influenza virus infections

account for many acute lower respiratory tract infections and it is estimated that 250,000–500,000 people die from severe influenza virus infections annually. While Semanya and Maroyi (2018) reported on 306 medicinal plant species used to treat and manage respiratory infections, a concerted effort to date has not been undertaken in categorising these medicinal plants specifically to respiratory viral and bacterial sources. This review focusing on southern African medicinal plants for viral infections forms part one of a two part review whereby the focus on bacterial pathogens is reviewed as Part 2 in a separate manuscript (Cock and Van Vuuren, 2020).

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<https://doi.org/10.1016/j.jep.2020.113194>

Received 18 March 2020; Received in revised form 30 June 2020; Accepted 15 July 2020

Available online 27 July 2020

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1.1. Viral respiratory infections

Several viruses can infect respiratory tissue and induce respiratory illnesses. Of these, the most common viral causes of respiratory disease are influenza virus, rhinoviruses, respiratory syncytial virus (RSV), parainfluenza virus, adenovirus, human metapneumovirus, and enterovirus.

1.1.1. Influenza

Influenza (often abbreviated to flu) is a highly infectious airborne disease caused by the influenza virus. There are four genus's of influenza virus, of which three genus's (A, B and C) can infect humans (Paules and Subbarao, 2017). Influenza virus D genus has never been reported as a human infection and instead only infects pigs and cattle. However, it is believed that this genus has the potential to infect humans and cross species infections may be reported in the future (Asha and Kumar, 2019). Of the other three classes of influenza virus, influenza virus A is the most important to human health and is the most virulent of the human influenza pathogens (Paules and Subbarao, 2017). Whilst this genus consists of only a single species, numerous serotypes have been described (listed in descending order of deaths caused):

- H1N1. This serotype has several viral sub-serotypes which have caused considerable mortality. The H1N1 serotypes were responsible for the Spanish influenza outbreak of 1918 (which infected approximately 500 million people worldwide and caused an estimated 50–100 million deaths) (Taubenberger and Morens, 2006), and the swine influenza outbreak of 2009 (which infected approximately 20% of the world's population and caused thousands of deaths) (Reddy et al., 2018).
- H2N2. This serotype was the cause of the Asian influenza outbreak of 1957. This serotype may have resulted from a mutation in ducks that subsequently crossed species to humans (Scholtissek et al., 1978). The death toll of this virus has been estimated to be between one and four million.
- H3N2 serotype caused the Hong Kong influenza outbreak of 1968, which is estimated to have killed at least a million people between 1968 and 1969. This serotype is believed to have descended from H2N2 via an antigenic shift mutation (Scholtissek et al., 1978).
- H5N1, also known as avian influenza or bird flu. Whilst this virus can infect humans and several other animal species, its virulence in humans is relatively benign compared to the previously described serotypes. This virus is highly pathogenic in many bird species and an outbreak of bird-adapted strain of H5N1 in 2004 in southeast Asia directly resulted in the deaths of tens of millions of birds. Hundreds of millions of more birds (particularly domestic fowl) were culled to inhibit the spread of the disease, causing serious economic hardship in the region. Airborne spread of this sub-serotype virus from birds to humans is not yet possible, although it is believed from genetic analyses that only a few mutations are required for this to occur (Sorrell et al., 2011), raising concerns of a future pandemic.
- H7N7 is a zoonotic serotype that can infect humans, pigs, horses, seals and birds by natural transmission routes in the wild, and has been used to infect mice in laboratory studies (Paules and Subbarao, 2017). The zoonotic nature of the virus indicates that it poses a future pandemic threat.
- H1N2 is also a zoonotic serotype, which infects humans, pigs and birds (Paules and Subbarao, 2017). Due to its cross-species infectivity, it is also believed to be a future pandemic threat.
- H9N2, H7N2, H7N3 and H10N7 are other bird-infective serotypes, although they can also infect humans, especially children (Paules and Subbarao, 2017).

A common feature of the influenza virus A serotypes, whether they infect humans or not, is their high rate of mutation and therefore their potential for major pandemics. If such pandemics occur, lack of

immunity, ease of transmission and increased virulence may cause major losses of life, as previously seen for the Spanish influenza outbreak over a 100 years ago. It is therefore important that therapies to treat these infections be developed to guard against future pandemics.

Influenza virus genus's B and C are less common than influenza virus A and are generally considered to be less of a concern due to their lower virulence and slower mutation rates (Paules and Subbarao, 2017). Indeed, influenza virus B mutates at a third to a half of the rate of influenza A. Furthermore, this virus only infects humans. The reduced rate of antigenic change, combined with the single species host infectivity (thereby inhibiting cross-species antigenic shifts), substantially decreases the chances of pandemic shifts occurring in these influenza genus's.

There are currently relatively few effective cures for any influenza virus species. The exception are the neuraminidase inhibitors which prevent influenza virus reproduction by inhibiting viral budding from the cell. Most other therapies target the symptoms of the illness to make the infected person feel better whilst their immune system fights the infection. However, influenza vaccines are now available against most influenza serotypes, although the vaccine effectiveness ranges from 10 to 60% (depending on the year and the serotypes targeted by the vaccine) (Osterholm et al., 2012). Therefore, many people will still contract influenza, despite receiving a vaccine and an effective therapeutic alternative is urgently required.

1.1.2. Enterovirus

Enterovirus is a particularly diverse genus of viruses, consisting of a number of medically relevant pathogens including polioviruses and rhinoviruses. Due to their particular relevance to respiratory disease, the rhinoviruses will be discussed separately in detail. Enteroviruses most commonly infect the gastrointestinal tract and are most readily transmitted via the intestine (accounting for their name) (Stalkup and Chilikuri, 2002). However, they frequently also infect the respiratory system. Most commonly, when enteroviruses infect respiratory tissue, they induce symptoms similar to the common cold. However, these infections can also cause substantially more serious symptoms including inflammation of the heart and surrounding tissue, inflammation of the membranes surrounding the brain and inflammation of the pancreas. There are currently no cures for any enterovirus-induced diseases. Instead, treatment is supportive and aims to alleviate the symptoms (e.g. providing analgesics for pain relief) and more effective therapies are required. For the polioviruses, effective vaccines already exist, which allow for the prevention of poliomyelitis. However, these vaccines are ineffective if a poliovirus infection is already established. To date, there are no effective vaccines for the other respiratory infective enteroviruses.

1.1.2.1. Rhinovirus. Rhinovirus is the predominant cause of the common cold and is the most infectious viral pathogen in humans (Baille et al., 2018). Indeed, it has been estimated that the average adult may contract two or three colds per year, whilst children may contract as many as eight colds annually. Like influenza viruses, rhinoviruses are prone to mutations, resulting in a large genetic diversity. Indeed, three species consisting of 160 main subtypes have been reported. Each of these viruses has different complements of surface antigens. Therefore, rhinovirus may evade the immune response and a cold will develop, even when the infected person has been exposed to several other rhinovirus subtypes. Similar to influenza virus, rhinovirus is largely spread via airborne transmission, although it may also be spread by direct contact.

Rhinovirus infections progress very rapidly. Indeed, the virus adheres to cell surface receptors within 15 min of entering the respiratory tract and the disease has an incubation period of approximately two days (although this can be as short as 20 h) (Baille et al., 2018). As well as being substantially less severe than influenza, the course of rhinovirus

infections is also much shorter, with recovery generally in seven to ten days. For these reasons, rhinovirus infections (and colds due to other viruses described below) are considered to be of less concern than influenza and substantially less research has aimed at finding a cure to the common cold. Despite this, rhinovirus infections can still cause substantial distress and even death in children, the elderly and immunocompromised individuals and research to develop a cure is still required, even if it is not considered as high a priority as the development of new influenza therapies. Unlike influenza, no effective rhinovirus vaccine is currently available.

1.1.3. Adenovirus

Adenoviruses can infect a broad range of vertebrate hosts and can induce a wide range of illnesses and symptoms, dependent on the tissue infected, the adenovirus species and serotype, and the severity of infection. They may infect the gastrointestinal tract (causing gastritis, the eye (causing conjunctivitis) or the bladder (causing cystitis), although they most frequently infect the respiratory tract and are the second most frequent cause of colds (after rhinoviruses) (Rubin, 1993). Adenoviruses are spread in a similar manner to the previously described viruses i.e. airborne respiratory droplets. However, they may also be spread by contact with faecal contaminated surfaces. Adenoviruses are stable for a particularly long time outside the body, which substantially enhances their transmission rates. Furthermore, they are stable in a variety of environments and are relatively resistant to chemical decontaminants. They can also infect a variety of animal hosts apart from humans, allowing for major antigenic shifts and the potential for pandemics.

Given their resistance to decontamination and ease of transmission, it is fortunate that adenovirus infections are generally relatively benign compared to other viral respiratory infections. Humans infected with adenoviruses are often asymptomatic, although when they do display symptoms, these may vary widely. For most adenovirus serotypes, these generally present with the same symptoms as the common cold. However, some serotypes can induce substantially more severe symptoms and may require medical intervention. Adenovirus serotype 14 is particularly virulent and can cause severe respiratory distress, which may be fatal in some people (Louie et al., 2008). Of concern, this serotype has mutated substantially since it was first detected and increased spread of the new virus has been noted in recent years. Despite this, very little research has targeted this virus to develop new therapies and further research is urgently required.

1.1.4. Parainfluenza

Despite their name similarity, parainfluenza viruses are not closely related to influenza viruses, although they share several symptom similarities. Human parainfluenza virus (HPIV) infections are particularly prevalent in children. It has been estimated that of the five million childhood lower respiratory tract infections reported in the United States each year, approximately a third of these are due to HPIV infections (Henrickson et al., 1994). HPIV can also infect the upper respiratory tract, although this is substantially less common. Four main HPIV serotypes have been described (Branche and Falsey, 2016):

- HPIV-1 is the most common serotype and is the major cause of croup.
- HPIV-2 also causes croup, as well as several other upper and lower respiratory tract diseases.
- HPIV-3 and HPIV-4 both cause bronchitis and viral pneumonia.

Despite the prevalence of HPIV infections, they are generally considered to be of low concern for most people. Infections in children last at least seven days and symptoms similar to colds are most common. Most children >10 years age are asymptomatic with HPIV infections. However, HPIV infections can be much more serious in younger children. HPIV-1 and HPIV-2 infections can induce severe upper respiratory tract distress in children up to four years of age. HPIV-3 can cause

bronchitis and viral pneumonia in infants (<1 year of age). Similarly, HPIV can cause severe pneumonia that can be fatal in immunocompromised people. Therefore, although HPIV research is relatively neglected, effective anti-HPIV therapies are required.

1.1.5. Human respiratory syncytial virus (HRSV)

Human respiratory syncytial virus (HRSV) is another common cause of respiratory virus infections, particularly in infants and children. Infections are very common and it is estimated that 60% of infants are infected in their first year and nearly all children are infected by 3 years of age (Glezen et al., 1986). In most infected people, HRSV infections are asymptomatic, or produce relatively benign symptoms, similar to a common cold. However, HRSV infections may induce severe bronchitis requiring hospitalisation in approximately 3% of the population and prior HRSV infections do not confer lifelong immunity (Hall et al., 2009). Instead, people may acquire repeated infections as early as 1 year after a prior infection. There is no cure for HRSV infections and treatment is supportive and aims to alleviate the disease symptoms and allow the infected persons immune response to combat the disease. In older people with a decreased immune response and other immunocompromised individuals, HRSV infections may be substantially more severe and in rare cases may result in death.

HRSV is very readily spread and avoiding infection is almost impossible (Glezen et al., 1986). Unlike other respiratory viruses where the route is mostly airborne, HRSV transmission is most frequently via direct contact. The virus is particularly hardy and remains viable on surfaces for up to 5 h. The virus is also relatively resistant to chemical decontaminants, making its prevention particularly difficult. For this reason, HRSV spreads rapidly through childcare centres and treatment facilities for the elderly. HRSV infections are most frequent in the colder months for most regions of the world, when people congregate together indoors, with closer contact and thus more efficient transmission.

1.1.6. Human metapneumovirus (HMPV)

HMPV infections are common causes of respiratory illness and are associated with 6–40% of viral respiratory infections in children seeking medical intervention. Indeed, serological studies indicate that nearly all children worldwide have been exposed to HMPV by 5 years of age (Kahn, 2006). However, as for HRSV, prior infections with HMPV do not provide life-long immunity and repeated infections are common in older children and in adults. Generally, HMPV infections result in mild upper respiratory tract infections and present with similar symptoms to the common cold. However, the symptoms may be substantially more severe in older people and immunocompromised individuals and whilst relatively rare, HMPV-associated fatalities may occur. HMPV infections may also produce substantially more severe symptoms in individuals with asthma or chronic obstructive pulmonary disease (COPD).

The method of transmission of HMPV is less understood than for the other respiratory-infective viruses although it is likely to spread via similar pathways (i.e. airborne transmission, direct contact) (Chow et al., 2016). There is currently no known cure for HMPV infections and there is relatively little research into developing a treatment as the disease is relatively benign in most people and is self-limiting, usually resolving in similar time as a common cold. However, ribavirin has shown efficacy in animal models and may be useful in severe HMPV infections (Kitanovski et al., 2013). A number of studies have also investigated the potential for a HMPV vaccine (Karron et al., 2017) although it is likely that this is still at least several years from development.

1.1.7. Coronaviruses

Coronaviruses also cause respiratory tract infection that are usually mild compared to many of the previously listed viruses. However, rarer coronaviruses such as the viruses those that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) induce substantially more severe symptoms and can even be lethal.

Lastly and more topically and important is the SARS-CoV-2 coronavirus serotype which has caused recent global panic. The identified 2019-nCoV genome has been sequenced to some beta-coronaviruses detected in bats, with initial zoonotic mutations from snake expected (Ji et al., 2020; She et al., 2020). This remains at present the number one global viral respiratory threat. To date, neither SARS nor MERS have yet had a significant impact on southern Africa and therefore are not a focus of this study. However, recent SARS-CoV-2 infection and mortality rates in South Africa have highlighted the global nature of COVID 19. Indeed, as at 13 May 2020, the number of infections in South Africa was in excess of 12,000 and the mortality rate was above 200 (worldometersinfo/coronavirus/). This figure is highly dynamic and is likely to be substantially higher by the time this review is published. Furthermore, due to the relatively high number of asymptomatic individuals with SARS-CoV-2 infections, these figures are likely to be substantially underestimated. The ease of transmission of this virus highlights the need to test southern African plants against this serotype in future studies.

It is noteworthy that all the respiratory viruses discussed here (with the exception of adenoviruses) are RNA viruses and this may impact on the efficacy of any prevention or therapy in the future. In general, RNA viruses incorporate mutations at a substantially faster rate than for DNA viruses. Indeed, the mutation rates in influenza A virus has been estimated to be approximately one mutation per genome per replication (Drake, 1993). This mutation rate is up to 300 times faster than reported for DNA viruses. It is likely that this high mutation rate may induce changes to viral surface proteins. As antibodies are produced against these proteins following prior exposure (either via exposure to the virus or through vaccination), this may impact on an individual's immunity to these viruses. This is particularly apparent for influenza viruses and annual influenza vaccinations include updated antigens to account for this and to provide for immunity to new and emerging strains. The mutability of the other RNA respiratory viruses also affects an individual's ability to respond to future reinfections. Indeed, it was noted in the sections discussing the individual respiratory viruses that prior exposure generally does not confer life-long immunity. Similarly, the mutability of the RNA viruses may provide them with resistance to antiviral drugs and the new strains should be screened against these drugs as those strains. This also highlights the need to develop new antiviral therapies.

Also noteworthy, influenza viruses, parainfluenza viruses, HRSV, HMPV and coronaviruses are enveloped viruses, whereas the viruses that cause colds (enteroviruses, rhinoviruses, adenoviruses) are non-enveloped viruses. Non-enveloped viruses have substantially greater stability than enveloped viruses outside of the host cell as lipid envelopes are relatively fragile and sensitive to denaturation by environmental factors (e.g. temperature and pH) and well as by detergents and other chemicals (Lucas, 2001). For this reason, using detergents and soaps to wash hands is considered an effective preventative measure for enveloped viruses including influenza virus and is recommended for the current SARS-CoV-2 pandemic. In contrast, the viruses that cause colds are non-enveloped and therefore more stable outside host cells. For this reason, they last for longer times, which accounts for the greater rate of spread of colds.

1.2. Spread of respiratory viruses

Viral respiratory infections are very common, largely due to their ease of transmission. Viral respiratory infections may be spread by inhalation when an infected individual coughs or sneezes, or even when they talk. Small droplets of saliva containing large numbers of the viral pathogen are released and dispersed into the air. If other individuals in the vicinity of the sick person breathe in these droplets, and they may become infected. Unless that person has already acquired immunity to the virus via prior exposure, it is likely that they will develop the illness. Thus, one of the most effective ways to retard the spread of respiratory viruses is via behaviour modification. If an infected person covers their

mouth when coughing or sneezing, the incidence of spread of the viral respiratory disease is dramatically reduced. Respiratory viruses may also be spread via direct contact with an infected person, or via indirect contact with items and surfaces onto which an infected person has coughed or sneezed. Frequent and effective use of hand washes and surface disinfectants may therefore also substantially reduce the risks of infection. As adenoviruses and enteroviruses may also infect the gastrointestinal tract, contact with objects and surfaces contaminated with faeces from an infected individual (particularly via the hands) may also result in respiratory infections. Disinfection of hands and surfaces also reduces the spread of these viruses.

1.3. Signs and symptoms of viral respiratory diseases

Whilst a number of different viral pathogens may cause respiratory disease, there is similarity between the symptoms of many of those infections. Coughing, sneezing, runny noses, sore throats, blocked airways and laboured breathing are common symptoms of viral respiratory infections. Fever may also be associated with some infections (e.g. influenza). Infected individuals may also suffer from headaches and/or muscle aches and pains, and lethargy is common. The onset of the symptoms begins within a day or two of contracting the virus and last for up to 14 days (or longer for influenza).

In addition to differences related to the viral pathogen, the site of the infection (i.e. upper or lower respiratory tract infections) also significantly affects the disease symptoms. Upper respiratory tract infections affect the upper respiratory passages (larynx, nasal cavity and nasal passages, as well as the pharynx). The common cold is an example of an upper respiratory infection. In addition to the symptoms listed above that are common for all viral respiratory infections, upper respiratory infections are also characterised by discomfort of the nasal passages, excess mucus production, nasal congestion, runny nose and a sore throat. Headache, muscular pain and fever may also occur.

Lower respiratory tract infections occur when the virus infects the bronchial tubes (causing bronchitis) or the alveoli (causing pneumonia). The severity of the symptoms is dependent on the infective virus and the severity of the infection. Less severe infections may present with similar symptoms to the common cold (described above). In more severe infections, a phlegm-producing cough, fever, difficulty breathing, chest pain and wheezing may also be evident. Many of the symptoms are common between upper and lower respiratory tract infections. However, the nature of the symptoms can help differentiate between the sites of infection. People with lower respiratory infections generally present with consistent coughing with high phlegm production as the most apparent symptom. For upper respiratory tract infections, sneezing, sore throats and headaches are more apparent.

1.4. Current treatment options for viral respiratory diseases

There are few effective treatments for viral respiratory diseases and medical intervention is generally not required for most individuals. Viral respiratory diseases are generally self-limiting and most people will recover with rest and the consumption of adequate volumes of fluids. In most cases, therapy aims to alleviate the symptoms rather than to treat the cause of the disease. Acetaminophen (paracetamol) is useful for relieving much of the pain and discomfort associated with viral respiratory infections. Antiviral medicines are usually not used except in severe and/or prolonged cases of influenza. As of 2020, six prescription influenza antiviral medications had been approved by the United States Food and Drug Administration (FDA):

- Three chemically and functionally related drugs: oseltamivir phosphate (known as Tamiflu®), zanamivir (marketed as Relenza®) and intravenous peramivir (Rapivab®), are used as pharmaceutical treatments of influenza (FDA, 2019). All of these medications block the viral neuraminidase enzymes, thereby inhibiting viral release

from infected cells. These neuraminidase inhibitors are effective against both influenza A and B viruses. They are relatively effective and generally are safe for most people to use, although side effects including nausea and vomiting have been reported in some people. The cost of these drugs can be prohibitive in some regions of the world (particularly in developing countries) and they are often not available in rural and isolated regions. Furthermore, influenza virus resistance is increasingly being reported to these drugs (Sheu et al., 2008) and new therapies are urgently required.

- Baloxavir marboxil (marketed as Xofluza®), is also effective for the treatment of influenza A and B infections (FDA, 2019). This drug functions by inhibiting the cap-dependent endonuclease activity of influenza viruses, thereby blocking influenza virus RNA synthesis. However, several influenza strains have rapidly developed resistance to this drug since its clinical introduction in 2018, already limiting its efficacy (Hayden et al., 2018). Furthermore, adverse side effects including bronchitis and diarrhoea are reported in >20% of people who take this drug.
- The adamantane drugs amantadine (Symmetrel®) and rimantadine (Flumadine®) target the M2 ion channel protein of influenza A viruses (FDA, 2019). Therefore, they are indicated for influenza A but are ineffective against influenza B viruses. However, several influenza A serotypes have developed high levels of resistance (>99%) to these drugs and they are no longer considered effective against H1N1 and H3N2 serotypes (Deyde et al., 2007).

Whilst influenza virus resistance to the neuraminidase and cap-dependent endonuclease inhibitors classes of drugs are still relatively low, this is likely to change in the future with continued overuse of these drugs. These drugs should be used sparingly and reserved for high risk individuals (children, the elderly and immunocompromised individuals). Furthermore, medical practitioners will also often prescribe antibiotics for viral respiratory infections. Antibiotics have no effects against viruses and they should not be used for viral respiratory diseases unless a secondary bacterial infection is suspected. The incorrect use of antibiotics for these purposes may result in antibiotic resistant bacteria and it is recommended that this practice should cease.

Plant-based and traditional medicines are also used by many cultures to treat viral respiratory infections and their symptoms. This is especially true in developing countries. In many areas (particularly in isolated and rural communities), consultation with traditional healers is prevalent and is often the primary healthcare modality. Furthermore, allopathic drugs are often perceived in these areas as being relatively ineffective and are generally expensive compared to traditional medicines. Isolated rural communities may have limited access to allopathic medical practitioners and conventional pharmaceuticals are often not readily available. An examination of the antiviral properties of traditional medicines against viral respiratory pathogens may highlight new leads for drug discovery and may provide effective new therapies to treat viral respiratory diseases.

2. Viral respiratory diseases: A South African context

Southern Africa has similar viral respiratory disease epidemiology trends to other regions with similar population densities. The incidence of viral respiratory diseases substantially increases in the colder winter months (commonly referred to as cold and flu season) (Gessner et al., 2011). Geographical differences for viral respiratory diseases are also evident in various parts of southern Africa. Viral respiratory diseases are substantially more frequent in cold mountainous regions. These regions tend to have lower temperatures and therefore people tend to congregate indoors for longer periods, facilitating viral transmission. Related ethnic correlations also occur. For example, the southern Sotho tend to have higher prevalence's of the viral respiratory diseases than other ethnic groups in South Africa. The increased prevalence is due to the living environments of this group, rather than genetic factors. As the

Southern Sotho often live in cold mountainous regions, they spend more time indoors in groups than many other ethnic groups. Thus, viral transmission rates are higher. Incidentally, the higher prevalence of the viral respiratory diseases in the southern Sotho correlates with the development and usage of substantially more therapies for these diseases than have been reported for other ethnic groups. Indeed, nearly three times the amount of plant species have been recorded for the treatment of respiratory virus diseases by the southern Sotho compared to the Zulu (as discussed later and summarised in Table 1). This is despite the population size differences between these groups and is in contrast to the substantially higher volume of studies reported for the Zulu ethnobotany. Indeed, Hutchings et al. (1996) and Ngwenya et al. (2003) are concerned only with Zulu ethnobotany, whereas many of the other texts used in this study examine the ethnobotany of multiple groups (Smith, 1888; Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001; Van Wyk et al., 2009). Similarly, a large proportion of the ethnobotanical surveys cited in our study also concentrate on Zulus and regions in Zulu areas. In contrast, a single book (Moffett, 2010) and limited ethnobotanical surveys (Kose et al., 2015; Moteetee et al., 2019) have focused specifically on southern Sotho ethnobotany.

High density lower socio-economic urban communities often have higher prevalence's and rates of transmission of viral respiratory infections than other populations. Living in high density conditions facilitates viral transmission rates. Rural communities may also have different disease profiles, with higher incidences of zoonotic viral strains than in urban populations. Some respiratory viruses can infect domestic animals and livestock, as well as humans. For example, then H1N1 swine influenza strain, as well as H7N7 and H1N2 serotypes infect both humans and pigs. The latter two serotypes also infect birds and other farm livestock. All of these viruses are readily infective by airborne transmission between species. The H5N1 serotype (avian flu) can also infect both humans and birds, but is not yet readily transmissible to humans by airborne routes. People living in rural communities may have close contact with livestock, providing an extra avenue for infection. Therefore, these serotypes are often more common in rural communities than in urban environments. Several other attributes are shared between lower socio-economic urban communities and rural communities. For example:

- both communities often have limited access to effective clinical treatment. Medical care is often not affordable to poor and/or rural people. Instead, these communities tend to be more reliant on traditional medicine. Alternatively, given the comparatively low concern about many of the viral respiratory diseases compared to other infectious pathogens, and their self-limiting nature, many people suffering from these illnesses forgo medical treatment and allow the infection to run their course.
- Economically disadvantaged people and those living in rural communities are often less educated and have less understanding of simple preventative measures (e.g. frequent hand washing, disinfecting surfaces etc.) that limit the transmission of viral respiratory diseases.

The prevalence and severity of symptoms of viral respiratory diseases often correlates with age. Indeed, several of these diseases are generally considered to be childhood diseases only. A very common childhood disease is HRSV and nearly 100% of children have contracted HRSV by the age of three (Glezen et al., 1986). Whilst prior contact does not provide lifelong immunity to this disease, it does provide some protection and adult HRSV infections are far less common. Parainfluenza is also substantially more common in children than in adults as most children contract a HPIV infection before the age of 10 years (Henrickson et al., 1994), conferring them a degree of immunity. In most children, this is a relatively innocuous disease, although the symptoms may be substantially more serious in infants and can be life threatening. Children are also more prone to influenza and colds than adults because

Table 1
Southern African plants used traditionally to treat viral respiratory illnesses.

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Acacia arenaria</i> Schinz	Fabaceae	Sand acacia (English), sanddoring (Afrikaans)	Root	A decoction is consumed to treat colds.	Von Koenen (2001)
<i>Acacia decurrens</i> Willd.	Fabaceae	Black wattle, early green wattle (English)	Trunk exudate/gum	Used to treat bronchitis.	Watt and Breyer-Brandwijk (1962)
<i>Acacia hebeclada</i> DC.	Fabaceae	Cattlepod acacia (English), kersdoringboom (Afrikaans)	Root	A decoction is consumed to treat colds.	Von Koenen (2001)
<i>Acacia karoo</i> Hayne	Fabaceae	Sweet thorn (English), soetdoring (Afrikaans), mooka (Tswana), umuNga (Zulu, Xhosa)	Leaves and bark	Used to treat colds. Preparation and application are not specified.	Watt and Breyer-Brandwijk (1962); Hutchings et al.(1996); Van Wyk et al. (2009)
<i>Acacia mearnsii</i> De Wild.	Fabaceae	Uwatela (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Acacia mellifera</i> (Vahl.) Benth.	Fabaceae	Hook thorn, black hook (English), swarthaak (Afrikaans)	Roots	Chewed to treat colds.	Von Koenen (2001)
<i>Acacia nilotica</i> (L.) Delile	Fabaceae	Redheart, scented thorn (English), lekkerreulpeul (Afrikaans)	Bark and leaves	Used to treat colds.	Hutchings et al.(1996); Von Koenen (2001)
<i>Acacia senegal</i> (L.) Willd.	Fabaceae	Three thorn tree (English), driedoringakasia (Afrikaans)	Gum (trunk exudate)	Used as an expectorant in people with colds and influenza.	Von Koenen (2001)
<i>Acacia sieberana</i> var. <i>woodii</i> (Burt Davy) Keay & Brenan	Fabaceae	Paperbark thorn (English), papierbasdoring (Afrikaans)	Leaf and bark	Decoctions are used as an expectorant in people with colds and influenza.	Von Koenen (2001)
<i>Achyranthes aspera</i> L.	Amaranthaceae	Devil's horsewhip (English), langplitskafblom (Afrikaans)	Roots	The Zulus use a decoction to treat bronchitis. Also used in Namibia to treat colds.	Von Koenen (2001); Watt and Breyer-Brandwijk (1962)
<i>Acokanthera oppositifolia</i> (Lam.) Codd.	Apocynaceae	Bushman's poison (English), boesmangif (Afrikaans), inhlungunyembe (Zulu), intlungunyembe (Xhosa)	Leaves	Leaf decoctions are a Xhosa remedy for colds. However, this species is highly toxic and caution is required.	Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009); Philander (2011).
<i>Acorus calamus</i> L.	Acoraceae	Indaluqwatha, indawolucwatha, uzulucwatha (Zulu)	Not specified	Used by the Zulu to treat colds and influenza.	Mhlongo and Van Wyk (2019)
<i>Adenopodia spicata</i> (E. Mey.) C.Presl	Fabaceae	Spiny splinter bean (English), stekelsplinterboontjie (Afrikaans), ibobo, ubobo, umbambangwe (Zulu)	Bark	The Zulus use a decoction to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Adiantum chilense</i> var. <i>sulphureum</i> (Kaulf.) Kuntze ex Hicken	Pteridaceae	Common maidenhair fern (English)	Leaves	The southern Sotho smoke the leaves to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Adiantum capillus-veneris</i> L.	Pteridaceae	Maidenhair fern (English), venushaar (Afrikaans)	Leaves	The southern Sotho smoke the leaves to treat colds.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Von Koenen (2001); Moffett (2010)
<i>Adansonia digitata</i> L.	Malvaceae	Baobab (English), kremetartboom (afrikaans)	Fruit	Boiled and consumed to treat colds.	Von Koenen (2001)
<i>Aeollanthus buchnerianus</i> Briq.	Lamiaceae	Rock sage (English), klipsalie (Afrikaans)	Leaves	The Sotho smoke the leaves to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Agathosma betulina</i> (P.J. Bergius) Pillans	Rutaceae	Bucgh (English), boegoe, letuling (Afrikaans)	Leaves	An infusion is drunk to treat colds.	De Beer and Van Wyk (2011)
<i>Albizia antunesiana</i> Harms	Fabaceae	Purple-leaved false thorn (English), persblaarvalsdoring (Afrikaans)	Bark	Chewed to treat colds.	Von Koenen (2001)
<i>Alepidea amatymbica</i> Eckl. & Zeyh.	Apiaceae	Kalmoes (Afrikaans), lesoko (Sotho), iqwili (Xhosa), ikhathazo (Zulu)	Roots and stem	Zulus burn the stems and inhale the smoke to treat colds. Zulu and Sotho use a root decoction is drunk to treat colds and influenza.	; Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Van Wyk et al. (2009); Moffett (2010); Philander (2011);
<i>Allium cepa</i> L.	Amaryllidaceae	Onion (English)	Bulb	Used to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Allium sativum</i> L.	Amaryllidaceae	Garlic (English)	Bulb	Used to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Aloe arborescens</i> Mill.	Xanthorrhoeaceae	Krantz aloe (English), kransaalwyn (Afrikaans), ikalene (Xhosa), inkalene, umhlabana (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Aloe maculata</i> All.	Xanthorrhoeaceae	Soap aloe, zebra aloe (English)	Leaves	The Zulu use a decoction to treat colds and influenza.	Watt and Breyer-Brandwijk (1962); Kose et al. (2015)
<i>Anemone caffra</i> Harv.	Ranunculaceae	Unknown	Roots	Zulus used the powdered roots as a snuff to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Anemone vesicatoria</i> (L. f.) Prantl	Ranunculaceae	Blister leaf (English), brandbelaar, katjiedriebelaar (Afrikaans)	Leaves and roots	Root decoctions are used to treat colds and influenza. No application is specified for the leaves	Van Wyk et al. (2009); Watt and Breyer-Brandwijk (1962)
<i>Anisodonte triloba</i> (Thunb.) D.M.Bates	Malvaceae	Wildsalie (Afrikaans)	Leaves	A leaf infusion is consumed to treat colds.	De Beer and Van Wyk (2011)
<i>Antiphonia pinnatisecta</i> (S.Moore) Merxm.	Asteraceae	Unknown	Roots	The San use an infusion to treat influenza.	Von Koenen (2001)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Aptosimum indivisum</i> Burch. ex Benth.	Scrophulariaceae	Kinkhosesbos, agdaeeneesbos (Afrikaans)	Not specified	Used to treat colds.	Hulley and Van Wyk (2019)
<i>Artemisia afra</i> Jacq. Ex Willd.	Asteraceae	African wormwood (English), als, alsem, wildeals (Afrikaans), lengana (Sotho, Tswana), umhloniyane (Xhosa, Zulu)	Leaves	Infusions and decoctions are used to treat coughs, colds, influenza and bronchitis. Fresh leaves may also be inserted directly into the nose.	Smith (1888); Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009); Moffett (2010); Kose et al. (2015).
<i>Asplenium cordatum</i> (Thunb.) Sw.	Aspleniaceae	Resurrection fern (English), skubcaring (Afrikaans)	Leaves and rhizome	Leaves are smoked by Sotho to treat colds. A rhizome decoction is drunk to treat colds and relieve sore throats.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Asplenium monanthes</i> L.	Aspleniaceae	Unknown	Leaves	Smoked by southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010).
<i>Asplenium trichomanes</i> L.	Aspleniaceae	Maidenhair spleenwort (English)	Leaves	Smoked by southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Baccharoides adoensis</i> var. <i>mossambiquensis</i> (Steetz) "Isawumi, El-Ghazaly & B.Nord."	Asteraceae	Unknown	Not specified	The Zulu use infusions to treat influenza.	Smith (1888); Watt and Breyer-Brandwijk (1962)
<i>Ballota africana</i> (L.) Benth.	Lamiaceae	kattekruid, kattekruie (Afrikaans)	Whole plant	In infusion is used to treat colds and influenza.	Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009); Hulley and Van Wyk (2019) Von Koenen (2001)
<i>Bauhinia petersiana</i> Bolle	Fabaceae	Camel's foot (English), koffiebos (Afrikaans)	Leaves	Boiled and the steam inhaled to treat colds and influenza.	Kose et al. (2015)
<i>Berkheya setifera</i> DC.	Asteraceae	Leleme la khomo (southern Sotho)	Roots and leaves	Used to treat colds. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Bidens pilosa</i> L.	Asteraceae	Black jack, beggars ticks, cobblerspegs, sticky beaks (English)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Moffett (2010).
<i>Blepharis spinosa</i> Phillips	Acanthaceae	Unknown	Not specified	Used by the Sotho to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Buddleja saligna</i> Willd.	Scrophulariaceae	False olive (English), witolien (Afrikaans), lelonthwane (southern Sotho), ungqeba (Xhosa), igqeba-elimhlope (Zulu)	Leaves	The Tswana use a leaf decoction to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Berkheya setifera</i> DC.	Asteraceae	Buffalo-tongue thistle (English), rasperdissel (Afrikaans), ikhakhasi (Zulu), indlebe-lenkomo (Xhosa), lelelema-khomo, ntsoantsane (southern Sotho)	Roots	A decoction prepared and consumed for coughs and colds.	Watt and Breyer-Brandwijk (1962)
<i>Brunsvigia grandiflora</i> Lindl.	Amaryllidaceae	Giant candellabria (English), reusekandelaarblom (Afrikaans)	Bulb	A decoction is prepared from the crushed bulb and consumed for coughs and colds.	Watt and Breyer-Brandwijk (1962)
<i>Bulbine frutescens</i> Willd.	Xanthorrhoeaceae	Unknown	Leaves	The dried leaves are smoked by the Sotho to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Bulbine narcissifolia</i> Salm-Dyck	Xanthorrhoeaceae	Khomo ea balisa	Bulbs/roots	Used to treat colds. Preparation and application not specified.	Kose et al. (2015)
<i>Carpobrotus edulis</i> (L.) N. E.Br.	Aizoaceae	Sour fig, Cape fig, Hottentot's fig (English), vyerank, ghaukum, ghoenavy, hotmotsyve, Kaapvy, perdevy, rankvy (Afrikaans), ikhambilamabulawo, umgongozi (Zulu)	Leaves	Juice from squeezed leaves is diluted in water and used to relieve sore throats associated with colds.	Hutchings et al.(1996); Felhaber and Mayeng (1997)
<i>Carissa bispinosa</i> (L.) Defs. ex Brenan.	Apocynaceae	Amathungulu (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Cassine transvaalensis</i> (Burr. Davy) Codd.	Celestraceae	Transvaal saffron (English), lepel, lepelhout, waterboom (Afrikaans)	Leaves	Adults chew the leaves and swallow the sap to treat influenza. An infusion is given to children for the same purpose.	Hutchings et al. (1996); Von Koenen (2001);
<i>Catha edulis</i> (Vahl) Endl.	Celestraceae	Bushman's tea (English), boesmanstee (Afrikaans), khat (Arabic)	Leaves	The Xhosa use the leaves to treat influenza.	Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009)
<i>Chamarea capensis</i> (Thunb.) Eckl. & Zeyh.	Apiaceae	Vinkelbol, vinkelwortel (Afrikaans)	Root	The infusions are drunk to treat colds.	Hulley and Van Wyk (2019)
<i>Cheilanthes eckloniana</i> Met.	Pteridaceae	Ecklon's lip fern, resurrection fern (English)	Root, leaves	A decoction is consumed by the Sotho to treat colds. The leaves are also smoked to treat colds.	Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Cheilanthes hirta</i> Sw.	Pteridaceae	Mamaoaneng (southern Sotho)	Root	A decoction is consumed by the southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Kose et al. (2015)
	Pteridaceae	Unknown	Root		Moffett (2010)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Cheilanthes involuta</i> var. <i>obscura</i> (N.C. Anthony) N.C. Anthony				A decoction is consumed by the Sotho to treat colds.	
<i>Chaenostoma floribundum</i> Benth.	Scrophulariaceae	Unknown	Root	The Southern Sotho use a decoction to treat colds in children.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Chloris virgata</i> Sw	Poaceae	Feather finger grass (English)	Not specified	Used by the Sotho to treat colds.	Moffett (2010)
<i>Chrysocoma ciliata</i> L.	Asteraceae	Beesbos (Afrikaans)	Leaves	A decoction is drunk to treat colds.	De Beer and Van Wyk (2011)
<i>Cinnamomum camphora</i> (L.) J.Presl.	Lauriaceae	Camphor tree (English), kanferboom (Afrikaans), uroselina (Zulu)	Essential oil (distilled from the wood)	Used to treat colds.	Van Wyk et al. (2009); Philander (2011).
<i>Clematis brachiata</i> Thunb.	Ranunculaceae	Morara oa thaba (southern Sotho)	Not specified	Used by the Sotho to treat colds.	Hutchings et al. (1996); Moffett (2010); Kose et al. (2015).
<i>Cleome angustifolia</i> Forssk.	Cleomaceae	Unknown	Roots	The San inhale the steam from boiling roots to treat influenza.	Von Koenen (2001)
<i>Cliffortia ilicifolia</i> L.	Rosaceae	Unknown	Not specified	Used by Boers as an expectorant to relieve the symptoms of colds.	Watt and Breyer-Brandwijk (1962)
<i>Cliffortia odorata</i> L.f.	Rosaceae	Wildewingerd (Afrikaans)	Not specified	An infusion is drunk to treat colds.	Watt and Breyer-Brandwijk (1962); Philander (2011);
<i>Conyza scabrida</i> DC.	Asteraceae	Bakhos, oondbos (Afrikaans), isavu (Xhosa)	Leaves	Infusions are consumed and powdered. Used as a snuff to treat colds and influenza.	Hutchings et al. (1996); Van Wyk et al. (2009); De Beer and Van Wyk (2011); Philander (2011); Hulley and Van Wyk (2019)
<i>Chloris virgata</i> Sw.	Poaceae	Feather-finger grass, Rhodes grass (English)	Roots	A decoction is added to the bath by Xhosa to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Chrysanthemum morifolium</i> Ramat.	Asteraceae	Unknown	Leaves and flowers	People with colds sleep on a pillow filled with leaves and flowers to relieve the symptoms.	Watt and Breyer-Brandwijk (1962)
<i>Clematis brachiata</i> Thunb.	Ranunculaceae	Ihlonzo leziduli, inhlongo, umdloza, umfufuna (Zulu)	Stem	The Xhosa sniff the bruised stem to treat colds.	Smith (1888); Watt and Breyer-Brandwijk (1962); York et al. (2011)
<i>Combretum molle</i> R.Br. ex G.Don	Combretaceae	Umbondo, umbondwe (Zulu)	Leaves	An infusion is drunk to treat colds.	York et al. (2011)
<i>Corymbia gummifera</i> (Gaertn.) K.D.Hill & L.A.S.Johnson	Myrtaceae	Red bloodwood (English)	Leaves	Essential oils are inhaled to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Citrus limon</i> (L.) Osbeck	Rutaceae	Lemon (English)	Fruit juice	Consumed to treat colds.	Watt and Breyer-Brandwijk (1962); York et al. (2011)
<i>Crassula alba</i> Forssk.	Crassulaceae	Unknown	Juice	The Zulu and Swati mix the juice with water as a nasal cleanser for influenza sufferers.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996)
<i>Crinum bulbispermum</i> (Burm.f.) Milne-Redh. & Schweik.	Amaryllidaceae	Orange River lily, Vaal River lily (English), Oranjierivierlelie (Afrikaans), umduze (Zulu)	Bulb	A decoction is prepared from the crushed bulb and consumed by the southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010);
<i>Crinum macowanii</i> Baker	Amaryllidaceae	umduze (Zulu)	Bulbs	A decoction is prepared from the crushed bulb and consumed by the southern Sotho to treat colds.	Van Wyk et al. (2009)
<i>Cymbopogon nardus</i> (L.) Rendle	Poaceae	Citronella grass (English)	Entire plant	Used to treat colds. Treatment and application is not specified.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996)
<i>Cyperus longus</i> L.	Cyperaceae	Galingale (English)	Tuber	The Zulu inhale the powdered tuber to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Datura</i> spp.	Solanaceae	Various common names for different species.	Not specified	Used by the Sotho to treat colds.	Moffett (2010)
<i>Dicrothamnus rhinocerotis</i> (L.f.) Koek.	Asteraceae	Rhinoceros bush (English)	Not specified	Used to treat influenza. Preparation and application methods are not specified.	Watt and Breyer-Brandwijk (1962)
<i>Dicoma anomala</i> Sond.	Asteraceae	Fever bush, stomach bush (English), maagbitterwortel, kalwerbossie, koorsbossie, gryshout, maagbossie (Afrikaans), inyongana (Xhosa), isihlabamakhondlwane, umuna (Zulu)	Roots	Powdered root bark is inhaled by the Sotho as a snuff to treat colds. A decoction may also be consumed for the same purpose.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Von Koenen (2001); Moffett (2010); Kose et al. (2015)
<i>Dicoma capensis</i> Less.	Asteraceae	Wilde karmedik, koorsbossie (Afrikaans)	Roots	Powdered root bark is inhaled by the Sotho as a snuff to treat colds. A decoction may also be consumed for the same purpose.	Hutchings et al. (1996); Van Wyk et al. (2009); De Beer and Van Wyk (2011)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Digitaria sanguinalis</i> (L.) Scop.	Poaceae	Crab grass (English)	Whole plant	A decoction is consumed to treat colds.	Smith (1888)
<i>Dioscorea dregeana</i> (Kunth.) D. Durand & Schinz.	Dioscoreaceae	Ingevu, intana ebovu, udakawa (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Dodonaea viscosa</i> (L.) Jacq.	Sapindaceae	Sand olive (English), sandolien, ysterbos (Afrikaans), mutata-vhana (Venda)	Leaves, twigs	Used to treat colds and influenza.	Nortje and Van Wyk (2015); Van Wyk et al. (2009); De Beer and Van Wyk (2011); Nortje and Van Wyk (2015); Hulley and Van Wyk (2019).
<i>Dolichothrix ericoides</i> (Lam.) Hilliard & B.L. Burtt.	Asteraceae	Klipanoster, berganoster (Afrikaans)	Not specified	Infusions are drunk to treat colds.	Hulley and Van Wyk (2019)
<i>Drimia altissima</i> (L.f.) Ker Gawl.	Asparagaceae	Tall white squill (English)	Bulb	The powdered bulb is ingested to treat influenza and bronchitis.	Watt and Breyer-Brandwijk (1962)
<i>Dysphania ambrosioides</i> (L.) Mosyak & Clemants	Amaranthaceae	Wormseed, Jesuit's tea (English), Ikhambi leslumo, isinuka, isinukamasimba, umanxiweni (Zulu)	Not specified	Used by the Zulu to treat colds and influenza.	; Hulley and Van Wyk (2019); Mhlongo and Van Wyk (2019); Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996)
<i>Elaphoglossum conforme</i> (Sw.) Schott	Pteridaceae	Unknown	Rhizome	A decoction is consumed by the southern Sotho to treat colds.	Moffett (2010)
<i>Elaphoglossum petiolatum</i> (Sw.) Urb.	Pteridaceae	Graceful tongue fern (English)	Rhizome	A decoction is consumed by the southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Empleurum uncapulare</i> (L.f.) Skeels	Rutaceae	Bergboegoe, bokboegoe, langblaarboegoe (Afrikaans)	Not specified	Used to treat colds and influenza, Preparation and application are not specified.	Hulley and Van Wyk (2019)
<i>Equisetum ramosissimum</i> Desf.	Equisetaceae	Branched horsetail (English)	Rhizome	Zulu and Sotho drink a decoction of the rhizome to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Eriocephalus africanus</i> L.	Asteraceae	Kapokbos, skaapkaroo (Afrikaans)	Not specified	Infusions are used to treat colds.	Hulley and Van Wyk (2019)
<i>Eriocephalus punctalatis</i> DC.	Asteraceae	Wild rosemary, Cape snowbush (English), kapokbos (Afrikaans)	Unspecified	Used to fumigate huts of people with colds.	Watt and Breyer-Brandwijk (1962)
<i>Erigeron bonariensis</i> L.	Asteraceae	Unknown	Leaves	A leaf infusion is consumed by Zulus to treat colds.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996)
<i>Eriosema cordatum</i> E. Mey.	Fabaceae	Ugwayana, umuthi wamadoda, umvusandoda (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Eriosema distinctum</i> N.E. Br.	Fabaceae	Ugqomfane, umvusandoda, uqonsi (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Erythrophleum suaveolens</i> (Guill. & Perr.) Brenan	Fabaceae	Woodland waterberry, water pear (English), waterpeer (Afrikaans)	Bark	The Zulu use the powdered bark as a snuff to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Eucalyptus camaldulensis</i> Dehnh.	Myrtaceae	Umgamthrin (Zulu)	Gum (trunk exudate)	The gum is dissolved in water and used to treat colds.	Watt and Breyer-Brandwijk (1962); Mhlongo and Van Wyk (2019)
<i>Eucalyptus globulis</i> Labill.	Myrtaceae	Blue gum (English)	Leaves	Decoctions and infusions are used to treat colds and influenza.	Smith (1888); Watt and Breyer-Brandwijk (1962)
<i>Eucomis autumnalis</i> (Mill.) Chitt.	Asparagaceae	Autumn pineapple lily, pineapple flower (English), wildepyntappel, krulkoppie (Afrikaans), ubuhlungu becanti, isithithibala esimathunzi (Xhosa), umathunga, ukhokho, umakhandakantsele (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Euryops</i> spp.	Asteraceae	Different names for different species	Not specified	Ingested to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Foeniculum vulgare</i> Mill.	Apiaceae	Vinkel, makvinkel (Afrikaans)	Not specified	Infusions are drunk to treat colds.	Hulley and Van Wyk (2019)
<i>Geranium incanum</i> Burm. f.	Geraniaceae	vrouebossie, bergtee, amarabossie (Afrikaans), ngope-sethsoha, tlaka (Sotho)	Leaves	Leaf infusions are used to treat bronchitis.	Van Wyk et al. (2009)
<i>Geranium ornithopodon</i> Eckl. & Zeyh.	Geraniaceae	Unknown	Leaves	A leaf decoction is consumed to treat colds.	Moffett (2010)
<i>Gerbera ambigua</i> (Cass.) Sch. Bip.	Asteraceae	Seboka (southern Sotho)	Roots	A root infusion is drunk to treat severe colds.	Kose et al. (2015)
<i>Gerbera piloselloides</i> (L.) Cass.	Asteraceae	Tsebe ea pela (southern Sotho)	Unspecified	The southern Sotho use it to fumigate huts of people with colds.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Moffett (2010); Kose et al. (2015);
<i>Gerbera viridifolia</i> (DC.) Sch. Bip.	Asteraceae		Unspecified	The southern Sotho inhale smoke from the burning plant	Watt and Breyer-Brandwijk (1962); Moffett (2010)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Gladiolus dalenii</i> Van Geel	Iridaceae	Blushing baberton daisy (English), griquateebossie (Afrikaans), lyeza lamazi (Xhosa) Parrot gladiolus, Natal lily (English), papegaai-gladiolus, wildeswaardlelie (Afrikaans), umnunge (Xhosa), udwendweni, uhlakahle (Zulu), khahla-e-khola (Sotho)	Corm	to treat colds. An infusion is consumed for the same purpose. A decoction is used by the southern Sotho to treat colds. Smoke from burning corms is inhaled for the same purpose.	Hutchings et al. (1996); Von Koenen (2001); Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Glycyrrhiza glabra</i> L.	Fabaceae	Liquorice, licorice (English)	Rhizome	Decoctions and infusions are used to treat colds, influenza and bronchitis.	Watt and Breyer-Brandwijk (1962)
<i>Gnidia anthyloides</i> (L.f.) Gilg.	Thymelaeaceae	Brandbossie (Afrikaans), indolo, intozwane (Zulu)	Roots	Used by the southern Sotho to treat influenza.	Hutchings et al. (1996); Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Gnidia kraussiana</i> Meisn.	Thymelaeaceae	Impevu, umsula wengwe, umahedeni (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Gomphocarpus fruticosus</i> (L.) W.T.Aiton	Apocynaceae	Milkweed (English), melkbos, tontelbos (Afrikaans), lebegana, lereke-la-ntja (Sotho), modimolo (southern Sotho), umsinga-lwesalukazi (Zulu)	Not specified	Used by the southern Sotho to treat colds.	Von Koenen (2001); Moffett (2010)
<i>Grangea maderaspatana</i> (L.) Poir.	Asteraceae	Unknown	Unspecified	A decoction is used by the Xhosa to treat colds and influenza. The crushed leaves may also be directly inserted into the nostrils for the same purpose.	Watt and Breyer-Brandwijk (1962)
<i>Gunnera perpensa</i> L.	Gunneraceae	Wild rhubarb, river pumpkin (English), wilde ramenas, ravierpampoer (Afrikaans), qobo (Sotho), rambola-vhadzimu (Venda), iphuzi, ighobo (Xhosa), ugobhe (Zulu)	Leaves and roots	Used to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Gymnosporia buxifolia</i> Szyszyl.	Celestraceae	Lemoendoring, wonedoring, pendoringbos (Afrikaans)	Roots	Root decoctions are consumed to treat colds.	Hulley and Van Wyk (2019); Watt and Breyer-Brandwijk (1962)
<i>Gymnosporia heterophylla</i> (Eckl. & Zeyh.) Loes.	Celestraceae	Gewone pendoring (Afrikaans)	Leaves	An infusion is consumed to treat colds and influenza.	Von Koenen (2001); Hutchings et al. (1996)
<i>Haplocarpha scaposa</i> Harv.	Asteraceae	Papetloana (southern Sotho)	Root	A decoction is consumed by the Xhosa to treat colds.	Kose et al. (2015); Watt and Breyer-Brandwijk (1962)
<i>Helichrysum appendiculatum</i> (L.f.) Less.	Asteraceae	Sheep's ears everlasting (English), skaapoorbossie (Afrikaans), senkotoana (southern Sotho), ibode, indlebeyemvu (Zulu)	Leaves	The leaves are eaten raw to treat colds.	Watt and Breyer-Brandwijk (1962); Smith (1888)
<i>Helichrysum caespitium</i> (DC.) Sond. Ex Harv.	Asteraceae	Phate ea ngaka (southern Sotho)	Leaves	Smoke from burning leaves is inhaled by the southern Sotho to treat colds.	Kose et al. (2015); Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Helichrysum cymosum</i> (L.) D.Don.	Asteraceae	Kooibos (Afrikaans)	Not specified	Used to treat colds. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Helichrysum dregeanum</i> Sond. & Harv.	Asteraceae	Bergankeerkaroo, vaalberganker (Afrikaans)	Leaves	The southern Sotho smoke the leaves to relieve colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Helichrysum cochleariforme</i> DC.	Asteraceae	Unknown	Not specified	Used to treat bronchitis. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Helichrysum luteoalbum</i> (L.) Rchb.	Asteraceae	Impepho, inkoldwane (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Helichrysum nudifolium</i> Less.	Asteraceae	Everlastings (English), hottentotsteebossie, kooigoed (Afrikaans), isicwe, indlebe zebhokwe, undleni (Xhosa), icholocholo, imphepho (Zulu)	Leaves and roots	Khoikhoi and Xhosa consume the leaves as a remedy for colds. Root decoctions are used for the same purpose.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Van Wyk et al. (2009)
<i>Helichrysum odoratissimum</i> (L.) Sweet	Asteraceae	Everlastings (English), kooigoed (Afrikaans) imphepho (Zulu)	Roots	Decoctions are consumed to treat colds.	Hulley and Van Wyk (2019); Kose et al. (2015); Moffett (2010); Van Wyk et al. (2009); Hutchings et al. (1996); Watt and Breyer-Brandwijk (1962)
<i>Helichrysum pedunculare</i> Hilliard & B.L.Burtt.	Asteraceae	Unknown	Roots	Root decoctions are consumed to treat coughs and colds.	Watt and Breyer-Brandwijk (1962)
<i>Helichrysum rugulosum</i> Less.	Asteraceae	Marotole, motlosa-ngaka, motoantoanyane (southern Sotho)	Unspecified	Used by the southern Sotho to fumigate huts of people with colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Hermannia cuneifolia</i> Jacq.	Malvaceae	Wilde heuning, genesbossie, pleisterbossie (Afrikaans)	Leaves	A leaf infusion is used to treat colds.	De Beer and Van Wyk (2011)
<i>Hermannia salvifolia</i> L.f.	Sterculiaceae	Katjiedrieblaar (Afrikaans)	Not specified		Hulley and Van Wyk, 2019

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Herniaria hirsuta</i> L.	Caryophyllaceae	Hairy rupture wort (English)	Root	Used to treat colds. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Hoodia gordonii</i> (Masson) Sweet ex Decne.	Apocynaceae	Hoodia, ghaap, kakimas (Afrikaans)	Fleshy stems	Used to treat colds. Preparation and application not specified.	Philander (2011)
<i>Hypoxis hemerocallidea</i> Fisch., C.A.Mey. & Ave-Lall.	Hypoxidaceae	Yellow star, star lily, star flower (English), sterblom, geelsterretjie, gifbol (Afrikaans), moli kharatsa, lotsane (southern Sotho); inkomfe, inkomfe enkulu (Zulu), inongwe, ilabatheka, ixhalanxa, ikhubalo lezithunzela (Xhosa), tshuka (Tswana)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Ilex mitis</i> (L.) Radlk.	Aquifoliaceae	Cape holly, African holly, water tree (English), waterboom, waterhout (Afrikaans), nonaname (Northern Sotho), ipuphuma (Zulu), unduma (Xhosa), phukgu, phukgile (Sotho), mutanzwa-khameol (Venda)	Leaves and bark	The Zulu pound the leaves and bark to produce a lather which is used to wash the bodies of influenza sufferers.	Watt and Breyer-Brandwijk (1962)
<i>Imperata cylindrica</i> (L.) Raeusch	Poaceae	Kunai grass, cogongrass (English)	Roots	The southern Sotho used the roots to treat colds.	Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Kalanchoe paniculata</i> Harv.	Crassulaceae	Hasioor (Afrikaans), indabaluluvolo (Zulu), sehlakwahlakwane (southern Sotho)	Roots	The southern Sotho chew the fresh root or use the powdered root as a snuff to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Laggera decurrens</i> (Vahl.) Merxm.	Asteraceae	Wolbos (Afrikaans)	Leaves and roots	Boiled and the stem is inhaled to treat colds.	Von Koenen (2001)
<i>Lantana camara</i> L.	Verbenaceae	Tickberry (English)	Leaves	Used to treat colds. Preparation and application are not specified.	Watt and Breyer-Brandwijk (1962); Von Koenen (2001)
<i>Lantana rugosa</i> Thunb.	Verbenaceae	Bird's brandy (English)	Leaves	The Xhosa use leaf extracts to treat colds.	Von Koenen (2001)
<i>Lebeckia sericea</i> Thunb.	Fabaceae	Silverpea (English), bloufluitjiesbos, vaalertjebos (Afrikaans)	Not specified	The Nama use the plant as a remedy for colds.	Watt and Breyer-Brandwijk (1962)
<i>Leonitis ocyimifolia</i> (Burm.f) Iwarsson	Lamiaceae	Wild dagga (English), wilddedagga (Afrikaans)	Leaves and stems	Used as a treatment for colds. Preparation and application not specified.	Hulley and Van Wyk (2019); Watt and Breyer-Brandwijk (1962)
<i>Leonotis ocyimifolia</i> var. <i>schinzii</i> (Gürke) Iwarsson	Lamiaceae	Unknown	Leaves and stems	The Tswana use a decoction to treat coughs and colds.	Watt and Breyer-Brandwijk (1962)
<i>Leonotis leonurus</i> (L.) R. Br.	Lamiaceae	Wild dagga (English), wilddedagga, duiwelstabak (Afrikaans), mvovo (Xhosa), uyshwala-bezinyoni (Zulu)	Leaves and stems	The Sotho, Zulu and Tswana use a decoction of the leaves and stems to treat coughs, colds and influenza.	Moffett (2010); Van Wyk et al. (2009); Smith (1888); Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Van Wyk et al. (2009); Moffett (2010); Hulley and Van Wyk (2019)
<i>Lessertia frutescens</i> subsp. <i>frutescens</i> Goldblatt & J.C. Manning	Fabaceae	Keurtjie, beeskeurtiebos, kankerbos (Afrikaans)	Not specified	An infusion is used to treat colds.	Hulley and Van Wyk (2019)
<i>Leucas martinicensis</i> (Jacq.) R.Br.	Lamiaceae	Tumbleweed (English), tolbossie (Afrikaans)	Leaves	An infusion is used to treat colds and influenza.	Von Koenen (2001)
<i>Leucas lavandulifolia</i> (Sm.) Raf.	Lamiaceae	Umagumede (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Leucas pechuelii</i> (Kuntze) Baker	Lamiaceae	Unknown	Entire plant	A decoction is made from the entire plant and sniffed to treat influenza.	Von Koenen (2001)
<i>Lichtensteinia interrupta</i> E. Mey.	Apiaceae	Umkhalaphanga (Zulu)	Roots	A root decoction is consumed by the Zulu, Xhosa and Southern Sotho to treat colds.	Smith (1888); Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Moffett (2010)
<i>Lippia javanica</i> (Burm F.) Spreng	Verbenaceae	Fever tea, lemon bush (English), koorbossie, beukesbossie, lemoenbossie (Afrikaans), inzinzinba (Xhosa), umswzwane, umswazi (Zulu)	Leaves and stems	The Xhosa, Zulu and Tswana drink a decoction to treat colds, influenza and bronchitis.	Watt and Breyer-Brandwijk (1962); York et al. (2011); Mhlongo and Van Wyk (2019)
<i>Lonchocarpus nelsii</i> (Schinz) Heering & Grimme	Fabaceae	Apple leaf (English), appleblaar (Afrikaans)	Roots	Smoke from the burning roots is inhaled to treat colds.	Von Koenen (2001)
<i>Lycopodium clavatum</i> L.	Lycopodiaceae	Clubmoss, stag-horn clubmoss, running clubmoss, ground pine (English)	Whole plant	Used by the southern Sotho to treat colds	Moffett (2010)
<i>Melolobium cardicans</i> (E. Mey.) Eckl. & Zeyh.	Fabaceae	Wild dagga (English), wilddedagga (Afrikaans)	Leaves and stems	A decoction of the leaves and stems is drunk to treat colds.	De Beer and Van Wyk (2011)
<i>Mentha aquatica</i> L.	Lamiaceae	Water mint (English)	Bark		

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Mentha longifolia</i> (L.) L.	Lamiaceae	Wild mint (English), kruisement, balderjan (Afrikaans), koena-ya-thabo (Sotho), inixina, inzinziniba (Xhosa), ufuthana, lomhlanga (Zulu)	Leaves, roots and stems	A decoction is used by Xhosa, Tswana and southern Sotho to treat colds. The Xhosa, Zulu and Sotho take a decoction or add the leaves to milk and consume to treat colds, influenza and bronchitis.	Watt and Breyer-Brandwijk (1962); Hutchings et al.(1996) Watt and Breyer-Brandwijk (1962); Hutchings et al.(1996); Van Wyk et al. (2009); Moffett (2010); De Beer and Van Wyk (2011); Hulley and Van Wyk (2019)
<i>Mentha spicata</i> L.	Lamiaceae	Spearmint (English), imboza (Xhosa)	Leaves	A decoction is used to treat colds.	Hulley and Van Wyk (2019)
<i>Metalasia densa</i> (Lam.) P. O.Karis	Asteraceae	Tee (southern Sotho)	Unspecified	Used by the southern Sotho to fumigate huts of people with colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Microglossa mespilifolia</i> (Less.) B.L. Rob.	Asteraceae	Inkhambi elimhlophe, umazambezi (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Milletia grandis</i> (E.Mey.) Skeels	Fabaceae	Ubobolwehlathi (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Mohria caffrorum</i> (L.) Desv.	Anemiaceae	Carrot fern, scented fern (English), brandbossie (Afrikaans)	Leaves	The southern Sotho smoke the leaves to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Mikania natalensis</i> DC.	Asteraceae	Ihlozi (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Monsonia burkeana</i> Planch. ex Harv.	Geraniaceae	Crane's bill (English), angelbossie, keitabossie, naaldbossie, teebos (Afrikaans)	Leaves and roots	A decoction is used by the Xhosa to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Monsonia emarginata</i> L'Hér.	Geraniaceae	Dysentery herb (English), geita, geitabossie, keitabossie, naaldbossie (Afrikaans)	Leaves and roots	A decoction is used by the Xhosa to treat colds.	Smith (1888); Watt and Breyer-Brandwijk (1962);
<i>Montinia caryophyllaceae</i> Thunb.	Montiniaceae	Pepperbush, wild colve-bush (English), bergklapper, peperbos (Afrikaans)	Leaves	Pulverised leaves are used as a snuff to treat colds.	Von Koenen (2001)
<i>Morella serrata</i> (Lam.) Killick	Myricaceae	Mountain waxberry, lance-leaved waxberry (English), smalbar-wasbessie, berg wasbessie, waterolier (Afrikaans), isibhara, umaluleka (Xhosa), lyethi, ulethi, umakhuthula (Zulu)	Not specified	Used by the Sotho to treat colds.	Moffett (2010)
<i>Myrothamnus flabellifolia</i> Welw.	Myrothamnaceae	Resurrection plant (English), bergboegoe (Afrikaans), uvukwabafile (Zulu)	Leaves	Leaf infusions are used to treat colds.	Watt and Breyer-Brandwijk (1962); Von Koenen (2001); Van Wyk et al. (2009)
<i>Nicotiana glauca</i> Graham	Solanaceae	Mustard tree, tree tobacco (English), tabakboom, wildetabak, volstruisgifboom (Afrikaans), mohlafotha (Sotho)	Leaves	Powdered leaves are used by the Sotho as a snuff to treat colds.	Moffett (2010)
<i>Nicotiana rustica</i> L.	Solanaceae	Strong tobacco, Aztec tobacco (English)	Leaves	Powdered leaves are used by the southern Sotho as a snuff to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Notobubon tenuifolium</i> (Thunb.) Magee	Apiaceae	Wildekoelsaad, wilde vinkel (Afrikaans)	Not specified	Used to treat colds. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Ocimum americanum</i> L.	Lamiaceae	Hoary basil (English), wilde basielkruid (Afrikaans)	Leaves	The leaves are burnt and the smoke inhaled to treat colds.	Von Koenen (2001)
<i>Oncosiphon piluliferum</i> L. f. Källersjö	Asteraceae	Stinkkruid (Afrikaans)	Not specified	Used to treat colds and bronchitis. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Oncosiphon suffruticosum</i> L. Källersjö	Asteraceae	Stinkkruid, wirmkruid (Afrikaans)	Whole plant	Used to treat influenza.	Van Wyk et al. (2009); Nortje and Van Wyk (2015); Hulley and Van Wyk (2019).
<i>Osmitopsis asteriscoides</i> Less.	Asteraceae	Bels, belskruie (Afrikaans)	Leaves	Used to treat influenza.	Van Wyk et al. (2009); Philander (2011)
<i>Otholobium polystictum</i> (Harv.) C.H.Stirt.	Fabaceae	Kite hook-leaved pea (English), vlieebos (Afrikaans), mohlonecha, mohlonepshoa (southern Sotho)	Root	Used by the southern Sotho to treat colds.	Moffett (2010); Watt and Breyer-Brandwijk (1962)
<i>Pachycarpus rigidus</i> E. Mey. ex Eckl. & Zeyh.	Apocynaceae	Ishongwe (Zulu)	Not specified	Used by the southern Sotho to treat colds.	Moffett (2010)
<i>Packera heterophylla</i> (Fisch.) E.Wiebe	Asteraceae	Unknown	Leaves	Smoke from burning leaves is inhaled by the Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Pechuel-Loeschea leubnitziae</i> (Kuntze) O. Hoffm.	Asteraceae	Bitterbos (mbiguous)	Leaves	Smoke from burning is inhaled to treat colds.	Von Koenen (2001)
<i>Pegolettia baccharidifolia</i> Less.	Asteraceae	Ghwarrieson, heuningdou (Afrikaans)	Not specified		Hulley and Van Wyk (2019)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Pellaea calomelanos</i> (Sw.) Link.	Pteridaceae	Hard fern (English), lehorometso (Sotho), inkomankomo (Zulu)	Leaves	Used to treat colds. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009); Moffett (2010); Philander (2011); Smith (1888)
<i>Pellaea ambiguou</i> (Sw.) Baker	Pteridaceae	Unknown	Leaves	The Sotho smoke the leaves to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Pentzia incana</i> (Thunb.) Kuntze	Asteraceae	Skaapkarooos, ankerkaroo, kleinskaapkarooos (Afrikaans)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Passiflora suberosa</i> L.	Passifloriaceae	Unyawo lenkukhu (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Pelargonium abrotanifolium</i> Jacq.	Geraniaceae	Bergsalie (Afrikaans)	Leaves	A leaf infusion is used to treat colds and influenza.	De Beer and Van Wyk (2011)
<i>Pelargonium graveolens</i> L'Her.	Geraniaceae	Rose geranium (English), wildemalva (Afrikaans)	Leaves	Leaves are steamed and vapours are inhaled to treat colds.	Van Wyk et al. (2009)
<i>Pelargonium ramosissimum</i> Willd.	Geraniaceae	Dassieboegoe, dassiebos (Afrikaans)	Leaves	the Xhosa consume decoctions or tinctures (preferred) to treat colds.	Smith (1888); Watt and Breyer-Brandwijk (1962); De Beer and Van Wyk (2011)
<i>Pentanisia prunelloides</i> (Koltzsch) Walp.	Rubiaceae	Wild verbena (English), sooibrandbossie (Afrikaans), setimamollo (Sotho), icimamlilo (Zulu)	Roots	Used to treat colds and influenza. Preparation and application were not specified	Van Wyk et al. (2009); Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Kose et al., 2015
<i>Persicaria lapathifolia</i> (L.) Delarbre	Polygalaceae	Uxhaphoxana, uxhaphozi (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Phyla scaberrima</i> (Juss. Ex Pers.) Moldenke	Verbenaceae	Unknown	Leaves	A decoction of the leaves is used to treat colds.	Smith (1888)
<i>Plectranthus ambiguus</i> (Bolus) Codd.	Lamiaceae	Iboza, imbatatane (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Plectranthus laxiflorus</i> Benth.	Lamiaceae	Citronella spur flower (English), sitrinella spoorsalie (Afrikaans), ubebebe (Xhosa)	Leaves	A decoction made from powdered leaves was used by the Zulu as an enema to treat influenza.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Ngwenya et al. (2003)
<i>Polygala schinziana</i> Chodat	Polygalaceae	Kanjengena (Afrikaans)	Roots	A decoction is consumed to treat coughs and colds.	Hutchings et al. (1996); Von Koenen (2001)
<i>Pleopeltis macrocarpa</i> (Bory ex Willd.) Kaulf.	Polypodiaceae	Lance leaf polypody (English)	Not specified	A decoction is consumed by the southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010);
<i>Protea repens</i> L.	Proteaceae	Sugarbush (English), suikerbos (Afrikaans)	Flowers	Syrup prepared from the flower nectar is used by people with colds and influenza as a cough mixture.	Van Wyk et al. (2009)
<i>Pteronia incana</i> (Brum.) DC.	Asteraceae	Skieterbos, keurtjiebos, kraakbos (Afrikaans)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Pulicaria scabra</i> (Thunb.) Druce	Asteraceae	Fleabane (English), aambeibos (Afrikaans), isithaphuka (Zulu)	Leaves	The powdered leaves are used by Zulus to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Pycureus nitidus</i> (Lam.) J. Raynal	Cyperaceae	Unknown	Rhizome	Used by the southern Sotho to treat colds. Preparation and application is not specified.	Watt and Breyer-Brandwijk (1962)
<i>Ranunculus capensis</i> Thunb.	Ranunculaceae	Blistering leaves (English), blandblare, katjiedriebelaar (Afrikaans)	Roots	A root infusion is consumed to treat colds.	Smith (1888)
<i>Ranunculus multifidus</i> Forssk.	Ranunculaceae	Buttercup flower (English), botterblom, brandblaar, geelbotterbom, kankerblaar (Afrikaans), hlapi (southern Sotho), uxhaphozi, ishaskazane (Zulu)	Leaf	The Zulu use bruised leaves to treat colds. The southern Sotho also use the leaves to treat colds.	Smith (1888); Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Moffett (2010)
<i>Rhigozum trichotomum</i> Burch.	Bignoniaceae	Driedoring (Afrikaans)	Stems	The Nama chew the stems to treat colds.	Von Koenen (2001)
<i>Rhoicissus tridentata</i> (L. f.) Willd. & R.B. Drumm.	Vitaceae	Northern Bushman's grape (English), noordelike boesmandruif, bitterdruif, droog-my-keel (Afrikaans), isaqoni, umnxeba, ulatile (Xhosa), isinwazi, umthwazi (Zulu), morara-oathaba (southern Sotho), murumbulamudzana (Venda)	Not specified	Used by the southern Sotho to treat colds.	Moffett (2010).
<i>Rhus divaricata</i> Eckl. & Zeyh.	Anacardiaceae	Fire thorn Karee, rusty leaved currant, mountain kuni-bush (English)	Roots	A root decoction is used to treat colds, influenza and bronchitis.	Watt and Breyer-Brandwijk (1962)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Rubus ludwigii</i> Eckl. & Zeyh.	Rosaceae	Wild raspberry, silver bramble (English), braambos, wildebraam (Afrikaans), itshalo, unomhloshane (Zulu), monoko-metsi (southern Sotho)	Roots	The southern Sotho use a root decoction to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Rumex lanceolatus</i> Thunb.	Polygalaceae	Tongblaar (Afrikaans)	Leaves	Fresh leaves are ground and used as a snuff to treat colds.	Von Koenen (2001)
<i>Ruta graveolens</i> L.	Rutaceae	Wynruit (Afrikaans)	Leaves	Leaf infusions are drunk to treat colds and influenza.	De Beer and Van Wyk (2011); Nortje and Van Wyk (2015); Hulley and Van Wyk (2019)
<i>Salix hirsute</i> Thunb.	Salicaceae	Cape willow (English), vaalwilger, wilgerboom (Afrikaans)	Bark	Used to treat colds and influenza.	Von Koenen (2001); Hulley and Van Wyk (2019)
<i>Salvia africana-lutea</i> L.	Lamiaceae	Bloebloomsalie (Afrikaans)	Not specified	A decoction is used by the Nama to treat colds.	Watt and Breyer-Brandwijk (1962); Philander (2011)
<i>Salvia chameleagnea</i> Berg.	Lamiaceae	Bloublomsalie (Afrikaans)	Leaves and flowers	A decoction is used by the Nama to treat colds.	Watt and Breyer-Brandwijk (1962); Hulley and Van Wyk (2019)
<i>Salvia dentata</i> Aiton	Lamiaceae	Bergsalie (Afrikaans)	Leaves	Leaf decoctions are drunk to treat colds.	De Beer and Van Wyk (2011); Nortje and Van Wyk (2015)
<i>Salvia microphylla</i> Kunth.	Lamiaceae	Roosalie, rooibloomsalie (Afrikaans)	Not specified	Infusions are drunk to treat colds.	Hulley and Van Wyk (2019)
<i>Salvia stenophylla</i> Burch. ex Benth.	Lamiaceae	Maagpynbos, fynblaarsalie (Afrikaans)	Leaves	A leaf infusion is consumed to treat cold and influenza.	Von Koenen (2001)
<i>Schistostephium flabelliforme</i> Less.	Asteraceae	Unknown	Not specified	An infusion is consumed to treat colds.	Smith (1888)
<i>Schkuhria pinnata</i> (Lam.) Kuntze. ex. Thell.	Asteraceae	Kleinkakiebos, klein-gousblom (Afrikaans)	Leaves	Powdered leaves are swallowed with water to treat colds and influenza.	Watt and Breyer-Brandwijk (1962); Von Koenen (2001)
<i>Schotia brachypetala</i> Sond.	Fabaceae	Weeping boer bean, tree fuchsia, African walnut (English), hullboerboon (Afrikaans), umfofofo, umgxam (Xhosa), ihluze, umgxamu, uvovovo (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Securidaca longipedunculata</i> Fresen.	Polygalaceae	Violet tree (English), krinkhout (Afrikaans)	Roots	A root infusion is used by the San to treat colds.	Von Koenen (2001)
<i>Searsia divaricata</i> (Eckl. & Zeyh.) Moffett	Anacardiaceae	Mountain kuni-bush (English)	Not specified	Used by the southern Sotho to treat colds.	Moffett (2010)
<i>Searsia erosa</i> (Thunb.) Moffett	Anacardiaceae	Broom karee, besembos (English)	Not specified	Used by the southern Sotho to treat colds.	Moffett (2010)
<i>Searsia lancea</i> (L.f.) F.A. Barkley	Anacardiaceae	African sumuc, willow rhus (English)	Leaves	Used to treat colds. Preparation and application is not specified.	Mulaudzi et al. (2012)
<i>Searsia natalensis</i> (Bernh. ex C.Krauss) F.A. Barkley	Anacardiaceae	Natal rhus (English)	Roots	A decoction is used to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Sersia undulata</i> (Jacq.) T. S.Yi, A.J.Mill. & J. Wen.	Anacardiaceae	Kuni-bush (English), koeniebos, garrabos (Afrikaans), t'kuni (Khoi)	Leaves, bark and roots	The Nama chew the leaves to relieve colds. A leaf decoction is consumed to treat colds. Alternatively, fresh leaves are chewed for the same purpose. No preparation is given for the bark and roots.	Van Wyk et al. (2009); Hulley and Van Wyk (2019); Watt and Breyer-Brandwijk (1962)
<i>Selaginella cafferorum</i> (Milde) Hieron	Selaginellaceae	Resurrection plant (English)	Not specified	Used by the southern Sotho to treat colds.	Moffett (2010); Kose et al. (2015)
<i>Senecio asperulus</i> DC.	Asteraceae	Moferefer (southern Sotho)	Unspecified	The southern Sotho use a decoction to treat colds and influenza.	Watt and Breyer-Brandwijk (1962); Moffett (2010); Kose et al. (2015)
<i>Senecio brachypodus</i> DC.	Asteraceae	Forest senecio (English)	Roots	An infusion is consumed by the southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Senecio dregeanus</i> DC.	Asteraceae	Unknown	Roots	A root decoction is consumed by southern Sotho to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Senecio rhyncholaenus</i> DC.	Asteraceae	Unknown	Leaves	The southern Sotho inhale the smoke from burning leaves to treat colds.	Watt and Breyer-Brandwijk (1962); Moffett (2010)
<i>Senna italica</i> Mill.	Fabaceae	Italian senna (English), elandsertjie (Afrikaans)	Root	The root is pounded, soaked in milk and consumed to treat influenza.	Watt and Breyer-Brandwijk (1962); Hutchings et al. (1996); Von Koenen (2001)
<i>Seriphium plumosum</i> L.	Asteraceae	Khoi-kooigoed, slangbos, slangbossie (Afrikaans)	Leaves	The Zulu boil the leaves and inhaled the steam to treat influenza.	Ngwenya et al. (2003)
<i>Siphonochilus aethiopicus</i> (Schweif.) B.L. Burt	Zingiberaceae	African ginger (English), isiphephetho, indungulo (Zulu)	Roots and rhizomes	Chewed to treat influenza.	Hutchings et al. (1996); Van Wyk et al. (2009); Philander (2011)
<i>Solanum capense</i> L.	Solanaceae	Nightshade (English)			

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Solanum americanum</i> Mill.	Solanaceae	Black nightshade (English)	Bark and roots Fruit	A decoction is drunk to treat colds. Ripe fruit is taken with honey to treat colds.	Smith (1888); Hutchings et al. (1996) Von Koenen (2001)
<i>Solanum refractum</i> Hook. & Arn.	Solanaceae	Nastergal, nasgal (Afrikaans)	Not specified	Infusions are drunk to treat colds.	Hulley and Van Wyk (2019)
<i>Spilanthes mauritiana</i> (A. Rich exPres.) DC.	Asteraceae	Isishoshokazane, isisinini (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Spirostachys africana</i> Sond.	Euphorbiaceae	African mahogany, African sandalwood, headache tree, jumping bean tree, tamboti (English) agelhout, angelhout, gifboom, melkhout, dandaleenhout, tambootie (Afrikaans), muonze (Venda), morekuri (Northern Sotho), umtamboti (Zulu), umthombothi (Xhosa)	Bark	Used to treat influenza. The preparation and application were not specified.	Mulaudzi et al. (2012)
<i>Stachys hyssopoides</i> Burch. ex Benth.	Lamiaceae	Pinksalie (Afrikaans), selaoane (southern Sotho)	Unspecified	Used by the southern Sotho to treat colds.	Moffett (2010)
<i>Sutherlandia frutescens</i> (L.) R.Br.	Fabaceae	Cancer bush (English), kankerbos (Afrikaans), 'musa-pelo, motlepel (Sotho), insiswa, unwele (Xhosa, Zulu)	Leaves	A decoction is used to treat influenza.	Van Wyk et al. (2009); De Beer and Van Wyk (2011); Nortje and Van Wyk (2015)
<i>Sutherlandia humilis</i> E. Phillips & R.A.Dyer	Fabaceae	Unknown	Leaves	A decoction is used to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Sutherlandia microphylla</i> Burch.	Fabaceae	Unknown	Leaves	Infusions or decoctions are used to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Syzygium cordatum</i> Hochst. ex Krauss	Myrtaceae	Waterberry (English), waterbessie, waterboom (Afrikaans), undoni (Zulu), umswi, umjomi (Xhosa), mawthoo (southern Sotho), motlho (Northern Sotho), mutu (Venda)	Leaves	Used to treat colds. Preparation and application not specified.	York et al. (2011); Mulaudzi et al. (2012); Mhlongo and Van Wyk (2019)
<i>Tagetes minuta</i> L.	Asteraceae	Ikhambi lempaka, usangwana (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Tarchonanthus camphoratus</i> L.	Asteraceae	Wild camphor bush(English), wildekanferbos, vaalbos (Afrikaans), sefahla (Sotho), mofahlana (southern Sotho), mathola (Xhosa), igqeba-elimhlophe (Zulu)	Leaves and twigs	Infusions or tinctures are taken to treat bronchitis.	Von Koenen (2001); Van Wyk et al. (2009)
<i>Tecoma capensis</i> (Thunb.) Lindl.	Bignoniaceae	Umunyane, uthswala benyoni (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Terminalia prunioides</i> M. A.Lawson	Combretaceae	Purple-pod Terminalia (English), deurmekaar, sterkbos (Afrikaans)	Root	A root infusion is consumed to treat colds.	Von Koenen (2001)
<i>Terminalia sericea</i> Burch. ex DC.	Combretaceae	Silver cluster leaf (English), vaalboom (Afrikaans), mususu (Venda)	Roots and leaves	Infusions are consumed to treat colds.	Hutchings et al. (1996)
<i>Tetradenia riparia</i> (Hochst.) Codd.	Lamiaceae	Misty plume bush, ginger bush (English), gemerbos, watersalie (Afrikaans), iboza, ibozane (Zulu)	Leaves	An infusion is used to treat stuffy and runny noses of people with colds and influenza.	Felhaber and Mayeng (1997); Van Wyk et al. (2009); York et al. (2011); Mhlongo and Van Wyk (2019); Van;
<i>Teucrium africanum</i> Thunb.	Lamiaceae	Drievingertee (Afrikaans)	Not specified	A decoction is used by Xhosa and Afrikaners to treat influenza.	Watt and Breyer-Brandwijk (1962); Hulley and Van Wyk (2019)
<i>Thamnosma africana</i> Engl.	Rutaceae	Flea bush (English)	Leaves and twigs	An infusion is consumed to treat colds and influenza.	Von Koenen (2001)
<i>Thesium costatum</i> A.W. Hill	Santalaceae	Kleinswartstorm (Afrikaans), marakalle (southern Sotho)	Not specified	The southern Sotho use multiple <i>Thesium</i> spp. to treat colds.	Watt and Breyer-Brandwijk (1962); Kose et al. (2015)
<i>Toddalia asiatica</i> (L.) Lam.	Rutaceae	Cockspur orange, climbing orange (English)	Root	The Venda use a root decoction to treat influenza.	Watt and Breyer-Brandwijk (1962)
<i>Trephrosia semiglabra</i> Sond.	Fabaceae	Unknown	Roots	The southern Sotho use a root decoction to treat colds.	Watt and Breyer-Brandwijk (1962)
<i>Tropaeolum majus</i> L.	Tropaeolaceae	Kappertjie (Afrikaans)	Not specified	Used to treat colds. Preparation and application not specified.	Hulley and Van Wyk (2019)
<i>Tulbaghia acutiloba</i> Harv.	Amaryllidaceae	Wild garlic (English), wilde knoffel (Afrikaans), konofolo, setotha-fotha (southern Sotho)	Whole plant	Used to treat colds. Preparation and application not specified.	Kose et al. (2015).
<i>Tulbaghia violacea</i> Harv.	Amaryllidaceae	Wild garlic (English), wilde knoffel (Afrikaans), isihaqa (Zulu)	Bulbs and leaves	Used to treat colds.	Van Wyk et al. (2009); Hulley and Van Wyk (2019); Mhlongo and Van Wyk (2019)
<i>Valeriana capensis</i> Thunb.	Caprifoliaceae	Cape valerian (English), wildebalderjan (Afrikaans)	Rhizome	Used to treat bronchitis.	Van Wyk et al. (2009)
<i>Vangueria infausta</i> Burch.	Rubiaceae	Wild medlar (English), wilde mispel (Afrikaans)	Leaves and roots	Infusions are consumed to treat colds.	Hutchings et al.(1996); Von Koenen (2001)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Vepris lanceolata</i> G. Don.	Rutaceae	White ironwood (English), witysterhout (Afrikaans), muhondwa (Venda), umzane (Xhosa), umozana (Zulu)	Root	The Zulu use the powdered root as a treatment for influenza.	Smith (1888); Watt and Breyer-Brandwijk (1962)
<i>Viscum capense</i> L.f.	Santalaceae	Cape mistletoe (English), lidjisteet, voelent (Afrikaans)	Whole plant	An infusion is used to treat bronchitis.	Van Wyk et al. (2009); Nortje and Van Wyk (2015)
<i>Volkameria glabra</i> (E. Mey.) Mabb. & Y.W. Yuan	Lamiaceae	Umqoqongo (Zulu)	Not specified	Used to treat colds and influenza. Preparation and application not specified.	Mhlongo and Van Wyk (2019)
<i>Waltheria indica</i> L.	Malvaceae	Unknown	Roots	The San chew the roots to treat colds and influenza.	Von Koenen (2001)
<i>Warburgia salutaris</i> (G. Bertol.) Chiov.	Canellaceae	Pepper-bark tree (English), peperbasboom (Afrikaans), mulanga, manaka (Venda), isibhaha (Zulu)	Bark	Used to treat coughs and colds.	Hutchings et al. (1996); Van Wyk et al. (2009)
<i>Withania somnifera</i> (L.) Dunal	Solanaceae	Indian ginseng, poison gooseberry, winter cherry (English), bitterappelliefie, koorshout (Afrikaans), ubuvuma (Xhosa), ubuvimbha (Zulu)	Root	The southern Sotho consume a decoction to treat colds and influenza.	Smith (1888); Watt and Breyer-Brandwijk (1962); Moffett (2010); Kose et al. (2015)
<i>Xysmalobium undulatum</i> (L.) W.T.Aiton.	Apocynaceae	Wild cotton (English), melkbos (Afrikaans)	Root	Decoctions prepared are applied to the chest to treat colds.	Von Koenen (2001); Watt and Breyer-Brandwijk (1962); Von Koenen (2001)
<i>Zanthoxylum capense</i> (Thunb.) Harv.	Rutaceae	Knobwood (English)	Bark	Used to treat colds. Preparation and application not specified.	Philander (2011)
<i>Zanthoxylum davyi</i> Waterm.	Rutaceae	Forest knobwood (English)	Bark	The Zulu eat the powdered bark to treat colds and severe coughs.	Watt and Breyer-Brandwijk (1962)
<i>Zingiber officinale</i> Roscoe	Zingiberaceae	Ginger (English), gemmer (Afrikaans)	Root	Used to treat colds, influenza and sinusitis.	Hulley and Van Wyk (2019)

of their relative lack of immunity to these diseases. Throughout the course of their life, humans encounter multiple respiratory viral pathogens. In response, we develop antibodies against these viruses which confer protection against future infections with the same virus. Thus, adults often only contract influenza infections every few years as they encounter influenza strains they have previously not contracted. The large number of viral pathogens that cause colds allows adults to potentially contract multiple colds within a single year. However, once a particular strain has been encountered, the immune system confers protection against future infections with that specific virus. In contrast, children will usually have encountered relatively few respiratory viruses and therefore have limited immunological protection so they may be infected far more frequently than adults.

The incidence and severity of viral respiratory infections is also higher and the symptoms more severe in older people. The immune systems of the elderly are less efficient than in the younger generation, allowing these diseases to last for longer periods and allowing the symptoms to be substantially more severe. Indeed, influenza and colds are of considerable concern in elderly people and the risk of mortality is substantially increased. Similarly, immunocompromised individuals are also at far greater risk of contracting a viral respiratory disease than the general population, and when they contract these diseases, the symptoms are often substantially more severe and may be life threatening (Nunes et al., 2014; Annamalay et al., 2016). This is particularly concerning for southern Africa. Sub-Saharan Africa, including South Africa, has a substantially higher prevalence of HIV infected people than many other regions of the world. Indeed, as of 2018, it was estimated that 7.52 million South Africans (equating to >13% of the entire population and 19% of the adult population) are living with HIV (Statistics South Africa, 2018). This is particularly concerning in a southern African context as these individuals with untreated HIV would have be expected to have greatly increased rates of respiratory virus infections, and the infections have far greater consequences. Timely diagnosis and the usage of highly active antiretroviral therapies (HAART) is necessary to overcome these more profound effects in individuals with HIV.

Vaccinations to some of the respiratory infective viruses are readily available. In particular, influenza vaccinations are updated annually to provide protection against the latest influenza strains. Their efficacy has

been improving in recent years, now consistently providing protection rates of 50–60%. These vaccinations are made readily available. Despite this, the uptake of these services is particularly low in South Africa. Indeed, it was recently estimated that <5% of South Africans received the influenza vaccination in 2015 (Solanki et al., 2018). As vaccination is currently the best preventative option for influenza, the rate of uptake is low and higher risk (children, the elderly and immunocompromised) people in particular would benefit from annual vaccinations.

3. Materials and methods

This study aimed to identify southern African plants which are used in traditional healing systems for the treatment of viral respiratory diseases in humans. This information was sourced from a variety of ethnobotanical books (Smith, 1888; Watt and Breyer-Brandwijk, 1962; Hutchings et al., 1996; Von Koenen, 2001; Ngwenya et al., 2003; Van Wyk et al., 2009), as well as ethnobotanical reviews (Hulley and Van Wyk, 2019; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Philander, 2011; Van Wyk et al., 2009). Google-Scholar, Science-Direct, PubMed and Scopus electronic databases were searched to identify original ethnobotanical research papers using the following terms as filters, and were searched both alone and as combinations: “South African”, “medicinal plant”, “traditional medicine”, “ethnobotany”, “respiratory infection”, “colds”, “influenza”, “bronchitis”, “respiratory syncytial virus”, “RSV”, “parainfluenza”, “rhinovirus”, “human metapneumovirus”. These terms were searched alone and as combinations. Only English language publications were used in the preparation of this review. This study is non-biased and does not have taxonomic preference (although several of the studies we review targeted specific families or genera). All species names were checked using the Plant List website (<http://www.theplantlist.org/>). Whilst most of the plant species included herein are native to southern Africa, introduced plant species were also included where there is evidence of their usage in at least one southern African traditional healing system. Our initial literature search identified two hundred and sixty-eight plant species that have been used as traditional remedies for viral respiratory diseases in southern Africa. The vast majority of these species are native to southern Africa, although, several introduced species were also included. For introduced

species to be included in this report, they must either be naturalised or widely cultivated, and there must be documented evidence that they are commonly used by at least one southern African ethnic group to treat viral respiratory disease.

Each plant species identified by this initial search were subjected to a further literature review to establish the extent (if any) of the scientific research into the efficacy of that species, and to scientifically validate their traditional use. Specific criteria to filter studies included the terms ethnomedicine, southern African medicinal plants and other key words related to viral respiratory infections. Only plants used to treat viral respiratory infections in humans are included in this study. Several studies documented the use of some southern African plants to treat viral respiratory diseases in livestock and domestic animals. However, these studies were excluded from this review unless they specifically mention the use of the plant species to also treat human respiratory viral infections. We aimed through this review to summarise traditional southern African ethnopharmacological knowledge on the treatment of viral respiratory diseases, and to discuss the plant species used traditionally to treat these infections. Through this study, we aim to foster further research into southern African plants as treatments for viral respiratory diseases by highlighting plant species traditionally used to treat those diseases.

4. Southern African medicinal plants used traditionally to treat viral respiratory diseases

Viral respiratory diseases exhibit several symptoms that are relatively generic and also occur with multiple other diseases. Traditional medicine practitioners often use plant preparations to target disease symptoms rather than specifically targeting the disease. Indeed, many ethnobotanical texts and reviews record the use of plants to treat symptoms such as coughs and runny noses. Many other diseases produce similar symptoms. For example, other bacterial respiratory diseases such as tuberculosis elicits similar symptoms. Likewise, the early phases of acquired immunodeficiency syndrome (AIDS), anthrax, bubonic plague, cytomegalovirus, Lyme disease, malaria, measles, rabies, severe acute respiratory syndrome (SARS) and smallpox (to list just a few) present with similar symptoms to the viral respiratory diseases and may be mistaken for influenza. Other ethnobotanical texts may list plants used to treat “chest complaints”, “breathing disorders” or other similar symptoms. In this study, only plant species that have specifically been reported to be used to treat viral respiratory infections are included. Where ambiguity occurs regarding a plants specific usage, that plant has been excluded from this study.

An extensive literature search identified 257 southern African plants used in at least one southern African traditional healing system to treat viral respiratory infections (Table 1). The high number of species used to treat these diseases is hardly surprising given the prevalence of these infections. Indeed, it is likely that this list is incomplete and has underestimated the number of species used for this purpose as we have excluded plant species from this record where there is ambiguity about their use. Whilst many of the ethnobotanical texts (Van Wyk et al., 2009; Von Koenen, 2001; Smith, 1888 etc.) examine plant use independent of ethnic groups, several studies examined the ethnobotanical usage by specific ethnic groups. Hutchings et al. (1996) and Ngwenya et al. (2003) itemise plant species used by the Zulu to treat viral respiratory diseases. Similarly, Moffett (2010) concentrates on southern Sotho plant usage, Adeniji et al. (2000) summarises Swazi medicinal plants and Gelfand et al. (1985) itemises the medicinal plants used by ethnic groups in Zimbabwe. Numerous ethnobotanical surveys used in the preparation of Table 1 also reports on medicinal plant use by ethnic groups in specific locations (Hulley and Van Wyk, 2019; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Philander, 2011; Van Wyk et al., 2009). Together, these studies provide an evaluation of the usage of southern African plants for the treatment of viral respiratory disease and allow for the detection of specific trends.

Interestingly, a high proportion of the studies which mention the usage of plants by specific ethnic groups to treat viral respiratory diseases relate to southern Sotho traditional medicine. Indeed, of the plant species that were listed as being used by specific ethnic groups, 70 species were listed as used by the southern Sotho, 26 species are listed as used by the Zulu, 16 species by the Xhosa, five species each by the Tswana and Nama, four species by the San, and one species each by the Venda and Khoikhoi. This is hardly surprising given the environments that each of these groups live in. The southern Sotho live at higher altitudes and in substantially cooler environments than the other ethnic groupings. These conditions require the Southern Sotho to spend greater periods of time indoors, living in close proximity, especially during the colder periods. Such conditions are ideal for the transmission of respiratory viruses and it is likely that the southern Sotho would contract these infections at higher rates than the groups living in warmer environments.

It is also noteworthy that the Southern Sotho has substantially more treatments for the common cold than they did for influenza. This is also likely to correspond to the transmission of these viruses. More than 200 viral serotypes (including over 160 rhinovirus serotypes) have been identified as causes of colds. Due to the antigenic variability of these viruses, otherwise healthy adults may catch up to two or three colds a year. In contrast, there are less influenza virus serotypes, although frequent mutations provide new antigenic variants. However, on average, otherwise healthy adults will only contract an influenza infection every five years. Thus, although influenza infections are substantially more severe than colds, the frequency that the southern Sotho contracted each illness would make cold treatments of particular importance to them.

A further trend regarding the usage of the medicinal plants was also evident. Previous studies have reported that decoctions and infusions are the most common methods for treating most pathogenic diseases (Cock et al., 2018, 2019). Whilst these methods of preparation and usage were also the most common for the treatment of respiratory viruses, burning the plant part and inhaling the smoke was substantially more common for this purpose than previously reported for the treatment of other diseases. This is not unexpected as burning of plant volatiles for pulmonary treatment regimens is common practice from a global perspective (Mohagheghzadeh et al., 2006) Indeed, of the 70 plant species specifically listed as used by the southern Sotho for the treatment of viral respiratory diseases, 21 of these were burned and the smoke inhaled. A further four of the southern Sotho medicinal plant species were burned and used to fumigate the huts of sick people. Inhaling the smoke from burning plant materials was less frequently used by other ethnic groups, although this treatment method was also used by the Zulu and Xhosa for one species each. A further four plant species were also smoked to treat viral respiratory disease, although the ethnic group was not specified for those species. Boiling the plant material and inhaling the steam was used for a further four plant species, although the ethnic group(s) using these species was only stipulated for one of these species (by the San). Several plant species were also powdered and used as a snuff. Five species used by the southern Sotho were administered in this way. The Zulu also used four plant species as snuffs, and a further two plant species (for which the ethnic group was not specified) were also used this way.

In some instances (five plant species) the fruit was indicated for treatment. It is possible that the vitamin C content was targeted here and hence symptomatic treatment was considered rather than a cure sought.

Two hundred and fifty-seven southern African plant species that are used in traditional medicine to treat viral respiratory infections are listed in Table 1. These plant species come from seventy-one families including Amaryllidaceae, Anaradiaceae, Apiaceae, Apocynaceae, Asphodelaceae, Aspleniaceae, Asteraceae, Celastraceae, Combretaceae, Fabaceae, Geraniaceae, Lamiaceae, Malvaceae, Myrtaceae, Poaceae, Polypodiaceae, Pteridaceae, Ranunculaceae, Rosaceae, Rutaceae, Scrophulariaceae, Solanaceae, Verbenaceae and Xanthorrhoeaceae (Fig. 1).

Few of these species have had their inhibitory activity validated against viral respiratory pathogens via *in vitro* testing (Table 2). Most species have only had their use to treat viral respiratory diseases documented in ethnobotanical surveys and laboratory-based studies are required to validate their traditional use. The Asteraceae, Fabaceae and Lamiaceae families were particularly well represented for the treatment of fungal skin infections, with 55, 28 and 23 species identified from these families respectively (Fig. 1). The higher representation of these families compared to other families may indicate that they have better potential against respiratory viruses. However, these are large families, each consisting of many species. Indeed, Asteraceae consists of nearly 33,000 individual species and has a wide global distribution (Bremer et al., 1992). Therefore, the greater representation of Asteraceae, Fabaceae and Lamiaceae is consistent with the higher number of species in these families.

Leaves were the most frequently used plant part for the treatment of viral respiratory infections across the traditional southern African healing systems (Fig. 2). Notably, several other studies have reported that leaves are the most frequently used plant part for the treatment of other pathogenic diseases (De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2015; Philander, 2011; Hulley and Van Wyk, 2019; Cock et al., 2018, 2019; Cock et al., 2019). Roots, bulbs, rhizomes and corms, are also commonly used to treat viral respiratory diseases (80 species). Bark is also relatively commonly used for this purpose (15 species). However, wild harvesting bark can damage trees and may even kill the plant. Therefore, tree bark should be used sparingly to avoid damage to the tree and allow for sustainable production. Further studies similar to those conducted by Zschocke et al. (2000) and Jena et al. (2017) can be undertaken to determine if plant part substitution can yield similar efficacies and therefore provide an alternate medicinal source that would require sustainable harvesting.

Many of the plant species traditionally used for the treatment of viral respiratory infections are herbaceous. This is advantageous for sustainable production of these medicines as herbaceous plants grow rapidly. The use of plant parts that does not extensively damage the plant is

preferred, particularly for endangered and threatened plant species. Unfortunately, the ethnobotanical records were incomplete for many plant species identified as treatments for viral respiratory diseases and we were unable to identify which plant part is used. Further ethnobotanical studies are required to clarify this.

5. Scientific studies into the therapeutic properties of southern African plants against viral respiratory diseases

Surprisingly few studies have examined the effects of southern African plants against viral respiratory infections (Table 2). Indeed, we were only able to find nine studies that have reported activity for southern African plants for activity against respiratory viruses. Not surprisingly given its prevalence and more serious nature, the influenza virus has been the most extensively studied. However, we were only able to find five studies that reported anti-influenza virus activity for some southern African plants (Lall et al., 2006; Michaelis et al., 2011; Rahmasaria et al., 2017; Mair et al., 2018; Mehrbod et al., 2018). The most extensive of these studies reported that five of the screened plants inhibited influenza virus A viral production against a H1N1 reference serotype (Mehrbod et al., 2018). Similarly, a preparation called EPs 7630 prepared from *P. sidoides* inhibited the replication of H1N1 and H3N2 influenza virus, parainfluenza virus, HRSV and human coronavirus strain 229E at 100 µg/mL (Michaelis et al., 2011), but did not affect H5N1 influenza strain or several adenoviruses and rhinoviruses. The susceptibility of the 229E coronavirus to this preparation is particularly interesting given the current SARS-CoV-2 pandemic and highlights this preparation as a potential treatment for COV-19. Whilst we were unable to find publications screening EPs 7630 against that virus, this would be a priority for future studies.

T. ventricosa was also particularly strong inhibitor of influenza virus replication, with an EC₅₀ of 0.05 µg/mL. This was notable inhibition and was similar to the inhibition recorded for the control antivirals amantadine hydrochloride and oseltamivir carboxylate. *C. spicata* and *P. viridiflorum* were also strong inhibitors of influenza virus A

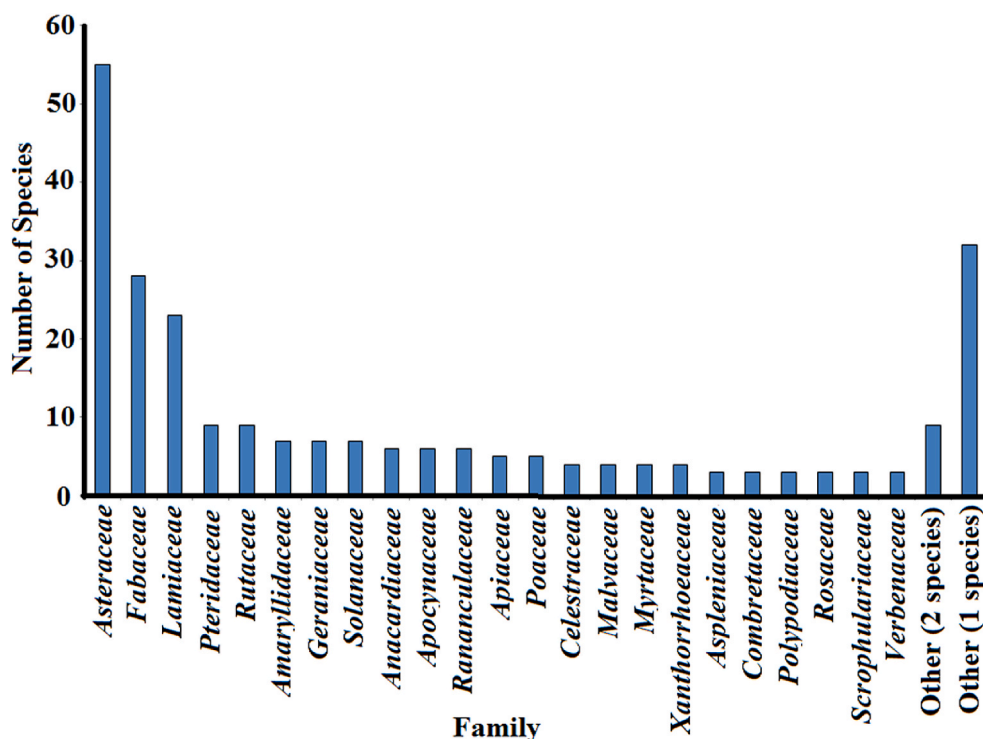


Fig. 1. The number of plant species per families related to medicinal plants for the treatment of viral respiratory infections. Others refers to the number of other genera (not named individually) that are represented by the indicated number of species.

Table 2
Scientific evaluations of the inhibitory activity of southern African plants against viral respiratory pathogens.

Plant Species	Common Name	Family	Plant Part Used	Formulation	Results	Reference
<i>Acokanthera schimperi</i> (A.DC.) Schweinf.	Unknown	Apocynaceae	Leaves	Multiple solvent extracts were tested.	Inhibited 50% parainfluenza production at a 1 in 10 dilution.	Bagla et al. (2012)
<i>Aspalathus linearis</i> (Burm.f.) R.Dahlgren	Red bush, bush tea (English), Rooibos (Afrikaans)	Fabaceae	Leaves	Leaf infusions	An IC ₅₀ value was not reported. Instead, the authors state that the extract inhibited influenza virus A and B production by 50% at 0.2% of the extract concentration (not stated in that study).	Rahmasaria et al. (2017)
<i>Barleria prionitis</i> L. subsp. <i>delagoensis</i> (Oberm.) Brummitt & J.R.I.Wood	Delagoa Bay barleria, porcupine flower (English)	Acanthaceae	Whole plant	DCM extract	Compounds isolated from the extract (6-O-transp-coumaroyl-8-O-acetylshanzhiside methyl ester and its cis isomer) inhibited syncytial virus (RSV) production (EC ₅₀ = 2.5 µg/mL)	Chen et al. (1998)
<i>Burkea africana</i> Hook.	Wild syringa (English)	Fabaceae	Bark	Purified saponins	Bark extracts displayed apparent antiviral activity in a cytopathic effect (CPE) assay. Eight individual saponins purified from the bark were potent inhibitors of H3N2 influenza Hong Kong strain, with IC ₅₀ values 0.05–0.27 µM.	Mair et al. (2018)
<i>Carissa spinarum</i> L.	Climbing num-num, small num-num (English), enkeldoringnoemnoem, ranknoemnoem, kleinnoemnoem (Afrikaans), mothokolo (Sotho)	Apocynaceae	Leaves	Multiple solvent extracts were tested.	Inhibited 25% parainfluenza production at a 1 in 10 dilution.	Bagla et al. (2012)
<i>Clerodendrum glabrum</i> E. Mey. var. <i>glabrum</i>	Tinderwood (English), tontelhout (Afrikaans), moswaapeba (Sotho), munukha-tshilongwe (Venda), umqwaqwanam (Xhosa), umQoqonga (Zulu)	Lamiaceae	Leaves	Methanol extract	Tested against influenza virus A. EC ₅₀ values of 110 µg/mL against both pre- and post-penetration phases of viral replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	Mehrbod et al. (2018)
<i>Crassula globularioides</i> subsp. <i>argyrophylla</i> (Diels ex Schönland & Baker f.) Toelken	Unknown	Crassulaceae	Aerial parts	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >6 µg/mL.	Beuscher et al. (1994)
<i>Cussonia spicata</i> Thunb.	Cabbage-tree (English), kiepersol (Afrikaans), umsenge (Zulu and Xhosa), motshetshe (Sotho)	Araliaceae	Leaves	Methanol extract	Tested against influenza virus A. EC ₅₀ values of 5–15 µg/mL against both pre- and post-penetration phases of viral replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	Mehrbod et al. (2018)
<i>Ekebergia capensis</i> Sparm.	Cape ash (English), essenhout (Afrikaans), mmidibidibi (Northern Sotho), umnyamathi (Zulu)	Meliaceae	Bark	Extracted with multiple solvents of varying polarity	Inhibited 75% parainfluenza production at a 1 in 10 dilution.	Bagla et al. (2012)
<i>Helichrysum armenium</i> DC	Unknown	Asteraceae	Leaves	Aqueous and ethanolic extracts	Inhibited parainfluenza virus production. MIC = 4 µg/mL	Kutluk et al. (2018)
<i>Helichrysum melanacme</i> DC.	Hotnotskooigoed (Afrikaans)	Asteraceae	Leaves	Ethanol extract	Inhibited influenza virus A production. IC ₅₀ = 10 µg/mL	Lall et al. (2006)
<i>Heteromorpha arborescens</i> (Spreng.) Cham. & Schltdl.	Parsley tree (English), wildepietersielele (Afrikaans)	Apiaceae	Root bark	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >25 µg/mL.	Beuscher et al. (1994)
<i>Holarrhena pubescens</i> Wall. ex G. Don	Fever-pod (English) Jasmine-tree (English)	Apocynaceae	Bark	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >10 µg/mL.	Beuscher et al. (1994)
<i>Jasminum fluminense</i> Vell.	River jasmine (English), rivier jasmyn (Afrikaans)	Olacaceae	Stems	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >50 µg/mL.	Beuscher et al. (1994)
<i>Pelargonium sidoides</i> DC.	Black pelargonium, South African geranium (English), kalwerbossie, rabassam (Afrikaans), ikubalo, iyeza lesikhali (Xhosa), khoara-e-nyenyane (Southern Sotho)	Geraniaceae	Unspecified	A proprietary preparation named EPs 7630 was tested.	EPs 7360 at a concentration of 100 µg/mL inhibited the replication of H1N1 and H3N2 influenza virus, parainfluenza virus, HRSV and human coronavirus strain 229E, but did not affect H5N1 influenza	Michaelis et al. (2011)

(continued on next page)

Table 2 (continued)

Plant Species	Common Name	Family	Plant Part Used	Formulation	Results	Reference
<i>Pittosporum viridiflorum</i> Sm.	Cheesewood (English), kasuur (Afrikaans), kgalagangwe (Northern Sotho), umkhwenkhwe (Zhosa, Zulu), umfusamvu (Zulu)	Pittosporaceae	Leaf	Aqueous, methanol, ethanol and acetone extracts	strain, or several adenoviruses and rhinoviruses. Tested against influenza virus A. EC ₅₀ values of 3–82 µg/mL against both pre- and post-penetration phases of viral replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	Mehrbod et al. (2018)
<i>Polygala lancifolia</i> A. St.-Hil. & Moq.	Purple broom (English), persboom, bloukappie (Afrikaans), hlokoa leleue (Sotho), ithethe (Zulu)	Polygalaceae	Aerial parts	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >12 µg/mL.	Beuscher et al. (1994)
<i>Pterocarpus angolensis</i> DC.	Bloodwood, paddle-wood, sealing-wax tree, wild teak, Transvaal teak (English), bloedhout, dolfhout, greinhout, kajatenhout, lakhout, wilde-kiaat (Afrikaans), morôtô (Sotho), umvangazi, umbilo (Zulu)	Fabaceae	Bark	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >12 µg/mL.	Beuscher et al. (1994)
<i>Rapanea melanophloeos</i> (L.) Mez.	Cape beech (English); boekenhout, beukehout (Afrikaans), isiCalabi, umaPhipha, iKhubalwane, isiQalaba sehlati (Zulu), isiQwane sehlati (Xhosa)	Primulaceae	Leaves and twigs	Aqueous, methanol, ethanol and acetone extracts	Tested against influenza virus A. EC ₅₀ values of 113 µg/mL against both pre- and post-penetration phases of viral replication. No direct interaction with viral hemagglutinin glycoprotein.	Mehrbod et al. (2018)
<i>Steganotaenia araliacea</i> Hochest.	Carrot tree (English)	Apiaceae	Root	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >5 µg/mL.	Beuscher et al. (1994)
<i>Tabernaemontana ventricosa</i> Hochst. ex. A.DC.	Forest toad tree (English), bospaddaboom (Afrikaans), uKhamamasane (Zulu)	Apocynaceae	Leaves	Extracted with multiple solvents of varying polarity	Tested against influenza virus A. EC ₅₀ values of 0.05 µg/mL against both pre- and post-penetration phases of viral replication. Solvent extracts were substantially more potent than aqueous extracts. No direct interaction with viral hemagglutinin glycoprotein.	Mehrbod et al. (2018)
<i>Xanthocercis zambeziaca</i> (Baker) Dumaz-le-Grand	Nyala tree (English), njalaboom, hoenderspoor (Afrikaans), mutshato (Venda)	Fabaceae	Leaves	Methanol and DCM extracts	DCM extract strongly inhibited rhinovirus type 2 production in HeLa cells at concentrations >60 µg/mL.	Beuscher et al. (1994)

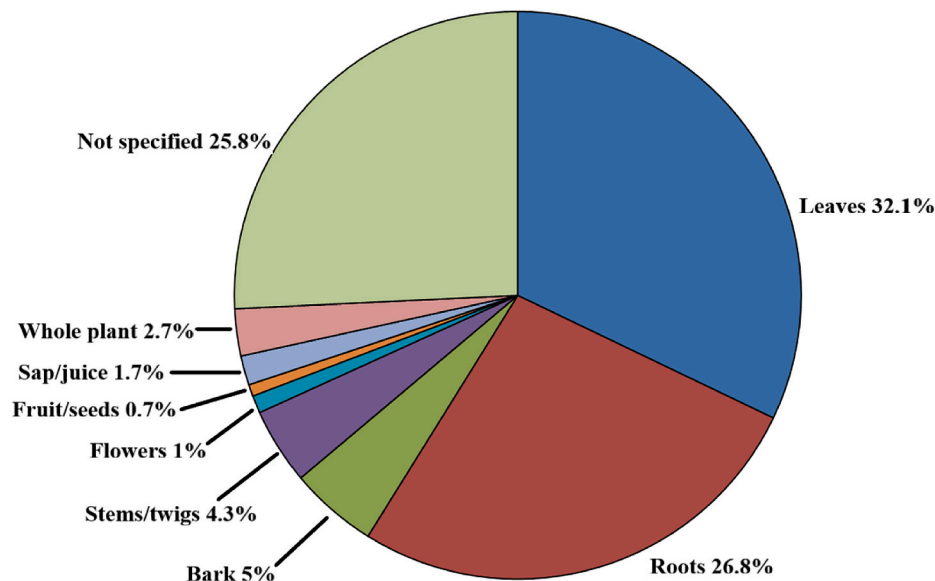


Fig. 2. Frequency of use of different plant parts to treat viral respiratory infections.

production, with EC₅₀ values as low as 5 and 3 µg/mL respectively. Noteworthy activity was also recorded for *C. glabrum* and *R. melanophloeos* extracts, albeit with substantially higher EC₅₀ values (110 and 113 µg/mL respectively). However, *T. ventricosa* also displayed some toxicity, with a selectivity index (SI) of 2 reported. This may limit the use of *T. ventricosa* extracts, as only relatively low concentrations would be considered safe to use to treat influenza A. The lowest toxicity and highest SI (8) was determined for *C. spicata*. This plant may therefore be the preferred therapeutic option for the treatment of influenza A H1N1 serotypes.

Two other studies also reported influenza virus inhibitory activity for *A. linearis* (Rahmasaria et al., 2017) and *H. melanacme* (Lall et al., 2006). The Lall et al. study (2006), screened *H. melanacme* extract (and purified compounds) against a single clinical strain of the virus designated strain Panama, which is a H3N2 influenza A serotype virus. Noteworthy inhibition of viral replication was reported in that study (IC₅₀ = 10 µg/mL). This was the only study that we found that screened against a H3N2 serotype, making it difficult to compare these results with those obtained from other studies. The Rahmasaria et al. (2017) study screened *A. linearis* extracts against a much more extensive panel of influenza viruses. Indeed, that study screened against five oseltamivir sensitive and one resistant influenza H1N1 serotype strains. Good activity was noted against all influenza strains, with IC₅₀ values < 5% of the extract concentration against all strains, and as low as 0.5% against one H1N1 strain. Interestingly, the inhibition of viral replication by the *A. linearis* extracts was not substantially different between the oseltamivir sensitive and resistant viral strains, further highlighting the potential of *A. linearis* extracts to treat influenza virus infections. Of further note, the *A. linearis* extracts were non-toxic and SI's were between 12 and 140.

Three studies also screened southern African plant extracts against parainfluenza virus (Michaelis et al., 2011; Bagla et al., 2012; Kutluk et al., 2018). The Kutluk et al. (2018) study screened *H. armenium* against parainfluenza and reported strong inhibition (MIC = 4 µg/mL). The Bagla et al. (2012) study screened a more extensive panel of plant extracts and reported noteworthy activity for *A. schimperi*, *C. edulis* and *E. capenses* (Bagla et al., 2012). However, that study screened extracts of varying concentrations at fixed dilutions, and measured the % inhibition of viral replication. IC₅₀ values were not determined, making it impossible to compare the efficacy of these extracts with other studies. However, notable inhibition was reported for all three plants and future studies are required to better quantify the anti-parainfluenza activity of these extracts and allow them to be benchmarked against other plant species. The Michaelis et al. (2011) study tested a proprietary preparation prepared from *P. sidoides* against parainfluenza virus at 100 µg/mL and reported inhibition of viral replication. However, a single concentration was tested so IC₅₀ values were not determined.

It was perhaps surprising given the prevalence of colds, that we were only able to locate two study that screened southern African plant extracts against rhinovirus (Beuscher et al., 1994; Michaelis et al., 2011), and only one study that screened against adenovirus and enterovirus strains, although the *P. sidoides* preparation tested in that study had no effects on adenovirus and enterovirus replication. Strong inhibition of rhinovirus production were reported for *C. swaziensis* (at concentrations >6 µg/mL), *H. arborescens* (at concentrations >25 µg/mL), *H. pubescens* (at concentrations >10 µg/mL), *J. fluminense* (at concentrations >50 µg/mL), *P. virgata* (at concentrations >12 µg/mL), *P. angolensis* (at concentrations >12 µg/mL), *S. araliacea* (at concentrations >5 µg/mL) and *X. zambesiaca* (at concentrations >60 µg/mL) (Beuscher et al., 1994). A single study also tested iridoid glycosides isolated from *B. prionitis* against RSV and reported EC₅₀ values as low as 2.5 µg/mL for the pure compounds (Chen et al., 1998). Unfortunately, that study did not test the crude extract against RSV and it is not known whether it also has noteworthy anti-RSV activity.

Interestingly, only a single species of plant (*C. glabra*) tested for the ability to inhibit the production of respiratory viruses corresponded to

plants used in traditional healing systems to treat those infections (Mhlongo and Van Wyk, 2019). A further four species were not recorded as being used traditionally to treat these infections, although are closely related to other species used for this purpose. The inhibitory activity of *H. armenium* (Kutluk et al., 2018) and *H. melanacme* (Lall et al., 2006) were screened against parainfluenza and influenza virus A respectively. Whilst there is no record of these plant species being used as traditional medicines to treat respiratory viral infections, ten other *Helichrysum* species are recorded as being used for these purposes (Table 1). Similarly, we found no evidence that *Carissa edulis* was used traditionally to treat parainfluenza despite it being tested for this activity (Bagla et al., 2012). However, the related species *C. bispinosa* is used to treat viral respiratory disease, although it is recorded for use against influenza, rather than parainfluenza infections (Mhlongo and Van Wyk, 2019). Similarly, we were unable to find evidence that *P. virgata* was used to treat colds, despite it being screened against rhinovirus (Beuscher et al., 1994). However, the related species *P. schinziana* was used traditionally to treat colds (Von Koenen, 2001; Hutchings et al., 1997). The inclusion of those species in the antiviral studies may have been on the basis of these taxonomic relationships, although this is not explained by the authors of those studies. It is likely that all other species were selected randomly for screening.

More recently, mechanistic computational modeling of the anti-influenza effects of quercetin-3-O-α-L-rhamnopyranoside isolated from the medicinal plant *R. melanophloeos* with known antiviral activity against H1N1 was undertaken. Results demonstrated that the compound was effective against influenza infection by regulating immunomodulatory properties, inhibiting the binding ability to viral receptors M2 transmembrane and neuraminidase of 2009 pandemic H1N1 and human RhoA cellular protein (Mehrbood et al., 2019).

6. Discussion

The development of viral resistance to the current complement of antiviral chemotherapies has necessitated the development of new drugs with novel targets. Two of the six drugs currently in clinical usage to treat influenza (the adamantane drugs amantadine and rimantadine) are no longer considered effective against H1N1 and H3N2 serotypes as they have developed almost complete resistance to these drugs (Deyde et al., 2007). Similarly, several influenza strains have developed resistance to baloxavir marboxil (which functions via a different mechanism to the adamantane drugs) (Hayden et al., 2018), effectively limiting its efficacy. The speed with which influenza A and B strains have developed resistance to this drug (it has been in clinical use for less than 2 years) indicates that it is likely to be of little therapeutic value in a short time. Only oseltamivir phosphate, zanamivir and peramivir are still effective against most influenza virus strains (FDA, 2019), although resistance to these drugs is also increasingly being reported (Sheu et al., 2008). The development of new influenza therapies are urgently required.

Ideally, new anti-influenza drugs should have different therapeutic mechanisms to the existing drugs to allow them to inhibit influenza strains that have acquired resistance to the other medications. New chemotherapies should also be effective at low concentrations and have low toxicity. Traditional plant-based medicines are attractive targets to combat respiratory viruses. Many traditional medicines have been used for hundreds of years and their efficacy has been demonstrated over long periods. Furthermore, due to their extensive usage, their toxicity and side effects are often known, and their safety verified. Additionally, traditional medicines are used as crude preparations that containing multiple components. These components may target different aspects of viral replication, which may not only increase the efficacy of the mixture, but also decrease the possibility of inducing further resistance in respiratory-infective viruses.

This study aimed to identify southern African plant species that had been specifically recorded as being used for the treatment of viral respiratory diseases. In order to maximise the number of plants used for

these purposes and highlight plants for future studies, we searched all available English language published records, including older literature sources dating back to the later part of the nineteenth century (Smith, 1888). Whilst, this has maximised the number of species that we have recorded, it is noteworthy that some older literature is prone to generalisations, without definitive evidence. However, with few exceptions, we were able to confirm the use of the plant species named in the older literature with similar reports in more recent reports. Indeed, of the species listed in Smith (1888) as used for the treatment of colds and influenza, all except four species (*L. asperifolia*, *P. sanguinale*, *R. capensis*, *S. flabelloforme*) were also listed in more recent studies as being used for the same purposes. Similarly, relatively few plant species were named in Watt and Breyer-Brandwijk (1962) without also being listed for the same uses in one or more other more recent publications. However, the use of older literature also presented further complications related to classification, with numerous taxonomic revisions occurring in the intervening period.

A further limitation was highlighted when using ethnobotanical texts and published ethnobotanical literature. Many of these publications discuss the southern African ethnic groups as homogenous entities under broad groupings such as Zulu, Xhosa, Sotho etc. This particularly applies to the older literature, although it is also true of many newer publications. Unfortunately, this implies that there is uniform traditional knowledge regarding the usage of medicinal plants throughout these groups, independent of geographic and other factors. This is a simplistic view and individual cohorts within these larger ethnic groups have a diversity of traditional knowledge arising from differing experiences and differing knowledge transfer pathways. As many publications summarise the traditional knowledge of entire ethnic groupings, our review has also listed the use of these plants in this way out of necessity and for reasons of brevity. However, several recent ethnobotanical studies not only record the usage of medicinal plants within broad ethnic groups, but also compare the usage between different regions within the same ethnic groupings. For example, Hulley and Van Wyk (2019) not only record the traditional knowledge of an ethnic group, but in individual villages within a region, thereby highlighting the heterogeneity of knowledge within that broader group. A discussion of the specific differences within different sub-populations of the various ethnic groups is beyond the scope of this review and the reader is referred to the individual studies cited in Table 1 for more detailed understanding of the heterogeneity of traditional knowledge.

Our study identified 257 plant species that are traditionally used to treat respiratory viral infections. Several previous studies have also examined the use of southern African plants to treat respiratory symptoms. However, those symptoms are common to other diseases as well as those caused by respiratory viruses. As the aim of our study was to categorise southern African medicinal plants based on their reported use to treat specific viral respiratory diseases, plant species listed to treat symptoms associated with colds and influenza without specifying their use against those diseases were excluded from our study. Therefore, we are confident that all species used in our study are used in southern African traditional medicine to treat these diseases. However, excluding species because of a lack of definitive ethnobotanical records may have substantially underestimated the number of species traditionally used against these diseases. Several otherwise promising species have not been included for this reason. For example, *P. sidoides* and *Cyclopia* sp. are reported to treat symptoms consistent with acute bronchitis and colds, as well as numerous other diseases (Michaelis et al., 2011). As these symptoms are generic, these species have not been included in our study. However, as they can alleviate some symptoms consistent with viral respiratory diseases, they should not be ignored and future studies to test their activity against respiratory viruses is required.

It is notable that most of plant species listed in our study were used traditionally to treat influenza (generally considered to be the most serious viral respiratory infection) and colds (the most prevalent respiratory disease). Given the number of plants traditionally used to treat

viral respiratory diseases, the low number of studies screening southern African plants for the ability to these viruses is surprising. Indeed, only one of the traditionally used species (*C. glabrum*) has been screened for the ability to block respiratory virus production to date (Mehrbood et al., 2018). That study tested the plant extracts against a single H1N1 influenza strain (Mehrbood et al., 2018) and the possible activity against other influenza strains (and against other respiratory-infective viruses) remains to be studied. Therefore, the remaining 256 plant species that have been used for hundreds of years to treat viral respiratory diseases are yet to be tested and much work is required.

There was a lack of studies investigating most of the other viral respiratory diseases discussed in this review other than colds and influenza. Distinguishing between the other respiratory viruses can be difficult. This is evident from the complete lack of ethnobotanical records of plant species used to treat parainfluenza, HRSV, HMPV and coronavirus induced diseases. Traditional healers would have been able to prescribe therapies to alleviate the symptoms of these diseases, although they are unlikely to have been able to distinguish them from a suite of respiratory and other diseases. Thus, researchers seeking herbal targets to test against those diseases may benefit from screening using plants recorded as remedies to coughs, sore throats, fevers and other generic respiratory symptoms. Many of these plants will also have been used to treat colds and influenza, so screening against the plants identified in this study is likely to yield promising leads against the other respiratory diseases.

It is likely that several factors may contribute to the relative neglect of studies screening southern African plants against respiratory viruses. As previously discussed, viral respiratory diseases are generally (and in some cases, erroneously) thought to be of low concern compared to other pathogenic diseases. However, even for those diseases for which this is true (e.g. colds), the prevalence of the disease makes the development of an effective therapy an attractive prospect. Viral assays are often more complex than many other bioassays (e.g. antibacterial assays), requiring specialised training and equipment, as well as expensive reagents. This may deter some researchers from the field. Furthermore, potential researchers may not be sure of which plants to target. It is hoped that this review may address this final point by providing a comprehensive listing of the southern African plant species known to be used to treat these diseases.

Whilst only one plant species traditionally used to treat viral respiratory diseases has had its antiviral activity verified, twenty-one other species have also been screened. The inclusions of these species may have been on the basis of taxonomic similarity to traditionally used species, or due to the author's bias towards a particular family or genus. Alternatively, inclusion in the studies may have been random. All of these are valid reasons for inclusion in screening studies. However, using a targeted approach that aims to screen the species used traditionally for these purposes is more likely to identify effective new therapeutic targets.

When a plant preparation displays good activity against one strain of respiratory virus, it is necessary to screen it against other strains of the same viral species. Different serotypes within a species, and different strains of those serotypes, often have very different susceptibility and resistance profiles. This is particularly apparent for the influenza viruses. Indeed, rapid and continual mutation resulting in antigenic shifts is the way that influenza virus is able to evade the immune response (and often, antiviral chemotherapies). Thus, newly developed influenza therapies (as well as therapies against other respiratory-infective viruses) should not only be tested against common viral strains. They should also be tested at regular intervals against new and emerging strains to evaluate their continued efficacy against viral respiratory diseases. This is particularly important for influenza virus due to the high probability of future pandemics for which medical science may have limited treatment options.

Notably, most of the plant species already screened for anti-respiratory virus activity were also tested concurrently for toxicity.

This is particularly true for the recent studies. Evaluation of toxicity is imperative to quantify the therapeutic potential of a plant-derived medicine as even the most promising preparation will be of limited value if it possesses substantial toxicity. Even when a plant preparation has previously been tested for toxicity in studies evaluating other therapeutic properties, it should also be tested in parallel with the antiviral studies to allow quantification of a selectivity index (SI) or therapeutic index (TI). Ideally, toxicity evaluation studies should also incorporate more than one assay model to provide confidence in the safety of the therapy, and to allow for comparisons between studies. Much work is required to screen southern African plants against respiratory viruses. This review provides a reference to aid in plant species selection to focus future studies.

7. Conclusions

Our study has highlighted 257 southern African plant species used traditionally to treat viral respiratory diseases (particularly influenza and colds). Despite extensive ethnobotanical records and the relatively large number of southern African plant species identified, only a single species has yet been tested for the ability to inhibit the growth of respiratory viruses on the basis of its ethnobotanical usage. Substantial further work is needed to test the other 256 species against the viral pathogens that they were traditionally used against. Furthermore, with some notable exceptions, the southern African plant species that have been tested against viral respiratory pathogens have generally only been tested against one, or at most, a few viral respiratory pathogens. Other viruses (particularly those whose diagnosis is more complicated), have been relatively neglected. Testing against other respiratory viruses is warranted. Given its prevalence and relatively serious nature, screening against influenza strains should be considered a priority. Similarly, given the high level of infections and mortality associated with the current COVID-19 pandemic, screening against the SARS-CoV-2 virus is also an attractive option which may highlight plant species for drug development. It is hoped that this review may highlight the more promising species for screening.

Acknowledgements

The authors are grateful to the Environmental Futures Research Institute, Griffith University, Australia, and the Department of Pharmacy and Pharmacology, University of the Witwatersrand, South Africa for the support provided to undertake these studies.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jep.2020.113194>.

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