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Review

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

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ARTICLE INFO

Keywords:

Southern African plants
Tuberculosis
Diphtheria
Pertussis
Whooping cough
Pneumonia
Traditional medicine

ABSTRACT

Ethnopharmacological relevance: Multiple plant species were used traditionally in southern Africa to treat bacterial respiratory diseases. This review summarises this usage and highlights plant species that are yet to be verified for these activities.

Aim of the study: This manuscript reviews the traditional usage of southern African plant species to treat bacterial respiratory diseases with the aim of highlighting gaps in the literature and focusing future studies.

Materials and methods: An extensive review of ethnobotanical books, reviews and primary scientific studies was undertaken to identify southern African plants which are used in traditional southern African medicine to treat bacterial respiratory diseases. We also searched for southern African plants whose inhibitory activity against bacterial respiratory pathogens has been confirmed, to highlight gaps in the literature and focus future studies. **Results:** One hundred and eighty-seven southern African plant species are recorded as traditional therapies for bacterial respiratory infections. Scientific evaluations of 178 plant species were recorded, although only 42 of these were selected for screening on the basis of their ethnobotanical uses. Therefore, the potential of 146 species used traditionally to treat bacterial respiratory diseases are yet to be verified.

Conclusions: The inhibitory properties of southern African medicinal plants against bacterial respiratory pathogens is relatively poorly explored and the antibacterial activity of most plant species remains to be verified.

1. Introduction

Four diseases account for the majority of bacterial respiratory infections globally. Of these, tuberculosis (caused by *Mycobacterium tuberculosis*) has the greatest burden and is classified as one of the top ten causes of death globally (Floyd et al., 2018). This disease is highly contagious and is readily spread via airborne transmission. Indeed, the World Health Organisation (WHO) estimates that more than 10 million people fell ill with tuberculosis in 2018, with 1.5 million people dying from the disease (WHO, 2019a). Of the people contracting *M. tuberculosis* infections, only 10% develop the active form of the disease and fall ill (Houben and Dodd, 2016). Therefore, it is estimated that a pool of 100 million new potentially infective people contracted *M. tuberculosis* infections in 2018. Bacterial pneumonia is also a considerable cause of mortality and morbidity. Indeed, it is classed as

the second highest cause of mortality of any communicable disease (after tuberculosis), with more than 800,000 deaths estimated in 2017 (WHO, 2018). Diphtheria and pertussis caused similarly high mortality rates prior to the widespread introduction of effective vaccination (Holý et al., 2017). Vaccines have been particularly effective and the rates of infection and mortality have decreased dramatically. For example, the number of reported cases of diphtheria decreased from >1 million cases in 1980 to approximately 4500 in 2018 (WHO, 2019b; Holý et al., 2017). Similar trends for the incidence of pertussis have been reported although it still causes a considerable health burden, with 150,000 new cases and 90,000 deaths reported in 2018 (WHO, 2019c; (Holý et al., 2017). This review concentrates on the use of southern African plants to treat these four diseases due to their relevance to southern African health. Whilst other bacteria such as *Legionella pneumophila* (Legionnaires disease) may also cause respiratory diseases, they make relatively minor

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<https://doi.org/10.1016/j.jep.2020.113204>

Received 18 March 2020; Received in revised form 7 July 2020; Accepted 20 July 2020

Available online 27 July 2020

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contributions to southern African health (Muchesa et al., 2018) and thus are not a focus of this review.

1.1. Tuberculosis

Tuberculosis (TB) is the most serious of the bacterial respiratory infections globally (Floyd et al., 2018). It is classified by the World Health Organisation (WHO) as one of the top ten causes of death globally, and the leading cause of death by a single pathogen, ranking substantially ahead of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) (WHO, 2019a). TB has a high infection rate due to its air-borne route of transmission. When an infected person coughs or sneezes (or even talks), small droplets of saliva containing the bacterium are released and dispersed into the air. If other individuals breathe in these droplets, they may also become infected. The spread from person to person is rapid and there is a high infection rate. Indeed, the WHO estimates that approximately a quarter of the world's population is infected with *M. tuberculosis* at any given time and thus at risk of developing TB (WHO, 2019a; Floyd et al., 2018). These high rates of infection also increase the risks of infection to non-infected members of the population.

Tuberculosis generally affects the lungs, although it can also infect other parts of the body. Most infections are asymptomatic and are known as latent TB. People with latent TB do not suffer from the disease's symptoms, nor do they generally spread the disease (Furin et al., 2019). However, they have the potential to spread the bacterium if the disease progresses and therefore they constitute a substantial potential disease reservoir. However, active TB infections are substantially more frequent in immune-compromised individuals, such as people with HIV/AIDS (Pawlowski et al., 2012). When active TB develops, there is a high mortality rate, with approximately 50% of afflicted individuals dying unless they receive timely and effective medical treatment (Floyd et al., 2018).

A number of symptoms are evident in people with TB: chronic coughing with blood containing sputum, fever, night sweats and rapid weight loss (which is responsible for the historical name 'consumption') (Furin et al., 2019). Medical intervention for TB most frequently involves vaccination and >90% of children are vaccinated globally. The efficacy of the vaccine is low, decreasing the risk of acquiring a *M. tuberculosis* by only 20%. However, once an infection occurs, the vaccination decreases the chances that the infection will develop from a latent to active form of TB by 60%. If active TB develops, treatment with antibiotics for 6–9 months is often effective in curing the disease and blocking the transmission from the infected person to others (Nguyen, 2016). However, limited classes of antibiotics are effective against *M. tuberculosis* as the cell wall blocks cell entry for most antibiotic classes. A combination of rifampicin, isoniazid, pyrazinamide and ethambutol is generally used to increase the efficacy of the treatment (Furin et al., 2019). Of considerable concern, there are increasing reports of *M. tuberculosis* strains with resistance to these antibiotics, rendering these combinations of little use (Nguyen, 2016). Effective new antibiotic therapies are urgently required to treat these resistant strains.

1.2. Diphtheria

Diphtheria is another bacterial infection that can cause substantial mortality. Indeed, 5–10% of infections result in death, although the mortality rate can be as high as 20% in children less than 5 years of age and in adults over 40 years old (WHO, 2019b; Holý et al., 2017). Outbreaks are rare in developed countries due to medical advances, although they are more common in developing populations. Diphtheria primarily affects the upper respiratory tract, causing symptoms that range from mild to severe (Truelove et al., 2019). The disease is caused by the bacterium *Corynebacterium diphtheria* and is transmitted in a similar way to TB: from person to person via air-borne pathways. Once a person breathes in the bacterium, disease progression is rapid, with

symptoms usually evident within 2–5 days after exposure. The symptoms may include a sore throat, fever, chills, fatigue, cyanosis, coughs, headaches, difficulty swallowing and swollen lymph nodes, resulting in swelling of the neck. Grey or white pseudo-membrane patches may also develop in the throat of infected people, restricting the airways and causing a 'barking' cough similar to that seen for croup. In severe cases, myocarditis, nerve inflammation, renal disease and decreased blood clotting (due to low platelet levels) may also occur.

The widespread usage of an effective vaccine has substantially reduced the incidence of diphtheria globally (WHO, 2019b; Holý et al., 2017). This vaccine is now routinely given to children (in conjunction with whooping cough and tetanus vaccines) as a three or four dose regimen. Immunity is not life-long and repeated vaccinations are recommended every ten years after the initial vaccination. The diphtheria vaccination is generally quite effective and has greatly reduced the incidence of the disease since its widespread introduction. Indeed, the WHO estimates that approximately 4500 cases of diphtheria are now reported each year, down from >1 million cases a year prior to 1980 (WHO, 2019b; Holý et al., 2017). When *C. diphtheriae* infections occur (generally in non-vaccinated people in developing countries), antibiotic therapy may be effective in curing the disease and blocking its further spread. Metronidazole, erythromycin, penicillin-G, rifamycin or clindamycin are most frequently used to treat diphtheria (Truelove et al., 2019). However, multi-antibiotic resistant *C. diphtheriae* strains are increasingly being reported (Floros et al., 2018; Mohankumar et al., 2018) and new antibiotic therapies are required.

1.3. Pertussis (whooping cough)

Pertussis (commonly known as whooping cough) is a highly contagious bacterial disease that infects large numbers of people annually despite the availability of an effective vaccine (Holý et al., 2017). Indeed, the WHO estimated that over 150,000 new cases were reported in 2018, with nearly 90,000 deaths (WHO, 2019c). However, not all cases are reported, particularly in developing countries, and it is likely that the WHO estimate substantially understates the prevalence of this disease. Indeed, other studies have estimated that there were 24.1 million pertussis cases and over 160,000 deaths of children under five years of age in 2014 (Yeung et al., 2017). Whilst these incidence rates remain unacceptably high, the introduction of a pertussis vaccine in the 1940's has resulted in dramatic reductions in regions that have introduced pertussis vaccination programs (Holý et al., 2017). For example, before the introduction of the vaccine, the incidence of pertussis in the United States of America was estimated to be approximately 180,000 annually (CDC, 2019). Following vaccination, the incidence in that country fell dramatically to an estimated 1000 new cases per year in 1976. Since that time, the incidence has risen again to nearly 19,000 in 2017.

Pertussis is caused by the bacterium *Bordetella pertussis* (Holý et al., 2017). It is an airborne disease and is spread in a similar manner to TB and diphtheria. Once a person is infected with the bacterium, it generally takes 6–20 days for the symptoms to become evident. Initially the symptoms are similar to a common cold, with a runny nose, fever and mild cough being common. These rapidly progress to the characteristic severe coughing fits, followed by a sudden inhalation, producing the 'whooping' sound that gives the disease the common name whooping cough. The disease is protracted, with the symptoms often lasting up to 10 weeks. The coughing can be so severe that it can cause subconjunctival haemorrhages, rib fractures, hernias, urinary incontinence and vertebral artery dissection (WHO, 2019c).

Vaccination is the main form of pertussis control and is approximately 70–85% effective, dependent on the *B. pertussis* strain (Holý et al., 2017). However, recent genetic shifts in the bacterium have rendered some strains less susceptible to the vaccine (Mooi et al., 2014). Furthermore, immunity conferred by vaccination is not life-long and has been estimated to only last 4–12 years (Wendelboe et al., 2005). If a

person contracts pertussis, macrolide antibiotics including erythromycin, clarithromycin or azithromycin are generally effective. However, macrolide resistant *B. pertussis* strains have been reported (Liu et al., 2018; Lönnqvist et al., 2018) rendering these antibiotics of little use. Effective new therapies are urgently required.

1.4. Bacterial pneumonia

Bacterial pneumonia is characterised by lung inflammation due to bacterial infections (Brooks, 2020). It is not a single disease and can be caused by multiple bacterial species including *Haemophilus influenzae*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus pneumoniae*. Bacterial pneumonia is a significant medical burden and causes considerable loss of life annually. Indeed, lower respiratory infections (of which bacterial pneumonia is the major mortality causing disease) are one of the highest causes of death of all communicable diseases (Brooks, 2020; WHO, 2018). The severity of bacterial pneumonia varies widely from mild to life-threatening, or even death. The severity is dependent on a number of factors including the bacterial species and strain causing the infection, the age of the infected person (children and older people tend to suffer more severe symptoms), the immunological status of the infected person, and their general health. The symptoms are generally the same irrespective of the bacterial species/strain or the age of the infected person and include chest pains, shortness of breath, frequent coughing which produces yellow or green coloured mucus, fever, lethargy and chills. In severe cases, infected individuals may develop complications including respiratory failure, sepsis, lung abscesses or empyema (accumulation of pus in the pleural cavity surrounding the lungs).

Infection with these bacteria is most frequently via similar transmission pathways as TB, diphtheria and pertussis (i.e. air-borne transmission), and is classified as community acquired pneumonia (Brooks, 2020). This accounts for the vast majority of bacterial pneumonia cases. However, hospital-acquired bacterial pneumonia (HCAP) is also relatively common and occurs when a sick patient (who has a compromised immune system due to an existing medical condition) contracts an infection whilst in hospital. Ventilator-acquired pneumonia (VAP) may also occur when contaminated equipment is used to ventilate a patient. However, whilst HCAP and VAP are significant issues, air-borne transmission is the major route of transmission.

In contrast to the other bacterial respiratory diseases already discussed, there are few effective vaccines to prevent bacterial pneumonia, although vaccines are available against *Pneumococcal* spp. (Brooks, 2020). Treatment for bacterial pneumonia is generally reactive and is reliant on the use of antibiotics to kill the infective bacteria. The specific antibiotic(s) used are dependent on the infective bacterium. Antibiotic therapy is generally effective against most infective strains, although resistance of bacterial pneumonia strains to antibiotics is becoming relatively common and antibiotic therapies are increasingly failing (Peyrani et al., 2019). Of particular concern, extremely resistant strains of *Klebsiella pneumoniae* have been reported in China and Greece (Cheesman et al., 2017). Both of these strains were resistant to nearly all frontline antibiotics. The same study reported that shortly after those resistant strains were isolated, another *K. pneumoniae* strain that was resistant to all classes of antibiotics was detected in the United States of America. This is particularly concerning as medical science has no effective treatment against that strain and new therapies are urgently required. Similarly, methicillin resistant *Staphylococcus aureus* (MRSA) and extended spectrum β -lactamase resistant (ESBL) strains of some bacterial causes of pneumonia are now relatively common (Cheesman et al., 2017). The development of new therapies that are effective against these antibiotic-resistant species is urgently required.

2. An overview of bacterial respiratory diseases in South Africa

The incidence of TB is particularly high in southern Africa (Nanoo

et al., 2015). Indeed, the WHO issues an annual global TB report on the 30 highest TB burden countries based on the number of cases and the severity of diseases burden (WHO, 2019a). Six southern African countries (Lesotho, Mozambique, Namibia, South Africa, Zambia, Zimbabwe) are included in that list. South Africa has the highest overall number of cases (301,000 total infections), which corresponds to the higher population numbers in South Africa compared to the other southern African countries. The TB rate as a percentage of population is approximately 5% for South Africa, which is similar to the rates in Mozambique and Namibia, and lower than the rates in Lesotho. Interestingly, the rates in Zambia (3.5%) and Zimbabwe (2%) were substantially lower and may correlate to the higher average temperatures (particularly in winter) in those countries. Alternatively, the lower rates may be due to less effective and incomplete reporting of these diseases in those countries. Due to the higher temperatures, it is likely that people in those countries spend less time in groups indoors, thus decreasing pathogen transmission. The southern African infection rates are substantially higher than the global average of 1%, demonstrating the health burden that TB has in southern Africa.

Notably, the WHO statistics only report the cases of active TB. As only approximately 10% of *M. tuberculosis* infections cause the active form of the disease, the actual infection rate may be as high as 50% of the population, providing a vast reservoir of bacteria for potent transmission of TB. Other studies have reported higher incidence of *M. tuberculosis* infection in specific populations. Screening studies in an adult population (<30 years old) in a mining community detected *M. tuberculosis* infections in 89% of the population (Hanifa et al., 2009). A similar study screened adolescent school students (12–18 years old) in rural regions of the Western Cape province of South Africa, within 100 km of Cape Town, and reported nearly 60% of the students had latent TB infections (Mahomed et al., 2011). Both of these studies screened specific groups and these statistics do not necessarily represent the overall prevalence of latent *M. tuberculosis* infections in the entire southern Africa region and the prevalence in urban regions of southern Africa may be substantially different.

The Hanifa et al. study (2009) highlights the prevalence of TB on the mining industry. The conditions under which miners may work constitute ideal conditions for the transmission of *M. tuberculosis*. Miners often work in enclosed spaces underground for extended periods. If a miner has TB, airborne transmission is highly likely under those conditions. Furthermore, miners often share equipment, which may further facilitate the spread of the bacterium. High density lower socio-economic urban communities also have higher incidences of *M. tuberculosis* infections than other regions of southern Africa. High density living provides ideal conditions for airborne transmission, thereby increasing the likelihood of person to person transfer. Of concern, antibiotic resistant *M. tuberculosis* strains are highly prevalent in southern Africa, with >90% of new infections reported to be resistant to several frontline antibiotics (WHO, 2019a). The high prevalence of resistant *M. tuberculosis* strains contributes to the overall burden of the disease in the region. Not only is it more difficult to treat the disease in infected people, but this also allows for further transmission of the bacterium.

The relatively low level of childhood vaccination uptake in several of the southern African countries also contributes to the levels of TB in the region. The WHO report (2019a) estimates that only 59% of children below five years of age have been immunised against TB in South Africa. This contrasts dramatically with the worldwide vaccination rates where it has been estimated that more than 90% of children below the age of five years have been vaccinated for TB. The low vaccination uptake in South Africa is surprising given the incidence of TB in the region and subsidisation of TB vaccination programs by the South African government. Vaccination is relatively cheap and is generally readily available in most areas of the country. We were unable to find a further breakdown of the vaccination statistics on a geographical and ethnic basis, but it is likely that low levels of uptake in isolated and rural communities skew the statistics for the entire country. Isolated and rural communities

often have limited access to clinical care, and when medical care is available, rural populations are often poor and may be unable to afford westernised health care. Instead, rural communities are often reliant on traditional healers. However, encouraging TB vaccination programs may be effective in reducing the infection levels in southern Africa, even amongst non-vaccinated people, by providing ‘herd immunity’, thereby reducing transmissibility.

Not surprisingly, the incidence of *M. tuberculosis* infections is also higher in health care workers than in the general population, due to their levels of exposure to respiratory pathogens. Indeed, one study estimated that the risk of contracting TB is approximately 2.5 times higher for medical professionals than the general population in several countries with similar socio-economic profiles as southern Africa (Joshi et al., 2006). Furthermore, that study demonstrated that specific health care sectors have substantially increased risks of contracting TB. In particular, the risks to workers in emergency departments, TB treatment facilities, clinical laboratories, and internal medicine departments were particularly high rates of infection. Within those departments, paramedics, nurses, patient attendants, ward attendants and radiology technicians had substantially increased risks of contracting a *M. tuberculosis* infection. Whilst that study examined the incidence of TB in the health care sector in other countries, it is likely that similar trends occur in southern Africa.

Immuno-compromised people also have higher rates of infection than non-immunocompromised people. Indeed, the WHO report on TB in the southern African countries (WHO, 2019a) estimated that 59% of individuals diagnosed with TB in 2018 in South Africa also had HIV/AIDS. Of further concern, people with HIV/AIDS had a substantially worse prognosis than the general population, with approximately twice the mortality rate. Whilst the WHO report did not break the data down on the basis of age, it is likely that similar trends would occur in children and in the elderly. Both of these groups have lower immuno-competence than healthy adults. Thus, they are likely to have higher incidences of TB, and higher rates of mortality once they contract a *M. tuberculosis* infection. However, we were unable to find statistics to support this and further studies are needed for confirmation.

The other bacterial respiratory diseases generally follow similar trends to other countries with similar socio-economic profiles. As with other regions of the world, widespread diphtheria and pertussis vaccination programs in children have substantially decreased the incidence of those diseases in southern Africa. Indeed, between January 2008 and March 2015, only four cases of diphtheria were reported in South Africa. An outbreak of diphtheria occurred in South Africa in March 2015, with fifteen confirmed cases in rural Kwa-Zulu Natal, of which four died (Mahomed et al., 2015). All but four of the infected people were either not vaccinated, or their vaccinations were out of date. The outbreak was rapidly contained and the incidence rates have remained low since. Similarly low rates of infection occurred throughout other southern African countries across the same period.

Pertussis is far more common than diphtheria in southern Africa. It is difficult to find incidence statistics for individual countries in southern Africa as the WHO provides figures for the African global region instead. According to the WHO, 14 million cases of pertussis were reported from a population of approximately one billion people, which equates to an infection rate of 1.4% of the population. However, vaccination programs are widespread in South Africa and have a far greater take up rate in southern Africa than in central, eastern and western Africa (WHO, 2019c), so it is likely that the incidence in South Africa (and other southern African countries) is substantially less than this. Pertussis is substantially more common in children than in adults and is one of the most common diseases in children under five years of age. It also has higher incidences in immuno-compromised people than in the general population. A recent study screened children hospitalised for respiratory illnesses in South Africa and reported that pertussis was the cause of approximately 7% of the cases of respiratory illness (Muloiwa et al., 2016). The rate was significantly higher in HIV positive children

(15.8%) and in HIV exposed but negative children (10.9%) than in HIV unexposed children (5.4%). Notably, there have been marked recent increases in the incidence of pertussis in the WHO African world region. Indeed, the number of reported *B. pertussis* infections in that region has increased from approximately 1.5 million to over 14 million between 2016 and 2018 (WHO, 2019d). Although specific figures for South Africa are not available from the WHO, it is likely that it has similar trends for those of the rest of the Africa region. It is likely that decreased rates of pertussis vaccination uptake in recent years may contribute to this trend. Indeed, a recent report by the Centre for Communicable Diseases (2018) reported that pertussis vaccination rates in South Africa had decreased to 66% of the population in 2016, allowing for the resurgence of the disease in the region.

Bacterial pneumonia is common in both children and adults in southern Africa and it is the most common cause of hospitalisation in South Africa. Indeed, approximately 12 million children were hospitalised and 1.2 million children died from bacterial pneumonia in 2010 in South Africa (Dept of Paediatrics and Child Health, South Africa, 2019). The same study also reported that bacterial pneumonia is the second most common cause of death in South African adults. The disease is substantially more common in immune-compromised individuals (both children and adults).

Pertussis and bacterial pneumonia transmission trends are similar to TB. High density urban living allows for efficient transmission of these diseases, therefore the incidence is higher under those conditions. Unfortunately, we were unable to locate occupation specific statistics as reported for TB and further research is required in that area. However, it is likely that similar trends occur (i.e. higher rates in occupations that require workers to work together in confined spaces such as mining; high rates in health care sector professionals through greater contact with infected people). However, these trends have not been reported for pertussis and bacterial pneumonia and further studies are required to confirm this.

3. Materials and methods

3.1. Search strategy

Our study aimed to identify southern African plants used traditionally to treat bacterial respiratory diseases in humans. A systematic search was undertaken using a variety ethnobotanical books (Smith, 1888; Watt and Breyer-Brandwijk, 1962; Van Hutchings et al., 1996; Von Koenen, 2001; Ngwenya et al., 2003; Wyk et al., 2009) and ethnobotanical reviews (Hulley and Van Wyk, 2017; De Beer and Van Wyk, 2011; Nortje and Van Wyk, 2011; Philander, 2011; Van Wyk, 2008). Ethnobotanical research articles published prior to June 2020 were also searched via Google-Scholar, Science-Direct, PubMed and Scopus using the following terms as filters, and were searched both alone and as combinations: “South African”, “medicinal plant”, “traditional medicine”, “ethnobotany”, “respiratory infection” “tuberculosis”, “pneumonia”, “bacterial pneumonia”, “pertussis”, “diphtheria”, “whooping cough”. All terms were searched alone and as combinations.

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. Specific criteria to filter studies included the terms ethnomedicine, southern African medicinal plants and other key words related to bacterial respiratory infections and the specific pathogens.

3.2. Eligibility criteria

A screening of publication titles was initially performed, and eligible publications were selected. The abstracts of were then read to ensure that the selected publications met the eligibility criteria. Full text manuscripts were retrieved for all publications that met the eligibility requirements and these were further studied.

3.2.1. Inclusion criteria

To meet the eligibility criteria for this study, a publication had to meet the following inclusion criteria:

- Only English language publications published prior to June 2020 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).
- For the ethnobotanical studies, the plant species must be stated to be used against the specific bacterial respiratory diseases examined in this study, rather against generic symptoms.
- For the screening studies, preparations prepared from plant extracts must have been screened against at least one of the pathogens responsible for the bacterial respiratory diseases. Alternatively, studies that tested the plant preparations against human or animal models with the bacterial respiratory diseases were also included in this study.
- 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.

3.2.2. Exclusion criteria

Studies with the following criteria were excluded from this study:

- Studies where the species identity was in doubt. By necessity, several relatively old publications were searched (e.g. Smith, 1888; Watt and Breyer-Brandwijk, 1962). Where possible, the species names were confirmed or updated using the Plant List website (<http://www.thepplantlist.org/>). Where a species name could not be definitively verified, that species was omitted from this study.
- Only plant species definitively described as being used to treat specific bacterial respiratory diseases are included in this study. Due to symptom similarity with numerous diseases, when a plant was described as being used to treat symptoms consistent with bacterial respiratory diseases without specifying the diseases they are used to treat were excluded from this study.
- Whilst plant species that are not native to southern Africa are included in this study, introduced plant species were excluded unless there is evidence of their usage in at least one southern African traditional healing system and their widespread cultivation in southern Africa.

3.3. Data collection

Ethnopharmacological studies from southern Africa that are linked with the treatment of bacterial respiratory disease were collected and examined in this study. Additionally, studies testing the activity of the southern African medicinal plants against the bacterial respiratory pathogens, or against infected human or animal models, were examined, irrespective of the study origin. The following data was collected:

- Genus, species and family name for each species examined in the individual publications. All species names were standardised using the Plant List website (<http://www.thepplantlist.org/>).
- Ethnic grouping that traditionally used the plant species medicinally. Where possible, the common and ethnic names were also collected.
- The plant part used and the method of preparation were collected (where available).
- For screening studies, the bacterial pathogen species and (where possible) the strain were listed and the MIC values (where available) are included.
- For animal and human trial studies, the animal model (where appropriate), route of administration, doses and toxicity data (where available) was noted.

All data was managed using Excel® software.

4. Results

4.1. South African medicinal plants used traditionally to treat bacterial respiratory diseases

One hundred and eighty-seven southern African plants which are used in at least one southern African traditional healing system to treat bacterial respiratory infections were identified following an extensive literature search (Table 1). As indicated in our review of southern African plants to treat viral respiratory infections (Cock and Van Vuuren, part one), several pathogenic respiratory diseases exhibit generic symptoms that are common with other bacterial diseases, as well as viral respiratory diseases. For example, the early stage symptoms of TB are often similar to those of influenza or severe acute respiratory syndrome (SARS). Similar symptoms are also evident for numerous other non-respiratory diseases including bubonic plague, Lyme disease, malaria, measles, rabies, and the early phases of AIDS. As ethnobotanical texts may report the usage of plant species to treat the symptoms of a disease, the specific disease treated is often not definitive. For this study, we have only included plant species that have specifically been reported for the treatment of bacterial respiratory infections in humans. Where the disease pathogen targeted by a plant is ambiguous, we have excluded that species from this study. Thus, it is likely that this list underestimates the number of plant species used to treat bacterial respiratory disease.

The relatively high number of plant species used to treat bacterial respiratory diseases may relate to the seriousness and relative prevalence of these infections. Indeed, the vast majority of the plants recorded for use against bacterial respiratory infections were used against bacterial pneumonia (139 species) or TB (81 species). Both of these diseases are relatively common in southern Africa and produce relatively high mortality rates. It is therefore perhaps not surprising that high numbers of plant species were identified for the treatment of these diseases.

Many of the ethnobotanical books, reviews and primary studies used in this review did not specify the preparation of the traditional medicine or how it was used and further studies are required to clarify this. However, many of the recent ethnobotanical surveys did report these details, further emphasising the importance of updated ethnobotanical information. From those studies, a further trend was also evident: decoctions and infusions were most widely used in the treatment of bacterial respiratory infections, with 64 plant-based medicines reported to be used in these ways. Previous studies have also reported that decoctions and infusions are the most common methods for treating most pathogenic diseases (Afolayan et al., 2014; Asong et al., 2019; Cock et al., 2018; Cock et al., 2019; De Beer and Van Wyk, 2011; Hulley and Van Wyk, 2017; Nortje and Van Wyk, 2011; Philander, 2011). Tinctures were prepared and consumed for a further four species, volatiles targeted from three species via inhalation, and a syrup was prepared and consumed from the fruit of various species. This contrasts dramatically with the preparation and usage of plant species to treat viral respiratory diseases, where inhalation was the main method of administration (unpublished results). The use of southern African plants to treat viral respiratory plants will be the basis of another manuscript in preparation.

A wide variety of families of southern African plant species including Apiaceae, Asparagaceae, Asphodelaceae, Apocynaceae, Asteraceae, Brassicaceae, Celastraceae, Combretaceae, Euphorbiaceae, Fabaceae, Lamiaceae, Lauraceae, Malvaceae, Moraceae, Myrtaceae, Polygonaceae, Rosaceae and Solanaceae (Fig. 1) were traditionally used to treat bacterial respiratory diseases. Although the bioactivity of several of these species has already been screened against bacterial respiratory pathogens via *in vitro* testing (Table 2), most species are yet to be screened against respiratory bacterial pathogens. Asteraceae (33 species) and Fabaceae (20 species) were commonly used traditionally to treat bacterial respiratory diseases (Fig. 1). Lamiaceae (9 species), Asparagaceae

Table 1
South African plants used traditionally to treat bacterial respiratory illnesses.

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Abrus precatorius</i> subsp. <i>africanus</i> Verdc.	Fabaceae	Bead vine, coral bead plant, coral bean, crabs eye, licorice vine, love bean, lucky bean creeper, prayer beads, weather vine (English), umkhokha (Zulu)	Leaves, roots	Used to treat TB and whooping cough. Preparation and application not specified.	Madikizela et al. (2013)
<i>Abutilon angulatum</i> (Guill. & Perr.) Mast.	Malvaceae	Unknown	Root	Used to treat bacterial pneumonia. Preparation and application are not specified.	Von Koenen (2001)
<i>Acacia eriloba</i> E.Mey.	Fabaceae	Camel thorn, giraffe thorn (English), kameeldoringboom (Afrikaans)	Leaves	Leaf infusions are drunk to treat bacterial pneumonia.	Von Koenen (2001)
<i>Acacia nilotica</i> (L.) Delile	Fabaceae	Redheart, scented thorn (English), lekkerreulpeul (Afrikaans)	Root	Used to treat TB. Preparation and application are not specified.	Watt and Breyer-Brandwijk (1962)
<i>Acacia xanthophloea</i> Benth.	Fabaceae	Fever tree (English)	Bark	Used to treat TB. Preparation and application are not specified.	McGaw et al. (2008)
<i>Aclepias crispa</i> P.J. Bergius	Apocynaceae	witvergeet, kalmoes (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application are not specified.	Hulley and Van Wyk, 2017
<i>Acorus calamus</i> L.	Acoraceae	Sweet flag (English), makkalmoes (Afrikaans), ikalamuzi (Zulu)	Root	Volatile compounds produced from the root are used to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Adenia fruticosa</i> Burt Davy	Passifloraceae	Green-stem (English)	Not specified	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Ajuga ophyrdis</i> Burch. ex Benth.	Lamiaceae	Senyarrla (Southern Sotho)	Roots	Used to treat TB. Preparation and application not specified.	Kose et al. (2015)
<i>Allium cepa</i> L.	Amaryllidaceae	Onion (English)	Bulb	Consumed to treat whooping cough.	Watt and Breyer-Brandwijk (1962)
<i>Allium sativum</i> L.	Amaryllidaceae	Garlic (English)	Bulb	Consumed to treat whooping cough and TB.	Watt and Breyer-Brandwijk (1962)
<i>Aloe arborescens</i> Mill.	Xanthorrhoeaceae	Krantz aloe (English), kransaalwyn (Afrikaans), ikalene (Xhosa), inkalane, umhlabana (Zulu)	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Aloe ferox</i> Mill.	Xanthorrhoeaceae	Cape aloe (English), Bitteraalwyn, Winkelaalwyn (Afrikaans), iKhala (Xhosa), iNhlaba (Zulu)	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Aloe maculata</i> All.	Xanthorrhoeaceae	Soap aloe, zebra aloe (English)	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Aloe nobilis</i> Haw.	Xanthorrhoeaceae	Golden toothed aloe	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Aloe plicatilis</i> (L.) Mill.	Xanthorrhoeaceae	Fan aloe, Franschoek aloe (English), waaieraalwyn, Franschoekaalwyn, bergaalwyn, tongaalwyn (Afrikaans)	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Anginon difforme</i> (L.) B. L.Burt.	Apiaceae	Wildeanys (Afrikaans)	Leaves	Leaf infusions were drunk by the Nama to treat TB.	Nortjie and Van Wyk (2015)
<i>Aptosimum depressum</i> Burch. ex Benth.	Scrophulariaceae	Unknown	Not specified	An infusion was used as a gargle to treat diphtheria.	Watt and Breyer-Brandwijk (1962)
<i>Artemisia afra</i> Jacq. ex Willd.	Asteraceae	African wormwood (English), als, alsem, wildeals (Afrikaans), lengana (Sotho, Tswana), umhloniyane (Xhosa, Zulu)	Leaves	The leaves are boiled and the steam inhaled to treat whooping cough and diphtheria. The resultant infusion can also be drunk for the same purposes.	Von Koenen, 2001; McGaw et al., 2008;
<i>Aspalathus cordata</i> (L.) R.Dahlgren	Fabaceae	Unknown	Leaves	An infusion is drunk to treat whooping cough.	Watt and Breyer-Brandwijk (1962)
<i>Aspalathus linearis</i> (Burm.f.) R.Dahlgren	Fabaceae	Red bush, bush tea (English), Rooibos (Afrikaans)	Leaves	An infusion is drunk to treat TB and whooping cough.	Watt and Breyer-Brandwijk (1962)
<i>Asparagus africanus</i> Lam.	Asparagaceae	Bush asparagus (English)	Root	Root infusions are consumed several times per day to treat TB.	Watt and Breyer-Brandwijk, 1962; Madikizela et al., 2013; Hulley and Van Wyk, 2017
<i>Asparagus capensis</i> L.	Asparagaceae	Katdoring (Afrikaans)	Root	Root infusions are consumed several times per day to treat TB.	Watt and Breyer-Brandwijk, 1962; Philander, 2011; Hulley and Van Wyk, 2017
<i>Asparagus densiflorus</i> (Kunth) Jessop	Asparagaceae	Katdoring (Afrikaans)	Root	Root infusions are consumed to treat TB.	Hulley and Van Wyk, 2017
<i>Asparagus falcatus</i> L.	Asparagaceae	Unknown	Leaves and roots	Root infusions are consumed to treat TB.	Pallant and Steenkamp, 2008; Madikizela et al., 2013; Van Wyk (2008)
<i>Asparagus linearis</i> (Burm.f.) R.Dahlgren	Asparagaceae	T'nuance, katdoring (Afrikaans)	Roots	Root infusions are consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Asparagus retrofractus</i> L.	Asparagaceae	Ming fern (English)	Root	Root infusions are consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Asparagus setaceus</i> (Kunth) Jessop	Asparagaceae	Asparagus fern, climbing fern, lace fern (English)	Root	Root infusions are consumed to treat TB.	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>Asparagus striatus</i> (L.f.) Thunb.	Asparagaceae	Bergappel, bergappeltjie, bobbejaanappel (Afrikaans)	Root	Root infusions are consumed several times per day to treat TB. Root infusions are consumed several times per day to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Asparagus suaveolens</i> (Burch.) Baker	Asparagaceae	Bushveld Asparagus, wild aspoaragus (English), katdoring (Afrikaans), mvane (Xhosa)	Root	Root infusions are consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Astridia velutina</i> (L. Bolus) Dinter	Aizoaceae	Unknown	Sap	used to treat diphtheria. Preparation and application not specified.	Von Koenen (2001)
<i>Buddleja saligna</i> Willd.	Scrophulariaceae	False olive (English), witoliën (Afrikaans), lelothwane (Southern Sotho), unqeba (Xhosa), igqeba-elimhlope (Zulu)	Leaves, stems	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Callilepis laureola</i> DC	Asteraceae	Oxe-eye daisy (English), Wile margriet (Afrikaans), amafuthomhlaba, ihlamvu, impila (Zulu)	Root	Preparation and application methods are not specified.	Watt and Breyer-Brandwijk (1962)
<i>Capparis tomentosa</i> Lam.	Capparaceae	Wooly caper-bush (English), wollerige kapperbos, wag-'n-bietjie (Afrikaans), inkunzi-ebomvu, iqwaningi, umqoqolo, ukhokhwana, umabusane (Zulu), imfishlo, intshihlo, intsihlo, umpasimani (Xhosa)	Bark, Roots	The bark is burned and the smoke is inhaled to treat TB. The Venda also drank a root decoction for the same purpose.	Watt and Breyer-Brandwijk, 1962; Pallant and Steenkamp, 2008
<i>Carissa edulis</i> (Forssk.) Vahl.	Apocynaceae	Simple-spined num-num, climbing num-num, small num-num (English), enkeldoringnoemnoem, ranknoemnoem, kleinnoemnoem (Afrikaans), mothokolo (North Sotho), murungulu (Venda)	Root, leaves	A root decoction is used by the Venda to treat TB. Leaf juice was gargled to treat diphtheria	Pallant and Steenkamp, 2008; Van Wyk, 2008
<i>Carpobrotus acinaciformis</i> (L.) L. Bolus	Aizoaceae	Eland's sourfig (English), elandssuurvy (Afrikaans)	Leaves	The boiled fruit is consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Carpobrotus edulis</i> (L.) N.E.Br.	Aizoaceae	Sour fig, Cape fig, Hottentot's fig (English), vyerank, ghaukum, ghoenavy, hotnotsveye, Kaapvy, perdevy, rankvy (Afrikaans), ikhambi-lamabulawo, umgongozi (Zulu)	Leaves	A leaf decoction is consumed to treat diphtheria. Leaf juice is consumed to treat TB.	al.Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 2009; Philander, 2011; Nortjie and Van Wyk, 2015
<i>Cassine aethiopica</i> Thunb.	Celastraceae	Saffron wood, forest saffron (English), saffraan, bossafraan (Afrikaans)	Leaves	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Cephalaria pungens</i> Szabó	Caprifoliaceae	Unknown	Roots	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Chaetachme aristata</i> Planch.	Ulmaceae	Thorny elm (English), basterwitpeer (Afrikaans)	Leaves	Used to treat TB. Preparation and application not specified.	Dzoyem et al. (2016)
<i>Chamaecrista mimosoides</i> (L.) Greene	Fabaceae	Boesmantee (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application are not specified.	Von Koenen (2001)
<i>Chenopodium ambrosioides</i> L.	Chenopodiaceae	Wormsalt (English), sinkingbossie (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application are not specified.	al.; Von Koenen, 2001; McGaw et al., 2008
<i>Chironia baccifera</i> L.	Gentianaceae	Bitterbos, skilparbos (Afrikaans)	Not specified	Infusions are used to treat TB and pneumonia.	Hulley and Van Wyk, 2017
<i>Chrysanthemum frutescens</i> L.	Asteraceae	Paris daisy (English)	Roots	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Chrysanthemum segetum</i> L.,	Asteraceae	Corn marigold (English)	Leaves	Decoctions are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Cinnamomum camphora</i> (L.) J.Presl.	Lauraceae	Camphor tree (English), kanferboom (Afrikaans), uroselina (Zulu)	Leaves. Essential oil (distilled from the wood)	The leaves are smoked by the Southern Sotho to treat TB. The bark is used to treat bacterial pneumonia, Preparation and application not specified.	Philander, 2011; Van Wyk et al., 2009; Watt and Breyer-Brandwijk, 1962
<i>Cissampelos capensis</i> L.f.	Menispermaceae	Dawidjies, fynblaarklimop (Afrikaans)	Leaves	Infusions are drunk to treat TB.	Hulley and Van Wyk, 2017
<i>Cliffortia odorata</i> L.f.	Rosaceae	Wildewingerd (Afrikaans)	Not specified	An infusion is drunk to treat diphtheria.	Watt and Breyer-Brandwijk (1962)
<i>Combretum molle</i> R.Br. ex G.Don.	Combretaceae	Velvet bush willow (English), fluweelboswilg, basterrooibos (Afrikaans), mokgwethe (Sotho), mugwiti (Venda), umBondwe-omhlope (Zulu)	Bark	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Combretum platypetalum</i> Welw. ex M.A. Lawson	Combretaceae	Unknown	Root	Root decoctions are drunk to treat bacterial pneumonia	Von Koenen (2001)
<i>Croton pseudopulchellus</i> Pax	Euphorbiaceae	Small lavender fever-berry (English), kleinlaventelkoorsbessie, sandkoorsbessie (Afrikaans), uHushane (Zulu)	Leaves	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Cryptocarya latifolia latifolia</i> Sond.	Lauriaceae	Bastard stinkwood, broad-leaved auel, broad-leaved quince (English), baster-	Bark	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Cyclopia genistoides</i> (L.) Vent.	Fabaceae	stinkhout, basterswartstinkhout, breëblaarkweper, pondo-kweper (Afrikaans), umgxaleba, umgxobothi (Xhosa), umhlangwenya, umkhondweni, umdlangwenya (Zulu), Honeybush tea (English), heuningbos (Afrikaans)	Leaves	infusions are drunk as an expectorant in people with TB.	Watt and Breyer-Brandwijk (1962)
<i>Dahlia pinnata</i> Cav.	Asteraceae	Garden dahlia (English)	Flowers	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Datura metel</i> L.	Solanaceae	Thorn apple, angel's trumpet (English)	Root	Dried roots are smoked to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Dicoma capensis</i> Less.	Asteraceae	Karmadik, baarbos, sandsalie (Afrikaans)	Leaves	Decoctions are drunk to treat TB.	Nortjie and Van Wyk (2015)
<i>Dichrostachys cinerea</i> (L.) Wight & Arn.	Fabaceae	Kalahari Christmas tree, sickle bush, bell mimosa, Chinese lantern tree (English)	Leaves and roots	Leaves and roots are burned and the smoke inhaled to treat TB and bacterial pneumonia.	Watt and Breyer-Brandwijk, 1962; Von Koenen, 2001;
<i>Diplorhynchus condylocarpon</i> (Müll. Arg.) Pichon	Apocynaceae	Wild rubber, horn-pod tree (English), horingpeulbos, melkbos (Afrikaans), muthowa (Venda)	Not specified	Used to treat TB. Preparation and application method not specified.	Watt and Breyer-Brandwijk (1962)
<i>Dodonaea viscosa</i> (L.) Jacq.	Sapindaceae	Sand olive (English), sandolien, ysterbos (Afrikaans), mutata-vhana (Venda)	Leaves, twigs	A decoction is drunk to treat TB and diphtheria. Also useful for the treatment of bacterial pneumonia.	al. Watt and Breyer-Brandwijk, 1962; McGaw et al., 2008; Hulley and Van Wyk, 2017
<i>Drosera capensis</i> L.	Droseraceae	Cape sundew (English), sondouw (Afrikaans)	Leaves	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Ekebergia capensis</i> Sparm.	Meliaceae	Cape ash, dogplum (English), essenhout (Afrikaans), mmidibidi (Sotho)	Leaves bark, roots	Used to treat TB. Preparation and application not specified.	Hulley and vanWyk, 2017
<i>Elytropappus rhinocerotis</i> (L.f.) Less.	Asteraceae	Rhinoceros bush (English)	Unspecified	Used to treat TB. Preparation and application methods are not specified.	Hulley and vanWyk, 2017
<i>Empleurum unicusulare</i> (L.f.) Skeels	Rutaceae	Bergboegoe (Afrikaans)	Unspecified	Used to treat bacterial pneumonia. Preparation and application methods are not specified.	Hulley and vanWyk, 2017
<i>Erigeron canadensis</i> L.	Asteraceae	Horseweed, coltstail, marestail, butterweed (English)	Leaf	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Eriocephalus africanus</i> L.	Asteraceae	Kapokbos, skaapkaroo (Afrikaans)	Not specified	Infusions are used to treat TB.	Hulley and vanWyk, 2017
<i>Erythrina humeana</i> Spreng.	Fabaceae	Umsinsana (Zulu)	Not specified	Used to treat TB. Preparation and application not specified.	Corrigan et al. (2011)
<i>Eucalyptus globulus</i> Labill.	Myrtaceae	Southern blue gum, Tasmanian blue gum (English)	Leaves	The leaves are boiled and the vapour is inhaled to treat TB and diphtheria.	Van Wyk, 2008; Watt and Breyer-Brandwijk, 1962
<i>Eucela natalensis</i> A. DC.	Ebenaceae	Natal guarri, Natal ebony, large-leaved guarri (English), Natalghwarrie, berggwarrie, swartbasboom (Afrikaans), umTshekisini, umKhasa (Xhosa), iDungamuzi, iChitamuzi, umZimane, umTshikisane, inKunzane, inKunzi-emnyama, umHlalanyamazane, umAnyathi (Zulu)	Roots	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Euphorbia heterophylla</i> L.	Euphorbiaceae	Japanese poinsettia, desert poinsettia, painted spurge, milkweed (English)	Leaves and flowers	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Euphorbia nerifolia</i> L.	Euphorbiaceae	Milk hedge, milk bush, oleander spurge, oleander-leaved euphorbia (English), melkbos (Afrikaans)	Stem latex	Used to treat whooping cough. Preparation and application method not specified.	Watt and Breyer-Brandwijk (1962)
<i>Felicia filifolia</i> (Vent.) Burt Davy	Asteraceae	Steenbokbossie, vaderlandsrapuisbos (Afrikaans)	Not specified	Used for the treatment of TB. Preparation and application not specified.	Hulley and Van Wyk, 2017
<i>Ficus carica</i> L.	Moraceae	Common fig (English)	Leaves and roots	A decoction of the roots and leaves is drunk to treat diphtheria.	Watt and Breyer-Brandwijk, 1962; Hulley and Van Wyk, 2017
<i>Ficus sur</i> Forssk	Moraceae	Cape fig, broom cluster fig (English)	Root and bark	The Zulu drink a decoction of the root and bark to treat TB.	al. Watt and Breyer-Brandwijk, 1962; Pallant and Steenkamp, 2008; Madikizela et al., 2013
<i>Ficus sycamorus</i> L.	Moraceae	Sycamore fig, common cluster fig, mulberry fig (English), trosvy, geelrierviery, geelstamvy, gewone trosvy, wildevyboom, sycamorusvy (Afrikaans), mogo, mogoboya, mohlole (Sotho), muhuhoya, muhuyu, muhuyu-lukuse, mutole, muvhuyu-vhutwa (Venda), mogoboya, umkhiwane	Fruit	A fruit infusion is drunk by the Venda to treat TB.	Pallant and Steenkamp (2008)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
		isikhukhuboya, umncongo, umkhiwane (Zulu)			
<i>Galenia africana</i> L.	Aizoaceae	Yellow bush (English), brakkraalbossie, geelbos, kraalbos, muisbos, muisgeelbossie, perdebos (Afrikaans), iqina (Xhosa)	Leaves	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Garcinia polyantha</i> Oliv.	Clusiaceae	Unknown	Bark	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Ginkgo biloba</i> L.	Ginkgoaceae	Ginkgo	Leaves	Decoctions and infusions are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Glycyrrhiza glabra glabra</i> L.	Fabaceae	Liquorice, licorice (English)	Rhizome	Root infusions are used to treat TB.	Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 2009
<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)	Leaves	Used to treat TB. Preparation and application method not specified.	Watt and Breyer-Brandwijk, 1962; Van Wyk et al., 2009;
<i>Gunnera perperna</i> L.	Gunneraceae	Wild rhubarb, river pumpkin (English), wilde ramenas, ravierpampoen (Afrikaans), qobo (Sotho), rambola-vhadzimu (Venda), iphuzi, ighobo (Xhosa), ugohe (Zulu)	Roots	Used to treat TB. Preparation and application method not specified.	McGaw et al. (2008)
<i>Gymnosporia buxifolia</i> (L.) Szyszyl.	Celestraceae	lemoendingoring, wondedoring, pendoringbos (Afrikaans)	Not specified	Used to treat TB. Preparation and application not specified.	Hulley and Van Wyk, 2017
<i>Helianthus tuberosus</i> L.	Asteraceae	Jerusalem artichoke (English)	Root/tuber	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Helichrysum crispum</i> (L.) D.Don.	Asteraceae	Hottentot's Bedding (English), Hotnotskooigoed, Hottentotskooigoed, Hottentotskruie, Kooigoed (Afrikaans)	Leaves, whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Helichrysum imbricatum</i> (L.) Less.	Asteraceae	Gold-and-silver (English)	Not specified	Used as a remedy for whooping cough. Preparation and application not specified.	Watt and Breyer-Brandwijk, 1962; McGaw et al., 2008;
<i>Helichrysum krausii</i> Sch. Bip.	Asteraceae	Straw everlasting (English), sewejaartjie (Afrikaans), isipheshane, isiqoqo (Zulu)	Flowers and seeds	Dried flowers and seeds are smoked to treat TB.	Watt and Breyer-Brandwijk, 1962; McGaw et al., 2008;
<i>Helichrysum melanacme</i> DC.	Asteraceae	Hotnotskooigoed (Afrikaans)	Leaves, whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Helichrysum nudifolium</i> (L.) Less.	Asteraceae	Everlastings (English), hottentotsteebossie, kooigoed (Afrikaans), isicwe, indlebe zebhokwe, undleni (Xhosa), icholocholo, imphepho (Zulu)	Leaves, whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Helichrysum odoratissimum</i> (L.) Sweet	Asteraceae	Everlantings (English), kooigoed (Afrikaans) imphepho (Zulu)	Leaves, whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Helichrysum vestitum</i> (L.) Willd.	Asteraceae	Cape snow (English)	Not specified	Used to treat diphtheria. Preparation. Application not specified.	; Watt and Breyer-Brandwijk, 1962; McGaw et al., 2008
<i>Helipterum eximium</i> (L.) DC.	Asteraceae	Unknown	Not specified	Used to treat diphtheria. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Helipterum speciosissimum</i> (L.) DC.	Asteraceae	Unknown	Not specified	Used to treat diphtheria. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Helipterum variegatum</i> DC.	Asteraceae	Unknown	Not specified	Used to treat diphtheria. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Hermannia sabvifolia</i> L. f.	Malvaceae	Katjiedrielaar (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application not specified.	Hulley and Van Wyk, 2017
<i>Hoodia gordonii</i> (Masson) Sweet ex Decne.	Apocynaceae	Hoodia, ghaap, kakimas (Afrikaans)	Fleshy stems	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Hoodia pilifera</i> subsp. <i>annulata</i> (N.E. Br.) Bruyns	Apocynaceae	Unknown	Fleshy stems	Used to treat TB. Preparation and application method not specified.	Watt and Breyer-Brandwijk (1962)
<i>Hypericum perforatum</i> L.	Hypericaceae	St John's wort (English)	Roots, leaves and flowers	Decoctions and infusions are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Indigofera tinctoria</i> L.	Fabaceae	True indigo (English)	Juice	consumed to treat whooping cough.	Watt and Breyer-Brandwijk, 1962; Madikizela et al., 2013;
<i>Jatropha zeyheri</i> Sond.	Euphorbiaceae	Verfbol (Afrikaans), sefapabadia (Sotho), ugodide (Zulu)	Unspecified	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Lactuca sativa</i> L.	Asteraceae	Lettuce (English)	Whole plant	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Lannea edulis</i> (Sond.) Engl.	Anacardiaceae	Wild grape (English), wildedruif (Afrikaans), muporotso (Venda)	Root	Decoctions and infusions of the root bark is drunk to treat whooping cough.	Van Wyk et al. (2009)
<i>Leonotis leonoris</i> (L.) R. Br.	Lamiaceae		Leaves and stems	A tincture is drunk to treat TB and whooping cough.	

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
		Wild dagga (English), wildedagga, duiwelstabak (Afrikaans), mvovo (Xhosa), uyshwala-bezinyoni (Zulu)			Watt and Breyer-Brandwijk, 1962; Pallant and Steenkamp, 2008; Dzoyem et al. (2016)
<i>Leucaena leucocephala</i> (Lam.) de Wit	Fabaceae	Wild tamarind, wild lead tree (English)	Bark leaves, seeds	Used to treat TB. Preparation and application not specified.	
<i>Lessertia frutescens</i> (L.) Goldblatt & J.C. Manning	Fabaceae	Keurtjie, beeskeurtiebos, kankerbos (Afrikaans)	Not specified	An infusion is used to treat TB.	Hulley and Van Wyk, 2017
<i>Leyssera gnaphalioides</i> L.	Asteraceae	Skilpadteebossie, hongertee, duinetee, teringteebos Afrikaans)	Leaf	An infusion is drunk to treat TB.	Watt and Breyer-Brandwijk (1962); McGaw et al. (2008)
<i>Malva neglecta</i> Wallr.	Malvaceae	Low mallow (English)	Roots	Decoctions and infusions are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Malva paviflora</i> L.	Malvaceae	Marshmallow, cheeseweed mallow, little mallow, small flower mallow (English)	Roots	Decoctions and infusions are drunk to treat TB.	Von Koenen (2001)
<i>Matricaria chamomilla</i> L.	Asteraceae	German chamomile, wild chamomile, scented mayweed (English)	Not specified	Used to treat diphtheria and TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Maytenus heterophylla</i> (Eckl. & Zeyh.) N. Robson	Celestraceae	Gewone pendoring (Afrikaans)	Leaves	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Melilotus alba</i> Ledeb.	Fabaceae	White sweet clover (English)	Whole plant	Decoctions and infusions are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Melolobium candicans</i> (E.Mey.) Eckl. & Zeyh.	Fabaceae	Wild dagga (English), wildedagga (Afrikaans)	Leaves and stems	A decoction of the leaves and stems is drunk to treat TB.	De Beer and Van Wyk (2011)
<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	Used to treat TB, whooping cough and diphtheria. Preparation and application method not specified.	Watt and Breyer-Brandwijk (1962)
<i>Mesembryanthemum tortuosum</i> L.	Aizoaceae	Koegoed, kanna (Afrikaans)	Not specified	Used to treat TB. Preparation and application not specified.	Hulley and Van Wyk 2017
<i>Montinia caryophyllacea</i> Thunb.	Montiniaceae	Pepper-bush, wild clove bush (English), bergklapper, peperbos (Afrikaans)	Leaves	The dried pulverised leaves are used as a snuff to treat TB.	Von Koenen (2001)
<i>Mundulea sericea</i> (Willd.) A.Chev.	Fabaceae	Cork bush, silver bush, (English), kurkbos, olifantshout, visboontjie, visgif, mangaanbos (Afrikaans), mosetla-thlou (Sotho), mukunda-ndou (Venda), umsindandlovu (Zulu)	Bark and roots	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Nasturtium officinale</i> R. Br.	Brassicaceae	Watercress (English)	Whole plant	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Nicotiana glauca</i> Graham	Solanaceae	Mustard tree, tree tobacco (English), tabakboom, wildetabak, volstruisgifboom (Afrikaans), mohlafotha (Sotho)	Leaves	Powdered leaves are used as a snuff to treat TB.	Von Koenen (2001)
<i>Nidorella anomala</i> Steetz	Asteraceae	Unknown	Whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Nidorella auriculata</i> DC.	Asteraceae	Unknown	Whole plant	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Olea europea</i> L.	Oleaceae	Wild olive (English) olienhout (Afrikaans), mohlware (Sotho), umnquma (Zulu, Xhosa), mutlhwari (Venda)	Leaves	A leaf decoction is used as a gargle to treat diphtheria.	Watt and Breyer-Brandwijk (1962); Von Koenen (2001);
<i>Oncosiphon suffruticosum</i> (L.) Källersjö	Asteraceae	Stinkkruid, wirmkruid (Afrikaans)	Whole plant	An infusion is drunk to treat bacterial pneumonia.	Van Wyk et al. (2009)
<i>Opuntia ficus-indica</i> (L.) Mill.	Cactaceae	Indian pear (English), turksvy (Afrikaans)	Leaves	Leaf infusions are drunk to treat whooping cough.	Von Koenen (2001)
<i>Opuntia vulgaris</i> Mill.	Cactaceae	Prickly pear (English)	Leaves	A leaf infusion is consumed to treat whooping cough.	Watt and Breyer-Brandwijk (1962)
<i>Pegolettia baccharidifolia</i> Less.	Asteraceae	Ghwarrieson, heuningdou (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application not specified.	Hulley and Van Wyk 2017
<i>Pelargonium graveolens</i> L'Hér.	Geraniaceae	Rose geranium (English), wildemalva (Afrikaans)	Leaves	Leaves are steamed and vapours are inhaled to treat TB.	Van Wyk et al. (2009)
<i>Pelargonium myrrhifolium</i> (L.) L'Hér	Geraniaceae	Unknown	Tuber	Used to treat TB. Preparation and application not specified.	Van Wyk (2008)
<i>Pelargonium ramosissimum</i> Willd.	Geraniaceae	Dassieboegoe (Afrikaans)	Tuber	Used to treat TB. Preparation and application not specified.	Van Wyk (2008)
<i>Pelargonium rentiforme</i> Curtis	Geraniaceae	Kidney-leaved pelargonium (English), rooirabas (Afrikaans), iyeza lesikhali, ikubalo, umsongelo (Xhosa)	Tuber	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Pelargonium sidoides</i> DC.	Geraniaceae	Black pelargonium (English), kalwerbossie, rabassam (Afrikaans), ikubalo, iyeza lesikhali (Xhosa), khoara-e-nyenyane (Southern Sotho)	Tuber	Used to treat TB and pneumonia. Preparation and application not specified.	McGaw et al. (2008); Hulley and Van Wyk 2017
	Geraniaceae	Kaneelbol, rooirabas (Afrikaans)	Tuber		Philander (2011)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Pelargonium triste</i> (L.) L'Hér				Used to treat TB and pneumonia. Preparation and application not specified.	
<i>Pentania prunelloides</i> (Klotzsch) Walp.	Rubiaceae	Wild verbena (English), sooibrandbossie (Afrikaans), setimamololo (Sotho), icimamlilo (Zulu)	Roots	The Xhosa drink a root infusion to treat TB.	Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009); Philander (2011); Madikizela et al. (2013)
<i>Pentzia incana</i> (Thunb.) Kuntze	Asteraceae	Skaapkarooobos, ankerkaroo, kleinskaapkarooobos (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application not specified.	Hulley and Van Wyk 2017
<i>Pharanceum lineare</i> L. f.	Molluginaceae	Droëdaskruie (Afrikaans)	Not specified	An infusion is consumed to treat TB.	Watt and Breyer-Brandwijk (1962); Van Wyk (2008);
<i>Polycarpaea corymbosa</i> (L.) Lam.	Caryophyllaceae	Old man's cap (English)	Not specified	Used to treat TB. Treatment and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Polygala fruticosa</i> P.J. Bergius	Polygonaceae	Butterfly bush, heart-leaf polygala (English), ertjieblom (Afrikaans), ulopesi, ulapesi, umabalabala (Xhosa), ithethe (Zulu)	Roots	Root decoctions are used by the Zulu to treat TB.	Watt and Breyer-Brandwijk (1962); Madikizela et al. (2013);
<i>Polygala myrtifolia</i> L.	Polygonaceae	September bush (English), septemberbossie, augustusbossie, blouertjie, langelede (Afrikaans), ulopesi, ulapesi, umabalabala (Xhosa), uchwasha (Zulu)	Aerial parts	Used to treat TB. Treatment and application not specified.	McGaw et al. (2008)
<i>Polygonum aviculare</i> L.	Polygonaceae	Knotgrass, bird weed, pig weed (English)	Not specified	Used to treat TB. Treatment and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Polysiphonia virgata</i> (C. Agardh.) Sprengel	Rhodomeleaceae	Red algae (English)	Not specified	Used to treat TB. Treatment and application not specified.	McGaw et al. (2008)
<i>Protea nitida</i> Mill.	Protaceae	Waboom (Afrikaans)	Not specified	Used to treat TB and pneumonia. Treatment and application not specified.	Hulley and Van Wyk 2017
<i>Prunus africana</i> (Hook. f.) Kalkman	Rosaceae	Red stinkwood, African almond (English), rooistinkhout, Afrika-amandel, Wildekersieboom (Afrikaans), inyazangomaelimnyama, inkokhokho, ngubozinyeweni, umdumezulu (Zulu); uMkakase, inyazangoma, itywina-elikhul, Umkhakhase (Xhosa), mogohloro (Sotho), mulala-maanga (Venda)	Bark	Used to treat TB. Treatment and application not specified.	McGaw et al. (2008)
<i>Prunus cerasus</i> L.	Rosaceae	Sour cherry, tart cherry, dwarf cherry (English)	Leaf	Used to treat TB. Treatment and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Prunus persica</i> (L.) Batsch	Rosaceae	Peach tree (English)	Leaves	Used to treat whopping cough. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Pteronia camphorata</i> (L.) L.	Asteraceae	Wakkerbos, koorsbos (Afrikaans)	Leaves and twigs	Leaf and twig infusions are drunk to treat TB.	Nortjie and Van Wyk (2015)
<i>Quercus</i> spp.	Fagaceae	Oak (English)	Bark	The bark is boiled and the fumes inhaled to treat diphtheria	Watt and Breyer-Brandwijk (1962)
<i>Rapanea melanophloeos</i> (L.) Mez	Primulaceae	Cape beech (English); boekenhout, beukehout (Afrikaans), isiCalabi, umaPhipha, iKhubalwane, isiQalaba sehlati (Zulu), isiQwane sehlati (Xhosa)	Leaves and twigs	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Rhynchosia caribaea</i> (Jacq.) DC.	Fabaceae	Unknown	Roots	A root extract is consumed to treat bacterial pneumonia.	Von Koenen (2001)
<i>Rhamnus prinoides</i> L'Hér	Rhamnaceae	Mofifi (Southern Sotho)	Branches	Used to treat bacterial pneumonia. Preparation and application not specified.	Kose et al. (2015)
<i>Ricinus communis</i> L.	Euphorbiaceae	Castor bean, castor oil plant (English)	Leaves	Used to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962)
<i>Rumex crispus</i> L.	Polygonaceae	Yellow dock (English)	Whole plant	Used to treat TB. Preparation and application methods are not specified.	McGaw et al. (2008)
<i>Salvia africana-lutea</i> L.	Lamiaceae	Bloebloomsalie (Afrikaans)	Not specified	A tincture is drunk to treat whooping cough.	Watt and Breyer-Brandwijk (1962)
<i>Salvia chamdaegnea</i> Berg.	Lamiaceae	Bloublomsalie (Afrikaans)	Leaves and flowers	Used to treat whooping cough. Preparation and application method not specified.	Watt and Breyer-Brandwijk (1962)
<i>Salvia microphylla</i> Kunth	Lamiaceae	Rooisalie, rooiblomsalie (Afrikaans)	Not specified	Infusions are drunk to treat bacterial pneumonia.	Hulley and Van Wyk 2017
<i>Schinus molle</i> L.	Anacardiaceae	Peruvian pepper (English), peperboom (Afrikaans)	Not specified	Used to treat bacterial pneumonia. Preparation and application not specified.	Hulley and Van Wyk 2017
<i>Searsia lancea</i> (L.f.) F.A. Barkley	Anacardiaceae	Makkaree, kareebloom (Afrikaans)	Not specified	Infusions are drunk to treat bacterial pneumonia.	Hulley and Van Wyk 2017
<i>Securidaca longpedunculata</i> Fresen.	Polygalaceae	Violet tree (English), krinkhout, rooipeultjie, seepbasboom (Afrikaans), mpesu (Venda), iphuphuma (Zulu)	Roots	A decoction is consumed by the Venda to treat TB.	Pallant and Steenkamp (2008)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Senecio serratuloides</i> DC.	Asteraceae	Two-day cure (English), ichazampukane, insukumbili, umaphozisa umkhuthelo (Zulu)	Aerial parts	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Solanum nigrum</i> L.	Solanaceae	Black nightshade (English)	Leaves	Fresh leaves are consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Solanum retrofractum</i> Vahl	Solanaceae	Nastergal, nasgal (Afrikaans)	Not specified	Used to treat TB. Preparation and application not specified.	Hulley and Van Wyk 2017
<i>Spergula arvensis</i> L.	Caryophyllaceae	Corn spurry (English)	Whole plant	An essential oil used to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Strophanthus grandiflorus</i> (N.E.Br.) Gilg	Apocynaceae	Unknown	Whole plant	An alcohol extract is consumed to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Sutherlandia frutescens</i> (L.) R.Br.	Fabaceae	Cancer bush (English), kankerbos (Afrikaans), 'musa-pelo, motlepele (Sotho), insiswa, unwele (Xhosa, Zulu)	Leaves	A decoction is used to treat TB.	Nortjie and Van Wyk (2015)
<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 by the Zulu to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962); Hutchings et al., (1996); Corrigan et al. (2011);
<i>Syzygium gerrardii</i> (Harv. ex Hook.f.) Burtt Davy	Myrtaceae	Unknown	Leaves	Used by the Zulu to treat TB. Preparation and application not specified.	Watt and Breyer-Brandwijk (1962); McGaw et al. (2008)
<i>Tabernaemontana elegans</i> Stapf	Apocynaceae	Toad tree (English), laeveldse paddaboom (Afrikaans), umKahlwana, umKhadu (Zulu)	Leaves, roots	Used to treat TB. Preparation and application not specified.	Pallant and Steenkamp (2008); Dzoyem et al. (2016)
<i>Taraxacum officinale</i> (L.) Weber ex F.H. Wigg	Asteraceae	Dandelion (English)	Flowers, leaves, roots, whole plant	Used to treat TB. Extracts were consumed orally to treat tuberculosis.	Sharifi-Rad et al. (2018); Smith (1895); Watt and Breyer-Brandwijk (1962)
<i>Terminalia phanerophlebia</i> Engl. & Diels	Combretaceae	Lebombo cluster-leaf (English), lebombotrosblaar (Afrikaans), amaNgwe-amnyama, amaNgwe-omphofu (Zulu)	Roots	Used to treat TB. Preparation and application not specified.	Madikizela et al. (2013)
<i>Terminalia sericea</i> Burch. ex DC.	Combretaceae	Silver cluster leaf (English), vaalboom (Afrikaans), mususu (Venda)	Roots and leaves	Decoctions and infusions are consumed to treat bacterial pneumonia.	McGaw et al. (2008); Van Wyk et al. (2009); York et al. (2011);
<i>Tetradenia riparia</i> (Hochst.) Codd	Lamiaceae	Misty plume bush, ginger bush (English), gemerbos, watersalie (Afrikaans), iboza, ibozane (Zulu)	Leaves, roots	Used to treat TB. Preparation and application not specified.	McGaw et al. (2008)
<i>Thesium hystrix</i> A.W. Hill	Santalaceae	Kleinswartstorm (Afrikaans)	Root	Large volumes of a root decoction are drunk to treat TB.	Smith (1895) Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009)
<i>Thymus serpyllum</i> L.	Lamiaceae	Breckland thyme, wild thyme, creeping thyme, elfin thyme (English)	Leaves and flowers	Used to treat whooping cough. Preparation and application methods are not specified.	Smith (1895); Watt and Breyer-Brandwijk (1962);
<i>Thymus vulgaris</i> L.	Lamiaceae	German thyme, common thyme (English)	Leaves	Leaf essential oil is used to treat whooping cough. Application methods is not specified.	Smith (1895); Watt and Breyer-Brandwijk (1962); McGaw et al. (2008);
<i>Trachyandra laxa</i> (N.E. Br.) Oberm.	Xanthorrhoeaceae	Unknown	Roots	Used to treat whooping cough. Preparation and application are not specified.	Von Koenen (2001)
<i>Trema orientalis</i> (L.) Blume	Cannabaceae	Pigeon wood (English), hophout (Afrikaans)	Leaves and fruit	Infusions of the leaves and fruit are drunk to treat bacterial pneumonia.	Von Koenen (2001)
<i>Trichilia emetica</i> Vahl	Meliaceae	Ixolo, umathunzini, umkhula (Zulu)	Leaves	Decoctions are used to treat pneumonia and whooping cough.	York et al. (2011)
<i>Trifolium pratense</i> L.	Fabaceae	Red clover (English)	Flowers	Infusions are drunk to treat TB and whooping cough.	Smith (1895); Watt and Breyer-Brandwijk (1962);
<i>Tulbaghia alliacea</i> L.f.	Amaryllidaceae	Wild garlic, woodland garlic (English), wildeknoflok (Afrikaans), molela (Southern Sotho), ishaladilezinyoka, umwelela (Zulu)	Bulbs	Used to treat TB. Preparation and application not specified.	Smith (1895); Watt and Breyer-Brandwijk (1962); Van Wyk (2008)
<i>Tulbaghia maritima</i> Vosa	Amaryllidaceae	Unknown	Bulbs	Used to treat TB. Preparation and application not specified.	Smith (1895); Watt and Breyer-Brandwijk (1962)
<i>Tulbaghia violacea</i> Harv.	Amaryllidaceae	Wild garlic (English), wilde knoffel (Afrikaans), ishaqa (Zulu)	Bulbs	Decoctions are drunk to treat TB.	Philander (2011); Smith (1895); Watt and Breyer-Brandwijk (1962); Van Wyk et al. (2009)
<i>Urtica urens</i> L.	Urticaceae	Annual nettle, burning nettle, sting nettle bush, dwarf stinging nettle (English), brandnekel (Afrikaans)	Bark	Bark infusions are drunk to treat TB, pneumonia and whooping cough.	Hulley and Van Wyk 2017
<i>Viscum capense</i> L. f.	Santalaceae	Cape mistletoe (English), lidjiesstee, voelent (Afrikaans)	Whole plant	Used to treat TB. Preparation and application not specified.	Philander (2011)
<i>Vitis vinifera</i> L.	Vitaceae	Common grape (English)	Fruit	A syrup prepared by boiling the fruit juice is used in the Transvaal to treat diphtheria.	Watt and Breyer-Brandwijk (1962)
	Canellaceae		Bark		McGaw et al. (2008)

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Table 1 (continued)

Plant species	Family	Common name(s)	Plant part used	Used for	References
<i>Warburgia salutaris</i> (G. Bertol.) Chiov.		Pepper-bark tree (English), peperbasboom (Afrikaans), mulanga, manaka (Venda), isibhaha (Zulu)		Used to treat TB. Preparation and application not specified.	
<i>Withania somnifera</i> (L.) Dunal	Solanaceae	Indian ginseng, poison gooseberry, winter cherry (English), bitterappelliefie, koorshout (Afrikaans), ubuvuma (Xhosa), ubuvimbha (Zulu)	Root	Alcohol root extracts are drunk to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Zanthoxylum capensis</i> (Thunb.) Harv.	Rutaceae	Knobwood (English)	Bark	The Zulu use a root bark decoction to treat TB.	Watt and Breyer-Brandwijk (1962)
<i>Ziziphus mucronata</i> Willd.	Rhamnaceae	Buffalo thorn (English), blinkblaar-wag-'n-bietjie (Afrikaans), umphafa, umlahlankosi, isilahla (Zulu), umphafa (Xhosa), mutshetshe (Venda), mokgaló, moonaona (Sotho)	Leaves, bark and roots	A decoction of the leaves, roots and bark is drunk to treat TB.	McGaw et al. (2008); Suliman (2010)

(9 species), Apocynaceae (8 species), Xanthorrhoeaceae (6 species), Aizoaceae, Geraniaceae, Euphorbiaceae, Polygonaceae and Solanaceae were also well represented with 5 species each. Four members of Combretaceae, and Malvaceae were also identified, as well as three members each of Amaryllidaceae, Celastraceae, Moraceae, Myrtaceae and Rosaceae. Two or less species of forty-one other families were also identified as being traditionally used to treat bacterial respiratory diseases.

Several trends regarding the plant part used traditionally were also apparent. The use of leaves was particularly common for the treatment of bacterial respiratory infections, with the use of leaves recorded for 68 southern African plant species (Fig. 2). Interestingly, leaves are also the most frequently used plant part for the treatment of many other pathogenic diseases (Afolayan et al., 2014; Asong et al., 2019; Cock et al., 2018; Cock et al., 2019; De Beer and Van Wyk, 2011; Hulley and Van Wyk, 2017; Philander, 2011). The roots of 58 plant species were also used to treat several bacterial respiratory diseases, whilst bark (15 species) and stems and twigs (10 species) were also relatively widely used. In contrast flowers, fruit and seeds were only rarely used to treat bacterial respiratory disease. In contrast, the whole plant of some species was used therapeutically in southern African traditional medicine. Complete ethnobotanical records were not available for 36 plant species and we were therefore not able to determine the part used traditionally to treat bacterial respiratory diseases.

4.2. Scientific studies into the growth inhibitory activity of South African plants against bacterial respiratory pathogens

Whilst the ethnobotanical usage of many southern African plants to treat bacterial respiratory infections are yet to be scientifically evaluated, 189 southern African plant species have been screened for the ability to inhibit the growth of bacterial respiratory infections (Table 2). Interestingly, only 42 species (indicated in bold within Table 2) (of the 186 species that are used in traditional medicine to treat bacterial respiratory diseases have been tested against one or more bacterial respiratory pathogens. This equates to approximately only 23% of the species traditionally used to treat bacterial respiratory diseases. The remaining 77% are yet to be evaluated against any of the respiratory pathogens. Furthermore, the majority of the plants species that have been screened have only been tested against a single bacterial respiratory pathogen and further studies are required to test them against other bacterial species and strains.

The vast majority of plants that have been tested against pneumonia-causing bacterial pathogens have been screened against *K. pneumoniae* and *P. aeruginosa*. Indeed, 139 plant species were tested against one or both of these pathogens. Eighty-nine plant species were also screened against *M. tuberculosis*, or other *Mycobacterium* spp. (*M. arum* and *M. smegmatis*) as TB model organisms. Furthermore, many of these species were screened against both the TB and pneumonia-causing

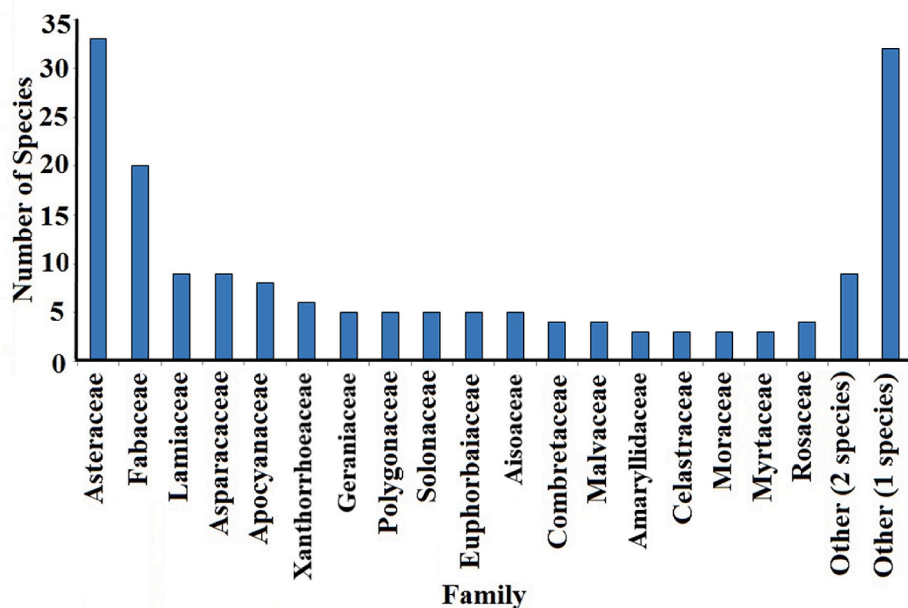


Fig. 1. The number of southern African plant species per family related to southern African medicinal plants for the treatment of bacterial respiratory infections. Others refers to the number of other genera (not named individually) that are represented by the indicated number of species.

Table 2
Scientific evaluations of the inhibitory activity of South African plants against bacterial respiratory pathogens.

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
Acacia nilotica (L.) Delile	Fabaceae	Scented-pod acacia (English), lekkerruikpeul (Afrikaans), mogohlo (Sotho), umNqawe (Zulu)	Leaf, bark and root extracts	<i>K. pneumoniae</i>	MIC = 780 µg/mL	Eldeen et al. (2005)
<i>Acacia sieberiana</i> DC.	Fabaceae	Paperbark thorn (English), papierbasdoring (Afrikaans), mphoka (Northern Sotho), musaunga (Venda), umKhamba (Zulu)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 800–2000 µg/mL	Suliman (2010); Eldeen et al. (2005)
Acacia xanthophloea Benth.	Fabaceae	Fever tree (English)	Bark extracts Leaf, bark and root extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	500 µg/mL 800 µg/mL	Lall and Meyer (1999) Eldeen et al. (2005)
<i>Acanthospermum glabratum</i> (DC.) Wild	Asteraceae	Unknown	Whole plant extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 670 µg/mL MIC = 3300 µg/mL	York et al. (2011)
<i>Agathosma betulina</i> (P. J.Bergius) Pillans	Rutaceae	Buchu (English), boegoe, rondebelaarboegoe (Afrikaans)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 1876 µg/mL	Cock and Van Vuuren (2015a)
<i>Aloe barberae</i> Dyer	Xanthorrhoeaceae	Tree aloe (English)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 780 µg/mL	Ndhala et al. (2009)
<i>Aloe marlothii</i> A.Berger	Xanthorrhoeaceae	Mountain aloe, flat-flowered aloe (English), bergalwyn (Afrikaans), inhlabi, umhlaba (Zulu)	Leaf extracts	<i>M. smegmatis</i> (model for tuberculosis) <i>K. pneumoniae</i>	MIC = 3330 µg/mL MIC = 2670 µg/mL	York et al. (2011)
<i>Abrus precatorius</i> subsp. <i>africanus</i> Verdc.	Fabaceae	Bead vine, coral bead plant, coral bean, crabs eye, licorice vine, red bead vine (English), umkhokha (Zulu)	Leaf and seed extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 780 µg/mL (leaf) MIC = 1560 µg/mL (seed)	Madikizela et al. (2013)
<i>Androstachys johnsonii</i> Prain	Picrodendraceae	Ironwood (English), musimbiri (Venda)	Root bark and leaf extracts	<i>K. pneumoniae</i>	MIC = 3000 µg/mL	Samie et al. (2005)
<i>Artemisia afra</i> Jacq. ex Willd.	Asteraceae	African wormwood (English), als, alsem, wildeals (Afrikaans), lengana (Sotho, Tswana), umhlonnyane (Xhosa, Zulu)	Leaf extracts	<i>P. aeruginosa</i> <i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	Inactive MIC = 1563 µg/mL MIC = 1560 µg/mL MIC = 1560 µg/mL	Mativandlela et al. (2008) Buwa and Afolayan (2009)
Asparagus africanus Lam.	Asparagaceae	Bush asparagus (English)	Leaf extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 390 µg/mL MIC = 1560 µg/mL	Madikizela et al. (2013)
Asparagus falcatus L.	Asparagaceae	Unknown	Leaf extracts	<i>H. influenzae</i> <i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC > 1000 µg/mL MIC = 390 µg/mL MIC = 3130 µg/mL	Pallant and Steenkamp (2008) Madikizela et al. (2013)
<i>Ballota africana</i> (L.) Benth.	Lamiaceae	kattekruide, kattekruie (Afrikaans)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 379 µg/mL	Cock and Van Vuuren (2015a)
<i>Bauhinia petersiana</i> Bolle	Fabaceae	Large white bauhinia (English), mubondo, mumwando, mun'ando or mupondo (Shona)	Leaf and root extracts	<i>M. tuberculosis</i>	MIC = 312 µg/mL	Dzoyem et al. (2016)
<i>Berberia discolor</i> (Klotzsch) Hemsl.	Rhamnaceae	Bird plum, brown ivory (English), voëlpruim (Afrikaans), mogogomo (Sepedi), nmumu, ubalatsheni-omkhulu, umadlozane, umhlungulo, uvuku (Zulu)	Bark acetone extract	<i>M. tuberculosis</i>	MIC = 10.5–12.5 µg/mL	Green et al. (2010)
<i>Brachylaena discolor</i> DC	Asteraceae	Coast silver oak (English), kusvaalbos (Afrikaans), phahla (Zulu), mphahla (Sotho), umPhahla (Xhosa)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 900 µg/mL MIC = 4000 µg/mL	York et al. (2011)
<i>Bridelia cathartica</i> Bertol.	Phyllanthaceae	Blue sweetberry, knobby bridelia (English)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 670 µg/mL MIC = 4000 µg/mL	York et al. (2011)
<i>Bridelia micrantha</i> (Hochst.) Baill.	Phyllanthaceae	Munzere (Venda)	Root, bark and seed extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 6000 µg/mL MIC = 6000 µg/mL	Samie et al. (2005)
<i>Brunsvigia grandiflora</i> Lindl.	Amaryllidaceae	Giant candelabra (English), reusekandelaarblom (Afrikaans)	Bark acetone extract Bulb extracts	<i>M. tuberculosis</i> <i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 25 µg/mL MIC = 3130 µg/mL	Green et al. (2010) Madikizela et al. (2013)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Calpurnia aurea</i> (Aiton) Benth.	Fabaceae	Calpurnia, wild laburnum, Natal laburnum, Cape laburnum (English), geelkeurboom, geelkeur, Natalse geelkeur (Afrikaans), inDloli, umSithshana (Xhosa), umKhiphampethu, inSiphane-enkulu, umHlahlambedu, umLalandlovana (Zulu)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 3130 µg/mL MIC = 80 µg/mL	Elisha et al. (2017)
<i>Carpobrotus edulis</i> (L.) N.E.Br.	Aizoaceae	Sour fig, Cape fig, Hottentot's fig (English), vyerank, ghaukum, ghoenavy, hotnotsvye, Kaapvy, perdevy, rankvy (Afrikaans), ikhambi-lamabulawo, umgongozi (Zulu)	Leaf extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 3125 µg/mL MIC = 320–1040 µg/mL	Buwa and Afolayan (2009)
<i>Cassia fistula</i> L.	Fabaceae	Purging cassia, holden shower tree (English)	Flower extract	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	Inactive Up to 13 mm zones of inhibition in disc diffusion assay. MIC not determined.	Duraipandiyand Ignacimuthu (2007); Buwa and Afolayan (2009) Cock and Van Vuuren (2015a)
<i>Cassia petersiana</i> (Bolle) Lock	Fabaceae	Dwarf Cassia (English), apiespeul (Afrikaans), Munembenembe (venda), Uhwabile, Umnembenembe (Zulu)	Bark acetone extract	<i>M. tuberculosis</i>	MIC = 50 µg/mL	Green et al. (2010)
<i>Cassine papillosa</i> (Hochst.) Kuntze	Celastraceae	Unknown	Bark extracts	<i>M. tuberculosis</i>	MIC = 1000 µg/mL	Lall and Meyer (1999)
<i>Chaetachme aristata</i> Planch.	Ulmaceae	Thorny-Elm (English), basterwitpeer (Afrikaans)	Leaf extracts	<i>M. tuberculosis</i>	MIC = 39 µg/mL	Dzoyem et al. (2016)
<i>Chamaecrista mimosoides</i> (L.) Greene	Fabaceae	Fishbone dwarf cassia (English), boesmanstee (Afrikaans), imbubu, umbonisela (Zulu), umnyana, unobothungwana (Xhosa)	Leaf and root extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL (roots)	Suliman (2010)
<i>Cheilanthes viridis</i> (Forssk.) Sw	Pteridaceae	Ikhambi, lesilonda (Zulu)	Leaf and stem extracts	<i>P. aeruginosa</i>	MIC = 460 µg/mL (leaves)	Kelmanson et al. (2000)
<i>Chenopodium ambrosioides</i> L.	Chenopodiaceae	Wormsalt (English), sinkingbossie (Afrikaans)	Aerial parts extracts Leaf and root extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 500 µg/mL MIC = 1500 µg/mL (leaves)	Lall and Meyer (1999) Lall and Meyer (1999)
<i>Citrus limon</i> (L.) Osbeck	Rutaceae	Lemon (English)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 2670 µg/mL	York et al. (2011)
<i>Clausena anisata</i> (Willd.) Hook.f. ex Benth.	Rutaceae	Unknown	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1670 µg/mL MIC = 1670 µg/mL	York et al. (2011)
<i>Clematis brachiata</i> Thunb.	Ranunculaceae	Ihlonzo leziduli, inhlongo, umdloza, umfufuna (Zulu)	Leaf and stem extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 2000 µg/mL	York et al. (2011)
<i>Clematis oweniae</i> Harv.	Ranunculaceae	Bridal wreath, traveller's joy, old man's beard (English), klimop, lemoenbloeisels (Afrikaans), ihlonzo leziduli, Inhlabanhlanzi (Zulu), ityolo (Xhosa), morarana-oa-mafehlo (Southern Sotho)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Suliman (2010)
<i>Clerodendrum glabrum</i> E.Mey.	Lamiaceae	Tinderwood (English), tontelhout (Afrikaans), moswaapeba (Sotho), munukha-tshilongwe (Venda), umqwaqwanam (Xhosa), umqoqonga (Zulu)	Leaf, bark and root extracts Leaf extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 156 µg/mL MIC = 4000 µg/mL	Dzoyem et al. (2016) Suliman (2010)
<i>Combretum apiculatum</i> Sond.	Combretaceae	Red bush willow (English), rooiboswilg (Afrikaans), umbondwe (Zulu), mohwelere (Pedi), muvuvha (Venda)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1600 µg/mL	Eloff (1999)
<i>Combretum bracteosum</i> (Hochst.) Engl. & Diels	Combretaceae	Hiccup nut (English), hikklimop (Afrikaans), uQotha (Xhosa)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1600 µg/mL	Eloff (1999)
<i>Combretum caffrum</i> (Eckl. & Zeyh.) Kuntze	Combretaceae	Eastern Cape bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 6000 µg/mL	Eloff (1999)
<i>Combretum celastroides</i> Welw. ex M.A. Lawson	Combretaceae	Trailing bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 3000 µg/mL	Eloff (1999)
<i>Combretum collinum</i> Fresen.	Combretaceae	Weeping bushwillow, bicoloured bushwillow (English), vaiërende boswilg (Afrikaans)	Leaf extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 315 µg/mL MIC = 555–1600 µg/mL	Cock and Van Vuuren (2015b) Eloff (1999); Cock and Van Vuuren (2015b); Eloff (1999)
	Combretaceae	Forest climbing bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>		Eloff (1999)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Combretum edwardsii</i> Exell.					MIC = 3000 µg/mL	
<i>Combretum erythrophyllum</i> (Burch.) Sond.	Combretaceae	River bushwillow (English), riviervaderlandswilg, rooiblaar, rooiblad (Afrikaans), umbondwe, umdubuwelandze, umhlabavane (Zulu), umdubu (Xhosa), miavana, modubo (Southern Sotho), modibo (Northern Sotho), mugavhi, mugwiti, muvuvhu (Venda)	Leaf extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 430 µg/mL MIC = 500–3000 µg/mL	Eloff (1999); Cock and Van Vuuren (2015b)
<i>Combretum hereroense</i> Shinz	Combretaceae	Russet bushwillow, mouse-eared combretum (English), kierieklapper (Afrikaans), mokabi (Sotho), mugavhi (Venda), umhlabavane (Zulu)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1600 µg/mL	Eloff (1999)
<i>Combretum imberbe</i> Wawra	Combretaceae	Leadwood (English), hardekool (Afrikaans), motswiri (Pedi), ummono (Sotho), umbondwe omnyama (Zulu), muhiri (Venda)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 3000 µg/mL	Eloff (1999)
<i>Combretum kraussii</i> Hochst.	Combretaceae	Forest bushwillow (English), bosvaderlandswilg (Afrikaans), uhwabhu, umdubu-wehlathi (Zulu), ulandile (Xhosa), modlubu (Sotho), muvuvhu, muvuvhu-wannda, muvuvhu-wa-thavhani (Venda)	Leaf extracts Leaf, bark and root extracts	<i>P. aeruginosa</i> <i>K. pneumoniae</i>	MIC = 1600 µg/mL MIC = 3125 µg/mL	Eloff (1999) Eldeen et al. (2005)
<i>Combretum microphyllum</i> Klotzsch	Combretaceae	Flame creeper (English)	Leaf extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 205 µg/mL MIC = 1650 µg/mL	Cock and Van Vuuren (2015b) Eloff (1999); Cock and Van Vuuren (2015b)
<i>Combretum mkuzense</i> J. D.Carr & Retief	Combretaceae	Maputaland bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1600 µg/mL	Eloff (1999)
<i>Combretum moggii</i> Exell	Combretaceae	Rock bushwillow (English), muvuvhatavha (Venda)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 3000 µg/mL	Eloff (1999)
<i>Combretum molle</i> R. Br. ex G.Don	Combretaceae	Umbondo, umbondwe (Zulu)	Leaf extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 500 µg/mL MIC = 1330 µg/mL MIC = 550–670 µg/mL MIC = 800–1870 µg/mL	Lall and Meyer (1999) Eloff (1999); York et al. (2011); Cock and Van Vuuren (2015b)
<i>Combretum mossambicense</i> (Klotzsch) Engl.	Combretaceae	Knobbly creeper (English), knoppiesklimp (Afrikaans)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 800 µg/mL	Eloff (1999)
<i>Combretum nelsonii</i> Dummer	Combretaceae	Waterberg bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 3000 µg/mL	
<i>Combretum paniculatum</i> Vent.	Combretaceae	Burning bush, forest flame creeper (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1600 µg/mL	
<i>Combretum woodii</i> Dummer	Combretaceae	Large-leaved forest bushwillow (English), grootblaarvaderlandswilg (Afrikaans), iWaphu (Zulu)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 800 µg/mL	
<i>Combretum padoides</i> Engl. & Diels.	Combretaceae	Thicket bushwillow (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 800 µg/mL	
<i>Combretum zeyheri</i> Sond.	Combretaceae	Large-fruited bushwillow, Zeyher's bushwillow (English), raasblaar, fluisterboom (Afrikaans), moduba-tshipi (Pedi), umbondwe wasembudwini (Zulu), mufhathelathundu (Venda)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 800 µg/mL	
<i>CreMASpora triflora</i> (Thonn.) K.Schum.	Rubiaceae	Unknown	Leaf extracts	<i>K. pneumoniae</i>	MIC = 80 µg/mL	Elisha et al. (2017)
<i>Croton megalobotrys</i> Müll.Arg.	Euphorbiaceae	Feverberry (English), koorsbessie, grootkoorsbessie (Afrikaans), motsibi (Sotho), muruthu (Venda)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 313 µg/mL	Selowa et al. (2010)
<i>Croton pseudopulchellus</i> Pax	Euphorbiaceae	Small lavender fever-berry (English), kleinlaventelkoorsbessie, sandkoorsbessie (Afrikaans), uHubeshane (Zulu)	Aerial parts extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Croton silvaticus</i> Hochstetter ex Krauss	Euphorbiaceae	Forest fever berry (English)	Leaf extracts	<i>P. aeruginosa</i>	MIC = 1250 µg/mL	Selowa et al. (2010)
<i>Conyza scabrata</i> DC.	Asteraceae	Oven bush (English), bakbesembossie, bakbos, oondbos (Afrikaans),	Leaf extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 300 µg/mL MIC = 2000 µg/mL	Seaman (2005)
<i>Cyperus articulatus</i> L.	Cyperaceae	Jointed flat sedge (English)	Root extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	Inactive MIC = 2670 µg/mL	York et al. (2011)
<i>Cryptocarya latifolia</i> Sond.	Lauraceae	Bastard stinkwood, broad-leaved laurel (English), baster-stinkhout,	Bark extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Datura stramonium</i> L.	Solanaceae	breëblaarkweper, breëblaar-kweper, pondo-kweper (Afrikaans), umdlangwenya, umthungwa (Zulu), umgxaleba, umgxoboth, umncatyana (Xhosa)	Leaf extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 300 µg/mL MIC = 4000 µg/mL	Seaman (2005)
<i>Dioscorea dregeana</i> (Kunth) T.Durand & Schinz	Discoreaceae	Ilabatheka (Zulu)	Tuber extracts	<i>P. aeruginosa</i>	MIC = 390 µg/mL	Kelmanson et al. (2000)
<i>Dioscorea sylvatica</i> Eckl.	Discoreaceae	Ilabatheka (Zulu)	Root and tuber extracts	<i>P. aeruginosa</i>	Inactive	Kelmanson et al. (2000)
<i>Dioscorea sylvatica</i> Eckl.	Discoreaceae	Forest elephant's foot (English)	Tuber extract	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 1000 µg/mL MIC = 4000 µg/mL	Seaman (2005)
<i>Dodonaea viscosa</i> subsp. <i>angustifolia</i> (L.f.) J.G.West	Sapindaceae	Sand olive (English)	Leaf extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB)	MIC = 5000 µg/mL MIC = 3125 µg/mL	Mativandilela et al. (2008)
<i>Drosera capensis</i> L.	Droseraceae	Cape sundew (English), sondouw (Afrikaans)	Leaf extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB)	Inactive MIC = 3125 µg/mL	Mativandilela et al. (2008)
<i>Diospyros mespiliformis</i> Hochst. ex A.DC.	Ebenaceae	African ebony, jackal-berry (Eng.); jakkalsbessie (Afr.); Musuma (Tshivenda); Mgula (Tsonga)	Leaf hexane extract	<i>M. tuberculosis</i>	MIC = 100 µg/mL	Green et al. (2010)
<i>Ekebergia capensis</i> Sparrm.	Meliaceae	Cape ash, dogplum (English), essenhout (Afrikaans), mmidibidi (Sotho)	Bark extracts Leaf extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 500 µg/mL Inactive MIC = 1330 µg/mL	Lall and Meyer (1999) York et al. (2011)
<i>Elaeodendron croceum</i> (Thunb.) DC	Celastraceae	Forest saffron (English)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 310 µg/mL	Elisha et al. (2017)
<i>Eriocephalus africanus</i> L.	Asteraceae	Wild rosemary (English), wilderoosmaryn, kapokbos (Afrikaans)	Leaf extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 500 µg/mL MIC = 500 µg/mL	Seaman (2005)
<i>Erythrina caffra</i> Thunb.	Fabaceae	Coast coral tree (English), kuskoraalboom (Afrikaans), umsinsi (Zulu), umsinti (Xhosa)	Root extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	Inactive MIC = 8000 µg/mL	York et al. (2011)
<i>Eucalyptus grandis</i> W. Hill	Myrtaceae	Red gum, flooded gum (English)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 670 µg/mL	York et al. (2011)
<i>Euclea natalensis</i> A. DC.	Ebenaceae	Natal guarri, Natal ebony, large-leaved guarri (English), Natalghwarrie, berggwarrie, swartbasboom (Afrikaans), umTshekisanani, umKhasa (Xhosa), iDungamuzi, iChitamuzi, umZimane, umTshikisane, inKunzane, inKunzi-emnyama, umHlalanyamazane, umAnyathi (Zulu)	Root extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Euphorbia tirucalli</i> L.	Euphorbiaceae	Pencil plant, rubber-hedge euphorbia (English), kraalmelkbos (Afrikaans)	Stem extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	Inactive MIC = 2670 µg/mL	York et al. (2011)
<i>Faidherbia albida</i> (Delile) A.Chev.	Fabaceae	Ana tree (English), anaboom (Afrikaans), mogabo (Pedi), umHlalankwazi (Zulu), muhoto (Venda)	Leaf and bark extracts	<i>K. pneumoniae</i>	MIC = 6269 µg/mL	Eldeen et al. (2005)
<i>Ficus sur</i> Forssk	Moraceae	Cape fig, broom cluster fig (English)	Bark and root extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 3130 µg/mL (bark and roots) MIC = 780–1560 µg/mL (roots)	Madikizela et al. (2013) Madikizela et al. (2013); Eldeen et al. (2005)
<i>Flueggea virosa</i> (Roxb. ex Willd.) Royle	Phyllanthaceae	Snowberry tree, white-berry bush (English), witbessiebos (Afrikaans), isibangamhlota sehlati, umyawayane (Zulu)	Leaf, root, bark and fruit extracts	<i>M. tuberculosis</i>	MIC = 312 µg/mL	Dzoyem et al. (2016)
<i>Galenia africana</i> L.	Aizoaceae	Yellow bush (English), brakkraalbossie, geelbos, kraalbos, muisbos, muisgeelbossie, perdebos (Afrikaans), iqina (Xhosa)	Bark extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>M. tuberculosis</i>	MIC = 1200 µg/mL (bark and roots) MIC = 780 µg/mL (roots) MIC = 310 µg/mL	Mativandilela et al. (2008)
<i>Gerrardina foliosa</i> Oliv.	Gerrardinaceae					

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Gunnera perpensa</i> L.	Gunneraceae	Krantz-berry (English), Umaluleka (Zulu), Umlulama (Zulu) Wild rhubarb, river pumpkin (English), wilde ramenas, ravierpampoen (Afrikaans), qobo (Sotho), rambola-vhadzimu (Venda), iphuzi, ighobo (Xhosa), uqobhe (Zulu)	Aqueous bark extracts Root extracts	<i>M. tuberculosis</i>	Inactive	Madikizela, and McGaw (2018) Lall and Meyer (1999)
<i>Helichrysum kraussii</i> Sch.Bip.	Asteraceae	Straw everlasting (English), sewejaartjie (Afrikaans), isipheshane, isiqoqo (Zulu)	Leaf and stem extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 1330 µg/mL	York et al. (2011)
<i>Helichrysum melanacme</i> DC.	Asteraceae	Hotnotskooigoed (Afrikaans)	Whole plant extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Helichrysum odoratissimum</i> Less.	Asteraceae	Everlantings (English), kooigoed (Afrikaans) imphepho (Zulu)	Whole plant extracts Whole plant extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 300–500 µg/mL MIC = 2000 µg/mL	Meyer, 1999; Seaman (2005); Lall and Seaman (2005)
<i>Heteromorpha arborecens</i> (Spreng.) Cham. & Schltld.	Apiaceae	Parsley tree (English), wildepietersielie (Afrikaans)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 160 µg/mL	Elisha et al. (2017)
<i>Heteromorpha trifoliata</i> (H.L.Wendl.) Eckl. & Zeyh.	Apiaceae		Acetone, ethanol and aqueous leaf extracts	<i>M. tuberculosis</i>	MIC = 80–5000 µg/mL	Madikizela, and McGaw (2018)
<i>Heteropogon contortus</i> (L.) P.Beauv. ex Roem. & Schult.	Poaceae	Tanglehead, spear grass (English), pylgras, assegaagrass (Afrikaans), isitupe (Zulu), selokana, seloka (Southern Sotho)	Leaf and stem extracts	<i>P. aeruginosa</i>	Inactive	Kelmanson et al. (2000)
<i>Heteropyxis natalensis</i> Harv.	Myrtaceae	Lavender tree, natal lavender (English), laventelboom (Afrikaans), inkunzi (Zulu), mudedede (Venda), inkhuzwa (Zulu).	Leaf bark and root extracts	<i>M. tuberculosis</i>	MIC = 312 µg/mL	Dzoyem et al. (2016)
<i>Hexalobus monopetalus</i> (A.Rich.) Engl. & Diels.	Annonaceae	Baboons' breakfast, Shakama plum (English), muhodzongwa, mukorongwa, mukwingiziri, munyani, mupodzongwa, mupodzongwa, musakama (Shona)	Leaf, stem, root, bark and fruit extracts	<i>M. tuberculosis</i>	MIC = 156 µg/mL	Dzoyem et al. (2016)
<i>Hypericum roeperianum</i> Schimp.ex A. Rich.	Hypericaceae	Unknown	Leaf extracts	<i>K. pneumoniae</i>	MIC = 160 µg/mL	Elisha et al. (2017)
<i>Hypoxis</i> spp.	Hypoxidaceae	Yellow stars, star lily, african potato (English), sterretjie, Afrika-patat (Afrikaans), inkomfe, ilabatheka (Zulu)	Root extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 5330 µg/mL MIC = 1670 µg/mL	York et al. (2011)
<i>Hypoxis colchicifolia</i> Baker			Bulb acetone and ethanol extracts Bark, acetone, aqueous and ethanol extracts	<i>M. tuberculosis</i>	MIC = 160–630 µg/mL MIC = 1250–2500 µg/mL	Madikizela, and McGaw (2018)
<i>Indigofera arrecta</i> A. Rich.	Fabaceae	African indigo (English)	Leaf and root extracts	<i>M. arum</i> (model for tuberculosis) <i>K. pneumoniae</i>	MIC = 780 µg/mL (leaves) MIC = 390 µg/mL (roots)	Madikizela et al. (2013)
<i>Kigelia africana</i> (Lam.) Benth.	Bignoniaceae	Sausage tree (English), worsboom (Afrikaans), umVunguta, umFongothi (Zulu), muvevha (Venda)	Leaf and fruit extracts	<i>K. pneumoniae</i>	MIC = 663 µg/mL	Arkhipov et al. (2014); Cock and Van Vuuren (2015a); York et al. (2011)
<i>Krauseola mosambicina</i> Pax & Hoffm.	Caryophyllaceae	Unknown	Leaf and stem extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1000 µg/mL MIC = 3000 µg/mL	
<i>Lantana rugosa</i> Thunb.	Verbenaceae	Bird's beer, bird's brandy (English), voëlbrandewyn, wildesalie (Afrikaans), utyani-bentaka, utywala bentaka (Xhosa), impema, ubukhwebezane, ubungungundwane, uguguvama (Zulu), mabele-mabutsoa-pele, molutoane (Southern Sotho).	Leaves and stems	<i>K. pneumoniae</i>	MIC = 3000 µg/mL	Suliman (2010)
<i>Leonotis intermedia</i> Lindl.	Lamiaceae	Minaret-flower (English), klipdagga (Afrikaans), fincane, isihlungu sedobo (Xhosa), joala-ba-li-nonyana, moseneke (Southern Sotho)	Leaf and stem extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 195 µg/mL (leaves) MIC = 3130 µg/mL (leaves and stems)	Madikizela et al. (2013)
<i>Leucaena leucocephala</i> (Lam.) De Wit	Fabaceae	Wild tamarind, white lead tree, lead tree, koa haole, ekoa, horse tamarind, jumbie bean, white popinac (English)	Leaf, bark and seed extracts	<i>M. tuberculosis</i>	MIC > 2500 µg/mL	Dzoyem et al. (2016)
	Lamiaceae	Unknown		<i>K. pneumoniae</i>		Suliman (2010)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Leucas martinicensis</i> (Jacq.) R.Br.			Leaf and flower extracts		MIC = 2000 µg/mL	
<i>Lippia javanica</i> (Burm. f.) Spreng	Verbenaceae	Fever tea, lemon bush (English), koorbossie, beukesbossie, lemoenbossie (Afrikaans), inzinzinba (Xhosa), umsuzwane, umswazi (Zulu)	Leaf, twig and root extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC > 2500 µg/mL MIC = 1000 µg/mL MIC = 538 µg/mL MIC = 630 µg/mL	Dzoyem et al. (2016) York et al. (2011); Cock and Van Vuuren (2015a); Elisha et al. (2017)
<i>Maesa lanceolata</i> Forssk.	Primulaceae	False assegai (English), valsassegai (Afrikaans), umalunguzalazikhakhona, inhlavubele, umaguqu, isidenda, ubhoqobhoqo (Zulu), intendekwane (Xhosa), muunguri (Venda)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Maytenus senegalensis</i> (Lam.) Excell	Celastraceae	Confetti spike-thorn, confetti tree (English), rooidoring, rooi-pendoring (Afrikaans), isihlangu, Isihlangwane (Zulu), sephatwa (Sotho), tshibavhe, tshiphandwa (Venda)	Aerial parts extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Morus mesozygia</i> Stapf	Moraceae	African mulberry, black mulberry (English)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 80 µg/mL	Elisha et al. (2017)
<i>Nidorella anomala</i> Steetz	Asteraceae	Unknown	Whole plant extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Nidorella auriculata</i> DC.	Asteraceae	Unknown	Whole plant extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Ozoroa obovata</i> (Oliv) R.Fern. & A.Fern.	Anacardaceae	Broad-leaved resin tree (English), Breë blaarharpuisboom (Afrikaans)	Leaf and bark extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 300–2000 µg/mL MIC = 1000–1700 µg/mL	Seaman (2005); York et al. (2011);
<i>Parinari capensis</i> Harv.	Chrysobalanaceae	Dwarf mobola-plum, sand apple (English), bosappel, gruisappeltjie, sandappeltjie, witappeltjie (Afrikaans), mobolo-oa-fatsi (Southern Sotho)	Root extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 1500 µg/mL	York et al. (2011)
<i>Peucedanum caffrum</i> Phil	Apiaceae	Unknown	Root extracts	<i>K. pneumoniae</i>	MIC = 6000 µg/mL	Suliman (2010)
<i>Pentanisia prunelloides</i> (Klotzsch) Walp.	Rubiaceae	Wild verbena (English), sooibrandbossie (Afrikaans), setimamollo (Sotho), icimamillo (Zulu)	Leaf and root extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 390 µg/mL (leaves) MIC = 390 µg/mL (roots)	Madikizela et al. (2013)
<i>Pelargonium betulinum</i> (L.) L'Hér. ex Aiton	Geraniaceae	Camphor-scented pelargonium, birch-leaved pelargonium (English), kanferblaar, maagpynbossie, suurbos (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 1000 µg/mL	Lalli et al. (2008)
<i>Pelargonium citronellum</i> J.J.A. Van der Walt	Geraniaceae	Citronella pelargonium, lemon-scented pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 3000 µg/mL	Lalli et al. (2008)
<i>Pelargonium cordifolium</i> Curtis	Geraniaceae	Unknown	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 1500 µg/mL	Lalli et al. (2008)
<i>Pelargonium crispum</i> (P.J.Bergius) L'Hér.	Geraniaceae	Lemon-scented pelargonium, crisped-leaf pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium cucullatum</i> (L.) L'Hér.	Geraniaceae	Hooded-leaf pelargonium, (English), wildemalva (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 1500 µg/mL	Lalli et al. (2008)
<i>Pelargonium fasciculaceum</i> E.M. Marais	Geraniaceae	Unknown	Leaf extracts	<i>K. pneumoniae</i>	MIC = 374 µg/mL	Cock and Van Vuuren (2015a)
<i>Pelargonium glutinosum</i> (Jacq.) L'Hér.	Geraniaceae	balm-scented pelargonium, sticky-leaf pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium graveolens</i> L'Hér.	Geraniaceae	Rose-scented pelargonium (English), wildemalva (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium greytonense</i> J.J.A. Van der Walt	Geraniaceae	Greyton pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 3200 µg/mL	Lalli et al. (2008)
<i>Pelargonium hermannifolium</i> Jacq.	Geraniaceae	Unknown	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 1500 µg/mL	Lalli et al. (2008)
<i>Pelargonium hispidum</i> Willd.	Geraniaceae	Hispid pelargonium (English), grofharig (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium panduriforme</i> Eckl. & Zeyh.	Geraniaceae	Balsam-scented geranium, fiddle leaf geranium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium papilionaceum</i> (L.) L'Hér. ex Aiton	Geraniaceae	Butterfly pelargonium (English), rambossie (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 4000 µg/mL	Lalli et al. (2008)
<i>Pelargonium pseudoglutinosum</i> R. Knuth	Geraniaceae	Unknown	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Pelargonium quercifolium</i> (L.f) L'Hér.	Geraniaceae	Oak-leaf pelargonium (English), muishondbos (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium radens</i> H. E. Moore	Geraniaceae	Rasp-leaved, multifid-leaved pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2500 µg/mL	Lalli et al. (2008)
<i>Pelargonium scabroide</i> R. Knuth	Geraniaceae	Unknown	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium scabrum</i> (L) L'Hér.	Geraniaceae	Rough-leaved pelargonium, three-pointed pelargonium (English), hoenderbos (Afrikaans)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium sublignosum</i> R. Knuth	Geraniaceae	Unknown	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium tomentosum</i> Jacq.	Geraniaceae	Peppermint-scented pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Lalli et al. (2008)
<i>Pelargonium vitifolium</i> (L.) L'Hér.	Geraniaceae	Vine-leaved pelargonium, balm-scented pelargonium (English)	Aerial parts extracts	<i>K. pneumoniae</i>	MIC = 4000 µg/mL	Lalli et al. (2008)
<i>Phymaspermum acerosum</i> (DC.) Källersjö	Asteraceae	Geelblombos (Afrikaans), isibhahasegeke, umhlonishwa (Zulu)	Acetone, ethanol and aqueous leaf extracts Acetone, ethanol and aqueous root extracts	<i>M. tuberculosis</i>	MIC = 80–630 µg/mL MIC = 40–310 µg/mL	Madikizela, and McGaw (2018)
<i>Piper capense</i> L.f.	Piperaceae	Wild pepper (English)	Root acetone extract	<i>M. tuberculosis</i>	MIC = –100 µg/mL	Green et al. (2010)
<i>Pittosporum viridiflorum</i> Sims	Pittosporaceae	Cheesewood, white cape beech (English), kasuur, witboekenhout (Afrikaans), umVusamvu, Umkhwenkwe, Umphushane (Zulu), kgalagangwe (Sotho), mosetela (Southern Sotho), mulondwane, mutanzwakhamele (Venda), umgqwengqwe (Xhosa)	Leaf extracts	<i>K. pneumoniae</i> <i>M. tuberculosis</i>	MIC = 160 µg/mL MIC = –310-2500 µg/mL	Elisha et al. (2017) Madikizela, and McGaw (2018)
<i>Plectranthus neochilus</i> Schltr.	Lamiaceae	Smelly spur flower, lobster flower (English), rotstuinsalie (Afrikaans)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1000 µg/mL MIC = 1330 µg/mL	York et al. (2011)
<i>Podocarpus elongatus</i> (Aiton) L'Hér. ex Pers.	Podocarpaceae	Breede River yellowwood (English), breeriviergeelhout, westelike geelhout (Afrikaans)	Leaf and stem extracts	<i>K. pneumoniae</i>	MIC = 1040 µg/mL	Abdillahi et al. (2008)
<i>Podocarpus falcatus</i> (Thunb.) R.Br. ex Mirb.	Podocarpaceae	Outeniqua yellowwood (English), Outeniekwageelhout (Afrikaans), mogöbagöba (Sotho), umsonti (Zulu)	Leaf and stem extracts	<i>K. pneumoniae</i>	MIC = 650 µg/mL	Abdillahi et al. (2008)
<i>Podocarpus henkelii</i> Stapf ex Dallim. & B. D.Jacks.	Podocarpaceae	Henkel's yellowwood (English), Henkel-se geelhout (Afrikaans), umSonti (Zulu)	Leaf and stem extracts	<i>K. pneumoniae</i>	MIC = 390 µg/mL	Abdillahi et al. (2008)
<i>Podocarpus latifolius</i> (Thunb.) R.Br. ex Mirb.	Podocarpaceae	Real yellowwood (English), opregte geelhout (Afrikaans), umkhomba (Xhosa), mogobagoba (Sotho), muhovho-hovho (Venda), umsonti (Zulu)	Leaf and stem extracts	<i>K. pneumoniae</i>	MIC = 650 µg/mL	Abdillahi et al. (2008)
<i>Polygala fruticosa</i> P. J. Bergius	Polygalaceae	Butterfly bush, heart-leaf polygala (English), ertjieblom (Afrikaans), ulopesi, ulapesi, umabalabala (Xhosa), ithethe (Zulu)	Leaf and root extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1560 µg/mL (leaves) MIC = 3130 µg/mL (roots)	Madikizela et al. (2013)
<i>Polygala myrtifolia</i> L.	Polygalaceae	September bush (English), septemberbossie, augustusbossie, blouertjie, langelede (Afrikaans), ulopesi, ulapesi, umabalabala (Xhosa), uchwasha (Zulu)	Aerial parts extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Pouzolzia mixta</i> Solms	Urticaceae	Soap nettle (English), muthanzwa (Venda)	Leaf, root and stem extracts	<i>K. pneumoniae</i>	MIC = 6000 µg/mL	Samie et al. (2005)
<i>Protorhus longifolia</i> (Bernh.) Engl.	Anacardiaceae	Red beech, purple currant, red Cape beech (English), rooi-boekenhout, rooimelkhout (Afrikaans), ikhubalo, isifuze (isiXhosa), umkomiso, uzintlwa (Zulu)	Leaf acetone and ethanol extracts	<i>M. tuberculosis</i>	MIC = –160-1250 µg/mL	Madikizela, and McGaw (2018)
<i>Pterocelastrus echinatus</i> N.E. Br.	Celastraceae	Hedgehog-tree, white candlewood (English), Ibholo (Xhosa), Inqayilibomvu (Zulu), Mutongola (Venda), Witekshout (Afrikaans)	Bark acetone and ethanol extracts Leaf acetone, aqueous and ethanol extracts	<i>M. tuberculosis</i>	MIC = –160-630 µg/mL MIC = –160-630 µg/mL	Madikizela, and McGaw (2018)
<i>Prunus africana</i> (Hook.f.) Kalkman	Rosaceae	Red stinkwood, African almond (English), rooistinkhout, Afrika-amandel	Leaf extracts	<i>M. arum</i> (model for TB)	Inactive	Madikizela et al. (2013)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
		(Afrikaans), inyazangoma-elimnyama, inkokhokho, ngubozinyeweni, umdumizulu (Zulu), uMkakase, inyazangoma, Itywina-elikhul, Umdumizulu (Xhosa), mogohloro (Sotho), mulala-maanga (Venda)		<i>P. aeruginosa</i> <i>K. pneumoniae</i>	MIC = 1500 µg/mL MIC = 1500–6000 µg/mL	Samie et al. (2005) Eldeen et al. (2005); Samie (2005)
<i>Psidium guajava</i> L.	Myrtaceae	Common guava, yellow guabva (English)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2000 µg/mL MIC = 670 µg/mL	York et al. (2011)
<i>Ptaeroxylon obliquum</i> (Thunb.) Radlk.	Rutaceae	Sneezewood (English), nieshout (Afrikaans), umThathi (Xhosa)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 1977 µg/mL	Cock and Van Vuuren (2015a)
Rapanea melanophloeos (L.) Mez.	Primulaceae	Cape beech, rapanea (English), boekenhout, kaapse, boekenhout, rooiboekenhout, swartbas (Afrikaans), ikhulwane, inhluthe, isicalabi, isiqalaba-sehlathi, umaphipa-khubalo, umhluti-wentaba, uvukwabafile (Zulu)	Leaf, bark and root extracts	<i>M. tuberculosis</i>	MIC = 150–500 µg/mL	Lall and Meyer (1999); Dzoyem et al. (2016)
Rhamnus prinoides L'Hér.	Rhamnaceae	Camdeboo, dogwood, glossy-leaf, shiny leaf, stinkwood (English), alinkbaar, hondepishout, kamdeboo-stinkhout, seerkeelboom (Afrikaans), ulenyenyeni, umgilindi, umhlinye, umnyenyeni (Zulu)	Leaf, bark, root, fruit and seed extracts	<i>M. tuberculosis</i>	MIC = 625 µg/mL	Dzoyem et al. (2016)
<i>Rhoicissus tridentata</i> (L. f.) Wild & R.B. Drumm.	Vitaceae	Bitter grape (English), Murumbulashedo (Venda)	Root, tuber and fruit extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 3000 µg/mL MIC = 3000 µg/mL	Samie et al. (2005)
			Leaf acetone extract	<i>M. tuberculosis</i>	MIC = 50 µg/mL	Green et al. (2010)
<i>Rhus dentate</i> Thunb.	Anacardiaceae	Nana-berry (English), Mubikasadza (Shona)	Bark acetone extract	<i>M. tuberculosis</i>	MIC = 50 µg/mL	Green et al. (2010)
Rumex crispus L.	Polygonaceae	Yellow dock (English)	Aerial parts extracts	<i>M. tuberculosis</i>	Inactive	Lall and Meyer (1999)
<i>Salix mucronate</i> Thunb.	Salicaceae	Cape willow (English), Safsaf-wilger, kaapse wilger, wildewilgerboom (Afrikaans), munengeledi (Venda), mogokare (Sotho), umngcunube (Xhosa), umnyezane, umzekana (Zulu)	Leaf, bark and root extracts	<i>K. pneumoniae</i>	MIC = 6250 µg/mL	Eldeen et al. (2005)
<i>Sansevieria hyacinthoides</i> (L.) Druce	Asparagaceae	Mother-in-law's tongue, piles root, bowstring hemp (English), skoonma-se-tong, aambeiwortel, haasoor (Afrikaans), kai, ghaiwortel (Khoi), isikhokolotho (Xhosa, Zulu), isikwendle, isitokotoko (Zulu)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	Inactive MIC = 4000 µg/mL	York et al. (2011)
<i>Scadoxus puniceus</i> (L.) Friis & Nordal	Amaryllidaceae	Paintbrush lily, snake lily (English), rooikwas (Afrikaans), isisphompho, umgola (Zulu)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2670 µg/mL MIC = 3000 µg/mL	York et al. (2011)
<i>Schkuhria pinnata</i> (Lam.) Kuntze ex Thell.	Compositae	Dwarf marigold (English)	Leaf extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i> <i>M. smegmatis</i>	MIC = 3000 µg/mL MIC = 270 µg/mL MIC = 270 µg/mL	Suliman (2010) Kudumela et al., 2018 Masiphephethu (2019); Masoko and Masiphephethu (2019). Green et al. (2010)
<i>Schotia brachypetala</i> Sond.	Fabaceae	Weeping boer-bean, tree fuchsia, African walnut (English), huilboerboon (Afrikaans) umfofofo (Xhosa), uvovovo (Zulu), molope (Northern Sotho), mutanswa (Venda), nwavilombe (Tsonga); umutwa (Tswana), uvovovo (Swati)	Bark acetone extracts	<i>M. tuberculosis</i>	MIC = 50 µg/mL	Green et al. (2010)
<i>Sclerocarya birrea</i> (A. Rich.) Hochst.	Anacardaceae	Marula (English), morula (Northern Sotho)	Bark extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1330 µg/mL MIC = 670 µg/mL	York et al. (2011)
Securidaca longipedunculata Fresen.	Polygonaceae	Violet tree (English), krinkhout, rooipeultjie, seepbasboom (Afrikaans), mpesu (Venda), iphuphuma (Zulu)	Roots	<i>Haemophilus influenzae</i>	Inactive	Pallant and Steenkamp (2008)
<i>Senecio deltoideus</i> Less.	Asteraceae	Canary creeper (English), undenze (Xhosa)	Leaf extracts	<i>Mycobacterium smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 1330 µg/mL MIC = 1330 µg/mL	York et al. (2011)
Senecio serratoloides DC.	Asteraceae	Two-day cure (English), ichazampukane, insukumbili, umaphozisa umkhuthelo (Zulu)	Aerial parts extracts Leaf extracts	<i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 5000 µg/mL MIC = 1330 µg/mL	Lall and Meyer (1999) York et al. (2011)

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Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Siphonochilus aethiopicus</i> (Schweinf.) B.L. Burtt	Zingiberaceae	Natal ginger, wild ginger (English), wildegemmer (Afrikaans), indungulo, isiphephetho (Zulu)	Root extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 1330 µg/mL MIC = 300 µg/mL MIC = 4000 µg/mL	Seaman (2005)
<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)	Bark extracts	<i>H. influenzae</i> <i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>P. aeruginosa</i> <i>K. pneumoniae</i>	MIC = 1000 µg/mL MIC = 300 µg/mL MIC = 1330 µg/mL MIC = 310 µg/mL MIC = 300–2000 µg/mL	Pallant and Steenkamp (2008) Seaman (2005) York et al. (2011) Samie et al. (2005) Cock and Van Vuuren (2015a); York et al. (2011); Samie et al. (2005); Seaman (2005) Dzoyem et al. (2016)
<i>Tabernaemontana elegans</i> Stapf	Apocynaceae	Toad tree (English), laevelde paddaboom (Afrikaans), umKhahlwana, umKhadu (Zulu)	Leaves, roots, rhizome, sap	<i>M. tuberculosis</i> <i>H. influenzae</i>	MIC = 1250 µg/mL Inactive	Pallant and Steenkamp (2008) Madikizela et al. (2013)
<i>Terminalia phanerophlebia</i> Engl. & Diels	Combretaceae	Lebombo cluster-leaf (English), lebombotrosblaar (Afrikaans), amaNgwe-amnyama, amaNgwe-omphofu (Zulu)	Leaf, root and twig extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 195 µg/mL (leaves and twigs) MIC = 195 µg/mL (twigs)	Cock and Van Vuuren (2015a); Cock and Van Vuuren (2015b); Eloff (1999)
<i>Terminalia pruinoides</i> M.A. Lawson	Combretaceae	Purple-pod terminalia (English), deurmekaar, sterkbos (Afrikaans)	Leaf extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 432 µg/mL MIC = 360–1600 µg/mL	York et al. (2011)
<i>Terminalia sericea</i> Burch. ex DC.	Combretaceae	Silver cluster leaf (English), vaalboom (Afrikaans), mususu (Venda)	Bark, root and leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 670 µg/mL MIC = 250–670 µg/mL MIC = 6000 µg/mL	York et al. (2011); Suliman (2010); Cock and Van Vuuren (2015a) Eloff (1999) Green et al. (2010)
<i>Tetradenia riparia</i> (Hochst.) Codd	Lamiaceae	Misty plume bush, ginger bush (English), gemberbos, watersalie (Afrikaans), iboza, ibozane (Zulu)	Bark acetone extract Root extracts Leaf extracts	<i>M. tuberculosis</i> <i>M. tuberculosis</i> <i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 25 µg/mL MIC = 300 µg/mL MIC = 1000 µg/mL MIC = 1750 µg/mL	Seaman (2005) York et al. (2011)
<i>Thymus vulgaris</i> L.	Lamiaceae	German thyme, common thyme (English)	Aerial parts extracts	<i>M. tuberculosis</i>	MIC = 500 µg/mL	Lall and Meyer (1999)
<i>Trema orientalis</i> (L.) Blume	Cannabaceae	Pigeonwood (English), hophout (Afrikaans), ifamu, iphubane, isakasaka, isikhwelamfene, sakasaka, ubathini, umbengele, umhangabhanganga, umdindwa, umsekeseke, umvangazi (Zulu)	Leaves, stems, roots, bark, fruit, twigs and seeds	<i>M. tuberculosis</i>	MIC = 312 µg/mL	Dzoyem et al. (2016)
<i>Trichilia dregeana</i> Sond.	Meliaceae	Forest mahogany, Cape mahogany, red ash (English), rooiesenhout, bosrooiesenhout, basteressenhout (Afrikaans), umKhuhlu, uMathunzini (Zulu), umKhuhlu (Xhosa), mmaba (Sotho), mutuhu, mutshikili (Venda)	Leaf, bark and root extracts	<i>K. pneumoniae</i>	MIC = 6250 µg/mL	Eldeen et al. (2005)
<i>Trichilia emetica</i> Vahl	Meliaceae	Natal mahogany (English), rooiesenhout (Afrikaans), mamba (Sotho), umathunzini (Zulu), umkhuhlu (Xhosa), mutuhu (Venda)	Leaf extracts	<i>M. smegmatis</i> (model for TB) <i>K. pneumoniae</i>	MIC = 2670 µg/mL MIC = 1670 µg/mL	York et al. (2011)
<i>Tulbaghia violacea</i> Harv.	Amaryllidaceae	Wild garlic (English), wilde knoffel (Afrikaans), isihaga (Zulu)	Root and leaf extracts	<i>M. arum</i> (model for TB) <i>K. pneumoniae</i>	MIC = 780 µg/mL MIC = 277 µg/mL	Buwa and Afolayan (2009) Cock and Van Vuuren (2015a)
<i>Vernonia colorata</i> (Willd.) Drake	Asteraceae	English bitter leaf, bitters tree (English)	Leaf, stems and root extracts	<i>P. aeruginosa</i>	MIC = 520 µg/mL (leaves)	Kelmanson et al. (2000)
<i>Vitex rehmannii</i> Gürke	Lamiaceae	Pipe-stem fingerleaf (English), umluthu (Zulu), munyongatshifumbu (Venda)	Leaf extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL	Suliman (2010)
<i>Warburgia salutaris</i> (G.Bertol.) Chiov.	Canellaceae	Pepper-bark tree (English), peperbasboom (Afrikaans), mulanga, manaka (Venda), isibhaha (Zulu)	Bark and leaf extracts Leaf acetone extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i> <i>M. tuberculosis</i>	MIC = 156 µg/mL MIC = 624 µg/mL MIC = 25 µg/mL	Dzoyem et al. (2016) Cock and Van Vuuren (2015a) Green et al. (2010)

(continued on next page)

Table 2 (continued)

Plant species	Family	Common name(s)	Extract tested	Test micro-organism	Activity	References
<i>Xerophyta retinervis</i> Baker	Velloziaceae	Black-stick lily (English), besembos, bobbejaanstert (Afrikaans), isigqumana, isiphmba (Zulu)	Bark extracts	<i>M. tuberculosis</i> <i>K. pneumoniae</i>	MIC = 300 µg/mL MIC = 500 µg/mL	Seaman (2005)
<i>Ximenia caffra</i> Sond.	Oleaceae	Sour plum (English), mutshili (Venda)	Leaf and root extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 3000 µg/mL MIC = 6000 µg/mL	Samie et al. (2005) Samie et al. (2005)
<i>Zanthoxylum davyi</i> Waterm.	Rutaceae	Forest knobwood (English)	Root and bark extracts	<i>K. pneumoniae</i>	MIC = 2000 µg/mL (bark)	Suliman (2010)
<i>Zornia milneana</i> Mohlenbr.	Fabaceae	Lukandulula (Venda)	Whole plant extracts	<i>K. pneumoniae</i> <i>P. aeruginosa</i>	MIC = 3000 µg/mL MIC = 3000 µg/mL	Samie et al. (2005)
<i>Ziziphus mucronata</i> Willd.	Rhamnaceae	Buffalo thorn (English), blinkblaar-wag-'n-bietjie (Afrikaans), umphafa, umlahlankosi, isilahla (Zulu), umphafa (Xhosa), mutshetshete (Venda), mokgaló, moonana (Sotho)	Bark extracts Leaf, bark and root extracts Bark extract	<i>M. smegmatis</i> (model for TB) <i>M. tuberculosis</i> <i>K. pneumoniae</i> <i>M. tuberculosis</i>	Inactive MIC = 156 µg/mL MIC = 4000 µg/mL MIC = 50 µg/mL	Mativandela et al. (2008) Dzoyem et al. (2016) Suliman (2010) Green et al. (2010)

Where multiple solvent extractions and/or multiple plant parts were tested for a plant species, the MIC values reported here were for the most active extract (as judged by MIC value). Plant species indicated in bold are species documented ethnobotanically (Table 1).

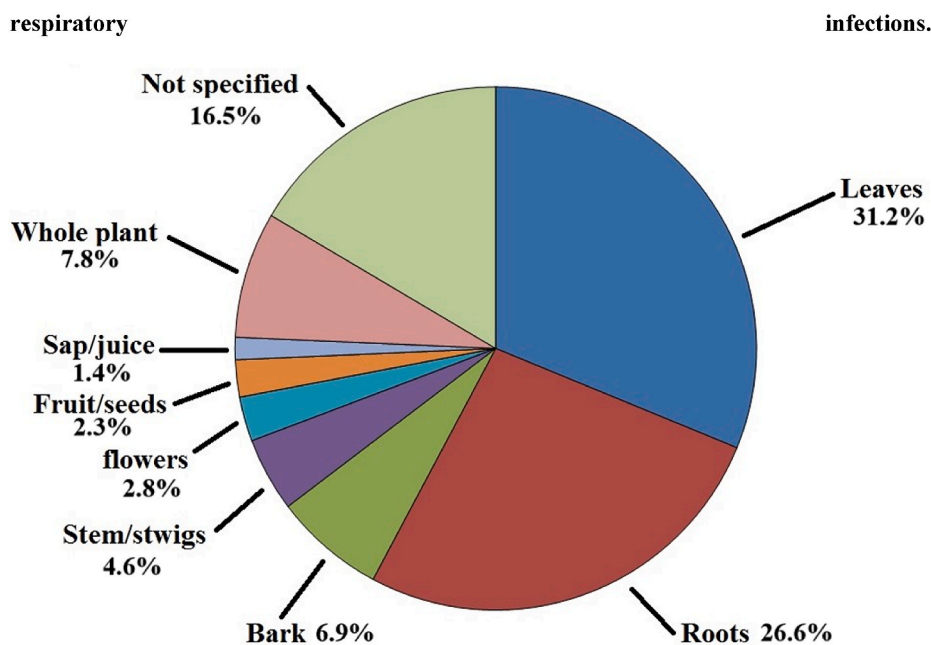


Fig. 2. Frequency of use of different southern African plant parts to treat bacterial respiratory infections.

bacteria. The high numbers of plants screened against these pathogens may be due to the serious consequences of contracting TB or pneumonia, both of which may result in mortality.

The high numbers of plants screened against the pneumonia-causing bacteria may also result from these bacteria also being implicated in several other illnesses. Often, when plant extracts are screened against these bacteria, the testing was targeting those other diseases. For example, several of the southern African plants screened against *K. pneumoniae* (*Agathosma betulina* (Berg.) Pillans, *Ballota africana* Benth., *Carpobrotus edulis* (L.) N.E. Br, *Combretum collinum* Fresen., *Combretum erythrophyllum* (Burch.) Sond., *Combretum microphyllum* Klotzsch, *Combretum molle* R.Br., *Kigellia africana* (Lam.) Benth., *Lippia javanica* (Burm. F.) Spreng, *Pelargonium fasciculata* Colvill ex Sweet, *Ptaeroxylon obliquum* (Thunb.) Radlk., *Syzygium cordatum* (Hochst.), *Terminalia pruinoides* Lawson, *Terminalia Sericea* Burch. ex DC., *Tulbaghia violacea* Harv., *Warburgia salutaris* (Bertol.f.) Chiov.) were tested in

studies focused on the trigger mechanisms of the autoimmune disease ankylosing spondylitis (Arkhipov et al., 2014; Cock and Van Vuuren, 2015; Cock and Van Vuuren, 2014). Despite the different focus, these studies also evaluate the use of the plants for the treatment of bacterial pneumonia.

Due to the important pathogenesis of TB in Southern Africa, a relatively large number of southern African plant species have already been screened for anti-*M. tuberculosis* activity (Green et al., 2010; Dzoyem et al., 2016; Madikizela and McGaw, 2018). However, the majority of plants identified as being used to treat TB are yet to be tested, and substantially more work is required in this field.

Other bacterial pathogens associated with respiratory diseases have been poorly studied with respect to validation and southern African medicinal plant use. Indeed, only four plants species were screened against *Haemophilus influenzae* (*Asparagus falcatus* (L.) Oberm., *S. longpedunculata*, *S. cordatum*, *T. elgans*) and we were unable to find any

studies that screened southern African plants against *C. diphtheriae* or *B. pertussis* (the causes of diphtheria and whooping cough respectively). These diseases all cause considerable distress. However, effective vaccines against *C. diphtheriae* or *B. pertussis* are available, and their use is now routine. Therefore, cures for these diseases are considered of lower priority, possibly accounting for the lack of screening against these pathogens. However, these vaccines are only effective as preventatives and are of little use if a pathogen infection occurs. Furthermore, neither vaccination nor prior exposure to *C. diphtheriae* or *B. pertussis* confer lifelong immunity and a vaccinated individual may still contract the disease several years after initial vaccination. Therefore, regular 'booster' vaccinations are required to prevent these diseases. Cures are still required to overcome the illness once infection with these bacteria occurs, and treatments for these diseases should not be neglected.

A critical analysis of the plant species studied in Table 2 demonstrates that 75% do not demonstrate noteworthy activities. It has been recommended (Van Vuuren and Holl, 2017), that efficacies ≤ 160 $\mu\text{g/mL}$ should only be considered as noteworthy. One does, however, need to take cognisance that each study may not have been tested against all known respiratory pathogens and as such, the plant species while not demonstrating efficacy against a particular tested bacterial strain, may prove to be more active against other bacterial strains not included in the pathogen set. Some plant species demonstrating noteworthy efficacy against *M. tuberculosis* include *B. discolor* (10.5–12.5 $\mu\text{g/mL}$), *B. micrantha* (25 $\mu\text{g/mL}$), *C. petersiana* (50 $\mu\text{g/mL}$), *D. mespiliformis* (100 $\mu\text{g/mL}$) (Green et al., 2010), as well as *C. aristata* (39 $\mu\text{g/mL}$), *C. glabrum* (156 $\mu\text{g/mL}$) and *H. monopetalus* (156 $\mu\text{g/mL}$) (Dzoyem et al., 2016). Other plant species also demonstrating noteworthy activity against *M. tuberculosis* were *P. acerosum*, *P. capense*, *P. longifolia*, *P. echinatus*, *R. melanophloeos*, *R. tridentate*, *R. dentate*, *S. brachyptala*, *T. sericea*, *W. salutaris* and *Z. mucronata* (Green et al., 2010; Dzoyem et al., 2016; Madikizela, and McGaw, 2018). Other plant species such as *C. aurea* and *C. triflora* demonstrated noteworthy efficacy against *K. pneumoniae* at 80 $\mu\text{g/mL}$ (Elisha et al., 2017). Other plant species demonstrating noteworthy activity against *K. pneumoniae* include *Heteromorpha* spp., *H. roeperianum*, *H. colchicifolia*, *M. mesozygia*, *P. viridiflorum* (Elisha et al., 2017; Madikizela, and McGaw, 2018). What is even more interesting is the fact that only four plant species (*C. aristata*, *T. sericea*, *W. salutaris* and *Z. mucronata*) were affiliated to traditional use (Table 1). Furthermore, only two bacterial species (*M. tuberculosis* and *K. pneumoniae*) correlated with noteworthy activity.

All the investigations that screened southern African plants against bacterial respiratory diseases used *in vitro* methods and none of the plant preparations have been evaluated *in vivo*. This is may be due to ethical concerns and the understandable global trend to replace *in vivo* test models (where possible) with *in vitro* testing. However, whilst the *in vitro* properties may be promising and indicate further evaluation is required, many other pharmacodynamic and pharmacokinetic factors also affect the safety and efficacy of all chemotherapies. Where promising activity is detected, further *in vivo* studies are required to evaluate the suitability of these plants for therapeutic use.

There are no records of ethnobotanical use to treat bacterial respiratory diseases for the other majority plant species that have been screened against bacterial respiratory pathogens. Indeed, 212 of the 254 plant species that have been already screened (approximately 83%) were selected for study for reason other than ethnobotanical usage. Those plant species were selected based on alternative criteria, including the investigators bias for a specific genus/family. For example, 21 *Combretum* species and three *Terminalia* species have been screened against bacterial respiratory pathogens (Cock and Van Vuuren, 2015a; Cock and Van Vuuren, 2015b; Madikizela et al., 2013; York et al., 2011; Eldeen et al., 2005; Eloff, 1999; Lall and Meyer, 1999) despite only two *Combretum* species and two *Terminalia* species being traditionally used for that purpose. The selection of the *Combretum* and *Terminalia* species correlates with the research background of specific researchers where interest in the plant family Combretaceae, was the focus. Plant species

from the family Combretaceae from other regions of the world have demonstrated similar interesting activities (Cock, 2015; Lima et al., 2012; Eloff, 1999) and therefore these species are good candidates for testing.

5. Discussion

Traditional herbal medicines are promising sources of potential new antibacterial chemotherapeutics. In many cases, their use has been documented for hundreds (or even thousands of years), aiding in species selection for study. Southern African traditional plant use has particularly good potential as there are high biodiversity levels and relatively good records of plant use. Through extensive review of the available ethnobotanical literature, we identified 187 plant species that are used in one or more southern African healing systems to treat either TB, diphtheria, pertussis or bacterial pneumonia. Surprisingly given the ease of transmission and severity of these diseases, only 42 of the identified species have been screened against bacterial causes of these diseases. All of those species were reported to be effective against one or more bacterial respiratory pathogens. However, the other 145 species identified as traditional treatments for respiratory diseases of bacterial origin remain to be screened.

Even when a plant species has been screened against a bacterial respiratory pathogen, they were usually only tested against one or two pathogens. The plants have been most extensively tested against TB and pneumonia causing pathogens, because of the ease of transmission and relatively high mortality rates caused by these diseases. However, with a few notable exceptions, those studies screen against bacterial strains that are also susceptible to other conventional antibiotics. Given the high incidence of multiple drug resistant strains of *M. tuberculosis* (~92% in southern Africa; WHO, 2019a) and of some pneumonia causing bacteria, testing against resistant strains of these bacteria is important to develop new therapies. Ideally, any new therapies targeting those pathogens should function via different mechanisms to the existing drugs so that they may also be effective in resistant bacterial strains. Thus, where a plant-based therapy has demonstrated efficacy towards one or more bacterial respiratory pathogens, follow-up studies should also test the preparations against resistant and neglected strains.

In comparison to TB and bacterial pneumonia, studies screening plant extracts against *C. diphtheriae* and *B. pertussis* are lacking. Indeed, we were unable to find any studies screening southern African plants against these bacteria. To an extent, this is understandable, particularly for *C. diphtheriae*. Highly efficient vaccines are available against this pathogen and the rates of new diphtheria infections in particular have decreased dramatically and there are now only approximately 4500 new infections reported annually worldwide (WHO, 2019b). However, when an individual is infected with *C. diphtheriae*, there is a 5–10% mortality rate. The incidence of pertussis has also declined substantially since the introduction of widespread vaccination programs, with the levels of infection decreased to 150,000 new cases in 2018, with nearly 90,000 deaths (WHO, 2019c). These rates are still concerning and studies seeking new cures for these diseases should not be ignored, particularly given the rapid emergence of antibiotic resistant strains of *C. diphtheriae* and *B. pertussis* in recent years.

Notably, all of the screening studies have only used *in vitro* models to screen the traditional medicines. We were unable to find any studies that screened the plants in *in vivo* systems. *In vitro* modelling is best regarded as an initial step in the developing of new drugs from natural sources. Activity in an *in vitro* system may not necessarily translate to activity *in vivo*. A large number of bioavailability issues will influence the activity of a plant preparation *in vivo*. Where promising activity is detected *in vitro*, the plant preparations should be re-screened using an appropriate *in vivo* model organism. Furthermore, pharmacodynamics and pharmacokinetic parameters should be examined so that appropriate doses and treatment regimens can be modelled.

Of the plants that have been screened for inhibitory activity against

the bacterial respiratory pathogens, few were also tested for toxicity. These plants have often been used therapeutically for hundreds of years and it is possible that researchers assume that they are safe and have therefore not focused on the toxicological aspects of the traditional medicine. Many of these plants have been screened for toxicity in other studies (Fennell et al., 2004; Steenkamp and Gouws, 2006). However, the focus of those studies was solely on evaluation of toxicity of the extracts, or on investigating the safety of the extracts in conjunction with different bioactivities. Toxicological screening studies should be performed in parallel with therapeutic screening studies to allow the safety index to also be reported. Differences in the methods used to process the plants, as well as differences between collection locations, seasons of collection etc. may result in substantial differences between phytochemical profiles of the different preparations. This may significantly alter their toxicity profiles of the different preparations. It may therefore not be valid to assume that the toxicity profile reported in one study also indicates that bioactive extracts in another study will also be safe. Instead, toxicity evaluations and bioactive screening studies should be included in the same report. Furthermore, to allow for comparisons between different studies, toxicity evaluations should ideally incorporate more than one toxicity model.

6. Conclusions

In conclusion, despite ethnobotanical records of a substantial number of southern African plant species used to treat bacterial respiratory diseases, many are yet to be tested for inhibitory activity against any respiratory bacterial pathogen and substantially more work is needed in this field. Indeed, one hundred and eighty-seven southern African plant species are recorded as traditional therapies for bacterial respiratory infections. Scientific evaluations of 178 plant species were recorded. Of the species evaluated for therapeutic properties, only 42 species were selected for screening on the basis of their ethnobotanical uses. Therefore, the potential of 146 species used traditionally to treat bacterial respiratory diseases are yet to be verified. Furthermore, the species that have been tested against some bacterial respiratory pathogens generally have only been tested against one or a few bacterial respiratory pathogens and testing against other bacteria is required. Furthermore, most plant species have only been tested against antibiotic-sensitive pathogen strains. Given the rapid development of antibiotic resistance, the southern African plant species identified in our study should also be screened against antibiotic resistant bacterial strains.

Whilst substantial effort is required to screen southern African plants against respiratory bacterial pathogens, a directed approach is recommended. Plant preparations should initially be screened against the pathogens for which they were traditionally used. Furthermore, testing against the pathogens that cause the more serious respiratory diseases (tuberculosis, bacterial pneumonia) is recommended to decrease the burden caused by these diseases. Diphtheria and pertussis are less of a concern than tuberculosis and pneumonia due to the development of effective vaccines against those pathogens. However, they also should not be neglected as the bacteria responsible for these diseases are increasingly evading the vaccines and are concurrently developing resistance to clinical antibiotics. It is hoped that this review will highlight promising species for testing, which may aid in the development of new therapies against bacterial respiratory diseases.

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 and by 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.2020.113204>.

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