AN ETHNOPHARMACOLOGICAL INVESTIGATION OF MEDICINAL PLANTS USED FOR CHILDHOOD AILMENTS IN THABA ‘NCHU, SOUTH AFRICA

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DECLARATION OF INDEPENDENT WORK

I, **Shudufhadzwani Ndou**, identity number [redacted], student number [redacted] do hereby declare that this research project submitted to the Central University of Technology, Free State, for the DEGREE MASTER OF HEALTH SCIENCES: BIOMEDICAL TECHNOLOGY, is my own independent work; and complies with the Code of Academic Integrity, as well as other relevant policies, procedures, rules and regulations of the Central University of Technology, Free State; and has not been submitted before to any institution by myself of any other person in fulfilment (or partial fulfilment) of the requirements for the attainment of any qualification.

Signature of student   Date

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SUMMARY

Medicinal plants have a long history of use worldwide (75-80% of the world's population) as traditional medicine to manage various ailments, including those affecting children. The use of medicinal plants is also fuelled by the outbreak of different childhood ailments, after-effects that emanate from modern medicine, and expensive (limited) healthcare services. This study was carried out to document the use of medicinal plants for childhood ailments in Thaba 'Nchu, Free State, South Africa, and evaluate three selected plants for phytochemical contents, cytotoxicity and antimicrobial activity.

Thirty traditional medicinal practitioners were interviewed through semi-structured interviews between November 2018 and March 2019. Medicinal plants were used to treat 19 diseases commonly found in children. The study revealed that depression of fontanelles has the highest frequency of mention (58) with an Informant Consensus Factor of 0.56, and bronchiolitis has the highest Informant Consensus Factor of 1.00. *Berkheya montana* (UV of 0.47 with 76% fidelity level) was the most frequently and popularly used medicinal plant species. *Solunum aculeatissimum (*UV of 0.30 with 43% fidelity level) was the least frequently and least popularly used medicinal plant species. *Aloe grandidentata* (UV of 0.17 with 10% fidelity level) was the least used medicinal plant in the selected study area. Roots (66%) were the dominant plant part utilised to prepare remedies for treating childhood ailments. As a result, three medicinal plants (*B. montana*, *S. aculeatissimum*, and *Aloe grandidentata*) were chosen for further investigation due to their abundance in the study area as well as the lack of focused and comprehensive research on their medicinal properties concerning ailments in children.

The presence of phytochemicals such as alkaloids, flavonoids, glycosides, phenols, phlobatannins, saponins, steroids, tannins, and terpenoids was analysed qualitatively in acetone, methanol and water extracts from *B. montana*, *S. aculeatissimum*, and *A. grandidentata*. Terpenoids were abundant in the all the extracts except the acetone extract of *A. grandidentata* and were the only phytochemicals detected in the water extract of *B. montana*. Flavonoids and Saponins were the least abundant phytochemicals in the extracts tested.

The cytotoxicity evaluation of extracts *from the three plants* was conducted using the Hoechst 33342 and propidium iodide (PI) dual staining method. Acetone and methanol extracts of *S. aculeatissimum* exhibited toxic effects at all tested concentrations. However, the water extracts of *S. aculeatissimum*, *B. montana*, and *A. grandidentata* demonstrated low or no cytotoxicity, while the methanol extracts of *A. grandidentata*, had no harmful effects on Vero cells. The minimal cytotoxic potential of water extracts is particularly significant for their traditional use in treating various illnesses in children.

The current study utilised both Gram-negative and Gram-positive bacterial species, including *Bacillus cereus, Clostridium perfringens, Enterobacter hormaechei, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, and Streptococcus pyogenes* in the evaluation of the antibacterial activity *of A. grandidentata, B. montana, and S. accutisimum extracts.* Methanol and acetone extracts of *B. montana* exhibited antibacterial activity against 9 and 4 bacterial species, respectively, with MIC values ranging from 2.5 to 1.25 mg/ml. The methanol and acetone extracts of *S. aculeatissimum* demonstrated the lowest MIC values of 2.5 to 0.625 mg/ml against 9 and 3 bacterial species, respectively. Additionally, *A. grandidentata* methanol and acetone extracts showed activity against 9 and 3 bacterial species at MIC values of 2.5 to 0.6 mg/ml. Documenting these plants will help preserve this knowledge for future generations and serve as a foundation for developing new drugs to treat childhood illnesses. The phytochemical analysis, toxicity, and antibacterial activity evaluation of *A. grandidentata*, *B. montana*, and *S. accutisimum* extracts justify using the plants to treat some childhood diseases mentioned in the study area.

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ABBREVIATIONS

%	Percentage
µg/Ml	Microgram per millilitre
ATCC	American Cell Culture Concentration
CAFSaB	Centre for Applied Food Sustainability and Biotechnology
CDC	Centre for Disease Control and Prevention
DMSO	Dimethyl Sulfoxide
DPPH	2, 2- dipheny- 1- picrylhydrazyl
g/L	Gram per Litre
GAE/g	Gallic acid equivalent per gram
Mg/ml	Milligram per millilitre
MIC	Minimum inhibitory concentration
mL	Millilitre
mm	Millimetre
mM	Millimolar
NSAID	Non-steroidal anti-inflammatory drugs
RIF	Rifampicin
SEM	Scanning Electron Microscopy
TB	Tuberculosis
TEM	Transmission Electron Microscopy
TLC	Thin Layer Chromatography
UNICEF	United Nations Children's Fund
WHO	World Health Organization

CHAPTER 1
BACKGROUND

1.1 Introduction and Rationale

Children are vulnerable to various illnesses and diseases, forming a large portion of the global disease burden (Donna & Chris, 2013). Children's immune systems are vulnerable, making them more susceptible to higher mortality risks (Brown, 2017; Donna & Chris, 2013; Lopez et al., 2006). This vulnerability is caused by several age-related issues, such as immune prematurity (Shaheen et al., 2017). Children with compromised immune systems experience a common range of ailments such as stomach-ache, fever, mucositis, vomiting, constipation, dyspepsia, pneumonia, wheezing, intestinal parasites, dysentery, convulsion (seizure), teething, measles, mumps, and eye flu (Allen, 2016; Dixit, 2011). Insufficient healthcare services and limited access to basic needs such as clean water and food in rural areas increase the chances of children acquiring diseases. Diseases affect children physiologically, mentally, socially, and physically, resulting in disability and, in extreme cases, death, significantly influencing children's quality of life (Allen, 2016; Khandaker et al., 2014).

Infectious diseases such as pneumonia, diarrhoea, and malaria are the main contributors to the mortality of children worldwide. Statistics recorded in 2021 by the United Nations International Children's Emergency Fund (UNICEF) indicated five million deaths in children globally (UNICEF, 2023; Ndlovu et al., 2021). Africa has over 70% of ailments such as pneumonia, diarrhoea, malaria, measles and acute otitis media that are common in children. In South Africa, childhood infections cause a heavy burden in terms of financial cost, health services and mortality (Jenkins, 2016).

South Africa has a high use of synthetic medicine for the management of childhood diseases. The frequently used drugs are acetaminophen, ibuprofen, and amoxicillin, salbutamol used for various ailments such as fever, pain, infections, asthma symptoms, inflammation and many more (Sakulchit & Goldman, 2017). However, the use of these synthetic medicine in the paediatric population leads to several side effects such as allergic reactions, gastrointestinal issues, drowsiness, behavioural changes, adverse effects on growth and developments, organ toxicity, increased risk of infections, antimicrobial resistance (Quaglietta et al., 2021; Dwyer & Bloch 2019;

Dadgostar, 2019; Fernandes & Norman, 2019; Sammons & Choonara, 2016; Philip, 2014; Cheng et al., 2011). The abovementioned side effects significantly impact children's quality of life (Ndhlovu et al., 2021). Therefore, there is a need to search for alternative treatments from medicinal plants that may be safe, effective, and cheap (Nieto, 2020; Mustafa, 2017).

An estimated 80% of the world's population, especially those living in rural and secluded areas, heavily rely on medicinal plants to treat diseases (Ekor, 2014). Throughout the world, the utilisation of medicinal plants for promoting children's health and overall wellness has been acknowledged for a considerable period (Ndhlovu et al, 2021). It is unsurprising considering that 50,000 plant species are utilised worldwide for medicinal purposes due to their availability and cultural acceptance (Chen et al., 2016). Moreover, the prevailing challenging economic conditions in many rural areas and the limited availability of modern medicine have led to a growing preference for the therapeutic use of medicinal plants (Ndhlovu et al., 2021).

Traditional knowledge of medicinal plants has been passed across generations mainly through oral tradition, especially in Southern Africa (Maluleka, 2017). However, the absence of preservation efforts and the impact of industrialisation, urbanisation and modernisation are somewhat contributors to the erosion and loss of indigenous knowledge (Fernández-Llamazares et al., 2021; Van Wyk & Prinsloo, 2018; Senanayake, 2006). Traditional knowledge on medicinal plant resources also contributes to the conservation and sustainability of biological diversity and needs to be recorded (Seile et al., 2022). These records can be in the form of these guidebooks or catalogues. A catalogue of medicinal plants includes details such as the scientific name of the plants, the common and local names, botanical descriptions, the plant part used, preparation and dosage, and their secondary metabolites (Van Wyk & Prinsloo, 2018). The mentioned details are a valuable tool for researchers and the public because they serve as a reference that will be available for future generations. Therefore, the current study investigated ethnopharmacological medicinal plants used to treat and manage Thaba' Nchu childhood ailments.

The medicinal properties of plants are derived from secondary metabolites. Hence, traditional indigenous knowledge must be incorporated to produce novel drugs (Maroyi, 2017). There is a voluminous amount of undocumented medicinal knowledge amongst the elders. Biological diversity should be conserved and sustained by applying traditional knowledge since it has deteriorated in the latest generation due to economic and social changes. The documentation of this knowledge is of paramount importance for researchers and the public because they serve as a reference that will be available for future generations.

1.2 Research Questions

This study was conducted to address the following research questions:

- Which medicinal plants do local traditional medicinal practitioners in Thaba ‘Nchu use to treat childhood illnesses and infections, and how do they prepare the remedies?
- Do the plants used for the treatment of childhood ailments have antimicrobial properties?
- What are the phytochemical constituents in the plants used for childhood infections?
- Are these plants safe for use in children?

1.3 Problem Statement

Childhood illnesses contribute significantly to the global burden of disease (Donna & Chris, 2013). Children are exposed to painful infections, which weaken their immune system; hence, they suffer disproportionality in terms of mortality risk (Brown, 2017; Donna & Chris, 2013; Lopez, 2006). Children’s immune systems develop, so their lives and those around them are affected when they become ill. Children can be affected biologically, psychologically, socially and physically, leading to disabilities or even death (Allen, 2016; Khandaker et al., 2014). According to modern healthcare or clinical practice, antimicrobial treatments are a prerequisite for the management/treatment of different infections. However, the indiscriminate use of these antimicrobial treatments in the paediatric population is high, leading to antimicrobial resistance (Buccellato et al., 2015). Antimicrobial resistance is a natural phenomenon that occurs in bacteria when antibiotics are overused, rendering antibiotics previously necessary in treating infections caused by these bacteria obsolete. Adverse and deleterious effects have been associated with antibiotic resistance, including treatment failure, extended hospital stay, increased cost of therapy, unpleasant side-effects of drugs, as last-line and more potent antibiotics are employed in addition to substantial financial constraints on the health care facilities alongside increased morbidity and mortality, etc. (Manyi-Loh et al., 2023; Friedman et al., 2016). Antibiotic resistance is a global menace that merits critical attention as it reduces the number of drugs available to combat bacterial infections. Therefore, alternative approaches/sources of treatment become obvious. The search for alternative antimicrobials from medicinal plants, which may be safe, effective and cheap, is considered (Nieto, 2020; Mustafa, 2017.

Over a fifth (22%) of the children in South Africa live far from primary health care facilities. However, the country employs a healthcare delivery strategy based on a decentralised primary healthcare system at the district level (Hall & Sambu, 2016). This challenge could be mitigated using available resources, including indigenous health knowledge lying dormant at the community level, especially in rural areas. Indigenous knowledge in Southern Africa is transmitted orally (Van Wyk & Prinsloo, 2018; Senanayake, 2006), and it is not documented or archived, thus indicating threats to extinction. Equally valuable knowledge about the use of medicinal plants is threatened. Additionally, the population could increase in marginal areas, leading to deforestation and the loss of medicinal plants (Zerabruk & Yirga, 2012). Apparently, the documentation of indigenous knowledge of the utilisation of medicinal plants in the form of accessible catalogues is imperative.

1.4 Aim and Objectives

This study aims to compile a catalogue of medicinal plants used to treat childhood infections in Thaba ‘Nchu, Free State, South Africa and to evaluate the antimicrobial activity for the selection of plants.

1.4.1 Specific objectives

To achieve the overall objective, specific objectives were presented as follows:

- To create a record of medicinal plants utilised for treating common ailments in children.
- To determine the secondary metabolites found in selected plant extracts.

- To evaluate the *in vitro* antimicrobial activity of the selected plant extracts.
- To examine the cytotoxic effects of the plant extracts on Human Vero cells.

1.5 Study Layout

The objectives were achieved through the steps outlined in Figure 1.1. An ethnobotanical survey was carried out to document the medicinal plants used to treat childhood ailments in Thaba 'Nchu. The ethnobotanical data were analysed to identify the most used plants in the area. The plant extracts were further investigated for their bioactive compounds, antimicrobial activity and cytotoxicity.

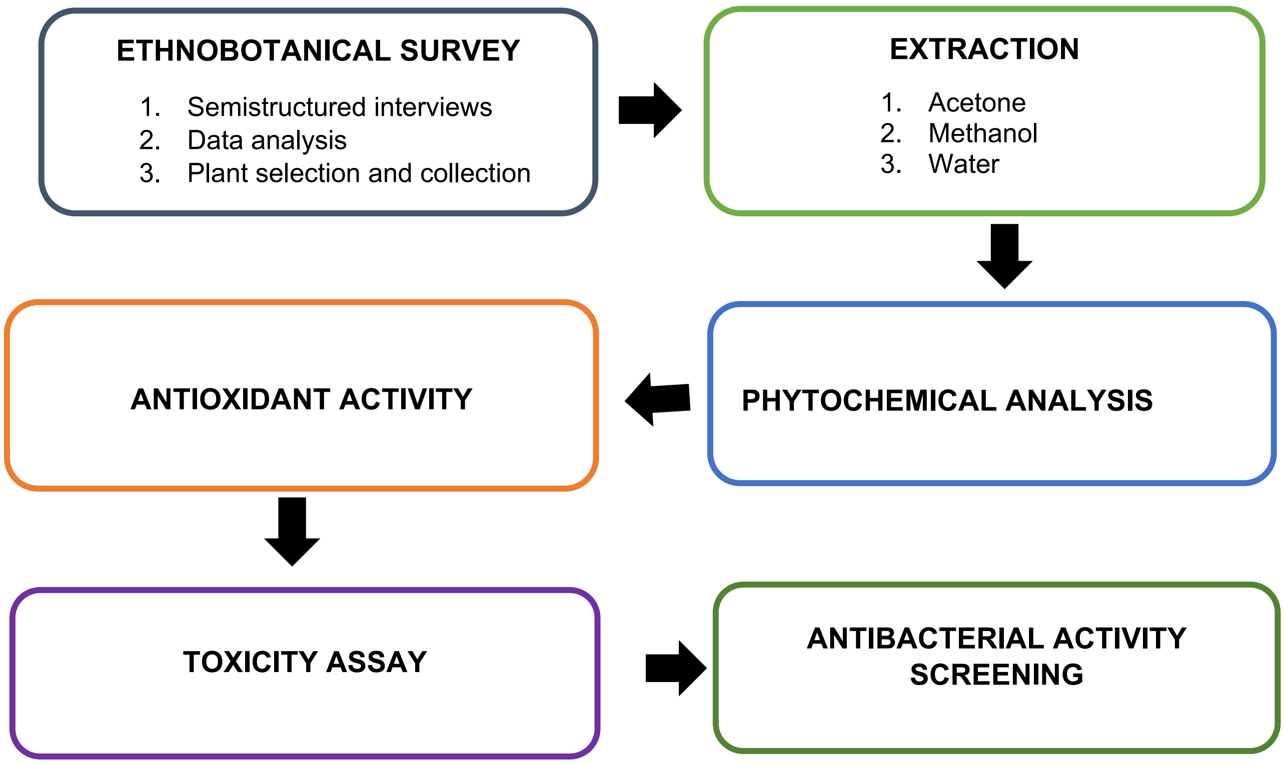

Figure 1.1: Procedures followed to achieve the objectives of this study

1.6 Study Overview

The current study consists of seven chapters. **Chapter 1** outlines the background, introduction, rationale, aims, objectives, and study outline. The literature review, ailments in children and secondary metabolites are given in **Chapter 2**. The medicinal plants used for treating common ailments in children of Thaba 'Nchu are documented in **Chapter 3** as an ethnobotanical survey. **Chapter 4** is the centre of phytochemical screening, total phenolic content, and total flavonoid content of *Aloe grandidentata,* *Berkheya Montana and Solanum aculeatissimum*. **Chapter 5** presented the *in vitro* cytotoxicity of these plant extracts. The antibacterial activity of the three plants was evaluated in **Chapter 6** using the microdilution method. The overall discussion and conclusion of the results reported in this study, as well as the conclusions and recommendations, are made available in **Chapter 7**.

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CHAPTER 2
LITERATURE REVIEW

2.1 Introduction

Development refers to the sequence of changes that occur from conception throughout the lifespan. It encompasses various domains, including a biological focus on physical growth and changes in the body (Keenan et al., 2016). Children play a crucial role in shaping the future due to their energy and potential. Early childcare experiences influence a child's growth and progress. Therefore, their proper development is essential for improving the world (Waldfogel, 2010).

Ensuring a child's future success is best achieved through investment in early childhood development. Allocating financial resources toward fostering children's growth and maximising their potential can yield substantial advantages for economies and societies because early childhood is the cornerstone of an individual's health and overall well-being (Wardlaw et al., 2013). The nation's development and success depend on its children's survival and well-being. In 2014, children comprised 34% of the total population, representing 29% of South Africa's population (Hall & Sambu, 2019; Buchner-Eveleigh, 2016). Such data should allow the government to tighten available health services.

2.2 Children's Right to Good Health

Good health is vital for human well-being, and compromised health in childhood significantly restricts the ability to experience life fully (Vaux, 1976). The right to health care establishes that all individuals are entitled to the "highest standard of health" (Gulliford & Morgan, 2013). In this context, every child deserves timely access to appropriate health services (Buchner-Eveleigh, 2016; Goldhagen et al., 2015). Despite the centrality of child health within primary health care programs, global child mortality remains alarmingly high: approximately 7.6 million children die annually, with more than 70% of these deaths attributable to preventable conditions such as diarrhea, pneumonia, and malnutrition.

2.3 Challenges of Good Health Services for Children

2.3.1 Lack of service delivery

Owing to the lack of a delivery system for the past 30 years, health systems worldwide have faced significant challenges. We live in a rapidly changing world that influences individual behaviours, even leading some people to relocate from rural areas to towns and cities (Malakoane et al., 2020). Access to healthcare can be limited for various reasons. Providing quality health care in South Africa is a constitutional obligation (Maphumulo & Bhengu, 2019). Although “access to health care” means having the opportunity to use the health care (Gulliford & Morgan, 2013), public health services do not meet the basic “standards for care and the needs of patients” (Maphumulo & Bhengu, 2019).

2.3.2 Poverty

Children represent the most susceptible part of society (Donna & Chris, 2013). Most children are cared for by their parents, who are primarily responsible for meeting their needs. However, poverty often makes this difficult. In cases where parents lack financial resources and rely on the state for healthcare services, children have the right to claim access to these services (Buchner-Eveleigh, 2016). It has been noted that children encounter unique obstacles concerning their right to health. Their physical and mental development makes them especially vulnerable to health challenges, including malnutrition and various illnesses (Heitkamp, 2018).

2.3.3 Diseases in children

The global annual estimation of preventable deaths in children is seven million (Tugume & Nyakoojo, 2019). There is a vulnerability to numerous types of illnesses in children due to their developing immune system and nutritional inadequacy, which are the main characteristics of illnesses in children (Shaheen et al., 2017; Donna & Chris, 2013). In this light, immunocompromised children are at greater risk of acquiring specific infections (Allen, 2016). Seven out of ten of the 10 million child deaths each year are linked to causes such as pneumonia and diarrhoea (Donna & Chris, 2013). The most common infections that affect children are respiratory, urinary, liver, skin, throat and gastrointestinal infections and kidney disorders (Shaheen et al., 2017; Mahady, 2005; Palombo & Semple, 2001). Some diseases that are of national importance are outlined below.

2.3.3.1 Stomach flu (Gastrointestinal tract illness)

Stomach flu is a collective term for gastrointestinal tract ailments/infections that result in vomiting, stomach ache, diarrhoea (Tshikalange et al., 2016). In some parts of Africa and South Africa, diarrhoea accounts for 46% and 19% of deaths for children, respectively (Awotiwon et al., 2016). Moreover, in South Africa, there are over 60000 cases of childhood diarrhoea per month and approximately 9000 child diarrhoeal deaths yearly (Chola et al., 2015). Diarrhoea is caused by various bacteria (*Campylobacter*, *Clostridium difficile*, *Escherichia coli*) and parasitic organisms such as *Giardia* or *Campylobacter* (Saaed & Ongerth , 2019. Children are more susceptible to gastrointestinal infections, which compromise body parts such as mouth, oesophagus, and small and large intestines, as shown in Figure 2.1. The drugs available for the treatment of gastrointestinal infections include: penicillin, amoxicillin, clarithromycin, azithromycin, albendazole, ceftriaxone, and cimetidine (Brink et al., 2016; Wittenberg, 2012). The overuse of these drugs produces diverse side effects (Table 2.1) such as chest pain, chills, cough, painful or difficult urination, pinpoint red spots on the skin, and bleeding gums. As a result, it is necessary to seek alternative drugs for addressing gastrointestinal disorders that come with fewer adverse effects. *Flourensia cernua, Mentha spicata* and *Phoradendron californicum* have potential benefits for gastrointestinal health (Julián-Flores et al., 2025).

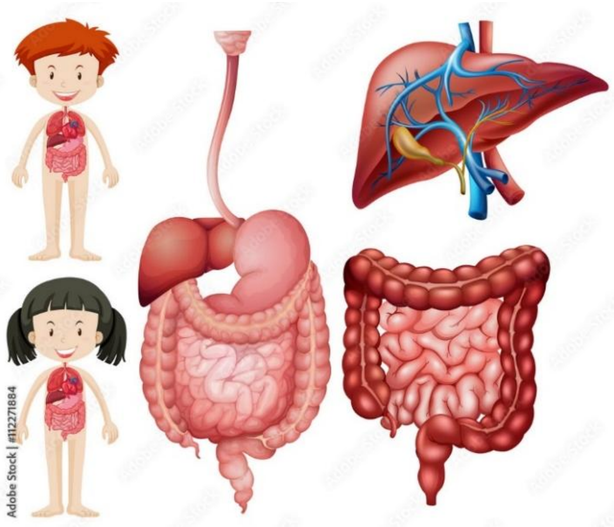


Figure 2.1: Organs affected by gastrointestinal tract infection

2.3.3.2 Upper respiratory tract infections (URTI) / Common cold

The common cold is classified as an infection affecting the nose, throat, and sinuses, spreading from child to child. The affected body parts are the upper airway, including the nose, sinuses, pharynx (throat), and larynx (voice box) (Pappas, 2017). Viruses, including rhinoviruses, coronaviruses, adenoviruses, and influenza viruses, primarily cause URTIs. The presence of rhinovirus infection triggers a concurrent inflammation of the paranasal sinuses. Bacterial infections can sometimes complicate URTIs, leading to conditions like bacterial sinusitis or streptococcal pharyngitis, pneumonia, meningitis, sepsis, and bronchitis (Hussain & Hussain, 2020; Thomas & Bomar, 2018). According to Cotton et al. (2008), the onset of the URTI in children is marked by a feeling of congestion in the nasal passages and irritation in the throat, usually accompanied by a mild increase in body temperature, reduced appetite, and muscle discomfort. The act of sneezing coincides with the emergence of a clear, watery discharge from the nose. This state can persist for as long as ten days in over one-third of individuals affected (Wu et al., 2022).

The primary objective of treating URTI is to alleviate the symptoms. A range of medications with different mechanisms of action is available to address these issues. These include adrenergic agonists, anticholinergics, antihistamines, antitussives, and expectorants (Ferrara et al., 2015). Common components found in these drugs encompass first-generation antihistamines, antipyretics such as paracetamol, and anti-inflammatory agents like ibuprofen (Farzam et al., 2019). Cough suppressants like dextromethorphan, expectorants such as guaifenesin, and decongestants like pseudoephedrine and phenylpropanolamine are also frequently present in these formulations (Korppi et al., 2022). The treatment of URIT has side effects, as indicated in Table 2.1.These side effects can be made better by the use of alternatives such as *Echinacea purpurea, Hedera helix, Pelargonium sidoides, Hypoxis hemerocallidea* medicinal plants (Ndhlovu et al., 2023).

2.3.3.3 Lower respiratory tract infections

Lower respiratory tract infection results from a viral (bronchitis and bronchiolitis) and bacterial (pneumonia) infection. According to van Eyk (2019), lower respiratory tract infections significantly contribute to childhood mortality in South Africa. Factors such as malnutrition, poor access to healthcare, and overcrowded living conditions can increase the risk and severity of these infections. Pneumonia affects the lungs and it is mostly caused by bacteria such as *Streptococcus pneumoniae, Staphylococcus aureus* and *Klebsiella pneumonia* (Sattar et al., 2023; Dixit, 2019).

Cough, elevated body temperature, discomfort in the chest, rapid breathing, and the generation of phlegm are common indications. Individuals with pneumonia might additionally manifest symptoms unrelated to breathing, including cognitive confusion, head pain, muscle aches, abdominal discomfort, queasiness, retching, and diarrhoea (Dangor et al., 2021; Donna & Chris, 2013). The primary objectives in managing LRTI is to enhance the quality of life by preventing pulmonary sequelae, diminishing cough, averting flare-ups, increasing physical endurance, optimising lung development where feasible, mitigating additional lung damage (via inflammation management, exacerbation prevention, and addressing root causes), and minimising potential complications (Burney et al., 2017).

Penicillin, ampicillin and aminoglycosides are the most commonly used therapies for this infection (Ampath, 2017). Patients with no access to effective medication are at high risk of developing major complications (such as septic shock, arthritis, osteomyelitis, meningitis, myocarditis and pericarditis) and death. Natural sources such as medicinal plants that include *Acacia modesta, Alhagi maurorum, Allium sativum, Astragulus tragacantha, Bergenia stracheyi, Capsella bursapastoris, Cardia* *myxa, Carthamus tinctorius* and *Elephantorrhiza elephantine* will limit these risks (Donà et al., 2017; Alamgeer et al., 2018; Mashile et al., 2019; Ndlovu et al., 2023).

2.3.3.4 Tuberculosis (TB)

Approximately one million children are affected by tuberculosis, and over 400,000 of them are currently receiving treatment. In 2019, cases of TB in children under 15 years around the globe reached 1.2 million, making TB the top cause of mortality in children (Dwilow et al., 2022). South Africa has one of the highest burdens of TB in the world, and children are particularly vulnerable. TB can be transmitted from adults or other children, and without appropriate diagnosis and treatment, it can lead to severe illness and death (van Der Walt & Moyo, 2018; Churchyard et al., 2014). About 96% of children with TB die before treatment is initiated globally (Dodd et al., 2017). Tuberculosis has narrow symptoms, and it is the most unrecognised cause of ailments and death in children (Perez-Velez & Marais, 2012). According to Attah (2018), TB infection in children and adults is the same, though children suffer the most consequences. The development of tuberculosis (TB) is influenced by factors such as immune system weakness, severe malnutrition, inadequate immunization, overcrowded living conditions, high population density, and limited access to proper treatment and medication. (VanValkenburg et al., 2022; Reddy et al., 2021). Figure 2.2 illustrates how *Mycobacterium tuberculosis* can infect nearly any organ, although the most common clinical signs and symptoms are located within the thoracic cavity and peripheral lymph nodes (Carabalí-Isajar et al., 2023). Plants such as *Agapanthus inapertus, Artemisia afra, Berchemia discolour, Bridelia micrantha, Cannabis sativa, Carica papaya, Citrus lemon, Combretum hereroense, Eriobotrya japonica, Eucalyptus camaldulensis, Eucomis pallidiflora, Hypoxis hemerocallidea, Lippia javanica, Myrothamnus flabellifolius, Salix mucronata, Terminalia sericea, Warbugia salutaris and Zanthoxylum capense* can be used for Tuberculosis management (Green et al., 2010; Semenya & Maroyi, 2019; Ndlovu et al, 2023).

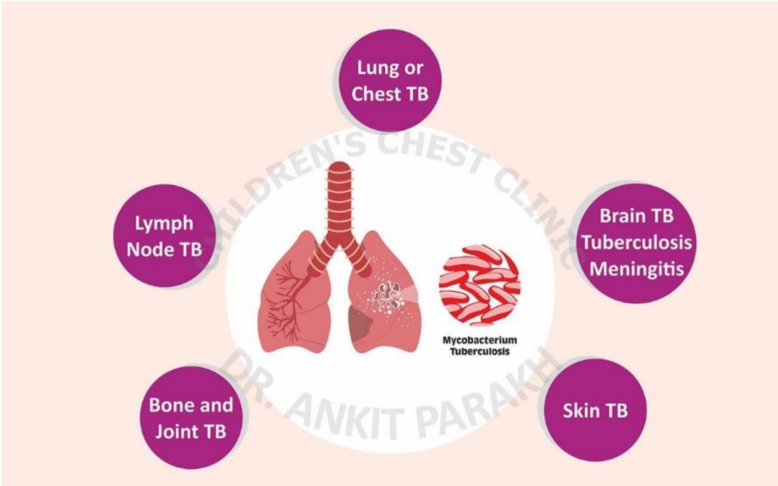


Figure 2.2: Different types of TBs that may affect children

2.3.3.5 Fontanelles abnormalities

The fontanelles are openings covered by membranes with two or more adjacent cranial bones. A newborn possesses six fontanelles: the anterior and posterior, with two on the sides at the back and two on the sides at the front of the head. This fontanelle takes on a diamond or rhomboid shape and is positioned at the intersection of the frontal and parietal bones (Woldeyes et al., 2020). A normal fontanelle should range between 5mm and 7mm, closing by the second month of birth. A fontanelle is considered abnormal when it is large or has a delayed closure (Figure 2.3) (Kiesler & Ricer, 2003). Achondroplasia, congenital hypothyroidism, craniosynostosis, Down syndrome, hydrocephalus, malnutrition, Meknes syndrome, microcephaly, rickets, Osteogenesis imperfecta and increased intracranial pressure are conditions that are linked to an enlarged fontanelle or delayed fontanelle closure. Infants with fontanelle abnormalities present an expanded head, a nasal bridge positioned lower than usual, a noticeable forehead prominence, and a shortened limb upon birth (D'Antoni, et al., 2017; Kiesler & Ricer, 2003).

Most abnormalities of the fontanelle require surgical intervention. These procedures aim to reduce pressure on the brain, reshape the skull, and support normal brain development (Sharma, 2013). Thyroid hormone replacement therapy is used to promote typical growth and development, which also encourages timely fontanelle closure. Bisphosphonates are prescribed to improve bone strength and are used alongside surgery when fractures occur (Boyce et al., 2014). Children diagnosed with

Menkes syndrome receive copper-histidine treatment. In addition, overall development should be supported through adequate nutrition that provides sufficient calories, protein, vitamins, and minerals. Plants used for the management of ailments that affect the fontanelle includes *Boscia foetida, Bulbine frutescens, Centaurea scabiosa, Cotyledon orbiculata, Disparago anomala, Gomphocarpus fruticosus, Helichrysum paronychioides, Hypoxis hemerocallidea, Siphonochilus aethiopicus, Solanum campylacanthum, Solanum lichtensteinii, Withania somnifera* (Ndhlovu et al., 2023).

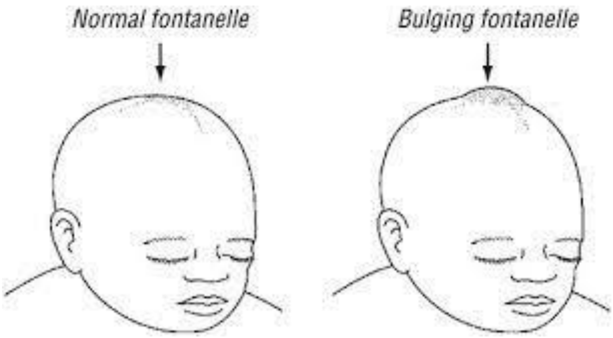


Figure 2.2: Difference between a normal and a bulging fontanelle (WHO, 2000)

2.4 Current drugs used to treat childhood ailments and their side effects

The treatment of childhood ailments has significantly improved with the availability of a range of medications designed to alleviate symptoms and promote recovery. Commonly used drugs in paediatrics include antibiotics for bacterial infections, analgesics for pain relief, corticosteroids for respiratory conditions, and antihistamines for allergic reactions. Antibiotics, such as amoxicillin, are frequently prescribed to treat infections like strep throat or ear infections in children. However, improper or excessive use of these drugs can lead to side effects, including gastrointestinal discomfort, allergic reactions, and the risk of antibiotic resistance (Table 2.1). Therefore, careful balance between therapeutic benefit and potential side effects has become a critical focus in paediatric care.

Table 2.1: Side effects of specific medicine administration in children

Side effect	Side effect explained	Example of drug/medication	Reference
Allergic reactions	Medication allergies in children can cause rashes, itching, swelling, and breathing problems, among other symptoms. Anaphylaxis is a severe allergic response that can be deadly.	Penicillin, Insulin, Chemotherapy drugs, Aspirin, Ibuprofen, Nonsteroidal anti-inflammatory drugs	Cheng, 2011
Gastrointestinal issues	Many medications can cause gastrointestinal side effects in children, including nausea, vomiting, diarrhoea, and stomach pain. These side effects can be particularly problematic in young children who may have dysarthria.	Tetracycline, Bisphosphonates, Potassium chloride, NSAIDs, Iron, Dopamine	Philpott et al., 2014 Fernandes & Norman, 2019
Drowsiness and sedation	Certain medications, such as antihistamines, cause drowsiness or sedation in children. This can affect their ability to concentrate, learn, or perform specific tasks.	Vallergan, Henergan	Iannelli, 2022
Behavioral changes	Some medications, such as certain types of antidepressants or stimulants used for attention deficit hyperactivity disorder (ADHD), may cause behavioural changes in children. These changes can include increased agitation, irritability, or mood changes.	Fluoxetine, Escitalopram, Sertraline, Citalopram	Dwyer & Bloch, 2019
Adverse effects on growth and development	Certain medications are used for long-term treatment and may impact a child's growth and development. Corticosteroids used to manage chronic conditions like asthma or autoimmune diseases can affect bone growth and increase the risk of osteoporosis.	Prednisone, Prednisolone, Dexamethasone	Gupta, 2012 Loke et al., 2014 Philip, 2014

Organ toxicity	The administration of medication can cause toxicity to specific organs in children. Some antibiotics, such as certain types of aminoglycosides, can potentially cause kidney damage or hearing loss.	Acetaminophen, Cisplatin, Methotrexate, NSAIDs, Aminoglycosides, Amphotericin	Faught et al., 2015 Mund et al., 2015 Sammons & Choonara, 2016
Increased risk of infections	Immunosuppressants used in organ transplant recipients or children with autoimmune disorders can weaken the immune system, increasing the child's susceptibility to infections.	Ibuprofen, Steroids, Azathioprine, Mercaptopurine, Tacrolimus, Methotrexate, Cyclosporine, Ampicillin Amoxicillin, Sulphathiazole, trimethoprim, Oxacillin	Orlicka et al., 2013 Quaglietta et al., 2021
Antimicrobial resistance	Antimicrobial resistance occurs when microorganisms such as bacteria, viruses, fungi, and parasites develop the ability to proliferate even when exposed to previously influenced medications. This adaptation allows these microorganisms to withstand the previously effective drugs against them.	Penicillin, Fluoroquinolone, Methicillin, Cephalosporins, Carbapenem	WHO, 2014 Dadgostar, 2019

2.5 Medicinal Plants

Traditional knowledge in South Africa is mainly passed down orally across generations. In this context, the absence of preservation efforts as well as. the impact of industrialisation, urbanisation and modernisation are contributors to the erosion and loss of indigenous knowledge (Fernández-Llamazares et al., 2021; Van Wyk & Prinsloo, 2018; Senanayake, 2006). The management of ailments with medicinal plants has been well practised before the emergence of conventional medicine. Medicinal plants are part of African traditional medicine, which is a system that is still widely used in the world today. It is utilised in all societies and is practised by most cultures (Teka et al., 2020). In rural areas of Ghana, herbal medicine is the first step in treating any illness (Ozioma & Chinwe, 2019). Traditional medicine is used by people of all ages, in both rural and urban settings to treat minor and chronic conditions. The use of traditional medicine has had a significant impact on people's lives, especially given the country's limited access to conventional healthcare.

According to the World Health Organization (WHO), traditional medicine is also known as botanical medicine, vegetable medicine, or phytomedicine. These preparations are derived from whole plants or plant parts such as the roots, leaves, bark and fruits as concoctions for human medicinal use (Ozioma et al., 2019). Traditional medicinal practitioners play a vital role in communities, exploiting their extensive knowledge of medicinal plants to create remedies for various diseases. The increasing use of medicinal plants in recent years highlights the discovery of potent bioactive compounds, which may serve as valuable leads in drug discovery. The ongoing interest in medicinal plants contribute to half of the drugs in the clinical world (Koparde et al., 2019). The challenges posed by conventional drugs can be effectively managed using medicinal plants, which present the best available option. Medicinal plants have a promising future on research and development of new therapeutic drugs (Shakya, 2016). Due to the toxicity and side effects of allopathic medications, the use of herbal medicine has increased in popularity, which has resulted in a rapid increase in the production of herbal drugs (Verma & Singh, 2008).

The role of medicinal plants as potent therapeutic agents has been recognised globally. Between 1950 and 1970, plant-based drugs such as deserpidine, rescinnamine, reserpine, vinblastine, and vincristine were introduced to the market (Verma & Singh, 2008). From 1971 to 1990, drugs including ectoposide, guggulsterone, teniposide, nabilone, plaunotol, lectinan, artemisinin, and ginkgolides were developed. Additionally, from 1991 to 1995, topotecan, gomishin, and irinotecan were introduced (Verma & Singh, 2008), motivating the ongoing search for medicinal plant-derived drugs that could be used to treat childhood diseases.

In South Africa, more than 90 medicinal plants are involved in developing various drugs, leading to a focus on new drug development and isolation of active compounds (Hatherley et al., 2015; Van Wyk, 2011). Plant-based medications entered modern medicine through their use as indigenous treatments, rooted in traditional beliefs, customs and oral traditions of communities and handed down through generations. The indigenous knowledge of TMPs to manage and treat childhood ailments requires scientific validation. This support will enable more medicinal plants to be marketed and documented, benefiting local communities (Giannenas et al., 2020).

2.6 Medicinal Plants and Secondary Metabolites

Various parts of medicinal plants are rich in secondary metabolites, which are organic compounds directly involved in the primary metabolic processes of growth and development (Elshafie et al., 2023). These secondary metabolites include alkaloids, terpenoids, flavonoids, phenols, tannins, steroids, and glycosides, and they play crucial roles in plant defence mechanisms against pathogens, herbivores and environmental stressors (Twaij & Hasan, 2022). These compounds exhibit significant pharmacological activities, making them valuable for drug discovery and development (Table 2.2). The biological activities of secondary metabolites has led to their use in the treatment of ailments ranging from cancer and cardiovascular diseases, infections and inflammatory conditions, including childhood diseases (Chaachouay & Zidane, 2024). As research continues to explore the potential of these compounds, medicinal plants remain a pivotal source of novel therapeutic agents.

2.6.1 Alkaloids

Alkaloids are a diverse naturally occurring chemical compounds with nitrogen atoms in their chemical structure. There are over 12,000 different alkaloids identified to date, and they include narcotic analgesics, morphine and codeine, apomorphine, morphine, strychnine, quinine, ephedrine, and nicotine, which are concentrated in specific plant parts such as leaves, seeds and bark (Gutiérrez-Grijalva et al., 2020; Eguchi et al., 2019). Alkaloids are an essential component of modern pharmaceuticals used in Parkinson’s disease, muscle relaxant papaverine, and the antimicrobial agents such as sanguinarine and berberine (Heinrich et al., 2021). Alkaloids are found in certain plant families including Amaryllidaceae, Lythraceae, Rhamnaceae and Solanaceae.

2.6.2 Flavonoids

Flavonoids are a diverse group of naturally occurring compounds found in plants, and they play a significant role in the plant kingdom. These compounds are known for their wide range of biological activities and have gained considerable medical attention (Nabil-Adam et al., 2023; Roy et al., 2022). Flavonoids have antimicrobial effects and are present in plants such as *Searsia undulate, Psidium guajava,* and *Aspalathus linearis*. Their subclasses include isoflavanoids, neoflavanoids, flavone, flavanones. (Jan & Abbas, 2018). Flavonoids have been widely researched for their potential health benefits. They are recognised for their antioxidant properties, allowing them to neutralise harmful free radicals in the body, thereby reducing oxidative stress and inflammation (Chaudhary et al., 2023). This may have a role in preventing chronic diseases such as cardiovascular disease, cancer, and neurodegenerative disorders (Ullah et al., 2020). Some flavonoids have demonstrated antiviral and antibacterial activities, making them potential candidates for developing pharmaceuticals or natural remedies for infectious diseases (Badshah et al., 2021).

2.6.3 Tannins

Tannins can be broadly categorised into hydrolysable and condensed (or non-hydrolysable) tannins (Dable-Tupas et al., 2023). Tannins are widely distributed across various plant parts and are particularly abundant in families such as Anacardiaceae (e.g., *Sclerocarya birrea*), Geraniaceae (e.g., *Geranium incanum*), and Combretaceae (e.g., *Terminalia arjuna*) (Ojewole et al., 2010; Ucella-Filho et al., 2022; Alshehri, 2024). These polyphenolic compounds exhibit diverse pharmacological properties, including anticancer, anti-inflammatory, and antioxidant activities, as well as notable cardiovascular and astringent effects (de Melo et al., 2023). Tannins, commonly present in plants such as green tea and oak bark, also demonstrate astringent and antimicrobial activities that contribute to wound healing and infection prevention (Rahman et al., 2021). In addition, their antiseptic properties underpin their therapeutic use in the treatment of gastrointestinal, respiratory, parasitic, neurological, dermatological, and hepatic disorders, including jaundice. They have further been employed in the management of urinary tract infections, inflammatory conditions, and malaria (Fraga-Corral et al., 2021).

2.6.4 Terpenoids and steroids

Terpenoids and steroids are the largest class of secondary metabolites, which include azadirachtin, artemisinin, menthol, sesquiterpenoids, carotene and steroids (Isah et al., 2018). They play an essential role in human physiology, where they are involved in regulating metabolism and immune response (Jahangeer et al., 2021). Terpenoids have demonstrated their effectiveness in preventing and treating various diseases, including cancer. They also exhibit properties such as antimicrobial, antifungal, antiparasitic, antiviral, anti-allergenic, antispasmodic, antihyperglycemic, anti-inflammatory, and immunomodulatory effects (Thoppil & Bishayee, 2011). Plants rich in terpenoids and steroids include Asparagaceae, Dioscoreaceae, Lamiaceae Typhaceae and Zingiberaceae (Olajide et al., 2024; Ghezal et al., 2017; Adham, 2015).

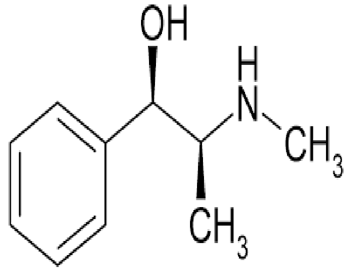
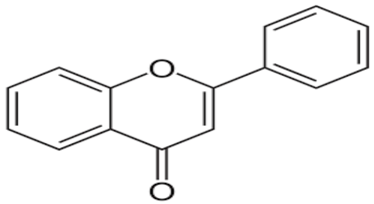
2.6.5 Coumarins

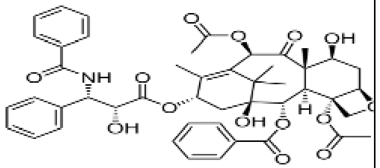
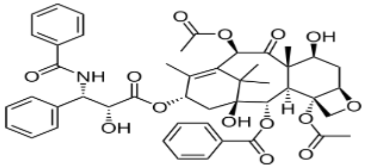
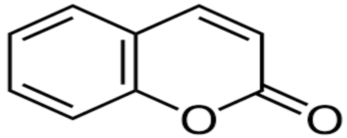
Coumarins belong to the benzopyrone family and are found naturally in many medicinal plants such as *Aloe ferox, Anthoxanthum odoratum, Bulbine natalensis, Coumarouna odorata, Cinnamomum cassia*, *Justicia pectoralis* and *Plumbango auriculata* (Sharifi-Rad et al., 2021). Coumarins have been investigated for their potential medicinal properties. Some coumarin derivatives, such as warfarin and acenocoumarin, are used as anticoagulant medications to prevent blood clotting. They work by interfering with the body's blood-clotting mechanisms (Sharifi-Rad et al., 2021; Verhoef et al., 2014). Coumarins exhibit a wide range of biological activities, including antioxidant, antifungal, anti-inflammatory, and antimicrobial (Annunziata et al., 2020; Naik et al., 2019; Pereira et al., 2018).

2.6.6 Phenolic compounds

Phenolic compounds are low molecular weight, naturally occurring compounds containing one or more phenolic groups. They are compounds produced by plants during their normal development or when they are in stressed conditions such as wounding, infection, and UV radiation exposure (Lin et al., 2016). Phenolic compounds are key bioactive constituents in medicinal plants and contribute to various pharmacological properties, including antioxidant, anti-inflammatory, antimicrobial, and anticancer activities (Sun & Shahrajabian, 2023). Phenolic acids, including gallic acid, caffeic acid, and ferulic acid, exhibit notable anti-inflammatory and pain-relieving properties, making them useful in treating inflammation and associated conditions. Lignans are utilized in several areas of healthcare and are considered highly important among the phenolic compounds examined for their health-related roles. They possess anticancer and hormone-modulating effects, offering potential benefits in hormone-related cancers (Rana et al., 2022). Phenolic compounds enhance the therapeutic value of medicinal plants, supporting their long-standing use in traditional medicine and increasingly drawing interest in modern pharmacological research.

Table 2.2: Secondary metabolites found in different plants

Secondary metabolites	Examples	Biological activities	Plants	Structure	References
Alkaloids	These are naturally occurring chemical compounds. Examples include morphine, strychnine, quinine, ephedrine, and nicotine.	They often have several pharmacological effects and are used as medications. The effects include narcotic analgesics, morphine, and codeine, apomorphine (a derivative of morphine) used in Parkinson's disease, the muscle relaxant papaverine, and the antimicrobial agents sanguinarine and berberine.	*Datura stramonium, Clivia miniate, Ziziphus mucronate, Punica granatum*		Rajput et al., 2022 Britannica Editors 2025
Flavonoids	They are plant metabolites that are also known as Vitamin B. Distinguishable flavonoids include isoflavonoids, neoflavanoids, flavone, and flavanones.	They have antimicrobial effects.	*Searsia undulata, Psidium guajava, Aspalathus linearis*		Janićijević et al., 2007; Samanta et al., 2011; Altemimi et al. 2017; Gutiérrez-Venegas et al., 2019; Galatro et al., 2024;

Tannins	Examples include gallotannin and condensed tannin.	They are rich in antiseptic effects and are often used to treat diarrhoea.	*Geranium incanum, Sclerocarya birrea*		
Terpenoids and steroids	They constitute the largest class of secondary metabolites, e.g., azadirachtin, artemisinin, menthol, sesquiterpenoids, carotene, and steroids.	Terpenoids demonstrate a broad spectrum of biological effects, including anti-inflammatory, antimicrobial, antiviral, analgesic, antitumor, and antifungal activities, among others	*Mentha longifolia Dioscorea dregeana Typha capensis Zingiber oficinale Drimia elata*		Altemimi et al., 2017; Maltseva et al., 2024; Khanam et al., 2025
Coumarins	Coumarins are found naturally in many plants. e.g., ethraquinones and naphthoquinones.	They are proven to exert antibacterial and antifungal activity	*Plumbango auriculata, Aloe ferox, Bulbine natalensis*		Sharifi-Rad et al., 2021; Tsivileva et al., 2022

2.7 Conclusion

This chapter reviews the profound effects of childhood diseases on global health care systems and examines medicinal plants used in treating these conditions. Furthermore, childhood diseases significantly contribute to global mortality rates, highlighting a critical public health challenge. These illnesses not only strain healthcare systems but also represent a significant cause of death among children, particularly in low- and middle-income countries where access to medical care may be limited. Medicinal plants that treat childhood diseases highlight their importance in traditional medicine and their potential as complementary therapies in modern healthcare. Medicinal plants are recorded to treat childhood conditions such as respiratory infections, gastrointestinal issues, skin disorders, etc. The therapeutic properties of these plants, attributed to the presence of bioactive compounds, highlight their relevance in paediatric care, particularly in areas where access to conventional drugs is limited. Flavonoids, phenolic acids, tannins, and lignans are particularly prevalent and studied for their therapeutic benefits. Flavonoids, such as quercetin, kaempferol, and catechins, are well-known for their antioxidant effects, which help neutralise free radicals and protect against oxidative stress-related diseases, including cardiovascular and neurodegenerative disorders. Therefore, it is essential to document and scientifically investigate the pharmacological properties of medicinal plants used by traditional healers to treat childhood diseases.

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CHAPTER 3

MEDICINAL PLANTS USED TO TREAT CHILDHOOD DISEASES IN THABA 'NCHU, FREE STATE PROVINCE, SOUTH AFRICA

3.1 Introduction

Diseases impact children physiologically, mentally, socially, and physically, resulting in disability and, in severe cases, death (Allen, 2016; Khandaker et al., 2014). In rural areas, poor healthcare services and limited access to necessities, including, clean water and food, contribute to higher childhood mortality rates (Ndhlovu et al., 2021). Children are more susceptible to infections than adults, increasing their risk of mortality (Brown, 2017; Lopez et al., 2006). Common diseases that affect children globally include gastrointestinal problems, respiratory, urinary tract issues, kidney disorders, liver conditions, ear, nose, throat diseases, eye infections, and dental anomalies (Shaheen et al., 2017). These conditions are attributed to biological vulnerability stemming from various age-related factors, such as immune system immaturity and nutritional deficiencies, which are key characteristics of illnesses in children (Shaheen et al., 2017). Reducing child mortality is a priority for Africa. Despite the use of curative treatments in hospitals, paediatric illnesses in South Africa continue to impose substantial financial, health service, and mortality costs (Simmons et al., 2021).

Although the prevalence of childhood illnesses varies significantly across different regions of the world (Sethuraman & Bhari, 2013), these diseases continue to be a significant cause of mortality in children (Brown, 2017). In addition to limited access to medication for treating childhood diseases in rural areas, the use of Western medicine faces challenges such as the emergence of multidrug-resistant strains of pathogens, leading to reduced drug efficacy. Additionally, conventional drugs can cause side effects in some children, including vomiting and allergic skin reactions (WHO, 2021; Kulyar et al., 2020). The shortage of health facilities in rural areas has led communities to rely on available resources, such as medicinal plants, to address childhood diseases. Medicinal plants are a readily available natural resource for many rural communities (Okaiyeto & Oguntibeju, 2021). Therefore, there is a demand for safe, efficient, affordable, and easily accessible alternative treatments from medicinal plants (Mustafa, 2017; Haq, 2004; Iwu et al., 1999).

Traditional medicine includes health practices, methods, knowledge, and beliefs that utilise plants for diagnosing, treating, and preventing illnesses and promoting overall well-being (Alzweiri et al., 2011; Lulekal et al., 2008). Most people rely on medicinal plants for primary health care needs (Srivastava et al., 1996). For example, the WHO reported that approximately 4 billion people rely on the healing properties of medicinal plants (Jamshidi-Kia et al., 2018). Herbal medicine offers a promising source of plant compounds that have been reported to exhibit various critical biological activities such as anti-inflammatory, antiviral, antitumor, antimalarial, antimicrobial, and analgesic effects (Shaheen et al., 2017).

Various studies have documented the use of medicinal plants for various ailments across different communities in South Africa (Moteetee & Kose, 2017; Balogun et al., 2016; Tshikalange et al., 2016; Possa & Khotso, 2015; Mahwasane et al., 2013). However, most studies have not specifically addressed ailments affecting children. In Thaba 'Nchu, people rely on traditional medicine informed by indigenous knowledge, but there is no documented information on the use of medicinal plants specifically for children in this area. Therefore, this study was conducted to document medicinal plants used to treat various illnesses in children in Thaba 'Nchu, Free State province, South Africa.

3.2 Materials and Methods

3.2.1 Study area

Thaba 'Nchu (29.197 S, 26.8209 E) is situated east of Bloemfontein, in South Africa's Free State province, covering an area of approximately 36.39 km^2 (Figure 3.1). The area lies within a grassland biome, characterised by warm summers and short, cold, dry winters. The rainy season extends from August to May, with vegetation thriving primarily between September and May (Geonames, 2022). The town consists of both urban and rural settlements, surrounded by land with a medium to high agricultural potential. Thaba 'Nchu's population of approximately 38,616 people is dominated by the Sotho and Tswana speaking people (Geonames, 2022). The area faces a high poverty rate; however, the local economy relies on food production, clothing, and other microbusinesses. As a result, many rural inhabitants are closely connected to using natural resources such as plants.

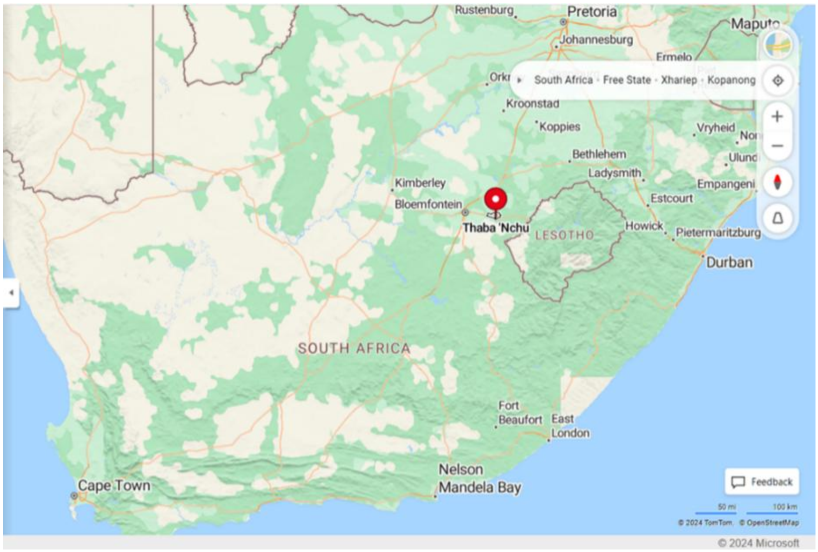

Figure 3.1: Map of South Africa showing Thaba 'Nchu (Source: Google Maps)

3.2.2 Data collection

The University Research and Innovation Committee (URIC) approved the study at the Central University of Technology. All ethical considerations regarding interactions with traditional healers were strictly observed. A traditional healers' association from the study area was used to recruit traditional medical practitioners (TMPs). Participants were then selected based on their willingness to participate. The aims and objectives of the study were explained to each participant in the local language, Sesotho, with the assistance of an interpreter when necessary, ensuring they fully understood what was required of them. Semi-structured interviews were conducted with 30 individual traditional healers. The importance of the participant's contributions to managing diseases in children in Thaba 'Nchu was emphasised. The questionnaire was designed to be voluntary and confidential, allowing respondents to skip any questions they found uncomfortable (Russell et al., 2005). The questionnaires solicited information on childhood diseases treated with medicinal plants, including the plant parts used, method of preparation, administration techniques, and dosages.

3.2.3 Voucher specimen collection

The area's chief TMP assisted with identifying and collecting the mentioned plants in the field. Furthermore, the collected plants were taken to the South African National Botanical Institute (SANBI) to verify and assign voucher specimen numbers.

3.2.4 Data analysis

The ethnobotanical data was recorded into Microsoft Word and an Excel spreadsheet. The data collected from the respondents were quantitatively analysed using the following indices.

3.2.4.1 Relative frequency of citation (RFC)

The Relative Frequency of Citation (RFC) determines the level of agreement among participants regarding the use of medicinal plants. The indices also show the local significance of each species. The RFC is calculated based on the percentage of participants who mentioned each plant species. Relative Frequency of Citation was calculated using the formula:

RFC = FC/N x 100

Where:

FC = number of times a particular species was mentioned.

N = total number of times that all species were mentioned.

The RFC value ranges between 0.00 and 1.00. It approaches 0 when no informants reference the plant as useful and approaches 1 when all informants consider it useful.

3.2.4.2 Informant Consensus Factor (ICF)

The ICF is used to measure the participant's knowledge of medicinal plants.

ICF = Nur ‑ Nt/Nur ‑ 1

Where:

NUR = number of use citations for each ailment

NT = number of plant species used.

The ICF value approaches 0 when plant selection is random and there is no exchange of information among participants. Conversely, the ICF approaches 1 when there is a clear selection of plants and active information exchange among participants.

3.3 Results and Discussion

3.3.1 Demographics

Six males (20%) and 24 females (80%) were interviewed in this study. The predominance of women in the survey may be attributed to their role as primary caregivers, making them more likely to address the healthcare needs of children. As shown in Figure 3.2, most respondents were between 50 and 59. This is consistent with recent ethnobotanical studies, which found that individuals in this age group typically possess a greater knowledge of medicinal plants (Wanjohi et al., 2020; Tefera & Kim, 2019).

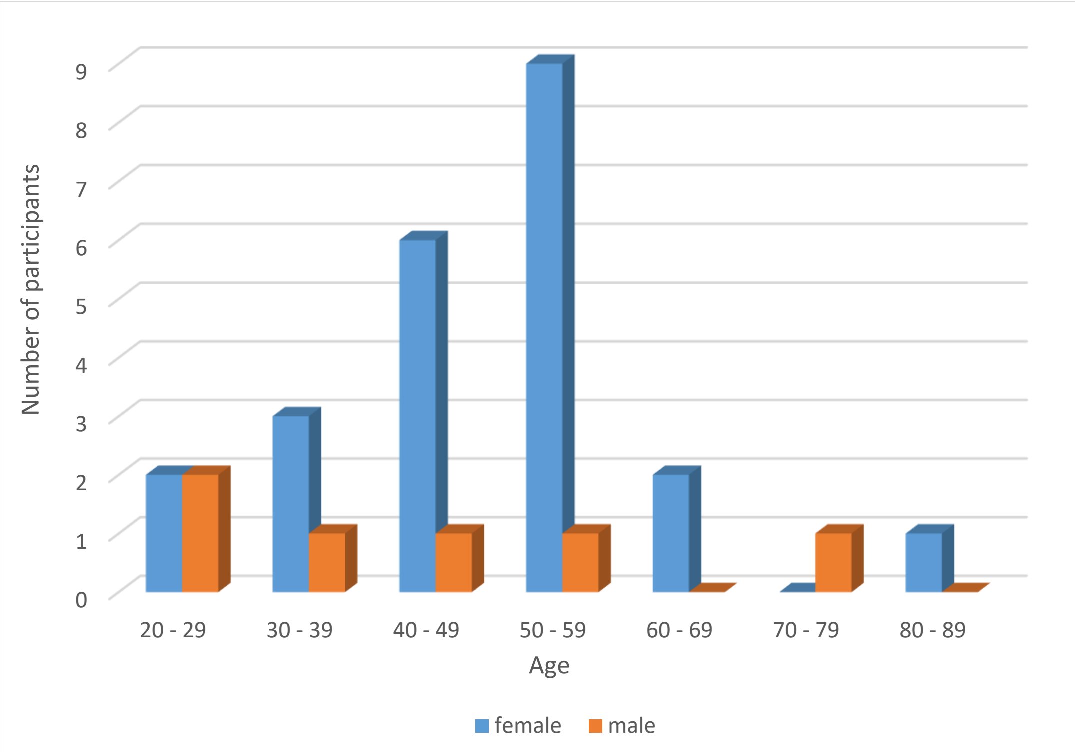

Figure 3.2. Demographic information of traditional medical practitioners who treat childhood illnesses in Thaba 'Nchu

3.3.2 Plants used to treat childhood diseases

The ethnobotanical survey revealed 60 medicinal plant species, belonging to 28 families that are used to treat childhood diseases in Thaba 'Nchu (Table 3.1) Plants most frequently mentioned for treating childhood diseases in this study include *B. montana* (23), *Pelargonium reniforme* (20), *Xysmalobium undullatum* (20), *Dicoma anamala* (17), *Solanum aculeatissimum* (13), *Polygala hottentotta* (10), *Allium sativum*

(7), and *Alepidea amatymbica* (6). In a similar study, Mhlongo and Van Wyk (2019) reported approximately 60 medicinal plants used to treat childhood diseases in KwaZulu-Natal. Plants from the genus *Berkheya* have been recorded in other studies to treat childhood diseases such as chest pains, stomach complaints, and sore eyes (Mhlongo & van Wyk, 2019; Hutchings & Scott, 1996). Medicinal plants from the genus *Solanum* have been used for a long time to treat abdominal discomfort, gastrointestinal disorders, earaches, skin rashes, scabies, and general body weakness (Asong et al., 2019; Mhlongo & van Wyk, 2019; Moffett, 2016; Bhat, 2014; Arnold & Gulumian, 1984). The recurrent use of genera such as *Berkheya* and *Solanum* across different regions underscores their longstanding role in traditional healthcare systems, particularly for conditions children.

Table 3.1: Medicinal plants used to treat childhood diseases in Thaba Nchu, Free State province, South Africa

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Achyranthes aspera Linnaeus. var. aspera	Lemanamana	Amaranthaceae	TN^{2}SMP1	Fontanelles	Roots	Decoction (Orally)	*Solanum aculeatissiumum*	3.33
Alepidea amatymbica Ecklon & Zeyher.	Lesoko	Apiaceae	TN^{2}SMP2	Sharp pain, chest sores, diarrhoea	Roots	Decoction (Orally)	-	20.0
Allium sativum Linnaeus.	Konofolo	Amaryllidaceae	TN^{2}SMP3	Fontanelles Sores in the mouth Ear Infection Sharp pain Chest pain	Tuber Leaves	Decoction (Orally)	*Berkheya multijuga* *Hirpicium armerioides* *Allium sativum*	23.33
Aloe greandidentata Salm.Dyck	Lekgala	Asphodelaceae	TN^{2}SMP4	Fontanelles Kwashiorkor Sores	Leaves	Decoction (Rectally) paste (Dermally)	-	10.0
Antedeschia aethiopica (L) Spreng	Mothebe	Araceae	TN^{2}SMP59	Eye infection	Whole plant	Decoction (Topically)	-	3.33
Anthospermum rigidum Ecklon & Zeyher. subsp. Rigidum	Phakisana	Rubiaceae	TN^{2}SMP5	Eye infection Tiredness	Whole plant	Decoction (Topically and orally)	-	6.67
Artemisia afra Jacq. ex Willd.	Lengana	Asteraceae	TN^{2}SMP6	Chest pain	Leaves	Decoction (Orally)	-	3.33

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Aster bakerianus Urtt Davy ex C.A. Sm.	Phoa	Asteraceae	TN^{2}SMP7	Fontanelles	Whole plant	Decoction (Orally)	-	6.67
Berkheya montana J.M.Wood & M.S.Evans	Mohatollo	Asteraceae	TN^{2}SMP8	Sharp pain Fontanelles Weakness/Tiredness/ Lethargy Chest Pain	Roots Roots Roots Whole plant	Decoction (Orally)	*Allium sativum* *Galium capense* *Capense Rubiaceae* *Gunnera perpensa*	76.67
Bulbine narcissifolia Salm-Dyck	Kgomoyabadisa	Asphodelaceae	TN^{2}SMP11	Sharp pain HIV (Immune boosting)	Roots Leaves and stem	Decoction (Orally)	*Dimorphotheca acutifolia Hermmania depressa* (HIV)	6.67
Chironia palustris Burch.	Lepshetlane	Gentianaceae	TN^{2}SMP56	Kwashiorkor	Roots	Decoction (Orally)	-	3.33
Clutia pulchella var. obtusata	Monyamafi	Euphorbiaceae	TN^{2}SMP12	Fontanelles	Roots	Decoction (Rectally)	-	3.33
Commelina africana (L.)	Tabolalefalo	Commelinaceae	TN^{2}SMP57	Sharp pain, Weakness/Tiredness, Rash Fontanelles Diarrhoea Fits/seizure	Roots Whole plant Leaves stem	Decoction (Orally) Decoction (Rectally)	*Xysmalobium undullatum*	23.33
Crabbea hirsute	Lephakhama	Acanthaceae	TN^{2}SMP13	Fontanelles	Whole plant	Decoction (Orally)	-	3.33
Cynodon dactylon (Linn.) Pers.	Mohlwatsepe	Poaceae	TN^{2}SMP14	Eye infection	Leaves	Decoction (Topical)	-	3.33
Dicoma anamala Harv. Form Sonderi	Hlwenya	Asteraceae	TN^{2}SMP16	Chest pains	Roots	Decoction (Orally)	*Dicoma anomala* *Hermmania depressa* *Xysmalobium undullatum*	56.67

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Dimorphotheca acutifolia Hutch.	Phela	Asteraceae	TN^2SMP17	Fits/seizure Ear infection	Roots	Decoction (Orally)	-	16.67
Drimia depressa (Baker) Jessop	Moretele	Hyacinthaceae	TN^2SMP18	Sores	Roots	Topically	*Drimia depressa* *Elephantorrhiza elephantina*	3.33
Elephantorrhiza elephantina (Burch.) Skeels	Mositsane	Fabaceae	TN^2SMP19	Loss of appetite Sores	Roots	Topically	*Elephantorrhiza elephantina* *Drimia depressa,*	6.67
Erigeron bonariensis L.	Lehamonyane	Asteraceae	TN^2SMP60	Sores	Leaves	Decoction (Topical)	-	3.33
Eucalyptus sp.	Bloukomo	Myrtaceae	TN^2SMP21	Chest pain	Leaves	Decoction (Topically)	-	6.67
Eucomis autumnalis subsp. Clavata	Mathethebale	Hyacinthaceae	TN^2SMP22	Sharp pain, Diarrhoea	Roots	Decoction (Orally)	-	6.67
Galium capense subsp. Capense Linn. *von Staden*	Maboni	Rubiaceae	TN^2SMP15	Fontanelles	Roots	Topically	-	3.33
Gazania linearis var. linearis	Tsikitlane	Asteraceae	TN^2SMP24	Fontanelles, sharp pain stock Bite	Leaves or Roots	Decoction (Orally)	*Gazania linearis,* *Melolobium microphyllum,* *Solanum aculeatissimum,* *Polygala hottentotta* *Berkheya montana*	13.33

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Gerbera piloselloides (L.) Cass.	Tsebeyapela	Asteraceae	TN^2SMP25	Ear infection	Whole plant	Decoction (Orally)	-	3.33
Gomphocarpus fruticosus (L.) W.T.Aiton	Moethimolo	Apocynaceae	TN^2SMP26	Weakness/Tiredness	Roots	Inhalant (Nasally)	-	3,.3
Gunnera perpensa L.	Qobo	Gunneraceae	TN^2SMP27	Fontanelles	Roots	Decoction (Orally)	*Gunnera perpensa* *Galium capense* *Berkheya montana*	3.33
Haplocarpha scapose Harv.	Papetlwane	Asteraceae	TN^2SMP10	Fontanelles	Roots	Decoction (Orally)	-	3.33
Hebenstretia dura Choisy	Tshitabaloi	Scrophulariaceae	TN^2SMP28	Weakness/Tiredness	Whole plant	Decoction (Nasally and topically)	-	3.33
Helichrysum caespititium (DC) Harv.	Phateyangaka	Asteraceae	TN^2SMP29	Chest pain Weakness/tiredness	Whole plant	Decoction (Orally)	-	6.67
Hermmania depressa N.E.Br	Seletjana	Sterculiaceae	TN^2SMP30	Chest pain Diarrhoea Vomiting HIV (immune boosting)	Roots Whole plant Whole plant Roots	Decoction (Orally)	*Dicoma anomala and Xysmalobium undullatum, Pelargonium reniforme Hermmania depressa Dimorphotheca acutifolia*	26.67
Hirpicium armerioides (DC.) Roessler	Shweshwe	Asteraceae	TN^2SMP23	Fontanelles Sharp pain	Roots	Decoction (Orally)	*Solanum aculeatissiumum,*	20.00

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
							Malva parviflora, Achyranthes aspera, Pelargonium reniforme, Berkheya montana and *Pentanisia prunelloides*	
Ipomea crassipes Hook.	Maime	Apiaceae	TN^{2}SMP31	Fontanelles	Roots	Decoction (Orally)	-	3.33
Kedrostis capensis (Sond.) A.Meeuse	Sesepasadinoha	Cucurbitaceae	TN^{2}SMP32	Fontanelles, Stock Bite, Sore throat, diarrhoea	Tuber or Whole plant	Decoction (Orally)	*Polygala hottentotta, Gazania linearis, Dicoma anamala, Xysmalobium undullatum*	20.00
Leucosidea sericea Ecklon & Zeyher.	Cheche	Rosaceae	TN^{2}SMP33	Diarrhoea	Whole plant	Decoction (Orally)	*Leucosidea sericea, Xysmalobium undullatum*	3.33
Malva parviflora L. Malva sylvestris L. Malvaceae	Tikamotse	Malvaceae	TN^{2}SMP35	Fontanelles Swelling Sores	Roots Roots Whole plant	Powdered Inhalant (Nasally) Paste (Topically)	*Solanum aculeatissiumum, Salix mucronata*	10.00
Melolobium microphyllum (L.f.) Ecklon & Zeyher.	Mofahlatoeba	Leguminosae	TN^{2}SMP9	Sharp pain	Whole plant	Decoction (Orally)	*Solanum aculeatissimum Polygala hottentotta Berkheya montana Gazania linearis*	3.33

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Metalasia muricata R.Br.	Teayabarwa	Astaraceae	TN^{2}SMP58	Swelling Chicken pox	Roots Whole plant	Decoction (Orally)	*Scabiosa columbaria*	10.00
Monsonia attenuata Harv.	Maleleka	Geraniaceae	TN^{2}SMP36	Fontanelles	Bark	Decoction (Orally)	-	3.33
Morus alba (Morus alba Linn.)	Mmalebere	Moraceae	TN^{2}SMP37	Loss of appetite	Roots	Decoction (Oral)	-	3.33
Pelargonium reniforme Curt.	Kgwara	Geraniaceae	TN^{2}SMP38	Diarrhoea Chest sores Fontanelles Vomiting	Roots Roots Whole plant Whole plant	Decoction (Orally)	-	66.67
Pentanisia prunelloides subsp. latifolia (Hochst.) Verdc.	Setimamollo	Rubiaceae	TN^{2}SMP34	Sharp pain Swelling Sores	Roots	Decoction (Orally, dermally or topically)	*Pentanisia prunelloides* and *Berkheya montana*	13.33
Polygala hottentotta C. Presl	Lehlokwanalatse la	Polygonaceae	TN^{2}SMP39	Sharp pain, Fontanelles, Weakness/Tiredness, Diarrhoea Bronchiolitis Stork Bite	Roots Whole plant	Decoction (Orally)	*Berkheya montana* *Gazania linearis* *Xysmalobium undullatum* *Solanum aculeatissiumum,* *Gazania linearis,* *Kedrostis capensis*	33.33

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Punica granatum L. Lythraceae	Gerenate	Punicaseae	TN^2SMP41	Diarrhoea, Vomiting	Fruits	Maceration (orally)	-	10.00
Rumex lanceolatus Thunb	Kgamane	Polygonaceae	TN^2SMP42	Sores in the mouth	Roots	Decoction (Orally)	-	3.33
Salix mucronata Thunb. subsp. subserrata (Willd.) R. H. Archer & Jordaan	Moduane	Salicaceae	TN^2SMP43	Swelling	Whole plant	Decoction and Infusion (Dermally)	-	3.33
Salvia repens Burch. ex Benth. var. repens	Mosisidi	Lamiaceae	TN^2SMP44	Sores in the mouth	Roots	Decoction (Orally)	*Allium sativum, Sorghum caffrorum, Salvia repens, Rumex lanceolatus, Bulbine narcissifolia*	3.33
Scabiosa columbaria L.	Selomi	Dipsacaceae	TN^2SMP45	Swelling Chicken pox	Roots	Decoction (Orally)	*Scabiosa columbaria Metalasia muricata*	6.67
Schkuria pinnata (Lam.) Kuntze ex Thell.	Setswamadi	Asteraceae	TN^2SMP46	Diarrhoea Fontanelles	Roots Whole plant	Decoction (Orally)	-	10.00
Searsia erosa Thunb.	Tsilabela	Anacardiaceae	TN^2SMP47	Diarrhoea	Roots	Decoction (Orally)	-	3.33
Senecio asperulus DC.	Moferefere	Asteraceae	TN^2SMP20	Fontanelles Swelling	Whole plant Roots	Decoction (Orally) Infusion (Dermally)	*Senecio asperulus, Withania somnifera* *Senecio asperulus*	6.67

Scientific name	Local name	Family	Voucher number	Specific use	Plant part used	Mode of preparation (administration)	Accompanying plants	RFC (%)
Senecio asperulus DC.	Makgonatsohle	Asteraceae	TN²SMP48	Weakness/Tiredness	Roots	Decoction (Orally)	*Senecio asperulus* and *Berkheya montana*	3.33
Solanum aculeatissimum Jacq.	Thola	Solanaceae	TN²SMP49	Fontanelles, Chest pain, Diarrhoea Weakness/Tiredness Sharp pain	Whole plant Roots	Inhalant (Nasally)	-	43.33
Sorghum caffrorum Var.	Mabele	Poaceae	TN²SMP50	Sores in the mouth	Leaves and Stem	Decoction (Orally)	-	3.33
Tulbaghia acutiloba Harv.	Moelela	Alliaceae	TN²SMP52	Rash	Roots	Decoction (Nasally and rectally)	-	3.33
Tulbaghia alliacea L.f.	Sefothafotha	Alliaceae	TN²SMP51	Fontanelles	Roots	Decoction (Orally)	-	6.67
Wahlenbergia depressa J.M.Wood & M.S.Evans	Sephephetho	Campanulaceae	TN²SMP53	Sharp pain	Roots	Decoction (Orally)	-	6.67
Withania somnifera (L.)	Moferongope	Solanaceae	TN²SMP54	Fontanelles Tiredness, Weakness/Tiredness Diarrhoea	Whole plant Roots	Decoction (Orally)	*Withania somnifera* *Senecio asperulus*	10.00
Xysmalobium undullatum (L.) W.T. Aiton	Pohotshehla	Apocynaceae	TN²SMP55	Sharp pain, Ear infection Fontanelles Chest pain,	Roots Whole plant	Decoction (Orally) Infusion (Topically)	*Xysmalobium undulatum* and Commelina Africana, *Dicoma anamala*	66.67

Fontanelles = meningitis, encephalitis, hydrocephalus, hypoxic-ischemic injury, trauma, and intracranial haemorrhage

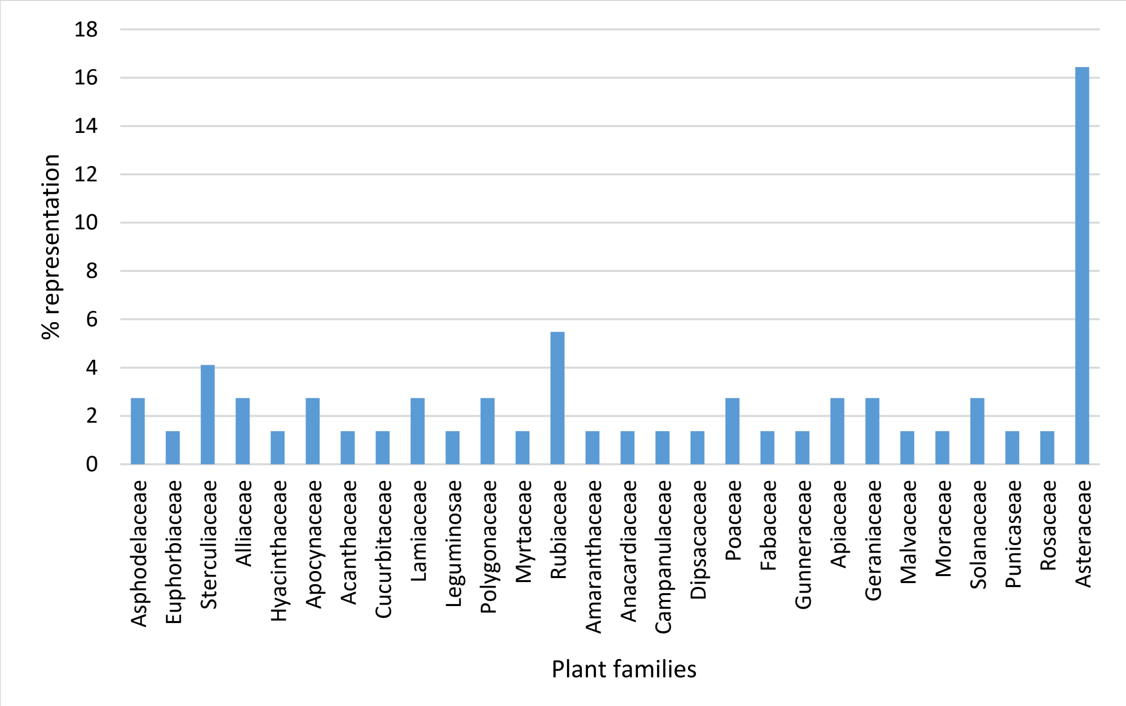

Figure 3.3: Families of medicinal plants used to treat childhood diseases in Thaba 'Nchu

The three most represented families were Asteraceae, Rubiaceae, and Sterculiaceae (Figure 3.3). Plant species from the Asteraceae family are widely distributed in various ecological regions, including arid and semiarid, forests, high altitude grasslands and urban green spaces. These characteristics are typical of most plants found in the study area, which is part of a grassland biome. Additionally, plants in the Asteraceae family can synthesise a wide range of secondary metabolites, including triterpenoids, flavonoids, polyacetylenes, alkaloids, benzofurans, benzopyrans, phenylpropane triterpene monols, diols, acetylenic compounds, methylated flavanols and flavones, inulin-type fructans, the cyclitols L-inositol and scyllitol, and fatty oils (Rolnik & Olas, 2021). Secondary metabolites play crucial roles in human health by providing therapeutic benefits, including antioxidant, anti-inflammatory, and antimicrobial properties, and nutritional support, and they are also key in the development of pharmaceuticals and health supplements (Elshafie et al., 2023). In addition, the Asteraceae family are the most utilised plant species in South Africa (Ndhlovu et al., 2021; Moteetee & Kos, 2017; Nalumansi et al., 2014). This may be due to the high concentration of bioactive compound present in plants belonging to this family (Atnafu et al., 2018). However, the families Sterculiaceae and Rubiaceae were represented by three and four plants, respectively.

3.3.3 Childhood diseases treated with medicinal plants in Thaba 'Nchu

Children have a weaker immune system, hence their susceptibility to different diseases. The use of medicinal plants to treat diseases is well established and significantly influences healthcare practices and childhood well-being. The present study recorded 19 childhood diseases treated through medicinal plants in Thaba 'Nchu. The study revealed that depression of fontanelles, diarrhoea, sharp pain, weakness/tiredness/lethargy, and vomiting are the most treated ailments in Thaba 'Nchu (Figure 3.4 and Table 3.2).

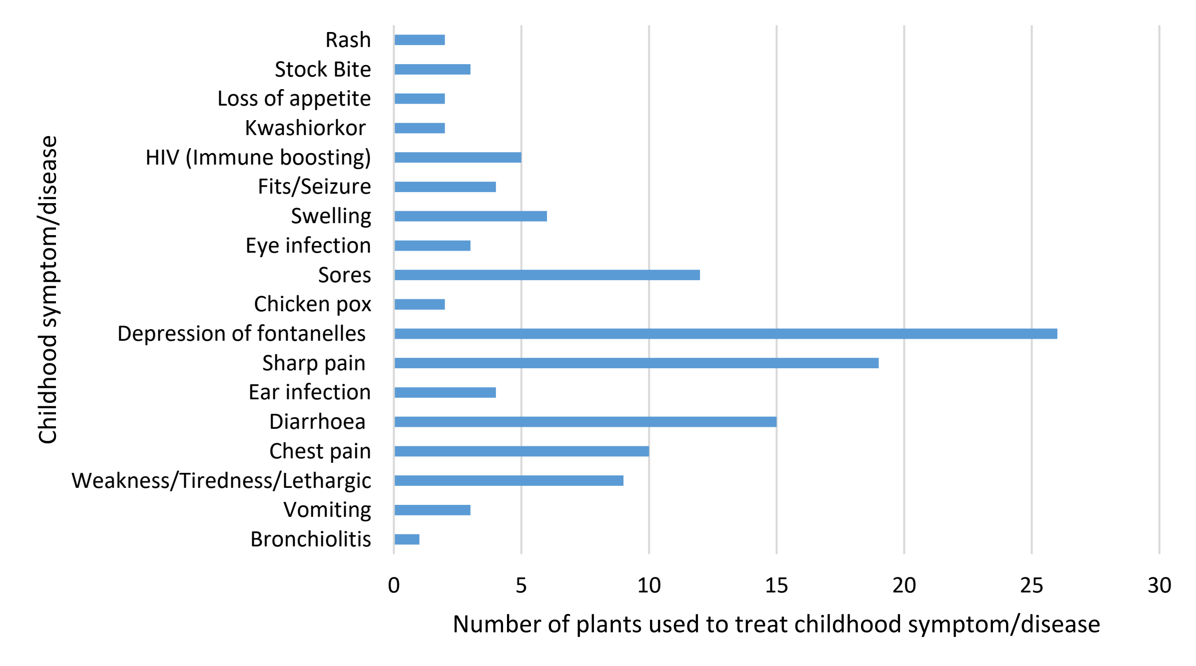

Figure 3.4: Diseases treated by various medicinal plants in Thaba 'Nchu

Depression of fontanelles refers to gaps between bones in the skull of an infant where three skull bones meet and are typically brought on by trauma, such as abdominal blunt trauma in pregnant women, and the use of obstetric forceps during delivery (Jarvis, 2011). This may lead to diseases such as meningitis, encephalitis, trauma, intracranial haemorrhage, hydrocephalus, and hypoxic-ischemic injury. Stomach ailments, depression of the anterior fontanelle, skin ailments, chest problems and pain, convulsions (fits/seizures), ear/eye ache, weakness, malnutrition, and gastrointestinal disorders have been reported amongst the most treated ailments for children in South Africa (Ndhlovu et al., 2021). Current findings correlate with those of Van Vliet (2012), who reported fontanelles, respiratory problems, diarrhoea, and earache as common childhood diseases that medicinal plants treat. The current study does not align with the study of Shaheen et al. (2017), who reported the highest ICF value for cardiovascular diseases (haemophilia and heart problems) at 0.5. They also found an ICF value of 0.2 for respiratory disorders (cough, diphtheria, Pertussis), 0.45 for constipation, vomiting, and diarrhoea, 0.16 for ear problems, 0.12 for dermatological issues, and 0.11 for eye infections (Figure 3.4).

Table 3.2: Categories of childhood diseases managed and treated with medicinal Plants in Thaba 'Nchu

English name	Sotho name	Frequency of mention	ICF
Bronchiolitis	Leleta	3	1.00
Chest pains	Sebuba	28	0.67
Chicken pox	Paterepotisi	3	0.50
Depression of fontanelles	Phowana	58	0.56
Diarrhoea	Letshollo/ Mala	40	0.64
Ear infections	Tsebe	9	0.63
Eye infections	Mahlo	4	0.33
Fits/seizures	-	4	0.00
HIV (Immune boosting)	Phamokate	5	0.00
Kwashiorkor	Kwashiorkor	2	0.00
Loss of appetite	-	2	0.00
Rash	Lekgopo le le sesane	2	0.00
Sharp pain	Letswejane	43	0.57
Sores	Diso	18	0.35
Stork Bites	Nogana	3	0.00
Swelling	Borurusi	7	0.17
Vomiting	Lehlatso	8	0.71
Weakness/tiredness/lethargy	Mohato	27	0.69

3.3.4 Plant parts used to treat childhood ailments in Thaba 'Nchu

In Thaba ʻNchu, different plant parts, including bark, fruits, leaves, and roots, are harvested by TMPs to prepare remedies (Figure 3.5). The results of this study indicate that roots (50%) are the most used part, followed by the whole plant (28%), leaves (14%), stems (4%), tubers (2%), fruits (1%), and bark (1%). Using roots more than the other plant parts is a common practice in traditional medicine (Jima & Megersa, 2018;

Mahwasane et al., 2013). Besides being available for harvest throughout the year, roots have high concentrations of bioactive compounds (Stéphane et al., 2021; Pal et al., 2011). The high usage of roots to treat childhood diseases in similar ethnobotanical studies is well documented (Shaheen et al., 2017; Nalumansi et al., 2014). However, in other studies, leaves have been reported to be the most used plant parts for managing childhood diseases (Ndlovu et al. 2021). This is because leaves can be harvested in large quantities and are easy to use (Shaheen et al., 2017). Overusing roots over other plant parts in Thaba 'Nchu negatively affects the sustainable utilisation of medicinal plant resources. Therefore, TMPs in Thaba 'Nchu must be educated on sustainable harvesting and uses of medicinal plants, including possibly developing medicinal plant gardens for future use.

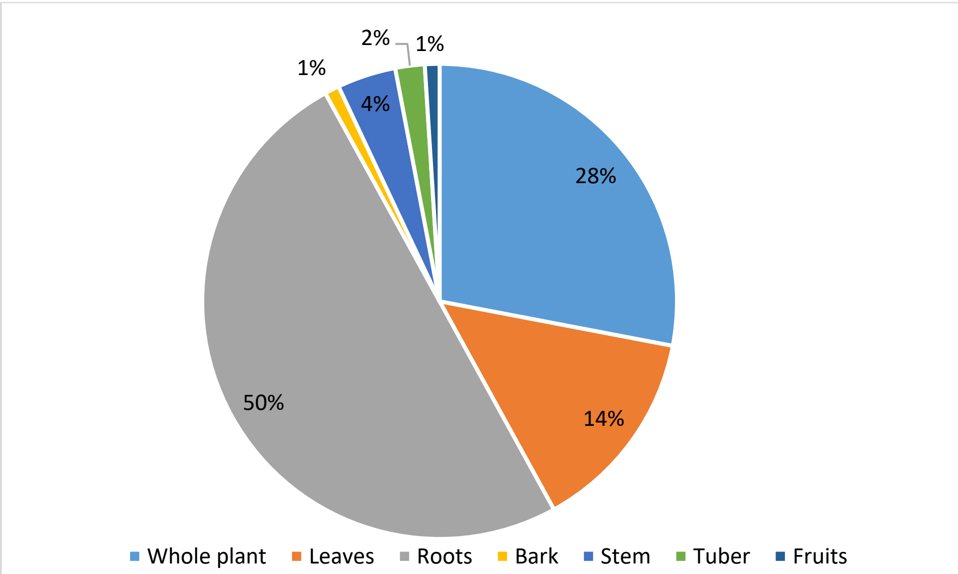

Figure 3.5: Medicinal plants parts used to treat childhood diseases in Thaba 'Nchu

3.3.5 Mode of preparation and route of administration

The result of the present study indicates that plant parts are prepared in four different ways for treating and managing childhood diseases in the area. As shown in Figure 3.6, the preferred modes of remedy preparation respectively is decoction (85%), infusion (8%), paste similarly to burn (3%) and maceration (1%). Reports by Ndhlovu et al. (2021) indicated that infusion is considered the most effective method for preparing plants to treat childhood diseases and general well-being in South Africa, primarily because it requires fewer resources.

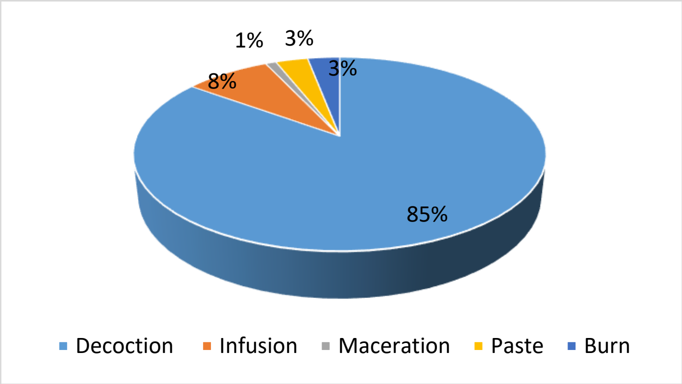

Figure 3.6: Mode of preparation for medicinal plants used to treat childhood diseases in Thaba 'Nchu

Figure 3.7 shows the route of administration includes oral (65%), Topical (16%), rectal (7%), dermal (6%), and nasal (6%). Oral administration is preferred for children, likely because it is easy to administer and generally well-accepted by young patients (Shaheen et al., 2017; Dambisya & Tindimwebwa, 2003).

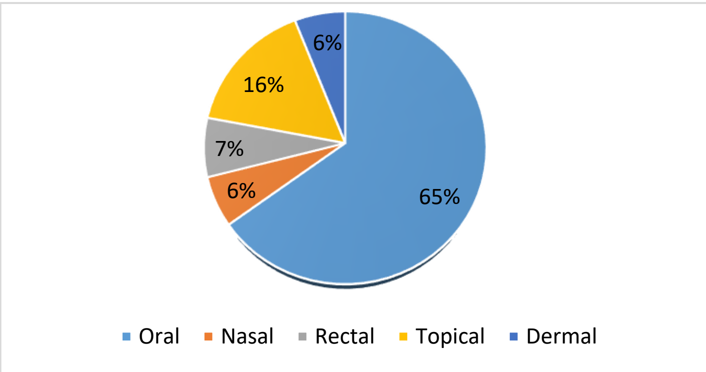

Figure 3.7: Route of administration for medicinal plants used to treat childhood diseases in Thaba 'Nchu

3.3.6 Ethnobotanical indices

Consensus analysis has been used in recent ethnobotanical studies to assess the reliability of data provided by various informants.

3.3.7 Relative frequency of citation

In this study, the RFC values ranged from 0.03 to 0.77. *B. montana* had the highest RFC value of 0.77, making it the most significant plant in Thaba 'Nchu. Among the documented herbaceous plant species, only four had RFC values greater than 0.5 (*B. montana*, *P. rigidus*, *G. caffrum*, and *D. anomala*), while the RFC values for the remaining 56 species ranged from 0.03 to 0.43. Notably, *B. montana*, *S. aculeatissimum*, and *A. grandidentata* were reported for the first time concerning ailments in children. According to the frequency of citation, *B. montana* is identified as the most useful plant for treating childhood ailments in the area.

3.3.8 Informant Consensus Factor

The informant consensus factor (ICF) was calculated for each reported disease and is detailed in Table 3.1. Bronchiolitis received the highest ICF score, indicating that TMPs frequently treat this ailment in children. Bronchiolitis is a serious condition characterised by inflammation of the airways, often caused by viral, bacterial, or fungal infections. The overuse of antibiotics for this condition can lead to side effects such as gastrointestinal issues or allergic reactions (Wopker, 2020). The ICF values for other diseases ranged from 0.17 to 1.00. In the current study, the highest frequency of mention was for depression of the fontanelles and sharp pain. Vomiting had the second-highest ICF value at 0.71. Other notable ICF values include weakness/tiredness/lethargy (0.69), which can affect children by impairing daily activities, causing mood swings, sleep issues, reduced social interactions, lower school attendance, decreased academic performance, and a diminished quality of life (Nunes, 2017). Chest pain, with an ICF of 0.67, is a significant concern due to its potential link to heart disease and mortality (Dogan, 2022). The ICF values for diarrhoea and ear infections were 0.63 and 0.64 respectively. A zero ICF value was observed for conditions such as fits/seizures, HIV (immune boosting), kwashiorkor, loss of appetite, snake bites, and rash. These results suggest a strong preference for specific plants and a sharing of information about treating sharp pain in children within the area.

3.4 Conclusion

Documenting the knowledge and medicinal plants used to treat childhood diseases is essential for preserving them for future generations. In Thaba 'Nchu, the use of medicinal plants represents an affordable and accessible healthcare system. Thirty traditional medical practitioners shared knowledge about 60 medicinal plants from 28 families. Nineteen childhood-related ailments are treated in the area, with common conditions including depression of fontanelles, diarrhoea, and sharp pain. The Asteraceae family was notably represented among these medicinal plants. *B. montana*, with an RFC value of 0.77, along with other plants such as *Pachycarpus rigidus*, *Geranium caffrum*, *Dicoma anomala*, and *S. aculeatissimum,* are the most commonly used by the Thaba 'Nchu community to manage childhood ailments. Roots are the most preferred plant part, and decoctions are typically used for oral administration. However, using roots could lead to the extinction of important plant species in the study area, highlighting the need for campaigns to educate the traditional healers' in the community about sustainable harvesting practices. This study lays a solid foundation for future research, which may include phytochemical studies, cytotoxicity tests, and evaluations of the pharmacological potential of the medicinal plants cited by the participants to assess their potential for development into new drugs that can be used to treat childhood diseases.

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CHAPTER 4
PHYTOCHEMICAL SCREENING OF PLANTS USED FOR CHILDHOOD AILMENTS

4.1 Introduction

In the past, conventional drugs were originally derived from medicinal plants. However, exploring natural products as bioactive molecules gained attention because conventional modern medicines could not effectively treat illnesses, infections, and diseases (Valgas et al., 2007). Furthermore, the issue of antibiotic resistance further compounded the crisis. There are limitless prospects of new drug leads due to the exceptional availability of multiple chemical compounds from natural products (Nasim et al., 2022). Due to safety concerns, natural-origin antimicrobials are now given much attention worldwide instead of synthetic ones. This attention is due to the benefit of human health, amongst many others, including anticarcinogenic, antiatherogenic, antiulcer, anti-thrombotic, anti-inflammatory, immune modulating, antimicrobial, vasodilatory, and analgesic effects (Tepal, 2016). Our bodies produce unstable molecules when physiological processes (cells using oxygen) occur, resulting in cell damage, which causes different disorders (Mondal et al., 2019).

Plants are considered the most vital and rich natural source of medicinal properties. A medicinal plant is described as any plant with substances that demonstrate healing effects or contains molecules/compounds that can serve as precursors or leads for semi-synthetic products (Siju et al., 2014). The non-nutritional substances occurring in plants are phytochemicals, which include saponins, tannins, alkaloids, alkenyl phenols, glycoalkaloids, flavonoids, sesquiterpenes, lactones, terpenoids and phorbol esters (Saeed et al., 2019). These substances can be found in plants like leaves, bark, flowers, fruits, and roots.

The quality of bioactive compounds present in plants varies depending on the environmental and climatic/weather conditions such as light intensity, availability of water, type of soil, temperature, and location (Quispe et al., 2018; Chandra et al., 2014). Quispe et al (2018) further explained that plants of the same species can have different amounts or types of bioactive compounds in various environments. Plants have about 12,000 identified phytochemicals which help to protect them against bacteria, fungi, predators, insects and herbivores (Kumar & Pandey, 2013; Sengul et al., 2009).

The selected plants *B. montana*, *S. aculeatissimum* and *A. grandidentata* are used in Thaba ‘Nchu for medicinal purposes in managing ailments in children. Therefore, it is essential to investigate the presence of active compounds in these plants as they may provide valuable information about managing ailments in children. The screening of phytochemicals in these plants not only helps uncover the plant extracts' constituents but is also vital in the search for bioactive agents that can be engaged in producing useful drugs (Pant et al., 2017). Therefore, the present study identified the secondary metabolites present in *B. montana*, *S. acculeatissimum,* and *A. grandidentata* extracts.

4.2 Materials and Methods

4.2.1 Collection, preparation, and storage of plant material

Different parts of the selected medicinal plants, *B. montana* (roots), *S. aculeatissimum* (whole plant) and *A. grandidentata* (leaves) were collected from various regions of Thaba ‘Nchu. Voucher specimens for all three plants were taken to the Free State Botanical Garden for identification and authentication. The plant materials were air-dried indoors at 40 ˚C, evaporating the water molecules, rendering the materials sufficiently dried and ready for grinding for 72 hours. Subsequently, each plant material was ground into powder using an electrical grinder, thus increasing its surface area (Chigayo et al., 2021). The powdered material of each plant was soaked in different solvents (100%) of varying polarities, including acetone, methanol, and distilled water in the ratio 1:1 (100g: 100ml) and extracted successively as indicated in Figure 4.1. This ratio leads to a higher extraction yield. The mixtures were shaken for 24hours on a shaker operated at 100 rpm and filtered through Whitman No.1 filter paper. The entire procedure was repeated three (3) times. Each filtrate was concentrated in an RV 3 Rotary Evaporator under reduced pressure at 5 ˚C, until the filtrate was reduced to one-third of the starting filtrate volume, resulting in different crude extracts. The different filtrates were stored in sterile bottles at -20 ˚C for storage and further analysis.

Figure 4.1: Plant material soaked in acetone, methanol, and distilled water

4.2.2 Preliminary phytochemical screening

The availability of phytochemicals (alkaloids, flavonoids, glycosides, phenols, phlobotanins, saponins, steroids, tannins and terpenoids) was determined independently. The determination was conducted using standard procedures described by Dhawan and Gupta (2017) and Tepal (2016). Qualitative tests were carried out as follows.

4.2.2.1 Test for alkaloids

About 0,01g of each extract of the selected plants was dissolved in 2mL of Wagner's reagent. After extract dissolution, the occurrence of alkaloids in the plant extracts was confirmed by the formation of a reddish- brown coloured precipitate.

4.2.2.2 Test for flavonoids

To each extract (0,01 g), a few drops of sodium hydroxide (NaOH) were added, resulting in the appearance of a yellow colour. Subsequently, three drops of sulfuric acid (H_2SO_4) were introduced against the wall of the test tube. The solution became colourless after adding a few drops, confirming the presence of flavonoids in the plant extracts.

4.2.2.3 Test for glycosides

A quantity (0,01 g) of the crude extract was mixed with 1mL of distilled water in a test tube. The mixture was shaken vigorously, after which three drops of aqueous sodium hydroxide (NaOH) were added. A yellow colour indicated the presence of glycosides.

4.2.2.4 Test for phenols

A certain quantity of each extract (0,01g) was dissolved in 1mL of the extraction solvent, followed by three drops of Iron (III) chloride. The change of colour of the solution to blue, green, red, or purple indicated the presence of phenols.

4.2.2.5 Test for phlobatannins

Specified quantity of each plant extract (0,01g) was dissolved in 1mL of distilled water. Three drops of 1% hydrochloric acid were added, and the formation of a red precipitate indicated the presence of phlobatannins.

4.2.2.6 Test for saponins

A portion of each extract (0,01g) was dissolved in 20 mL of distilled water in a test tube sealed with parafilm. The test tubes were grouped together, and their contents mixed vigorously for about 15 minutes by shaking. Foam formation at the top of the test tubes indicated a positive test or the presence of saponins.

4.2.2.7 Test for steroids

Approximately 0,01 g of each plant extract was weighed and introduced into a test tube. One (1) mL of sulphuric acid (H_2SO_4) was added to the wall of the test tube. The formation of a dark-red-green colour indicated the presence of steroids.

4.2.2.8 Test for tannins

Ten milligrams (0,01g) of each extract were dissolved in water in a test tube, followed by filtration of the solution using a Whitman No.1 filter paper. Three drops of ferric chloride solution were added to the filtrate, and a bluish colour indicated the presence of tannins (Anyasor et al., 2010).

4.2.2.9 Test for terpenoids

About 0,01 mg of each extract was dissolved in the respective extraction solvent in a test tube. Subsequently, two (2) mL of chloroform was added to each test tube, followed by 3 mL of Sulphuric acid (H_2SO_4), which was introduced against the wall of the test tube. A reddish-Brown colouration confirmed the presence of terpenoids.

4.3 Results and Discussion

4.3.1 Preliminary phytochemical screening

The results from the evaluation of bioactive compounds in the plants studied are presented in Table 4.1. All the plants showed positive test results, but the positivity spectrum depended on the abundance of the active compound of interest. The phytochemical screening revealed the presence of alkaloids, glycosides, phenols, phlobotanins, steroids, tannins and terpenoids which were more abundant compared to flavonoids and saponins. The abundance of alkaloids, steroids, phenols, and terpenoids was notable in the roots of *B. montana*, the whole plant of *S. aculeatissimum*, and the leaves of *A. grandidentata*. The methanol extracts of *B. montana* roots and *S. acculeatissimum* whole plant showed abundant alkaloids, steroids and terpenoids. The results were equally positive for the aqueous extracts of the three studied plants. These results are similar to other studies performed elsewhere (Dubale et al., 2023; Oloya et al., 2022).

Table 4..1: Phytochemical screening of *B. montana, S. aculeatissimum*, and A. grandidentata **extracts**

	B. montana			*S. aculeattissimum*			*A. grandidentata*		
	Acetone	**Methanol**	**D. Water**	**Acetone**	**Methanol**	**D. Water**	**Acetone**	**Methanol**	**D. Water**
Alkaloids	++	++	-	+	++	-	-	-	+
Flavonoids	-	-	-	-	-	+	-	+	+
Glycosides	+	+	-	-	++	-	-	+	+
Phenols	-	-	-	++	++	-	++	-	-
Phlobatannins	+	++	-	+	+	+	-	-	-
Saponins	-	+	-	-	-	+	-	-	-
Steroids	++	++	-	++	++	++	++	-	-
Tannins	-	-	-	-	+	+	++	++	-
Terpenoids	++	++	++	++	++	++	-	++	++

++: Abundant; **+**: Present; **-**: Absent

The phytoconstituents detected are known to have medicinal properties. Overall, 89 % of the extracts showed the presence of terpenoids and tested negative only in the acetone leaf extracts of *A. grandidentata*. Terpenoids are part of the organic compounds with structural features, including acetate units that make them capable of playing a role in human physiology, owing to their antimicrobial and antidiarrheal activities (Tiwari et al., 2011; Yadav & Agarwala, 2011). Terpenoids are present in *Burkheya sp*. and found in the family *Asteraceae*. According to Perveen and Al-Taweel (2018), terpenoids can be grouped into monoterpenes, sesquiterpenes, diterpenes, sesterpenes, and triterpenes depending on their carbon units. They have been reported effective in treating diarrhoea, colds, diabetes, sore throats, coughs, and respiratory infections (Kose et al., 2015).

Plants of the Solanaceae family, such as *S. aculeatissimum,* are rich in alkaloids and steroids. Most plant-derived alkaloids have demonstrated biological activities, including anti-inflammatory, antimalarial, antimicrobial, cytotoxicity, antispasmodic and pharmacological effects (Al-Reza, 2022; Thite et al*.,* 2013). This compound class is regularly used in medicines due to their well-known biological activities. They have been reported to be effective against intestinal ailments, sores, colds, chills, wounds, fever, asthma, enema, syphilis, rheumatism, removes retained conception products, bed sores, haemorrhoids, ringworms, gall sicknesses, chest complaints. These findings follow a previous study by Kose et al. (2015).

In the present study, *A. grandidentata*, a member of the Asphodelaceae family, was tested, and this swollen and succulent leaf plant was observed to contain alkaloids, flavonoids, glycosides, phenols, steroids, tannins and terpenoids. The data support findings of previous studies that investigated the phytochemicals in the leaf extracts of *Aloe* sp. (*Aloe berhana*, *Aloe ferox*, *Aloe vera*, *Aloe maculate*, *Aloe striatula*) and noted the occurrence of aloin, anthraquinones and pre-anthraquinone positive. The afore-mentioned molecules possess strong anti-inflammatory effects and antimicrobial activity (Kose et al., 2015; Radha & Laxmipriya, 2015; Dagne & Yenesew, 1994). Flavonoids are polyphenols with an aromatic ring and hydroxyl groups, capable of absorbing free radicals and binding metal ions that may accelerate reactive oxygen species formation, leading to lipid peroxidation (Shen et al., 2022). This group of compounds have the potential to act as potent antioxidants, and this ability relies mainly on their molecular structure, the position of the hydroxyl group and other features in their chemical structure (Iqbal et al., 2015). The flavonoids help to combat diseases in the human body; hence, they are of great significance in maintaining human health in addition to anti-inflammatory, antiangiogenic, anti-allergic effects, analgesic and antioxidant (Kamal et al., 2012). Flavonoids were present in the aqueous extracts than the methanol and acetone extracts, making the studied plants less potent water-soluble antioxidants for preventing oxidative cell damage (Radha & Laxmipriya, 2015).

Tannins are said to demonstrate antiviral, antibacterial and antitumour activities (Kumari & Jain, 2012). In the current study, tannins were detected on the methanol and aqueous extracts derived from all the parts of *S. aculeatissimum* (leaves, stem, and roots), and acetone and methanol leaf extracts of *A. grandidentata.* In addition, the methanol extracts of *S. acculeatissimum* had the most glycosides. These glycosides are present in the acetone and aqueous extracts of *B. montana* and *A. grandidentata.* Glycosides are secondary metabolites in plants in the Asphodelaceae, Asteraceae, and Solanaceae families (Dubale et al., 2023).

Furthermore, the abundance of phenols in the parts of *S. aculeatissimum* and the leaves of *A. grandidentata* suggests potential for their antimicrobial activity (Radha & Laxmipriya, 2015). Although phenols can be extracted from dried plant samples, their absence in the roots of *B. montana* might be due to influences attributed to the extraction time, the temperature, the solvent-to-solid ratio, and the surface area of the plant sample, which reveals the incompatible activities of solubilization and analyte degradation by oxidation as explained by Dai and Mumper (2010).

In this study, *B. montana* roots contained phlobatannins, which have useful applications in ethnomedicinal practices for wounds in children (Wadood et al., 2013; Lalrinzuali et al., 2015). The presence of saponins was equally noted only in the methanol extracts of *B. montana* and aqueous extracts of *S. aculeatissimum*. These findings contradict previous studies, wherein saponins were present in leaves of *A. maculata*, a member of the Asphodelaceae (Kose et al., 2015). Saponins are recognised for their ability to reduce inflammation (Yadav & Agarwala, 2011) and exhibit antimicrobial properties (Kamal et al., 2012). Additionally, they possess medicinal benefits that enhance the immune system, aid in clearing the lungs and chest, and are used for cleansing incisions made on children (Kose et al., 2015). These phytoconstituents identified in the roots, leaves and the whole parts of the different plant extracts may be responsible for the biological activities in these selected plants, thus serving as scientific evidence and the reason for their use in traditional medicine by the natives of Thaba Nchu (Iqbal et al., 2015).

4.4 Conclusion

The findings of this study revealed the presence of medically valuable compounds within the roots of *B. montana*, various parts of *S. aculeatissimum*, and the leaves and roots of *A. grandidentata*. Identified phytochemicals included alkaloids, flavonoids, glycosides, phenols, phlobatannins, saponins, steroids, tannins, and terpenoids, all of which have demonstrated bioactivity in previous research. These compounds are particularly relevant for their therapeutic potential in managing childhood diseases. This suggests that the roots of *B. montana*, parts of *S. aculeatissimum*, and the leaves of *A. grandidentata* could serve as promising sources of natural antimicrobial agents and valuable drug precursors for treating infections commonly experienced by children. Such properties are crucial in the context of increasing antimicrobial resistance, which poses a significant challenge in paediatric medicine. Therefore, further research is strongly recommended to evaluate the specific antimicrobial effects of these secondary metabolites, as they could lead to innovative, plant-based therapeutic options for combating infections and other health conditions affecting children. Additionally, expanding studies to explore dosage, toxicity, and compound isolation will be essential in understanding the full scope of their medicinal potential and ensuring safety and efficacy for use in paediatric populations.

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CHAPTER 5

IN VITRO CYTOTOXICITY ACTIVITY OF MEDICINAL PLANT EXTRACTS USED FOR CHILDHOOD AILMENTS IN THABA 'NCHU

5.1 Introduction

Toxicity refers to the adverse effects of substances on living organisms, while cytotoxicity specifically describes the detrimental effects at the cellular level, which can lead to cell death (Odaudu & Akinsi, 2022). *In vitro* cell culture systems are commonly used to assess cytotoxicity, where a substance is deemed toxic if it disrupts cell attachment, alters cell morphology, impairs growth, or induces cell death (Zhang, 2018; Riss et al., 2019). Given that plant-derived extracts are often intended for various medicinal purposes, understanding their cytotoxicity is especially critical when considering treatments for childhood diseases. Research by Saeed et al. (2016) indicates that toxicity and cytotoxicity can be classified into several categories, including chemical toxicity, organ-specific cytotoxicity, and basal cell toxicity. This is particularly relevant for evaluating the safety of traditional remedies used for treating ailments in children.

In many rural communities, traditional folk medicine remains the primary healthcare option, often leading to self-medication with herbal remedies (Kasilo & Nikiema, 2014; Savatagi et al., 2025). While these remedies can provide accessible and affordable treatments, there is limited awareness regarding their potential toxicity, particularly concerning the risk of drug interactions and unknown biological effects (van Wyk & Prinsloo, 2020). Many medicinal plants contain complex phytoconstituents that may be beneficial but can also exhibit toxic effects (Pittler et al., 2003). Therefore, it is essential to evaluate the toxicity of plant-based substances before their application as treatments for childhood illnesses, as both children and adults can be adversely affected by toxic compounds.

Recent research has emphasised the need for systematic studies of natural products and their phytochemicals to ascertain their antimicrobial activity and safety before use in pediatric medicine (Anywar et al., 2021). Toxicological evaluations are crucial for confirming the safety of herbal medications (Oloya et al., 2022). Various cytotoxicity tests, which assess how well cells can proliferate in the presence of a test compound, provide essential preliminary data for selecting plant extracts with potential therapeutic benefits, especially those with antineoplastic properties (Nobakht et al., 2014).

While certain medicinal plants exhibit promising biological activity, their potential toxicity must not be overlooked, as some secondary metabolites may have harmful effects (Somaida et al., 2020). Previous studies, such as those by Anajwala (2012), have demonstrated cytotoxicity in plant extracts, emphasising the need to assess their safety carefully. Although *S. aculeatissimum*, *A. grandidentata*, and *B. montana* contain beneficial terpenoids, insufficient data exist regarding their safety in paediatric applications. Therefore, this study aims to evaluate the toxicity profiles of these solvent extracts to ensure their safe use in treating childhood diseases.

5.2 Materials and Methods

5.2.1 Sample preparation

The plant extracts were prepared by grinding each plant material into powder using an electrical grinder, thus increasing its surface area (Chigayo et al., 2021). The powdered material of each plant was soaked in different solvents (100%) of varying polarities, including acetone, methanol, and distilled water in the ratio 1:1 (100g: 100ml) and extracted successively. This ratio leads to a higher extraction yield. The mixtures were shaken for 24hours on a shaker operated at 100 rpm and filtered through Whitman No.1 filter paper. The entire procedure was repeated three (3) times. Each filtrate was concentrated in an RV 3 Rotary Evaporator under reduced pressure at 5 °C, until the filtrate was reduced to one-third of the starting filtrate volume, resulting in different crude extracts. The different filtrates were stored in sterile bottles at -20 °C for storage and further analysis.

The test extracts were redissolved in dimethyl sulfoxide (DMSO) to a concentration of 200 mg/ml, and it was kept at 4 ˚C until further bioassays.

5.2.2 Hoechst and propidium iodide cytotoxicity assay

Vero cells, derived from the African green monkey kidney, were maintained at 37°C in a humidified incubator with 5% CO_2. The cells were cultured in 10 cm dishes using

DMEM supplemented with 10% FBS. Cell purity was assessed by seeding 4000 cells per well in 96-well microtiter plates with 100 µL of medium, allowing for cell adherence at 37°C and 5% CO_2 for 24 hours before treatment with plant extracts. Each extract was diluted in culture medium to concentrations of 50, 100, and 200 µg/mL, and 100 µL of the diluted extracts was added to the wells. The cells were then incubated for 48 hours. To assess cytotoxicity, the treatment medium was replaced with 100 µL of Hoechst 33342 nuclear dye (5 µg/mL) and incubated at room temperature for 20 minutes. Propidium iodide (100 µg/mL) was then added to stain dead cells. The cells were imaged using the ImageXpress Micro XLS Widefield Microscope (Molecular Devices) with a 10x Plan Fluor objective and DAPI and Texas Red filter cubes. Nine image sites were captured per well, covering approximately 75% of the well's surface area.

5.2.3 Data quantification

The screening assay was achieved by quantifying life and lifeless cells using the ImageXpress Micro XLS Widefield Microscope (Molecular Devices). The images obtained were evaluated using the MetaXpress software and Multi-Wavelength Cell Scoring Application Module. A Microsoft Excel spreadsheet was used for data analysis and processing.

5.3 Results and Discussion

The cytotoxicity of the three plant species was assessed using a dual staining technique that employed the nuclear dye Hoechst 33342 and propidium iodide (PI). In this procedure, life cells were identified by their positive staining with Hoechst 33342, while dying or dead cells stained positively with PI. A total of nine extracts were screened against Vero cells, with Melphalan serving as a positive control in the experimental setup. The red line on the results graph (Figure 5.1) indicated half the total cell count of the untreated control group, marking the threshold for potential cytotoxicity among the extracts tested.

Among the nine extracts evaluated, the acetone and methanol extracts of *S. aculeatissimum* exhibited pronounced cytotoxic effects on the cells. This was evidenced by the total cell count falling below the red line at concentrations of 50 µg/mL, 100 µg/mL, and 200 µg/mL, indicating a significant decrease in cell viability. These results are consistent with previous research by Shokrzadeh et al. (2010), which found that *Solanum nigrum* demonstrated notable toxicity against the HepG2 cell line and a moderate effect on the CT26 cell line. Furthermore, Shokrzadeh et al. (2010) highlighted the potential toxicity of S. nigrum on HeLa cells while reporting a relatively lower impact on Vero cells, as Patel et al. (2009) noted.

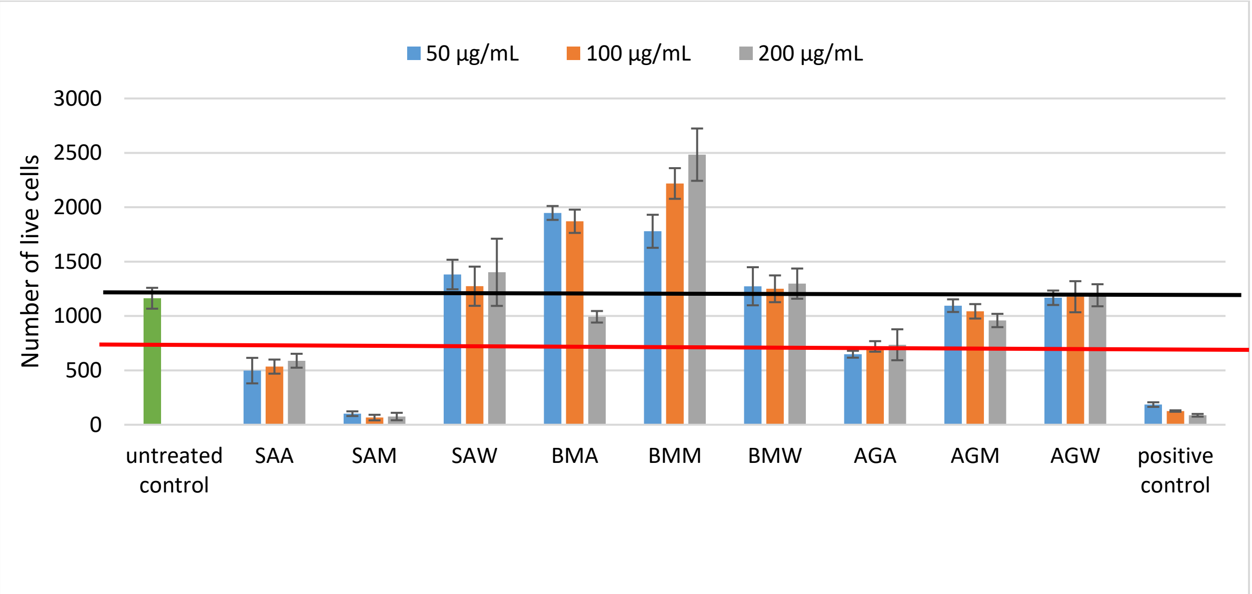

Figure 5.1: Total number of feasible cells.

Error bars indicate the SD of quadruplicate values performed as a single experiment. SAA=Solanum aculeatissimum Acetone, SAM=Solanum aculeatissimum Methanol, SAW=Solanum aculeatissimum Water, BMA= Berkheya montana Acetone, BMM= Berkheya Montana Methanol, BMW=Berkheya montana Water and AGA= Aloe grandidentata AGM= Aloe grandidentata Methanol, AGW= Aloe grandidentata Water

The *Solanum* genus is recognised for its diverse bioactive compounds, including alkaloids, flavonoids, and phenolic compounds, all known for their toxic effects (Kaunda & Zhang, 2019; Kortei et al., 2020; Thejaswini et al., 2023). The current study identified that the extracts from *S. aculeatissimum* contained a variety of these phytochemicals, specifically alkaloids, flavonoids, phenols, saponins, and tannins, all of which have been documented to exhibit cytotoxic effects on human cells (Pascoal et al., 2019). The low cytotoxicity of all the aqueous and *B. montana* and *A. grandidentata* extracts is encouraging, which warrants further investigation on these plants. This finding underscores the importance of evaluating plant extracts' safety and therapeutic potential, particularly when considering their application in traditional medicine and the treatment of childhood diseases, where the balance between efficacy and toxicity is crucial.

5.4 Conclusion

In conclusion, evaluating the cytotoxicity of the extracts from *S. aculeatissimum, B. montana,* and *A. grandidentata* highlights the necessity of rigorous safety assessments for plant-derived remedies, particularly in treating childhood diseases. The pronounced cytotoxic effects observed in the acetone and methanol extracts of *S. aculeatissimum* suggest that while certain extracts may possess therapeutic potential, they also carry inherent risks that must be carefully considered. Conversely, the low cytotoxicity exhibited by the aqueous extracts of *B. montana* and *A. grandidentata* is promising, indicating a safer profile for potential use in traditional medicine. This emphasises the importance of continued research into these plants to fully understand their bioactive compounds, ensuring that their applications can be both effective and safe for vulnerable populations, such as children, who may rely on natural remedies for their health needs.

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CHAPTER 6

ANTIBACTERIAL ACTIVITY OF SOLVENT CRUDE EXTRACTS OF SELECTED SOUTH AFRICAN PLANTS

Introduction

Bacteria, fungi, and viruses present a major risk to human health, particularly for immunocompromised individuals. These pathogens are capable of causing a wide range of infections that disproportionately affect children, contributing to conditions like pneumonia and diarrhea, which together account for roughly 2 million child deaths each year (Panayidou, 2014). The virulence factors of these pathogens enable them to evade the host's immune responses, facilitating infection and reproduction within the body.

Understanding the mechanisms of these bacterial pathogens is crucial for developing effective treatments. The emergence of antimicrobial resistance has led to a resurgence of infectious diseases, as many common pathogens have developed resistance to drugs such as penicillin and ciprofloxacin (Elisha et al., 2017). This resistance presents a significant challenge to healthcare systems globally and is often exacerbated by the misuse and overuse of antibiotics (Aliero & Afolayan, 2006). Additionally, conventional antimicrobials can cause serious side effects, including hypersensitivity and immune suppression (Al-Jabri, 2005).

There are bacterial species that are significant pathogens in childhood diseases. *Clostridium perfringens* causes gastrointestinal infections; *Pseudomonas aeruginosa* and *Entrobacter hormaechei* are linked to respiratory, urinary, and skin infections; *Staphylococcus epidermidis* is responsible for bloodstream infections; *Streptococcus pneumoniae* contributes to pneumonia and middle ear infections; *Streptococcus pyogenes* causes conditions like strep throat, scarlet fever, and impetigo; *Bacillus cereus* leads to symptoms of diarrhoea and vomiting; and *Enterococcus faecalis* can cause meningitis.

There is a growing interest in exploring natural products, particularly medicinal plants, as alternatives for developing new antimicrobial agents in this context. In South Africa, the traditional use of medicinal plants dates back to the 1850s, with around 3,000 species recognised for their medicinal properties (Van Wyk, 2011). These plants contain various secondary metabolites that exhibit antibacterial activity and may help combat infections in children while minimising the adverse effects of synthetic drugs.

This study evaluated the *in vitro* antibacterial properties of crude extracts from *B. montana, S. aculeatissimum,* and *A. grandidentata* against various bacterial and yeast strains. Identifying effective plant-based antibacterials could lead to safer treatment options for childhood infections and contribute to addressing the pressing issue of antimicrobial resistance. By harnessing the therapeutic potential of these natural products, we can develop innovative solutions for managing childhood diseases caused by resistant pathogens.

6.1 Materials and Methods

6.1.1 Serial dilution of solvent crude plant extracts

Extracts of *B. montana, S. acculeatissimum* and *A. grandidentata* were prepared using the same method described in Chapter 4. The different plant extracts were serially diluted two-fold to obtain different concentrations (2.5mg/ml, 1.25mg/ml, 0.625mg/ml, 0.312mg/ml, and 0.156mg/ml) of each plant extract. The microdilution method was employed as per the method of Njume et al. (2011). Stock solutions of nine extracts (i.e., methanol, acetone, and aqueous extracts of each plant) were prepared to obtain a concentration of 5mg/mL as a stock concentration. The initial dilution was prepared by adding 0.5 mL of the stock solution to 0.5 mL of distilled water. This resulted in a solution of the analyte with a concentration of 2.5mg/ml, which was also confirmed by using the formula $C_1V_1=C_2V_2$, (5mg/ml) (0.5ml) = (C_2) (1ml), C_2 = 2.5mg/ml. The process was repeated until a final solution at a 0.156mg/ml concentration was made, as shown in the example in Figure 6.1.

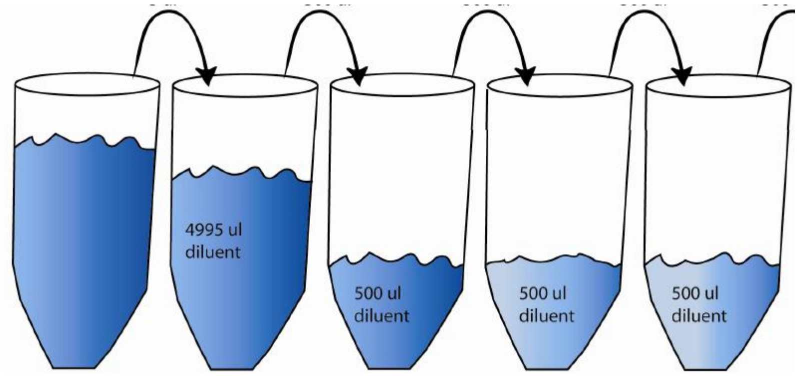

Figure 6.1: Serial dilution method

6.1.2 Preparation of an inoculum of microorganisms

The bacterial species were collected from the National Health Laboratory Services, Bloemfontein, South Africa. Fourteen microbial species were used in the screening of antimicrobial activity. They included *Bacillus cereus* (ATCC 13061), *Clostridium perfringens* (13124), *Enterobacter hormaechei* (700323), *Enterococcus faecalis* (ATCC), *Escherichia coli* (13762), *Escherichia coli* RESISTANT (ATCC 13846), *Pseudomonas aeruginosa* (ATCC 27853), *Staphylococcus aureus* (ATCC 11632), *Staphylococcus epidermidis* (ATCC 12228), *Streptococcus pneumoniae* (ATCC 49619) and *Streptococcus pyogenes* (ATCC 8668). The microbial species were grown by inoculating them into Mueller Hinton broth, followed by incubation and shaking at 100 rpm for 24 hours to maintain their purity and viability. Thereafter, their growth was stored on Mueller-Hinton agar plates at 4°C until further use. Prior to the investigation, the test organisms were revived by inoculating bacterial growth in 100mL Mueller Hinton broth, aliquoted into different sterile test tubes labelled with the reference organism and incubated overnight at 37 ˚C. The turbidity of the growth culture of each microbial strain was adjusted to conform to the concentrations of McFarland Standards (0.08 – 0.1 McFarland standard read at 625nm for bacterial species by diluting with 100mL Mueller Hinton broth (Marasini et al., 2015).

6.1.3 Determination of the minimum inhibitory concentration (MIC) of the plant solvent extracts

The collected plant materials were air-dried indoors at 40 °C for 72 hours, ensuring removal of moisture before grinding. Each dried sample was then pulverized using an electric grinder to increase surface area (Chigayo et al., 2021). The powdered material was extracted successively in 100% acetone, methanol, and distilled water at a 1:1 ratio (100 g:100 mL). The mixtures were shaken for 24 hours at 100 rpm and filtered through Whatman No. 1 filter paper, and this procedure was repeated three times. All filtrates were concentrated using a rotary evaporator at 5 °C under reduced pressure to one-third of their original volume, yielding crude extracts. The extracts were then stored in sterile bottles at −20 °C for further analysis.

The antibacterial activity of the nine extracts was evaluated using the broth microdilution method to determine the minimum inhibitory concentration (MIC) as per the method of Elisha et al. (2017). The 96-well microtiter plates were filled with a combination of 80 µL of the stock concentration of the plant extracts that were serially diluted with broth to concentrations ranging from 2.5mg/mL to 0.16 mg/mL. 80 µL of each standardised bacterium was dispensed into the wells and labelled A – E in triplicate. The negative control consisted of the bacteria only, while the positive control consisted of 80 µl of the test bacterium plus 80 µL of 0.125mg/mL chloramphenicol (a conventional antibiotic). The plates were sealed with parafilm and incubated at 37 ˚C for a duration depending on the test organism. Subsequently, the wells were filled with 4 mg/mL of INT (p-iodonitrotetrazolium violet) stain to differentiate between the living and dead cells and determine the MIC.

6.2 Results and Discussion

6.2.1 The antibacterial activity of the plant extracts

The antimicrobial activity evaluation of *B. montana, S. aculeatissiumum* and *A. grandidentata* extracts was determined by the dilution microplate method against different microorganisms which cause illnesses and infections in children. Results in this antibacterial activity were analysed using the method highlighted in Figure 6.2, and the MIC values are displayed in Table 6.1.

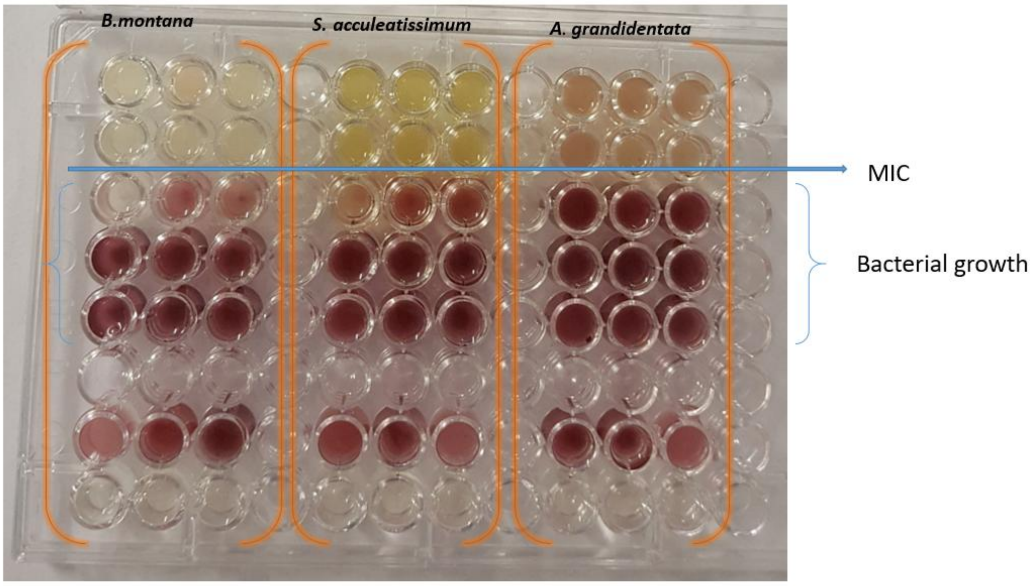

Figure 6.2: Methanolic extracts of the studied plants tested against S. pneumoniae showing MIC value 1.25 mg/ml

The methanolic extracts of *B. montana* roots exhibited significant antibacterial activity, with minimum inhibitory concentration (MIC) values ranging from 2.5 to 1.25 mg/mL against several bacterial pathogens, including *C. perfringens, P. aeruginosa, S. epidermidis, S. pneumoniae, S. pyogenes, B. cereus, E. faecalis,* and *E. hormaechei*. The acetone extracts of *B. montana* also showed antibacterial effects against *B. cereus, E. faecalis, E. coli, S. pneumoniae, and S. pyogenes*, with MICs in the same range. Similarly, the methanol extracts of *S. aculeatissimum* demonstrated activity against all bacterial strains tested, whereas its acetone extracts were effective against only four strains. For *A. grandidentata*, the methanol extracts exhibited antibacterial effects across all tested bacterial species, with MIC values between 2.5 and 0.6 mg/mL. In comparison, acetone extracts were active against *B. cereus, E. faecalis and C. pyogenes* at MICs of 2.5 to 1.25 mg/mL.

Table 6.1: MIC values against the different bacterial and yeast strains

		B. montana			***S. aculeatissimum***			***A. grandidentata***			**CHPL**	**AMPT B**
Microbial species	**Gram (+ or -)**	***M**	***A**	***aq**	***M**	***A**	***aq**	***M**	***A**	***aq**		
B. cereus	+	2.5	2.5	-	2.5	1.25	-	2.5	1.25	-	<0.1	<0.1
C. perfringens	+	1.25	-	-	1.25	-	-	1.25	-	-	-	-
E. hormaechei	+	2.5		-	2.5	-	-	2.5	-	-	-	-
E. faecalis	+	2.5	1.25	-	2.5	2.5	-	1.25	1.25	-	-	-
E. coli	+	2.5	2.5	-	1.25	-	-	1.25	-	-	<0.1	<0.1
P. aeruginosa	+	1.25	-	-	0.625	-	-	0.625	-	-	<0.1	<0.1
S. epidermidis	-	1.25	-	-	2.5	-	-	2.5	-	-	<0.1	<0.1
S. pneumoniae	-	1.25	2.5	-	1.25	2.5	-	1.25	-	-	<0.1	<0.1
S. pyogenes	-	1.25	2.5	-	0.625	2.5	-	1.25	2.5	-	-	-

*aq=Aqueous extracts, *A= Acetone extracts, *M= Methanol extracts, *CHPL= Chloramphenicol, *AMPT B= Amphotericin B; All experiments were conducted in triplicates; (-) = No antimicrobial activity was found

Several studies corroborate the antibacterial activity observed in the methanolic and acetone extracts of *B. montana*, *S. aculeatissimum*, and *A. grandidentata* indicating that these plants have bioactive compounds with therapeutic potential. This is evident because from the current study, tannins were detected on the methanol and aqueous extracts derived from all the parts of *S. aculeatissimum* (leaves, stem, and roots), and acetone and methanol leaf extracts of *A. grandidentata*. In previous literature, methanolic extracts of *B. montana* roots have demonstrated inhibitory effects on *Staphylococcus aureus* and *Escherichia coli*, attributed to phenolic compounds like tannins and flavonoids, which disrupt bacterial cell walls and inhibit nucleic acid synthesis (Cowan, 1999; Eloff, 1998). Additionally, saponins and alkaloids in *B. montana* are known for their antimicrobial properties, particularly against Gram-positive bacteria, aligning with its effectiveness against *Bacillus cereus* and *Streptococcus species*.

For *S. aculeatissimum*, similar antibacterial effects have been reported, particularly against respiratory and gastrointestinal pathogens. Methanol extracts of this plant exhibit multiple biological activities, including anti-inflammatory, antibacterial, antioxidant, anti-obesity, and anti-cancer effects. They also contain the steroidal glycoalkaloids solasonine and solamargine, whose membrane-disrupting properties likely enhance the extract's broad antibacterial activity, particularly against *S. epidermidis* and *S. pneumoniae* (Burger et al., 2018; Yang et al.,2025). These glycoalkaloids have demonstrated bactericidal activity by compromising bacterial cell membranes and causing leakage of cellular contents.

Earlier research on *A. grandidentata* identified its methanol extracts as effective against *E. coli* and *P. aeruginosa*, similar to findings in this study (Ibrahim et al., 2013). This antibacterial activity may be linked to the plant's high content of terpenoids and flavonoids, which interfere with bacterial enzymes and DNA replication. Specifically, terpenoids like camphor and menthol are known to penetrate bacterial cell walls, while flavonoids inhibit DNA gyrase, leading to bacterial cell death (El-Saadony et al., 2025).

The findings of this study further the potential of *B. montana, S. aculeatissimum,* and *A. grandidentata* as natural sources of antibacterial agents. Their active compounds, including alkaloids, glycoalkaloids, saponins, terpenoids, and flavonoids, offer a multi-targeted approach to combating bacterial infections in childhood diseases (Smith et al., 2008). Further investigation into these compounds' specific mechanisms of action and synergistic effects could enhance the therapeutic potential of these plants in paediatric antibacterial treatments.

6.3 Conclusions

In conclusion, the findings from this study highlight the promising antibacterial potential of *B. montana*, *S. aculeatissimum*, and *A. grandidentata*, particularly against bacterial strains associated with common childhood diseases. The inhibitory effects observed, with low MIC values across multiple bacterial species, suggest that these plants contain potent bioactive compounds, including alkaloids, glycoalkaloids, saponins, terpenoids, and flavonoids. Each compound class contributes to antibacterial action through mechanisms such as cell wall disruption, enzyme inhibition, and interference with DNA replication. Given the role of these pathogens in ailments such as gastrointestinal infections, respiratory conditions, skin infections, bloodstream infections, and meningitis in children, these plant extracts offer potential as alternative or complementary treatments for managing paediatric bacterial infections. To fully realise their therapeutic potential, further research is warranted to identify optimal extraction methods, examine specific mechanisms of action, and assess the synergistic effects of these compounds. Such studies could lead to the development of plant-based antibacterial therapies, addressing an urgent need for safer, effective alternatives in treating bacterial infections in children.

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CHAPTER 7
GENERAL DISCUSSION AND CONCLUSION

7.1 Introduction

In South Africa, medicinal plants are an important aspect of our lives. Medicinal plants are essential in managing and treating different illnesses in children in the Thaba 'Nchu area. There are over 45,000 plant species in Africa, and about 30,000 higher plant species, which contribute 10% of the world's flora, of which 3400 medicinal plant species belong to South Africa (Ndhlovu et al., 2019; Linder, 2014; Williams, 2013). Cape Floral Kingdom is the most diverse flora on earth, and Limpopo has a rich plant diversity in South Africa (Ndhlovu et al., 2019; Van Wyk et al., 2009). Free State has over 350 plant species used for medicinal purposes (Dingaan & Du Preez, 2017). According to Ndhlovu et al. (2021), there are 29 studies in the form of articles, books and dissertations with information of 194 plants used for treating ailments in children in nine provinces of South Africa. Despite these publications, there is still insufficient well-detailed documentation on the use of medicinal plants on children in the past years.

Children are highly vulnerable to a variety of illnesses and diseases, making them a major contributor to the global disease burden. This persists despite the widespread availability and use of conventional medications designed for prevention and treatment. However, these medications are frequently associated with adverse effects in children, which can complicate their management and lead to additional health concerns (Rieder, 2019). Medicinal plants are globally utilised because of their natural availability and the presence of secondary metabolites and beneficial biological properties that can help address the drawbacks of conventional drugs (Brown, 2017; Lopez et al., 2006).

As medicinal plants represent a good alternative, especially in South Africa where many of them are used for treatment of various diseases including those related to children. Although certain medicinal plants exhibit notable pharmacological properties, investigating their potential toxicity remains critically important (Somaida et al., 2020). Secondary metabolites such as alkaloids, saponins, glycosides and tannins found in S. aculeatissiumum extracts are known to exhibit toxic effects to humans and animals.

The toxic effects may range from neurotoxicity, hepatotoxicity, gastrointestinal irritation, hemolysis of red blood cells and reduced nutrient absorption when consumed in excessive amounts (Pan et al., 2014; Francis et al., 2002; Gleadow and Woodrow., 2002; Khanbabaee and Van Ree., 2011). Therefore, this study focused on documenting medicinal plants used for treating and managing childhood diseases in Thaba ‘Nchu.

7.2 Results

The current study findings showed that a smaller percentage of males (20%) participated in the ethnobotanical survey conducted on plants used to treat childhood diseases than females (80%) in Thaba ‘Nchu. The higher representation of women in the survey can be attributed to their primary caregiver role for children. Women are known to be experienced in addressing children's healthcare needs and therefore possess greater knowledge of using medicinal plants to manage childhood illnesses.

A total of sixty medicinal plants from 28 different families were recognised for their use in treating childhood diseases in Thaba ‘Nchu. The most frequently cited species were *Berkheya montana, Pachycarpus rigidus, Geranium caffrum, Dicoma anamala,* and *Solanum aculeatissimum*. Decoctions were the primary remedy preparation method, with remedies being administered orally (65%), topically (16%), rectally (7%), dermally (6%), and nasally (6%). These findings contribute to preserving this traditional knowledge for future generations and provide a valuable basis for selecting medicinal plants for further studies, including potential drug development.

Table 7.1 summarises the experimental results used to validate using the selected medicinal plants to treat childhood ailments documented in **Chapter 3**. *B. montana*, *S. aculeatissimum*, and *A. grandidentata* were selected for pharmacological investigation to validate their use in the treatment of childhood diseases.

Table 7.1: Summary of the experimental results obtained in the study

	***Aloe grandidentata* (leaves)**	***Burkheya montana* (roots)**	***Solanum aculeatissimum* (whole plant)**
Phytochemical screening	Alkaloids, flavonoids, glycosides, phenols, steroids, tannins, terpenoids	Alkaloids, glycosides, phlobotannins, saponins, steroids, terpenoids	Alkaloids, flavonoids, glycosides, phenols, phlobotannins, saponins, steroids, tannins, terpenoids
Antibacterial activity (Minimum Inhibitory Concentration)	Methanol (9 microorganisms at 0.625 mg/ml - 2.5 mg/ml) Acetone (3 microorganisms at 1.25 mg/ml - 2.5 mg/ml)	Methanol (9 microorganisms at 1.25 mg/ml - 2.5 mg/ml) Acetone (5 microorganisms at 1.25 mg/ml - 2.5 mg/ml)	Methanol (9 microorganisms at 0.625 mg/ml-2.5 mg/ml) Acetone (4 microorganisms at 1.25 mg/ml - 2.5 mg/ml)
Cytotoxicity	Methanol: Non-toxic Acetone: Non-toxic Aqueous: Non-toxic	Methanol: Non-toxic Acetone: Non-toxic Aqueous: Non-toxic	Methanol: Toxic Acetone: Toxic Aqueous: Non-toxic

7.3 Discussion and Conclusion

The phytochemical constituents detected across *B. montana*, *S. aculeatissimum*, and *A. grandidentata* methanol, acetone and water extracts include alkaloids, flavonoids, glycosides, phenols, steroids, tannins, terpenoids, and phlobatannins. These secondary metabolites are recognised for their biological activity and are crucial to the therapeutic properties of medicinal plants (Hussein et al., 2019). The medicinal value of these plants is attributed to these phytochemical compounds, which exert distinct and targeted effects on the human body to treat various health ailments, including childhood diseases (Agidew, 2022). These secondary metabolites contribute to medicinal plants' pharmacological properties such as hypoglycemic, antidiabetic, antioxidant, antimicrobial, anti-inflammatory, anticarcinogenic, and antimalarial activities (Yadav et al., 2014). Therefore, the presence of the identified compounds in *B. montana, S. aculeatissimum,* and *A. grandidentata* could explain why these plants are utilised in treating childhood diseases in Thaba 'Nchu.

In the current study, the methanol and acetone extracts of *S. aculeatissiumum* were toxic against the Vero cell line. Secondary metabolites such as alkaloids, saponins, glycosides, and tannins found in *S. aculeatissiumum* extracts are known to exhibit toxic effects on humans and animals. Hence, the secondary metabolites identified in *S. aculeatissiumum* extracts could have played a role in the toxicity observed in this study. The toxicity demonstrated in this study does not indicate that *S. aculeatissiumum* extracts must be discarded; however, they must be used cautiously. Therefore, to fully understand the toxicity of *S. aculeatissiumum,* further invitro-cytotoxicity studies need to be conducted on isolated compounds.

Medicinal plants and natural remedies offer the potential to complement conventional treatments, reduce reliance on synthetic drugs, and mitigate the adverse effects of some pharmaceuticals. The current study revealed that *Aloe grandidentata, B. montana* and *S. aculeatissimum* extracts showed antibacterial activity against *Bacillus cereus, Clostridium perfringens, Enterobacter hormaechei, Enterococcus faecalis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae and Streptococcus pyogenes* at various MICs. Some of these microorganisms are known to be causatives for some of the childhood diseases such as pneumonia, diarrheal and emetic syndromes, urinary tract infections, wound, soft tissues and skin infections, neonatal meningitis, sepsis, respiratory infections, pharyngitis and many other childhood diseases. Therefore, the observed activity of *Aloe grandidentata*, *B. montana*, and *S. aculeatissiumum* extracts against the aforementioned microorganisms provides strong evidence supporting the traditional use of these plants in treating childhood diseases caused by these pathogens. This validates their potential as alternative therapeutic agents, particularly in combating infections associated with these bacteria. The findings also underscore the importance of further exploring these plants to isolate and characterise the bioactive compounds responsible for their antimicrobial properties. Such research could lead to developing novel drug agents that address the growing challenges of antimicrobial resistance and enhance the list of available therapies for childhood and other infectious diseases.

7.4 Limitations of the Study

- The plants chosen for further investigation were determined by their availability in the study area, even if ethnobotanical surveys identified them as the most used plants for managing childhood diseases.
- Plant materials were collected from a single location, which may not represent the full chemical variability of the species.
- Seasonal and environmental differences might have affected the phytochemical composition of the plant, limiting generalizability.
- The selected plants were evaluated for their antimicrobial properties exclusively against bacterial species.
- The antimicrobial activity was perfomed only *in vitro*, this might not accurately be a reflection of how the compound on the plant would act on the living organism. The study could not be performed on human due to ethical approval processes.
- Resource constraints led to the screening of limited phytochemical groups leaving many compounds unidentified, this is because advanced analytical techniques such as LC-MS were not available to fully characterize active constituents of the plants.

7.5 Future Recommendations of the Study

Further analysis of the plant extracts/isolated compounds should be conducted.

- Identifying bioactive compounds using LC-MS should be conducted to increase the potential for developing new drugs from plants to treat childhood ailments and lead to the discovery of novel compounds.
- More research (Bio screening assay, hatching techniques and Sulfohodamine cytotoxicity assay) is needed to fully validate and understand the efficacy and safety of these plants for paediatric healthcare.
- Antimicrobial activity (antiviral, antibacterial and antifungal activity) of these plant extracts and their isolated compounds must be evaluated against other bacterial strains and fungi related to childhood ailments.

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APPENDICES

INFORMATION BROCHURE

PROJECT TITLE: An ethnopharmacological investigation of medicinal plants used for childhood ailments in Thaba 'Nchu, South Africa

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Introduction (purpose of study)

You are being asked to take part in a research study. In order to participate, you must be 18 years (older). Before you decide to participate in this study, it is important that you understand why the research is being done and what it will involve. Please read the following information carefully. Please ask the researcher if there is anything that is not clear or if you need more information. The decision to participate, or not, is up to you. The purpose of the study is investigate medicinal plants used to treat childhood infections in the Free State and determine their antimicrobial activity and to compile a catalogue of medicinal plants used to treat childhood infections for documentation purposes as well as a reference text for community members.

What is involved in the study?

If you decide to participate in the study you will be interviewed to share your knowledge and experience about childhood infections and the medicinal plants used to treat them. You will also be asked questions about how you prepare the plants for treatment as well as where you find or buy the plants. The researcher or assistants will be taking down notes on your responses or record you with your permission. Later on in follow-up visits you will be asked to identify the plants you mentioned in the interviews. You may also be asked to accompany the researcher on plant collection field trips to ensure the correct identification of the medicinal plants.

Time frame

This research is expected to last for two years so we expect to make frequent visits to see you especially during spring and summer and to let you know the outcomes of the study.

Benefits

We can't guarantee that you will personally experience benefits from participating in this study. It is reasonable to expect future benefits like the following from the information we find in this study:

- Help in creating an Ecostore (area for product development) for the medicinal plants used for infections in children.
- Fundamental knowledge on medicinal plants used for treatment of infections in children
- Full access to research processes and results
- Full access to the catalogue published in Sesotho and English
- Preserving the knowledge for future generations on the use of medicinal plants, their safety and efficacy
- Influence on planting medicinal plants in gardens

Risks

From this research, the risks or discomfort to the participant will be minimal or non- existent. The study is all about day to day, time to time experience you get when treating infections in children. You will never be put in a position where you may feel awkward, self-unconscious, or ashamed. There will be no damage to your financial standing, employability, or reputation.

Your rights as a research participant and Confidentiality

Participation in this study is completely voluntary and anonymous. Information gathered during the research will be used solely for the purpose of this study and all efforts will be made to ensure the confidentiality of participants' personal information. Indirect quotes will be used to avoid tracing it back to the individual if data will be published. Most of the data you provide will be grouped with other participants. Please note that while your name will be recorded with the data, it will not be used in the report. All identifiable data will be stored securely on a computer with password-restricted access and only the researcher (and supervisor if applicable), and ethics committee members will have access to it. All identifiable information will be destroyed at the end of the study or after 15 years, whichever comes first.

Please take time to read this entire form and ask questions before deciding whether to take part in this research project. If you decide not to participate there will not be any negative consequences. Please be aware that if you decide to participate, you may withdraw from the study at any time and your data will be returned to you or destroyed. You may also decide not to answer any specific question.

Contacts for questions or problems

If you have questions about the study, any problems, or think that something unusual or unexpected is happening you can contact:

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051 - 507 4023
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If you have any questions or concerns about your rights as a research participant, contact:

Prof Samson Mashele Dean Faculty of Health and Environmental Sciences, Central University of Technology **Tel: (051) 5073111** Email: **smashele@cut.ac.za**	**Prof Carlu van der Westhuizen** Assistant Dean: Research, Innovation & Engagement Faculty of Health and Environmental Sciences, Central University of Technology Tel: **(051) 5073788** Email: **cvdwesth@cut.ac.za**

INFORMED CONSENT FORM

Thank you for your participation. By submitting this form you are indicating that you have read the description of the study, are over the age of 18, and that you agree to the terms as described in the short questionnaire that follows:

I have read and I understand the provided information and have had the opportunity to ask questions. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving a reason and without cost. I understand that I will be given a copy of this consent form. I voluntarily agree to take part in this study. **I have had all my questions answered to my satisfaction**.

Yes ☐

No ☐

I grant permission for the research to be recorded and saved for purpose of review by the researcher, supervisor / principal investigator, and ethics committee.

Yes ☐

No ☐

I grant permission for the research recordings to be used in presentations or documentation of this study.

Yes ☐

No ☐

Participant's Name: ____

Address: ____

Contact details: ____

Signature ____________________________ Date __________

Investigator's signature ____________________________ Date __________

Verbal consent *(Applicable when participants cannot read or write)*

I hereby declare that I have read explained and clarify the contents of the data sheet to the research participant. The nature and purpose of the study were explained. The possible risks and benefits of the study were also explained. The research participant has undoubtedly showed that he/she is aware of the right to withdraw from the study at any time, for any reason and without threatening his/her relationship with the research team. I hereby certify that the research participant has verbally agreed to participate in this study.

Participant's Name: ____

Address: ____

Contact details: ____

Signature ______________________________ Date __________

Investigator's signature _____________________________ Date __________

INTERVIEW QUESTIONS FOR TRADITIONAL HEALERS

1. DEMOGRAPHIC INFORMATION

1.1 Name and Surname

1.2 Gender

1.3 Date of birth / Age

1.4 Location/Residence

1.5 What is your marital status? Single Married Divorced Widowed

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1.6 How did you become a traditional healer?

1.7 What is your employment status/ occupation?

1.8 Religion

1.9 Ethnic group

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2. KNOWLEDGE ATTRIBUTE

2.1 Do you have any knowledge on the use of medicinal plants?

2.2 Do you use medicinal plants to treat illnesses in children?

____

2.3 How long (time in years) have you been treating children with medicinal plants?

____

2.4 How many children have you treated so far?

____

3. PLANT KNOWLEDGE

3.1 Which illnesses do you treat in children?

3.2 Which plants can be used to treat illnesses mentioned in children? (Local name in Sotho)

3.3 Do you use all the plants you mentioned above?

3.4 What is the age group of the children in which the plant is used for?

3.5 Basic description of the plant (Tree/ Herb/ Shrub/Climber)

3.6 Where is the plant collected) (Sources of the plant)

3.7 Are the plants abundant, rare, scarce or difficult to find in the place of collection? Compared to other years.

3.8 When is the plant harvested? (Season and time of the day)

3.9 Do you cultivate the plant?

3.10 What plant part(s) do you use?

3.11 Is the plant used individually or with a mixture of other plants? What other plants or items do they mix it with? Proportions

3.12 Do you use it fresh or dry?

If dry, how do you dry and store it after collection and for how long?

3.13 How do you prepare the plant for the remedies? 3.14 What is the mode of administration for children?

3.15 What dosage should they take, and for how long?

3.16 What are the Contraindications?

3.17 What are the side effects that can be observed?

3.18 What are the cultural observations?

The way the plant is supposed to be handled according to the culture.

Is it used for medicinal purposes only? If No, what other things is it used for?