Review Article

A Review of Plant-Based Therapies for the Treatment of Urinary Tract Infections in Traditional Southern African Medicine

Ian Cock,1,2 Nothando Mavuso,3 and Sandy Van Vuuren3

1School of Environment and Science, Griffith University, Brisbane 4111, Australia
2Environmental Futures Research Institute, Griffith University, Brisbane, Australia
3Department of Pharmacy and Pharmacology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, Gauteng 2193, South Africa

Correspondence should be addressed to Sandy Van Vuuren; sandy.vanvuuren@wits.ac.za

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Urinary tract infections (UTIs) are amongst the most common bacterial infections globally, with ∼11% of the world’s population contracting at least one infection annually. Several South African plants are used in traditional healing systems to treat UTIs, yet the therapeutic potential of these plants against bacteria that cause UTI remains poorly explored. This study documents southern African plant species used traditionally to treat UTIs. An extensive literature review was undertaken to document the southern African plant species that are used in traditional South African medicine to treat UTIs, thereby highlighting gaps in the current research that require further study. One hundred and fifty-three southern African plant species that are used to treat UTIs were identified. Eighty-five southern African plants were identified as having noteworthy inhibitory activity against the major UTI-causing bacteria. Few of those studies screened against all of the bacterial causes of UTIs, and none of those studies examined the mechanism of action of the plant preparations. Furthermore, many of those studies did not test the toxicity of the plant extracts, so an evaluation of the safety for therapeutic usage was lacking. Substantial further research is to determine their potential for therapeutic use.

1. Introduction

Urinary tract infections (UTIs) are amongst the most common human infections globally. Indeed, it has been estimated that nearly 800 million people (equating to approximately 11% of the global population) develop at least one UTI in any given year [1, 2]. They are substantially more common in women than in men, with the prevalence in women estimated to be approximately five times higher than in males [3]. Indeed, it is expected that more than half of female population of the world will contract at least one UTI in their lifetime, with a substantial proportion experiencing recurrent infections [1]. With the exception of a spike in UTI occurrence in women aged 14–24 years old, the prevalence of UTIs generally increases with age, with the highest incidence in women over 65 years of age [4]. The difference in rates of UTIs between men and women is related to anatomical differences between the genders. As the urethra is located closer to the anus and is shorter in women than in men, women are substantially more susceptible to infections by uropathogens [5]. Additionally, individual health status affects the incidence of UTIs. For example, immunocompromised individuals and sufferers of chronic uncontrolled diabetes mellitus have substantially increased incidences of UTIs as their weakened immune systems are unable to effectively combat infections [3].

Lifestyle and environmental factors also contribute to the prevalence of UTIs. Older adults often accumulate multiple medical conditions, and their treatment and management regimens may increase the risks of contracting UTIs. In particular, catheterisation substantially increases the incidence of UTIs, especially by Gram-negative bacterial pathogens [1]. Indeed, healthcare-associated UTIs have been estimated to account for approximately 10% of UTI cases,
with 75% of these being reported in female patients [6, 7]. Additionally, prolonged antibiotic usage to treat other medical conditions weakens the immune response, thereby increasing the susceptibility to UTIs. In younger women, increased sexual activity between the ages of 18 to 39 years of age increases both the incidence of UTIs and the frequency of recurrence [4]. Any region of the urinary tract may become infected, including the kidneys, bladder, urethra, and ureter [8]. When the UTIs occur in the lower regions of the urinary tract, the infection is known as a bladder infection (cystitis). Infections in the upper urinary tract (pyelonephritis) are commonly referred to as kidney infections.

1.1. Types of Urinary Tract Infections. Urinary tract infections are classified as either complicated or uncomplicated. Complicated infections occur in people with underlying conditions or abnormalities in any part of the genitourinary tract, making the infection more serious and more challenging to treat than uncomplicated infections. In contrast, uncomplicated UTIs are classified as infections occurring in the absence of comorbidities or other anatomical urinary tract and renal abnormalities [9]. The incidence of complicated UTIs is substantially lower than that of uncomplicated UTIs, which occur in otherwise healthy people with normal genitourinary tract anatomy [10]. However, uncomplicated infections are generally easier to manage, and treatment with a short course of antibiotics is usually effective. Urinary tract infections in children and males are generally categorised as uncomplicated infections due to their low probability of comorbidities [8]. Notably, complicated UTI-causative pathogens are linked to increased rates of antimicrobial resistance. Therefore, the development of effective therapies to treat these conditions is vital, not only to decrease the effects of these infections, but also to slow the development of further antibiotic-resistant bacterial strains.

1.2. Causes of Urinary Tract Infections. Interestingly, there can be notable differences between the infectious agents responsible for uncomplicated and complicated UTIs. The vast majority of these pathogens are normal components of the gastrointestinal or vaginal microflora, thereby increasing the chances that they cause UTIs. For both classes of UTI, uropathogenic *Escherichia coli* are the leading infective agent, accounting for approximately 75 and 65% for uncomplicated and complicated UTIs, respectively [1]. *Klebsiella pneumoniae* accounts for a further 6% and 8% of uncomplicated and complicated UTIs. The bacterium *Staphylococcus saprophyticus* causes about 6% of uncomplicated UTIs yet does not significantly contribute to complicated UTIs. In contrast, *Enterococcus* spp. contribute substantially to complicated UTI cases (~11%), yet contribute less to uncomplicated UTIs (~6%). Other bacteria also contribute significantly, albeit with substantially lower rate, to the incidence of UTIs. In particular, *Proteus* spp. (particularly *Proteus mirabilis*) and *Pseudomonas aeruginosa* each cause approximately 2% of both uncomplicated and complicated cases of UTIs. Other pathogens may occasionally also cause UTIs. For example, *Staphylococcus aureus* induces a low number of cases of UTIs, although these are generally considered a special case as they are usually secondary to blood *S. aureus* infections. UTIs can also be caused by fungal and viral pathogens, albeit with a substantially lower prevalence than reported for bacterial UTIs. In this review, we focus on the major bacterial causes of UTIs. Therefore, whilst numerous studies have screened traditional medicines for the ability to inhibit *S. aureus*, those studies generally focussed on other diseases (e.g., skin disorders), and we have not listed those studies herein due to the minor role of this bacteria in inducing UTIs. Likewise, *Candida albicans* infections are a common cause of urethra infections and are thus commonly classed as urethritis rather than a UTI. Therefore, we do not include studies examining the effects of southern African plants to inhibit *C. albicans* growth in this review. Numerous other studies have examined the effects of southern African plants against *C. albicans*, and the reader is directed to those studies [11–13]. Notably, those studies generally screened against *C. albicans* for reasons not associated with UTIs.

The pathogens that cause UTIs usually enter the urinary tract via the urethra. Bacteria are transferred to the urethra from the bowel. When they colonise the bladder, they attach to the bladder wall and form a biofilm, which helps the pathogens to evade the host’s immune response [14]. Improper urogenital area hygiene, sexual intercourse, and exposure to unfavourable hygiene products (e.g., scented and chemical filled feminine products and contraceptives) may aid in the introduction of pathogens to the urinary tract and create suitable growth conditions for infections to develop [10]. Other risk factors for contracting an uncomplicated UTI include sexual intercourse with a new sexual partner, use of contraceptives, and a history of previous recurrent UTIs. Risk factors for complicated UTIs are underlying diseases, use of catheters, abnormal genitourinary anatomy and physiology, hospitalisation, and exposure to antibiotics [10].

1.3. Symptoms of Urinary Tract Infections. Urinary tract infections may present in several ways including increased and persistent urgency to urinate, painful burning sensations associated with urination, increased frequency of urination, lower volumes for each urinary event, and cloudy and foul smelling urine. Pain in the lower abdomen, back, and pelvic area is also a relatively common symptom of UTIs, especially in women [8]. Occasionally, UTIs may result in blood in the urine, which may present as red-, pink-, or cola-coloured urine. Infection in the kidney may present with symptoms including nausea and vomiting, fever, and upper back pain (most commonly on a single side) [10]. Many of these signs and symptoms are generic, and UTIs are frequently overlooked or misdiagnosed as other conditions, particularly in older people.

1.4. Current Treatments. In most cases, UTIs are relatively easy to treat with a course of broad-spectrum antibiotics, although fluoroquinolones (including ciprofloxacin) are
African traditional systems are perhaps the most extensively studied and verified, although many of the therapies are yet to be extensively studied and verified, and substantially more work is needed in this field.

It is estimated that approximately 700,000 tons of plant materials are used each year in South Africa to produce herbal remedies worth 1.2 to 2.5 billion South African Rands annually [25–28]. Not only are these products widely used in South Africa by practitioners of traditional medicine, but they are also becoming increasingly popular as complementary and alternative medicines in combination with allopathic pharmaceuticals. Indeed, some plant products (e.g., Harpagophytum procumbens (Burch.) DC. Ex Meisn., commonly known as devil’s claw extracts) are commonly sold at pharmacies globally, and it is no longer necessary to visit a traditional Muthi market to obtain products developed from them. However, a substantial portion of traditional plant use in South Africa does use plant materials obtained and prepared following traditional methods. Depending on the plant species used, a variety of different parts including roots, flowers, leaves, bulbs, and stems may be used medicinally, and the individual parts may have substantially different properties and uses [29]. Traditional beliefs have a deep influence within the majority of the ethnic cultures in South Africa and are particularly prevalent in rural communities [30]. Even in urban communities, a large portion of the South African population is reliant on traditional medicine as their primary mode of healthcare [31]. Indeed, that study postulated that the demand for traditional medicines in South Africa will increase in future years due to stress associated with urban lifestyles.

Despite their widespread use, there is a relative lack of information on the proper use and preservation of plant medicines. Medicinal plants are considered (often erroneously) to have fewer adverse effects [32] and are often more accessible and affordable than Western/allopathic medications [33]. A substantial number of South Africans (especially rural populations) are dependent on self-medication with plant-based medicines, and the involvement of the community in managing the use and preservation of plant species may result in successful strategies for sustainable use [34]. South African ethnobotanical literature has been relatively well recorded, although the medicinal properties of many species used traditionally are yet to be rigorously verified. There has been a substantial increase in studies screening and validating the use of South African traditional medicines in recent years, highlighting the potential of several species [35]. Of the therapeutic properties examined, the antibacterial activity of South African plants has received the most attention, although many species remain relatively neglected. Numerous plants have been reported to have antimicrobial activity, with a substantial recent increase in interest in this field. However, very few of those studies have specifically focussed on UTIs. Instead, screening against bacterial pathogens that cause gastrointestinal diseases [36, 37], skin disease [38, 39], or autoimmune diseases [40, 41] have received far greater attention. Notably, many of the same bacterial species screened in the other studies are also amongst the pathogenic causes of UTIs. Whilst the focus of those studies is not UTIs, they are included in this

1.5. The Use of Medicinal Plants in Urinary Tract Infection Treatment. The launch and development of the WHO Traditional Medicine Strategy 2014–2023 aimed to support the development and implementation of proactive policies and action plans to improve the role traditional medicine plays in population health [24]. The strategy focuses on developing new health systems (including the use of complementary and traditional medicinal products) as a high priority. A re-examination of traditional medicines is an attractive option for the development of new therapies to treat pathogenic infections as plant-derived medicines have often been used for hundreds (in some cases, thousands) of years. Furthermore, the traditional use by some cultures has been relatively well documented. Asian, Middle Eastern, and African traditional systems are perhaps the most extensively

generally avoided as the side effects are often regarded as outweighing the benefits. The most common treatments include trimethoprim/sulfamethoxazole, fosfomycin, nitrofurantoin, cephalaxin, and ceftriaxone. However, due to overuse and misuse of commonly used clinical antibiotics, the emergence of antibiotic-resistant pathogens is increasingly common, resulting in the failure of the main antibiotic chemotherapy options [15]. Antibiotic resistance has been a driving force of new drug development initiatives, and implementation of alternative treatment identification and new antibiotic therapies are urgently required.

The development of antibiotic-resistant bacteria is increasingly resulting in antibiotic therapy failures, and chronic UTIs are becoming more frequent [1]. Additionally, the relatively high rate of UTI recurrence poses a challenge to the effective treatment of these infections [16]. Indeed, that study estimated that approximately 24% of people contracting a UTI will develop a recurrent infection within six months of the original infection. Of further concern, approximately 5% of people who develop a UTI will experience more than three recurrences per year [17].

Foxman and Buxton [18] suggest that empirical treatments of UTIs should be reconsidered due to the following reasons:

(i) The frequency of antibiotic-resistant E. coli strains, many of which have resistance to multiple antibiotics including fluoroquinolones [15], is increasing. The increasing incidence of extended spectrum β-lactamase (ESBL) UTI pathogens that are resistant to the commonly used β-lactam class of antibiotics is particularly concerning [19, 20].

(ii) Even relatively short courses of currently used antibiotic therapies may significantly affect the gut microflora, resulting in other health issues developing [21]. These therapies may also disrupt the urogenital microbiome, resulting in other unforeseen issues. Thus, the benefits of empirical antibiotic therapy may not outweigh the risks [22, 23]. New and innovative strategies to prevent UTI recurrences and alternative therapies for their treatment are considered a high priority [18].
study as they were screened against the same bacterial species.

2. Materials and Methods

This study aimed to record and document the southern African medicinal plants that are used traditionally to treat UTIs. A variety of ethnobotanical books [42–46], as well as multiple peer reviewed journal articles, were consulted to compile this list. The online resources Google Scholar, PubMed, Scopus, and ScienceDirect were used to identify and access original scientific research studies. The following terms were used as filters and were searched for both alone and as combination: “Southern Africa,” “South African,” “Lesotho,” “Swaziland,” “Namibia,” “Botswana,” “Zimbabwe,” “Zambia,” “Mozambique,” “traditional medicinal plant,” “ethnobotany,” “urinary tract infection,” “UTI,” “bladder,” and “uropathogens.” The initial search aimed to document all of the plant species used in southern Africa to treat UTIs. Our study was nonbiased and did not favour the traditional knowledge of one ethnic group over others. Despite this, substantially more information was available about Zulu traditional medicine due to the prevalence of reports on that topic in the available literature. Whilst most of these species are native South African plants, introduced species were not excluded, where they had been incorporated into the traditional medicine systems of at least one South African ethnic group. Following the initial literature review, a further review was undertaken to identify the species that have been screened for their ability to inhibit one or more of the bacterial pathogens that cause UTIs.

2.1. Eligibility Criteria. Ethnobotanical books and peer reviewed journal articles were searched using the specific key words noted above. Published studies were identified and their abstracts were read to establish their relevance to this study. The full content of publications that were deemed relevant were then examined thoroughly to ensure that the eligibility criteria were met.

2.2. Inclusion Criteria. The following inclusion criteria for eligibility of the study were considered:

(i) Publications written in English and prior to April 2021 were used in this review.
(ii) Our study was nonbiased and without any taxonomic preference.
(iii) For the ethnobotanical survey (Table 1), only plant species that are recorded to treat UTIs are included. Any plants recorded to treat individual nonspecific symptoms were excluded unless it could be determined that they were specifically used to treat UTIs.
(iv) For the biological activity studies presented in Table 2, only studies that screened against the major bacterial causes of UTIs were included, irrespective of whether the focus of the study was UTIs or the bacteria tested were selected because of their association with a different disease.

(v) Only studies screening against the common causes of UTIs were evaluated in this review, irrespective of their focus. For example, studies that screened southern African plants against E. coli were included in this study, even if their focus was on gastrointestinal diseases rather than UTIs.

(vi) Ethnobotanical studies on the flora of southern African region included South Africa and those countries immediately surrounding it.

2.3. Exclusion Criteria. The following criteria were used to exclude some studies:

(i) Where name changes and families of plant species were encountered, particularly in older publications, websites such as The Plant List (http://www.theplantlists.org/) and South African National Biodiversity Institute (SANBI) (http://www.sanbi.org) were used to confirm species identification.
(ii) Plant species that were recorded to treat generic symptoms of UTIs that are common to other illnesses, without specifically stating their use in treating UTIs, were excluded from this study.
(iii) Studies that screened against bacteria that only cause UTIs secondary to other diseases were excluded. Therefore, studies screening South African plants for S. aureus, which only causes UTIs secondary to blood S. aureus infections, were not included in this study.
(iv) Only screening studies that tested against bacterial pathogens were included in this study. Publications that screened South African plants for fungi, viruses, or protozoa were excluded.
(v) The use of introduced plant species were excluded from this study unless they are extensively used as part of southern African traditional medicine of at least one South African ethnic group.

2.4. Data Collection. A thorough literature search for publications on southern African medicinal plants used traditionally to treat UTIs was undertaken and is summarised in this study. Additionally, in vivo and in vitro biological screening of South African medicinal plants for bacterial pathogens that cause UTIs are summarised, regardless of the origin of the study. The following data was collected for each species:

(i) Species name, family name, and common name for each species recorded in the individual publications were collected
(ii) Common names and the names used by different ethnic groups (where appropriate) were collected from individual publications and from the SANBI red list website
(iii) The plant part used, method of preparation, and mode of administration were recorded where that information was provided
| Plant species                          | Family                        | Common name                                           | Part of plant used | Uses                                      | References |
|---------------------------------------|-------------------------------|-------------------------------------------------------|--------------------|-------------------------------------------|------------|
| *Acacia sieberiana* var. *woodii*     | Leguminosae                   | Paperbark thorn (Eng); papierbaskerdor (Afr)         | Bark and roots     | Urinary tract ailments                    | [46]       |
| (Burtt Davy) Keay & Brenan            |                               |                                                       |                    | Urinary tract infection                   |            |
| *Acokanthera oppositifolia* (Lam.) Codd | Apocynaceae                   | Inhluengyembe (Zulu)                                  | Not specified      | Urinary ailments                          | [43]       |
| *Afroaster hispida* (Thunb.) J.C.Manning & Goldblatt | Asteraceae                  | Udlutshana (Zulu)                                     | Not specified      | Urinary ailments                          | [47]       |
| *Agathaoma betulina* (P.J.Bergius) Pillans | Rutaceae                     | Buchu (Eng); boeoe (Afr); bocho (Sotho)              | Leaves             | Bladder and kidney ailments               | [45, 48, 49] |
| *Agathaoma capensis* (L.) Dummer      | Rutaceae                     | Spicy buchu (Eng); anysboeoe, steenbokboeoe (Afr)    | Leaves             | Urinary ailments                          | [50]       |
| *Agathaoma serratifolia* (Curtis) Spreeht | Rutaceae                     | Langblaarboeoe, kloofboeoe (Afr); long buchu (Eng)   | Leaves             | Bladder and kidney ailments               | [45]       |
| *Albizia adianthifolia* (Schum.) W.Wight | Leguminosae                   | Lisyengelele, usolo, umgadankawu (Zulu)              | Not specified      | Urinary tract infection                   | [47]       |
| *Aloe ferox* Mill.                    | Xanthorrhoeaceae              | Bitteraalwyn (Afr); bitter aloe (Eng)                 | Leaves, roots, and stems | Kidney and bladder ailments               | [51]       |
| *Aloe zebrina* Baker                  | Xanthorrhoeaceae              | Sebraaalwyn (Afr); zebra aloe (Eng)                   | Leaves             | Urinary and bladder ailments              | [46]       |
| *Antiphiona pinnatisecta* (S.Moore) Merxm. | Compositae                   | Unknown                                               | Roots              | Bladder ailments                          | [46]       |
| *Antizoma angustifolia* (Burch.) Miers ex Harv. | Menispermaceae              | Maagbitterwortel (Afr)                                | Roots              | Kidney and bladder ailments               | [52]       |
| *Aptosimum procumbens* (Lehm.) Burch. ex Steud. | Scrophulariaceae          | Brandbos (Afr)                                        | Leaves             | Bladder ailments                          | [42–44]    |
| *Arctopus echinatus* L.               | Apiaceae                     | Alsem (Afr); African wormwood (Eng); mhlonyana (Zulu) | Leaves, roots, and stems | Kidney and bladder ailments               | [49, 51]    |
| *Asparagus africanus* Lam.            | Asparagaceae                  | African asparagus (Eng); kadoring (Afr); isigob (Zulu) | Not specified      | Bladder and kidney ailments               | [46]       |
| *Asparagus asparagoides* (L.) Druce   | Asparagaceae                  | Makholela (Sotho)                                     | Roots              | Urinary tract infection                   | [48]       |
| *Aster bakerianus* Burtt Davy ex C.A.Sm. | Compositae                 | Idlutshane, uholshana (Zulu)                          | Leaves             | Urinary tract infection                   | [43]       |
| *Baccharoides adoensis* var. *kotschyana* (Sch.Bip. ex Walp.) | Compositae                    | Innyathelo (Zulu)                                     | Stems and leaves   | Urinary tract infection                   | [43]       |
| *Ballota africana* (L.) Benth.        | Lamiaceae                     | Kattekruid (Afr)                                      | Leaves             | Bladder and kidney ailments               | [50]       |
| *Berkeyha Setifera* DC.               | Compositae                   | Ikhakhase, umlumumuba (Zulu); lelema-la-khomo (Sotho) | Root               | Urinary and kidney ailments               | [47, 54]    |
| *Bolusanthus speciosus* (Bolus) Harms | Leguminosae                   | Umhlo (Zulu); tree wisteria (Eng); vanwykshout (Afr) | Barks, leaves, and stems | Kidney ailments                           | [55]       |
| *Boophone disticha* (L.F.) Herb.      | Amaryllidaceae                | Gifbol (Afr)                                          | Bulb               | Bladder ailments                          | [42–44]    |
| *Bowoea volubils* Harv.               | Asparagaceae                  | Climbing onion (Eng); knolklomip (Afr); iguleni (Zulu) | Bulb               | Bladder ailments                          | [43, 48]    |
| *Brachylaena discolor* DC.            | Compositae                   | Bosvaalbos (Afr); ipahla (Zulu)                       | Leaves             | Urinary ailments                          | [43]       |
| *Bulbine abyssinica* A.Rich           | Xanthorrhoeaceae              | Wildekopieva (Afr)                                    | Leaves             | Bladder ailments                          | [56, 57]    |
| *Bulbine latifolia* (L.) Spreng.      | Xanthorrhoeaceae              | Red carrot (Eng); rooiwortel (Afr)                     | Root               | Bladder and kidney ailments               | [48, 57]    |
| *Cardiospermum halicacabum* L.         | Sapindaceae                   | Balloon vine (Eng); blaasaklimop (Afr)                | Stems and leaves   | Bladder ailments                          | [43, 46, 58] |
| *Carica papaya* L.                    | Caricaceae                    | Papaya, pawpaw (Eng)                                  | Not specified      | Bladder ailments                          | [42]       |
| *Cenchrus ciliaris* L.                | Poaceae                      | Buffalograss (Eng); bloubuffelgras (Afr); idungamuzi (Zulu) | Roots              | Urinary tract infection                   | [43, 59, 60] |
| *Centaura benedicta* (L.) L.           | Compositae                   | Karmedik (Afr)                                        | Not specified      | Urinary and kidney ailments               | [50]       |
| *Chironia baciffa* L.                 | Gentianaceae                  | Bitterbos, sarsaparilla (Afr)                         | Not specified      | Urinary ailments                          | [50]       |
Table 1: Continued.

| Plant species                     | Family          | Common name                                      | Part of plant used | Uses                                           | References |
|-----------------------------------|-----------------|--------------------------------------------------|--------------------|------------------------------------------------|------------|
| Chrysanthemoides monilifera (L.) Norl. | Compositae      | Bietou, bessiebos (Afr)                          | Whole plant        | Urinary and kidney ailments                    | [50]       |
| Cissampelos capensis L.f.         | Menispermaceae  | David’s root (Eng); gifhondjie, dawidjeswortel (Afr) | Roots and leaves   | Bladder ailments                               | [42–44, 46]|
| Cleome gynandra L.                | Cleomaceae      | African cabbage, spiderwisp (Eng); snottierbelletjie (Afr) | Not specified      | Bladder ailments                               | [42]       |
| Clilfortia odorata L.f.           | Rosaceae        | Wildewingerd (Afr); wild vine (Eng)              | Leaves             | Bladder ailments                               | [48]       |
| Clivia miniata (Lindl.) Bosse     | Amaryllidaceae  | Benediction lily (Eng); boslelie (Afr); umayime (Zulu) | Bulb               | Urinary ailments                               | [43]       |
| Coix lacryma-jobi L.              | Poaceae         | Job’s tears, adlay (Eng)                         | Not specified      | Bladder ailments                               | [42]       |
| Combretum kraussii Hochst.        | Combretaceae    | Umduba, umdubu omhilope, umdubu wamanziz (Zulu)  | Not specified      | Urinary and bladder ailments                   | [47]       |
| Commelina africana L.             | Commelinaceae   | Idangabane (Zulu); khpo (Sotho)                  | Root               | Bladder ailments                               | [43]       |
| Conostomium natalense (Hochst.) Bremek | Rubiaceae      | Wild pensa (Eng); umbophe, uncolosi (Zulu)       | Not specified      | Urinary ailments                               | [61]       |
| Conyza scabrifolia DC.            | Compositae      | Oondbos, bakbos, padders (Afr)                    | Leaves             | Bladder infection                              | [51]       |
| Crinum macowanii Baker            | Amaryllidaceae  | River fly (Eng); umduze (Zulu)                   | Bulb               | Urinary ailments                               | [43]       |
| Crinum moorei Hook. f.            | Amaryllidaceae  | Umduze (Zulu)                                    | Bulb               | Urinary ailments                               | [43]       |
| Crossyphus guttata (L.) D.Müll-Dobles & U.Müll-Dobles | Amaryllidaceae | Gifbol (Afr)                                     | Bulb               | Bladder ailments                               | [42–44]   |
| Cryptolepis oblongifolia (Meisn.) Schl. | Apocynaceae | Bokhoring, melkobs (Afr); mukanjazaza (Sotho)    | Not specified      | Bladder ailments                               | [42]       |
| Cassonia paniculata Eckl. & Zeyh. | Araliaceae      | Motsetse (Sotho)                                 | Not specified      | Kidney and bladder ailments                    | [54, 62]   |
| Cyathula achyranthoides (Kunth) Moq. | Acanthaceae    | Unknown                                          | Not specified      | Bladder ailments                               | [63]       |
| Cynodon dactylon (L.) Pers.       | Poaceae         | Dog’s tooth (Eng); krookgras (Afr)                | Rhizome            | Urinary ailments                               | [46]       |
| Datura stramonium L.              | Solanaceae      | Thornapple, jimsonweed, devil’s snare (Eng)      | Leaves             | Bladder ailments                               | [42]       |
| Dicoma capensis Less.             | Compositae      | Karmedik, wilde karmedik (Afr)                    | Leaves             | Bladder and kidney ailments                    | [44, 45, 56, 57] |
| Diosma oppositifolia L.           | Rutaceae        | Buchu, Bitter buchu (Eng)                         | Leaves             | Bladder and kidney ailments                    | [48]       |
| Diosma prama I.Williams Hochst. ex A.D.C | Rutaceae        | Steenbokboege (Afr)                              | Not specified      | Urinary and kidney ailments                    | [50]       |
| Diospyros mespiliformis Hochst. ex A.D.C | Ebenaceae      | Ikhambi lesdu, umazambazi (Zulu)                 | Not specified      | Urinary ailments                               | [47]       |
| Dipcaia gracilissimum Baker       | Asparagusaceae  | Oumasegroottoon (Afr)                            | Not specified      | Bladder ailments                               | [63]       |
| Dipsca viride (L.) Moench         | Asparagusaceae  | Ugibisila, ugenileni, umakhweya (Zulu)           | Not specified      | Urinary tract infection                       | [47]       |
| Dipsca gracilissimum Baker        | Asparagusaceae  | Oumasegroottoon (Afr)                            | Not specified      | Bladder ailments                               | [64]       |
| Dodonaea viscosa (L.) Jacq.       | Sapindaceae     | Basterol, sandolain, yterbros (Afr); sand olie (Eng); umqumbu (Zulu) | Leaves             | Bladder and kidney ailments                    | [5, 50, 51]|
| Drimia elata Jacq.                | Asparagusaceae  | Satin squill (Eng); brandui, jeukbol (Afr); umqumbu (Zulu) | Not specified      | Urinary ailments                               | [44]       |
| Dysphania ambrosioides (L.) Mosaykin & Clemants | Amaranthaceae | Ikhambi lesumo, uzansikwesibay (Zulu)            | Not specified      | Urinary ailments                               | [47]       |
| Elytrigappus rhinocerotes (L.f.) Less. | Asteraceae     | Renosterbos (Afr)                                | Leaves             | Bladder and kidney disorders                  | [49]       |
| Elymus repens (L.) Gould           | Poaceae         | Couch grass (Eng)                                | Not specified      | Bladder ailments                               | [42]       |
| Empleurus unicapsulare (L.f.) Skeels | Rutaceae        | Bergboege, langblaarboege (Afr)                   | Whole plant        | Urinary and kidney ailments                    | [50]       |
| Eriosephalus punctulatus DC.      | Compositae      | Kapokbos (Afr)                                   | Whole plant        | Bladder and kidney ailments                    | [50]       |
| Eriosephalus distinctum N.E.Br.   | Leguminosae     | Ubangalala omkhulu (Zulu)                         | Roots              | Urinary ailments                               | [43]       |
Table 1: Continued.

| Plant species | Family          | Common name                          | Part of plant used | Uses                            | References |
|---------------|-----------------|--------------------------------------|--------------------|---------------------------------|------------|
| Erythrina caffra Thunb. | Leguminosae | Coral tree (Eng); kaffirboom (Afr); umsinsi (Zulu) | Leaves          | Urinary ailments                | [43]       |
| Erythrina lysistemon Hutch. | Leguminosae | Umsinsi (Zulu)                        | Leaves          | Bladder ailments                | [47]       |
| Euclea natalensis A.DC. | Ebenaceae | IsiZimane, umshekisane (Zulu)         | Bark             | Urinary tract infection         | [47, 65]   |
| Euclea undulata Thunb. | Ebenaceae | Gharwarie, gharwarieboom, gharwiebos (Afr) | Whole plant      | Urinary and kidney ailments     | [43, 50]   |
| Eucomis autumnalis (Mill.) Chitt | Asparagaceae | Mathethebane (Soho)                   | Tubular roots    | Urinary ailments                | [58]       |
| Euphorbia milii Des Moul. | Euphorbiaceae | Crown of thorns (Eng)                 | Not specified    | Bladder ailments                | [64, 66]   |
| Euphorbia tithymaloides L. | Euphorbiaceae | Redbird flower (Eng)                  | Not specified    | Bladder ailments                | [64, 66]   |
| Exomis microphylla (Thunb.) Aellen | Amaranthaceae | Hondepisbos, hondebossie (Afr)        | Whole plant      | Urinary ailments                | [50]       |
| Faidherbia albida (Delile) A.Chev. | Leguminosae | Anatree (Eng); anaboom (Afr)          | Bark             | Bladder ailments                | [46]       |
| Foeniculum vulgare Mill. | Apiaceae | Vinkel, makukinkel, soetvinkel (Afr)   | Whole plant      | Bladder ailments                | [50]       |
| Galenia africana L. | Aizoaceae | Kraalbos (Afr)                        | Leaves           | Bladder ailments                | [42–44]    |
| Galium tomentosum Thunb. | Rubiaceae | Red storm (Eng); rooistorm, doodief (Afr) | Not specified    | Bladder ailments                | [48, 56]   |
| Geranium incanum Burm.f. | Geraniaceae | Carpet geranium (Eng); horlosie, bergte, vrouette (Afr); tlako (Sotho) | Not specified    | Bladder ailments                | [56, 64]   |
| Grewia caffra Meisn. | Malvaceae | Upata, ihathu (Zulu)                  | Roots, bark      | Bladder ailments                | [67]       |
| Grewia occidentalis L. | Malvaceae | Cross berry (Eng); ikloko, imahlele (Zulu) | Roots            | Bladder ailments                | [43]       |
| Grewia robusta Burch. | Malvaceae | Bokbos (Afr)                          | Whole plant      | Urinary ailments                | [50]       |
| Gunnera perpensa L. | Gunneraceae | Ugooho, izibuzulu (Zulu)              | Not specified    | Bladder ailments                | [47]       |
| Helichrysum crispum (L.) D. Don | Compositae | Kooigoed (Afr)                        | Leaf             | Bladder and kidney ailments     | [49]       |
| Helichrysum odoratissimum (L.) Sweet | Compositae | Pheto (Sotho); kooigoed, kooibos (Afr) | Leaves, roots, and stems | Bladder ailments                | [50, 56]   |
| Helichrysum patulum (L.) D.Don | Compositae | Honey everlasting (Eng); kooigoed (Afr); impetpo (Zulu) | Not specified    | Bladder ailments                | [42]       |
| Hibiscus pusillus Thunb. | Malvaceae | Blaasbossie (Afr)                     | Whole plant      | Stems and Leaves                | [50]       |
| Hibiscus mastersianus Hiern | Malvaceae | Monarch rosemallow (Eng)              | Urinary ailments | Urinary ailments                | [46]       |
| Hibiscus pedunculatus L.f. | Malvaceae | Pink mallow (Eng); indola ebonvu (Zulu) | Leaves           | Urinary ailments                | [43]       |
| Hoslandia opposita Vahl | Lamiaceae | Bird gooseberry (Eng); uyaweyaye (Zulu) | Not specified    | Urinary ailments                | [46]       |
| Hypoxis hemicallidea Fisch., C.A.Mey. & Avé-Lall. | Hypoxidaceae | Inkanfe (Zulu); yellow star (Eng)    | Not specified    | Bladder ailments                | [47, 50]   |
| Hypoxis rigidula Baker | Hypoxidaceae | Ilabatheka, inkomfe, umhungulo (Zulu); African potato (Eng) | Not specified    | Bladder ailments                | [47, 50]   |
| Indigofera cassioides DC. | Leguminosae | Unknown                               | Not specified    | Bladder ailments                | [42]       |
| Ipomoea pes-caprae (L.) R.Br. | Convolvulaceae | Beach morning glory, goat’s foot (Eng); strandpatat (Afr) | Not specified    | Bladder ailments                | [42]       |
| Jasminum abysinicum Hochst. ex DC. | Oleaceae | Mthundangazi                          | Roots            | Bladder ailments                | [68]       |
| Kedrostis capensis A. Meeuse | Cucurbitaceae | Sesepa sa linoha (Sotho)             | Tubular roots and leaves | Urinary tract infection         | [69]       |
| Ledebouria marginata (Baker) Jessop | Asparagaceae | Bokhoe (Sotho)                       | Root bulb        | Urinary tract infection         | [70]       |
| Leonotis leonurus (L.) R.Br. | Lamiaceae | Klip dagga, wild dagga (Afr)          | Stems with leaves and flowers | Bladder and kidney disorders, and | [49]       |
| Lessertia frutescens (L.) Goldblatt & J.C.Manning | Leguminosae | Kalkoenblom, keurtjie (Afr)           | Leaves           | Kidney and urinary ailments     | [50, 56]   |
| Plant species                  | Family            | Common name                        | Part of plant used | Uses                             | References   |
|-------------------------------|-------------------|------------------------------------|--------------------|----------------------------------|--------------|
| Matricaria chamomilla L.      | Compositae        | Chamomile (Eng)                    | Not specified      | Bladder ailments                 | [42]         |
| Melianthus pectinatus Harv.   | Melianthaceae     | Kriekiebos, lidjiebos (Afr)        | Root               | Urinary tract infection          | [56]         |
| Mentha longifolia (L.) L.     | Lamiaceae         | Wild mint (Eng); uutfhana lomhlanga (Zulu) | Leaves             | Bladder and kidney ailments      | [49, 52, 68] |
| Mervilla plumbea (Lindl.)     | Asparagaceae      | Inguduzu, untapotosis, untangana zibomvana (Zulu) | Not specified     | Bladder ailments                 | [47, 50]     |
| Mesembryanthemum cordifolium L.f. | Aizoaceae       | Ibohlololo (Zulu)                 | Leaves             | Bladder ailment                  | [44, 47, 53] |
| Mesembryanthemum crystallinum L. | Aizoaceae        | Common ice plant, crystalline ice plant (Eng); soutraai, volsruuslaai (Afr) | Not specified     | Bladder ailments                 | [42]         |
| Mikania capensis DC.          | Compositae        | Umldonzo, umholoz (Zulu)           | Roots              | Urinary ailments                 | [42, 43]     |
| Millettia obliqua Dunn        | Leguminosae       | Unknown                            | Blister bush (Eng); bergseldery (Afr) | Kidney and bladder ailment | [42, 52]     |
| Notobubon galbanum (L.) Magee | Apiaceae          | Blue water lily (Eng); blowswaterlelie (Afr); izubu, iziba, uqobho (Zulu) | Not specified     | Urinary tract infection          | [46, 47, 49] |
| Nymphaea nouchali Burm.f.     | Nymphaeaceae      | Leaves                             | Urinary tract infection | [46, 49]             |              |
| Ocimum americanum L.          | Lamiaceae         | Hoary basil (Eng); wilde basielkruid (Afr) | Not specified     | Urinary tract infection          | [46]         |
| Ocotea bullata (Burch.) E. Meyer in Drege | Lauraceae | Stinkwood, laurel wood (Eng); umnkani, umhlungulu (Zulu) | Wild olive (Eng); olyfhout, olenhout (Afr); isadlulambezo (Zulu) | Urinary ailments | [43, 58]     |
| Olea europaea L.              | Oleaceae          | Snuff-box tree (Eng); snuikalbassie (Afr) | Roots and bark    | Urinary tract infection          | [43, 46]     |
| Oncoba spinosa Forssk.        | Salicaceae        | Foie e kubedu (Sepedi); mudoro (Venda) | Roots              | Urinary ailments                 | [63]         |
| Opuntia ficus-indica (L.) Mill. | Cactaceae        | Large caltrops (Eng)               | Leaves and twigs   | Bladder and kidney ailments      | [42]         |
| Pedaliunum murex L.           | Pedaliaceae       | Ghwarriseson, heuningdou (Afr)     | Leaves and twigs   | Bladder and kidney ailments      | [42]         |
| Pegoletia baccharidifolia Less. | Compositae       | Rooriaboras (Afr); gooseberry-leaved Pelargonium (Eng) | Leaves and stems  | Urinary tract infection          | [51, 68]     |
| Pelargonium grossularioides (L.) L’Hér. | Geraniaceae | Rooriaboras (Afr)                 | Roots              | Urinary tract infection          | [56]         |
| Pelargonium hypoleucum Turcz. | Geraniaceae       | Rooriaboras (Afr)                 | Roots              | Bladder and kidney ailments      | [51, 68]     |
| Pelargonium ramosissimum Wildl. | Geraniaceae      | Dassieboegoe, dassiebos (Afr)      | Leaves and stems   | Bladder and kidney ailments      | [43]         |
| Pentanisia prunelloides (Klotzsch) Walp. | Rubiaceae | Sooihrandboossie (Afr); icimamlilo (Zulu) | Roots              | Bladder and kidney ailments      | [43]         |
| Pentstemon crispus (Mill.) Nyman ex A.W.Hill. | Apiaceae | Pietersielie (Afr); parsley (Eng) | Leaves             | Bladder ailments                 | [49, 66]     |
| Phytolacca heptandra Retz.    | Phytolaccae       | Inkbessie (Afr); ingubivumile (Zulu) | Not specified     | Urinary ailments                 | [43]         |
| Portulaca quadrigula L.       | Portulacaceae     | Pigweed, wild purslane (Eng); kanniiedood (Afr) | Not specified     | Urinary tract infection          | [46, 42]     |
| Prunus persica (L.) Batsch    | Rosaceae          | Peach (Eng)                        | Leaves             | Bladder and kidney ailments      | [42]         |
| Ranunculus multifidus Forssk. | Ranunculaceae     | Botterblom, brandblare (Afr); uxsaphozi (Zulu) | Leaves             | Urinary ailments                 | [43]         |
| Rhamnus prinoides L’Hér.      | Rhamnaceae        | Mofifi (Sotho)                     | Root               | Kidney and bladder ailment       | [54]         |
| Rhicissus tridentata (L.) Wild & R.B.Drumm. | Vitaceae | Wild/bitter grape (Eng); bobbejaantou, wildedruif (Afr); isinwazi (Zulu) | Stems              | Urinary ailments                 | [43, 64]     |
| Rhynchosia caribaea (Jacq.) DC. | Leguminosae      | Snoutbean (Eng); rankboontjie (Afr); isilhalasengomni (Zulu) | Roots              | Bladder ailments                 | [46]         |
| Rhynchosia minima (L.) DC.    | Leguminosae       | Leat snoutbean, burn-mouth-vine (Eng) | Roots              | Bladder ailments                 | [46]         |
Microsoft Excel was used for statistical data analysis.

3. Results

3.1. Plants Used Traditionally to Treat Urinary Tract Infections. Numerous South African plant species have been recorded to treat pathogenic diseases. This knowledge has traditionally been passed down from generation to generation by word of mouth, and some of this knowledge has now been recorded in ethnobotanical publications, although it is likely that substantial information is not yet readily available. A total of 153 plants from fifty-two families were recorded in the literature for the treatment of UTIs (Table 1). Out of the fifty-two families, Compositae had the greatest number of entries.

| Plant species                      | Family            | Common name                                      | Part of plant used | Uses                                  | References |
|------------------------------------|-------------------|--------------------------------------------------|--------------------|---------------------------------------|------------|
| Rhyynosia sublobata (Schum.) Meikle| Leguminosae       | Twiner of barren ground (Eng)                    | Roots              | Bladder ailments                      | [46]       |
| Ricinus communis L.                | Euphorbiaceae     | Olieboom, olieblaar (Afr)                        | Leaves             | Urinary and kidney ailments           | [47, 50]   |
| Rotheca hirsuta (Hochst.) R.Fern    | Lamiaceae         | Butterfly bush, wild violet (Eng); umathanja, lukiskisi (Zulu) | Not specified | Urinary ailments                      | [64]       |
| Ruta graveolens L.                 | Rutaceae          | Wynruit (Afr)                                    | Leaves             | Urinary tract infection and bladder ailments | [49, 56] |
| Salix woodii Seemen                | Salicaceae        | Wild willow (Eng)                                | Bark               | Urinary ailments                      | [69]       |
| Salix mucronata Thunb.             | Salicaceae        | Cape willow (Eng); vaalwilger (Afr)              | Bark               | Bladder ailments                      | [46]       |
| Salvadoria persica L.              | Salvadoraceae     | Toothbrush tree, real mustard tree (Eng); kerriebos (Afr) | Roots             | Urinary tract infection              | [46]       |
| Solavia microphylla Kunth          | Lamiaceae         | Baby sage, Graham’s sage, blackcurrant sage (Eng) | Roots              | Urinary ailments                      | [50]       |
| Scadoxus puniceus (L.) Friis & Nordal| Amaryllidaceae    | Imdume likaholiyole, uhloleyile, umphompo (Zulu) | Not specified | Urinary ailments                      | [47]       |
| Solanum aculeastrum Dunal R.Br.    | Solanaceae        | Gifappel (Afr); umthuma, untumane (Zulu)         | Fruit              | Urinary tract infection and kidney ailments | [47, 48] |
| Sutherlandia frutescens (L.)       | Fabaceae          | Keurtjies, kankerbossie (Afr)                     | Leaves and stems    | Bladder and kidney ailments           | [49]       |
| Tarchonanthus camphoratus L.       | Compositae        | Camphor bush (Eng); wilde kanferbos (Afr); igceba elimhlohe (Zulu) | Not specified | Urinary ailments                      | [64]       |
| Teucrium trifidum Retz.            | Lamiaceae         | Katjiedriebaar (Afr)                             | Leaves             | Bladder ailments                      | [56, 57]   |
| Thesium hystrix A.W.Hill           | Santalaceae       | Kleinswartsboom (Afr)                            | Roots              | Bladder ailments                      | [42]       |
| Tragia meyeriana Müll.Arg.         | Euphorbiaceae     | Stinging nettle (Eng); ubangalala, imbabazane (Zulu) | Not specified | Bladder ailments                      | [42, 43]   |
| Tragia rupestris Sond.             | Euphorbiaceae     | Ubangalala, imbabazane (Zulu)                    | Roots              | Bladder ailments                      | [43]       |
| Trichilia emetica Vahl             | Meliaceae         | Red rash (Eng); basteressenhout (Afr); ixolo, umkhuhlu (Zulu) | Bark              | Kidney ailments                       | [43]       |
| Trifolium africanum Ser.           | Leguminosae       | (Eng); wildeklawer (Afr); moqoiqoi, moqophi (Sesotho) | Not specified | Bladder ailments                      | [63]       |
| Typha capensis (Rohrb.) N.E.Br.    | Typhaceae         | Papkuil (Afr)                                    | Not specified      | Bladder and kidney ailments           | [46]       |
| Urtica urens L.                    | Urticaceae        | Small nettle (Eng); dog nettle (Eng)             | Bark               | Bladder pains                        | [58]       |
| Warburgia salutaris (G.Bertol.) Chiov. | Canellaceae   | Isibaha (Zulu)                                   | Leaves             | Urethral ailments                     | [67]       |
| Withania somnifera (L.) Dunal      | Solanaceae        | Winter cherry (Eng); geneesblaar (Afr)            | Roots              | Bladder ailments                      | [46]       |
| Xanthium strumarium L.             | Compositae        | Kankerroos (Afr)                                 | Not specified      | Bladder ailments                      | [42]       |
| Xysmalobium undulatum (L.) W.T.Aiton| Apocynaceae       | Wild cotton (Eng); melkbos (Afr)                 | Not specified      | Bladder ailments                      | [46]       |
| Zantedeschia albomaculata (Hook.) Baill. | Araceae        | Arum lilies, calla lilies, pig lily (Eng); varblom (Afr); mohalaliito (Sotho) | Not specified | Urinary ailments                      | [54, 62–64]|
| Zea mays L.                        | Poaceae           | Corn (Eng); umbila (Zulu)                        | Not specified      | Bladder ailments                      | [42]       |
Table 2: Plant species with noteworthy activity that have been tested against urinary tract bacterial pathogens.

| Plant species                        | Plant part used | Pathogens screened | MIC values                      | Toxicity evaluation                      | References |
|--------------------------------------|-----------------|--------------------|----------------------------------|------------------------------------------|------------|
| Acacia karoo Hayne                   | Leaves          | E. coli            | (M) 414 μg/mL; (W) 458 μg/mL     | Non-toxic in Artemia                    | [71]       |
| Acacia nicoitica (L.) Delile          | Root and bark   | E. coli            | Root and bark: (E) 780 μg/mL; (W) 6250 μg/mL | Not determined                           | [72]       |
| Acacia sieberiana DC.                | Root and bark   | E. coli            | Root and bark: (E) 92–780 μg/mL; (W) 1560 μg/mL | Not determined                           | [72]       |
| Agathosma betulina (Berg.) Pillans    | Leaves          | K. pneumoniae      | (M) 1876 μg/mL; (W) 2387 μg/mL   | Not toxic in human epithelial kidney cells | [73]       |
|                                      |                 | P. mirabilis       | (M) 878 μg/mL.                  | Not determined                           | [41]       |
| Alchornea cordifolia (Schumach. And Thonn.) Müll. Arg. | Leaves, stem | E. coli            | Leaves: (M) 63 μg/mL; (E) 63 μg/mL | Not determined                           | [74]       |
|                                      |                 | K. pneumoniae      | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not determined                           | [74]       |
|                                      |                 | P. mirabilis       | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not determined                           | [74]       |
|                                      |                 | S. saprophyticus   | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not determined                           | [74]       |
| Alchornea laxiflora (Benth.) Pax & Hoffm. | Leaves, root, stem | E. coli            | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | LC_{50} = 100–140 μg/mL in HeLa cells | [74]       |
|                                      |                 | K. pneumoniae      | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not toxic in human epithelial kidney cells | [74]       |
|                                      |                 | P. mirabilis       | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not toxic in human epithelial kidney cells | [74]       |
|                                      |                 | S. saprophyticus   | Leaves: (M) 125 μg/mL; (E) 125 μg/mL | Not toxic in human epithelial kidney cells | [74]       |
| Aloe ferox Mill.                     | Leaves          | E. coli            | (W) > 8000 μg/mL.                | Not toxic in human epithelial kidney cells | [73]       |
| Aloe marlothii A.Berger              | Leaves          | E. coli            | (M) 1250 μg/mL; (M) 1250 μg/mL   | Not determined                           | [75]       |
| Apodytes dimidiata E.Mey ex am.      | Not stated      | E. coli            | (A) 2500 μg/mL; (A) 310 μg/mL    | Not determined                           | [76]       |
| Artemisia afra Jacq. Ex Wildl.        | Leaves          | E. coli            | (W) 3000 μg/mL.                 | Not toxic in human epithelial kidney cells | [74]       |
| Ballota africana (L.) Benth.          | Leaves          | K. pneumoniae      | (M) 438 μg/mL; (W) 379 μg/mL     | Non-toxic in Artemia                    | [41]       |
|                                      |                 | P. mirabilis       | (M) 4278 μg/mL.                 | lethality assay                          | [40]       |
| Bolosanthus speciosis (Bolus) Harms   | Leaves          | E. coli            | (A) 80 μg/mL.                   | LC_{50} = 53 μg/mL in Vero cells         | [77]       |
| Brachylaena discolor                  | Not stated      | E. coli            | (A) 630 μg/mL; (A) 310 μg/mL    | Not determined                           | [76]       |
| Calpurnia aurea (aiton) Benth.        | Leaves          | E. coli            | (A) 40 μg/mL.                   | LC_{50} = 57 μg/mL in Vero cells         | [77]       |
| Carpobrotus edulis (L.) N.E. Br.      | Leaves          | P. mirabilis       | (M) 205 μg/mL; (W) 561 μg/mL    | Non-toxic in Artemia                    | [40]       |
|                                      |                 | Proteus vulgaris   | (M) 670 μg/mL; (W) 1246 μg/mL   | lethality assay                          | [40]       |
| Cissus quadrangularis (Linn.)         | Stems           | E. coli            | (M) 1259 μg/mL; (M) 2500 μg/mL  | Not determined                           | [75]       |
| Clausena anisata (Wildl.) Hook ex Benth. | Not stated    | E. coli            | (A) 310 μg/mL; (A) 310 μg/mL    | Not determined                           | [76]       |
| Clerodendron glabrum E.Mey            | Not stated      | E. coli            | (A) 310 μg/mL; (A) 630 μg/mL    | Not determined                           | [76]       |
| Plant species                  | Plant part used | Plant part screened | MIC values                                      | Toxicity evaluation                  | References |
|-------------------------------|-----------------|---------------------|------------------------------------------------|--------------------------------------|------------|
| Combretum kraussii            | Leaves          | E. coli             | Root and bark: (E) 1560 μg/mL; (W) 3125 μg/mL | Not determined                       | [72]       |
| Hochst.                      |                 |                     |                                                |                                      |            |
| Cremastra triflora            | Leaves          | E. coli             | (A) 50 μg/mL                                   | LC₅₀ = 14 μg/mL in Vero cells         | [77]       |
| (Thonn.) K.Schum.             |                 |                     |                                                |                                      |            |
| Heteromorpha arborescens      |                 | E. coli             | (M) 4000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (EA) > 8000 μg/mL; (H) > 8000 μg/mL | Not determined                       | [78]       |
| Ficus sur                    | Root and bark   | E. coli             | (M) 1000 μg/mL; (W) > 8000 μg/mL; (D) 1000 μg/mL | Non-toxic in Artemia lethality assay  | [80]       |
| Gumbo                       | Root and bark   | E. coli             | (M) 1250 μg/mL; (W) > 8000 μg/mL; (D) 4000 μg/mL | Non-toxic in Artemia lethality assay  | [80]       |
| Gymnosporia senegalensis      | Roots           | E. coli             | (M) 156 μg/mL; (W) 312 μg/mL; (E) 156 μg/mL; (A) 312 μg/mL | Not determined                       | [82]       |
| (Lam.) Loes.                 |                 |                     |                                                |                                      |            |
| Hydnora africana             | Bark            | E. coli             | (M) > 8000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (EA) > 8000 μg/mL; (H) > 8000 μg/mL | Not determined                       | [78]       |
| Thunb.                      |                 |                     |                                                |                                      |            |
| Heteromorpha arborescens      | Leaves          | E. coli             | (A) 180 μg/mL                                   | LC₅₀ = 81 μg/mL in Vero cells         | [77]       |
| (Spreng.) Cham & Schldll.    |                 |                     |                                                |                                      |            |
| Gymnosporia senegalensis      | Roots           | E. coli             | (M) > 8000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (EA) > 8000 μg/mL; (H) > 8000 μg/mL | Not determined                       | [78]       |
| (Lam.) Loes.                 |                 |                     |                                                |                                      |            |
| Hydnora africana             | Bark            | E. coli             | (M) 200 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (EA) > 8000 μg/mL; (H) > 8000 μg/mL | Not determined                       | [78]       |
| Wendl. Eckl. & Zeyh.         | Not stated      | E. coli             | (A) 630 μg/mL                                   | Not determined                       | [76]       |
| Plant species                  | Plant part used | Pathogens screened | MIC values                  | Toxicity evaluation                          | References |
|-------------------------------|----------------|-------------------|-----------------------------|----------------------------------------------|------------|
| Heteropyxis natalensis Harv.  | Leaves         | E. coli           | (M) 382 μg/mL               | Non-toxic in Artemia lethality assay          | [71]       |
| Hypericum roeperianum G.W. Schimp. ex A. Rich. | Leaves | E. coli           | (A) 130 μg/mL               | LC50 = 66 μg/mL in Vero cells                | [77]       |
| Hypoxis hemerocallidea Fisch. Mey. & avé-Lall. | Leaves | E. coli           | (M) 4000 μg/mL; (W) 4000 μg/mL; (D) > 8000 μg/mL; (E) > 8000 μg/mL; (H) > 8000 μg/mL | Not determined | [78]       |
| Indigofera daleoides Harv.    | Whole plant    | E. coli           | (M) 78 μg/mL; (E) 146 μg/mL; (A) 78 μg/mL | Not determined                              | [82]       |
| Indigofera frutescens Linn. f. | Not stated     | E. coli           | (A) 160 μg/mL               | Not determined                              | [76]       |
| Jatropha zeheri Sond.         | Root           | E. coli           | (A) 20 μg/mL                | Not determined                              | [76]       |
| Kigelia africana (Lam.) Benth. | Leaves         | E. coli           | (M) 827 μg/mL; (W) 681 μg/mL | Non-toxic in Artemia lethality assay          | [71]       |
| Leucosidea sericea Eckl. & Zeyh. | Not stated     | E. coli           | (A) 80 μg/mL                | Not determined                              | [76]       |
| Lippia javanica (Burm.f.) Spreng. | Leaves         | E. coli           | (M) 439 μg/mL; (W) 192 μg/mL | Non-toxic in Artemia lethality assay          | [71]       |
| Maesa lanceolata Forssk.      | Leaves         | E. coli           | (A) 40–310 μg/mL; (A) 20–310 μg/mL | LC50 = 2.4 μg/mL in Vero cells          | [76, 77] |
| Mellettia grandis (E.Mey.) Skeels | Not stated     | E. coli           | (A) 310 μg/mL               | Not determined                              | [76]       |
| Melia azedarach L.            | Not stated     | E. coli           | (A) 310 μg/mL               | Not determined                              | [76]       |
| Morus mesozygia Stapf.        | Leaves         | E. coli           | (A) 20 μg/mL                | LC50 = 41 μg/mL in Vero cells               | [77]       |
| Nymania capensis (Thunb.) Lindb. | Leaves         | E. coli           | (M) > 8000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL | Non-toxic in Artemia lethality assay          | [80]       |
| Ozoroa insignis Delile         | Stem bark      | E. coli           | (M) 156 μg/mL; (W) 156 μg/mL; (E) 156 μg/mL; (A) 156 μg/mL | Not determined                              | [82]       |
| Pelargonium sidoides DC.      | Leaves         | E. coli           | (W) > 8000 μg/mL            | Non-toxic in Artemia lethality assay          | [73]       |
| Pittosporum viridiflorum Sims | Leaves         | E. coli           | (A) 110 μg/mL               | LC50 = 55 μg/mL in Vero cells               | [74]       |
| Pelargonium fasiculata (L.) Alton | Leaves         | K. pneumoniae     | (M) 374 μg/mL; (W) 432 μg/mL | Non-toxic in Artemia lethality assay          | [41]       |
| Ptaerocarpus angolensis DC.   | Bark           | E. coli           | (M) 630 μg/mL; (M) 2500 μg/mL | Not determined                              | [75]       |
| Ptaeroxylon obliquum (Thunb.) Radl. | Leaves         | K. pneumoniae     | (M) 1977 μg/mL; (W) 239 μg/mL; (M) 511 μg/mL; (W) 727 μg/mL | Non-toxic in Artemia lethality assay          | [41]       |
| Plant species                                      | Plant part used | Pathogens screened | MIC values                                                                 | Toxicity evaluation                      | References |
|---------------------------------------------------|-----------------|--------------------|-----------------------------------------------------------------------------|------------------------------------------|------------|
| *Prunus africana* (Hook. f.) Kalkman              | Roots           | *E. coli*          | (M) > 8000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (H) > 8000 μg/mL      | Not determined                           | [78]       |
| *Panica granatum* L.                              | Roots           | *E. coli*          | (M) 78 μg/mL; (W) 78 μg/mL; (E) 78 μg/mL; (A) 78 μg/mL                    | Not determined                           | [82]       |
| *Riccinus communis* Linn.                         | Leaves and stem | *E. coli*          | (M) 400 μg/mL; (M) 780 μg/mL                                               | Not determined                           | [75]       |
| *Rhicinus rhomboidea* (E. Mey ex Harv.) Planch.   | Leaves          | *E. coli*          | (M) 306 μg/mL; (W) 333 μg/mL                                               | Non-toxic in *Artemia* lethality assay   | [71]       |
| *Rhicinus tridentata* (L.f.) Wild & R.B.Drumm.    | Roots           | *E. coli*          | (M) > 8000 μg/mL; (W) > 8000 μg/mL; (D) > 8000 μg/mL; (H) > 8000 μg/mL      | Not determined                           | [78]       |
| *Sacrostemma viminalis* R. Br.                    | Stem            | *E. coli*          | (M) 1250 μg/mL; (M) 1250 μg/mL                                             | Not determined                           | [83]       |
| *Schkuhria pinnata* (Lam.)                        | Shoots          | *E. coli*          | (M) 310 μg/mL; (M) 1250 μg/mL                                              | Not determined                           | [75]       |
| *Schotia bractopetalia* Sond.                     | Leaves          | *E. coli*          | (M) 505 μg/mL; (W) 312 μg/mL; (E) 491 μg/mL; (A) 312 μg/mL                 | Non-toxic in *Artemia* lethality assay   | [71]       |
| *Spirostachys africana* Sond.                     | Stem bark       | *E. coli*          | (M) 156 μg/mL; (W) 312 μg/mL; (E) 156 μg/mL; (A) 156 μg/mL                 | Not determined                           | [82]       |
| *Syzygium cordatum* (Hochst.)                     | Leaves and bark | *P. mirabilis*     | (M) 969 and 474 μg/mL (bark and leaves respectively); (W) 932 and 49 μg/mL (bark and leaves respectively) | Non-toxic in *Artemia* lethality assay   | [40]       |
| *P. vulgaris*                                     |                 |                    | (M) 751 and 641 μg/mL (bark and leaves respectively); (W) 1325 and 658 μg/mL (bark and leaves respectively) |                                         | [40]       |
| *Strychnos madagascariensis* Poir.                | Leaves          | *E. coli*          | (M) 580 μg/mL; (W) 593 μg/mL                                               | Non-toxic in *Artemia* lethality assay   | [71]       |
| *Strychnos mitis* S.Moore                         | Not stated      | *P. aeuruginosa*    | (A) 40 μg/mL; (A) 160 μg/mL                                               | Not determined                           | [76]       |
| *Sutherlandia frutescens* (L.) R.Br.              | Leaves          | *E. coli*          | (W) > 8000 μg/mL                                                            | Not toxic in human epithelial kidney cells | [73]       |
| *Terminalia panerophlebia* Engl. & Diels.         | Not stated      | *P. aeuruginosa*    | (A) 80 μg/mL; (A) 80 μg/mL                                                | Not determined                           | [79]       |
| *Terminalia prinoides* M.A. Lawson                | Leaves          | *P. aeuruginosa*    | (A) 278 μg/mL; (W) 624 μg/mL; (M) 432 μg/mL; (W) 531 μg/mL; (M) 313 μg/mL; (W) 224 μg/mL; (M) 926 μg/mL; (W) 379 μg/mL | Non-toxic in *Artemia* lethality assay   | [71] [41] |
| *Terminalia sambesiaca* Engl. & Diels.            | Not stated      | *P. aeuruginosa*    | (A) 60 μg/mL; (A) 60 μg/mL                                                | Not determined                           | [79]       |
representation, with nineteen species reported as treatments for UTIs (Figure 1). Leguminosae were also commonly used as UTI therapies, with fourteen plant species reported [42, 43]. Asparagaceae, Rutaceae, and Lamiaceae were also well represented, with eight, six, and six species used to treat UTIs, respectively. Five species each of Amaryllidaceae, Solanaceae, and Malvaceae, as well as four species of both Euphorbiaceae and Poaceae, and three species of Geraniaceae and Xanthorrhoeaceae were also used for this purpose. A further twenty-four plant families were represented by two or fewer individual species. Of these, Aiptosimium procumbens (Lehm.) Burch. ex Steud, Arctopus echinatus L., Boophone disticha (L.f.) Herb., Bowieve volubilis Harv., Cardiospermum halicacabum L., Cissampelos capensis L., Galenia africana L., Helichrysum odoratissimum (L.) Sweet, and Zantedeschia albomaculata (Hook.) Baill. have been cited by several sources that also experimentally validated their use for the treatment of UTIs [47, 62, 64].

Approximately 47% of the plant species identified in our study were cited by multiple sources as traditional UTI therapies, indicating that screening and validation of those species should be prioritised.

The main plant parts used to prepare therapies to treat UTIs are leaves (27%), followed by roots, bulbs, and rhizomes (22%) (Figure 2). For 48 plant species (31%), the specific plant part used was not specified in the cited literature. For Solanum capense L. and Pelargonium ramosissimum Willd., both leaves and stems were used to treat UTIs, so both parts are recorded in Table 1 for that purpose [43, 58]. Fruits were found to be the least used parts as they are only available for short periods seasonally and may not be always readily available.

### 3.2. Dosage and Toxicity

Long term use of medicinal plants to treat diseases has resulted in the assumption that medicinal plants are nontoxic and safe for therapeutic use [39]. Of the plants specified for traditional use for UTIs (Table 1),

### Table 2: Continued.

| Plant species | Plant part used | Plant part | Pathogens screened | MIC values | Toxicity evaluation | References |
|---------------|----------------|------------|--------------------|------------|---------------------|------------|
| **Terminalia sericea** Burch. ex DC. | Leaves | E. coli K. pneumoniae P. mirabilis P. vulgaris | (M) 396 µg/mL; (W) 276 µg/mL (M) 254 µg/mL; (W) 318 µg/mL (M) 417 µg/mL; (W) 103 µg/mL (M) 508 µg/mL; (W) 520 µg/mL | Non-toxic in *Artemia* lethality assay | [40] |
| **Trichilia dregana** Sond. | Leaves | E. coli E. faecalis | (M) 1000 µg/mL; (W) > 8000 µg/mL; (D) 8000 µg/mL; (W) > 8000 µg/mL; (D) 4000 µg/mL | Non-toxic in *Artemia* lethality assay | [80] |
| **Trichilia emetica** Vahl. | Leaves | E. coli | (M) 1000 µg/mL; (W) > 8000 µg/mL; (D) 8000 µg/mL | Non-toxic in *Artemia* lethality assay | [80, 84] |
| **Tulbaghia violacea** Harv. | Leaves | E. coli K. pneumoniae P. mirabilis | Roots: (M) 387 µg/mL; Leaves: (M) 30 µg/mL Roots: (M) 526 µg/mL; (W) 613 µg/mL Leaves: (W) 125 µg/mL | LC₅₀ = 772 µg/mL in *Artemia* lethality assay | [41] [40] |
| **Turraea floribunda** Hochst. | Leaves | E. coli | (M) 4000 µg/mL; (W) > 8000 µg/mL; (D) 4000 µg/mL | Non-toxic in *Artemia* lethality assay | [80] |
| **Turraea obtusifolia** Hochst. | Leaves | E. coli | (M) 2000 µg/mL; (W) > 8000 µg/mL; (D) 8000 µg/mL | Non-toxic in *Artemia* lethality assay | [80] |
| **Vepris reflexa** I. Verd. | Not stated | E. coli P. aeruginosa | (A) 600 µg/mL; (A) 1250 µg/mL | Not determined | [79] |
none had their therapeutic dosage ranges recorded. It is noteworthy that several of these species have been reported to contain cardiac glycoside toxins (for example, *Bowiea volubilis* and *Acokanthera oppositifolia*) [70, 85, 86] and cucurbitacin (widely distributed in the Cucurbitaceae, Rubiaceae, Euphorbiaceae, and Cruciferae families), which have several adverse effects and toxicities [87]. Further studies into the pharmacological and safety profiles of the majority of the plants listed in Table 1 are required to determine their safety for the treatment of UTIs. Indeed, a common trend noted was that information on dosage and toxicity is lacking, not only for the treatment of UTIs, but in the records listing South African plant use against many other diseases.

3.3. **Scientific Studies on the Effects of Southern African Plants against Urinary Tract Infections.** In a review of South African plants that have been studied for their antimicrobial properties, it was concluded that, before 2017, there had been no specific uropathogenic studies focusing on the antimicrobial activities of southern African medicinal plants [35]; however, pathogens such as *E. coli* were included in other screening studies. For example, *E. coli* is also associated with gastrointestinal diseases, and some strains of this pathogen cause diarrhoea [88]. It is therefore not surprising that studies screening South African plants against *E. coli* more frequently focus on its involvement in those diseases [73, 77, 82]. *Escherichia coli* is also a widely studied bacterium and is often included in studies performing screening
against generic bacterial panels. Whilst these studies do not focus on the involvement of *E. coli* in UTIs, they have still been reported in this study as they demonstrate inhibitory activity against this bacterium, regardless of infection site. Similarly, *P. mirabilis* and *K. pneumoniae* are also associated with other diseases, including the autoimmune diseases, rheumatoid arthritis, and ankylosing spondylitis, respectively [40, 41]. Furthermore, *Pseudomonas aeruginosa* not only causes UTIs, but also has been associated with several other diseases [89]. Studies that screened southern African plant extracts for these bacteria were also included, regardless of the disease state that was the focus of the study.

A total of 85 plants used in southern African traditional medicine to treat UTIs have been tested for inhibitory activity against at least one UTI-causing bacterium. Not surprisingly, the inhibitory properties of southern African traditional medicine plants against *E. coli* were particularly well studied. Indeed, 82 species (96% of the total plant species screened) have previously been reported to inhibit *E. coli* growth at a noteworthy concentration. Notably, the majority of the plant species that have been screened against *E. coli* have also been screened against one or more other UTI-causing bacteria. Screening of southern African plants against *P. aeruginosa* has also received substantial attention, with 36 southern African plants reported to have noteworthy activity against this species. This is important as *P. aeruginosa* is resistant to many conventional antibiotics. Therefore, plant species with activity against this bacterium may be particularly promising, not only against UTIs, but also against other diseases in which *P. aeruginosa* causes pathogenesis, including multiple sclerosis [89] and cystic fibrosis [84]. Particularly, good *P. aeruginosa* inhibitory activity was reported for two *Terminalia* spp. (*T. phanerophlebia* and *T. sambesiaca*), with MICs of 80 and 60 μg/mL, respectively [79]. *Proteus* spp. and *K. pneumoniae* were each screened against 14 southern African plant species. Nearly all of the plants screened against those bacteria were tested in two separate studies that used the same panels of plant species [40, 41]. Both of those studies screened a larger panel of South African medicinal plants than listed here, and only those plant species with appreciable activity are reported herein. Notably, we were only able to find reports of *S. saprophyticus* inhibitory activity for two closely related South African plants of the genus *Alchornea* (*A. cordifolia* and *A. laxiflora*) [74]. As this bacterium is responsible for approximately 6% of uncomplicated UTIs, screening of South African plants for this bacterium is a priority for future studies.

Notably, 46 of the bacterial screening studies reported herein did not test toxicity within the same study, and it is therefore not possible to determine therapeutic indexes. Therefore, whilst the plant species examined in those studies may have noteworthy antibacterial activity, it is not possible to comment on their safety and therefore their potential as therapies to treat UTIs. Of the plants that were screened for toxicity alongside antibacterial activity, *LC*₅₀ values that indicate a lack of toxicity were reported for 28 plant species. Of concern, 11 plant species (*A. laxiflora*, *Bolusanthus speciosus*, *Calpurnia aurea*, *Cremaspora triflora*, *E. croceum*, *Heteromorpha arborescens*, *Hypericum roeperianum*, *Maesa lanceolata*, *Morus mesozygia*, *Pittosporum viridiflorum*, and *Tulbaghia violacea*) were reported to have appreciable toxicity, and therefore caution is recommended for their use. Of particular concern, *LC*₅₀ values of 2–14 μg/mL were reported for *C. triflora*, *E. croceum*, and *M. lanceolata*. Given the MIC values of these plant species against *E. coli*, the therapeutic indexes (as low as 0.008) can be calculated, indicating that these extracts are extremely unsafe for therapeutic use as the extracts are toxic at ~1% of the concentration required to achieve the therapeutic effect. However, it is noteworthy that all of these low *LC*₅₀ values in Vero cells were determined in a single study [77]. That study also reported low *LC*₅₀ values (lower than 100 μg/mL) for every plant species that was tested in that study, and therefore the results may be an anomaly of that study. The toxicity of these plant species needs to be verified in future studies to evaluate their safety for therapeutic use.

4. Discussion and Conclusion

Urinary tract infections are one of the most widespread classes of infectious diseases globally, yet the development of new therapies to treat these infections remains relatively neglected. Whilst UTIs cause discomfort, they rarely cause mortality or serious morbidity except in immune-compromised individuals. It is likely that the relative lack of severity of these infections may contribute to the low number of studies into the effects of southern African plants specifically targeted at bacteria that cause these infections. Indeed, most of these studies have occurred in the most recent 15-year period. Interestingly, the increase in research in this field coincides with increases in the incidence of antibiotic resistance. Several studies have already screened some South African plants for the ability to inhibit UTI-causing bacteria. Indeed, Table 2 summarises studies screening 85 plant species against UTI-causative bacteria.

Surprisingly, despite 153 plant species identified with documented uses to treat UTIs, only 85 species have been reported to have noteworthy inhibitory activity against the main UTI-causative bacteria species. Furthermore, most of the tested plants were not selected for screening based on their traditional use to treat UTIs. Instead, in many cases, the plant species were screened against the bacteria based on their involvement in other diseases. *Escherichia coli* is a common gastrointestinal bacterium, and several studies screened plant extracts against this bacterium to examine its potential to treat diarrhoea. The studies described in this review focussed on the main bacterial species that can cause UTIs (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *P. mirabilis*, and *S. saprophyticus*). Combined, these bacteria account for >90% of the cases of uncomplicated UTIs, highlighting their importance to those studies [11]. However, for these pathogens, we were only able to locate a single study that tested South African plants against *S. saprophyticus* [74], and future studies screening plants against this bacterium are required. Furthermore, other bacterial species are also responsible for a significant proportion of UTIs. In particular, unspecified *Enterococcus* spp. account for approximately 6%
and 11% of uncomplicated and complicated UTIs, respectively [11], and therefore future studies screening South African plants against these pathogens are warranted. Furthermore, our review focussed on the bacterial causes of UTIs as they account for nearly all reported cases. However, C. albicans, as well as some viruses and protozoa, may also cause UTIs and should not be neglected in future studies. Further studies are required to screen those species against the other major causes of UTIs. Additionally, all the previous studies have screened plant species against UTI-causative bacteria that are susceptible to conventional antibiotic therapies. To date, screening plants against antibiotic-resistant bacterial strains has been largely neglected. As there have been substantial increases in the prevalence of antibiotic-resistant bacterial pathogens in recent years, it is important that the plants identified herein are also screened against resistant bacterial strains to further evaluate the potential in clinical environments. Furthermore, when examining antimicrobial efficacy, it must be noted that UTIs are very often biofilm-borne, and this aspect has been neglected in the screening. Only one study [78] focussed on 14 plant species utilising bacterial communication systems via quorum sensing signalling and in biofilm studies. Clearly, this area remains untapped, and there is a possibility for plant species to not only act on planktonic bacterial cells, but also inhibit or prevent biofilm formation.

It appears that plant species selection for several studies was based more on plant availability rather than ethnobotanical use. Another aspect of the previous studies is that the plant part tested does not always correlate with the part traditionally used. It is likely that availability may also have been a significant factor in selection of plant part in those studies. However, the chemistry may differ substantially between different plant parts, and they may therefore induce completely different biological activities. Where possible, screening and evaluation studies should test the plant part used traditionally, as well as an approximation of how it was processed for use. These factors may have significant impacts on the toxicity of the preparation. Future studies testing an approximation of the traditional plant preparations are therefore required to validate the traditional use of these plants to treat UTIs.

To be useful in the treatment of UTIs, an extract (or purified compound derived from an extract) must have relatively low toxicity. This is particularly true for the treatment of recurrent infections. Surprisingly, many of the plant species screened for inhibitory activity against UTI-causative bacteria were not tested for toxicity in the same studies. This may be because many of these plants have been used in traditional healing systems for hundreds of years without reported toxicity and are therefore assumed to be safe. However, some plant species are prepared by different methods to test bioactivity from the preparation method used by traditional medicine practitioners. Different preparation methods may dramatically alter the phytochemical composition of different preparations and therefore may also affect their toxicity profiles. Indeed, several studies reported toxic, carcinogenic, and mutagenic effects for extracts prepared from plants traditionally used as medicines [33]. Several of the studies highlighted in this review have also investigated the toxicity of southern African plant species traditionally used to treat UTIs [40, 41, 71, 73, 77, 80]. Whilst most of those studies reported that the plant extracts were nontoxic, one study reported very low LC50 values against Vero cells for several plant species, indicating that those species may not be safe to use medicinally. However, the results of that study may be erroneous as all the plant species tested had low LC50 and verification of these results is required. Of further note, several different toxicity assays (human cell lines, Vero monkey kidney cells, Artemia nauplii assays) were used to screen the plant species in different studies, making comparisons difficult between studies. Ideally, toxicity studies should incorporate more than one toxicity assay to allow for better comparisons between studies.

Ethnobotanical records have already identified several promising plant species used in traditional South African medicinal systems to treat UTIs, and several of those species (as well as multiple species for which a traditional use against UTIs was not recorded) have already been tested against one or more UTI-causative bacteria. Further research is required to screen all identified species against each of the UTI-causative bacteria (rather than just one or two of them) and against antibiotic-resistant bacterial strains that are becoming increasingly common. Additionally, all previous studies have tested the plant extracts in vitro. As considerably different effects may be seen in vivo due to bioavailability differences, studies in animal models are also required.

Overall, there is evidence that southern African medicinal plants have potential to treat UTIs and, with further in-depth analysis, could be the new alternative to cranberry juice which is internationally recognised as a safe natural alternative for treating infections of the urinary tract.

Data Availability

All data are included within this study and are also available from the corresponding author on request.

Conflicts of Interest

The authors declare no conflicts of interest.

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