South African Journal of Botany 185 (2025) 194–204

Contents lists available at ScienceDirect

South African Journal of Botany

journal homepage: www.elsevier.com/locate/sajb

South African medicinal plants traditionally used to treat gonorrhoea: A comprehensive review

Thilivhali E. Tshikalange [a], Fatimah Lawal [b], Mcebisi J. Mabuza [b,*], Mahwahwatse J. Bapela [b]

[a] Department of Life and Consumer Sciences, University of South Africa, Private Bag X01, FL, 1710, South Africa
[b] Department of Plant and Soil Sciences, University of Pretoria, Hatfield 0028, South Africa

ARTICLE INFO

Edited by Dr N. Makunga

Keywords:
Medicinal plants
South Africa
Gonorrhoea
Ethnopharmacology
Phytochemistry
Cytotoxicity
Antigonococcal activity

ABSTRACT

Gonorrhoea is the second most common sexually transmitted infection (STI) and a major health issue in South Africa. This review provides a detailed list of South African medicinal plants used to treat gonorrhoea. The study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Researchers used databases like Google Scholar, Scopus, ScienceDirect, and Web of Science. Search terms included "medicinal" plants, "traditional use," "gonorrhoea," "venereal diseases," "sexually transmitted infections," and "South Africa." Plant species were verified through the South African National Biodiversity Institute (SANBI) and the New Plants of Southern Africa (NEWPOSA) online databases. A total of 28 plant species from 21 families were identified in South Africa for treating gonorrhoea. The Fabaceae and Maliaceae families, with three plant species each, were the most commonly used for this purpose. However, only 44 % of these species have undergone pharmacological testing against *Neisseria gonorrhoeae*. The remaining 56 % have not been evaluated for gonococcal activity. Although some phytoconstituents have been isolated, few antigonococcal compounds have been documented. Cytotoxicity tests have mostly been conducted *in vitro*, with limited evidence from *in vivo* studies. *In vivo* evaluations are essential for accurately determining the clinical safety of crude extracts and isolated compounds. Future research should focus on validating the antigonococcal properties of South African medicinal plants, isolating phytoconstituents, and conducting *in vivo* safety assessments.

1. Introduction

Gonorrhoea, an infection caused by the gram-negative diplococcus bacterium *Neisseria gonorrhoeae*, is the second most common sexually transmitted infection (STI) worldwide (World Health Organization (WHO), 2024). In South Africa, its prevalence has placed significant pressure on the healthcare system, with the burden increasing annually (WHO, 2024). This rise is primarily attributed to inadequate routine screening and diagnosis practices. Currently, diagnoses are mainly based on reported symptoms, which contributes to the growing number of gonorrhoea cases each year (Meyer and Buder, 2020). While deaths from gonorrhoea have declined over the past decade, new infections continue to rise, especially in sub-Saharan Africa, which reports the highest rates (WHO, 2024). Many new gonorrhoea cases occur among individuals aged 15 to 49 years, particularly in informal settlements (Michalow et al., 2025). The populations most at risk include pregnant women and newborns (WHO, 2024). *Neisseria gonorrhoeae* thrives in warm, moist environments, especially within mucous membranes and the urogenital tracts of both males and females (Yeshanew and Geremew, 2018). It can also grow in the anus, throat, and eyes, particularly affecting young infants shortly after birth (WHO, 2024). Novel therapies are needed, as *N. gonorrhoeae* is resistant to most of the currently used antibiotics (Yakobi et al., 2024).

Indigenous South African medicinal plants have been used for centuries to treat venereal diseases, including gonorrhoea (Dembetembe et al., 2022; Masevhe and Tshisikhawe, 2018; Mulaudzi et al., 2015, 2011; Naidoo et al., 2013). In many rural areas, a significant proportion of people rely on traditional medicine for their primary healthcare needs. In South Africa, rural communities increasingly turn to traditional healers for the treatment of sexually transmitted infections and urinary tract infections (Semenya et al., 2013). The ongoing use of traditional medicine is supported by its affordability, accessibility, and cultural significance in many developing countries (Cleary et al., 2013). Numerous traditional healers utilize specific medicinal plants to combat

* Corresponding author.
E-mail address: mabuzamcebisi@gmail.com (M.J. Mabuza).

https://doi.org/10.1016/j.sajb.2025.07.052
Received 31 March 2025; Received in revised form 27 July 2025; Accepted 29 July 2025
Available online 9 August 2025

STI pathogens and alleviate symptoms such as sores, inflammation, and pain associated with these infections (Naidoo et al., 2013). These plants have been used for generations and may contain active ingredients effective against gonorrhoea. Although no commercial antigonococcal antibiotic derived from plants has been developed yet, the plant kingdom holds vast potential for future discoveries (Newman and Cragg, 2020).

This paper reviews studies on South African plants used to treat gonorrhoea, emphasizing current ethnomedicinal knowledge as well as the pharmacological and phytochemical research conducted on their extracts and isolated constituents.

2. Methodology

The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) as outlined in Fig. 1. Literature was obtained from published scientific journal articles, books, and dissertations. The databases utilized were Science Direct, Scopus, Web of Science, and Google Scholar. The key search terms applied included "medicinal plants", "traditional use", "gonorrhoea", "venereal diseases", "sexually transmitted infections", and "South Africa". Additionally, keywords such as "antigonococcal activity" were used to retrieve publications documenting antigonococcal bioactivity in South African plant species.

2.1. Inclusion and exclusion criteria

Articles focused on subjects that did not relate to the ethnomedicinal, ethnopharmacology, phytochemistry, and cytotoxicity of South African plant species used to treat gonorrhoea were excluded. Furthermore, articles that had no full text available, those not written in the English language, and articles not peer reviewed were also excluded. Other studies that met this criterion were retrieved for eligibility screening. The SANBI and NEWPOSA databases were consulted to verify South African species.

2.2. Data extraction

The sourced articles were exported to Mendeley reference management software (Mendeley version 2.115.0). A total of 220 resources were retrieved from Science Direct (11), Scopus (30), Google Scholar (89), and Web of Science (90). The primary screening involved the reading of each title and abstract. In total, 150 articles were screened for eligibility, and only 68 were eligible and have been included in this review.

3. Results

Table 1 summarizes the ethnomedicinal data obtained for plants used in South African traditional medicine for the treatment of gonorrhoea. The species identified are widely distributed across South Africa's provinces and are traditionally used to treat gonorrhoea and other venereal ailments. A total of 28 species from 21 different families and 27 genera are documented (Table 1). Dicotyledons account for 23 of the total number of species, while 5 species represent monocotyledons. It is common to observe more dicotyledonous species because they are the most diverse compared to monocots. *Widdringtonia nodiflora* is the only species that produces seeds without bearing fruit, hence it's the only gymnosperm. The Maliaceae and Fabaceae families both have three species each. Nanacardiaceae, Combretaceae, and Polygalaceae families each have two plant species, while the rest of the plant families have a single species (Table 1).

From these plant species (Table 1), the frequently used plant parts were the roots (37 %), followed by the leaves (28 %), stem bark (22 %), bulbs (2 %), fruits (7 %), and the whole plant (4 %) (Fig. 2).

4. Discussion

4.1. South African plants that are used to treat gonorrhoea

When assessing the different plant parts traditionally used to treat

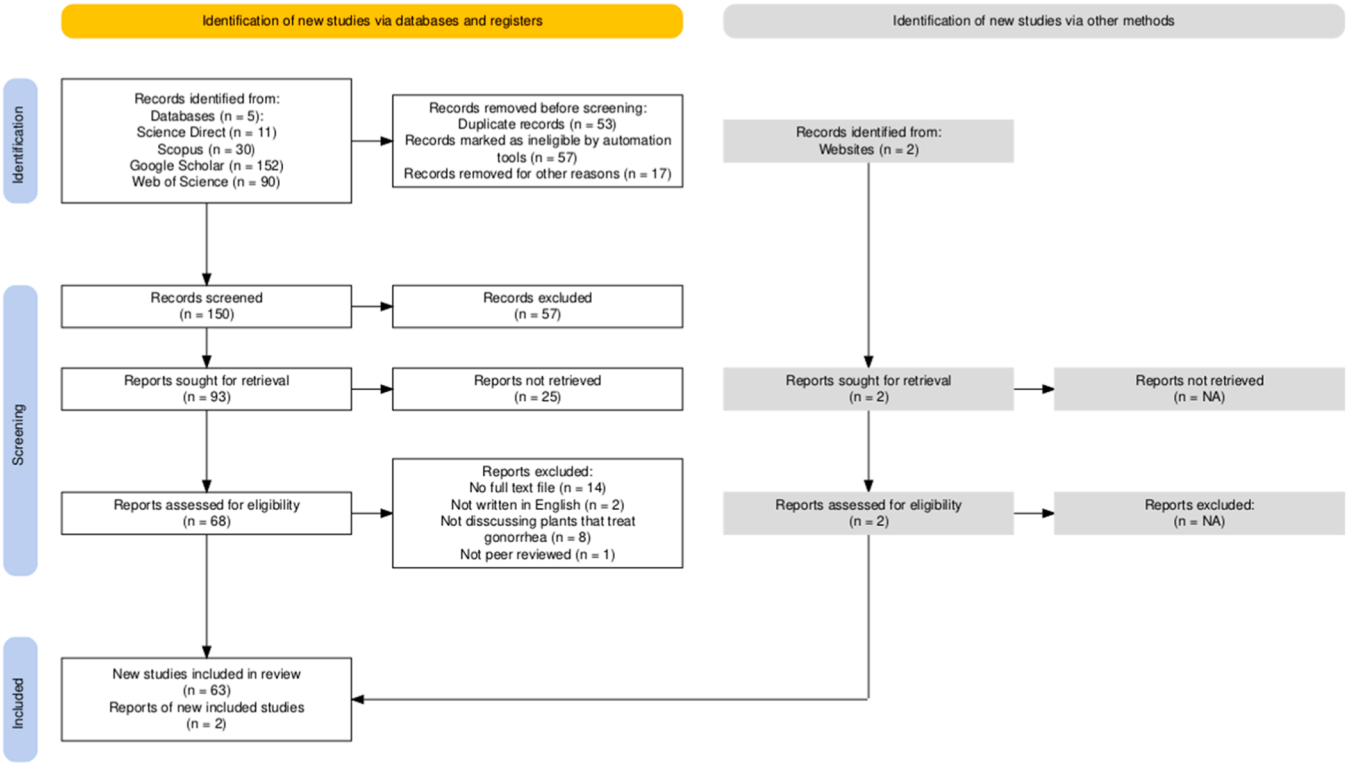

Fig. 1. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) diagram of this study (Haddaway et al., 2022).

Table 1
Medicinal plants traditionally used to treat gonorrhoea in South Africa.

Species /Vernacular name	Natural/ Cultivated	Distribution	Ethnomedicinal uses	Plant part used,	Antigonococcal activity	Toxicological reports	Active substances
Anacardiaceae							
Harpephyllum caffrum Bernh ex. Krauss/ Umgwenya (X)	Natural and cultivated	Eastern Cape, KwaZulu-Natal, Limpopo, Mpumalanga	Decoction taken orally to treat gonorrhoea. Treats acne and eczema. Powdered burnt stem bark is used treat sprains and bone fractures (Buwa and Van Staden, 2006; Hutchings and Scott, 1996; Van Wyk and Gericke, 2000).	Stem bark and leaves	The leaf extracts displayed poor antigonococcal activity with a 38 % inhibition (Shabana et al., 2011).	The ethanolic leaf extract was cytotoxic to human liver, colon and larynx carcinoma cells. They were non cytotoxic against non-cancerous human embryonic kidney cells (HEK-293 cell line) with CC_{50} values >100 µg/ml (Shabana et al., 2011; Twilley et al., 2017).	No records
Lannea edulis (Sond.) Engl./Umgabunkhomo (Z) Mutshutshungwa (V)	Natural and cultivated	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West	Gonorrhoea, menstrual pain, infertility, bilharzia, fever and bronchitis (Pooley and Boon, 2010).	Roots, stem bark, and fruits	No records	The Brine shrimp lethality assay (BSLA) report showed that the leaves were moderately safe (Sohni et al., 1995; Tafadzwa, 2009).	No records
Apiaceae							
Arctopus echinatus L./ Sieketroos (A)	Natural	Eastern Cape, Western Cape	Syphilis, gonorrhoea, epilepsy, bladder ailments, glandular swellings and water retention (Magee et al., 2006).	Roots	No records	No records	No records
Apocynaceae							
Gomphocarpus fruticosus (L.) W.T. Aiton subsp. *Fruticosus*/Lebegane (S) Mubvafhisa (V)	Natural	Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape, Western Cape	Leaf decoctions are administered as sedative and also used to treat headaches, tuberculosis and gonorrhoea (Van Wyk and Gericke, 2000).	Roots and leaves	Antigonococcal activity was reported in the aqueous and acetone root extracts at 66 % and 85 % inhibition, respectively (Mulaudzi et al., 2015).	Cytotoxic against different human cancer cell lines (Fouche et al., 2008); Non cytotoxic against non-cancerous human embryonic kidney cells (HEK-293 cell line) with CC_{50} values >100 µg/ml; cytotoxic to cancerous HeLa cell lines (Twilley et al., 2017).	No records
Asparagaceae							
Asparagus concinnus (Baker) Kies	Natural	Eastern Cape	Roots boiled to treat gonorrhoea (Chauke et al., 2015).	Roots	No records	No records	No records
Asphodelaceae							
Aloe ferox Mill./Ikhala (X)	Natural and cultivated	Eastern Cape, Free State, KwaZulu-Natal, Western Cape	Leaves used to treat syphilis and gonorrhoea,. Also used as laxative as well as treating treat arthritis septic wounds (Pooley, 1993).	Leaves	Antigonococcal activity was reported at MIC value of 0.5 mg/ml (Kambizi and Afolayan, 2008).	Low cytotoxicity on THP-1 human leukemic monocyte; Minimal cytotoxicity of gel and leaf extract on HaCaT and other cell lines (Fox et al., 2017; Yeol and Kim, 2017)	Aloin, chrysophanol and aloe emodin (Not tested, but present in active extracts) (Kambizi and Afolayan, 2008).
Asteraceae							
Helichrysum caespititium Sond./Boriba (S)	Natural	Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, Northern Cape, North West	Whole plant decoctions used to treat gonorrhoea (Maroyi, 2019; Pooley, 2003).	Whole plant	Antigonococcal activity observed at MIC of 0.06 mg/ml (Seleteng-Kose et al., 2019).	Isolated ploroglucinol (caespitate) showed no toxicity to Vero monkey kidney cells *in vitro* cytotoxicity assay (Mathekga, 2001)	10-Methyl-8-(propan-17-ylidene) naphthalen-9-yl)-11-vinyl-14-hydroxyfuran-16-one (MIC – 60 µg/ml) (Bassey et al., 2021).
Balanophoraceae							
Sarcophyte sanguinea Sparrm subsp. *sanguinea*/ Umavumbuka (Z)	Natural	Eastern Cape, KwaZulu-Natal, Limpopo, Mpumalanga	It treats HIV/AIDS, gonorrhoea, wounds, dysentery, diarrhoea, sore throat, swollen glands and also used for irregular menstrual cycles (De Wet et al., 2008).	Stem bark	Antigonococcal activity was reported for both organic and aqueous extracts with MIC values of 0.31 and 0.25 mg/ml, respectively (Naidoo et al., 2013).	Stem crude extract displayed no cytotoxicity against human embryonic kidney epithelial (Graham, HEK-293) cells with CC_{50} values >100µg/ml (Naidoo et al., 2013).	No records

(*continued on next page*)

Table 1 (*continued*)

Species /Vernacular name	Natural/ Cultivated	Distribution	Ethnomedicinal uses	Plant part used,	Antigonococcal activity	Toxicological reports	Active substances
						Hepatotoxic at tested concentration of 100μg/ml) (Ramulondi, 2017)	
Bignoniaceae							
Kigelia africana (Lam.) Benth/Umvongothi (Z) Muvevha (V)	Natural	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga	Syphilis, sores, and **gonorrhoea** (Oyebanji et al., 2015).	Leaves and fruits	No records	The aqueous and organic leaf extracts showed 22 % and 16 % inhibition, respectively on human embryonic kidney epithelial cells (Naidoo et al., 2013); cytotoxicity report of different plant part extracts and isolated compounds in various *in vitro* studies on different human cancer cell lines (Bello et al., 2016); Organic root extracts noncytotoxic in BSLA (Mbunde et al., 2016).	No records
Combretaceae							
Combretum molle R.Br. ex G/Mugwiti (V) Umbondo (Z)	Natural	Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West	**Gonorrhoea**, syphilis, malaria, pneumonia, fever, dysentery, and leprosy (Van Wyk and Van Wyk, 1997).	Leaves and roots	No records	Non cytotoxic against Vero monkey kidney cells and non-cancerous human embryonic kidney cells (HEK-293 cell line) with CC_{50} values >100 μg/ml (Twilley et al., 2017).	No records
Terminalia sericea Burch. ex DC/Mususu (V) Imkhonono (Z)	Natural	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape	Syphilis, gonorrhoea, tonsils, mouth thrush, diabetes, diarrhoea and infant food supplement (Palgrave et al., 2002; Palmer and Pitman, 1972).	Leaves, roots, and stem bark	No records	Cytotoxic (CC_{50} = 24 μg/ml) to Vero monkey kidney cells (Tshikalange et al., 2005); Aqueous root and leaf extracts very cytotoxic to different cancer cell lines (Fyhrquist et al., 2006)	No records
Cupressaceae							
Widdringtonia nodiflora (L.) Powrie/Thaululo (V) Unwele-lwe-entaba (Z)	Natural and cultivated	Eastern Cape, Free State, KwaZulu-Natal, Limpopo, Mpumalanga, Western Cape	Gonorrhoea, syphilis, gout, rheumatism, oedematous swelling, menstrual, uterine infection (Tlakula and Tshikalange, 2015).	Resin in bark, leaves and roots	No records	No records	No records
Fabaceae							
Albizia adianthifolia (Schumach.)/Igowane (Z) Mafahla-nare (P) Muelela (V)	Natural	Eastern Cape, KwaZulu-Natal, Limpopo, Mpumalanga	Gonorrhoea and bronchitis (Naidoo et al., 2013a; van Vuuren and Naidoo, 2010).	Stem bark and roots		Stem bark extract non-cytotoxic to human embryonic kidney epithelial (Graham, HEK-293) cells CC_{50} >100μg/ml (Naidoo et al., 2013); cytotoxicity of methanol extract of leaves, stem bark and roots on different cancer cell line as well as non-cancerous cell lines (CC_{50} > 50 μg/ml) (Kuete et al., 2016)	No records
Peltophorum africanum Sond/Musese (V) Huilboom (A) Isikhaba-mkhombe (Z)	Natural	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West	Syphilis, gonorrhoea, wound healing, tooth ache, sore throat, eye infection, dysentery, diarrhea and clears internal parasites (De Wet et al., 2012; Naidoo et al., 2013).	Leaves and roots.	Moderately active against *N. gonorrhoea* with MIC value of 1.6 mg/ml (Mamba, 2017).	Root extract non-cytotoxic to human embryonic kidney epithelial cells (CC_{50} >100μg/ml) (Naidoo et al., 2013). Root ethanol extract non-cytotoxic to Vero Kidney monkey cells (CC_{50} = 133.3μg/ml) (T. Tshikalange et al.,	No records

(*continued on next page*)

Table 1 (*continued*)

Species /Vernacular name	Natural/ Cultivated	Distribution	Ethnomedicinal uses	Plant part used,	Antigonococcal activity	Toxicological reports	Active substances
						2016). Root methanol extract non-cytotoxic to Vero monkey kidney cells (CC_{50} = 137.2 µg/ml) (A. Samie et al., 2009); 70 % acetone extract of roots and leaves non cytotoxic to Vero cells (CC_{50} > 300 µg/ml) (Madikizela et al., 2017)	
Bolusanthus speciosus (Bolus) Harms/ umHolo (Z) Mukamba (V)	Natural and cultivated	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga	Abdominal cramps and stomach problems and gonorrhoea, kidney infection and enema (Venter and Venter, 1996).	Stem bark and roots	No records	Crude leaf extract cytotoxic to Vero monkey kidney cells (CC_{50} < 50 µg/ml) (Ahmed et al., 2012); bark acetone extract very cytotoxic to Vero monkey kidney cells (CC_{50} = 2.7 µg/ml) (Samie et al., 2009); cytotoxicity of isolated compound from leaves on bovine dermis cells (CC_{50} = 30.69 µg/ml) and Vero cells (CC_{50} = 74.68 µg/ml) (Aderogba et al., 2007).	No records
Gunneraceae							
Gunnera perpensa Linn./ Iphuzi (Z) Shamboḓavhadzimu (V)	Natural and cultivated	Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Western Cape	Decoction treat gonorrhoea, syphilis and urinary infections (Buwa and Van Staden, 2006).	Roots	No records	70 % Acetone extract of roots and leaves non cytotoxic to Vero cells (CC_{50} >1000 µg/ml) (Madikizela et al., 2017); weak toxicity of rhizome in BSLA (LC_{50}- 137.62 mg/100 ml), non-cytotoxic to Human HEK293 and HepG2 cell lines (CC_{50} > 200 µg/ml) (Simelane et al., 2012)	No records
Liliaceae							
Albuca nelsonii N.E. Br./ Intelezi (X)	Natural and cultivated	Eastern Cape, Free State, KwaZulu-Natal	Decoction used for gonorrhoea (Buwa and Van Staden, 2006).	Bulbs	No records	No records	No records
Malvaceae							
Waltheria indica L./ Monkey bush (E) Delelemukula (V)	Natural	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape	Urinary tract infections and **gonorrhoea** (Magwede et al., 2019).	moots	No records	Acetone root extract non-cytotoxic to Vero cells (CC_{50} = 131 µg/ml) (Mongalo et al., 2017); report of toxicity from mild to toxic from different studies of extracts from different parts of plants (Zongo et al., 2013)	No records
Meliaceae							
Ekebergia capensis Sparrm./Mmidibidi (S)	Natural and cultivated	Eastern Cape, KwaZulu-Natal, Limpopo, Mpumalanga	**Gonorrhoea**, headache, dysentery, heartburn, chronic coughs, and intestinal worms (Palgrave et al., 2002; Venter and Venter, 1996; Van Wyk and Gericke, 2000).	Root, stem bark and leaves	The petroleum ether and dichloromethane leaf extracts were active, displaying 77 % and 96 % antigonococcal inhibition, respectively (Mulaudzi et al., 2011).	Isolated triterpenoid compounds from roots tested against Vero cells and different cancer cell lines (Irungu et al., 2014); acetone extract was toxic to against Vero cells (CC_{50} = 12.5µg/ml) (Kimutai et al., 2016)	No records
Trichilia dregeana Sond./ Mutuhu (V)			Gonorrhoea and syphilis (De Wet et al., 2012; Tlakula and Tshikalange, 2015).	Stem bark and leaves	The organic extract displayed antigonococcal activity at MIC value of 2.0 mg/ml (Naidoo et al., 2013a).	Leaf extract non-cytotoxic to human embryonic kidney epithelial cells CC_{50} >100µg/ml (Naidoo et al., 2013).	No records

(*continued on next page*)

Table 1 (*continued*)

Species /Vernacular name	Natural/ Cultivated	Distribution	Ethnomedicinal uses	Plant part used,	Antigonococcal activity	Toxicological reports	Active substances
Trichilia emetica Vahl./ Mutshikili (V) Umkhuhlu (X) Umkhuhlu (Z)	Natural and cultivated	KwaZulu-Natal, Mpumalanga, Limpopo	Used as an enema for general cleansing, gonorrhoea, syphilis, and stomach complaints (Hutchings and Scott, 1996; Mabogo, 2012; Pooley and Boon, 2010).	Stem bark	No records	Methylene chloride of leaf extracts were toxic to J774 macrophage-like murine cell line (CC_{50} = 36.5 μg/ml) (Hoet et al., 2004), The leaf water extracts were non-toxic to fibroblast cells (W138) (CC_{50} >100μg/ml) (Bero et al., 2009); leaf extract toxic to lymphocyte (CC_{50} = 2.5 μg/ml), dichloromethane extract of bark also toxic to Vero cells (CC_{50} = 50 μg/ml) (Komane et al., 2011)	No records
Olacaceae							
Ximenia caffra Sond./ Mutshili (V) Umthunduluka (Z)	Natural and cultivated	Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West	Infertility, tonsillitis, fever, gonorrhoea, bilharziasis, diarrhoea and dysentery (Palgrave et al., 2002; Palmer and Pitman, 1972; Van Wyk and Van Wyk, 1997; Venter and Venter, 1996).	Roots and leaves.	No records	Root ethanol extract moderately cytotoxic to Vero kidney monkey cells (CC_{50} = 91.0 μg/ml) (Tshikalange et al., 2016); Root extract non-cytotoxic to human embryonic kidney epithelial cells CC_{50} > 100 μg/ml (Naidoo et al., 2013); Toxicity in brine shrimp lethality test (Moshi et al., 2004); Acetone leaf and bark extracts non-cytotoxic to Vero cells (CC_{50} >100 μg/ml) (Samie et al., 2009)	Vomifoliol (Nair et al., 2013).
Podocarpaceae							
Afrocarpus falcatus (Thunb.) C.N.Page Synonym *Podocarpus falcatus* (Thunb.) R. Br. ex Mirb./Umgeya (X)	Natural and cultivated	Eastern Cape, KwaZulu-Natal, Limpopo, Mpumalanga, Western Cape	Gonorrhoea and headaches, gall sickness (Beentje, 1994).	Fruits	No records	Report of toxicity of stem and leaf extracts to HEpG2 cells at all test and the percentage concentration with viability of cells <50 % (Abdillahi et al., 2012)	No records
Polygalaceae							
Polygala fruticosa P. J. Bergius/Umabalabala (X)	Natural and cultivated	Cape region, KwaZulu-Natal, and the Karoo	Gonorrhoea (Hutchings and Scott, 1996; Van Wyk and Gericke, 2000).	Roots, leaves and whole plant	Both organic and aqueous extracts each displayed antigonococcal activity with MIC value of 2.0 mg/ml (van Vuuren and Naidoo, 2010).	Aqueous extract non-toxic at low doses administered to mice in acute toxicity test and did not significantly affect liver and kidney physiology (Mukinda and Eagles, 2010); Isolated compounds from roots were cytotoxic to human colorectal adenocarcinoma cell line (Addo et al., 2015)	No records
Securidaca longepedunculata Fresen./Mpesu (V) Violet-tree (E) Krinkhout (A)	Natural	Gauteng, Limpopo, North West	Gonorrhoea, headaches, tuberculosis, toothache, infertility, constipation and inflammation (Hutchings and Scott, 1996; Van Wyk and Gericke, 2000).	Roots	No records	Non-cytotoxic to monocytic THP-1 cells (CC_{50} > 125 μg/ml) (Luo et al., 2011); Aqueous extract cytotoxic to Ehrlich ascites carcinoma cells (CC_{50} = 67 μg/ml) (Lawal et al., 2012); Report of toxicity in BSLA as well as toxicity of some solvent extracts in acute toxicity studies with mice (Mongalo et al., 2015)	No records
Rhamnaceae							

(*continued on next page*)

Table 1 (*continued*)

Species /Vernacular name	Natural/ Cultivated	Distribution	Ethnomedicinal uses	Plant part used,	Antigonococcal activity	Toxicological reports	Active substances
Ziziphus mucronata Willd. subsp. *mucronata*/ Umphafa (X) Mokgalo (P) Mutshetshete (V) Mukhalu, Mutshetshete (V) Buffalo thorn (E) Wag-'n-bietjie (A)	Natural	Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape	Gonorrhoea, painful sores, chest pains, and dysentery (Hutchings and Scott, 1996; Venter and Venter, 1996).	Roots, stem bark and leaves	The dichloromethane crude extract displayed poor cytotoxicity on the brins shrimp assay, inducing mortality at 15 % (Van Vuuren et al., 2015).	The leaf extracts displayed poor cytotoxicity on L6 rat skeletal cells with CC_{50} values of 58, 69, 63 and 80 µg/ml for the dichloromethane, ethyl acetate, methanol and decoction, respectively (Mabuza et al., 2025). Minimal cytotoxicity of the hexane stem bark extracts displayed no cytotoxicity with CC_{50} value > 50 µg/ml (Buthelezi et al., 2024).	No records
Santalaceae							
Osyris lanceolata Hochst. & Steud./Mpeta (V) Rotslooibas (A)	Natural	Eastern Cape, Free State, Gauteng, KwaZulu-Natal, Limpopo, Mpumalanga, North West, Northern Cape	The roots and leaves are prepared as tonics to treat various ailments including gonorrhoea (Palgrave et al., 2002; Pooley and Boon, 2010; Van Wyk and Van Wyk, 1997).	Roots and bark	The dichloromethane and ethanolic root extracts were active displaying inhibition of 82 % and 87 %, respectively (Mulaudzi et al., 2011).	No cytotoxicity observed on PLP2 cells. The best inhibitory effects were observed with the aqueous extract for HepG2 and HeLa cell lines (Rached et al., 2016).	No records
Vitaceae							
Cissus quadrangularis L./ Tshiuvhulusi (V) Cactus vine (E)	Natural	Limpopo, Mpumalanga	Treats gout, syphilis, sexually transmitted disease, piles, scurvy, asthma, eyes infection, wounds healing, fractured, diarrhoea, dysentery, and aphrodisiac (van Vuuren and Naidoo, 2010; Van Wyk and Gericke, 2000).	Leaves	No records	Anticancer activity (Bhujade et al., 2013)	No records

A – Afrikaans.
E – English.
P – Pedi.
S – Sotho.
X – Xhosa.
T – Tshivenda.
Z – Zulu.

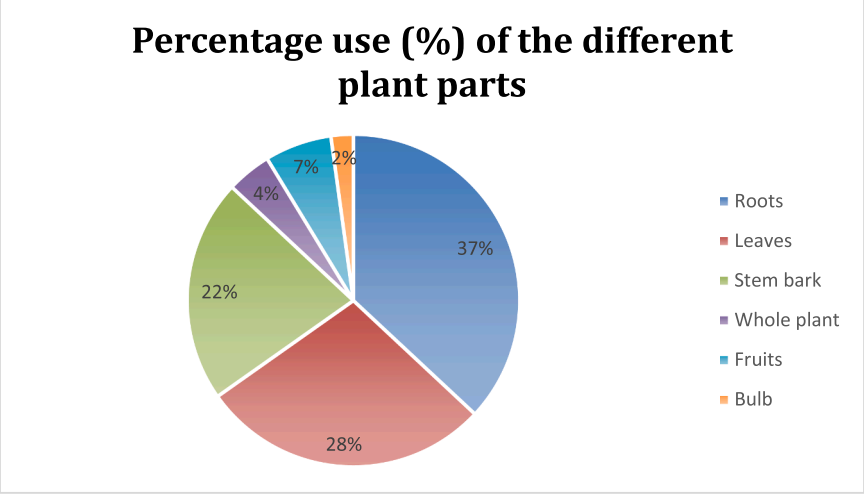

Fig. 2. Plant parts from South African medicinal plants are frequently used to treat gonorrhoea.

gonorrhoea, the roots are mostly targeted by traditional healers as they are perceived to contain concentrated bioactives (Moeng, 2010). This is followed by the leaves, stem, and to a lesser extent, the bulbs and fruits (Fig. 1). A major concern with the use of plant roots and stem bark for medicinal purposes is the potential threat they pose to the sustainability and conservation status of these plants. The collection of the stem bark and roots of plants can induce plant damage, and they are not easily regenerated as compared to the leaves, which can be sustainably harvested. To validate the ethnomedicinal uses of plants, other renewable plant parts should be tested for activity. Alternatively, bioactive compounds acquired from the roots may be synthesized in an attempt to avoid the continued unscrupulous harvesting of roots.

4.2. Antigonococcal activity of South African medicinal plants

4.2.1. Antigonococcal activity

The plant species listed in Table 1 are frequently utilized by traditional healers and indigenous people to treat gonorrhoea and other STIs. Many studies have documented their biological activity against various STI-causing pathogens, including gonorrhoea (Buwa and Van Staden, 2006; De Wet et al., 2012, 2012; Mongalo et al., 2016; Mulaudzi et al., 2013, 2011; Naidoo et al., 2013; Omogbene et al., 2024; Semenya et al., 2013). However, research validating the traditional use of these species specifically against *N. gonorrhoea* remains limited. The scientific validation of the bioactivity and clinical safety of species used in traditional medicine is crucial, as these findings not only benefit the scientific community but also provide valuable insights for indigenous people and anyone interested in utilizing natural remedies.

From the 28 documented species, only 8 have been subjected to *in vitro* antigonococcal activity. In most of the ethnobotanical studies focusing on either STIs, venereal diseases, or antimicrobial activity of South African plant species, *N. gonorrhoea* is seldom included in the list of pathogens evaluated. Only three studies that assessed the antimicrobial activity of South African species included *N. gonorrhoea* as a pathogen to be tested (Mulaudzi et al., 2015; Naidoo et al., 2013a; Seleteng-Kose et al., 2019). Only one study has specifically focused on assessing herbal remedies derived from South African plants for activity against *N. gonorrhoeae* (Mulaudzi et al., 2015).

The leaves of *P. fruticosa* were extracted using dichloromethane: methanol (1:1) and water. Both the dichloromethane: methanol (1:1) and the aqueous extracts displayed significant antigonococcal activity with an MIC value of 2.0 mg/ml (van Vuuren and Naidoo, 2010). The organic extract (dichloromethane: methanol) of *T. dregeana* displayed good activity against *N. gonorrhoea* with an MIC value of 2.0 mg/ml (Naidoo et al., 2013). In the same study by Naidoo et al. (2013), the organic and aqueous extracts of *S. sanguinea* displayed bioactivity with MIC values of 0.31 and 0.25 mg/ml, respectively. The organic extracts displayed notable activity, while the aqueous extracts only displayed activity for *P. fruticosa* and *S. sanguinea* (Mulaudzi et al., 2015; Naidoo et al., 2013a). The roots of *P. africanum* were tested on *N. gonorrhoea,* and an MIC value of 1.6 mg/ml was reported (Mamba, 2017). An MIC of 0.06 mg/ml was observed on the organic extract of *H. caespititium*, indicating high antigonococcal activity of the whole plant extract (Seleteng-Kose et al., 2019). The methanolic leaf extract of *Apalone ferox* displayed significant antigonococcal activity with an MIC value of 0.5 mg/ml (Kambizi and Afolayan, 2008).

Gomphocarpus fruticosus displayed antigonococal activity when tested against *N. gonorrhoeae*, with the aqueous and acetone extracts exhibiting 66 % and 85 % inhibition, respectively (Mulaudzi et al., 2015). Furthermore, the ethanolic leaf extract of *H. caffrum* showed poor activity, with a 38 % inhibition when tested against *N. gonorrhoeae* (Shabana et al., 2011a). Other plants showing good inhibition include *X. caffra, B. speciosus*, and *O. lanceolata* (Mulaudzi et al., 2011). The disk diffusion method used in these studies is not reliable, and the results obtained could vary significantly if the microdilution assay is applied. Recent studies on the antibacterial activity of various plant species have opted for the microdilution assay due to its enhanced efficiency, reproducibility, and capability to test multiple antimicrobials (Eloff, 2019) simultaneously.

Although *T. emetica, W. indica, A. nelsonii, G. perpensa, A. adianthifolia, W. nodiflora, T. sericea, C. molle, K. africana, A. echinatus,* and L. *edulis* are traditionally used to treat *N.* gonorrhoea, there is currently no record of studies scientifically validating their ethnomedicinal use for gonorrhoeae. This represents a significant research gap among South African plants that are traditionally employed to treat venereal ailments. Prioritizing more research to validate the antigonococcal activity of these plants is essential, given that gonorrhoea is the second most prevalent STI globally, with a high burden also observed in South Africa. Further studies on these species could enhance our understanding, and the next commercial antibiotic to treat gonorrhoea may potentially originate from a botanical species.

4.2.2. Antigonococcal phytochemicals from South African plants

Of the documented species (Table 1), antigonococcal constituents have been isolated only from *X. caffra, A. ferox*, and *H. caespititium*. The bisnorsesquiterpene vomifoliol, an active constituent isolated by bioassay-guided fractionation of dichloromethane leaf extract of *X. caffra*, showed good activity against *N. gonorrhoeae* (Fig. 3). However, the antigonococcal activity of vomifoliol (63.1 % inhibition) was reduced as compared to the activity of the whole plant extract (78.8 % inhibition). This suggests that the antigonococcal activity of the extract could have been due to the synergistic effect of vomifoliol and other compounds present in the plant extract (Nair et al., 2013).

Aloin, chrysophanol, and aloe emodin were isolated from bioactive extracts of *A. ferox*. They have not been tested for activity, however, they are thought to contribute to the observed activity in *A. ferox* (L Kambizi and Afolayan, 2008). The constituent 10-methyl-8-(propan-17-ylidene) naphthalen-9-yl)-11-vinyl-14-hydroxyfuran-16-one was isolated from *H. caespititium* and displayed activity against *N. gonorrhoea* with an MIC value of 60 μg/ml (Bassey et al., 2021). While several studies demonstrated significant activity of crude extracts derived from South African plant species, the isolation of the antigonococcal phytoconstituents from species used to treat gonorrhoea has not been conducted for most of the species.

4.2.3. Cytotoxicity of South African plants used to treat gonorrhoea

Extensive *in vitro* cytotoxicity studies have been conducted for most of the documented species, except for *A. echinatus, A. concinnus, W. nodiflora,* and *A. nelsonii* (Table 1). The vast majority of the species exhibit cytotoxicity to different plant parts. Additionally, the extraction solvents also display varying cytotoxicity for the same plant parts. The human cell lines used in the cytotoxicity tests produce different results for either extracts from the same plant parts or extracts with the same solvent of extraction (Table 1). *In vitro* cytotoxicity studies do not translate to the clinical safety of these documented species. Although some species are regarded as cytotoxic when tested on certain cell lines based on *in vitro* assessments, the findings may not be conclusive. Pathogens exhibit different behaviors *in vitro* and *in vivo*, and the same applies to *N. gonorrhoeae*. Generally, *in vivo* tests are deemed conclusive because the pathogen is observed in a living organism.

Typically, antimicrobial studies on medicinal plants with antigonococcal activity in South Africa focus on *in vitro* cytotoxicity screening (Bassey et al., 2021; Kambizi and Afolayan, 2008; Nair et al., 2013). In most cases, *in vivo* studies are conducted only for pure compounds, with crude extracts being examined to a lesser extent. This is often due to the high costs of *in vivo* tests, leading most researchers to focus on isolated pure compounds or the most active crude extracts. There is a significant research gap regarding the *in vivo* cytotoxicity of species used to treat gonorrhoea in South Africa. Therefore, clinical safety must be established based on *in vivo* assessments rather than solely depending on *in vitro* tests. Further *in vivo* studies are necessary to determine the clinical safety of the species documented in Table 1.

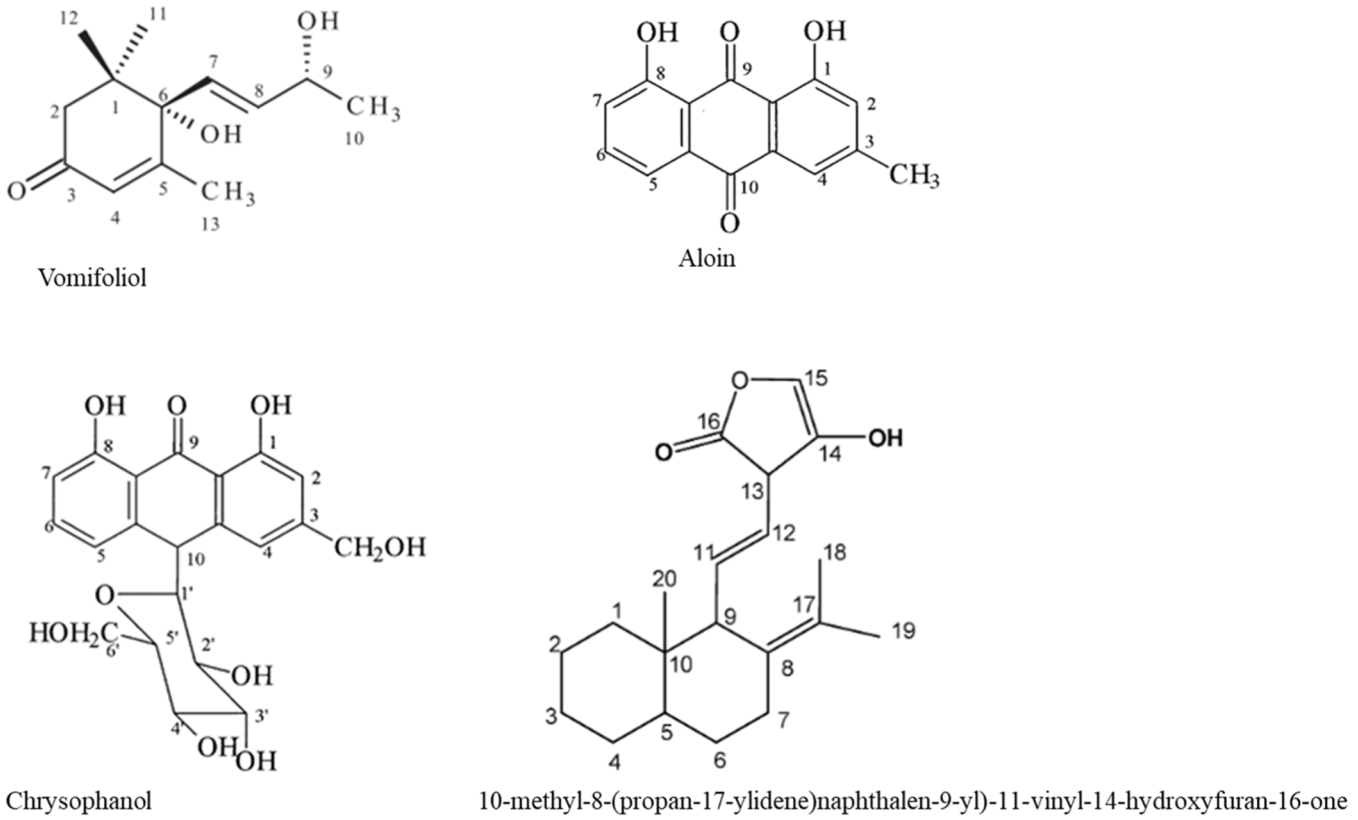

Fig. 3. Isolated antigonococcal constituents isolated from some South African medicinal plants, which are traditionally used to treat gonorrhoea.

5. Future perspectives

Over the past few decades, numerous South African medicinal plants traditionally utilized to treat various STIs have undergone scientific investigation. Efforts have also focused on the bio-guided isolation of active compounds from these plants. However, our findings indicate that more research is needed regarding the plants traditionally used in the treatment of gonorrhoea. Most documented studies have concentrated on validating traditional uses, with antimicrobial research primarily directed toward other clinically significant STI pathogens, rather than *N. gonorrhoeae*. It is well-known that gonorrhoea is the second most prevalent STI, yet, concerning the South African medicinal plants used to treat it, few studies have confirmed their ethnomedicinal significance, as observed in our findings. Moreover, bioactive substances within these species have not been thoroughly examined, revealing another important gap in phytochemical research.

Phytochemical studies are crucial because, in the drug discovery process, pure compounds are generally favoured over crude extracts. To date, not a single antibiotic derived from plants has been developed to treat gonorrhoea. This ongoing situation is primarily attributable to inadequate phytochemical analysis of many species traditionally used to treat various STIs, including gonorrhoea. Current advances in the field of metabolomics should also be leveraged, as they could facilitate the discovery of novel compounds with therapeutic potential. An ideal approach would involve testing different parts of each plant for their effectiveness against major STI pathogens, determining and documenting which pathogens show the greatest susceptibility, selecting the most active plant extracts for compound isolation, considering the synergistic effects of co-occurring compounds, assessing bioactivity as well as cytotoxicity of these compounds, and elucidating the modes of action of the active compounds.

6. Conclusion

The current review presents a comprehensive account of what has been accomplished and the research gaps that need to be filled concerning plants used in the treatment of gonorrhoea. Much still needs to be done in terms of validating the ethnobotanical uses of these plants and also exploring the option of bio-prospecting from them. Only about 44 % of these plants have been tested for their antigonococcal activity. The remaining 56 % are yet to be validated for their antigonococcal ethnomedicinal use. Bioactive substances have only been isolated in two species, further highlighting the scant phytochemical research conducted on species displaying antigonococcal activity. Cytotoxicity screening has predominantly been conducted *in vitro*; hence, *in vivo* studies are essential to conclusively determine the clinical safety of South African medicinal plant species.

CRediT authorship contribution statement

Thilivhali E. Tshikalange: Writing – review & editing, Supervision, Funding acquisition. **Fatimah Lawal:** Writing – original draft, Methodology, Formal analysis, Data curation. **Mcebisi J. Mabuza:** Writing – review & editing. **Mahwahwatse J. Bapela:** Writing – review & editing, Supervision.

Declaration of competing interest

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

Acknowledgments

The authors wish to acknowledge the research grant supported by

the National Research Foundation (NRF) in South Africa.

References

Abdillahi, H.S., Verschaeve, L., Finnie, J.F., Van Staden, J., 2012. Mutagenicity, antimutagenicity, and cytotoxicity evaluation of South African *podocarpus* species. J. Ethnopharmacol. 139, 728–738. https://doi.org/10.1016/j.jep.2011.11.044.

Addo, E.M., Chai, H., Hymete, A., Yeshak, M.Y., Slebodnick, C., Kingston, D.G.I., Rakotondraibe, L.H., 2015. Antiproliferative constituents of the roots of Ethiopian *Podocarpus falcatus* and structure revision of 2 α -hydroxynagilactone F and nagilactone I. J. Nat. Prod. 78, 827–835. https://doi.org/10.1021/np501062f.

Aderogba, M.A., McGaw, L.J., Ogundaini, A.O., Eloff, J.N., 2007. Antioxidant activity and cytotoxicity study of the flavonol glycosides from *Bauhinia galpinii*. Nat. Prod. Res. 21, 591–599. https://doi.org/10.1080/14786410701369557.

Ahmed, A.S., Elgorashi, E.E., Moodley, N., McGaw, L.J., Naidoo, V., Eloff, J.N., 2012. The antimicrobial, antioxidative, anti-inflammatory activity, and cytotoxicity of different fractions of four South African *Bauhinia* species used traditionally to treat diarrhoea. J. Ethnopharmacol. 143, 826–839. https://doi.org/10.1016/j.jep.2012.08.004.

Eloff, J.N., 2019. Avoiding pitfalls in determining antimicrobial activity of plant extracts and publishing the results. BMC. Complement. Altern. Med. 19, 1–8. https://doi.org/10.1186/s12906-019-2519-3.

Bassey, K., Mamabolo, P., Cosa, S., 2021. An andrographolide from *Helichrysum caespitium* (Dc.) sond. Ex harv., (Asteraceae) and its antimicrobial, quorum sensing, and antibiofilm potentials. Biology. (Basel) 10, 1224. https://doi.org/10.3390/biology10121224/s1.

Beentje, H.J., 1994. Kenya: Trees, shrubs, and Lianas. National Museums of Nairobi, Nairobi.

Bello, I., Shehu, M.W., Musa, M., Zaini, M., Mahmud, R., 2016. *Kigelia africana* (Lam.) Benth. (Sausage tree): phytochemistry and pharmacological review of a quintessential African traditional medicinal plant. J. Ethnopharmacol. 189, 253–276. https://doi.org/10.1016/j.jep.2016.05.049.

Bero, J., Ganfon, H., Jonville, M., Frédérich, M., Gbaguidi, F., Demol, P., Moudachirou, M., Quetin-leclercq, J., 2009. *In vitro* antiplasmodial activity of plants used in Benin in traditional medicine to treat malaria. J. Ethnopharmacol. 122, 439–444. https://doi.org/10.1016/j.jep.2009.02.004.

Bhujade, A., Gupta, G., Talmale, S., Das, S.K., Patil, M.B., 2013. Induction of apoptosis in A431 skin cancer cells by *Cissus quadrangularis* Linn stem extract by altering bax-bcl-2 ratio, release of cytochrome c from mitochondria, and PARP cleavage. Food Funct. 4, 338–346. https://doi.org/10.1039/c2fo30167a.

Buthelezi, M.N., Tshililo, V.T., Kappo, A.P., Simelane, M.B.C., 2024. Phytochemical evaluation of *ziziphus mucronata* and *xysmalobium undulutum* towards the discovery and development of anti-malarial drugs. Malar. J. 23, 1–13. https://doi.org/10.1186/s12936-024-04976-1.

Buwa, L.V., Van Staden, J., 2006. Antibacterial and antifungal activity of traditional medicinal plants used against venereal diseases in South Africa. J. Ethnopharmacol. 103, 139–142. https://doi.org/10.1016/j.jep.2005.09.020.

Chauke, M., Shai, L., Mogale, M., Tshisikhawe, M., Mokgotho, M., 2015. Medicinal plant use of villagers in the Mopani district, Limpopo province, South Africa. African J. Traditional, Complem. Alternat. Med. 12, 9–26. https://doi.org/10.4314/ajtcam.v12i3.2.

Cleary, S., Birch, S., Chimbindi, N., Silal, S., McIntyre, D., 2013. Investigating the affordability of key health services in South Africa. Soc. Sci. Med. 80, 37–46. https://doi.org/10.1016/j.socscimed.2012.11.035.

De Wet, H., Dludla, P.M., Mkhaliphi, S.E., Shabalala, S.N.M., 2008. An ethnopharmacological investigation of home grown plants used for treating diarrhoea and wound infections in the Mbazwana area. Maputaland. South African J. Botany 74, 365–366. https://doi.org/10.1016/j.sajb.2008.01.050.

De Wet, H., Nzama, V.N., Van Vuuren, S.F., 2012. Medicinal plants used for the treatment of sexually transmitted infections by lay people in northern Maputaland, KwaZulu–Natal Province, South Africa. South African J. Botany 78, 12–20. https://doi.org/10.1016/j.sajb.2011.04.002.

Dembetembe, T.T., Lall, N., Kritzinger, Q., 2022. The use of South African medicinal plants in the pursuit to treat gonorrhoea and other sexually transmitted diseases. In: Chassagne, F. (Ed.), Medicinal Plants as Anti-Infectives. Academic Press, pp. 183–207. https://doi.org/10.1016/b978-0-323-90999-0.00001-x.

Fouche, G., Cragg, G.M., Pillay, P., Kolesnikova, N., Maharaj, V.J., Senabe, J., 2008. *In vitro* anticancer screening of South African plants. J. Ethnopharmacol. 119, 455–461. https://doi.org/10.1016/j.jep.2008.07.005.

Fox, L.T., Mazumder, A., Dwivedi, A., Gerber, M., Plessis, J., Hamman, H., 2017. *In vitro* wound healing and cytotoxic activity of the gel and whole-leaf materials from selected aloe species. J. Ethnopharmacol. 200, 1–7. https://doi.org/10.1016/j.jep.2017.02.017.

Fyhrquist, P., Mwasumbi, L., Vuorela, P., Vuorela, H., 2006. Preliminary antiproliferative effects of some species of *Terminalia, Combretum,* and *Pteleopsis* collected in Tanzania on some human cancer cell lines. Fitoterapia 77, 358–366. https://doi.org/10.1016/j.fitote.2006.05.017.

Haddaway, N., Page, M., Pritchard, C., McGuinness, L., 2022. PRISMA2020: an R package and shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimized digital transparency and open synthesis. Campbell. Syst. Rev. 18, e1230. https://doi.org/10.1002/cl2.1230.

Hoet, S., Opperdoes, F., Brun, R., Adjakidjé, V., Quetin-leclercq, J., 2004. *In vitro* antitrypanosomal activity of ethnopharmacologically selected Beninese plants. J. Ethnopharmacol. 91, 37–42. https://doi.org/10.1016/j.jep.2003.11.008.

Hutchings, A., Scott, A.H., 1996. Zulu Medicinal plants: An inventory. University of Natal Press, Pietermaritzburg.

Irungu, B.N., Orwa, J.A., Gruhonjic, A., Fitzpatrick, P.A., Landberg, G., Kimani, F., Midiwo, J., Erdélyi, M., Yenesew, A., 2014. Constituents of the roots and leaves of *Ekebergia capensis* and their potential antiplasmodial and cytotoxic activities. Molecules. 19, 14235–14246. https://doi.org/10.3390/molecules190914235.

Kambizi, L., Afolayan, A.J., 2008. Extracts from *Aloe ferox* and *withania somnifera* inhibit *Candida albicans* and *Neisseria gonorrhoea.* Afr. J. Biotechnol. 7, 012–015. https://doi.org/10.4314/ajb.v7i1.58301.

Kimutai, N., Njenga, E.W., Jeruto, P., Kosgey, J., Kipkorir, N., Mutai, C., Ng'eny, L., Korir, R., 2016. Antimicrobial activity and cytotoxicity of selected medicinal plants found in Nandi County. Kenya. African J. Pharmacol0 Therapeutics 4, 86–91.

Komane, B.M., Olivier, E.I., Viljoen, A.M., 2011. *Trichilia emetica* (Meliaceae) – A review of traditional uses, biological activities and phytochemistry. Phytochem. Lett. 4, 1–9. https://doi.org/10.1016/j.phytol.2010.11.002.

Kuete, V., Tchinda, C.F., Mambe, F.T., Veronique, P., Efferth, T., 2016. Cytotoxicity of methanol extracts of 10 Cameroonian medicinal plants towards multi-factorial drug-resistant cancer cell lines. BMC. Complement. Altern. Med. 16, 267–279. https://doi.org/10.1186/s12906-016-1253-3.

Lawal, R.A., Ozaslan, M.D., Odesanmi, O.S., Karagoz, I.D., Kilic, I.H., Ebuehi, O.A.T., 2012. Cytotoxic and antiproliferative activity of *Securidaca longepedunculata* aqueous extract on Ehrlich ascites carcinoma cells in Swiss albino mice. Int. J. Appl. Res0 Natural Products 5, 19–27.

Luo, X., Pires, D., Aínsa, J.A., Gracia, B., Mulhovo, S., Duarte, A., Anes, E., Ferreira, M.U., 2011. Antimycobacterial evaluation and preliminary phytochemical investigation of selected medicinal plants traditionally used in Mozambique. J. Ethnopharmacol. 137, 114–120. https://doi.org/10.1016/j.jep.2011.04.062.

Mabogo, N., 2012. The Ethnobotany of the Vhavenda. University of Pretoria, Pretoria.

Mabuza, M.J., Kaiser, M., Tshikalange, T.E., Yusuf, A.A., Bapela, M.J., 2025. *In vitro* antiplasmodial activity and cytotoxicity of three *Ziziphus* (Rhamnaceae) species from South Africa. J. Ethnopharmacol 349, 119918. https://doi.org/10.1016/j.jep.2025.119918.

Madikizela, B., Ndhlala, A.R., Rengasamy, K.R.R., Mcgaw, L.J., Staden, J.Van, 2017. Pharmacological evaluation of two South African commercial herbal remedies and their plant constituents. South African J. Botany 111, 291–298. https://doi.org/10.1016/j.sajb.2017.03.038.

Magee, A.R., Van Wyk, B.-E., Van Vuuren, S.F., 2006. Ethnobotany and antimicrobial activity of Sieketroos (*Arctopus* species). South African J. Botany 73, 159–162. https://doi.org/10.1016/j.sajb.2006.06.009.

Magwede, K., Van Wyk, B., Van Wyk, A., 2019. An inventory of Vhavenḓa useful plants. South African J. Botany 122, 57–89. https://doi.org/10.1016/j.sajb.2017.12.013.

Mamba, P., 2017. Bioactivity of Selected Medicinal Plants Used for the Treatment of Sexually Transmitted Diseases. University of Pretoria, Pretoria.

Maroyi, A., 2019. *Helichrysum caespititium* (DC.) Harv.: review of its medicinal uses, phytochemistry, and biological activities. J. Appl. Pharm. Sci. 9, 111–118. https://doi.org/10.7324/japs.2019.90616.

Masuvhe, L., Tshisikhawe, M.P., 2018. Ethnobotanical survey of medicinal plants used by Vhavenda in the treatment of gonorrhoea at Dzimauli village, Vhembe District of Limpopo Province, South Africa. South African J. Botany 115, 322. https://doi.org/10.1016/j.sajb.2018.02.166.

Mathekga, A.D.M., 2001. Antimicrobial Activity of *Helichrysum* species and the Isolation of a New Phloroglucinol from *Helichrysum caespititium.* University of Pretoria, Pretoria.

Mbunde, M.V.N.M., Innocent, E., Mabiki, F., Andersson, P.G., 2016. Ethnobotanical survey and toxicity evaluation of medicinal plants used for fungal remedy in the Southern Highlands of Tanzania. J. Intercult. Ethnopharmacol. 6, 84–96. https://doi.org/10.5455/jice.20161222103956.

Meyer, T., Buder, S., 2020. The laboratory diagnosis of *Neisseria gonorrhoeae*: current testing and future demands. Pathogens. 9, 91. https://doi.org/10.3390/pathogens9020091.

Michalow, J., Hall, L., Rowley, J., Anderson, R.L., Hayre, Q., Chico, R.M., Edun, O., Knight, J., Kuchukhidze, S., Majaya, E., Reed, D.M., Stevens, O., Walters, M.K., Peters, R.P.H., Cori, A., Boily, M.C., Imai-Eaton, J.W., 2025. Prevalence of chlamydia, gonorrhoea, and trichomoniasis among male and female general populations in sub-Saharan Africa from 2000 to 2024: a systematic review and meta-regression analysis. eClinical Medicine 83, 103210. https://doi.org/10.1016/j.eclinm.2025.103210.

Moeng, T., 2010. An Investigation Into the Trade of Medicinal Plants by Muthi Shops and Street Vendors in the Limpopo Province, South Africa. University of Limpopo, Turfloop.

Mongalo, N., McGaw, L., Adebayo, S., Finnie, J., Van Staden, J., 2016. Cytotoxicity, antimicrobial, and anti-inflammatory properties of South African medicinal plants used to treat sexually transmitted and related opportunistic infections. South African J. Botany 103, 335. https://doi.org/10.1016/j.sajb.2016.02.119.

Mongalo, N.I., McGaw, L.J., Finnie, J.F., Staden, J.Van, 2017. Pharmacological properties of extracts from six South African medicinal plants used to treat sexually transmitted infections (STIs) and related infections. South African J. Botany 112, 290–295. https://doi.org/10.1016/j.sajb.2017.05.031.

Mongalo, N.I., McGaw, L.J., Finnie, J.F., Staden, J.Van, 2015. *Securidaca longipedunculata* Fresen (Polygalaceae): a review of its ethnomedicinal uses, phytochemistry, pharmacological properties, and toxicology. J. Ethnopharmacol. 165, 215–226. https://doi.org/10.1016/j.jep.2015.02.041.

Moshi, M.J., Cosam, J.C., Mbwambo, Z.H., Kapingu, M., Nkunya, M.H.H., 2004. Testing beyond ethnomedical claims : brine shrimp lethality of some Tanzanian plants. Pharm. Biol. 42, 547–551. https://doi.org/10.1080/13880200490897920.

Mukinda, J.T., Eagles, P.F.K., 2010. Acute and sub-chronic oral toxicity profiles of the aqueous extract of Polygala fruticosa in female mice and rats. J. Ethnopharmacol. 128, 236–240. https://doi.org/10.1016/j.jep.2010.01.022.

Mulaudzi, R., Ndhlala, A.R., Kulkarni, M.G., Finnie, J.F., Van Staden, J., 2013. Anti-inflammatory and mutagenic evaluation of medicinal plants used by Venda people against venereal and related diseases. J. Ethnopharmacol. 146, 173–179. https://doi.org/10.1016/j.jep.2012.12.026.

Mulaudzi, R.B., Ndhlala, A.R., Kulkarni, M.G., Finnie, J.F., Van Staden, J., 2011. Antimicrobial properties and phenolic contents of medicinal plants used by the Venda people for conditions related to venereal diseases. J. Ethnopharmacol. 135, 330–337. https://doi.org/10.1016/j.jep.2011.03.022.

Mulaudzi, R.B., Ndhlala, A.R., Van Staden, J., 2015. Ethnopharmacological evaluation of a traditional herbal remedy used to treat gonorrhoea in Limpopo province, South Africa. South African J. Botany 97, 117–122. https://doi.org/10.1016/j.sajb.2014.12.007.

Naidoo, D., Van Vuuren, S.F., Van Zyl, R.L., De Wet, H., 2013. Plants traditionally used individually and in combination to treat sexually transmitted infections in northern Maputaland, South Africa: antimicrobial activity and cytotoxicity. J. Ethnopharmacol. 149, 656–667. https://doi.org/10.1016/j.jep.2013.07.018.

Nair, J., Mulaudzi, R., Chukwujekwu, J., Van Heerden, F., Van Staden, J., 2013. Antigonococcal activity of *ximenia caffra* sond. (Olacaceae) And identification of the active principle. South African J. Botany 86, 111–115. https://doi.org/10.1016/j.sajb.2013.02.170.

Newman, D.J., Cragg, G.M., 2020. Natural products as sources of new drugs over the nearly four decades from 01/1981 to 09/2019. J. Nat. Prod. 83, 770–803. https://pubs.acs.org/doi/10.1021/acs.jnatprod.9b01285.

Omogbene, T.O., Lawal, I.O., Amoo, S.O., Adam, A.A., Gebashe, F.C., Aremu, A.O., 2024. Plants used for the management of venereal diseases in sub-Saharan Africa: a systematic review and critical assessment of their research status. Trop. Med. Health 52, 1–37. https://doi.org/10.1186/s41182-024-00651-y.

Oyebanji, B.O., Olatoye, O.S., Oyewole, O., 2015. Effects of methanolic leaf, bark, and fruit extracts of *Kigelia africana* on haematology and erythrocyte membrane stability in rats. Sokoto J. Veterinary Sci. 13, 1–5. https://doi.org/10.4314/sokjvs.v13i2.1.

Palgrave, C., Drummond, R., Moll, E., 2002. Trees of Southern Africa. Penguin Random House, Cape Town.

Palmer, E., Pitman, N., 1972. Trees of Southern Africa: covering all known indigenous species in the Republic of South Africa, South-West Africa, Botswana, Lesotho & Swaziland. Balkema, Cape Town.

Pooley, E., 1993. Complete Field Guide to Trees of Natal, Zululand & Transkei. Natal Flora Publications Trust, Durban.

Pooley, E., Boon, R., 2010. Pooley's Trees of Eastern South Africa. Flora and Fauna Publications Trust, Durban.

Pooley, Elsa., 2003. Mountain flowers : a Field Guide to the Flora of the Drakensberg and Lesotho. Flora Publications Trust, Durban.

Rached, W., Calhelha, R.C., Fernandes, Â., Carvalho, A.M., Bennaceur, M., Marouf, A., Barros, L., Santos-Buelga, C., Ferreira, I.C.F.R., 2016. Phytochemical characterization and bioactive properties of *Osyris quadripartita* Salzm. Ex decne. Leaves from Algeria. RSC. Adv. 6, 72768–72776. https://doi.org/10.1039/c6ra11787b.

Ramulondi, M., 2017. Toxicology and Herb-Drug Interaction of Selected Anti-Hypertension Plants Used by Lay Persons in Northern Kwazulu-Natal (South Africa). University of Zululand, KwaDlangezwa.

Samie, a, Obi, C.L., Lall, N., Meyer, J.J.M., 2009. *In vitro* cytotoxicity and antimicrobial activities, against clinical isolates of *Campylobacter* species and *entamoeba histolytica*, of local medicinal plants from the Venda region, in South Africa. Ann. Trop. Med. Parasitol. 103, 159–170. https://doi.org/10.1179/136485909x384992.

Seleteng-Kose, L., Moteetee, A., van Vuuren, S., 2019. Medicinal plants used for the treatment of sexually transmitted infections in the Maseru District, Lesotho: antimicrobial validation, phytochemical and cytotoxicity studies. South African J. Botany 122, 457–466. https://doi.org/10.1016/j.sajb.2019.01.035.

Semenya, S., Potgieter, M., Erasmus, L., 2013. Indigenous plant species used by Bapedi healers to treat sexually transmitted infections: their distribution, harvesting, conservation, and threats. South African J. Botany 87, 66–75. https://doi.org/10.1016/j.sajb.2013.03.001.

Shabana, M.M., El Sayed, Aly M., Yousif, M.F., El Sayed, A.M., Sleem, A.A., 2011. Bioactive constituents from *Harpephyllum caffrum* Bernh. And *Rhus coriaria* L. Pharmacogn. Mag. 7, 298–306. https://doi.org/10.4103/0973-1296.90410.

Simelane, M.B.C., Lawal, O.A., Djarova, T.G., Musabayane, C.T., Singh, M., Opoku, A.R., 2012. Lactogenic activity of rats stimulated by Gunnera perpensa L. (Gunneraceae) from South Africa. Afr. J. Tradit. Complement. Altern. Med. 9, 561–573.

Sohni, Y.R., Davis, C.L., Deschamps, A.B., Kale, P.G., 1995. Frameshift mutations in Salmonella induced by the extracts of medicinal herbs *Lannea edulis* (Sond.) Engl. And *Monotes glaber* Sprague. Environ. Mol. Mutagen. 25, 77–82. https://doi.org/10.1002/em.2850250111.

Tafadzwa, M., 2009. Screening of Some Traditional Medicinal Plants from Zimbabwe for Biological and Antimicrobial Activity. University of Zimbabwe.

Tlakula, P.K., Tshikalange, T.E., 2015. The ethnobotanical survey and conservation of medicinal plants that are used by the local people of Thulamela municipality, Limpopo Province. South African J. Botany 98, 203. https://doi.org/10.1016/j.sajb.2015.03.129.

Tshikalange, T., Mamba, P., Adebayo, S., 2016. Antimicrobial, antioxidant, and cytotoxicity studies of medicinal plants used in the treatment of sexually transmitted diseases. Int. J. Pharmacogn. Phytochem. Res. 8, 1891–1895.

Tshikalange, T.E., Meyer, J.J.M., Hussein, A.A., 2005. Antimicrobial activity, toxicity, and the isolation of a bioactive compound from plants used to treat sexually transmitted diseases. J. Ethnopharmacol. 96, 515–519. https://doi.org/10.1016/j.jep.2004.09.057.

Twilley, D., Langhansová, L., Palaniswamy, D., Lall, N., 2017a. Evaluation of traditionally used medicinal plants for anticancer, antioxidant, anti-inflammatory, and anti-viral (HPV-1) activity. South African J. Botany 112, 494–500. https://doi.org/10.1016/j.sajb.2017.05.021.

Twilley, D., Langhansová, L., Palaniswamy, D., Lall, N., 2017b. Evaluation of traditionally used medicinal plants for anticancer, antioxidant, anti-inflammatory, and anti-viral (HPV-1) activity. South African J. Botany 112, 494–500. https://doi.org/10.1016/j.sajb.2017.05.021.

Van Vuuren, S.F., Naidoo, D., 2010. An antimicrobial investigation of plants used traditionally in southern Africa to treat sexually transmitted infections. J. Ethnopharmacol. 130, 552–558. https://doi.org/10.1016/j.jep.2010.05.045.

Van Wyk, B., Van Wyk, P., 1997. Field Guide to Trees of Southern Africa. Penguin Random House South Africa, Cape Town.

Venter, F., Venter, J.-A., 1996. Making the Most of Indigenous Trees. Briza Publications.

WHO, 2024. Gonorrhoea (Neisseria Gonorrhoeae infection) [WWW Document]. World Health Organization. URL. https://www.who.int/news-room/fact-sheets/detail/gonorrhoea-(neisseria-gonorrhoeae-infection (accessed 4.13.25).

Van Wyk, B.-E.Van, Gericke, N., 2000. People's Plants: A Guide to Useful Plants of Southern Africa. Briza Publications, Pretoria.

Yakobi, S.H., Magibile, Y.B., Pooe, O.J., 2024. A systematic review of Neisseria gonorrhoeae drug resistance development in South Africa. Brazilian J. Microbiol. 55, 1053–1063. https://doi.org/10.1007/s42770-024-01281-6/figures/4.

Yeol, W., Kim, K., 2017. Anti- Anti-*Propionibacterium* acnes and the anti-inflammatory effect of *Aloe ferox* miller components. J. Herb. Med. https://doi.org/10.1016/j.hermed.2017.03.009.

Yeshanew, A.G., Geremew, R.A., 2018. *Neisseria gonorrhoeae* and their antimicrobial susceptibility patterns among symptomatic patients from Gondar town, North West Ethiopia. Antimicrob. Resist. Infect. Control 7. https://doi.org/10.1186/s13756-018-0376-3.

Zongo, F., Ribuot, C., Boumendjel, A., Guissou, I., 2013. Botany, traditional uses, phytochemistry and pharmacology of Waltheria indica L. (syn. *Waltheria americana*): a review. J. Ethnopharmacol. 148, 14–26. https://doi.org/10.1016/j.jep.2013.03.080.