



A Review on Ethnomedicine, Pharmacological Activity and Phytochemistry of *Rhoicissus tridentata* (L.f.) Wild & Drumm

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ABSTRACT:

Rhoicissus tridentata (L.f.) Wild & Drumm, a perennial climbing shrub belonging to the family Vitaceae, is a traditional medicinal plant of importance in southern Africa. Traditionally used to manage reproductive disorders, gastrointestinal ailments, inflammatory conditions, and liver diseases. This review critically evaluates its ethnomedicinal, phytochemical, and pharmacological data. The literature on *R. tridentata* was comprehensively retrieved from several scientific databases, including ResearchGate, Google Scholar, Scopus, ScienceDirect, SciFinder, and Elsevier journals. Relevant publications published between 1995 and 2025 were identified and reviewed using keywords such as “ethnomedicine,” “bioactive metabolites,” and “pharmacological properties” of *R. tridentata*. Phytochemical investigations have revealed the presence of diverse secondary metabolites, including triterpenoids, flavonoids, phenolic acids, tannins, alkaloids, saponins, sterols, and anthocyanins. These compounds contribute to the plant’s pharmacological activities, including antimicrobial, anti-inflammatory, antioxidant, uterotonic, hepatoprotective, antidiabetic, antiproliferative, and antiplasmodial effects, as shown in both *in vitro* and *in vivo* studies. Despite these promising findings, limited data exist on the pharmacokinetics, bioavailability, and molecular mechanisms of its bioactive constituents. This review highlights the therapeutic potential of *R. tridentata* as a promising source of bioactive natural products and emphasizes the need for further pharmacological, toxicological, and

clinical studies to support its development into standardized phytomedicines.

KEYWORDS:

Rhoicissus tridentata; Traditional medicine; Phytochemistry; medicinal plant, pharmacological activity, Safety profile

1. Introduction

The genus *Rhoicissus* Planch., belonging to the family Vitaceae, comprises a group of woody climbers or shrubs native to sub-Saharan Africa. Members of this genus are closely related to grapevines (*Vitis* spp.) and are characterized by the presence of tendrils, trifoliolate leaves, small, clustered flowers, and fleshy, globose berries. Among the various species, *Rhoicissus tridentata* (L.f.) Wild & Drumm. stands out as one of the most widely recognized and utilized in traditional medicine across southern Africa. The plant has undergone several taxonomic revisions, with subspecies such as *R. tridentata* subsp. *tridentata* and subsp. *Cuneifolia* is commonly identified in botanical literature. It is also known by several vernacular names, including Bushman’s grape in English, *isinwazi* in Zulu, and *umnxeba* in isiXhosa, Ndurutua in Swahili, reflecting its deep integration into local cultures and ethnobotanical practices (1,2).

R. tridentata is a vigorous climber or occasionally a shrub with leathery trifoliolate leaves that are

toothed along the margins. The small greenish-yellow flowers appear in dense clusters and give rise to fleshy berries that ripen from red to black. The plant's tuberous roots and lignotubers are often the primary parts used for medicinal purposes. It is widely distributed throughout southern Africa, occurring in diverse habitats such as savannahs, forest margins, rocky outcrops, and woodland areas, particularly in South Africa's Eastern Cape, KwaZulu-Natal, Limpopo, and Mpumalanga provinces (3, 4). It holds a prominent position in African traditional medicine. The roots and bark are frequently employed to induce or ease labor, enhance fertility, and relieve menstrual disorders. Decoctions and infusions are also used to manage stomach ailments, bladder and kidney problems, swollen glands, and general body pains. In several South African communities, the species is a key ingredient in *isihlambezo*, an herbal preparation traditionally consumed during late pregnancy to strengthen the uterus and facilitate childbirth (1, 5, 6). These wide-ranging applications suggest the presence of potent bioactive compounds underlying its pharmacological efficacy.

Preliminary phytochemical investigations into *R. tridentata* have revealed the presence of several bioactive compound classes. These include triterpenoids, phenolic acids, flavonoids, alkaloids, and sterols, which are often associated with the observed medicinal properties (7,8). In line with its traditional uses, initial pharmacological studies have demonstrated promising antibacterial, anti-inflammatory, uterotonic, antidiabetic, and antioxidant activities in various *in vitro* and limited *in vivo* models (1,6,8).

Despite growing research interest, significant gaps remain in our understanding of *R. tridentata*. Comprehensive toxicological assessments are limited, and the pharmacokinetic properties of its bioactive constituents are poorly characterized. Moreover, there has been little exploration of chemotypic variation across subspecies or geographical regions, which may influence both chemical composition and biological activity. To date, no single review has systematically synthesized the existing knowledge on the botany, phytochemistry, traditional uses, and pharmacology of *R. tridentata*, providing a consolidated foundation for future studies.

Therefore, this review aims to integrate and critically evaluate the available information on *R. tridentata*, highlighting its ethnomedicinal relevance, phytochemical diversity, and

pharmacological potential. Furthermore, it seeks to identify knowledge gaps and proposed directions for future research, particularly concerning its bioactive compounds, mechanisms of action, and safety profile.

2. Literature Survey Databases

This review is based on a systematic analysis of literature retrieved from major scientific databases, including ResearchGate, Google Scholar, Scopus, ScienceDirect, SciFinder, and Elsevier. Supplementary information on the botany, geographical distribution, traditional uses, phytochemistry, and pharmacological properties of *R. tridentata* was obtained from the reference lists of relevant journal articles, book chapters, and academic texts. The literature search covered publications from 1995 to 2025.

Only studies related to the keywords "*Rhoicissus tridentata*", "phytochemistry", "traditional medicine", "pharmacological activity", "antimicrobial activity", "toxicity", "uterotonic activity", and "bioactive compounds" were included in this review, while literature unrelated to these themes was excluded. The compiled information was critically evaluated to synthesize current knowledge, identify existing research gaps, and highlight promising directions for future investigations.

Ethnomedicine

R. tridentata (L.f.) Wild & R.B. Drumm., commonly known as the grape ivy, wild grape, or "isihaqa" in isiZulu, is a perennial climbing shrub belonging to the family Vitaceae. It is widely distributed across southern Africa, particularly in South Africa, Botswana, Zimbabwe, Mozambique, Kenya, Burundi, and Eswatini, where it plays a significant role in traditional medicine (1,9).

Traditionally, various parts of *R. tridentata*, including the roots, tubers, and leaves, are used to treat a broad spectrum of ailments. The roots are decocted or chewed to manage female reproductive disorders, such as infertility, menstrual pain, menorrhagia, abdominal pain during menstruation, postpartum recovery, and labour induction, earning it the reputation of a "women's health tonic" (1, 10). The root juice, extracted through chewing, is traditionally ingested to ease abdominal cramps and digestive discomfort.

The plant is also widely used to treat erectile dysfunction, heartburn, peptic ulcers, diarrhea, renal disorders, epilepsy, and sexually transmitted infections (STIs) (1, 11). Root or tuber infusions are used as antiemetics in children, for treating general ailments, and for cuts, sores, and sprained ankles. Roots warmed over a fire are pressed against swollen glands to reduce inflammation, while decoctions are consumed to relieve stomach ailments and eye infections.

In veterinary medicine, *R. tridentata* is traditionally used to treat heartwater, redwater, and internal parasites in livestock. The tuberous roots are sometimes boiled and fed to young animals, especially those that have lost their mothers, as a nutritional and restorative tonic (11). The bulbs are squeezed in 10 ml of water and given to cattle for fertility (12).

Additionally, the plant exhibits hepatoprotective effects, being used to prevent or manage liver damage (1). Its sap is reported to possess healing and anesthetic properties, which support its topical application on wounds and sores. Root and leaf preparations are also applied externally for broken bones, cuts, and swollen tissues.

Its applications in reproductive, gastrointestinal, hepatic, and musculoskeletal disorders suggest the presence of anti-inflammatory, antispasmodic, antimicrobial, and antioxidant compounds supporting its inclusion in further phytochemical and pharmacological studies (1, 13). Table 1 shows the traditional medicinal uses of *R. tridentata*.

Table 1: Ethnomedicinal uses of *R. tridentata* (L.f.) Wild & R.B. Drumm.

Plant part used	Traditional preparation	Traditional use	References
Roots / Tubers	Decoction, infusion, or juice extracted through chewing	Infertility, menstrual pain, menorrhagia, labor induction, postpartum recovery, abdominal pain during menstruation, and as a women's health tonic	(1, 13)
Roots / Tuber juice	Chewed and ingested	Ease of ingestion and relief of abdominal discomfort and digestive problems	(1, 9)
Roots (heated)	Warmed and pressed against the skin	Swollen glands, inflammation, and local pain relief	[5, 6]
Root decoction/ infusion	Taken orally	Erectile dysfunction, heartburn, peptic ulcers, diarrhea, renal disorders, and general body ailments	(1, 13)
Root or leaf preparations	Topical application or poultice	Cuts, sores, broken bones, sprained ankles, and wound healing	(13)
Root infusions/ sap	Oral or topical use	Epilepsy, menorrhagia, eye infections, sexually transmitted infections (STIs), and antiemetics for children	(1, 13)
Leaf extracts/ sap	Topical application	Treatment of sores, wounds, and eye infections; sap has anesthetic and healing properties	(1, 10)
Roots / Tubers (boiled)	Fed to livestock	Nutritional tonic for young animals (especially orphans); treatment for heartwater, redwater, and internal parasites	(9)
Whole plant (various)	Decoction or infusion	Liver protection (hepatoprotective), general tonic, anti-inflammatory, antioxidant	(1, 13)

Phytochemicals

Phytochemical investigations of *R. tridentata* have revealed a rich diversity of secondary metabolites that contribute to its wide range of pharmacological activities. Studies on the root bark, stem bark, and tuber extracts identified catechin, epicatechin, gallic acid, epigallocatechin gallate (EGCG), condensed

tannins, and other polyphenolic compounds, which were strongly associated with the plant's antioxidant properties (14). Similarly, Brookes and Katsoulis reported the presence of catechins, proanthocyanidins, gallic acid, sterols, triterpenoids, and triacontanol in root and branch extracts (15). Methanolic extracts were particularly enriched with proanthocyanidins and condensed tannins, which demonstrated

potent antioxidant and uterotonic activities. In contrast, non-polar extracts contained sterols and triterpenoids linked to anti-inflammatory, immune-enhancing, cholesterol-lowering, and possible central nervous system effects.

Further phytochemical profiling of the dichloromethane/methanol (1:1) ultrasound-assisted extract revealed the presence of flavonoids, tannins, and anthocyanins, including quercetin, kaempferol, fisetin, ellagic acid, and petunidin 3-galactoside. This extract exhibited moderate antibacterial activity against several zoonotic bacterial pathogens and demonstrated a bactericidal mode of action. Acute toxicity studies also indicated low toxicity, with an oral LD₅₀ greater than 5000 mg/kg (16).

In another study, phytochemical investigations of methanol–water extracts from the roots and lignotubers led to the isolation of several flavonoids, stilbene glycosides, triterpenoids, sterols, fatty acids, and phenolic compounds (3). The acetone fraction yielded asiatic acid, arjunolic acid, β-sitosterol, catechin, quercetin 3-O-rhamnoside, trans-resveratrol

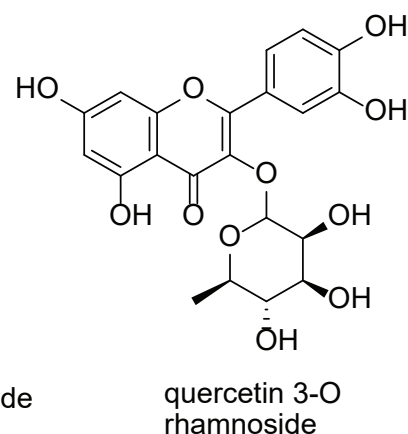
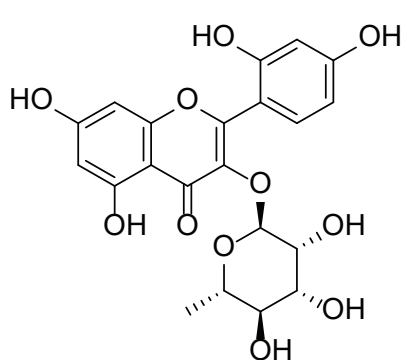
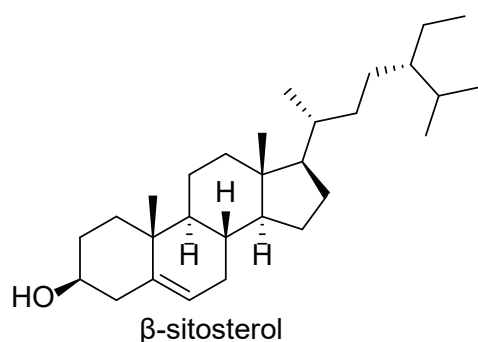
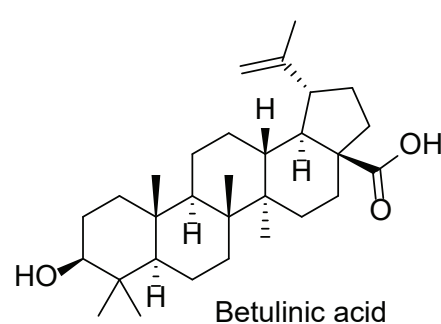
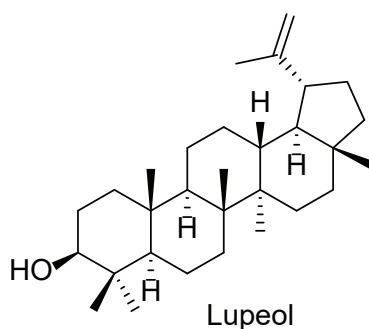
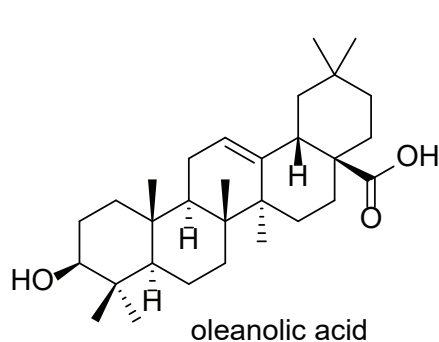
3-O-β-glucopyranoside, morin 3-O-α-L-rhamnopyranoside, and linoleic acid. Among these compounds, a mixture of asiatic acid and arjunolic acid exhibited the strongest uterotonic activity, while β-sitosterol also stimulated uterine contractions. Conversely, morin 3-O-α-L-rhamnopyranoside and trans-resveratrol 3-O-β-glucopyranoside displayed relaxant effects on uterine smooth muscle.

The coexistence of these diverse bioactive constituents provides a strong chemical basis for the broad spectrum of pharmacological activities attributed to *R. tridentata*. Experimental studies have demonstrated antibacterial, antifungal, antidiabetic, uterotonic, and antioxidant activities, thereby supporting many of its traditional medicinal uses. These findings highlight *R. tridentata* as a valuable source of bioactive natural products with significant potential for modern drug discovery and therapeutic development. Table 2 summarizes the major bioactive compounds and their reported activities, while Figure 1 illustrates some of the key compounds isolated from *R. tridentata*.

Table 2: Bioactive Compounds and Reported Activities of *R. tridentata*.

Chemical Class	Representative Compounds	Reported Activities	Mode/ mechanism of action	References
Phenolic compounds & Flavonoids	Quercetin, Kaempferol, Luteolin, Fisetin, Ellagic acid, Morin 3-O-α-L-rhamnopyranoside, and their glycosides	Antioxidant, uterotonic	Free radical scavenging and reduction of oxidative stress.	(14, 15)
		Antioxidant	Neutralization of reactive oxygen species (ROS) and inhibition of lipid peroxidation	(14)
		Antioxidant, anti-inflammatory	ROS scavenging and modulation of inflammatory mediators.	(14, 15)
		Antioxidant, antimicrobial	ROS scavenging and modulation of inflammatory mediators	(14)
		Uterine relaxant	Modulation of smooth muscle contractile pathways	(3)
		Uterine relaxant, antioxidant	Relaxation of uterine smooth muscle and oxidative stress reduction	(3)
Tannins	Hydrolyzable and condensed tannins	Antioxidant, uterotonic	Enhancement of antioxidant defense and smooth muscle contraction	(15)
		Antioxidant, antimicrobial	Protein precipitation, microbial membrane disruption, and free radical scavenging	(14, 15)

Chemical Class	Representative Compounds	Reported Activities	Mode/ mechanism of action	References
Triterpenoids & Sterols	Lupeol, Betulinic acid, β -sitosterol, Asiatic acid	Anti-inflammatory, cholesterol-lowering, uterotonic	Modulation of inflammatory pathways and stimulation of uterine contractions	(3, 15)
		Anti-inflammatory, immune-enhancing	Inhibition of inflammatory mediators and immune modulation	(15)
Alkaloids	Pheophytin, lycorine	Antimicrobial, cytotoxic, antioxidant	Prevention of oxidative damage and microbial inhibition	(3)
Saponins	Asiatic acid, Arjunolic acid	Uterotonic, antioxidant	Enhancement of smooth muscle contraction and antioxidant activity	(3)
Anthocyanins & Proanthocyanidins	Cyanidin, Procyanidin derivatives	Antioxidant, pigmentation, free radical scavenging	Anthocyanin-mediated free radical scavenging	(16)
Polyunsaturated fatty acid	Linoleic acid	Anti-inflammatory	Regulation of inflammatory mediators and membrane stabilization	(3)
Long-chain fatty alcohol	Triacontanol	Possible CNS and metabolic effects	Regulation of metabolic and signaling pathways	(15)



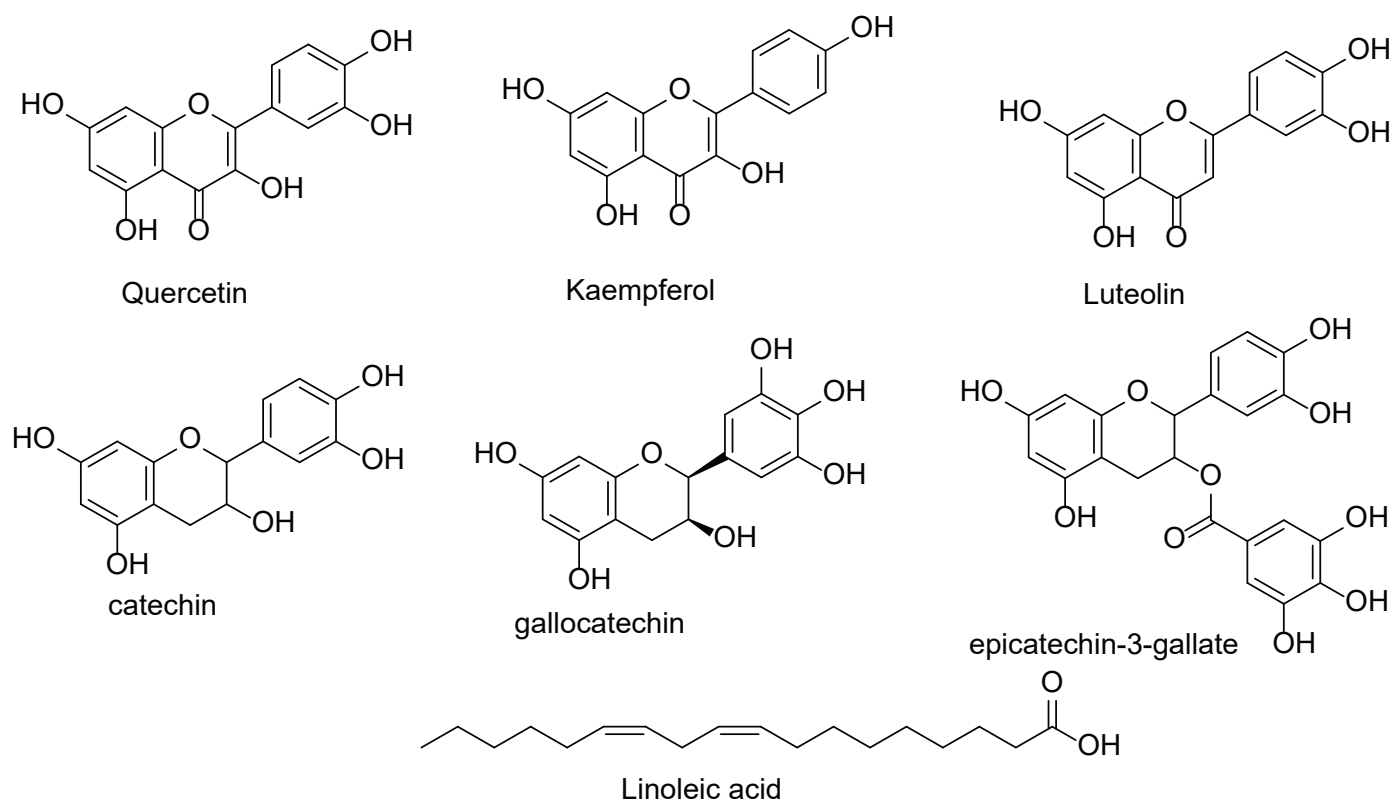


Figure 1: Some of the bioactive compounds isolated from *R. tridentata*.

Pharmacological Activities

R. tridentata has been widely reported to exhibit a broad spectrum of pharmacological activities, including antioxidant, antimicrobial, antiproliferative, antiplasmodial, uterotonic, hepatoprotective, and antidiarrheal effects. These pharmacological properties collectively support its traditional use in managing various ailments and highlight its potential as a valuable source of therapeutic compounds.

Antimicrobial Activity

The antibacterial and antibiofilm activities of *R. tridentata* root extracts against selected bacterial pathogens have been investigated and demonstrated moderate antimicrobial potential (17). The study revealed that the methanol extract exhibited minimum inhibitory concentrations (MICs) ranging from 0.13 to 4 mg/mL against *Chromobacterium violaceum*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, and *Serratia marcescens*. Hexane and aqueous extracts showed MIC values of 2–4 mg/mL against *Chromobacterium violaceum*, while the ethyl acetate extract demonstrated an MIC of 4 mg/mL against *Staphylococcus aureus* only. In contrast, the dichloromethane extract showed no inhibitory activity against the tested microorganisms. None of the extracts inhibited

the growth of *Escherichia coli*. Overall, the antibacterial activities of the methanol, water, ethyl acetate, and hexane extracts were less potent than those of ciprofloxacin, the standard drug, which exhibited an MIC of 0.063 mg/mL.

In addition to direct antibacterial effects, the methanol extract demonstrated notable antibiofilm and anti-virulence activities. The extract significantly disrupted microbial adhesion by reducing the initial attachment of important pathogens, including *Staphylococcus aureus*, *Proteus mirabilis*, and *Serratia marcescens*, by approximately 50%. Furthermore, the extract inhibited bacterial quorum sensing, as evidenced by more than 50% inhibition of violacein production in *Chromobacterium violaceum*, with a calculated IC_{50} of 2.58 mg/mL. These findings collectively indicate that *R. tridentata* possesses antibacterial, anti-adhesion, and quorum-sensing inhibitory properties, thereby providing scientific support for its traditional use in the treatment of urinary tract infections (UTIs) and highlighting its potential as a source of novel antipathogenic agents.

Another study investigated the antimicrobial activity of methanol leaf and root extracts of *R. tridentata* using the disc diffusion method against selected bacterial and fungal strains (12). The findings showed that methanol extracts

at 20 mg/mL exhibited significant antimicrobial activity compared with tetracycline (30 µg/mL), the reference drug. The methanol leaf extract demonstrated limited activity, producing an inhibition zone diameter (IZD) of only 4 mm against *Salmonella typhimurium*. In contrast, the methanol root extract displayed broader antimicrobial activity, with inhibition zone diameters ranging from 4–10 mm or more against a wide spectrum of microorganisms, including *Proteus mirabilis*, *Proteus morgani*, *Proteus vulgaris*, *Pseudomonas solanacearum*, *Pseudomonas syringae*, *Salmonella* spp., *Shigella boydii*, *Staphylococcus aureus*, *Alcaligenes faecalis*, *Streptococcus faecalis*, *Streptococcus pyogenes*, *Staphylococcus epidermidis*, *Bacillus cereus*, *Bacillus coagulans*, *Bacillus pumilus*, *Bacillus stearothermophilus*, *Klebsiella pneumoniae*, *Micrococcus luteus*, *Mycobacterium smegmatis*, and *Candida albicans*.

The methanol root extract demonstrated pronounced inhibitory activity against both Gram-positive and Gram-negative bacteria, as well as the fungal pathogen *Candida albicans*. Although no antifungal reference drug was included for comparison, the results suggest considerable antifungal potential. These findings confirm that the roots of *R. tridentata* are the most therapeutically valuable part of the plant, containing diverse bioactive compounds with significant antimicrobial properties. The results further validate the traditional medicinal use of *R. tridentata* in the treatment of infectious diseases.

In a comprehensive analysis, the antimicrobial efficacy of *R. tridentata* was investigated by preparing extracts from various plant parts using methanol, acetone, and hexane solvents; essential oils were also examined in specific assays (18). The study employed both disc diffusion and microdilution techniques to evaluate antibacterial activity. Experiments employed 10 µL of a 50 mg/mL gentamycin solution as the positive control, while 15 µL (6%) dimethyl sulfoxide (DMSO) served as the negative control. Results demonstrated that extracts derived from the roots and tubers exhibited potent, broad-spectrum inhibition against all tested bacterial strains. The potency was quantified by Minimum Inhibitory Concentration (MIC) values, which ranged from 0.75 mg/mL against *Bacillus cereus* to over 12 mg/mL against the more resilient *Pseudomonas aeruginosa*. In stark contrast, extracts obtained from the fruits displayed markedly lower activity, with all MIC

values exceeding 12 mg/mL, underscoring the superior efficacy of the underground components. Consequently, *R. tridentata* was classified among the most therapeutically promising plants, demonstrating significant activity against both Gram-positive and Gram-negative bacteria, a distinction it shared with other notable species, such as *Syzygium cordatum* and *Peltophorum africanum*.

The antimicrobial efficacy and activity against the human immunodeficiency virus (HIV) were evaluated for extracts from plant species traditionally used in southern Africa to manage sexually transmitted infections (STIs) (19). This investigation targeted the recombinant HIV-1 enzyme. In the assay, doxorubicin (100 µg/mL) served as the positive control, and a mixture of lysis buffer and reaction components served as the negative control. Among the tested species, *R. tridentata* displayed superior antimicrobial action, most notably against *Neisseria gonorrhoeae*, which it inhibited at a minimal concentration (MIC) of 0.40 mg/mL. It was also effective against *Candida albicans* and *Gardnerella vaginalis* (MIC 0.80 mg/mL), and *Oligella ureolytica* (MIC 1.60 mg/mL). Furthermore, *R. tridentata* exhibited significant inhibition of HIV-1 reverse transcriptase, achieving 75.50% inhibition at 100.00 µg/mL, a result approaching the 96.50% inhibition of the doxorubicin control. These pronounced activities position *R. tridentata* as a promising candidate for the development of novel multi-target therapeutic agents against sexually transmitted infections.

In a study by Tshikalange investigating medicinal plants for the treatment of sexually transmitted diseases, a broth microdilution assay was used to evaluate *R. tridentata* (19). The extract demonstrated broad-spectrum antimicrobial activity, with the highest potency against *Candida albicans*, *Escherichia coli*, and *Staphylococcus aureus*, each with a low MIC of 0.8 mg/mL. It was also effective against *Klebsiella oxytoca* (1.6 mg/mL) and *Klebsiella pneumoniae* (3.1 mg/mL), while showing moderate activity against *Neisseria gonorrhoeae* (6.3 mg/mL). These results confirm the significant antimicrobial potential of *R. tridentata*, supporting its traditional use.

Anti-inflammatory Activity

A scientific investigation into the traditional Zulu medicinal plant, *R. tridentata*, provides validation for its use in treating inflammation (12). The study focused on the plant's ability

to inhibit cyclooxygenase-1 (COX-1), a key mediator of the inflammatory process. The results demonstrated that a methanolic root extract significantly suppressed COX-1 activity, revealing a direct mechanism for its anti-inflammatory effects. This finding provides a pharmacological explanation for the plant's traditional use in alleviating pain and swelling and promoting wound healing. Conversely, aqueous extracts of the plant showed negligible anti-inflammatory activity. Importantly, the same potent methanolic root extract has previously been documented to possess broad-spectrum antimicrobial properties. The convergence of these two activities, a potent anti-inflammatory within a single extract, provides compelling scientific support for the ethnobotanical use of *R. tridentata* in treating conditions like cuts and wounds, where both infection and inflammation are concurrent concerns.

A study investigating the anti-inflammatory potential of various *Rhoicissus* species, including *R. tridentata*, employed a cyclooxygenase-1 (COX-1) enzyme inhibition assay to evaluate their efficacy (20). The research focused on methanolic extracts prepared specifically from the plant's roots. The results demonstrated that the methanolic root extract of *R. tridentata* collected from KwaZulu-Natal, South Africa, inhibited the COX-1 enzyme. Since COX-1 is a key catalyst in the prostaglandin biosynthetic pathway that mediates the inflammatory response, this inhibitory activity provides strong preliminary evidence of the plant's potential as an anti-inflammatory agent. This finding offers scientific support for the traditional use of *R. tridentata* in treating conditions associated with inflammation.

Mamba & Tshikalange also assessed the effect of *R. tridentata* on the anti-inflammatory enzyme 15-lipoxygenase (15-LOX) (19). In the assay, the enzyme solution was prepared at 200 units/mL in 2 M borate buffer at pH 9. For each test, 12.5 microliters of the plant extract or a control substance was combined with 487.5 microliters of the 15-LOX solution. The investigation revealed that *R. tridentata* exhibited inhibitory activity, with a calculated half-maximal inhibitory concentration (IC_{50}) of 87.39 micrograms per milliliter against the 15-LOX enzyme. This finding further supports the proposition that plant species in the genus *Rhoicissus* hold promise as sources of anti-inflammatory agents.

Antioxidant Activity

In a separate investigation of antioxidant properties, Tshikalange also evaluated medicinal plants used for the treatment of sexually transmitted diseases, including *R. tridentata*, using the DPPH free-radical scavenging assay (19). The results revealed that *R. tridentata* possesses extreme antioxidant activity, significantly outperforming the ascorbic acid control. This was determined by its remarkably low half-maximal inhibitory concentration (IC_{50}) of 0.06 $\mu\text{g/mL}$, indicating superior free-radical quenching capability compared to vitamin C ($IC_{50} = 1.44 \mu\text{g/mL}$). This finding highlights a potent antioxidant mechanism within the plant, which may contribute to its therapeutic effectiveness.

Opoku et al. (2002) conducted an *in vitro* evaluation of the antioxidant potential of methanolic extracts from the roots, stems, and leaves of *R. tridentata* (21). Using multiple assays, including DPPH free radical scavenging, xanthine oxidase inhibition, lipid peroxidation prevention, DNA protection, and Fe^{2+} chelation, the study revealed that *R. tridentata* exhibited vigorous, dose-dependent antioxidant activity. The extracts achieved up to 98% inhibition in the DPPH assay and demonstrated remarkable ferrous ion chelation, effectively preventing the formation of hydroxyl radicals. Additionally, they significantly inhibited xanthine oxidase and protected against lipid and DNA oxidative damage. Among the species evaluated, *R. tridentata* demonstrated the most potent antioxidant effects. The study concluded that the plant's high free radical-scavenging and metal-chelating capacities underpin its traditional medicinal use in Zulu ethnomedicine for managing oxidative stress-related ailments and inflammation, thereby supporting its therapeutic relevance in conventional healing systems.

Uterotonic Activity

The pharmacological effects of an aqueous root extract of *R. tridentata* were evaluated on isolated rat uterine and ileal tissues (22). The extract produced direct, concentration-dependent contractions in both organs. When the tissues were pretreated with the muscarinic receptor blocker atropine (40 nM) or the cyclooxygenase inhibitor indomethacin (5 mM), the contractile effects of the extract were abolished entirely, indicating that muscarinic receptors and cyclooxygenase-derived metabolites mediate

these responses. In contrast, pretreatment with the serotonergic receptor antagonist methysergide (1 mM) and the α -adrenoceptor blocker prazosin (2 mM) did not alter the extract's contractile action. These findings suggest that the stimulatory effect of the *Rhoicissus* extract on uterine and intestinal smooth muscles operates through muscarinic and prostaglandin-related pathways, rather than serotonin or adrenergic receptor mechanisms.

A study was conducted to assess how the contractile effects of *R. tridentata* extracts change with the seasons (23). Researchers compared the activity of crude aqueous preparations from various plant parts, collected at three-month intervals over a two-year period, using isolated rat uterine tissue. The findings revealed that extracts from specimens gathered during the summer and autumn seasons exhibited a contractile potency four to five times greater than those harvested in winter or spring. Among the plant components, tubers induced the most intense uterine contractions, followed by stems, roots, and leaves in descending order. These outcomes underscore the critical importance of standardizing the harvest period for *R. tridentata* to ensure consistent biological activity.

Mshengu isolated and identified the bioactive uterotonic constituents of *R. tridentata*. Each compound was evaluated for uterotonic activity on uterine smooth muscle obtained from rats treated with stilboestrol. Among these, the combined fraction of asiatic and arjunolic acids exhibited the strongest contractile response, with an EC_{50} value of 0.02129 μ g/mL for contraction amplitude (3). These findings provide pharmacological evidence supporting the traditional use of *R. tridentata* to promote childbirth and facilitate labor. Interestingly, morin 3-O- α -L-rhamnopyranoside and trans-resveratrol 3-O- α -glucopyranoside induced relaxation of the uterine muscle, indicating that the plant contains both stimulatory and inhibitory constituents acting on uterine tissue.

Ascaricidal Activity

Nalule investigated the *in vitro* anthelmintic activity of ethanol and aqueous root tuber extracts of *R. tridentata* against adult *Ascaris suum* using a worm motility inhibition assay (24). Extracts were evaluated at different concentrations and compared with Albendazole and Goodwin's solution as controls. Both extracts

produced significant, dose-dependent inhibition of worm motility ($F(5, 53) = 4.14$, $p = 0.005$; $R^2 = 0.90$), though the extraction method did not significantly affect this relationship ($F(10, 53) = 1.02$, $p = 0.450$). The ethanolic extract demonstrated higher potency ($ED_{50} = 12.3$ mg/mL) compared to the aqueous extract ($ED_{50} = 23.5$ mg/mL), although their maximal effects were statistically similar ($p = 0.082$). Phytochemical screening confirmed the presence of bioactive secondary metabolites. These results validate the traditional ethno-veterinary use of *R. tridentata* as an antiparasitic agent and emphasize that solvent choice influences efficacy. Further *in vivo* studies are recommended to assess safety and therapeutic potential.

A study was conducted to evaluate the *in vitro* anthelmintic efficacy of *R. tridentata* extracts, determining their median effective dose (ED_{50}) using an *Ascaris* model (25). The calculated ED_{50} for *R. tridentata* was 4.36 mg/mL. The most pronounced effect was observed at the highest tested concentration, 10.00 mg/mL, which first showed activity after 12 hours and reached a 100% response rate by 24 hours. Lower concentrations of 4.00, 6.00, and 8.00 mg/mL also initiated their effect at the 12-hour mark. The maximum response for the 4.00 and 6.00 mg/mL doses was attained after 48 hours, while the 8.00 mg/mL dose reached its peak effect at 36 hours. The lowest dose of 2.00 mg/mL only began to show a response after 24 hours and achieved a 90% efficacy at the 48-hour endpoint. These findings indicate that *R. tridentata* possesses significant potential for developing treatments against helminth infections in livestock.

Antiproliferative Activity

In a study screening Zulu medicinal plants for antineoplastic potential, the antiproliferative activity of *R. tridentata* was evaluated *in vitro* against the human hepatoma (HepG2) cell line (26). The method involved preparing both aqueous and methanolic extracts from the plant's roots. The antiproliferative effect was assessed using the MTT assay, which measures cell viability and proliferation after exposure to the plant extracts. The results demonstrated that *R. tridentata* possesses significant anticancer potential. Specifically, the aqueous root extract of *R. tridentata* exhibited remarkably high activity, showing 96.27% inhibition of cell proliferation. The corresponding methanolic root extract of the same subspecies also showed strong, though slightly lower, activity at 87.01%

inhibition. This finding suggested that the root of *R. tridentata*, exceptionally when prepared as a traditional water-based decoction, contains potent bioactive compounds that inhibit the growth of cancer cells, thereby providing scientific validation for its ethnobotanical use.

Dube and colleagues investigated the *in vitro* cytotoxic effects of stigmasterol derivatives synthesized from *R. tridentata* against breast cancer cells (27). Stigmasterol (1) was chemically modified via acetylation, epoxidation, oxidation, and dihydroxylation to produce eight new derivatives, whose structures were confirmed by NMR, IR, MS, and melting-point analyses. The compounds were evaluated for cytotoxicity against hormone receptor-positive (MCF-7), triple-negative (HCC70), and non-tumorigenic (MCF-12A) breast cell lines using the resazurin assay. While native stigmasterol showed no cytotoxicity ($EC_{50} > 250 \mu M$), several derivatives displayed enhanced activity. Specifically, 5,6-epoxystigmast-22-en-3 β -ol and stigmast-5-ene-3 β ,22,23-triol were selectively potent against MCF-7 cells ($EC_{50} = 21.92 \mu M$ and $22.94 \mu M$, respectively), and stigmastane-3 β ,5,6,22,23-pentol was most active against HCC70 cells ($EC_{50} = 16.82 \mu M$). This study demonstrates that structural modification of stigmasterol enhances its anticancer potential, identifying novel derivatives with promising activity against breast cancer cell lines.

Hepatoprotective Activity

A study was conducted to evaluate the *in vivo* hepatoprotective properties of *R. tridentata* in rats with carbon tetrachloride (CCl_4)-induced acute liver damage (28). Male Sprague-Dawley rats were separated into three groups. Two groups received an injection of CCl_4 , while the third control group was given an equivalent volume of olive oil. Two hours after the CCl_4 administration, one of the intoxicated groups was treated with an extract of *R. tridentata* via oral gavage. The olive oil control group was euthanized after two hours. Subjects from the two CCl_4 groups were humanely killed at 24, 48, and 72-hour intervals post-treatment. Researchers measured the serum activities of the enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST), as well as glucose-6-phosphatase (G-6-Pase). They also assessed lipid peroxidation (LPO) in liver tissue and microsomal fractions by quantifying malondialdehyde (MDA) levels. The results showed that CCl_4 intoxication caused a statistically significant increase ($p <$

0.05) in all measured variables, except G-6-Pase, which showed a significant decrease. Treatment with the *R. tridentata* extract following CCl_4 poisoning significantly lowered ($p < 0.05$) the elevated concentrations of ALT, AST, and LPO, while simultaneously increasing ($p < 0.05$) the depressed levels of G-6-Pase. Based on these findings, it can be concluded that *R. tridentata* contains active compounds that confer a protective effect against chemical-induced liver injury.

Antidiabetic Activity

The *in vivo* antidiabetic activity of *R. tridentata* was evaluated using streptozotocin (STZ)-induced diabetic rats (29). The experimental animals were divided into three groups: control, diabetic control, and treatment groups. Blood glucose levels were monitored at regular intervals using standard glucose measurement procedures. Diabetic rats were administered oral doses of the aqueous root extract for 7 to 14 days. The results showed that the extract significantly reduced blood glucose levels in STZ-induced diabetic rats compared to the untreated diabetic control group ($p < 0.05$). The hypoglycemic effect was dose-dependent and comparable to that of the standard reference drug, tolbutamide. Importantly, the extract did not cause hypoglycemia in normal (non-diabetic) rats, suggesting that its glucose-lowering action is specific to hyperglycemic conditions. The findings indicate that the aqueous root extract of *R. tridentata* possesses significant antidiabetic activity, supporting its traditional use in diabetes management.

A research investigation was designed to assess the antidiabetic properties of aqueous leaf extracts from *R. tridentata* using mice with alloxan-induced diabetes (4). The findings confirmed that the extracts possessed blood glucose-lowering effects. Specifically, aqueous whole-stem extracts of the plant, when administered via both intraperitoneal injection and oral routes, successfully reduced blood glucose concentrations at all four tested dosages (50, 100, 200, and 300 mg/kg body weight). This hypoglycemic effect was observed from the first hour through to the sixth hour after administration, though it did not follow a clear dose-dependent pattern. The study further concluded that intraperitoneal administration of the herbal extract produced a more potent therapeutic effect than oral administration.

Antiplasmodial Activity

Koech and colleagues investigated the anti-malarial activity and safety of *R. tridentata* extracts (30). Leaf and root materials were extracted using various solvents, including methanol, water, hexane, dichloromethane, and ethyl acetate, and evaluated against drug-sensitive and drug-resistant *Plasmodium falciparum* strains. Safety was assessed using monkey kidney cells. Results showed that the anti-malarial activity was solvent-dependent, with methanolic and aqueous extracts exhibiting the highest efficacy, achieving approximately 58% parasite inhibition, and demonstrating low toxicity and a high safety margin. Hexane extracts showed weaker activity (36% inhibition) and reduced safety. *R. tridentata* possesses moderate anti-malarial properties, and its therapeutic potential is maximized when polar solvents, such as methanol and water, are used for extraction, yielding extracts that are both effective and safe. The study emphasizes the importance of the extraction method in harnessing the plant's medicinal properties.

Toxicity

Toxicity studies show that *R. tridentata* is generally considered safe at low doses, but high doses (5 g/kg body weight) or prolonged use may cause organ toxicity, particularly in the kidneys and liver. In a cytotoxicity assessment conducted by Tshikalange on medicinal plants for the treatment of sexually transmitted diseases, the safety profile of *R. tridentata* was evaluated using an XTT assay on Vero cells (19). The results demonstrated a favorable outcome, with the plant extract exhibiting a half-maximal effective concentration (EC₅₀) of 88.5 µg/mL. This value indicates low cytotoxicity, especially when compared to the potent positive control, Actinomycin D, which had an IC₅₀ of 0.009 µg/mL. The significant disparity between the toxicity of the extract and the control substance suggests that *R. tridentata* has a wide therapeutic window, indicating its potential safety for further pharmacological development. This low cytotoxicity further strengthens its profile as a promising and safe therapeutic candidate.

The *in vivo* toxicity of *R. tridentata* was evaluated using Wistar rats (29). Acute and sub-acute toxicity tests were performed by administering different oral doses of the aqueous extract and monitoring the animals for any signs of

mortality, behavioral alterations, or physiological abnormalities. Additionally, histopathological examinations of liver and kidney tissues were conducted to assess potential organ damage. The results revealed that no deaths or toxic symptoms occurred, even at high doses of up to 5 g/kg body weight. Histological analysis confirmed the absence of significant tissue damage or pathological changes in the liver and kidney samples. Therefore, the extract was considered non-toxic and safe at the tested concentrations. These findings suggest that *R. tridentata* exhibits a favorable safety profile, supporting its potential therapeutic use without causing acute or subacute toxic effects in animal models.

The safety profile of aqueous *R. tridentata* extracts was evaluated through *in vitro* cytotoxicity tests on monkey kidney Vero cells and human fibroblast cells (31). The results established a no-observed-effect concentration of 8.00 µg/mL for the Vero cell line, a threshold below which no cell death occurred. At this same concentration, human fibroblast viability remained at 100%. Pharmacokinetic considerations estimated that the maximum achievable concentration in the bloodstream would be 6.10 µg/mL. Since this systemic concentration is below the established safety threshold of 8.00 µg/mL for Vero cells, the study concluded that *R. tridentata* exhibits no significant cellular toxicity. This nontoxic characteristic was further corroborated by its safe profile in tests on other cell lines, including human hepatoma, kidney epithelial, and histiocytoma cells, as well as mouse Leydig cells (31).

A sub-acute toxicity study of *Rhoicissus tridentata* root extracts was conducted in 84 Wistar albino rats treated orally for 28 days with doses of 187.5–1500 mg/kg body weight (32). An acute toxicity test in mice showed no mortality at 2000 and 5000 mg/kg, indicating low acute toxicity. During the sub-acute study, animals showed normal weight gain, although mild effects such as polyuria and transient lethargy were observed. Hematological analysis revealed reduced RBC count, hematocrit, MCH, and MCHC, while biochemical parameters showed increased ALT, GGT, and creatinine levels, indicating potential liver and kidney toxicity. Histopathology confirmed hepatic necrosis and renal tubular damage, demonstrating dose-dependent toxicity after prolonged exposure.

3. Conclusion

R. tridentata holds significant ethnomedicinal value and demonstrates diverse pharmacological properties that align with its traditional uses. The plant's bioactive constituents, particularly triterpenoids, flavonoids, and phenolic compounds, confer potent antimicrobial, anti-inflammatory, antioxidant, antiplasmodial, and uterotonic effects. Evidence from both *in vitro* and *in vivo* studies validates its therapeutic applications, while toxicological evaluations affirm its relative safety at tested doses.

However, the absence of extract standardization, comprehensive pharmacokinetic, clinical, and long-term safety data limits its translational potential. Future research should focus on isolating and characterizing active compounds, elucidating their mechanisms of action, and evaluating synergistic interactions among constituents. Standardization of extraction procedures and dosage formulations will be crucial in advancing *R. tridentata* from a traditional remedy to an evidence-based natural therapeutic agent with global pharmacological relevance.

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