Review
Sciences of Phytochemistry

Mimusops zeyheri as an Understudied Source of Bioactive Compounds: A Critical Evaluation of Pharmacological Evidence and Drug Discovery Prospects

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Abstract: *Mimusops zeyheri* is a multipurpose African plant traditionally used as both a food source and a medicinal resource in several communities. Despite its ethnomedicinal importance, scientific evidence on its phytochemical constituents, pharmacological properties, and safety profile remains fragmented and underexplored. This review aimed to critically evaluate the nutritional value, phytochemical composition, pharmacological activities, and safety profile of *M. zeyheri*, identify major research gaps, and highlight its potential as a source of bioactive compounds for natural product–based drug discovery. A narrative literature review was conducted using major scientific databases, including PubMed, Scopus, Web of Science, ScienceDirect, and Google Scholar from their inception to March 2026. Relevant studies published in English were retrieved using keywords related to *M. zeyheri*, phytochemistry, pharmacological activity, nutritional composition, antioxidant activity, antimicrobial effects, and toxicity. Eligible studies were screened and analyzed to extract information on ethnomedicinal uses, proximate composition, phytochemical constituents, experimentally reported biological activities, and toxicological evaluations. Available studies indicate that *M. zeyheri* contains diverse phytochemicals such as phenolic compounds, flavonoids, terpenoids, tannins, alkaloids, and saponins, which are associated with several pharmacological activities. Experimental investigations have demonstrated antidiabetic activity (approximately twofold increase in GLUT-4 translocation), antimicrobial activity against multiple bacterial strains, antioxidant activity (56% DPPH radical scavenging at 20 µg/mL), and significant inhibition of Caco-2 and HEK-293 cell proliferation at 80 mg/L, supporting some of its traditional therapeutic applications. Preliminary studies also suggest relatively low *in vitro* toxicity. *M. zeyheri* represents an underexplored yet promising plant with significant potential for pharmacological research and natural product–based drug discovery.

Introduction

Mimusops zeyheri Sond. (family Sapotaceae), commonly known as Transvaal red milkwood, represents a compelling case study in the critical gap between rich ethnobotanical knowledge and rigorous scientific validation within Southern African medicinal flora. This indigenous tree, distributed across rocky hillsides and riverine basins from South Africa to eastern Africa, is deeply embedded in local cultural practices for both nutrition and medicine (1). Its fruits are consumed as a health snack in rural communities, providing essential vitamins, minerals, and macronutrients, while its leaves, bark, roots, and seeds are deployed in traditional remedies for a remarkably broad spectrum of ailments, including wounds, skin infections, convulsions, scorpion stings, snake bite, erectile dysfunction, menstrual cramps, sexually transmitted infections, tuberculosis symptoms, inflammatory conditions, pain, diabetes, arthritis, malaria, asthma, among other (1–3). This dual role as a functional food and a therapeutic agent positions *Mimusops zeyheri* at a vital nexus for addressing food security and public health challenges in the region. However, despite this extensive traditional use, the species remains significantly under-investigated from a phytochemical and pharmacological standpoint, creating an urgent need for a systematic synthesis that bridges indigenous knowledge with modern scientific inquiry.

The current state of research on *Mimusops zeyheri* is

characterized by a focus on its nutritional and basic quality attributes rather than its bioactive potential. Studies have successfully documented the proximate composition of its fruits and seeds, confirming their value as a source of nutrients (4). Studies have also confirmed the presence of important compounds such as phenolics and flavonoids in the fruit, alongside a profile of amino acids and unsaturated fatty acids in the seeds (1). While these findings validate its role as a nutritional resource, they fall short of identifying the specific secondary metabolites responsible for its wide-ranging medicinal applications. Preliminary biological assessments, such as cytotoxicity screenings and in vitro cell proliferation studies, have been conducted, but these remain at the crude extract level and lack the mechanistic depth required to confirm or explain traditional uses (1).

This knowledge gap is particularly striking when viewed against the backdrop of the broader Sapotaceae family, which is renowned for its rich and diverse array of bioactive secondary metabolites. A powerful strategy for understanding *Mimusops zeyheri*'s potential is through informed botanical inference from its close relatives, most notably *Mimusops elengi*. A comprehensive review of *Mimusops elengi reveals* a phytochemical profile dominated by triterpenoids (including lupeol and betulinic acid), flavonoids (such as quercetin and kaempferol glycosides), and saponins (5). These compound classes are not merely chemical curiosities; they possess well-documented and highly relevant pharmacological activities.

Triterpenoids like lupeol and betulinic acid are celebrated for their potent anti-inflammatory, antimicrobial, and anticancer properties (6). Flavonoids are powerful antioxidants and modulators of immune function, often exhibiting significant activity against microbial pathogens and inflammatory cascades (7). The presence of such compounds in *Mimusops elengi* provides a strong, evidence-based hypothesis that analogous metabolite classes are likely present in *Mimusops zeyheri*, given their shared taxonomic lineage. It should be emphasized that this comparison is offered as a taxonomically informed, hypothesis-generating framework rather than direct evidence for *Mimusops zeyheri*. Confirming whether these compound classes and associated bioactivities actually occur in *Mimusops zeyheri* remains an essential and currently unmet research priority.

Notably, *Mimusops zeyheri* is ecologically and functionally distinct from its better-studied congener *Mimusops elengi*: whereas *Mimusops elengi* is native to South and Southeast Asia and is cultivated primarily as an ornamental valued for its fragrant flowers and use in Ayurvedic medicine, *Mimusops zeyheri* is a wild, indigenous Southern and Eastern African species occupying rocky hillsides, riverine basins, and bushveld, and is used chiefly as a dual-purpose food and medicinal resource by rural communities rather than as an ornamental. This distinct ecological and ethnobotanical profile underscores the need for species-specific investigation rather than reliance on inference alone. Unlike several closely related *Mimusops* species occurring within overlapping geographical ranges, *Mimusops zeyheri* is particularly recognized across southern and eastern Africa as an underutilized indigenous fruit tree with combined nutritional, ethnomedicinal, and socioeconomic importance.

The objective of this review is to integrate species-specific evidence for *Mimusops zeyheri* with informed botanical inference from related phytochemical patterns within the Sapotaceae, to provide a comprehensive synthesis of the plant's medicinal potential, phytochemical composition, and pharmacological effects. Understanding these dimensions is critical not only for academic and therapeutic advancements but also for guiding conservation and sustainable utilization strategies for this under-researched species.

Methodology

This study employed a narrative literature review approach to comprehensively evaluate the nutritional composition, phytochemical constituents, pharmacological activities, safety profile, and drug discovery potential of *Mimusops zeyheri*. Relevant scientific literature was retrieved from Google Scholar, PubMed, Scopus, Web of Science, and ScienceDirect from inception to March 2026. Searches were conducted using combinations of the species name and terms related to ethnomedicinal use, phytochemistry, nutritional composition, pharmacological activity, antioxidant activity, antimicrobial activity, cytotoxicity, and toxicity. Boolean operators (AND/OR) were used where supported by the respective database.

Studies were included if they (i) reported original data on *Mimusops zeyheri* in a peer-reviewed source, and (ii) were published in English. Studies were excluded if they (i) reported exclusively on other *Mimusops* species without generating or presenting data specific to *Mimusops zeyheri*, (ii) were conference abstracts, theses, or grey literature without accompanying peer-reviewed data, or (iii) could not be retrieved in full text. Searches covered the period from database inception to March 2026. Given the very small number of species-specific primary studies available for *Mimusops zeyheri*, no minimum methodological-quality threshold was applied for exclusion. Instead, design-related limitations of individual studies (e.g., in vitro-only testing, small sample size, lack of statistical validation) are flagged narratively at the relevant points in the text.

The retrieved publications were carefully screened and critically analyzed to extract information on the plant's ethnomedicinal uses, proximate and nutritional composition, phytochemical profile, experimentally reported pharmacological activities, and toxicological data. Data were synthesized thematically and organized into major sections. The collected information was then integrated to highlight current knowledge limitations and to position *Mimusops zeyheri* as a potentially valuable species for future pharmacological investigation and natural product–based drug discovery.

Botanical Description and Taxonomy

Taxonomic Classification

Mimusops zeyheri Sond., commonly known as the Transvaal red milkwood or milkwood, is an indigenous fruit tree belonging to the family Sapotaceae within the order Ericales(1). The Sapotaceae family comprises approximately 53 genera and over 1,200 species distributed mainly across tropical and subtropical regions.

Members of this family are typically characterized by evergreen growth habits, the presence of milky latex, hard timber, and the production of diverse secondary metabolites(1, 8). Leaves in this family are generally simple, alternate, and often leathery. The plant is classified as follows: **Kingdom:** Plantae; **Clade:** Angiosperms; **Order:** Ericales; **Family:** Sapotaceae; **Genus:** *Mimusops*; **Species:** *Mimusops zeyheri* Sond.

The species is known by several vernacular names, including Transvaal red milkwood (English), moepel (Afrikaans), mmupudu (Northern Sotho), umpushane (Zulu), nhlantswa (Tsonga), and mubululu (Venda) (9). Within the genus *Mimusops*, the species is recognized for its ecological, cultural, and nutritional importance, although it remains relatively underexploited compared with other indigenous fruit trees (1, 3, 10).

Etymology and Related Taxa

The generic name *Mimusops* originates from the Greek words *mimo* (ape) and *ops* (resembling), possibly referring to the appearance of the flowers or corolla structure (11). The species epithet *zeyheri* honors the German botanist C.L.P. Zeyher (1799–1858), a notable plant collector in southern Africa (11). Within South Africa, four milkwood species are recognized in the genus. The family Sapotaceae includes several economically significant species, such as *Manilkara zapota*, a South American tree whose latex is traditionally used in chewing gum production, and *Palaquium gutta*, a species historically exploited for gutta-percha used in industrial applications, including adhesives (9).

Morphological Description

Mimusops zeyheri occurs as a shrub or small to medium-sized tree that may reach up to 25 m in height and typically exudes milky latex when injured (12). The bark ranges from almost smooth to roughly reticulately fissured and varies in colour from grey to dark brown or black (see **Figure 1**). The tree forms a dense, rounded crown, while young branches are usually covered with reddish-brown pubescence. The leaves are spirally arranged, often appearing in clusters at the ends of branches. They are simple and entire, with petioles measuring approximately 0.5–3.5 cm in length. Leaf blades are oblong-elliptical to obovate-elliptical or lanceolate, measuring about 3.5–11.5 cm by 1.5–5.5 cm, with a cuneate base and typically a shortly acuminate apex. The texture is leathery, initially with reddish-brown pubescence on the lower surface that gradually becomes glabrescent, and numerous lateral veins are present (12).

The flowers occur in axillary fascicles of up to seven and are bisexual and actinomorphic. They possess pedicels approximately 1–3 cm long and curved. The calyx consists of two whorls of four sepals each, while the creamy-white corolla has a short tube and eight lobes, each bearing two appendages. Eight stamens alternate with eight hairy staminodes, and the ovary is superior and typically eight-celled. The fruit is an ellipsoid to ovoid or nearly globose berry, reaching up to 4.5 cm in length and turning yellow-orange upon ripening. Each fruit typically contains one or two ellipsoid seeds measuring about 1–2 cm in length with a shiny pale-brown surface and a small circular basal scar (12).

Distribution and Habitat

The natural distribution of *Mimusops zeyheri* spans several regions of southern and eastern Africa. The species occurs widely in the northern provinces of South Africa, as well as in Mozambique, Eswatini (Swaziland), Zimbabwe, Botswana, Zambia, Malawi, Tanzania, and Angola (13). The species thrives in diverse ecological settings, including rocky outcrops, wooded hillsides, forest margins, riverine vegetation, and open dry woodland or bushveld (9). It is also commonly associated with riparian woodland, sandy or infertile alluvial soils, termite mounds, and occasionally swamp forests and thickets (13). The species is generally adapted to summer rainfall regions at medium to low altitudes and shows moderate tolerance to frost, although severe frost conditions may limit its growth (9). Flower buds typically develop toward the end of the rainy season, while fruits ripen between March and June in parts of southern Africa (12).

Taxonomic Relationships and Species Differentiation

Within the genus, *Mimusops zeyheri* shares morphological



Figure 1. Flower buds (A), Flowers (B), Bark (C), and Fruits (D) of *Mimusops zeyheri* (12).

Table 1. Summary of ethnomedicinal uses of *Mimusops zeyheri*.

Use/Condition	Plant Part(s) Used	Preparation Method(s)	Administration Method(s)	Reference
Wounds and skin infections	Leaves, bark	Decoction, pounded paste	Topical	(3, 13)
Gastrointestinal disorders and ulcers	Bark, leaves	Decoction, infusion	Oral	(3)
Diabetes mellitus	Fruits, leaves	Decoction, dietary use	Oral	(3)
Pain, inflammation, headaches	Leaves, whole plant	Decoction	Oral	(17)
Respiratory ailments (cough)	Leaves	Decoction	Oral	(3)
Painful gums and oral conditions	Leaves	Decoction or mouthwash	Gargling/oral rinse	(17)
Female fertility and libido	Fruits	Air-dried fruit preparation	Oral	(17)
Male fertility and sperm productivity	Seeds	Various preparations	Oral	(17)
Candidiasis	Roots	Infusion	Oral	(13)
Snake bites	Leaves	Traditional preparation	Topical/oral	(17)
CulturaL/spiritual practices	Leaves	Burning or ritual preparation	Smoke inhalation/ritual use	(17)

similarities with closely related species such as *Mimusops obovata* and *Mimusops caffra*, which occur within overlapping geographical ranges (1). Distinguishing features among these species often involve subtle differences in leaf morphology, petiole length, and fruit size or shape (14). The species also closely resembles *Mimusops obtusifolia* (syn. *Mimusops fruticosa*), a species distributed in eastern Africa, including Kenya, Tanzania, Malawi, Zimbabwe, and Mozambique (12). However, *Mimusops obtusifolia* differs in having leaves with rounded apices and generally glabrous or sparsely pubescent undersides, as well as slightly smaller fruits.

Advances in molecular phylogenetics, including analyses of complete chloroplast genomes of related taxa such as *Mimusops coriacea*, support the placement of *Mimusops zeyheri* within the core *Mimusops* lineage. Additionally, scanning electron microscopy studies of seed coat ornamentation have identified distinctive microstructural patterns that aid in distinguishing *Mimusops zeyheri* from other congeners, including *Mimusops laurifolia* and *Mimusops elengi* (14, 15). These morphological and molecular approaches collectively contribute to improved taxonomic resolution within the genus.

Ethnobotanical Uses

Ethnomedicinal Applications

Mimusops zeyheri is widely recognized in traditional medicine across southern and eastern Africa, where various plant parts are used to manage numerous health conditions (**Table 1**). Quantitative ethnobotanical indices such as Relative Frequency of Citation (RFC) and Use Value (UV) demonstrate a high level of reliance on *Mimusops zeyheri* among rural populations, particularly for the treatment of wounds, gastrointestinal disorders, and metabolic diseases such as diabetes (1, 16). Ethnobotanical studies indicate that leaves, fruits, seeds, roots, and bark are employed in different therapeutic preparations depending on the ailment and cultural context (1–3). Traditional practitioners frequently prepare remedies as decoctions or infusions, which facilitate the extraction of bioactive compounds and improve safety by reducing potential contaminants (3).

The leaves are among the most used plant parts and are typically prepared as decoctions or pounded pastes to treat coughs, ulcers, wounds, and inflammatory conditions. In some communities, they are also used for managing painful gums, skin infections, and snake bites (3, 17). Bark preparations, usually in the form of decoctions or infusions, are traditionally applied to wounds and ulcers and are also used to treat sexually transmitted infections and gastrointestinal disorders (13). Root infusions are used for systemic infections and candidiasis, while multi-herb decoctions combining *Mimusops zeyheri* with other medicinal plants are employed in the management of metabolic disorders, reproductive health conditions, and inflammatory diseases (2).

Ethnomedicinal surveys conducted in regions such as the City of Tshwane Metropolitan Municipality and the Vhembe Biosphere Reserve in South Africa reveal that the species is used to treat diverse ailments, including diabetes mellitus, ulcers, gastrointestinal disorders, headaches, tonsillitis, inflamed gums, sexually transmitted infections, erectile dysfunction, menstrual cramps, and gynecological infections (3). Additionally, the plant is believed to enhance immunity and is used in traditional treatments for childhood conditions such as *hlogwana* (meningitis-like symptoms) and *khehlane* (sunken chest) (3).

Traditional preparation techniques for *Mimusops zeyheri* remedies are diverse and reflect a sophisticated ethnopharmacological knowledge system. Decoction is the most common preparation method, accounting for approximately 34–39% of reported uses, followed by infusion (25–33%) (3, 17). Other methods include fermentation, cold extraction, tincture preparation, powder formulation, and the preparation of pounded pastes or ointments for topical use. In certain cultural contexts, plant parts may also be burned for smoke inhalation or used in spiritual rituals (3, 17). Oral administration is the predominant route (approximately 55%), followed by topical application (20%), inhalation (10%), and bathing or soaking (10%). Less common administration methods

include the application of poultices or the use of ashes applied to small incisions (17).

Food and Nutritional Uses

Beyond its medicinal applications, *Mimusops zeyheri* is an important wild food resource in rural communities. The fruits are widely consumed fresh due to their sweet, floury pulp and are also processed into jams, jellies, and fermented beverages (12, 13). In some communities, fruits are air-dried and later consumed as cereal-like foods, contributing to household nutrition and food security (13). The fruits are particularly valued for their high vitamin C content and pleasant taste, making them popular among both humans and wildlife such as birds, monkeys, and baboons (9). The seeds also possess nutritional and functional importance. They contain crude protein, ether extract, amino acids, fatty acids, vitamin E, and dietary fiber, and may be processed to obtain oils with potential medicinal and nutritional applications (3, 18). These attributes highlight the species as a promising underutilized indigenous fruit with potential contributions to dietary diversification and rural livelihoods.

Non-Medicinal and Socioeconomic Uses

Beyond its medicinal relevance, *Mimusops zeyheri* provides several non-medicinal benefits that contribute to rural livelihoods, ecosystem services, and cultural practices across southern and eastern Africa. The species is particularly valued as a wild food resource, with its fruits widely consumed fresh or processed into various food products. The yellow to orange fruits possess a sweet, floury pulp that can be eaten raw, dried for later consumption, or processed into jams, jellies, and fermented beverages (12, 13). In some communities, dried fruits are ground or prepared as cereal-like foods, contributing to household food security and seasonal nutrition supply (17). The fruits are also an important ecological food source for wildlife, including birds and primates, which facilitates seed dispersal and supports ecosystem dynamics (9).

The species also has economic and utilitarian importance due to its wood properties. The heartwood is creamy brown to reddish-brown, relatively hard, fine-grained, and moderately durable, making it suitable for furniture production, tool handles, and general carpentry (12). Branches are traditionally used as firesticks in friction-based fire-making methods, while the tree may also serve as a fuelwood resource in rural communities (13). In some agricultural systems, farmers intentionally retain the tree within cultivated fields because it is believed to enhance soil fertility and contribute to agroecological stability (12, 13).

In addition to these practical uses, *Mimusops zeyheri* is occasionally cultivated as an ornamental species, particularly due to its dense canopy and evergreen foliage, which provide shade in home gardens, savanna landscapes, and recreational areas (9). Its aesthetic value has also led to the occasional commercialization of seedlings and potted plants in horticultural markets outside Africa (12). The species also holds cultural and spiritual significance in some communities. For example, certain traditional practices involve the use of plant materials during rituals associated with ancestral communication or spiritual cleansing (17). These diverse applications highlight the species as a multi-purpose indigenous tree with potential contributions to nutrition, traditional medicine, rural economies, and ecological sustainability.

Nutritional Value and Proximate Analysis

The nutritional significance of *Mimusops zeyheri* is reflected in the diverse macro- and micronutrient composition reported in different plant parts. In the Gauteng Province of South Africa, the species is widely recognized as a food plant, with its fruits representing the most frequently utilized component and accounting for approximately 47% of all recorded plant uses (3). The fruits are commonly consumed fresh, dried for storage, or processed into pulp-based beverages mixed with water or milk. Nutritional evaluation indicates that the fruits possess a remarkably high vitamin C content of about 90 mg/100 g, exceeding that of several indigenous and exotic fruits and highlighting their importance in nutritional supplementation and poverty alleviation initiatives(3). In addition, the fruits contain appreciable levels of simple carbohydrates, including fructose, glucose, and sucrose, further supporting their role as an important dietary energy source (19). Proximate analysis of the fruits has also revealed high dry and organic matter contents, alongside measurable protein and ash contents (4, 20).

The seeds of *Mimusops zeyheri* also contribute substantially to the plant's nutritional profile. Studies have reported the presence of lipids, proteins, oleic acid, and vitamin E in the seeds (18). Oil extracted from the seeds yields approximately 14.04% lipids and contains significant levels of linoleic acid (18.87%) (21). Other fatty acids reported include myristic acid, pentadecanoic acid, palmitic acid, margaric acid, stearic acid, arachidic acid, behenic acid, lignoceric acid, palmitoleic acid, 8-heptadecenoic acid, oleic acid, 11-eicosenoic acid, erucic acid, nervonic acid, α-linolenic acid, γ-linolenic acid, and 11,14,17-eicosatrienoic acid (21). Omega-3, 6, and 9 were also found to be present in the seed oil extract (21). In addition, the seeds contain proteins and vitamin E (1.97 ± 0.75 µg/g), further supporting their potential value as a dietary supplement and plant-derived oil source (18, 20). Amino acid profiling further demonstrated that glutamic acid is the predominant amino acid (1.29 g per 100 g) in the seed (18). Other amino acids reported in varying amounts include arginine, serine, aspartic acid, glycine, threonine, alanine, tyrosine, proline, hydroxyproline, methionine, valine, phenylalanine, isoleucine, leucine, histidine, and lysine (18).

Mineral profiling of the leaves has revealed the presence of several essential elements, including nitrogen (6.33 mg/kg), phosphorus (0.33 mg/kg), potassium (1.25 mg/kg), calcium (0.39 mg/kg), magnesium (0.06 mg/kg), zinc (29 mg/kg), copper (14 mg/kg), iron (409 mg/kg), aluminium (74.07 mg/kg), and manganese (51.85 mg/kg) (22). Trace element analysis of the roots also detected small amounts of chromium, arsenic, and lead in samples collected from Botswana (22). Collectively, these findings demonstrate that various parts of *Mimusops zeyheri* possess notable nutritional and proximate components, supporting its importance as a functional food resource and highlighting its potential contribution to dietary

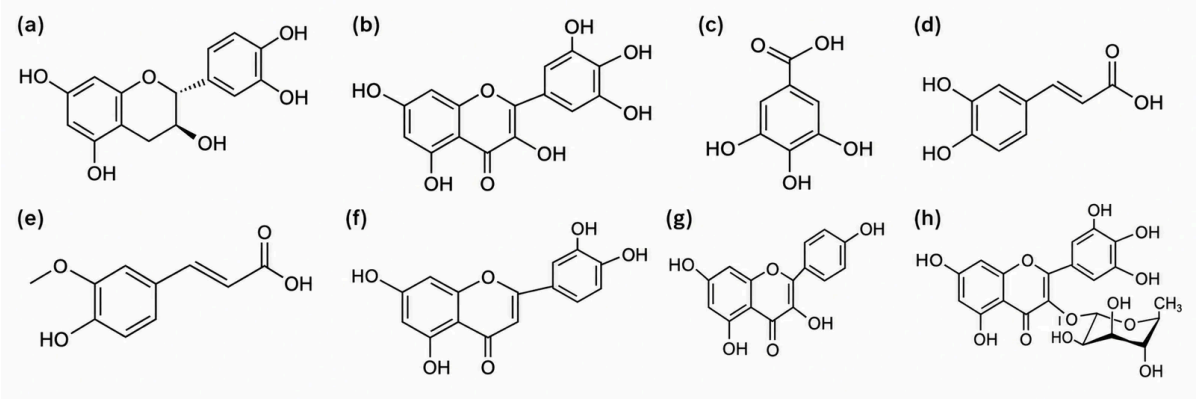


Figure 2. 2D structures of phytochemicals identified from *Mimusops zeyheri*; (a) = catechin, (b) = myricetin, (c) = gallic acid, (d) = caffeic acid, (e) = ferulic acid, (f) = luteolin, (g) = kaempferol, and (h) = myricitrin.

diversification and nutritional security.

Phytochemical Constituents

Phytochemical investigations of *Mimusops zeyheri* remain relatively limited, with only a few studies reporting the presence of specific bioactive compounds in different plant parts. Nevertheless, available evidence suggests that the species contains a range of phenolic and secondary metabolites that may contribute to its reported pharmacological and ethnomedicinal properties.

Qualitative phytochemical screening of leaf extracts reveals the presence of diverse classes of secondary metabolites. Methanolic leaf extracts were reported to contain phenols, alkaloids, flavonoids, terpenoids, tannins, quinones, saponins, and glycosides, indicating a chemically diverse phytochemical profile. In contrast, acetone extracts lacked detectable phenolic compounds, highlighting the influence of extraction solvents on phytochemical recovery (23). Similar qualitative analyses of fruit pulp extracts revealed the presence of phenols, saponins, and terpenoids when extracted with ethanol, distilled water, and methanol (24).

High-performance liquid chromatography (HPLC) analyses have identified several phenolic constituents in extracts of *Mimusops zeyheri*. Detected compounds include catechin, myricetin, gallic acid, caffeic acid, ferulic acid, luteolin, kaempferol, and myricitrin (**Figure 2**), all of which are well-known plant-derived polyphenols associated with antioxidant and anti-inflammatory activities (25). These compounds belong primarily to the flavonoid and phenolic acid classes, which are commonly implicated in plant defense mechanisms and therapeutic bioactivities.

Pharmacological Activities

Although ethnomedicinal evidence strongly supports the therapeutic potential of *Mimusops zeyheri*, experimental pharmacological investigations remain relatively limited. Most available studies are based on in vitro assays, and the molecular mechanisms underlying the observed bioactivities are still poorly characterized (**Table 2**).

Table 2. Reported pharmacological activities of *Mimusops zeyheri*.

Pharmacological Activity	Experimental Model	Key Findings	Reference
Antidiabetic	Muscle cell glucose uptake assay	Increased glucose absorption and GLUT-4 translocation; modulation of IRS-1/PI3K/Akt pathway at 500 µg/mL	(26)
Antibacterial	In vitro bacterial assays	Activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, *Staphylococcus aureus*	(25)
Antimycobacterial	*Mycobacterium smegmatis* assay	Acetone and methanol extracts showed the strongest inhibition	(23)
Antioxidant	DPPH radical scavenging assay	56% radical scavenging activity at 20 µg/mL	(25)
Antioxidant	ABTS and DPPH assays	Demonstrated free radical scavenging activity (exact IC50/percentage inhibition values not reported in the primary source)	(24)
Antibacterial	Well diffusion and MIC assays	Activity against *S. aureus* and *E. coli*	(24)
Antiproliferative	Caco-2 and HEK-293 cell lines	Inhibition of cell proliferation; cytostatic effect at 80 mg/L	(20)
Anticancer / Cytotoxic	Breast cancer cell lines (MDA-MB-231, MCF-7)	Low but measurable cytotoxicity; cell-line dependent response at 20-120 µg/mL	(21)

Consequently, the current pharmacological evidence base is fragmented, highlighting a substantial need for comprehensive in vivo and clinical investigations to validate traditional claims and elucidate mechanisms of action.

Antidiabetic Activity

Current evidence for the antidiabetic activity of *Mimusops zeyheri* is limited to a single in vitro study. The extract significantly increased glucose uptake at 1 and 3 h of incubation and produced an approximately twofold increase in GLUT-4 translocation, suggesting enhanced glucose utilization by peripheral tissues. Notably, GLUT-4 and GLUT-1 mRNA levels remained unchanged, indicating that the observed increase in GLUT-4-mediated glucose uptake was not associated with increased transcription of the GLUT-4 gene. Rather, the findings suggest modulation at the post-transcriptional or protein-trafficking level, although the available study did not establish the precise mechanism. At 500 µg/mL, *Mimusops zeyheri* extract significantly enhanced GLUT-4 expression/translocation in the presence of insulin, while components of the IRS-1/PI3K/Akt pathway were also modulated (26).

Antimicrobial Activity

Several studies have evaluated the antimicrobial potential of *Mimusops zeyheri*. Leaf extracts have demonstrated broad-spectrum antibacterial activity against multiple pathogenic bacterial strains, including *E. coli*, *K. pneumoniae*, *Pseudomonas aeruginosa*, *B. subtilis*, and *S. aureus*; however, the same extracts showed no significant antifungal activity against *Candida albicans* (25).

Additional investigations using solvent extracts of the leaves (dichloromethane, ethyl acetate, acetone, and methanol) revealed selective antibacterial activity. Methanol extracts generally yielded the highest extraction efficiency, followed by acetone, dichloromethane, and ethyl acetate (23)**.** Antimicrobial assays demonstrated inhibitory activity against *Mycobacterium smegmatis* and *S. aureus*, with acetone and methanol extracts exhibiting the strongest effects. However, none of the crude extracts inhibited *E. coli* in this particular study (23)**.** Methanolic extracts have also shown antibacterial activity against *S. aureus* and *E. coli* in well diffusion and minimum inhibitory concentration assays (24).

Antioxidant Activity

The antioxidant potential of *Mimusops zeyheri* has been evaluated using radical scavenging assays. In a DPPH assay, hydromethanolic extracts exhibited a 56% radical scavenging activity at 20 µg/mL, indicating moderate antioxidant capacity (25). Additional studies have confirmed antioxidant activity using both ABTS and DPPH assays, suggesting that phenolic constituents in the plant contribute to its ability to neutralize reactive oxygen species (24). Such antioxidant properties may partly explain the plant's traditional use in managing inflammatory and metabolic disorders.

Antiproliferative and Cytotoxic Activity

The antiproliferative potential of *Mimusops zeyheri* has also been investigated, particularly in relation to cancer cell lines. Seed oil extracts inhibited proliferation of Caco-2 and HEK-293 cells in a concentration-dependent manner, with significant suppression reported at 80 mg/L. Importantly, this inhibitory effect occurred without substantial induction of cell death, suggesting a cytostatic rather than cytotoxic mechanism (20).

Further studies examining breast cancer cell lines reported variable cytotoxic responses; notably, this work evaluated a range of seed oil concentrations (20-120 µg/mL) rather than the single 80 mg/L concentration used in the Caco-2/HEK-293 study, and this difference in concentration range and cell-line model should be borne in mind when comparing the two sets of findings. Seed oil exhibited measurable cytotoxic effects against the hormone-independent breast cancer cell line MDA-MB-231, particularly after 72 h of incubation, although the overall cytotoxicity remained relatively low (21). In contrast, the hormone-dependent cell line MCF-7 showed negative cytotoxicity during early incubation periods (24-48 h), indicating a temporary increase in cell viability before returning to near-neutral effects at 72 h. These findings suggest a cell-type-dependent biological response, emphasizing the need for further mechanistic and in vivo investigations (21).

Safety and Toxicity

The available safety evidence for *Mimusops zeyheri* is currently limited to a single in vitro investigation, as no in vivo toxicity studies have yet been reported. In muscle cell viability assays using the MTT method, extracts of *Mimusops zeyheri* exhibited negligible cytotoxic effects, maintaining approximately 97% cell viability at concentrations of 5 mg/mL (26). Interestingly, lower concentrations (1.25 mg/mL) produced mitogenic effects, increasing cell viability indicators by approximately 21% compared with untreated controls. The estimated LC_{50} values were greater than 5000 µg/mL, further supporting the low toxicity of the extract under experimental conditions (26).

Research Gaps and Future Directions

Despite the growing scientific interest in *Mimusops zeyheri*, the pharmacological investigation of this species remains at a relatively incipient stage, particularly when compared with other medicinal plants that have successfully progressed into advanced drug discovery pipelines. Current studies provide preliminary evidence supporting several biological activities, but the depth, methodological rigor, and translational relevance of these investigations remain limited. Consequently, substantial research opportunities exist for positioning *Mimusops zeyheri* as a promising candidate in modern pharmacological and drug discovery research.

One of the most critical limitations in the current literature is the inadequate characterization of the plant's phytochemical composition. While several phenolic compounds and classes of secondary metabolites have been reported, most studies rely on qualitative screening or limited chromatographic identification, which provides only a superficial understanding of the plant's chemical diversity. Given that many successful drugs derived from natural products originate from structurally unique phytochemicals, the incomplete chemical characterization of *Mimusops zeyheri* represents a missed opportunity.

Future research should focus on comprehensive metabolomic profiling using high-resolution analytical techniques, including LC–MS/MS, GC–MS, and NMR spectroscopy, to systematically identify and characterize the plant's chemical constituents. Importantly, bioassay-guided fractionation should be employed to isolate and structurally elucidate compounds responsible for observed pharmacological activities. Such an approach would enable the identification of novel lead compounds and facilitate structure–activity relationship (SAR) studies, which are essential for rational drug development (27).

Another major gap concerns the lack of detailed mechanistic insights underlying the pharmacological effects attributed to *Mimusops zeyheri*. Although some studies suggest involvement of pathways such as the insulin signaling cascade associated with glucose metabolism, these observations remain preliminary and insufficient to establish definitive molecular targets. For a plant to transition from ethnopharmacological relevance to pharmaceutical development, it is essential to determine precise molecular mechanisms of action (28). Future studies should therefore employ modern molecular pharmacology tools, including gene expression profiling, proteomics, receptor binding assays, and pathway-specific reporter systems, to elucidate the intracellular signaling networks influenced by the plant's bioactive constituents. Understanding the molecular targets of these compounds would significantly enhance the credibility of the plant as a source of drug candidates.

Most pharmacological investigations of *Mimusops zeyheri* have been conducted in in vitro experimental systems, which, although valuable for preliminary screening, do not adequately reflect physiological complexity. The absence of well-designed in vivo pharmacological studies limits the interpretation of efficacy, pharmacokinetics, bioavailability, and systemic safety. To advance the pharmacological validation of the plant, future research should utilize relevant animal disease models, particularly for metabolic disorders, infectious diseases, inflammatory conditions, and cancer. Such studies would allow evaluation of therapeutic efficacy, dose-response relationships, metabolic stability, and potential off-target effects, thereby bridging the gap between laboratory findings and potential clinical application.

Although preliminary in vitro toxicity assays suggest that *Mimusops zeyheri* extracts may exhibit relatively low cytotoxicity, the toxicological profile of the plant remains largely undefined. This represents a significant limitation, particularly considering the potential development of plant-derived compounds for therapeutic use. Comprehensive toxicological evaluations are necessary to establish the safety of the plant and its bioactive constituents. These studies are also critical for determining safe dosage ranges and identifying potential adverse effects associated with prolonged use.

Preliminary findings indicating antiproliferative effects of *Mimusops zeyheri* seed oil against certain cancer cell lines are particularly intriguing, yet the anticancer potential of the plant remains largely unexplored. Considering that many anticancer agents have historically been derived from natural products, this area warrants significantly greater research attention. Future investigations should explore whether compounds from *Mimusops zeyheri* influence key oncogenic pathways, including apoptosis regulation, cell cycle control, oxidative stress modulation, mitochondrial dysfunction, and epigenetic signaling. Furthermore, studies should evaluate activity across a broader panel of cancer cell lines and incorporate in vivo tumor models to determine therapeutic relevance.

Despite the presence of chemically diverse phytoconstituents, *Mimusops zeyheri* has received no attention in computational drug discovery research. Advances in computer-aided drug design (CADD) provide powerful tools for identifying potential drug candidates from plant-derived compounds. Integrating phytochemical databases of *Mimusops zeyheri* with molecular docking, pharmacophore modeling, molecular dynamics simulations, and ADMET predictions could accelerate the identification of promising lead molecules. Such approaches would help prioritize compounds for experimental validation and significantly enhance the efficiency of natural product–based drug discovery efforts.

From a pharmacological standpoint, *Mimusops zeyheri* represents an underexplored yet highlypromising reservoir of bioactive natural products. Its ethnomedicinal relevance, nutritional importance, and preliminary pharmacological activities suggest that the species may harbor novel compounds with therapeutic potential. However, realizing this potential requires a systematic and multidisciplinary research approach, integrating phytochemistry, molecular pharmacology, toxicology, computational modeling, and translational biomedical research. If these critical gaps are addressed, *Mimusops zeyheri* could emerge as a valuable source of lead molecules for the development of new antidiabetic, antimicrobial, antioxidant, or anticancer agents. Consequently, intensified scientific investigation of this species is warranted, not only to validate its traditional uses but also to harness its potential contributions to modern pharmacotherapy and natural product–based drug discovery.

Conclusion

Mimusops zeyheri is an underexplored African medicinal plant with considerable ethnomedicinal relevance, nutritional value, and emerging pharmacological potential. Available evidence indicates that the species contains diverse phytochemicals and exhibits preliminary antidiabetic, antimicrobial, antioxidant, and antiproliferative activities, supporting some of its traditional therapeutic applications. However, the current evidence base remains limited and is dominated by in vitro studies, with relatively few pharmacological investigations and no clinical evidence to substantiate efficacy or safety in humans.

From a translational perspective, the available evidence supports two complementary development pathways. Standardized extracts or enriched fractions could be explored for nutraceutical or functional-food applications where nutritional and antioxidant properties are prioritized, whereas bioassay-guided fractionation and structural characterization could facilitate the isolation of individual lead compounds for pharmaceutical development. Progress toward either pathway will require reproducible chemical standardization, mechanistic validation, pharmacokinetic characterization, and

appropriate safety assessment.

Declaration

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Not applicable.

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