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Review Article

The Renaissance of Indian Jujube: Novel Perspectives on the Medicinal and Nutraceutical Applications of *Ziziphus Mauritiana*

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ABSTRACT

Ziziphus mauritiana (commonly known as Indian jujube) is a fruit-bearing tree widely used in traditional medicine due to its reputed antidiabetic, antioxidant, anti-inflammatory, antimicrobial, and neuroprotective properties. Despite its extensive ethnopharmacological use, comprehensive scientific evaluation of its bioactive compounds and therapeutic potentials remains limited. This study systematically reviewed recent in vitro and in vivo investigations focusing on the phytochemical profiling, extraction optimization, and pharmacological activities of *Ziziphus mauritiana* fruit, seeds, and leaves. Various solvent extraction methods were evaluated for polyphenol and flavonoid content. Biological activities were assessed through antioxidant assays (DPPH, ABTS), anti-inflammatory models, antimicrobial tests against bacterial strains, antidiabetic effects in streptozotocin-induced diabetic rats, and neuroprotective studies in rodent models. Extracts of *Ziziphus mauritiana* demonstrated significant antioxidant activity attributed to high levels of polyphenols and flavonoids. Seed and fruit extracts exhibited potent antimicrobial effects against clinically relevant bacterial pathogens. In diabetic rat models, fruit extracts significantly reduced blood glucose levels and improved oxidative stress markers. Anti-inflammatory and analgesic activities were confirmed in rodent studies. Neuroprotective effects were indicated by attenuation of neurodegeneration markers in Parkinson's disease models. The bioactive compounds present in *Ziziphus mauritiana* support its traditional medicinal use, especially for managing diabetes, inflammation, oxidative stress, and neurodegenerative disorders. Further clinical studies are warranted to validate these findings and develop potential therapeutic applications.

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INTRODUCTION

Ziziphus mauritiana Lam., commonly known as Indian jujube or “ber,” is a multipurpose plant belonging to the family Rhamnaceae. Native to South Asia and Africa, it is now widely cultivated in tropical and subtropical regions across the globe. Its adaptability to drought-prone and semi-arid climates, along with its nutritional and medicinal value, has made it an important species in both agricultural and ethnopharmacological contexts [01]. Traditionally, different parts of *Z. mauritiana* including the fruit, seeds, leaves, bark, and roots have been used to treat a wide range of ailments such as digestive disorders, fevers, wounds, skin infections, insomnia, and respiratory issues in systems like Ayurveda, Unani, and Chinese traditional medicine [02]. The fruits are consumed fresh or dried and are known for their rich composition of vitamin C, dietary fiber, polyphenols, and antioxidants, making them valuable in nutritional as well as medicinal contexts [03]. Recent scientific investigations have validated many of these traditional uses, revealing antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, antimicrobial, and neuropharmacological properties across various plant parts and extract types [04]. These pharmacological effects have been attributed to a diverse range of phytoconstituents such as flavonoids (quercetin, kaempferol), alkaloids, triterpenoids, saponins, tannins, and cyclopeptide alkaloids [05]. Given the broad therapeutic potential of *Z. mauritiana*, this review aims to provide a comprehensive overview of its ethnomedicinal uses, phytochemical composition, extraction methods, pharmacological properties, and commercial applications, while highlighting areas for future research and clinical validation.

Ethnomedicinal Uses

Ziziphus mauritiana Lam. holds a significant place in traditional medicine systems across Asia, Africa, and the Middle East. Its diverse applications reflect the cultural and geographical variation in medicinal practices. The plant has been widely employed to address various ailments, often using specific parts such as fruits, leaves, seeds, bark, and roots [06]. In Ayurveda, the fruits of *Z. mauritiana* commonly known as “bor” are used as a cooling agent and a digestive tonic. They are recommended for the management of diarrhea, dysentery, and jaundice. The seeds are considered beneficial for treating insomnia and anxiety, while the leaves and bark are used topically for wound healing and skin infections [07]. Similarly, Unani practitioners utilize the plant’s parts to alleviate respiratory conditions, including cough and asthma, due to its expectorant properties [08]. Ethnobotanical surveys from different regions have documented the use of *Ziziphus mauritiana* in treating fever, inflammation, and gastrointestinal disturbances. In African traditional medicine, the fruit pulp is used to manage hypertension and diabetes, while decoctions of roots and leaves serve as antiseptics and anti-inflammatory agents [09]. Additionally, tribal communities in India apply leaf paste on wounds and use bark extracts for fever and malaria [10]. The mode of application varies from oral consumption of fruit juices and decoctions to external applications of pastes and poultices. These ethnomedicinal practices have guided scientific investigations into the pharmacological properties of the plant, supporting its widespread use and suggesting potential therapeutic benefits [11].

Botany, Cultivation, and Chemistry

Ziziphus mauritiana Lam. is a hardy, drought-resistant, deciduous shrub or small tree that typically grows between 5 to 10 meters in height.



It belongs to the family Rhamnaceae and is characterized by its thorny branches, ovate leaves, and small greenish-yellow flowers that develop into edible, round to oval-shaped fruits commonly referred to as “ber” [12]. The fruit varies in color from green to yellow, red, or brown, depending on the variety and maturity stage. The plant thrives in tropical and subtropical climates and is well adapted to semi-arid and arid regions due to its ability to withstand prolonged dry spells and poor soil conditions [13]. It is widely cultivated across India, Pakistan, Africa, and parts of Australia, serving both nutritional and medicinal purposes. Propagation is mainly through seeds, though vegetative methods like grafting and cuttings are also employed to maintain cultivar characteristics [14]. Phytochemically, *Z. mauritiana* is a rich source of diverse bioactive compounds distributed across its various parts. The fruits are known for their high content of vitamin C, carotenoids, flavonoids (quercetin, kaempferol), phenolic acids, and dietary fiber, which contribute to their antioxidant and nutritive properties [15]. Leaves and seeds contain alkaloids, including cyclopeptide alkaloids, saponins, tannins, triterpenoids, and sterols, which are associated with various pharmacological activities such as anti-inflammatory, hepatoprotective, and neuroprotective effects [16]. Advanced analytical techniques such as gas chromatography–mass spectrometry (GC-MS), high-performance liquid chromatography (HPLC), and nuclear magnetic resonance (NMR) spectroscopy have been employed to characterize these compounds and confirm their structures [17]. The presence of these phytoconstituents underpins the plant’s therapeutic potential and justifies its widespread use in traditional medicine.

Phytochemical Constituents of *Ziziphus mauritiana*

The therapeutic potential of *Ziziphus mauritiana* is primarily attributed to its rich and diverse phytochemical composition. These bioactive compounds are distributed across its fruits, leaves, seeds, bark, and roots, and are broadly categorized into major and minor constituents based on their concentration and pharmacological relevance. The following section provides an in-depth overview of the major classes of phytochemicals, their traditional uses, pharmacological activities, and modern applications.

1. Flavonoids (Quercetin, Kaempferol, Rutin)

Flavonoids are among the most abundant and pharmacologically significant secondary metabolites in *Z. mauritiana*. Compounds such as quercetin, kaempferol, and rutin have been extensively studied for their health-promoting effects.

- **Traditional Uses:** Flavonoid-rich preparations have been used in traditional medicine to alleviate inflammation, gastrointestinal disturbances such as diarrhea, and as general health tonics [18].
- **Pharmacological Activities:** These polyphenolic compounds exhibit strong antioxidant and free radical-scavenging abilities. They also modulate inflammatory signaling pathways, enhance hepatic function, and offer neuroprotection by interacting with key enzymes and receptor systems in the central nervous system [19].
- **Modern Applications:** Owing to their multifunctional biological effects, flavonoids are widely incorporated into nutraceuticals, functional foods, and anti-aging supplements. Their roles in cardiovascular protection and cognitive enhancement are being actively explored [20].



2. Alkaloids (Cyclopeptide Alkaloids, Mauritine)

Alkaloids such as cyclopeptide alkaloids (e.g., mauritine types A and B) are predominantly found in the seeds and bark of the plant.

- **Traditional Uses:** These alkaloid-rich plant parts have traditionally been used to manage insomnia, anxiety, and febrile conditions in folk medicine systems [21].
- **Pharmacological Activities:** Cyclopeptide alkaloids exhibit a range of neuropharmacological effects including sedative, anticonvulsant, and CNS-depressant actions. Additionally, they possess notable antimicrobial properties by interfering with microbial membrane integrity and enzyme activity [22].
- **Modern Applications:** These compounds are under investigation for the development of new central nervous system (CNS)-targeted drugs and as natural antimicrobial agents in pharmaceutical formulations [23].

3. Triterpenoids and Saponins

Triterpenoids and their glycosylated derivatives, saponins, are key constituents with widespread pharmacological significance.

- **Traditional Uses:** Traditionally, preparations containing these compounds have been used for treating wounds, skin infections, and inflammatory conditions [24].
- **Pharmacological Activities:** These compounds display potent anti-inflammatory and hepatoprotective effects. Mechanistically, they inhibit the production of pro-inflammatory cytokines such as TNF- α and IL-6 and enhance hepatic cellular regeneration [25].

- **Modern Applications:** Due to their immunomodulatory properties, triterpenoids and saponins are being utilized in cosmetic formulations, skin-healing ointments, and as adjuvants in vaccine delivery systems [26].

4. Phenolic Acids (Gallic Acid, Caffeic Acid)

Phenolic acids are important antioxidant constituents found particularly in the fruits and leaves.

- **Traditional Uses:** They have been applied as antiseptics and for the treatment of digestive issues like diarrhea and dysentery [27].
- **Pharmacological Activities:** Phenolic acids act as potent antioxidants and antimicrobials. They inhibit oxidative stress by neutralizing reactive oxygen species (ROS) and also suppress bacterial proliferation through enzymatic inhibition [28].
- **Modern Applications:** Currently, these compounds are used as natural preservatives in food and beverage industries and are being promoted as functional ingredients for promoting gut health [29].

5. Vitamins and Minerals

The fruits of *Z. mauritiana* are a rich source of essential micronutrients including vitamin C, iron, calcium, and phosphorus.

- **Traditional Uses:** These nutritional properties have led to the widespread traditional use of the fruits to enhance vitality and prevent deficiency-related ailments [30].
- **Pharmacological Activities:** Vitamin C plays a central role in immune defense, collagen synthesis, and wound healing. Minerals like zinc and iron support enzymatic reactions critical to metabolism and tissue repair [31].



- **Modern Applications:** These micronutrients are widely included in health supplements, fortified food products, and beverages designed to boost overall wellness and immunity [32].

Minor Phytochemicals

Although present in smaller concentrations, the minor phytochemicals in *Z. mauritiana* exhibit considerable bioactivity and complement the actions of major constituents.

1. Tannins

- **Traditional Uses:** Tannins are utilized for their astringent properties, commonly in the treatment of diarrhea and dysentery [33].
- **Pharmacological Activities:** These polyphenols exhibit antimicrobial, antioxidant, and anti-inflammatory actions by precipitating proteins and scavenging free radicals [34].
- **Modern Applications:** Tannins are used in pharmaceutical preparations as anti-diarrheal agents and are increasingly being incorporated into natural wound care products [35].

2. Sterols (β -Sitosterol)

- **Traditional Uses:** β -Sitosterol has been traditionally used in herbal remedies for urinary and prostate-related disorders [36].
- **Pharmacological Activities:** It is known for its cholesterol-lowering properties, owing to its structural similarity to cholesterol, which enables it to competitively inhibit absorption in the intestine [37].
- **Modern Applications:** β -Sitosterol is incorporated into functional foods and dietary supplements formulated for cardiovascular and prostate health [38].

3. Fatty Acids (Oleic Acid, Linoleic Acid)

- **Traditional Uses:** Oils extracted from the seeds have been used topically to promote skin healing and hydration [39].
- **Pharmacological Activities:** These essential fatty acids support skin regeneration, possess anti-inflammatory properties, and help restore skin barrier function [40].
- **Modern Applications:** Fatty acid-rich oils are widely included in cosmeceuticals, skin creams, and therapeutic lotions [41].

Table 1: Overview of Phytochemicals in *Ziziphus mauritiana*: Traditional Uses, Pharmacological Activities, and Modern Applications

Phytochemical Class	Major Compounds	Traditional Use	Pharmacological Activity	Modern Application
Flavonoids	Quercetin, Kaempferol	Anti-inflammatory, tonic	Antioxidant, neuroprotective	Nutraceuticals, cognitive enhancers
Alkaloids	Cyclopeptide alkaloids (Mauritine)	Sedative, antipyretic	CNS depressant, antimicrobial	CNS drugs, antimicrobials
Triterpenoids/Saponins	Various	Wound healing, anti-inflammatory	Immunomodulatory, hepatoprotective	Cosmetics, vaccine adjuvants
Phenolic Acids	Gallic acid, Caffeic acid	Antiseptic, anti-diarrheal	Antioxidant, antimicrobial	Functional foods, natural preservatives
Vitamins/Minerals	Vitamin C, minerals	Nutritional supplement	Immune support, metabolic health	Fortified foods, dietary supplements



Tannins	Various	Astringent for diarrhea	Antimicrobial, antioxidant	Pharmaceuticals, wound care
Sterols	β -Sitosterol	Urinary, prostate health	Cholesterol-lowering, anti-inflammatory	Functional foods, supplements
Fatty Acids	Oleic acid, Linoleic acid	Skin nourishment	Skin regeneration, anti-inflammatory	Cosmeceuticals, skincare

Extraction Methods of *Ziziphus mauritiana*

The extraction of phytochemicals from *Ziziphus mauritiana* plays a critical role in the isolation, identification, and development of therapeutic agents. Proper extraction techniques ensure maximum recovery of bioactive constituents such as flavonoids, alkaloids, saponins, and triterpenoids, while maintaining their structural integrity and biological activity. This section provides an overview of the conventional and modern extraction methods applied to different parts of *Z. mauritiana*, along with factors affecting extraction efficiency.

1. Selection and Preparation of Plant Material

Before extraction, the selection of appropriate plant parts (fruits, leaves, seeds, bark, or roots) is based on ethnobotanical or pharmacological relevance. The plant material is typically:

- Collected at the right stage of maturity
- Shade-dried or oven-dried at temperatures below 40–50°C to prevent degradation
- Ground into a fine powder to increase surface area for solvent penetration [42]

Particle size, drying method, and moisture content significantly influence extraction yield and quality [43].

2. Conventional Extraction Techniques

2.1. Maceration

Maceration is one of the simplest and oldest extraction methods. Plant material is soaked in solvents such as ethanol, methanol, or water for several hours to days with occasional stirring.

- **Advantages:** Minimal thermal degradation; suitable for thermolabile compounds
- **Limitations:** Time-consuming and may result in low efficiency for hard plant tissues like seeds and bark [44]

2.2. Soxhlet Extraction

This continuous hot percolation method is commonly used for extracting lipophilic constituents from powdered plant materials.

- **Solvents Used:** Ethanol, methanol, chloroform, and petroleum ether
- **Typical Application:** Isolation of flavonoids, triterpenoids, fatty acids, and alkaloids from *Z. mauritiana* [45]
- **Drawbacks:** Long extraction times and risk of thermal degradation for heat-sensitive compounds

2.3. Percolation

Percolation involves the slow movement of solvent through a packed column of plant material. It is more efficient than maceration and allows continuous extraction.

- **Application:** Commonly used in the preparation of fluid extracts and tinctures from *Z. mauritiana* fruits and leaves [46]



3. Modern/Advanced Extraction Techniques

With the rise in demand for more efficient, eco-friendly, and selective extraction techniques, modern technologies have been adopted for phytochemical recovery from *Z. mauritiana*.

3.1. Ultrasound-Assisted Extraction (UAE)

This method uses ultrasonic waves (20–40 kHz) to disrupt plant cell walls, enhancing solvent penetration and compound release.

- **Advantages:** Shorter extraction time, low solvent consumption, higher yields
- **Application:** Efficient extraction of polyphenols, flavonoids, and phenolic acids from fruit peels and leaves [47]

3.2. Microwave-Assisted Extraction (MAE)

Microwaves generate localized heating within plant tissues, leading to faster release of intracellular contents.

- **Solvents:** Often combined with ethanol or water
- **Pros:** Faster than Soxhlet or maceration; suitable for thermally stable compounds
- **Reported Use:** Extraction of triterpenoids and alkaloids from *Z. mauritiana* seeds and bark [48]

3.3. Supercritical Fluid Extraction (SFE)

This technique uses supercritical CO₂ (sometimes modified with ethanol) as a green solvent for nonpolar compound extraction.

- **Advantages:** Solvent-free final product, high selectivity, no residual toxicity
- **Application:** Recovery of fatty acids and sterols from seeds and pulp oil of *Z. mauritiana* [49]

- **Challenges:** High equipment cost and technical expertise required

4. Solvent Selection

Table No.02 - The choice of solvent greatly impacts the extraction of specific phytochemicals:

Solvent	Target Compounds	Polarity
Water	Tannins, glycosides, polysaccharides	Polar
Ethanol/ Methanol	Flavonoids, alkaloids, saponins	Mid-polar
Chloroform	Terpenoids, some alkaloids	Non-polar
Hexane	Fatty acids, sterols	Non-polar

5. Extraction Yield and Quality Considerations

Extraction efficiency is determined by the following factors:

- **Plant part and age:** Leaves and fruits tend to yield more polyphenolics, whereas seeds are rich in fatty acids and alkaloids
- **Moisture content:** Excessive moisture can reduce solvent diffusion and increase microbial growth
- **pH and temperature:** Each class of compound has an optimal extraction pH and thermal stability range
- **Solvent-to-material ratio:** Typically ranges from 10:1 to 20:1 (mL/g) for optimal yield [51]

Standardization of extraction protocols ensures consistency in phytochemical content and reproducibility of pharmacological studies.

6. Fractionation and Purification

Crude extracts may be subjected to liquid-liquid partitioning using solvents of increasing polarity (e.g., hexane, chloroform, ethyl acetate, water) to obtain enriched fractions. Further purification involves chromatographic techniques such as:



- Thin Layer Chromatography (TLC)
- Column Chromatography
- High-Performance Liquid Chromatography (HPLC) [52]

These techniques help isolate individual compounds like quercetin, mauritine, and gallic acid for pharmacological and structural analysis.

Plant Part Based Review of *Ziziphus mauritiana*

1. Leaves

- **Traditional Uses:** Used in folk medicine to treat asthma, diabetes, inflammation, hepatic disorders, wounds, and fever [53].
- **Phytoconstituents:** Rich in flavonoids (quercetin, kaempferol), phenolic acids (gallic acid, chlorogenic acid), saponins, and terpenoids (betulinic, oleanolic acid) [54].
- **Modern Evidence:**
 - **Anti-inflammatory:** Methanolic extract inhibited the NF- κ B pathway in LPS-induced macrophages and OVA-induced airway inflammation in mice (250–500 mg/kg) [53].
 - **Antioxidant & Analgesic:** Ethyl acetate fraction reduced paw edema, IL-6, TNF- α , and CRP levels in rats at 500 mg/kg, demonstrating potent antioxidant effects [55].
 - **Hepatoprotective:** Pre-treatment normalized ALT, AST, SOD, and GSH levels in ethanol-induced hepatotoxic rats [59].

2. Fruits

- **Traditional Uses:** Consumed fresh or dried to relieve digestive ailments, fevers, cuts, and mild laxative issues [65].
- **Phytoconstituents:** Contain vitamin C, phenolic compounds, flavonoids, and sugars [54].
- **Modern Evidence:**

- **Anti-inflammatory & Antioxidant:** Extract reduced TNF- α and IL-6 levels in rodents; effectiveness comparable to indomethacin [60].
- **Hepatoprotective:** Aqueous fruit extract (250–500 mg/kg) restored liver function markers in CCl₄-intoxicated rats [59].

3. Seeds

- **Traditional Uses:** Used as sedative, antiemetic during pregnancy, and poultice for diarrhea and rheumatism [65].
- **Phytoconstituents:** Cyclopeptide alkaloids (mauritine), fatty acids, and steroids [56], [57].
- **Modern Evidence:**
 - **Antidiabetic:** Aqueous-ethanol extract (800 mg/kg) significantly reduced blood glucose and increased insulin sensitivity in diabetic rats [61], [62].
 - **Anticancer:** Cytotoxic effects against HL-60 leukemia cells (IC₅₀ $\approx$ 40 μ g/mL); apoptosis observed in vitro [57].
 - **Immunostimulant:** Lectin fraction enhanced antibody response and macrophage activation [63].

4. Bark & Stem

- **Traditional Uses:** Decoctions used to treat diarrhea, gingivitis, and dysentery; poultices for wounds; root infusions used as febrifuge and emmenagogue [68].
- **Phytoconstituents:** Tannins, alkaloids (e.g., mauritine C), saponins, steroids [56].
- **Modern Evidence:**
 - **Multimodal Action:** Methanol bark extract (400 mg/kg) showed antidiarrheal (76%), analgesic (69%), and hypoglycemic (44%) activity in mice [66].



- **Anticancer:** Inhibited proliferation of lung and breast cancer cell lines ($GI_{50} \approx 28-29 \mu\text{g/mL}$) [67].
- **Tyrosinase Inhibition:** Methanolic bark extract showed significant enzyme inhibitory activity (in vitro) [70].
- **Phytoconstituents:** Tannins, glycosides, alkaloids, steroids [56].
- **Modern Evidence:**
 - **Immunomodulatory:** Root extract inhibited chemiluminescence in vitro ($IC_{50} = 55 \mu\text{g/mL}$), indicating immunosuppressive potential [69].
 - **Hepatoprotective:** Root extract reduced serum ALT, AST, ALP, and inflammatory markers (IL-6, TNF- α) in a silica-induced liver toxicity model [69].

5. Roots

- **Traditional Uses:** Used for wound healing, rheumatism, gout, and as a febrifuge and purgative agent [68].

Table No. 03 - Correlation of Traditional Uses and Modern Findings with Key Constituents in *Ziziphus mauritiana* Plant Parts

Plant Part	Traditional Use	Key Constituents	Modern Evidence
Leaves	Anti-inflammatory, hepatic, asthma	Flavonoids, phenolics, terpenoids	NF- κ B inhibition [53], hepatoprotection [59], analgesic activity [55]
Fruits	Digestive aid, laxative, fever	Vitamin C, flavonols, phenolic acids	Hepatoprotective [59], anti-inflammatory [60]
Seeds	Sedative, antiemetic, anti-diarrheal	Cyclopeptide alkaloids, steroids	Antidiabetic [61], [62], cytotoxic (HL-60) [57], immunostimulant [63]
Bark & Stem	Antidiarrheal, wound healing	Tannins, alkaloids, saponins	Antidiarrheal [66], anticancer [67], tyrosinase inhibition [70]
Roots	Febrifuge, purgative, joint disorders	Tannins, alkaloids, glycosides	Hepatoprotective [69], immunomodulatory [69]

Commercial and Industrial Applications of *Ziziphus mauritiana*

The wide-ranging bioactivities and nutritional profile of *Ziziphus mauritiana* have paved the way for its extensive use in various commercial sectors, including nutraceuticals, cosmetics, and food industries. This chapter explores the current industrial utilization of the plant, highlighting product developments, market trends, and future potential.

Nutraceutical Applications

Nutraceuticals derived from *Z. mauritiana* capitalize on its rich content of vitamins, antioxidants, flavonoids, and minerals, promoting health beyond basic nutrition.

- **Dietary supplements:** Standardized extracts rich in flavonoids and vitamin C are incorporated into capsules and powders marketed for immune support, anti-aging, and cardiovascular health [70]. Clinical investigations validate these benefits by demonstrating antioxidant activity and metabolic regulation [71].
- **Functional foods and beverages:** Juices and dried fruit powders are used as functional ingredients enhancing dietary fiber and antioxidant intake [72]. The fruit's pleasant flavor and high nutrient density make it a popular additive in health drinks and snack bars [73].
- **Herbal formulations:** Traditional herbal blends and modern phytopharmaceuticals



include *Z. mauritiana* extracts for managing diabetes, liver health, and inflammation [74].

livestock, contributing to sustainable agricultural practices [82].

Cosmetic and Personal Care Industry

Due to its anti-inflammatory, antioxidant, and skin-healing properties, *Z. mauritiana* has gained prominence in natural and cosmeceutical products.

- **Skin care products:** Extracts rich in saponins, fatty acids (oleic and linoleic acid), and flavonoids are formulated into creams, lotions, and serums targeting skin hydration, anti-aging, and wound healing [75]. The seed oil is used for its emollient and regenerative properties [76].
- **Hair care formulations:** Seed oil and leaf extracts are utilized in shampoos and conditioners for scalp nourishment and reduction of dandruff, leveraging their antimicrobial and anti-inflammatory effects [77].
- **Sun protection and anti-pollution cosmetics:** Flavonoid-rich extracts provide photoprotective effects and combat oxidative stress caused by UV radiation and environmental pollutants [78].

Food Industry

- **Fresh and dried fruit markets:** The fruit of *Z. mauritiana* is widely sold fresh in tropical and subtropical regions. Its drought resistance allows cultivation in semi-arid regions, supporting local economies [79].
- **Processed products:** Jams, jellies, pickles, and chutneys from *Z. mauritiana* fruit have commercial demand for their unique taste and nutritional benefits [80]. Its use in bakery products as natural flavor and fiber enhancer is emerging [81].
- **Animal feed:** Leaves and seed cake residues serve as high-protein fodder supplements for

Pharmaceutical and Veterinary Uses

- **Standardized extracts:** Pharmaceutical companies are exploring *Z. mauritiana* for developing formulations targeting diabetes, inflammation, and infections based on validated pharmacological properties [83].
- **Veterinary applications:** The plant extracts are employed traditionally and experimentally to treat parasitic infections and skin diseases in animals, with growing interest in commercial veterinary phytomedicines [84].

Industrial and Other Applications

- **Bioactive compounds isolation:** Phytochemicals like cyclopeptide alkaloids and triterpenoids are isolated for research and commercial exploitation as lead compounds in drug discovery [85].
- **Biodegradable packaging and biofuel:** Preliminary studies suggest the potential use of biomass residues of *Z. mauritiana* in developing eco-friendly packaging materials and bioethanol production, supporting green industry initiatives [86].

Toxicology and Safety Studies of *Ziziphus mauritiana*

While *Ziziphus mauritiana* has demonstrated significant pharmacological potential, assessing its safety profile is essential before wider therapeutic or commercial use. Toxicological evaluations including acute, sub-acute, and chronic toxicity studies, as well as genotoxicity and cytotoxicity assessments, provide crucial insights into its risk-benefit balance.

Acute Toxicity Studies



Acute toxicity tests generally involve single-dose administration to animals to identify lethal dose (LD₅₀) and observe adverse effects.

- **Experimental findings:** Oral administration of aqueous and ethanolic extracts of *Z. mauritiana* leaves, fruits, and seeds in rodents showed no mortality or significant behavioral changes up to 2000 mg/kg body weight [87, 89]. These results suggest a high margin of safety under acute exposure conditions.
- **Observations:** Mild transient effects like sedation or slight gastrointestinal discomfort were occasionally reported but resolved without intervention [88].

Sub-acute and Chronic Toxicity

Repeated dose toxicity evaluates long-term safety and potential organ-specific toxicity.

- **Sub-acute studies:** Rodents treated with daily doses of 500–1000 mg/kg leaf or seed extracts for 28 days exhibited no significant alterations in hematological, biochemical parameters (liver enzymes ALT, AST, kidney markers), or histopathology of vital organs [90].
- **Chronic studies:** Limited data exist on chronic exposure; however, preliminary 90-day studies reported no toxicity signs, supporting the safety of prolonged consumption at therapeutic doses [91].

Genotoxicity and Mutagenicity

Assessment of DNA damage or mutagenic potential is vital for evaluating carcinogenic risk.

- **In vitro studies:** AMES test performed with *Z. mauritiana* fruit and leaf extracts showed no mutagenic activity in *Salmonella typhimurium* strains TA98 and TA100, both with and without metabolic activation [92].

- **Comet assay:** Extracts did not induce DNA strand breaks in mammalian cell lines, indicating absence of genotoxic effects [93].

Cytotoxicity Studies

While cytotoxicity against cancer cells is desirable, effects on normal cells must be minimal.

- **Selective cytotoxicity:** Phytoconstituents such as cyclopeptide alkaloids exhibit cytotoxicity against tumor cell lines, but toxicity assays using normal fibroblasts or epithelial cells reported minimal adverse effects at therapeutic concentrations [94].

Safety in Human Use

- **Traditional use evidence:** Centuries of ethnomedicinal use with no widespread reports of toxicity or adverse effects suggest good tolerability in humans [95].
- **Clinical trial data:** Limited clinical studies report no serious adverse events related to *Z. mauritiana* extract supplementation; mild gastrointestinal disturbances were the most common minor complaint [96].

Potential Toxic Components and Contraindications

- Certain alkaloids at very high doses could theoretically cause CNS depression, necessitating caution in patients with neurological conditions [97].
- Allergic reactions are rare but possible, warranting allergy testing in sensitive individuals [98].

The existing toxicological evidence supports a favorable safety profile for *Ziziphus mauritiana* at doses used traditionally and in experimental models. However, further detailed chronic toxicity and human safety studies are essential to confirm



long-term safety, especially for pharmaceutical development. The increasing scientific validation of *Ziziphus mauritiana*'s therapeutic properties has led to numerous patents encompassing its pharmaceutical, pharmacological, and traditional medicine applications. This chapter summarizes key patented inventions highlighting novel formulations, extraction techniques, and therapeutic uses under Ayurveda, Unani, and modern herbal medicine systems.

Pharmaceutical and Pharmacological Patents

- **Standardized extracts and formulations:** Several patents describe extraction methods yielding high concentrations of active phytochemicals such as flavonoids and cyclopeptide alkaloids for use in treating metabolic disorders, inflammation, and neurological conditions. For instance, patented formulations of *Z. mauritiana* extracts combined with other herbal actives have shown synergistic antidiabetic and hepatoprotective effects [99].
- **Novel drug delivery systems:** Innovations include nanoformulations and sustained-release oral dosage forms enhancing bioavailability and therapeutic efficacy of *Ziziphus* phytoconstituents. Patents have claimed liposomal encapsulation of saponins and alkaloids for improved CNS targeting [100].
- **Antimicrobial and wound healing applications:** Patents also cover topical gels and ointments containing *Ziziphus mauritiana* extracts, demonstrating enhanced wound healing, antimicrobial, and anti-inflammatory activities. Such formulations are aimed at treating skin infections, burns, and ulcers [101].

3. Herbal, Ayurvedic, and Unani Patents

- **Traditional medicine formulations:** Numerous patents protect multi-herb compositions where *Ziziphus mauritiana* is a principal ingredient, used for managing digestive disorders, insomnia, and respiratory ailments according to Ayurveda and Unani principles [102].
- **Herbal supplements and nutraceuticals:** Patents include capsules and powders marketed as herbal tonics, immunity boosters, and adaptogens derived from fruit and leaf extracts, with claims supported by phytochemical standardization and efficacy data [103].
- **Extraction and preparation methods:** Innovations in solvent extraction, microwave-assisted extraction, and enzymatic hydrolysis methods to maximize yield and preserve bioactive profiles have been patented for industrial scale production of herbal formulations [104].

4. Industrial and Commercial Patents

- **Cosmeceutical products:** Patents exist for facial creams, anti-aging serums, and hair care products utilizing *Ziziphus mauritiana* seed oil and flavonoid-rich extracts for skin nourishment, photoprotection, and hair strengthening [105].
- **Food and beverage applications:** Patented processes for developing fortified beverages, functional snacks, and natural preservatives using *Ziziphus* fruit powder capitalize on its antioxidant and nutritional profile [106].

Emerging Patent Trends

- **Synergistic herbal combinations:** There is growing interest in combinational patents that blend *Ziziphus mauritiana* with other medicinal plants to target complex diseases such as diabetes, neurodegeneration, and liver



disorders, emphasizing multitargeted therapy [107].

- **Biotechnological approaches:** Recent patents explore tissue culture propagation, genetic modification, and biosynthesis of specific bioactive molecules from *Ziziphus* species for enhanced yield and consistency [107].

The spectrum of granted patents on *Ziziphus mauritiana* reflects its expanding role from traditional remedies to modern therapeutic agents and commercial products. Continued innovation and rigorous scientific validation will likely accelerate patenting activity and industrial application of this versatile medicinal plant.

Further Research Prospective

Pharmacological mechanisms:

More detailed molecular studies are needed to elucidate signaling pathways and receptor interactions of its bioactive compounds, particularly in neuroprotection and immunomodulation.

Clinical trials:

Robust randomized controlled trials with standardized extracts are essential to confirm efficacy, optimal dosing, and safety in humans for various indications such as diabetes, liver disorders, and neurodegenerative diseases.

Bioavailability and pharmacokinetics:

Research should focus on improving the absorption, distribution, metabolism, and excretion (ADME) profiles of key phytochemicals, employing novel delivery systems like nanoparticles and liposomes.

Synergistic effects:

Investigations on combinations with other medicinal plants may reveal enhanced therapeutic effects and reduced toxicity, especially in complex diseases.

Genetic improvement and biotechnology:

Advanced molecular breeding and tissue culture techniques can aid in developing high-yielding, pest-resistant cultivars with optimized phytochemical profiles.

Commercial and Industrial Value

Ziziphus mauritiana holds significant commercial promise due to its multifaceted applications:

Nutraceuticals:

Its fruits and extracts are increasingly used in dietary supplements aimed at boosting immunity, improving digestion, and providing antioxidant support.

Pharmaceuticals:

Standardized extracts are being developed as adjunct therapies for diabetes, liver protection, and CNS disorders, fueling patenting and product development.

Cosmetics and personal care:

Seed oil and flavonoid-rich extracts feature prominently in anti-aging creams, sunscreens, and hair care formulations, capitalizing on their antioxidant and skin regenerative properties.

Food industry:

Dried fruits, powders, and beverages made from *Ziziphus mauritiana* are marketed as functional foods and natural preservatives, catering to health-conscious consumers.



Animal Uses

Veterinary medicine:

Traditional use of *Ziziphus* parts in treating digestive issues, wounds, and infections in livestock has gained scientific support, with extracts showing antimicrobial and anti-inflammatory effects beneficial in animal health management.

Feed additive:

Its leaves and fruits serve as nutritious fodder, improving the health and productivity of ruminants in arid regions due to their protein and mineral content.

Animal husbandry:

Research into supplementation with *Ziziphus* extracts indicates potential improvements in immunity and stress resilience among livestock, although further studies are warranted.

Agricultural Uses

Drought-resistant crop:

Ziziphus mauritiana thrives in semi-arid and arid climates, making it valuable for afforestation, soil conservation, and combating desertification.

Agroforestry:

Its integration into farming systems enhances biodiversity, provides shade, and contributes organic matter to soil, improving overall farm sustainability.

Soil enrichment:

The tree's leaf litter contributes to nutrient cycling, and its root system stabilizes soil, reducing erosion.

Pollinator support:

Flowers attract bees and other pollinators, supporting local ecosystems and crop pollination services.

Genetic resource:

Wild and cultivated varieties offer genetic diversity for breeding programs aimed at yield improvement and stress tolerance.

CONCLUSION

Ziziphus mauritiana emerges as a highly versatile and valuable plant with deep roots in traditional medicine and significant promise in modern pharmacology and industry. Its rich phytochemical profile including flavonoids, alkaloids, saponins, phenolic acids, vitamins, and minerals underpins a broad spectrum of pharmacological activities such as antioxidant, anti-inflammatory, hepatoprotective, antidiabetic, neuroprotective, and antimicrobial effects. These properties have been validated through extensive in vitro, in vivo, and preliminary clinical studies. Traditional applications in Ayurveda, Unani, and other ethnomedicinal systems align well with modern scientific findings, highlighting the therapeutic relevance of different plant parts. Innovations in extraction methods and formulation technologies have further expanded its usability across nutraceuticals, pharmaceuticals, cosmetics, and functional foods, demonstrating its considerable commercial and industrial value. Moreover, *Ziziphus mauritiana* contributes significantly to animal health and agricultural sustainability. Its role as a drought-resistant species capable of enhancing soil quality and supporting agroforestry underscores its environmental and economic importance, particularly in semi-arid and arid regions. Safety and toxicological evaluations indicate a favorable profile, yet ongoing research



is essential to comprehensively establish long-term safety and optimize therapeutic regimens. Future research priorities include detailed mechanistic studies, well-designed clinical trials, bioavailability enhancement, and genetic improvement to maximize yield and phytochemical consistency. In summary, *Ziziphus mauritiana* holds vast potential as a natural resource bridging traditional wisdom and modern science. Continued interdisciplinary research and innovation are crucial to fully harness its medicinal, agricultural, and commercial benefits, thereby promoting health, sustainability, and economic development worldwide.

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