DOI: 10.55522/jmpas.V14I6.6989 ISSN NO. 2320 – 7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Review article

Ziziphus xylopyrus (Retz.) Willd.: A comprehensive review of the phytochemistry and multifaceted pharmacology of an underexplored medicinal plant

Shyalu Gajbhiye*

Babasaheb Bhimrao Ambedkar University Lucknow, Uttar Pradesh, India

Corresponding author: Shyalu Gajbhiye, ✉ shalugajbhiye02@gmail.com, **Orcid Id**: https://orcid.org/0009-0008-3622-6390

Babasaheb Bhimrao Ambedkar University Lucknow, Uttar Pradesh, India

Received - 20-11-2025**, Revised** - 28-11-2025, **Accepted** - 26-12-2025 **(DD-MM-YYYY)**

Refer This Article

Shyalu Gajbhiye, 2025. *Ziziphus xylopyrus (Retz.) Willd.*: A comprehensive review of the phytochemistry and multifaceted pharmacology of an underexplored medicinal plant. Journal of medical pharmaceutical and allied sciences, V 14 - I 6, Pages - 05 – 08. Doi: https://doi.org/10.55522/jmpas.V14I6.6989.

ABSTRACT

Ziziphus xylopyrus (Retz.) *Willd*., a member of the Rhamnaceae family, is a perennial shrub traditionally used across the Indian subcontinent for treating a diverse range of ailments, including liver disorders, ulcers, diarrhea, diabetes, and skin infections. Despite its rich ethnomedicinal history, scientific validation of its therapeutic claims remains fragmented. This comprehensive review synthesizes contemporary research to critically evaluate the botanical, phytochemical, and pharmacological profile of *Z. xylopyrus*. The analysis consolidates evidence demonstrating significant hepatoprotective, antiulcer, antimicrobial, antioxidant, anti-inflammatory, and wound-healing activities, primarily attributed to bioactive constituents such as flavonoids (quercetin, quercitrin), cyclopeptide alkaloids (xylopyrines, amphibine-H, nummularine-K), and tannins. A critical examination of methodologies, including extraction techniques and *in-vivo* models, is presented. The review identifies that methanolic and ethanolic extracts, particularly from roots, stem bark, and leaves, exhibit the most potent bioactivity. While promising, the existing research is characterized by a predominance of preliminary studies. This article concludes by highlighting significant research gaps, including the need for rigorous bioactivity-guided fractionation, detailed mechanistic studies, toxicological profiling, and standardization of extracts. We posit that *Z. xylopyrus* holds substantial promise as a source of novel phytopharmaceuticals but requires a systematic, translational research approach to bridge traditional knowledge with evidence-based therapeutic application.

Keywords: *Ziziphus xylopyrus*, Hepatoprotective, Antiulcer, Antimicrobial, Cyclopeptide alkaloids, Quercetin, Ethnopharmacology, Drug discovery.

INTRODUCTION

The global resurgence of interest in plant-based medicine is driven by the search for safer, multi-target therapeutic agents, particularly in the management of chronic and drug-resistant conditions [1]. Herbal medicine, rooted in ethnobotanical traditions, serves as an invaluable reservoir for drug discovery. *Ziziphus xylopyrus* (Retz.) Willd., commonly known as "Jujab" or "Ghonta," is one such botanical species endemic to the Indian subcontinent, whose therapeutic potential remains underexplored in the mainstream scientific literature [2, 3]. It is a large, straggling shrub found in regions of India, Pakistan, Nepal, and Sri Lanka.

Traditional healers have employed various parts of the plant—roots, stem bark, leaves, fruits, and seeds—for ailments ranging from liver complaints, fever, and diarrhoea to diabetes, skin infections, and ulcer management [4, 5]. The Ayurvedic Pharmacopoeia of India acknowledges its use, particularly for dental health (as dental sticks from the bark) and in pyorrhoea [6]. Despite this documented traditional use, a cohesive scientific narrative validating these claims and elucidating the mechanisms of action is lacking.

Recent years have seen a spike in focused pharmacological studies on *Z. xylopyrus*. Key among these are investigations into its

hepatoprotective efficacy against paracetamol-induced liver damage [7], its potent antiulcer activity [8], and its broad-spectrum antimicrobial properties [9]. These activities are underpinned by a rich phytochemical repertoire, including unique cyclopeptide alkaloids (e.g., xylopyrine A-H), flavonoids, tannins, and terpenoids [10, 11].

This review aims to collate and critically analyze the available scientific data on *Z. xylopyrus*. It will: (1) Outline its botanical and ethnomedicinal profile; (2) Detail its phytochemical constitution; (3) Systematically review its pharmacological activities with a focus on hepatoprotection, gastroprotection, and antimicrobial action; (4) Critique the methodological approaches of key studies; and (5) Identify pressing research gaps and future directions for the development of standardized phytomedicines from this promising species.

Botanical and ethnomedicinal profile

Botanical description and distribution

Ziziphus xylopyrus is a large, straggling shrub or small tree reaching 6-10 meters in height. Young shoots are covered with rusty tomentose hairs. A distinguishing characteristic is the presence of paired spines on younger branches—one straight and the other curved—with swollen nodes at the leaf scars. The leaves are simple, alternate, with a glabrous surface, rounded base, obtuse apex, and serrulate margins (2-7 cm long). The flowers are small, yellowish-white, and borne in compact clusters. The fruit is a globular, drupaceous berry, dark brown, about 1.2-1.8 cm in diameter, with an astringent taste and a hard, stony endocarp [5, 12].

The plant is distributed across tropical and subtropical regions of South Asia, specifically in Pakistan, Northwestern, Central, and South India, Sri Lanka, Nepal, and Bangladesh [3]. Its taxonomy is as follows: Kingdom: Plantae; Phylum: Magnoliophyta; Class: Magnoliopsida; Order: Rosales; Family: Rhamnaceae; Genus: *Ziziphus*; Species: *xylopyrus* [12].

Traditional and ethnomedicinal uses

Ethnobotanical surveys document the extensive use of *Z. xylopyrus* by various indigenous communities across India [4, 5, 13]:

General uses

Treating obesity, urinary troubles, diabetes, fever, diarrhoea, insomnia, digestive disorders, and skin infections.

Specific applications

The bark is used as an astringent and for making teeth-cleaning sticks. Root and bark decoctions are used for liver complaints. Leaf paste is applied for headaches, chest pain associated with cough, and skin conditions like rashes and boils. Fruit preparations are used for diabetes and diarrhoea. The plant is also used in ethnoveterinary medicine for livestock diseases [14].

Other uses

The fruit yields a black dye for leather tanning, and the plant serves as a host for lac insect cultivation [15].

This diverse traditional pharmacopoeia provides a strong rationale for targeted scientific investigation into its pharmacological properties.

Phytochemical constituents

The therapeutic potential of *Z. xylopyrus* is grounded in its complex phytochemistry. Different plant parts contain distinct classes of bioactive compounds (Table 1). The presence of flavonoids and cyclopeptide alkaloids is of particular pharmacological interest. Flavonoids like quercetin and quercitrin are well-known for their potent antioxidant, anti-inflammatory, and cytoprotective activities, which can explain several of the plant's observed effects [15]. Cyclopeptide alkaloids, a characteristic class for the Rhamnaceae family, are nitrogen-containing cyclic compounds often associated with antimicrobial, antiplasmodial, and sedative activities, making them prime candidates for further drug discovery efforts [10, 16].

Table 1: Major Phytochemical Constituents of *Ziziphus xylopyrus* by Plant Part

Plant Part	Major Phytoconstituents
Leaves	Flavonoids (Quercetin, Quercitrin), Tannins, Phenolic compounds, Saponins, Carbohydrates.
Stem & Root Bark	**Cyclopeptide Alkaloids** (Xylopyrine A-H, Amphibine-H, Nummularine-K), Oleanolic acid, Tannins (~7.2%), 7,3',4'-trihydroxyflavan-3,4-diol.
Fruits	Oleanolic acid, Reducing sugars, I-Leucocyanidin, Vitamin C, Carotene, Citric acid, Sucrose.
Flowers	Flavonoids (Quercitrin, Rutin, Kaempferol), Phenolic acids (Ferulic acid, p-Coumaric acid).
Seeds	Fatty acids (Oleic, Linoleic, Myristic), Sterols.

Pharmacological activities: a critical synthesis hepatoprotective activity

One of the most robustly studied activities of *Z. xylopyrus* is its hepatoprotective effect. Mishra and Kori (2024) conducted a pivotal study evaluating the methanolic (MZX) and aqueous (AZX) root extracts against paracetamol-induced hepatotoxicity in Wistar rats [7].

Methodology and key findings

Hepatotoxicity was induced using paracetamol (1000 mg/kg p.o. for 7 days). Test groups received MZX or AZX at 100 and 200 mg/kg doses, with silymarin as the standard. Pre-treatment with MZX (200 mg/kg) most effectively normalised elevated serum markers (AST, ALT, ALP, bilirubin), reduced hepatic lipid peroxidation (MDA), and restored antioxidant enzymes (SOD, Catalase). It also normalised the disturbed lipid profile. Histopathological analysis confirmed that MZX (200 mg/kg) treatment preserved near-normal hepatic architecture, comparable to the silymarin group [7].

Interpretation

The study clearly demonstrates a dose-dependent hepatoprotective effect, with the methanolic extract being superior, likely due to better extraction of non-polar bioactive flavonoids and alkaloids. The mechanism appears to involve potent antioxidant activity, mitigating paracetamol-induced oxidative stress—a key pathway in drug-induced liver injury.

Antiulcer activity

The antiulcer potential of *Z. xylopyrus* leaf extracts was investigated and corroborated in reviews [5, 8].

Methodology and key findings

Khan et al. evaluated an ethanolic extract (500 mg/kg), its ethyl acetate fraction (EA, 50 mg/kg), and an isolated precipitate fraction (ppt., 50 mg/kg) against HCl/ethanol-induced gastric ulcers in rats, using ranitidine as the standard [8]. The isolated fraction exhibited exceptional activity, with an ulcer inhibition of 93% (Ulcer Index: 4.00 ± 0.54), nearly matching ranitidine (95% inhibition).

Interpretation

This study is significant as it moves beyond crude extract evaluation. The remarkable efficacy of the isolated fraction suggests the concentration of active antiulcer principles, potentially the flavonoids like quercetin/rutin identified in the extract. The proposed mechanism is linked to the antioxidant and cytoprotective potential of these compounds, shielding the gastric mucosa from necrotising agents [5].

Antimicrobial activity

The antibacterial potential of *Z. xylopyrus* is highlighted in research by Das et al. (2023) and reviews.

Methodology and key findings

Das et al. tested crude methanolic leaf extract and successive solvent fractions against a panel of bacteria. The ethyl acetate (EtOAc) fraction showed the broadest and strongest activity, particularly against *Pseudomonas aeruginosa* (68.96% inhibition vs. amoxicillin), *Enterobacter aerogenes* (75%), and *Bacillus pumalis* (72%) [17].

Interpretation

The superior performance of the EtOAc fraction indicates that medium-polarity antimicrobial compounds (like certain flavonoids and alkaloids) are effectively extracted. The notable activity against *P. aeruginosa*, a notorious drug-resistant pathogen, is of high interest. However, the lack of Minimum Inhibitory Concentration (MIC) data limits the quantitative assessment of potency [16].

Other validated pharmacological activities

Comprehensive reviews catalogue other significant activities:

Antioxidant

Leaf and fruit extracts exhibit significant free radical scavenging activity in DPPH, ABTS, and ferric reducing assays, with leaf extract being more potent.

Analgesic & Anti-inflammatory

Methanolic stem bark extract showed a significant reduction in pain and inflammation in rodent models.

Antidiarrheal

Ethanolic fruit extract showed 89.88% protection in castor oil-induced diarrhoea in rats.

Antidepressant

Flavonoid-rich fractions from leaves showed activity in forced swim and tail suspension tests.

Wound healing

Ethanolic extracts promoted wound contraction and epithelization in rat models.

Anticataract & antisteroidogenic

Preliminary *in vitro* and *in vivo* studies suggest potential in these areas.

Critical methodological appraisal and research gaps

A critical analysis of the reviewed studies reveals a promising yet preliminary stage of research, characterised by several methodological limitations that define the current research gaps (Table 2) [18].

Table 2: Critical Research Gaps and Future Directions for *Z. xylopyrus*

Research Gap	Description & Implication	Recommended Future Action
Lack of Bioactivity-Guided Fractionation	Most studies stop at crude extracts. The active molecule(s) for each effect are unknown.	Employ systematic bioassay-guided isolation from active fractions (e.g., the antiulcer ppt. fraction, hepatoprotective MZX) to identify lead compounds.
Superficial Mechanistic Elucidation	Studies show *efficacy* but not *mechanism*. Pathways and molecular targets are unclear.	Use *in-vitro* models (cell lines) to probe pathways: Nrf2/ARE for antioxidant/hepatoprotection; NF-κB for inflammation; effects on gastric acid/PGE2 for antiulcer.
Incomplete Toxicological & Pharmacokinetic Data	Acute toxicity data exist, but sub-acute/chronic toxicity, genotoxicity, and ADME profiles are absent.	Conduct OECD guideline-compliant sub-chronic toxicity studies. Perform preliminary pharmacokinetic studies on key isolated compounds.
Absence of Standardisation	No chemical or biological markers for quality control. Reproducibility is a concern.	Develop HPLC or LC-MS methods to standardise extracts using marker compounds (e.g., quercetin, a specific xylopyrine).
Under-explored Traditional Indications	Claims for antidiabetic, antipyretic, and immunomodulatory effects lack scientific validation.	Design targeted studies to evaluate these traditionally cited activities using relevant models.

The hepatoprotection study by Mishra and Kori, while robust in its phenomenological approach, exemplifies the need for Gap #2. Its strong evidence necessitates follow-up *in-vitro* work on HepG2 cells to confirm cytoprotection and map the activation of the Nrf2 antioxidant pathway. Similarly, the exceptional antiulcer activity of the isolated fraction by Khan et al. (Gap #1) creates an urgent need to characterise its chemical composition. The antimicrobial study by Das et al. would be strengthened by determining MIC/MBC values and investigating synergy with existing antibiotics.

To realize its full potential, future research must be strategically directed along the translational pipeline:

Future perspectives

Isolation and characterisation

Prioritise bioactivity-guided isolation of lead compounds.

Deep mechanistic studies

Employ molecular and cellular biology techniques to elucidate precise mechanisms.

Preclinical development

Conduct thorough ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity) studies of standardized extracts or pure compounds.

Standardization

Develop robust analytical methods for quality control.

Clinical validation

Initiate well-designed pilot clinical trials for specific, high-potential indications.

CONCLUSION

Ziziphus xylopyrus emerges as a pharmacologically rich and culturally significant medicinal plant with scientifically validated potential in hepatoprotection, gastroprotection, and antimicrobial therapy. The convergence of traditional wisdom and modern pharmacological evidence is compelling, with cyclopeptide alkaloids and flavonoids as likely key bioactive agents.

However, its journey from a traditional remedy to a credible, evidence-based phytopharmaceutical is incomplete.

In conclusion, *Ziziphus xylopyrus* stands as a testament to the vast, untapped potential residing in ethnomedicinal flora. With a concerted effort towards rigorous, translational research, it holds the promise of yielding novel therapeutic agents or standardized herbal supplements for some of contemporary medicine's persistent challenges, particularly in areas of hepatotoxicity, gastropathy, and antimicrobial resistance.

REFERENCES

1. Yuan H, Ma Q, Ye L, 2016, The Traditional Medicine and Modern Medicine from Natural Products. Molecules. 21(5), Pages 559. Doi:10.3390/molecules21050559.
2. Sharma VK, Rajak AK, Chauhan NS, et al, 2011. A rare medicinal herb Ziziphus xylopyrus (Retz.) Willd. Pharmacogn J. 3(18), Pages 18-23.
3. Modi A, Jain S, Kumar V, 2014. Ziziphus xylopyrus (Retz.) Willd: A review of its folkloric, phytochemical and pharmacological perspectives. Asian Pac J Trop Dis. 4(Suppl 1), Pages S1-S6. Doi:10.1016/S2222-1808(14)60410-6.
4. Jain A, Katewa SS, Chaudhary BL, et al, 2004. Folk herbal medicines used in birth control and sexual diseases by tribals of southern Rajasthan, India. J Ethnopharmacol. 90(1), Pages 171-177. Doi:10.1016/j.jep.2003.09.041.
5. Mansoori MH, Kaur C, Gupta MK, et al, 2018. Ziziphus xylopyrus (Retz.) Willd.: A plant of enormous biomedical potential. Int J Green Pharm. 12(2, Suppl), Pages S322-S329.
6. Mishra SK, Kori ML, 2024. Evaluation of Hepatoprotective Potential of Zizyphus xylopyrus Extract. Int J Pharm Qual Assur. 15(4), Pages 2115-2122. Doi:10.25258/ijpqa.15.4.3.
7. Khan W, Reetesh C, Rohit D, et al, 2014. Pharmacological screening (anti-ulcer activity) of the ethanolic extract of "Zizyphus xylopyrus" (Retz.) wild. J Med Pharm Allied Sci. 3(4), Pages 220-222. Doi:10.55522/jmpas.V3I4.0056.
8. Das B, Mangala P, Joshi N, et al, 2023. Phytochemical Investigation and Evaluation of Antibacterial Activity of Zizyphus Xylopyrus (Retz) Willd Leaf Extract. J Adv Zool. 44(S-2), Pages 4369-4378.
9. Singh AK, Pandey MB, Singh VP, et al, 2007. Xylopyrine-A and xylopyrine-B, two new peptide alkaloids from Ziziphus xylopyra. Nat Prod Res. 21(12), Pages 1114-1120. Doi:10.1080/14786410701553810.
10. Pandey MB, Singh AK, Singh JP, et al, 2008. Three new cyclopeptide alkaloids from Ziziphus species. J Asian Nat Prod Res. 10(8), Pages 709-713. Doi:10.1080/10286020802016499.
11. Yadav M, Meena AK, Rao MM, et al, 2011. Review on Ziziphus xylopyrus: A potential traditional drug. J Pharm Res. 4(4), Pages 922-923.
12. Raghavendra HL, Prashith Kekuda TR, Monica AS, et al, 2015. Phytochemical analysis, antifungal and antioxidant activity of leaf and fruit of Ziziphus xylopyrus (Retz.) Willd (Rhamnaceae). Sci Technol Arts Res J. 4(2), Pages 83-88.
13. Reddy KN, Trimurthulu G, Reddy CS, 2006. Ethno veterinary medicine for treating livestock in eastern Ghats of Andhra Pradesh. Indian J Tradit Knowl. 5(3), Pages 368-372.
14. Batiha GE, Beshbishy AM, Ikram M, et al, 2020. The Pharmacological Activity, Biochemical Properties, and Pharmacokinetics of the Major Natural Polyphenolic Flavonoid: Quercetin. Foods. 9(3), Pages 374. Doi:10.3390/foods9030374.
15. Jain S, Sharma C, Khatri P, et al, 2011. Pharmacognostic and phytochemical investigations of the leaves of Ziziphus xylopyrus (Retz) Wild. Int J Pharm Life Sci. 3(1), Pages 122-125.
16. Devi S, Pandey VB, Singh JP, 1987. Peptide alkaloids from Ziziphus species. Phytochemistry. 26(12), Pages 3374-3375. Doi:10.1016/S0031-9422(00)82494-3.
17. Singhal U, Goyal A, Solanki NS, et al, 2012. Pharmacognostical study on fruit of Ziziphus xylopyrus (Retz.) Wild. Int J Drug Dev Res. 4(4), Pages 263-267.
18. Jena BK, Ratha B, Kar S, 2012. Wound healing potential of Zizyphus xylopyrus Willd. (Rhamnaceae) stem bark ethanol extracts using in vitro and in vivo model. J Drug Deliv Ther. 2(4), Pages 41-46.