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Ziziphus oenoplia (L.) Mill. : A Comprehensive Review on Pharmacological Aspects

Sourav Kumar M*

PG Scholar,

Department of Pharmacology, Srinivas College of Pharmacy,

Valachil, Post Farangipete, Mangalore, Karnataka, India-574143.

Satish S [1]*

Professor,

Department of Pharmacology, Srinivas College of Pharmacy,

Valachil, Post Farangipete, Mangalore, Karnataka, India-574143.

Abstract: *Ziziphus oenoplia* (L.) Mill., commonly known as Jackal jujube or *Rhamnus oenoplia*, is a plant with a rich history in traditional medicine across various cultures. This review comprehensively examines its pharmacological aspects, focusing on its diverse medicinal properties and therapeutic potential.

Objective: The pharmacological profile of *Z. oenoplia* encompasses a wide array of bioactive compounds such as alkaloids, flavonoids, saponins, and polyphenols. These constituents contribute to its various biological activities, including antioxidant, anti-inflammatory, antimicrobial, and anticancer effects. The plant has shown promising results in experimental models for conditions like diabetes, cardiovascular diseases, and neurodegenerative disorders, highlighting its potential as a therapeutic agent. Furthermore, *Z. oenoplia* exhibits significant pharmacological activities related to wound healing, hepatoprotection, and immunomodulation. Traditional uses of the plant in treating skin diseases, digestive ailments, and respiratory disorders are also validated through scientific research. The review consolidates information from ethnopharmacological studies, phytochemical analyses, and preclinical investigations to provide a holistic perspective on the medicinal properties of *Z. oenoplia*. Challenges in research, such as standardization of extracts and clinical trials, are discussed to delineate future research directions.

Conclusion: *Z. oenoplia* emerges as a promising candidate for further pharmaceutical development owing to its diverse pharmacological activities and traditional uses. This review underscores the importance of exploring its potential in modern medicine while respecting and integrating its traditional knowledge systems.

Keywords- *Ziziphus oenoplia*, antioxidant, hepatoprotective, anthelmintics.

I. INTRODUCTION

Traditional medicine, deeply intertwined with cultural heritage, reflects the lifestyle and ancient practices of societies. Highly developed systems such as Indian, Chinese, and Arabian traditional medicines are widely practiced globally, reaching countries like Malaysia and America. Approximately 80% of the world's population relies on traditional medicines, emphasizing their widespread use and cultural significance. [1] *Ziziphus oenoplia*, a crucial shrub, thrives in hot regions like India, Ceylon, Tropical Asia, and Australia. Originating from India during the Vedic period, Ayurveda, with texts like Susruta Samhita and Charaka Samhita, extensively documents the therapeutic usage of plants, including *Z. oenoplia*, also known as "makai" in Hindi or "Jackal Jujube" in English. This shrub, distributed across regions from the Indian subcontinent to northern Australia, offers various pharmacological properties such as being a blood purifier and a remedy for abdominal pain and fever. In Uttar Pradesh, India, it's frequently employed for liver diseases. Its roots possess diverse medicinal qualities, including antiulcer, antioxidant, and wound-healing properties. *Z. oenoplia* is integral to Ayurveda, treating ailments like ulcers, stomach aches, and asthma, owing to its astringent, digestive, and antiseptic properties. Across cultures, Ziziphus plants are utilized for treating digestive disorders, urinary troubles, diabetes, skin infections, and other ailments, showcasing their versatile medicinal applications. Rich in alkaloids, flavonoids, phenolic content, and terpenoids, *Z. oenoplia* holds promise for medicinal efficacy, reflecting the wealth of traditional herbal knowledge passed down through generations. [2]

II. TAXONOMY

Ziziphus oenoplia (L.) Mill., commonly known as Jackal jujube or Indian jujube, belongs to the family Rhamnaceae within the order Rosales. This perennial shrub is characterized taxonomically as part of the plant kingdom (Plantae), and it falls under the clades of tracheophytes, angiosperms, eudicots, and rosid dicots. Formerly classified under the genus Rhamnus as *Rhamnus*

oenoplia L., it was later reclassified under the genus Ziziphus by Mill, hence its current scientific name. *Z. oenoplia* is distinguished by its small, round fruits and thorny branches, typical of the Ziziphus genus. It is native to various regions including India, China, and parts of Africa, where it has a rich history of traditional medicinal use. The plant's taxonomy underscores its botanical relationship with other species within the Ziziphus genus, such as Ziziphus mauritiana and Ziziphus jujuba. This taxonomic classification not only helps in understanding its phylogenetic relationships but also aids in the identification and study of its diverse biological activities and medicinal properties.

III. DESCRIPTION OF *Ziziphus oenoplia*

Ziziphus oenoplia is a small deciduous tree or shrub that typically grows up to 6 meters (20 feet) in height. It has a dense, bushy crown with spreading branches and a rough, greyish-brown bark. The tree's trunk is usually short and crooked.

Leaves: *Ziziphus oenoplia* leaf is pale green in colour and has a characteristic odour, mucilaginous taste, leaflet appeared as alternate compound leaves. Ovate to ovate lanceolate in shape, entire or crenate, glabrous margin, symmetrical base and it has a three prominent nerves with numerous transverse nervules. Flowers appear yellowish green in sub-sessile axillary cymes.

Bark: The upper surface of the bark exhibited a rough texture and displayed a greenish-brown coloration. Notably, several ridges were evident on this surface, and characteristic thorns, a hallmark of Ziziphus species, were also observed. contrast, the lower surface of the bark appeared smooth and had a greenish tint. This surface was notably finer and possessed a soft, tactile quality, providing a gentle touch. The upper surface further revealed the alternate arrangement of leaves, while the lower surface showcased an obovate apex, indicating palmate venation patterns. [3]

Flowers: The tree produces small, inconspicuous flowers that are yellowish-green in color. The flowers are usually bisexual and are borne in clusters. They have five sepals and petals, and the stamens are also in multiples of five.

Fruits: *Ziziphus oenoplia* is primarily cultivated for its edible fruits, which are known as 6 Indian jujubes. The fruits are small, round, and berry-like, measuring around 1 to 2 centimeters in diameter. They have a thin, edible skin that is initially green but turns yellowish-brown as it ripens. The flesh is sweet and crisp, with a flavor reminiscent of apples. The fruits contain a hard stone-like seed in the center.

Roots: *Ziziphus oenoplia* has a well-developed and extensive root system. The roots consist of a combination of primary roots, secondary roots, and fine, fibrous roots. The root system of *Ziziphus oenoplia* tends to be shallow and widely spread. The majority of the roots are found in the upper layers of soil, within the top 30 centimeters (12 inches) of the ground. The lateral spread of the roots can extend beyond the tree's canopy, helping to anchor the plant firmly in the soil and absorb water and nutrients from a larger area. [4,5]

IV. ETHNOMEDICINAL USES

Ziziphus oenoplia (L.) Mill., known by various vernacular names such as Jackal jujube or Indian jujube, holds a significant place in traditional medicine systems across different regions where it is indigenous. The plant has been extensively utilized for its medicinal properties, addressing a wide range of health conditions. In Indian traditional medicine (Ayurveda and Siddha), various parts of *Z. oenoplia* are employed for treating digestive disorders. The fruits and leaves are often used to alleviate conditions such as diarrhea, dysentery, and abdominal pain. The roots and bark, known for their astringent properties, are utilized in formulations aimed at treating oral ulcers, gingivitis, and other oral ailments. In parts of Africa, *Z. oenoplia* is used in ethnomedicine to manage skin diseases such as eczema and dermatitis. The crushed leaves or extracts are applied topically to soothe itching and inflammation, showcasing its dermatological benefits. Furthermore, the plant's fruits are consumed fresh or dried in many cultures as a dietary supplement believed to enhance vitality and overall health. They are also used traditionally to alleviate fatigue and as a natural remedy for insomnia and anxiety. Additionally, *Z. oenoplia* finds use in folklore medicine for its purported ability to boost immunity and aid in recovery from illnesses. Herbal preparations made from its various parts are often administered to promote general well-being and resilience against common infections. These ethnobotanical uses underscore the plant's cultural significance and highlight its potential as a source of novel therapeutic compounds warranting further scientific investigation and validation. Integrating traditional knowledge with modern pharmacological research can provide insights into the efficacy and safety of *Z. oenoplia* as a medicinal resource. [6]

V. PHARMACOLOGICAL ACTIVITIES

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY

The antibacterial and antifungal properties of *Ziziphus oenoplia* (L.) root extract on ethanol were investigated by means of the disc diffusion method against a variety of bacteria and fungi. Six gram-negative bacteria (*Escherichia coli, Pseudomonas aeruginosa, Salmonella typhi, Vibrio cholerae, serretia, and Klebsiella pneumoniae*) and two gram-positive (*Staphylococcus aureus and Enterococci*) bacteria were significantly inhibited by the extract. *Aspergillus niger, Aspergillus flavus, Candida albicans,* and *Rhizopus oryzae* were the four fungi against which the antifungal activity were determined to be strong. It can be used in folk medicine around the globe to cure a wide range of illnesses, including infections caused by bacteria and fungi. [7,8]

WOUND HEALING ACTIVITY

It is evident that the hexane extracts of bark, and the hexanes, dichloromethane and ethyl acetate extracts of leaves of *Z. oenoplia*, exhibit wound healing potential. The wound healing potential of the hexanes extract of leaves may be mainly due to lupeol, which is to be confirmed. This study offers scientific evidence of the traditional knowledge of using the leaf of *Z. oenoplia* for wound

healing. Additional research is being conducted on these extracts to determine the active ingredients that promote wound healing. [9]

ANTHELMINTIC ACTIVITY

An investigation was carried out to assess the anthelmintic activity of various extracts of *Zyziphus oenoplia* (L.) root.All extracts exhibited anthelmintic activity, with the aqueous extract showing efficacy at 10mg/ml concentration, while ethanol, chloroform, and petroleum extracts induced paralysis and motility at similar concentrations. Moreover, other test concentrations also demonstrated anthelmintic effects. Notably, The chloroform extract, at a concentration of 20 mg/ml, demonstrated effectiveness similar to that of the standard drug albendazole. Additionally, ethanol, petroleum ether, and aqueous extracts displayed significant effects beyond 40 mg/ml concentration, albeit less potent than chloroform extract. This study underscores the concentration-dependent nature of the extracts, with the chloroform extract is showing itself to be the most potent, despite all extracts possessing anthelmintic properties. Further research is needed to identify the key chemical constituents responsible for the observed anthelmintic activity. [10]

ANTIOXIDANT ACTIVITY

Significant antioxidant activity is shown in both ethanol and the aqueous extract of *Z. oenoplia*, which increases their potential as therapeutic agents in the prevention of degenerative diseases associated with oxidative stress. Using the DPPH method, ethanol extracts and three solvent fractions of *Z. oenoplia* fruit were examined for their ability to scavenge free radicals. There was significant antioxidant activity in the crude ethanol extract. In addition, the chloroform fraction demonstrated substantial activity as compared to ascorbic acid. According to these results, *Z. oenoplia* fruit extracts have antioxidant qualities because they scavenge DPPH radicals. To discover and isolate these potentially active phytoconstituents and ascertain their potential antioxidant function, more studies on their pharmacological activity would be necessary. [11,12]

HEPATOPROTECTIVE

In a dose-dependent manner, the ethanolic extract of *Ziziphus oenoplia* roots effectively restored the significantly increased serum enzymatic activity of bilirubin, alkaline phosphatase, glutamic oxaloacetic transaminase, and glutamate pyruvate transaminase induced by INH + RIF treatment. Moreover, it also reversed the decreased activities of superoxide dismutase, catalase, glutathione S-transferase, and glutathione peroxidase towards normal levels in a dose-dependent manner. Additionally, the extract considerably reduced hepatic malondialdehyde production in the livers of rats intoxicated with INH + RIF in a dose-dependent manner. Histopathological analysis of rat liver slices provided additional evidence in favour of these biochemical results. The study's findings indicate that *Z. oenoplia*'s ethanolic extract has strong hepatoprotective qualities against rats' liver damage brought on by INH + RIF. [13,14]

ANTIULCER ACTIVITY

The antiulcer activity of *Ziziphus oenoplia* is significant in both the total alcoholic extract and its ethanol fraction at a dose of 300mg/kg. However, the chloroform and aqueous fractions did not show any significant effect at the same dose. The parameters assessed included ulcer index, pH and volume of gastric juice, free acidity, and total acidity. Interestingly, the ethanol fraction of *Ziziphus oenoplia* exhibited greater potency compared to the total alcoholic extract. Initial phytochemical screening indicated that the complete alcoholic extract contained alkaloids, flavonoids, tannins, and triterpenes, whereas the ethanol and aqueous fractions contained flavonoids, tannins, and phenolics. Alkaloids were identified in the chloroform fraction. [15,16]

ANTIPLASMODIALACTIVITY

The bioassay-guided fractionation of the EtOAc extract from Thai *Ziziphus oenoplia var. brunoniana* roots is led to the isolation of four novel 13-membered cyclopeptide alkaloids, which were given the names ziziphine N–Q. Ziziphine N and Q showed substantial antiplasmodial action against Plasmodium falciparum, with IC50 values of 3.92 and 3.5 µg/mL, respectively. Furthermore, with a MIC value of 200 µg/mL, both drugs exhibited feeble antimycobacterial action against Mycobacterium tuberculosis. This work emphasizes the promise of *Ziziphus oenoplia var. brunoniana* roots as a source of bioactive chemicals, notably for treating malaria and tuberculosis, however more research is needed to clarify their mechanisms. [17]

ANTICANCER ACTIVITY

Scientists discovered that betulinic acid could be extracted from a variety of Ziziphus species, including *Z. oenoplia*, *Z. mauritiana*, and *Z. rugosa*. The substance exhibited targeted cytotoxicity towards human melanoma cell lines. [Cichewitz and others, 2004]. Mahapatra et al. (2011) evaluated the antiangiogenic activity of an ethanolic extract of *Z. oenoplia* root using the chick chorioallantoic membrane (CAM) model in 9-day-old fertilized chick eggs. Ethanolic extract was observed to increase the number of capillaries on treated CAM surfaces in 9-day-old fertilized chick eggs. These findings revealed a considerable angiogenic potential for *Z. oenoplia* in the ethanolic extract of the root. [18,19]

ANALGESIC AND ANTI- NOCICEPTIVE ACTIVITY

A study was performed to evaluate the analgesic and anti-nociceptive activities of hydroalcoholic extract from *Ziziphus oenoplia* leaves. Swiss mice were administered doses orally. Analgesic effects were evaluated using the acetic acid-induced writhing, Eddy's hotplate, and tail flick models, while anti-nociceptive effects were evaluated using the tail immersion model. Acetic acid-induced activity was observed at 90 minutes. Analgesic effects in the tail flick model were dose-dependent and comparableto morphine sulfate. Significant pain-reducing effects were noted in the early phase of the formalin-induced paw licking model. The extract demonstrated effectiveness in both non-narcotic and narcotic pain models, indicating potential action through peripheral and central mechanisms, likely due to the alkaloids and terpenoids it contains. [20]

PANCREATIC LIPASE INHIBITORY ACTIVITY

This study explored the antioxidant and pancreatic lipase inhibitory properties of *Ziziphus oenoplia* (L.) Mill. leaves through in vitro and in silico methods. Four extracts were obtained: petroleum ether, ethyl acetate, ethanol, and aqueous. The ethyl acetate extract exhibited superior peroxide scavenging and pancreatic lipase inhibition compared to ascorbic acid and orlistat. Molecular docking against the pancreatic lipase–colipase complex identified four potential molecules. Molecular dynamics simulations of molecules revealed strong interactions. ADMET predictions using Swiss ADME and ADMET suggested these compounds as leads for pancreatic lipase inhibition. *Ziziphus oenoplia* (L.) Mill. leaves may yield bioactive compounds for developing safe pancreatic lipase inhibitors. The ethyl acetate extract, especially, demonstrated notable potential, hinting at future polyherbal formulations for obesity-related disorders with optimized efficacy and safety profiles. This study lays a foundation for further chemical, genomic, and proteomic investigations to validate these promising leads. [21]

ANTIDIARRHOEAL ACTIVITY

The study evaluates the potential antidiarrhoeal activity of "methanol extract of *Z. oenoplia* root" (ZOM) in experimental diarrhoea, induced by castor oil and magnesium sulphate in rat at 200 and 400 mg/kg b.w. Both doses were given orally, showed significant antidiarrhoeal activity comparable with that of the standard drug loperamide. On the basis of these findings, it can be assumed that *Z. oenoplia* could be a potential source for novel discovery for antidiarrhoeal. These results may support the fact that this plant is used traditionally to cure diarrhoea. [22]

ANTI-ALLERGIC AND ANTI-INFLAMMATORY ACTIVITIES

Study focused on isolating and testing the most active lectin from *Ziziphus oenoplia* seeds for its anti-allergic and anti-inflammatory properties. The most active lectin, designated ZOSL (*Ziziphus oenoplia* seed lectin), was isolated from dried *Ziziphus oenoplia* seeds. The anti-allergic and anti-inflammatory activities of ZOSL were assessed in vivo using the Arthus reaction and anaphylactic shock models on Wistar albino rats. ZOSL was identified as a monomeric lectin with a molecular weight of 25 kD. Oral administration of ZOSL to Wistar rats demonstrated preventive effects against anaphylactic shock and Arthus reaction. This shows ZOSL exhibited anti-allergic and anti-inflammatory activities in Wistar albino rats, suggesting its potential as a natural therapeutic agent. [23]

HYPOGLYCEMIC ACTIVITY

The ethanol extract of *Ziziphus oenoplia* barks was found to have a better hypoglycemic effect, because it was more effective than aqueous extract in lowering the blood glucose level of diabetic rats. Since repeated administration of both ethanolic and aqueous extracts did not show any changes in the autonomic and behavioral responses in rats during the experimental period, *Z. oenoplia* may be considered as an alternative treatment for diabetes. Produced significant reduction in blood glucose level especially to reduce the postprandial glucose levels, liver enzymes level and lipid components, it is further required to investigate the responsible principle compounds for the inhibitory action of α-amylase and α-glucosidase. This may be beneficial for the development of new antidiabetic agents from native plant resources; hence, a further investigation was needed to explore the possible mechanism of action. [24,25]

IN-VITRO ANTI-DENATURATION ACTIVITY

The study investigated the anti-denaturation activity of root extract of *Ziziphus oenoplia*. The root part of *Ziziphus oenoplia* was extracted with ethyl acetate, 90% ethanol, and water using a Soxhlet apparatus. The crude extracts were subjected to investigation for anti-denaturation study using a method designed by William's et al. Phytochemical analysis revealed the presence of carbohydrates, alkaloids, phenolic compounds, tannins, and saponins. All the extracts of *Ziziphus oenoplia* protected Bovine Serum Albumin (BSA) from denaturation more than 97% at a concentration of 1µg/ml. [26]

Scientific investigations into *Z. oenoplia* have revealed a rich array of bioactive compounds, including alkaloids, flavonoids, saponins, and polyphenols, which contribute to its various pharmacological activities such as antioxidant, anti-inflammatory, antimicrobial, and potentially anticancer effects. These findings corroborate many of its traditional uses and provide a scientific basis for exploring its therapeutic potential.However, despite the promising ethnobotanical and pharmacological evidence, several challenges remain. Standardization of extracts, identification of active compounds, and rigorous clinical trials are necessary steps to validate its safety, efficacy, and dosage in clinical settings. Moving forward, future research should focus on further elucidating the mechanisms of action of *Z. oenoplia* compounds, exploring potential synergies with conventional therapies, and investigating sustainable cultivation practices to ensure a stable supply of this valuable botanical resource.

Overall, *Z. oenoplia* represents a promising avenue for the development of new therapeutic agents and underscores the importance of integrating traditional knowledge with modern scientific inquiry in the pursuit of improved health outcomes. By bridging these disciplines, *Z. oenoplia* holds the potential to make meaningful contributions to global healthcare and pharmaceutical innovation.

VI. CONCLUSION

In conclusion, *Ziziphus oenoplia* (L.) Mill. emerges as a plant of significant ethnopharmacological importance, deeply rooted in traditional medicinal practices across diverse cultures. Its widespread use in treating ailments ranging from digestive disorders to skin conditions reflects its versatility and perceived efficacy in folk medicine.

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