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Ziziphus jujuba Mill.: A Comprehensive Review of its Phytochemistry and Pharmacological Potential

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Abstract

Ziziphus jujuba Mill., commonly known as jujube or Chinese date, is a medicinally important plant belonging to the family *Rhamnaceae*. Widely cultivated across Asia, the Middle East, and parts of Europe, this plant has long been used in traditional medicine systems such as Ayurveda, Traditional Chinese Medicine, and Unani. Various parts of the plant including fruits, leaves, seeds, bark, and roots possess a rich array of phytoconstituents such as flavonoids, saponins, triterpenoids, polysaccharides, phenolic acids, and alkaloids, which contribute to its broad pharmacological profile.

This review provides a comprehensive evaluation of the Pharmacognostic features, phytochemistry, traditional applications, and scientifically validated pharmacological activities of *Z. jujuba*. The plant exhibits antioxidant, anti-inflammatory, hepatoprotective, neuroprotective, anxiolytic, hypoglycaemic, immunomodulatory, wound healing, and antimicrobial effects across various experimental models. Its therapeutic potential has also been demonstrated in disorders related to the nervous system, metabolic syndrome, and liver dysfunction. The bioactivity is largely mediated through modulation of oxidative stress, neurotransmitter balance, inflammatory pathways, and immune responses.

Despite its promising pharmacological actions, further clinical trials, toxicological evaluations, and standardization of active constituents are essential to validate its safety and efficacy in modern medicine. *Ziziphus jujuba* stands as a valuable candidate for future phytopharmaceutical development, bridging traditional knowledge with contemporary therapeutic approaches.

Keywords: *Ziziphus jujuba*, jujube, phytochemistry, pharmacological activity, traditional medicine, phytopharmacology

1. Introduction

Ziziphus jujuba Mill., commonly known as jujube or red date, belongs to the *Rhamnaceae* family and is a small to medium-sized deciduous tree This species is extensively grown due to its therapeutic value and edible fruit yield. Native to China, jujube has been domesticated and used for over 3,000 years and is now grown across various parts of Asia, the Middle East, and even some regions of Europe. Its adaptability to drought, salinity, and a wide range of soil types has facilitated its spread along historical trade routes such

as the Silk Road. The fruit is traditionally consumed in both fresh and dried forms and is well known in many cultures for its therapeutic effects[1-3].

In traditional Chinese and Persian healing practices, jujube has historically been regarded as a highly valued medicinal plant. In ancient texts, it is documented as a valuable fruit for strengthening the digestive system, enhancing sleep, purifying blood, and improving vitality. Its therapeutic applications span a wide range of ailments including gastrointestinal disorders, respiratory conditions, and anxiety-related symptoms. In Persian medicine, it has been used to treat fevers, liver ailments, and respiratory tract irritations. In modern times, scientific interest in *Ziziphus jujuba* has grown due to its diverse pharmacological properties, such as antioxidant, anti-inflammatory, hepatoprotective, immunomodulatory, neuroprotective, and anticancer effects. This review aims to consolidate traditional knowledge and recent scientific findings on the phytochemistry and pharmacological potential of jujube to support its continued and expanded use in nutraceuticals and herbal medicines[4-8].

Synonyms of *Ziziphus jujuba*

English: Jujube, Chinese Date, Red Date, Indian Jujube

Chinese: Hong Zao/Red Date

Hindi: Ber

Arabic: Nabq/Innab

Regional/Traditional Names:

- **Siddha Medicine:** *Elanthai*
- **Ayurveda:** *Badari*
- **Unani:** *Ber, Unnab*

2. Phytochemistry

Ziziphus jujuba is a rich source of a wide range of phytochemicals that contribute to its nutritional and therapeutic properties. The fruits, leaves, seeds, roots, and bark have all been found to contain various classes of bioactive compounds. The major phytoconstituents identified in the jujube plant include flavonoids, saponins, alkaloids, terpenoids, phenolic acids, polysaccharides, tannins, amino acids, and vitamins. Among these, flavonoids and saponins are considered the primary bioactive groups responsible for its antioxidant, anti-inflammatory, and immunomodulatory effects. The fruit of *Z. jujuba* contains high levels of ascorbic acid (vitamin C), along with B-complex vitamins, minerals such as potassium, calcium, and phosphorus, and carbohydrates that contribute to its high nutritional value. Flavonoids such as kaempferol, quercetin, and rutin have been isolated from the fruit and leaves, exhibiting strong free-radical scavenging activity. Polysaccharides extracted from the fruit and seeds show significant immunostimulatory and hepatoprotective effects. In addition, triterpenic acids like oleanolic acid and ursolic acid are found in the fruit peel and bark, known for their anti-inflammatory and hepatoprotective properties. The seeds of *Z. jujuba* are rich in fatty acids and contain saponins and alkaloids that contribute to their sedative and hypnotic effects. The roots and bark also contain phenolic compounds and triterpenoids with antimicrobial and anti-inflammatory actions. The presence of such a diverse array of phytochemicals underscores the plant's multifaceted therapeutic potential and supports its use in traditional medicine systems. Ongoing research continues to explore the pharmacological relevance of these constituents for developing new herbal formulations and natural health products[6, 8-10].

3. Pharmacognostic Overview of Different Plant Parts

3.1. Leaves

The leaves of *Ziziphus jujuba* Mill. are simple, ovate to elliptic in shape, typically measuring 2.5–7.0 cm in length and 1.5–3.5 cm in width, though they may reach up to 9 cm under favourable conditions. They are arranged alternately on the branches, possess finely serrated margins, and exhibit a leathery texture with a glossy, bright green upper surface and fine hairs on the underside. A key identifying feature is the presence of three prominent basal veins. Traditionally, these leaves have been used in various ethnomedical practices for treating inflammation, insomnia, and microbial infections. Pharmacological studies have revealed that *Z. jujuba* leaves possess significant antioxidant, anti-inflammatory, antimicrobial, hypoglycaemic, neuroprotective, and hepatoprotective properties. Methanolic and aqueous extracts are rich in flavonoids, phenolics, and saponins, which contribute to their free radical scavenging and insulin-sensitizing effects in diabetic models. Moreover, the leaves exhibit anxiolytic and sedative properties via modulation of GABAergic pathways and demonstrate antimicrobial efficacy against both gram-positive and gram-negative bacteria, underscoring their broad therapeutic potential[11-15].

3.2. Fruits

The fruits of *Ziziphus jujuba* Mill., commonly known as jujube or Chinese date, are drupe-type, spherical to oblong in shape, typically measuring 2–3 cm in length and 1.5–2 cm in diameter. These fruits are rich in bioactive compounds such as vitamin C, flavonoids (rutin, quercetin), phenolics, triterpenic acids (betulinic acid, oleanolic acid), polysaccharides, and saponins. Pharmacologically, jujube fruits exhibit a wide range of activities. They possess strong antioxidant properties due to their high phenolic content, which helps neutralize free radicals and reduce oxidative stress. Additionally, jujube fruits have been shown to exert neuroprotective effects, including anti-Alzheimer's and antiepileptic activity, largely through cholinesterase inhibition and modulation of neurotransmitter levels. The fruits also demonstrate immunomodulatory, hypoglycaemic, hypolipidemic, anti-inflammatory, hepatoprotective, and anti-anxiety effects in various in vivo and in vitro models. These pharmacological properties make *Ziziphus jujuba* fruit a valuable candidate for the development of nutraceuticals and therapeutic agents[7, 16-20].

3.3. Seeds

The seeds of *Ziziphus jujuba* Mill., also known as jujube or Chinese date, are oblong or oval in shape, typically measuring 1.0–1.5 cm in length and 0.4–0.6 cm in diameter. Enclosed within the hard endocarp of the drupe fruit, the seeds are brown in colour and possess a smooth, glossy surface. Traditionally, jujube seeds (commonly called "Suan Zao Ren" in Chinese medicine) have been used as a sedative and anxiolytic. Pharmacologically, *Z. jujuba* seeds exhibit sedative, hypnotic, anxiolytic, neuroprotective, antioxidant, and anti-inflammatory activities. The primary bioactive constituents responsible for these effects include jujubosides (A and B), flavonoids, fatty oils, and saponins. Jujuboside A, in particular, has been shown to potentiate GABAergic transmission, reduce locomotor activity, and improve sleep latency and duration in experimental models. Moreover, extracts from jujube seeds have demonstrated cognitive-enhancing and anti-epileptic potential through their action on neurotransmitter systems and oxidative stress pathways. These pharmacological effects support the ethnopharmacological use of *Z. jujuba* seeds in managing insomnia, anxiety, and neurodegenerative conditions[4, 21-23].

3.4. Bark

The bark of *Ziziphus jujuba* Mill., belonging to the Rhamnaceae family, is brown to dark Gray in colour, rough in texture, and longitudinally fissured. Harvested from mature woody parts of the plant, the bark commonly exhibits a thickness between 3 and 6 mm. Anatomically, the bark contains thick-walled

sclerenchyma, phloem fibres, and prominent groups of calcium oxalate crystals. Traditionally, the bark has been employed in various ethnomedicinal systems, including Ayurveda and Traditional Chinese Medicine, for the treatment of fevers, inflammation, and digestive disorders. Pharmacological studies have revealed that the aqueous and methanolic extracts of *Z. jujuba* bark possess diuretic, anti-inflammatory, antimicrobial, antioxidant, and wound healing properties. These effects are primarily attributed to the presence of flavonoids, saponins, alkaloids, and phenolic compounds. In experimental models, the bark extract has shown significant diuretic activity, comparable to standard drugs like furosemide, by increasing urinary output and electrolyte excretion. Moreover, its anti-inflammatory action is linked to the inhibition of prostaglandin synthesis, while antioxidant effects are due to free radical scavenging by phenolic constituents. These findings support the therapeutic potential of *Z. jujuba* bark as a natural remedy for renal and inflammatory conditions[24-26].

3.5. Roots

The roots of *Ziziphus jujuba* Mill., a deciduous plant of the Rhamnaceae family, are typically long, fibrous, and branched, with a brownish exterior and a pale yellowish-white interior. The root system is well-developed and penetrates deep into the soil, which supports the plant's drought resistance. Traditionally, the roots have been used in various traditional medical systems, particularly in Chinese and Korean medicine, to treat ailments such as insomnia, fatigue, and liver disorders. Pharmacologically, *Z. jujuba* root extracts have shown sedative, hepatoprotective, analgesic, and antioxidant activities. The roots are rich in bioactive compounds such as saponins (notably jujubosides A and B), flavonoids, alkaloids, and triterpenes, which are believed to contribute to their therapeutic effects. In experimental studies, jujube root extracts have been shown to modulate the central nervous system, improving sleep and reducing anxiety-like behaviours in rodent models. Additionally, root extracts have exhibited protective effects against chemically induced liver damage, likely by reducing oxidative stress and preserving hepatocyte function. These pharmacological findings support the traditional use of *Ziziphus jujuba* roots in herbal medicine and suggest their potential for development into phytopharmaceuticals[23, 27-29].

4.Pharmacological activity

4.1. Antioxidant Activity

Ziziphus jujuba exhibits notable antioxidant activity, which is primarily attributed to its high content of phenolic compounds, flavonoids, and polysaccharides. Various plant parts including the leaves, fruits, and seeds have been used for extraction with solvents such as methanol, ethanol, and water, and evaluated mainly through in vitro models using DPPH, FRAP, and hydroxyl radical scavenging assays. A methanolic extract of the leaves demonstrated strong antioxidant activity, showing a phenolic content of 2.8% and effective free radical scavenging. Fruit extracts have also shown genotype-dependent antioxidant potential due to variations in phenolic composition. Furthermore, water-extracted polysaccharides from the fruit, especially acidic fractions, have demonstrated strong antioxidant effects, including superoxide and hydroxyl radical scavenging as well as metal ion chelation. confirmed that the structure and uronic acid content of these polysaccharides influence their antioxidant potency. These findings collectively support the role of Z. jujuba as a promising natural antioxidant with potential applications in traditional medicine and nutraceutical development[7, 8, 11].

4.2. Anti-Inflammatory Activity

Ziziphus jujuba has demonstrated significant anti-inflammatory effects in both in vitro and in vivo models, attributed mainly to its rich content of triterpenic acids, flavonoids, and jujubosides. To assess anti-

inflammatory activity, fruit-derived extracts of *Z. jujuba* prepared using hydroalcoholic, ethanolic, and essential oil bases have been tested in standard experimental models like carrageenan-induced rat paw edema, granuloma induction, and TPA-mediated dermatitis in murine subjects. One study using hydroalcoholic fruit extract reported a dose-dependent reduction in granuloma tissue formation, likely due to suppression of nitric oxide production. The ethanolic fruit extract was shown to significantly reduce paw inflammation by downregulating COX-2 expression and activity, suggesting a mechanism similar to that of diclofenac sodium. Essential oil from jujube also showed notable efficacy in reducing ear thickness and water content in a dermatitis mouse model, highlighting its topical anti-inflammatory potential. Among the six bioactive compound classes isolated from *Z. jujuba*, triterpenic acids such as ursolic acid and oleanolic acid exhibited the most potent effects by inhibiting splenocyte proliferation and inflammatory cytokine expression via the NF-κB signalling pathway. Collectively, these findings confirm the anti-inflammatory potential of *Z. jujuba*, supporting its traditional use and encouraging further exploration as a natural alternative to synthetic anti-inflammatory drugs[19, 30-32].

4.3. Antimicrobial Activity

Ziziphus jujuba has demonstrated broad-spectrum antimicrobial activity attributed to its rich composition of bioactive phytochemicals such as flavonoids, tannins, saponins, alkaloids, phenolics, and terpenoids. Extracts prepared from various parts of the plant—particularly the fruits, leaves, seeds, and essential oils using solvents like ethyl acetate, ethanol, and aqueous mediums have shown inhibitory effects against Gram-positive (e.g., *Staphylococcus aureus*, *Bacillus subtilis*) and Gram-negative bacteria (e.g., *E. coli*, *Salmonella typhi*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*), as well as fungi like *Aspergillus Niger* and *Phomopsis azadirachtae*. Notably, ethyl acetate fractions of jujube extract demonstrated potent antimicrobial action against *P. aeruginosa*, *Bacillus pumilis*, and *Enterobacter aerogenes*, indicating the solvent's role in enhancing activity by extracting specific antimicrobial constituents. A peptide called Snakin-Z, isolated from jujube, exhibited strong antibacterial and antifungal activity, with Gram-negative bacteria showing higher sensitivity compared to Gram-positive strains. Additionally, essential oil extracted from jujube fruits showed superior antimicrobial efficacy, in some cases outperforming conventional antibiotics like vancomycin against clinical isolates. These findings support the potential use of *Z. jujuba* as a natural antimicrobial agent, particularly in the context of increasing antibiotic resistance[32-35].

4.4. Sedative Activity

Ziziphus jujuba has long been used in traditional Chinese medicine (TCM) for its calming and sleep-inducing effects. Among the various parts of the plant, the seeds are especially valued for their sedative and hypnotic properties. Research has confirmed that these effects are largely attributed to the presence of triterpenic saponins, flavonoids, and phenolic compounds found in the seeds. In particular, ethanolic extracts prepared from the seeds have shown significant pharmacological activity in preclinical models. Using in vivo mouse models, studies have demonstrated that administration of the ethanolic seed extract significantly increased the duration of sleep and reduced sleep onset time, indicating its potent sedative and hypnotic action. The mechanism of action is believed to involve modulation of the serotoninergic and monoaminergic neurotransmitter systems, both of which are closely associated with mood regulation and sleep-wake cycles. Moreover, in vitro studies suggest that triterpenic saponins may directly influence central nervous system pathways, supporting their role as the primary bioactive constituents responsible for these effects. Given the increasing interest in natural remedies for insomnia and anxiety, the sedative activity of *Z. jujuba* offers a promising plant-based therapeutic alternative. Its use is further supported by

traditional applications and modern pharmacological data, making it a valuable candidate for further development into standardized phytotherapeutic agents for sleep-related disorders[20, 36].

4.5. Anticancer Activity

Ziziphus jujuba has shown promising anticancer potential due to its rich composition of bioactive compounds, especially triterpenic acids, betulinic acid, and phenolics. The fruit of the plant is commonly used, and ethanolic or methanolic extracts are generally employed to isolate active constituents. In in vitro models, particularly HepG2 liver cancer cells, the fruit extract has demonstrated strong anticancer activity by reducing cell viability in a concentration-dependent manner, inducing apoptosis, and altering the cell cycle. Among the active constituents, lupane-type triterpenoids such as 3-O-p-coumaroylalphitolic acid have shown enhanced cytotoxic effects, suggesting the structural importance of coumaroyl substitution. Betulinic acid, another potent triterpenoid extracted from *Z. jujuba* and *Z. mauritiana*, has exhibited selective toxicity toward human melanoma cells and has entered preclinical development for cancers such as lung, ovarian, and cervical types. Notably, the apoptotic effect of betulinic acid is p53- and CD95-independent, making it a versatile agent for cancer therapy. These findings establish *Ziziphus jujuba* as a valuable candidate for the development of natural anticancer therapies[37-39].

4.6. Gastrointestinal Protective Activity

Ziziphus jujuba exhibits significant gastrointestinal protective effects, traditionally recognized in Chinese medicine for warming and tonifying the spleen and stomach. The fruit and stem bark are commonly used plant parts, and aqueous and ethanolic extracts are employed in various experimental models. In animal studies, the aqueous carbohydrate-rich fraction of the fruit, containing glucose, fructose, pectin polysaccharides, and hemicellulose, improved intestinal conditions in hamsters by reducing the mucosal exposure to harmful substances such as ammonia. Ethanolic extracts of the stem bark notably decreased ulceration, submucosal swelling, and bleeding in gastric tissues in murine models. Additionally, jujube extract delayed diarrhoea onset and reduced stool output in a dose-dependent manner. These protective effects are mediated by enhanced intestinal antioxidant status, regulation of inflammatory cytokines, and modulation of tight junction proteins and gut microbiota, which collectively preserve intestinal barrier integrity. Clinical trials have further validated the efficacy and safety of jujube extract in treating chronic idiopathic constipation without adverse effects on hepatic or renal function, highlighting its therapeutic value in managing digestive disorders[25, 40].

4.7. Neuroprotective Activity

Ziziphus jujuba has demonstrated significant neuroprotective effects through a variety of mechanisms, making it a promising candidate for the treatment of neurological disorders. In traditional Chinese medicine, it is a major component of herbal formulas like *Ganmai Dazao Tang* and *Chaihu Guizhi Tang*, commonly used for depressive illnesses. The therapeutic effects are attributed to the presence of neuroactive flavonoids such as quercetin, kaempferol, and rutin, which improve PC-12 cell viability, reduce lactate dehydrogenase release, and attenuate intracellular ROS. In vivo studies using cerebral ischemia models in gerbils demonstrated that oral gavage of jujube extract increased SOD1 expression in the hippocampal CA1 region and decreased lipid peroxidation, thereby protecting neurons. Similarly, rats with focal cerebral ischemia treated with the extract exhibited reduced MDA and NO levels and elevated SOD levels in the cerebral cortex, striatum, and hippocampus. In experimental models of Alzheimer's disease, treatment with aqueous *Z. jujuba* extract mitigated oxidative stress, reduced neuroinflammatory responses, and restored cholinergic signalling. It enhanced hippocampal neurogenesis, improved synaptic plasticity, and significantly reversed memory deficits in behavioural assays like the Morris water maze.

Both HEJF and MEZJ extracts showed anticonvulsant effects in PTZ-induced seizure models by restoring antioxidant balance, inhibiting acetylcholinesterase and butyrylcholinesterase, and improving seizure threshold and cognition-related outcomes. These extracts restored GSH levels and inhibited AChE and BChE activity, while also prolonging myoclonic latency and improving cognitive behaviour. Combined therapy of HEJF with phenytoin or phenobarbital further enhanced seizure protection. Snakin-Z, a newly identified peptide derived from jujube fruit, exhibited strong DPPH radical scavenging activity and effectively inhibited the enzymatic functions of AChE and BChE. Additionally, co-treatment with HEJF and silymarin offered neuroprotection in focal cerebral ischemia models by reducing oxidative markers. These diverse findings—spanning antioxidative, anti-inflammatory, anti-apoptotic, cholinergic-modulatory, and anti-seizure mechanisms—strongly suggest that *Z. jujuba* has multifaceted neuroprotective potential, particularly against disorders such as AD, epilepsy, cerebral ischemia, and cognitive impairments[41, 42].

4.8. Antiaging Activity

The anti-aging potential of *Ziziphus jujuba* has been demonstrated using both topical and systemic models involving its leaves and fruits. A hydroalcoholic extract (80%) of the leaves was formulated into an emulsion at a 4% concentration and evaluated for stability (phase separation, pH, conductivity, etc.) over four weeks under various temperature and humidity conditions. This formulation was topically applied to healthy human volunteers (n=13) over an 8-week period, showing improvements in skin parameters such as melanin content, erythema, moisture, elasticity, and sebum content, indicating skin-rejuvenating effects. In a separate in vivo study using *Drosophila melanogaster* as the model organism, jujube fruit powder was administered orally at doses of 30 mg/mL and 150 mg/mL. The higher dose significantly extended lifespan and enhanced general health, suggesting systemic anti-aging effects. These findings highlight the anti-aging efficacy of *Z. jujuba* leaf and fruit extracts, particularly when prepared using hydroalcoholic solvents and evaluated through dermatological and model organism-based methodologies[43-45].

4.9. Wound Healing Activity

The wound healing activity of *Ziziphus jujuba* has been demonstrated through various in vivo and clinical studies using both its leaf and fruit extracts. Ethanolic and aqueous extracts of *Z. jujuba* leaves were formulated into ointments at a concentration of 5% w/w and evaluated in Wistar albino rats using the excision wound model. The efficacy was compared with 0.2% w/w nitrofurazone as the standard, and parameters such as wound closure rate, wound contraction, epithelial tissue regeneration, and angiogenesis were assessed, showing significant enhancement in healing. In a separate in vivo study, jujube fruit extract was tested on second-degree burn wounds, where it significantly accelerated healing compared to control groups treated with Vaseline and silver sulfadiazine. Additionally, a double-blind, controlled clinical trial on 100 lactating women demonstrated that topical application of jujube fruit lotion significantly reduced nipple fissure pain by the 7th and 14th days of intervention. Furthermore, water-soluble glucans isolated from *Z. jujuba* were found to promote cell migration and survival—key mechanisms involved in tissue repair—further supporting its potential as a natural wound healing agent[11, 46-48].

4.10. Anti-Asthmatic and Anti-Allergic Activity

The anti-asthmatic and anti-allergic potential of *Ziziphus jujuba* has been established through a variety of ex vivo and in vivo experimental models, primarily using its fruit extract and isolated saponins such as jujuboside B. Studies have demonstrated that jujube fruit extract significantly reduces asthmatic episodes and allergic responses by stabilizing mast cells, thereby inhibiting the release of histamine and other inflammatory mediators. The observed pharmacological effects—anti-anaphylactic, anti-inflammatory,

antihistaminic, and immunomodulatory—are attributed to its phytoconstituents, including flavonoids and steroidal saponins. In in vivo asthma models, both the crude fruit extract and jujuboside B were found to suppress airway inflammation and bronchoconstriction, supporting their traditional use in respiratory disorders. These effects are believed to involve multiple mechanisms, such as inhibition of mast cell degranulation, modulation of cytokine release, and suppression of IgE-mediated responses. The findings validate traditional claims and support the therapeutic potential of *Z. jujuba* as a natural agent for managing asthma and allergic conditions[49-52].

4.11. Antidiabetic Activity

The antidiabetic activity of *Ziziphus jujuba* has been explored using both in vitro and in vivo experimental models, primarily focusing on its fruit extract. Triterpenoids derived from *Z. jujuba* fruit extract were shown to enhance glucose uptake in L6 myotubes by stimulating GLUT4 translocation, indicating improved glucose utilization at the cellular level. In vivo studies using streptozotocin-induced diabetic rat models demonstrated that prolonged treatment with alcoholic extract of *Z. jujuba* fruit significantly reduced blood glucose levels. These effects are attributed to mechanisms such as enhanced insulin secretion and improved insulin receptor sensitivity. The results suggest that the fruit of *Ziziphus jujuba*, especially when extracted with ethanol, possesses potent antidiabetic properties and supports its traditional use in managing diabetes[53, 54].

4.12. Hepatoprotective Activity

Ziziphus jujuba has exhibited liver-protective properties in murine models, where damage was induced by hepatotoxins such as carbon tetrachloride, paracetamol, and ethionine, utilizing both fruit and leaf extracts. Ethanolic–water extracts of the leaves significantly reduced serum ALT, AST, and hepatic MDA levels while increasing the antioxidant biomarkers SOD, GSH, and GSH-Px. Histopathological analysis confirmed a reduction in tissue injury, suggesting protective effects against oxidative and inflammatory hepatic damage. Quantitative HPLC-DAD analysis identified 15 major constituents, with flavonoids suspected to be the key bioactive compounds responsible for the observed hepatoprotection. Similarly, fruit pulp extracts and jujube-derived polysaccharides enhanced antioxidant defences, modulated NRF2 and NF-κB signalling, and improved liver histology and enzyme profiles in ischemia-reperfusion injury models. Maslinic acid from jujube pulp also demonstrated efficacy against CCl_4-induced toxicity, indicating a multi-component, multi-target mechanism underlying the hepatoprotective activity of *Z. jujuba*[13, 55].

4.13. Anti-Alzheimer's Activity

Neuroprotective effects against Alzheimer's disease have been linked to bioactive constituents of *Ziziphus jujuba* fruit, notably oleamide and the peptide Snakin-Z. Oleamide, extracted from the fruit, exhibited neuroprotective effects in scopolamine-induced cholinergic toxicity models, where it enhanced choline acetyltransferase (ChAT) activity, suggesting its role in restoring acetylcholine levels critical for memory and cognition. Meanwhile, Snakin-Z demonstrated dual anticholinesterase activity by inhibiting both acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), along with strong antioxidant properties that may reduce oxidative stress implicated in Alzheimer's pathogenesis. These findings support the traditional use of jujube in cognitive enhancement and highlight its potential as a natural therapeutic agent for neurodegenerative diseases like Alzheimer's[16].

4.14. Antiepileptic Activity

The hydroalcoholic extract of *Ziziphus jujuba* fruit (HEJF) demonstrated significant antiepileptic potential in rat models of generalized tonic-clonic seizures and tonic hindlimb extension. HEJF not only exhibited

anticonvulsant activity but also mitigated seizure-induced cognitive deficits by enhancing learning and memory, reducing oxidative stress, and inhibiting cholinesterase activity. Biochemically, it decreased malondialdehyde (MDA) levels while elevating glutathione, indicating a neuroprotective antioxidant effect. Furthermore, co-administration of HEJF with sub-therapeutic doses of conventional antiepileptic drugs like phenytoin and phenobarbital enhanced their efficacy without altering serum drug concentrations, suggesting favourable pharmacodynamic interactions. However, Carbamazepine did not exhibit any notable pharmacological interaction. These findings position HEJF as a promising adjunctive natural therapy in epilepsy management[56, 57].

4.15. Anti-Melanogenic Activity

Ziziphus jujuba has demonstrated promising anti-melanogenic effects, supporting its traditional and emerging use in dermatological applications, particularly for skin brightening and treating hyperpigmentation. Clinical studies have reported that jujube syrup, when administered twice daily for eight weeks, significantly reduced facial hyperpigmentation, pigment counts, and pigmented area percentages compared to placebo, indicating its safety and efficacy in humans. Phytochemicals such as jujuboside A and B, epiceanothic acid (EPA), and 6-feruloylspinosin (FRS), isolated from *Z. jujuba* seeds, effectively suppressed α-MSH-induced melanogenesis in zebrafish larvae and B16F10 melanoma cells, highlighting their melanin-inhibitory properties. Furthermore, cold extracts of jujube fruit reduced melanin synthesis by up to 30% in vitro, while hot extracts showed negligible effects, suggesting that extraction methods impact bioactivity. Methanolic extracts (80%) prepared using Soxhlet and percolation techniques demonstrated significant inhibition of tyrosinase and melanogenesis, suggesting potential benefits in treating melasma, hyperpigmentation, and acne-associated dark spots. These findings suggest that *Z. jujuba* extracts could serve as dermatologically safe skin-lightening agents in cosmetic formulations[10, 58, 59].

4.16. Anti-Influenza Activity

Ziziphus jujuba exhibits antiviral potential, notably against influenza viruses, primarily due to the presence of betulinic acid (BA), a pentacyclic triterpene isolated from its fruit Betulinic acid (BA) exhibited strong antiviral effects against the A/PR/8 influenza virus in both A549 lung epithelial cell lines and C57BL/6 mouse models. At a concentration of 50 μM, BA inhibited influenza viral replication effectively without significant cytotoxicity. In vivo, BA treatment significantly attenuated pulmonary damage associated with influenza infection. This included reductions in tissue necrosis, inflammatory cell infiltration, and pulmonary edema when compared to both vehicle-treated and oseltamivir-treated mice, suggesting its therapeutic potential in managing influenza infections through anti-inflammatory and antiviral mechanisms[60].

4.17. Anti-Genotoxic Activity

Ziziphus jujuba exhibits notable anti-genotoxic activity primarily due to its rich polyphenolic content and potent antioxidant constituents like betulinic acid. These compounds help protect genetic material from oxidative stress-induced DNA damage. In vitro and in vivo studies have shown that jujube fruit extracts significantly reduce genotoxic effects caused by agents such as methyl methane sulfonate (MMS), hydrogen peroxide (H_2O_2), and hydroquinone by enhancing antioxidant enzyme activity. The polyphenolic and hydroalcoholic extracts have been particularly effective in decreasing chromosomal aberrations and DNA strand breaks, especially at lower concentrations due to their high antioxidant capacity. Comparative studies also demonstrated that *Z. jujuba* provides better Geno protective effects than *Origanum majorana*.

These findings highlight the potential of *Z. jujuba* as a natural anti-genotoxic agent, though further mechanistic and clinical studies are needed to confirm its therapeutic efficacy[61, 62].

4.18. Immunomodulatory Activity

Ziziphus jujuba demonstrates significant immunomodulatory activity, primarily attributed to its polysaccharide components. Among these, Ju-B-2 was found to enhance splenocyte proliferation in a dose-dependent manner, while Ju-B-3 showed no such effect. Further studies on mice revealed that crude and purified water-soluble polysaccharide fractions—particularly ZSP3 and ZSP4—stimulated proliferation of peritoneal macrophages and splenic cells, and also exhibited anti-complementary activity. Notably, the sub-fraction ZSP3c, rich in pectin with 49% esterification, showed the most potent immunostimulatory response. Additionally, jujube extract (JE) increased mucosal immune responses in fish by enhancing total immunoglobulin, lysozyme, and protease activities in the skin, along with upregulating immune-related cytokine genes such as TNF-α, IL-10, IL-8, and IL-1β. Moreover, ziziphus-arabinan, a water-soluble polysaccharide from jujube, has shown anti-complementary effects through both classical and alternative pathways. The results underscore *Z. jujuba*'s promise as a natural immune-modulating compound with applicability in clinical settings and aquaculture systems[18, 63, 64].

4.19. Biochemical and haematological activity

The consumption of *Ziziphus jujuba* fruit has been shown to influence several haematological and biochemical parameters, indicating its potential role in metabolic regulation and immune support. Studies revealed that jujube fruit significantly increased red blood cell (RBC) and white blood cell (WBC) counts, suggesting a hematopoietic and immunostimulatory effect. Interestingly, it also led to a decrease in platelet counts, which may reflect its role in modulating blood coagulation. In terms of biochemical parameters, jujube fruit demonstrated hypoglycaemic and hypolipidemic properties by effectively lowering blood glucose, triglyceride, and cholesterol levels. These findings highlight the potential therapeutic benefits of *Ziziphus jujuba* in managing haematological imbalances and metabolic disorders such as diabetes and hyperlipidaemia[65].

5. Discussion

Ziziphus jujuba Mill. has emerged as a multifunctional medicinal plant with rich ethnopharmacological relevance and a growing body of scientific evidence supporting its therapeutic applications. This review comprehensively outlines the phytochemistry, morphology, and pharmacological properties of various plant parts—including leaves, fruits, seeds, bark, and roots—highlighting its wide pharmacological spectrum. Each part of the plant offers unique bioactive constituents that contribute to its medicinal properties. For instance, the flavonoids, triterpenoids, and polysaccharides prevalent in the fruit are mainly responsible for its antioxidant, hepatoprotective, and neuroprotective effects. Similarly, jujubosides found in the seeds contribute to its sedative and anti-anxiety effects, while the roots and bark possess anti-inflammatory and antimicrobial activities.

Experimental evidence from in vitro, in vivo, and preliminary clinical studies supports the therapeutic efficacy of *Ziziphus jujuba* in treating diverse ailments, including sleep disorders, digestive and respiratory conditions, metabolic disturbances, neurological disorders, and inflammatory diseases. The plant has also shown promising results in advanced pharmacological applications, such as anti-aging, anti-cancer, anti-epileptic, and anti-genotoxic therapies. Notably, the plant's effects are often mediated via modulation of oxidative stress, inflammatory mediators, neurotransmitter activity, and immune signalling pathways.

Despite the promising pharmacological potential, challenges remain. Many studies are preliminary, with limited clinical translation. Standardization of extracts, elucidation of bioactive compounds, detailed toxicological profiling, and well-designed clinical trials are crucial to fully harness the therapeutic value of *Z. jujuba* and transition it from traditional to evidence-based modern medicine.

6. Conclusion

To conclude, *Ziziphus jujuba* Mill. stands out as a plant of considerable botanical and pharmacological value, deeply rooted in traditional medicine and rich in bioactive compounds. The diverse bioactive constituents present in its various parts validate many of its traditional uses and open avenues for therapeutic applications. From antioxidant and hepatoprotective properties to neuroprotective, immunomodulatory, and anti-inflammatory effects, *Z. jujuba* presents a valuable natural source for the development of herbal medicines and nutraceuticals.

The integration of traditional knowledge with modern pharmacological validation strongly supports its future application in integrative and alternative medicine. However, to ensure efficacy and safety in humans, further research is warranted especially large-scale clinical trials and advanced mechanistic studies. With continued scientific exploration, *Z. jujuba* may be positioned as a vital phytopharmaceutical agent in global health care.

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