Review Article

Ziziphus mauritiana: A Comprehensive Review on Ethnopharmacological, Phytochemical and Pharmacological Properties

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ABSTRACT

Plants of traditional importance that belong to the Rhamnaceae family are classified according totheir taxonomic categorization as *Ziziphus mauritiana (Z. mauritiana*). This fruit is also known asIndian jujube, Ber, or Chinese date. It is thought that this species originated in Southeast Asia'sIndo-Malaysia area. The plant species in issue has become significantly more naturalised in tropical locations, which include the Indian subcontinent, the Middle East, and South Africa. What's being discussed here is a small arboreal specimen or thorny perennial shrub withevergreen leaves. *Z. mauritiana* is a plant that is not used much but has the ability to treat a variety of illnesses. It is known that numerous plant parts, such as leaves, seeds, and fruits, havetherapeutic qualities based on ancient literary sources. *Z. mauritiana* exhibits exceptional medicinal properties that are associated with a diverse array of functional metabolites that include derivatives, such as terpenoids, flavonoids, and alkaloids. This plant is effective in treatingor preventing a variety of illnesses because it contains a variety of phytochemicals, bioactive compounds, vitamins, and other ingredients. The study looked at the pharmacological propertiesand medicinal benefits of plants, with an emphasis on their anxiolytic, antioxidant, anti-microbial,anti-cancer, anti-diabetic, and anti-ulcer properties. The current classified data on the pharmacological and toxicological effects of *Z. mauritiana*, as well as its botanical characteristics,traditional usage, phytochemistry, and phytochemistry, is reviewed and critically evaluated in this review paper.

Keywords: *Ziziphus mauritiana*, functional metabolites, pharmacological activities, anti-diabetic, anti-Steroidogenic.

INTRODUCTION

Around the world, *Z. mauritiana* trees may be found in regions with dry and semi-arid climates. In India, the aforementioned fruit is commonly used as a wild fruit. Many rural residents who live in arid areas depend heavily on *Z. mauritiana* trees for their livelihoods. These people depend on the trees for a variety of products, such as building materials, herbs, organic manureand forest litter, food, wood fuel (firewood) and building materials[1]. This plant's fruits have a high nutritional value and are an excellent source of vitamins and energy. Furthermore, they also help to generate revenue. Traditional medicine has been known to use the fruits, seeds, leaves, bark, roots, and other elements of the *Z. mauritiana* tree to treat fever, inflammatory diseases, insomnia, and skin issues[2]. *Z. mauritiana* is categorised as a species of tropical fruit tree. The plant in issue is a small tree or prickly perennial shrub that may grow up to 15 metres in height. Its crown grows in a spreading manner, and its trunk is at least 40 centimetres in diameter. This plant is further distinguished by many hanging branches and stipular spines. There is variation in the fruit's size and form. The item in issue can be oval, obovate, oblong, or round, and dependingon the kind, its length can be anywhere from 1.25 to 2.5 inches (2.5 to 6.25 cm). The tissue has a solid feel and is coloured somewhat white. At its somewhat under ripe stage, this fruit has a moderate amount of juice and a pleasant aroma. The fruit's exterior has a thin, tight, glossy, and smooth feel. It is seen most frequently in areas with tropical or subtropical climates. This plant species was originally native to India, but it has now spread far over tropical regions, from Africa to Afghanistan and China, Malaysia, Australia, and certain Pacific islands. In some areas, like Australia and Fiji, the species may form dense colonies and display invasive behaviour.

Furthermore, in Northern Australia, it has been recognised as a noteworthy environmental weed.The tree in question grows quickly and has a modest lifetime. It may reach heights of 10 to 40 feet (3 to 12 metres) in a short amount of time.

Native to India, *Z. mauritiana* is a fruit prized for its remarkable nutritional content and endurance. *Z. mauritiana* is a traditional botanical species that belongs to the Rhamnaceae family. The fruit is often known as "Ber" in Hindi and "Badrah" in Sanskrit within the Indian setting. The plant species in issue was originally found in the Middle East and the Indian subcontinent, but because of its high nutritional content, it is now grown in tropical andsubtropical climates. There is potential for using this plant in phytomedicine as well as the food sector[3].

The exceptional capacity of Ziziphus plants and bushes to adapt to adverse situations allows them to survive in a wide range of habitats. Cattle eat the plant, and its fibrous fibre is historically used to make high-quality charcoal, fuel, and a variety of agricultural equipment. Traditional medicine greatly benefits from the use of medicinal plants

in treating a wide range ofillnesses. Agreat deal of work has been done to assess the many pharmacological traits that theseplants exhibit.

The present study offers a thorough overview of the several facets of *Z. mauritiana* action, hence augmenting its potential as a strong therapeutic agent for a multitude of disorders.

Geographical Distribution

The species in question is thought to be native to southern Asia, eastern Africa, and several Indian Ocean islands. Research has indicated that it originated in India. Chinese apple, or *Z. mauritiana*,is widely distributed in Australia's northern regions, with the northern and central parts of Queensland exhibiting the highest abundance of the species. Additionally, the plant has been imported and grown in Southeast Asia, encompassing Malaysia and the Philippines, as wellas southern Africa. For the past four centuries, the fruit has been cultivated in China and India.

Z. mauritiana, sometimes referred to as Indian jujube, is a fruit crop that shows promise both in its native environment and in certain areas where it has been introduced. It is important to note,nevertheless, that *Z. mauritiana* is not now grown anywhere in Australia. In Fiji, *Z. mauritiana* is proliferating and may be seen growing along roadsides and in agricultural regions[4].

Morphology

Z. mauritiana is a tiny tree or shrub with prickly leaves that can grow up to 15 metres in height. Its trunk is at least 40 metres in diameter. The stem of *Z. mauritiana* grows quickly andhas a longlifetime. It has a structure that is hierarchical and may reach heights of fifteen metres. Its overallbeauty is enhanced by the dispersed crown and loose twigs on the stem. The plant's leaves are arranged alternately and have an ovate or four-sided elliptic form with a rounded tip and three prominent longitudinal veins that seem to be sunken at the base of the leaf. The bottompart of the tree has a variety of colours, ranging from fresh and pale green to grey green, whilethe foliage has a dark green colour and a glossy aspect around its periphery. Small and golden in colour, the flower structures are made of tiny petals that arise from the leaf axils. flowers: The blooms are small, yellow in colour, have delicate petals, and are located in the leaf axils of the plant. There is variation in the sizes and characteristics of the edible fruits. The shape of wild treefruits is tinyand spherical, with a diameter of around 3cm. On the other hand, the fruits of domesticated trees are often bigger, with measurements of around 5 cm in length and 4 cm in breadth. In addition, the tree fruits that are grown have different profiles that fall into four categories: oval, circular, obovate, or oblong[5].

Chemical Composition

Chemicals found in leaves include protein, amino acids, flavonoids, alkaloids, glycoside, terpenoids, saponins, fibres, tannin, and phenolic compounds. Fruits are rich in vitamin C, carotene, phosphorus, calcium, and protein. Carbohydrates such sucrose, glucose, fructose, andstarch are found in pulp. Alphitolic acid, betulinic, maslinic, oleanolic, ursolic, 3-O-trans- alphitolic, 3-O-cis-p-alphitolic, 3-O-cis-pcoumaroylalphitolicacide, and spinosin are examples of triterpene and triterpene saponins. The primary ingredients of it are also jujuboside B, swertisin,zizyphus saponins I, II, and III. *Z. mauritiana* seeds include the following: sucrose, docosanoic acid, stearic acid, palmitoleic acid, spinosin, beta-sitosterol, daucosterol, daucosterol-6 octadecanoate, betulinic aldehyde, ceanothic acid, frangufoline, and spinosin. There are over 150 cyclopeptide alkaloids produced by *Ziziphus* species. Pectin A, glycoside, triterpenoic acid, lipids, and alkaloids are all present in *Z. mauritiana*[6].

Nutritional Value: The fruit of *Z. mauritiana* is very nutritious. It has more iron than an apple, which is important because iron helps oxygen pass through the body. Studies have also shown that the edible parts of this fruit have higher concentrations of important nutrients and minerals,such as iron, zinc, calcium, salt, magnesium, and vitamin C. Ascorbic acid levels in 100 grammesof pulp have been reported to be between 70 and 165 milligrammes. Finally, fruits from this plant are known to be high in vitamin A and the B complex of vitamins. The fruits of

Z. mauritiana have an energy value of 20.9 kcal per 100 grammes of pulp in addition to their nutritional value. Rich in proteins, carbs, and several micronutrients such as zinc (Zn), iron (Fe), copper (Cu), phosphorus (P), sodium (Na), potassium (K), and calcium (Ca), fruit is a very nutrient-dense diet. During their seasonal availability, *Z. mauritiana* fruit intake takes major nutritional relevance in Zimbabwe[7].

There are two possible flavours for the edible part of the Ber fruit: sour and sweet. The edible part of Ber, both sweet and sour, has a dry weight that varies from 21.1 g to 24.1 g per 100 grammes. According to Shumaila Zulfiqar Butt et.al (2021), the edible component's dry weight of100 grammes is made up of different amounts of crude fibre (4.9 to 7.3 grammes), crude proteins (7.9 to 8.7 grammes), fat (0.8 to 1.5 grammes), andcarbohydrates (79.5 to 83.2 grammes) in relation to each other.

Toxicological Investigation

For all the extracts studied, Owolarafe et al. found a decrease in mitotic index percentage and a dose-dependent decrease in root tip length with an increase in extract concentration. The ethanol extract had the greatest significant effect on mitotic index. The authors also evaluated cytotoxicity and genotoxicity parameters, such as mitotic index, root tip growth length, and chromosomal aberration. Additionally, the EC50 values for the aqueous, ethanol, ethyl acetate, and hexane extract were 81.30, 52.01, 90.68, and 112.30 mg/l, respectively. Lastly, it was noted that all four extracts included chromosomal abnormalities such as sticky

telophase, bridging anaphase, c-mitosis, and vagrant chromosomes, and that the percentage of these aberrations decreased as extract concentrations rose. Therefore, based on the study's findings, it is possible todraw the conclusion that the plant extracts (*Z. mauritiana* (Lam)) are cytotoxic and genotoxic in nature, and that the plant extracts' antimutagenic bioactive principles may be the cause of theobserved decrease in the percentage of chromosomal aberration[8].The percentage of viable cells in ethanol and aqueous extracts of *Z. mauritiana*-treated horse cutaneous fibroblast cells isexamined by Karela et al. *Z. mauritiana*'s ethanolic and aqueous extracts did not exhibit cytotoxicity over the whole concentration range. These findings suggest that *Z. mauritiana* has agreater potential for medicinal usage[9]

In order to determine the acute and subchronic toxicity of *Z. mauritiana* leaf aqueous extract on Wistar rats, Owolarafe et al. undertook a research. Their investigation's conclusions showed that the extract had non-toxic qualities, as shown by an LD50 value higher than 5000 mg/kg body weight. Additionally, the subchronic toxicological assessment showed no appreciable negative effects on the majority of haematological parameters—white blood cell count being the only exception. Nevertheless, the assessment did identify certain changes in liver function measures, such as a 400 mg/kg body weight rise in blood GGT activity. Furthermore, there were variations in the amounts of sodium, potassium, bicarbonate, and creatinine in the serum, which are indicators of renal function. The liver and kidney have altered histoarchitecture, according to histopathological analysis[10]. Yangora et al. looked at the sub-chronic harmful effects of oral administration of the *Z. mauritiana* plant's methanolic root extract. The biochemical measurements did not show any significant alterations. But when comparing the medium and higher treated groups' liver and kidney histological analyses to those of the control group, minordifferences were found. These abnormalities included mild tubular necrosis and hyperplasia of inflammatory cells in the kidney and minor vacuolation and hepatic necrosis in the liver. These findings suggest that regular and frequent use of *Z. mauritiana* root extract may pose less risk when administered at lower dosages[11].

PHARMACOLOGICAL ACTIVITIES

Plants have a great deal of medicinal promise for the treatment of chronic illnesses and are important repositories of various naturally occurring pharmacological chemicals. The use of herbalremedies and pharmaceutical products generated from them is thought to play a major partin theglobal progress of clinical medicines. Likewise, *Z. mauritiana* has garnered noteworthy acknowledgement for its effectiveness in managing an array of ailments. For instance, this plant'sleaves are used to treat TB and a variety of other circulatory system-related illnesses. Furthermore, the combination of leaf juice and buffalo's milk has been shown to be therapeutically effective in treating smallpox[12]. This plant's leaves are ground into a paste that is applied to wounds to relieve burning sensations. Traditionally, the combination of newly picked

Z. mauritiana leaves and cumin has been used as a therapeutic intervention for urinary tract infections[13]. Furthermore, this plant's botanical root is mixed with cow's milk and usedas a treatment for diarrhoea. Traditional practitioners advise their patients to take a fresh *Z. mauritiana* root internally to relieve hoarseness in their throats. The majority of this plant's ingredients show promise in treating a range of illnesses. Traditionally, this plant's roots and stemshave been used to treat diarrhoea and dysentery medicinally. This plant has significant analgesic,anti-inflammatory, and anti-allergic qualities in its root bark[14]. Z. *maurititiana* has shown to bea highly effective treatment for pregnancy-related problems, including symptoms like nausea, vomiting, and abdominal discomfort. It has been shown that *Z. mauritiana* leaves have promise medicinal properties that might help treat a variety of illnesses, including fever, liver problems, and asthma. The usefulness of extracts made from several *Z. mauritiana* ingredients in the management of diabetes, inflammation, and cancer has been demonstrated by empirical research[15].The major metabolite makeup of the plant, comprising tannins, saponins,phlobatannins, alkaloids, flavonoids, and steroids, is responsible for its many pharmacological effects. The chemical components, sections utilised for extraction, or entire plant extracts are responsible for *Z. mauritiana*'s pharmacological effect.

Antidiabetic Activity

The pathological disease known as diabetes is characterised by hyperglycemia, or abnormally elevated blood glucose levels. Jarald et al. conducted a study to look at the potential effects of several *Z. mauritiana* fruit extracts on diabetes. Petroleum ether, chloroform, acetone, and aqueous extracts were among the extracts that were investigated. Antihyperglycemic extracts were shown to have hypoglycemic effects at two different dosage levels (200 and 400 mg/kg). The extracts indicated above showed a little but significant drop in blood glucose levels[16]. *Z. mauritiana* seed extract's possible hypoglycemic effect was assessed in diabetic mice treated withalloxan in a different study. Three different dosages per kilogramme of body weight—100, 400, and 800 mg—were given. The sub-acute studies observed a reduction in the mortality rate and weight loss following the administration of the extract. In terms of blood glucose level, bodyweight reduction, and death rate, the group that got the combined therapy (800 mg/kg seed extract + 10 mg/kg glyburide) showed more notable benefits. Furthermore, both normal and diabetic rats' glucose tolerance was improved by the extract. The results show that the extract reduces blood glucose levels in a synergistic manner[17]. *Z. mauritiana* fruit extracts were also shown to have a dose-dependent effect on blood glucose, total protein, albumin, and lipid profilelevels[18]

Anticancer Activity

Using both in vitro and in vivo tests, the current work sought to investigate the anticancer activities of the aqueous-ethanolic seed extract of *Z. mauritiana*. Using the MTT assay, the extract was examined in vitro against a range of cell lines, including HL-60, Molt-4, HeLa, and the normal cell line HGF. Furthermore, the extract was given to Swiss albino mice with Ehrich ascitescarcinoma as part of the in vivo assessment. Notably, the proliferation of HL-60 cells wasreportedto be significantly inhibited, leading to the cell cycle arrest via dosage-dependentactivation of apoptosis. Agarose gel electrophoresis was used to verify the existence of DNA fragmentationin HL-60 cells after a three-hour incubation period with the extract. When a plant extract was given to Swiss albino mice suffering from Ehrlich ascites carcinoma, the tumour volume and number of viable tumour cells were significantly decreased. Haemoglobin content, red blood cellcount, mean survival duration, tumour inhibition, and percentage longevity were also improved[19]. In order to determine if the methanol extract from *Z. mauritiana* leaves inhibits the growthof A549 cells, a subset of human lung epithelial cancer cells, Prakash et al. conducted a research. The study also sought to explore the possible mechanism by whichreactive oxygen species (ROS) are formed to induce apoptosis. Reactive oxygen species (ROS) generation and accumulation in the cytosol were examined as part of the assessment of oxidative stress. Meanwhile, the MTT assay was used to analyse the possibility of anti-cancer activity, along with cell morphology analysis and nuclear condensation evaluation to establish when apoptosis began[20]. According to a research, the anti-proliferation effect of *Z. mauritiana* Fruit Extract Nanoparticles on MCF-7 breast cancer cell lines is caused by the generation of reactive oxygen species (ROS) and the activation of apoptosis through a Fas-mediated mechanism[21].

Antibacterial Activity

A study was done to create silver nanoparticles by varying the amount of fruit extract from *Z. mauritiana*. The generated nanoparticles' antibacterial and antifungal qualities were then assessed, along with their possible impact on hair formation. Comparing the aqueous extractof

Z. mauritiana fruit to its ethanolic, methanolic, chloroform, and ethyl acetate extracts, it was found that the former's efficiency against Gram-positive bacteria was considerably greater. The gram-negative bacterial fungus species showed decreased sensitivity to silver nanoparticles (AgNPs). Several ratios of *Z. mauritiana* fruit extract were used in a study to create silver nanoparticles. Following this, the antibacterial and antifungal qualities of the produced nanoparticles were assessed in addition to their possible impacts on hair growth. When comparedto the ethanolic, methanolic, chloroform, and ethyl acetate extracts of *Z. mauritiana* fruit, the effectiveness of the fruit's aqueous extract mediated AgNPs against Gram-positive bacteria was demonstrated to be much greater. The fungus species that are members of the Gram-negative bacteria showed a decreased sensitivity to silver nanoparticles (AgNPs). The antibacterialactivity of as-synthesised silver nanoparticles was assessed against a variety of bacterial species, including Bacillus subtilis, Pseudomonas aeruginosa, Escherichia coli, and Staphylococcus aureus. A minimum inhibitory concentration (MIC) of 2.5 µg/ml demonstrated that the nanoparticles effectively inhibited the development of S. aureus. MIC of 5 µg/ml was themoderate inhibitory impact of the nanoparticles against E. coli[22].

Anti-Steroidogenic Activity

A research was conducted on female Sprague Dawley rats with artificially created polycystic ovaries to evaluate the beneficial effects of *Z. mauritiana* leaves on testosterone, estradiol, progesterone, LH hormones, blood glucose, and total cholesterol levels. The leaf extract of *Z. mauritiana* shown notable effectiveness in connection to the levels of several hormones and totalcholesterol. *Z. mauritiana* bark ethyl acetate extract possesses anti-steroidogenic properties The crude extract significantly increased the levels of ascorbic acid and cholesterol in the ovaries of mice given it, stopped the natural oestrus cycle in adult female mice at the oestrus stage, and significantly decreased the wet stress on the ovaries. The anti-fertility effect of crude extract was intended to be reversible; average estrus rotation and ovarian steroidogenesis were restored following the scheduled 27-day cessation of treatment with wheedle out[23].

Immunomodulatory

Immunomodulation is the term for the process of controlling and adjusting the immune response, which may entail increasing or decreasing the activity of the immune system. Immunostimulant treatment may improve both the innate and adaptive immune responses, strengthening the host's defences against infections. *Z. mauritiana* root extract was evaluated byAfzal et al. for its immunomodulatory, cytotoxic, and antioxidant capabilities. The results showedthat the root extract has these properties[24]. Mice were used to assess the immunomodulatory activity of *Z. mauritiana* aqueous-ethanolic seed extract. Different immunocytes were studied inhumoral and cell-mediated immune responses in mice immunised with sheep red blood cells (SRBCs). Similar to levamisole, the seed extract raised humoral immune response, cell-mediated immunity, and Th-1 cytokine IFN-γ while lowering Th-2 cytokine IL-4 at higher dosages[25]. Butleet al. isolated and purified lectin from *Z. mauritiana* seeds and used sheep blood cells to assess its immunomodulatory effect by lysosomal enzyme activity, phagocytic activity, XTT lymphocyte proliferation, and MTT cytotoxicity. Tripeptide constituted the purified lectin. At a maximal concentration of 200 µg/ml, the lectin demonstrated little cytotoxicity to sheep lymphocytes, with an effective dose of 12.5 µg/ml. In comparison to controls, lymphocyte proliferation rose significantly with

effective dosage, outpacing that of traditional mitogens such as LPS ($p<0.0001$) and Con-A. When macrophages were exposed to pure lectin (12.5 µg/ml), their phagocytic and lysosomal enzyme activity was higher than that of the control. There was nophagocytic or lysosomal enzyme activity in the atropine solution used as a negative control[26].

Anti-Diarrhoeal Activity

The concentration-dependent suppression of spontaneous pendular contractions in the rabbit jejunum and the inhibition of acetylcholine-induced contractions in the rat ileum were used to assess the antidiarrheal activity of the methanolic root extract. Using extract dosages of 25 and 50 mg/kg, an experimental investigation was carried out on mice to assess the effects ofgastrointestinal transit. The capacity of the extracts to prevent castor oil-induced fluid buildup and diarrhoea was investigated[27]. At dosages of 200, 400, and 800 mg/kg body weight, the aqueous leaf extract of *Z. mauritiana* was efficacious in preventing castor oil-induced diarrhoeain albino rats of the Wistar strain. The percentage inhibition was 51.05, 54.48, and 58.10%, respectively, and the amount of faeces dropped[28]. Using a mouse model, Ay et al. evaluated the antidiarrheal qualities of the methanolic crude extract made from *Z. mauritiana* leaves in theirstudy. Compared to the conventional medication loperamide (administered at a dosage of 50 mg/kg body weight), which demonstrated a reduction of approximately 67.24% in diarrhoea, the administration of a crude extract at a dosage of 400 mg/kg body weight resulted in a significant reduction in diarrhoea by approximately 52.02%[29].

Antioxidant Activity

The assessment conducted on *Z. mauritiana* included ascorbic acid concentration, total phenolics,flavonoids, and total antioxidant activity determination. The study's conclusions showthat ascorbic acid and total phenolics are present in large amounts in Indian jujube, with values ranging from 19.54 to 99.49 mg/100 g and 172 to 328.6 mg GAE/100 g, respectively[30]. The presence of polyphenolic compounds, which contribute to their antioxidant capabilities, can be linked to the significant DPPH scavenging activity of *Z. mauritiana* leaf extracts[31]. The pulp and leaves of *Z. mauritiana* have higher concentrations of several antioxidants and secondary metabolites; the pulp extract's antioxidant potential was demonstrated to be greater than that of the leaf extract[32]. The antioxidant activity of *Z. mauritiana* hydroalcoholic extracts wasexamined using 2,2-diphenyl-1-picrylhydrazyl and -carotene assays. The methanolic extracts derived from the pulp and leaves of this substance display a multitude of biologically active constituents and have significant antibacterial activity against a wide range of tested bacterial strains. When evaluating the primary and secondary oxidation products, it was demonstrated thatthe extract lowers the oxidation of soybean oil. Its antioxidative impact is enhanced as a result[33]. *Z. mauritiana* L. was shown to have antioxidant activity in a variety of in vitro techniques utilising ethanolic and hexane extracts, such as hydroxyl radical, DPPH radical, lipid peroxidation, and superoxide radical standardisation protocols. When compared to the ascorbicacid solution, the ethanol extract exhibits more antioxidant activity than the hexane extract. Itis thought that these active components, either acting alone or in combination, may be responsible for the documented antioxidant activity of certain plant species[34].

Positive Inotropic and Chronotropic

Good inotropic and chronotropic effects were shown by the aqueous extract of *Z. mauritiana* onthe heart of rats. The administration of propanolol as a pretreatment to the heart impeded these advantageous effects. It was hypothesized that *Z. mauritiana* possesses a restricted number of adrenomimetic compounds that are highly likely to exert their effects on the rat heart through theactivation of β adrenoreceptors[35].

Hepatoprotective

Shahnawaz et al. prepared silver nanoparticles loaded with biomolecules found in *Z. mauritiana*extract, followed by an assessment of the anticancer potential against hepatic cancer. The preventive effect of the aqueous extract derived from *Z. mauritiana* fruit was evaluated in relation to liver damage induced by CCL4. Different groups of rats were treated with either 250 or 500 mg/kg of fruit extract, or 100 mg/kg of silymarin (standard), prior to the administration of CCl4. Liver histology supported the findings. In silico investigations, major components of *Z. mauritiana* have demonstrated a significant affinity for the Rho family-alpha serine/threonine protein kinase. An anticancer assessment found that the synthesised nano formulation effectivelyreduces proinflammatory cytokines, oxidative stress, and tumour necrosis factor-, interleukin-6, interleukin-1, and nuclear factor kappa beta (NF-kB). However, minor abnormalities in the hepatic cells were found by the histological investigations[36]. Dahiru et al. examined *Z. mauritiana* leaf extract at 200 and 400 mg/kg bw in an alcohol-induced hepatotoxicity experiment that lasted six weeks. Rats given alcohol showed considerably greaterlevels of ALT, AST, bilirubin, and hepatic lipid peroxidation, but their glutathione, total antioxidantstatus, and body weight were lower than those of the control group. Rats were given an aqueous extract of *Z. mauritiana* prior to alcohol exposure, and this dramatically decreased ALT, AST, bilirubin, and lipid peroxidation. *Z. mauritiana* extract significantly improved overall antioxidant status and decreased glutathione in comparison to the alcohol-only group[37]. Z. mauriatiana alcoholicand ethyl acetate leaf extract is assessed by Dhananjay et al. for its ability to prevent hepatotoxicity caused by paracetamol. Total proteins were raised and elevated AST, ALT, ALP, and total bilirubin levels were decreased by ethyl acetate extract (400 mg/kg), ethanol extract (300 mg/kg), and standard (Silymarin). Ethyl acetate and ethanolic extract decreased inflammatory collection and removed lipid vacuoles in liver sections,

according to histopathological examinations[38].

Hypertension

Active flavonoids found in *Z. mauritiana*, such as tannins and saponins, are believed to heal glomerulosclerosis and reduce blood pressure spikes. Shown the ability of *Z. mauritiana* leaf extract to prevent glomerulosclerosis and lower blood pressure[39]. Mohebbati and colleagues assessed the effects of *Ziziphus jujuba* hydroalcoholic extract on cardiovascular responses in acute NG-nitro-L-arginine methyl ester (L-NAME) hypertensive rats. According to their results, long-term *Ziziphus jujuba* extract consumption, especially at the lowest dosage, mitigated the cardiovascular reactions brought on by L-NAME. These findings lead the authors to hypothesise that *Ziziphus jujuba* may be helpful in preventing nitric oxide (NO) deficiency-related hypertension[40]

Anxiolytic Activity

We evaluated the anxiolytic effect of *Z. mauritiana* leaf ethanolic extract using light and dark boxand raised pulse maze paradigms. Furthermore, the extract's possible effect on neurotoxicity was investigated using Rota-rod apparatus. The results of the studies offer support for the use of diazepam and extract from *Z. mauritiana*. The extract did not show any indications of neurotoxicity, according to the Rota-rod test findings. Thus, it can be seen that *Z. mauritiana* leafextract has anxiolytic qualities[41]. In mirrored chamber, raised plus maze, and light/dark models, Rakesh Kumar et al.'s study of the chloroform extract demonstrated a substantial anxiolytic effect at a level of 400 mg/kg. *Z. mauritiana* Lam. leaves have a chloroform extract that has anxiolytic properties. This action may be related to the plant's pentacyclic triterpenoid's propensity for binding $GABA_A$ receptors on the receptor site for benzodiazepines[42].

Thrombolytic Activity

Thrombolytics, sometimes referred to as clot-busting agents, are a family of pharmaceuticals usedto break up blood clots. Using an in-vitro and in-vivo animal model, Khokon et al.evaluated the pharmacological characteristics of methanolic seed and stem bark extracts of *Z. mauritiana* and discovered that the stem bark extract had more thrombolytic and anti- inflammatory potential[43].

Anti-Inflammatory Activity

Wistar rats were used to test the anti-inflammatory properties of the methanolic extract made from *Z. mauritiana* leaves using the cotton pellet-granuloma technique. The methanol extract of *Z. mauritiana* leaves inhibits the weight of cotton pellets in a dose-dependent manner. When the extract was given at a 500 mg/kg dosage, it showed a 31.1% protective impact against inflammation, whereas at a 250 mg/kg dosage, the protection rate was 16.9%[44]. The bioactivity of the *Ziziphus mauritiana* plant's methanol leaf extract is examined by Abdullah et al. The anti-inflammatory properties and activities were tested using the carrageenan-induced paw edoema technique. At a dosage of 400 mg/kg body weight of rats, the results demonstrated a71.83% decrease in inflammation[45]. The results of the study suggest that the aqueous extract obtained from *Z. mauritiana* root bark has a greater degree of efficiency in inhibiting the complement system. Following fractionation of the aqueous extract, a fraction demonstrating inhibitory activity against the complement system, COX-1, COX-2, and 5-LOX enzymes wasisolated. The RAW 264.7 cell line has been used to demonstrate the effectiveness of the *Z. mauritiana* active fraction in inhibiting the production of pro-inflammatory mediators, including TNF-α, COX-2, and iNOS. The active fraction showed protective properties against anaphylactic shock and the arthus response in vivo when given orally to Wistar rats on a regular basis. According to the results, there are notable anti-allergic and anti-inflammatory properties in the aqueous extract obtained from the separated fraction of *Z. mauritiana* root bark[46]. *Z. mauritiana* Lam leaves suppress the NFκB signalling pathway, which has anti-inflammatory capabilities against OVA-induced airway inflammation in mice and LPS-stimulated RAW 264.7 macrophages. At higher doses, *Z. mauritiana* reduced NO, ROS, and pro-inflammatory cytokinesin LPS-stimulated RAW 264.7 macrophages. It also reduced the expression of the ICAM,VCAM, and Muc5C genes. Mucus hypersecretion and decreased lung leukocyte infiltration were seen during the histopathological study. It did this by blocking p65-mediated IκB-α translocation in the NFκB, which decreased lung inflammation.

Analgesic Activity

The tail-flicking technique was used to test the antinociceptive effect of *Z. mauritiana* methanolextract. The distal section of the rats' tails—roughly 1-2 cm—were placed on the heat-emitting surface in order to quantify the animals' and rodents' reaction times to radiant heat. Reaction time increased somewhat with the extract; however, this was observed to vary on dose[47]. Acetic acid caused the mice to writhe, while an ethanolic bark extract from *Ziziphus mauritiana* show that significant inhibition of the activity at dosages of 250 mg and 500 mg/kg[48].

Wound healing Activity

Ziziphus mauritiana fruits ability to heal wounds and their antioxidant qualities were studied by Shady et al. Compared to both the untreated and conventional therapy groups, the extract significantly accelerated the healing process when given topically to excision wounds. TGF-1, VEGF, and Type I collagen expression were all upregulated in conjunction with this improvement, although TNF- and IL-1 levels were down. Because of its anti-inflammatory and antioxidant qualities, *Ziziphus mauritiana* may find application as a substitute treatment for wound healing[49].

Anti-asthmatic Activity

Mohan et al. evaluated the protective effects of *Z. mauritiana* Lam leaves against OVA-induced airway inflammation in mice and LPS-stimulated RAW 264.7 macrophages. Higher dosages of *Z. mauritiana* decreased pro-inflammatory cytokines, NO, and ROS in LPS-stimulated RAW 264.7 macrophages. It effectively reduced total and differential leukocytes as well as AHR at a dosage of 500 mg/kg. It also reduced the expression of the ICAM, VCAM, and Muc5C genes. Consequently, it decreased lung inflammation by blocking the NFκB signalling pathway's p65- mediated IκB-α translocation[50].

Anti-platelet aggregating activity

The use of *Ziziphus jujuba* seed ethanolic extract was utilised in the investigation of its impact on platelet aggregation generated by collagen, thrombin, and arachidonic acid (AA). The study'sfindings showed that the ethanolic extract of *Ziziphus jujuba* seeds and aspirin, a popular antiplatelet medication at a dosage of 300 µg/ml, both shown comparable effectiveness in the collagen and AA models. The ethanolic extract of *Ziziphus jujuba* seeds shown more efficacy thanaspirin in the thrombin-induced platelet aggregation paradigm. The aspirin exhibited anIC50 value of 325.9 ± 2.2, whereas the ethanolic extract had an IC50 value of 181.3 ± 1.6. The mice administered with an ethanolic extract made from *Ziziphus jujuba* seeds showed longer bleedingtimes and had a preventive effect against acute pulmonary thromboembolism. These results offer more proof of the extract's ability to prevent platelet aggregation[51].

Hair growth-promoting effect

The in-vivo method proved that *Z. jujuba* seed-derived essential oils might stimulate the growthof new hair. The application of 1% and 10% essential oils had better results than the control treatment in terms of hair length, weight, thickness, and relative area of hair follicle, according to an experimental research done on BALB/c mice[52]. Found that while comparing oils, the activity of 1% essential oil was higher than that of 10% essential oil.

Anti- Obesity

This study looks at the possible ability of *Ziziphus mauritiana* Lam bark powder (ZMBP) to reduceobesity in rats that have been fed a high-fat diet (HFD). After receiving ZMBP for 90 days, obese rats showed a reduction in body weight increase of 16.33% at 250 mg/kg and 17.38% (P<0.05) at 500 mg/kg when compared to the obese control group. When compared to the obese controlgroup (9.73+2.39 U/mg of protein), the activity of pancreatic lipase was seen tobe considerably lower in the groups supplied with 250 mg/kg (5.13+0.71 U/mg of protein) and 500 mg/kg (4.01+0.86 I/mg of protein). The inhibitory activity on pancreatic lipase is responsiblefor the observed antiobesity effect[53].

Preventive effect on memory score deficit

Lestari et al. looked at how *Z. mauritiana* Lam extract affected the hypertensive white rats' abilityto remember things after being exposed to NaCl and prednisone. When 800 mg/kg BW/day of NaCl and Prednisone were administered to white hypertensive Wistar rats, a significant preventative impact on memory score deficit was seen. discovered that administering jujube leaves extract (*Z. mauritiana* Lam) to white Wistar rats withhypertension prevented theirmemory score deficit. To ascertain the possible anti-amnestic qualities of extracts from *ziziphus mauritiana* L. leaves, Gajbhare et al. carried out a pharmacological evaluation in a follow-up investigation. According to the study, the leaf extract significantly affected the rats' cognitive abilities, particularly with regard to learning and memory[54]

Cholesterol-Lowering Activity

Lailatusholihah et al. looked at the impact of decreasing cholesterol. On the basis of the results, ithas been noted that the methanol extract made from *Ziziphus mauritiana* (Bidara leaf) extract significantly lowers cholesterol levels—by around 80.45%. The existence of many active secondary metabolites, including as flavonoids, tannins, and triterpenoids, is responsible for thisimpact[55].

Conclusion and future perspectives

One important species in the forestry area is *Z. mauritiana*. The aforementioned tree provides leaves for fibre, fuel, charcoal, and feed, among other uses. The *Z. mauritiana* plant has several medicinal qualities, including anti-inflammatory, anti-cancer, antidiabetic, anti-ulcer, antioxidant, and thrombolytic activity. It also shows promise in the treatment of a number of illnesses. The plant's great potency can be attributed to the presence of flavonoids, alkaloids, saponins, terpenes, and other medicinally active compounds. The literature review establishes that the plant holds significant importance and use in the field of medicinal plants, with potential for extensive future applications.[56]

Not only does it have biological properties and is used as food, but it also benefits society economically. Bioactive substances found in *Z. mauritiana* have a variety of biological effects. This plant species also has a high content of important nutrients including proteins and carbs, which improves its nutritional profile. Pharmacological investigations have provided evidence for the traditional usage of *Z. mauritiana* by establishing a link between the biological activity and secondary metabolite composition of the plant and its ethnopharmacological applications. The precise mechanisms of action, however, have not been studied.

Using pharmacological tests to investigate the safety of *Z. mauritiana* is an important and required undertaking, even though consumers of this medicinal species have not reported experiencing any negative effects. Given this, we would like to invite research teams to performthorough

toxicological analyses on *Z. mauritiana* in order to verify its safety.

Key findings

431 chemical components of this genus have been identified through phytochemical studies. Thetwo primary classes are flavonoids and cyclopeptide alkaloids. For both in vitro and in vivo applications, the crude extracts and separated compounds exhibit antibacterial, antitumor, antidiabetic, antidiarrheal, anti-inflammatory, antipyretic, antioxidant, and hepatoprotective qualities. Toxicity studies suggest that Ziziphus species is safer at therapeutic levels.

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