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A systematic review on *Ziziphus mauritiana*

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Abstract

Ziziphus is a genus from the Rhamnaceae family. *Ziziphus mauritiana* is a species of *Ziziphus* mainly found in Afghanistan, Malaysia, Algeria, Nepal, Egypt, Pakistan, Southern Africa, Kenya, Japan, Australasia, Brazil, and India. It is commonly known as Ber, Kul, Bogori, Bera, Jangri, Vadari, and Regu. This plant consists of various chemical constituents including alkaloids, flavonoids, terpenoids, saponins, phenolic acid, quinones, tannin, and chlorogenic acid. These plants have lots of traditional activities such as diarrhea, wounds, asthma, constipation, sleeplessness, urinary diseases, abscesses, gastrointestinal disorders, peptic ulcers, skin diseases, fever, liver diseases, and abdominal pains. Pharmacological activities of *Ziziphus mauritiana* are antioxidant, anti-inflammatory, anti-diabetes, anti-fungal, anti-diarrheal, anticancer, anti-plasmodial, anti-microbial, immunomodulator, antifertility, hypotensive, antinephritic, antispastic, and hepatotoxicity. The ultimate target of this paper is to convey all the relevant data related to this plant till now.

Keywords: *Ziziphus mauritiana*, phytochemical, pharmacological activities, traditional activities

Introduction

The word ziziph on is used to describe jujube and is related to the Arabic name *Ziziphus*. There are several additional names for it, including bell, jujube, Indian cherry, dessert apple, Indian plum, ber, and Chinese apple (IM *et al.*, 2017) [3]. The genus *Ziziphus* is a relatively widespread plant found all over the world. The tropical shrub *Ziziphus mauritiana* is indigenous to Southeast Asia, the Indian subcontinent, Iran, and Africa. *Ziziphus mauritiana* Mill. (The Chinese jujube) and *Ziziphus mauritiana* Lam. (the Indian jujube) are main domesticated jujubes. These species have been cultured all throughout the world. *Ziziphus mauritiana* yields fruits from February to March with red color and more luscious flesh, similar to litchi. Several parts of *Ziziphus mauritiana* are utilised for medical and nutritional purposes. It offers several health benefits, including anti-cancer, anti-diabetic, anti-microbial, antioxidant, anti-diarrheal, hepatoprotective, and anti-asthma properties. Carbohydrates, carbs, mucilages, proteins, sugar, and vitamins are abundant in the *Ziziphus mauritiana*.

Other species

- *Ziziphus jujuba* Lam.
- *Ziziphus quadrilocularis*
- *Ziziphus jujuba* (Chinese jujube)
- *Ziziphus lotus* Lam
- *Ziziphus parryi* Torr
- *Ziziphus xylopyus*
- *Ziziphus rotundata* D.C.
- *Ziziphus abyssinica* Hochst.
- *Ziziphus joazeiro*
- *Ziziphus talanai*

Common names

Rajabadari (Sanskrit); Bogari (Kannada); Kul, Ber, Boroi (Bengali); Vadari (Tamil); bor (Gujarati); Beri (Punjabi); Ber (Hindi); Bar, bera (Marathi); Bodori (Uriya); Badaram (Malayalam); Regu (Telugu); Ber (Urdu); Bozoi, Kool, Kul (Bangladesh); Jangri (Sindhi);

Oriya (Barkoli, Bodokoi, Bodori); Bogori (Assamese); Azufaifo, Yuyuba (Spanish); Ber (Himachal Pradesh), Bidara, Dara, Widara (Indonesia); Berra (Afghanistan).

Morphology and Distribution

Ziziphus mauritiana is a spiny, evergreen shrub with a trunk diameter of 40 cm. It has the capacity to grow up to 15 metres tall. Its bark has a dark grey color. The leaf color ranges from light green to dark green; the leaf length is 4.9-12 cm; the leaf width is 3.6-6 cm; the leaf shape is oblong, circular; the leaf base is broad, circular, oblique, obtuse, narrow; the petiole length is 1-3 cm; the leaf top is circular, obtuse, flat, and the leaf area is 15-60 cm (Muhammad *et al.*, 2013)^[41]. The sepals of flowers are dorsally tomentose, styles are 2mm long. Flowers have an unpleasant odor. Flowers are tiny, greenish-white or yellow, hermaphrodite, and found in sessile or short-peduncled auxiliary cymes. During flowering, pedicels are 2-4 mm long and 3-6 mm long during fruiting (Mahajan *et al.*, 2009)^[13]. The fruit shape varies from round to oval and its weight varies from 3.8 to 39.5 g.

Z. Mauritiana is inborn with wild temperate climates in India, Algeria, Afghanistan, Kenya, Malaysia, South Asia, Pakistan, Africa, Japan, Egypt, Nepal, Eurasia, America, Australia, and the Pacific Islands. This plant is also available in Madhya Pradesh, Rajasthan, Punjab, Bihar, Himachal Pradesh, Tamil Nadu, Maharashtra, and Uttar Pradesh. Ber cultivars have produced promising germplasms by unique characteristics, including required adaptation (Thar Sevika, Gola, Thar Bhubhraj, Umran,), varied quality characters (Illaichi, Banarasi, Karaka,), stable and tall yield (Seb, Ponda).

Taxonomical classification

- Family-Rhamnaceae
- Species-*Ziziphus mauritiana* (Indian jujube)
- Class-Dicotyledonae
- Genus-*Ziziphus*
- Kingdom-Plantae
- Phylum-Spermatophyta
- Subphylum-Angiospermae
- Order-Rhamnales
- Domain-Eukaryote

Parts used: Bark, Leaf, Fruits, Seed, Root.



Fig 1: Whole Plant



Fig 2: Flower



Fig 3: Leaf and fruit

Phytochemical Constituents

Alkaloid

Alkaloids are found in all parts of the plant. Mainly stem of *Ziziphus mauritiana* contains alkaloid. Mauritine-A, mucronine, mucronine-D, nummularine-A and B, sativanine-B, and amphibine-H are among the ring structure peptide alkaloids found in the stem. Isoboldine, asimilobine, iusiphine, norisoboldine, Coclaurine, and iusirne are chemicals found in Leaves. Ring structure peptide alkaloids are polyamidic compounds having a side chain. The nature of side chain can be basic or neutral depending on the presence of a terminal nitrogen atom. They have a ring with 13, 14, or 15 members. The ziziphine-A type and nummularine-C type are two of the 13-membered cyclopeptide alkaloids. Frangulanine-B, integerrine, amphibine-F, aduotine-Z, pandamine, amphibine-B are some of the 14-member ring alkaloids. The 15-member ring alkaloid is a mucronine-A. Benzoylhypaconine, Coclaurine, Dauricoline, Ephedradine C, Magnoflorine, Neojiangyouaconitine, Nortropanoline, 14-Benzoylaconine, Lirioferine, Ephedradine C, Gentianamine, and Sanjoinine A are all present in *Ziziphus mauritiana* fruit. They show antimicrobial, anti-inflammatory, anti-infectious, antiplasmodial, antidiabetic, sedative, anticonvulsant, and antioxidant properties.

Flavonoids

Flavonoids are the next essential chemicals present in *Ziziphus* species. Many flavonoids have been isolated from fruits and seeds including 6-feruloylspinosin, pigenin-6-C- β -D-glucopyranoside, Puerarin, Isospinosin, Kaempferol 3-O-

robinobioside, Isovitexin-O- β -D-glucopyranoside, Quercetine-3-O-robinobioside, 6-feruloylisosposin, Quercetine-3-O-rutinoside, Kaempferol 3-O-rutinoside and zivulgarin (Mahajan *et al.*, 2009) [13]. From the leaves of *Ziziphus mauritiana* nine phenolic acids are extracted such as vanillin, hydroxybenzoic acid, vanillic acid, chlorogenic acid, caffeic acid, protocatechuic acid, ferulic acid, ortho and paracoumaric acids, were recognized and quantified. Cyanidin3, 5-diglucoside, Gallocatechin Isoetin-7-O-D, Licurazide, Nelumboside B, glucopyranosyl-2'-O-D-xylopyranoside, Quercetin-3-gentiobioside, and Quercetin rhamnogentiobioside are all found in the fruit juice. The methanolic extract of *Ziziphus mauritiana* fruit contain maximum amount of flavanoids instead of other constituents.

Terpenoids

Triterpenoids are one of the plant's most important active ingredients. The main terpenoids are colubrinic acid, maslinic acid, alphitolic acid, oleanolic acid and triterpene saponin. *Z. Mauritiana*, *Z. spina* Christi, and *Z. jujuba* fruits, seeds, leaves, and flowers have yielded 43 terpenoids. Several investigations have discovered that terpenoids derived from *Ziziphus mauritiana* have anti-inflammatory, antimicrobial, cyclooxygenase-2 inhibitory, antiplasmodial, antimycobacterial, anti-complementary, and cytotoxic activities. Betulonic acid, Ganoderic acid, Istanbulin, Ecliptasaponin B, Coumaticacid, Ginsenoside Rh4, Lactiflorin, Phytolaccagenin, Poricoic acid, Qinghaosu, and Sweroside are all found in *Ziziphus mauritiana* fruit juice.

Another investigation discovered three new therapeutic substances from roots of *Ziziphus mauritiana* such as Zizimauritic acids A, B, and C. Nor-triterpenes with a distinct A-nor-E-seco spiro-lactone ceanothane-type triterpene skeleton, as well as three known triterpenes, betulinic acid, ceanothic acid and ceanothenic acid were identified in *Z. Mauritiana* roots.

Saponin

From *Ziziphus mauritiana* seed, saponins are extracted include jujubosides A, B, A1B1, C, the protojujubosides A, B, B1 and acetyljujuboside B. Most of the known biological activities of *Ziziphus* are attributed to these polyphenols, which include hemolytic, antibacterial, insecticide, cholesterol control, anticancer activity, anxiolytic and sweetness inhibiting qualities, calmodulin inhibitors, and molluscicide action. The seed, fruit and leaves parts of *Z. Mauritiana*, *Z. jujuba* and *Z. spina* christi contain about 31 saponins (Mahajan *et al.*, 2009) [13].

Steroids, Cholinergic acid, Cerebroside, Nucleoside /Nucleobase, Phenolic, Tanin, Volatile oil, Emodins, Quinones, Resins, Carboxylic acid (Dahiru *et al.*, 2006) [23].

Traditional uses

Diarrhea, wounds, Asthma, Fever, Sleeplessness, Urinary diseases, scabies, Peptic ulcer, Abscesses, Skin disease, heartburn, Liver diseases, Constipation, diuretic, biliousness, Gastrointestinal disorders, astringent, nausea, and Abdominal pains.



Fig 4: Pharmacological effects of *Ziziphus mauritiana*

Anti-Inflammatory

Ziziphus mauritiana's fruit, leaf, and seed all have anti-inflammatory properties. Huang q in tang first recommended fruit for this activity. This plant's leaf extract in methanol exhibits anti-inflammatory properties against carrageenan-induced paw edema at 200-400 mg/kg given orally. Adipocyte differentiation and glucose absorption experiments in Wistar rats were utilized to assess the anti-inflammatory activity of the chloroform and aqueous extracts of *Ziziphus mauritiana* bark. When given orally to rats, chloroform extract at a dosage of 200 mg/kg was found to have anti-inflammatory properties. When tested using IC50 values, the root bark's aqueous extract inhibited 5-

LOX-2, and COX2 (Cyclooxygenase 2) more effectively. Results show that the MAF, an aqueous extract of *Z. mauritiana*'s root bark, has strong anti-allergic and anti-inflammatory activities. This plant does not show any side effects like ulceration or bleeding which is common in NSAIDs. The anti-inflammatory effects of *Ziziphus mauritiana* also prevent inflammations caused by 5HT and histamine.

Antioxidant effect

Antioxidant mean-against oxidation. An antioxidant is chemical that prevents the oxidation of free radical. A substance with one or more unpaired electrons in its outer

orbital is referred to as a free radical. They are responsible for many diseases such as Cerebrovascular, Cancer, Arteriosclerosis, Atherosclerosis, Senility, Aging), Gastrointestinal Ulcerogenesis, Cystic Fibrosis, Behcet's Disease, Hemorrhagic Shock, Crohn's disease, Cataracts, Sunburn, Ulcers, Osteoporosis, Diabetes Mellitus, Emphysema, Rheumatoid Arthritis, Cardiovascular Disorders, Neurodegenerative Diseases (e.g. Parkinson, Alzheimer's, Huntington's disease, AIDS (Bhuiyan *et al.*, 2009) [34]. *Ziziphus mauritiana's* antioxidant action can be used to cure all of the diseases listed above. Researcher from Burkina Faso stated that polyphenols are present in this plant. Polyphenols were responsible for 98.63% reduction of DPPH (diphenyl-2-picryl hydrazyl free radical) and serve an important role in mediating the antioxidant function by scavenging free radicals in *Ziziphus mauritiana*. Methanolic extract of *Ziziphus mauritiana* increased its inhibitory action with increase in concentration when tested for DPPH radical scavenging activities. The antioxidant activity of *Ziziphus mauritiana* leaf extracts in various solvents was evaluated using various methods. By DPPH assay, the ethanol extract had the highest activity, with an IC50 of 19.44 0.79 g/ml, compared to standard ascorbic acid. Result show that antioxidant activity of *Ziziphus mauritiana* due to flavonoids and phenolic acid (Lekha *et al.*, 2020). Some phyto-constituent in this plant also show brilliant activity when tested using Cupric reducing Antioxidant capacity assay (CUPRAC) and Ferric-Reducing Antioxidant Power assay (FRAP). The FRAP assay was performed by Benzie *et al.*, (1996) and the CUPRAC assay was performed by Apak *et al.*, (2004). The leaf extract of this plant show better activity than the stem and bark extract. A Researcher from Niger also stated that Ethanol and hexane leaf extract show very prominent free radical scavenging activity (Abalaka *et al.*, 2009) [27]. The result of Bhuiyan showed that ethanolic extracts of the fruit of *Zizyphus mauritiana* (Local and Narikeli kul) showed potential free-radical scavenging activity.

Antidiabetic activity

Diabetes is a major public health issue that affects large populations all over the world. It raises the risk of various diseases, including atherosclerotic and nephrotoxicity. The *Ziziphus mauritiana* has less side effect instead to all other synthetic drugs like sulfonylureas, thiazolidinediones, biguanides, α -glucosidase inhibitors and meglitinide derivatives. The researchers tested antihyperglycemic effect of many extracts such as chloroform, crude aqueous, petroleum ether, ethanol, and acetone of *Zizyphus mauritiana* fruit on rats at 200 and 400 mg/kg. The non-polysaccharide fraction of *Ziziphus mauritiana* aqueous and aqueous extract showed significant anti-hyperglycemic effects. The administration of *Ziziphus mauritiana* seed extract to rats lowered glucose tolerance in both normal and diabetic mice. Single doses of *Ziziphus mauritiana* seed extract (100, 400, 800 mg/kg), glyburide (anti-diabetic medicine) (10 mg/kg), and the combination of both significantly lower blood sugar levels at 2, 4, and 6h. At 2 hours, the combination of both had an antihyperglycemic impact and reduced glucose levels more effectively than glyburide alone. According to the study, bark extract reduced blood glucose levels by a greater percentage than seed extract at both doses. This plant shows an anti-diabetes effect in a dose-dependent manner.

Anticancer activity

Cancer is characterized by uncontrolled cell proliferation. Lung cancer, liver cancer, stomach cancer, breast cancer and colorectal cancer are the most frequent cancers. Using doxorubicin as a reference, the dichloromethane root extract of this plant revealed significant anticancer activity with an IC50 of 20.340.9. Anticancer activity was also determined by using the MTT assay to examine cell viability. MTT [3-(4, 5-Dimethylthiazol-2-yl)-2, 5-Diphenyltetrazolium Bromide] assay was used to measure the metabolically active mitochondria of intact cells. According to the MTT assay, *Ziziphus mauritiana* has high action against hela cancer (cervical carcinoma malignancy). According to the graph, *Ziziphus mauritiana* shows more anticancer activity than other species of *Ziziphus*. This plant inhibits HL-60, Molt-4, and Hela with IC50 values of 20 g/mL and 40 g/mL. This plant extract has no substantial inhibitory effect on the Normal human gingival fibroblast cell line. Researcher Aisha Ashraf uses a bench-top potato disc experiment to test the anticancer activity of hexane, methanol, and chloroform leave extracts of *Ziziphus mauritiana* against *Agrobacterium tumefaciens* which is a plant pathogen. This is mainly responsible for the induction of neoplastic disease (Crown gall tumor) in dicotyledonous plants. Researchers observed that tested solvent extracts significantly reduced *A. tumefaciens* proliferation and had anti-tumor efficacy. The study of Chan *et al.* and Shin *et al.* shows that *Ziziphus mauritiana* has activity against hepatocellular carcinoma and gastric cancer.

Anxiolytic activity

Anxiety condition can be cured with certain medications like benzodiazepine and cognitive-behavioral therapy. Benzodiazepines are most given drugs for anxiety treatment. However, Benzodiazepine use has been restricted due to potential side effects such as sleepiness, dizziness, confusion, disorientation, amnesia, breathing difficulties, and loss of balance. As a result, researchers' focus has switched to novel medications with no harmful effects. The *Z. Mauritiana* Lam. leaves contain alkaloids, saponins, flavonoids and tannins as major chemical constituents and it shows good anxiolytic activity than diazepam. The ethanolic extract of *Ziziphus mauritiana* leaf shows better activity at 50,100,200 mg/kg dose on albino rat. The *Z. Mauritiana* treated animals spend extra time in open arms (Elevated plus maze) and bright area (Light Dark box) than diazepam treated animals.

Anti-microbial activity

The crude extract of jujube fruit demonstrated a positive antibacterial impact on gram-positive and gram-negative bacteria and fungus, suggesting that this fruit has stronger antimicrobial characteristics than standard antibiotics such as vancomycin. This fruit extract also shows good activity in pediatric infection. The ethanolic extract of *Ziziphus mauritiana* leaves shows antimicrobial activity against many bacterial strains such as *Klebsiella pneumonia*, *Staphylococcus aureus*, *Staphylococcus aureus epidermidis*, *Escheichia coli* and *Salmonella Dublin*. The different seed extract of *Ziziphus mauritiana* such as ethyl acetate, acetone, ethanol, methanol, chloroform, pet-ether and distilled water of *Ziziphus mauritiana* shows activity against six micro-organisms. *Aspergillus flavous*, *Pseudomonas fluorescence*, *Candida albicans*, *Bacillus subtilis*,

Escherichia coli and *Xanthomonas oryzae* are six different bacteria. The ethyl acetate extract of seed demonstrate highest activity on these micro-organism. The *Ziziphus mauritiana*-AgNPs were discovered to be selective against *S. aureus*, a gramme positive bacterial strain.

Conclusion

In recent years, many pharmaceutical drugs are innovative from herbal plants. Herbal plants play a very important role in drug discovery. *Ziziphus mauritiana* is the best herbal plant which is mainly located in desert and wild temperature areas. It is commonly known as Ber, Bera, etc. This plant's entire part is high in phytochemical compounds. These phytoconstituents have many traditional and pharmacological effects which are present in this review article.

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Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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