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REVIEW ARTICLE

Ziziphus Jujuba: A Phytopharmacological Review

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ABSTRACT

In the last few decades there has been an exponential growth in the field of Herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects. One such medicinal plant is *Ziziphus jujuba* Mill, a member of the family Rhamnaceae, commonly known as Bor, grows mostly in Europe, southern and eastern Asia, and Australia, especially the inland region of northern China. Jujuba has a long history of usage as a fruit and remedy. The main biologically active components are vitamin C, phenolics, flavonoids, triterpenic acids, and polysaccharides. It is used traditionally as tonic and aphrodisiac and sometimes as Hypnotic-sedative and Anxiolytic, anticancer (Melanoma cells), Antifungal, Antibacterial, Antiulcer, Anti-inflammatory, Cognitive, Antispastic, Antifertility/contraception, Hypotensive and Antinephritic, Cardiotonic, Antioxidant, Immunostimulant, and Wound healing properties. The aim of this paper is to scrutinize the available literature related to the restorative activity of the ber plant as an herbal medicine on mammalian physiology and to accumulate those scientifically valid data in a nut shell in the form of a mini review.

KEYWORDS

Ziziphus Jujuba, Pharmacology, Phytochemical Constituents, Herbal Medicine

INTRODUCTION

Various species of Ziziphus are used medicinally in India, China and Japan. The plant *Ziziphus jujuba* is also known as Ber, jujube. It taxonomically belongs to the family Rhamnaceae. The *Ziziphus jujube* Pers. mostly found almost all parts of areas.[1] The leaves used for hypoglycemic effects, reduction of sweetness judgements, as diuretic, emollient, expectorant, to promote hair growth, anticancer, sedative, blood purifier and in treatment of diarrhoea.[2,3,4] Fruits used as liver tonic, as an antioxidant, hepatoprotective, protective effect, weight gain, increases stamina and reported to have anticancer effects.[5,6,7,8,9]

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Chemically, *Ziziphus jujuba* contains Flavonoids, Saponins, tannins, Vitamin A, Vitamin B, sugars, mucilage, calcium, phosphate & iron. The pulp contains moisture, protein, fat, carbohydrate, calcium, phosphorus, iron, carotene, thiamine, riboflavin, Vitamin C. Ground seeds on extraction with petroleum ether gave 33% of bright yellowish oil. Fatty acid composition of the oil contains oleic acid-71.7%, Linoleic acid- 15%.[10] *Ziziphus jujube* fruits are very rich in vitamins C and B1 and B2.[11] Compared with other edible fruits, one fruit of ber per day would meet the diet requirements for vitamin C and vitamin B complex for an adult man as recommended by FAO/WHO.it is also known to have a high vitamin P content. It enhances the action of vitamin C. presence of Pectin-A in *Ziziphus jujube* fruit is also reported.[12] The aim of

present article is to explore the medicinal importance of the plant *Ziziphus jujuba*.

Morphology

Jujubes are species of the genus *Ziziphus* Tourn. ex L. *Zijihus* belongs to the family Rhamnaceae named after the genus *Rhamnus*. The Rhamnaceae have fruits which are drupes or are dry and are closely related to another family, Vitaceae, which includes major economic species whose fruits are berries. The name *Ziziphus is* related to an Arabic word and ancient Greeks used the word ziziphon for the jujube. There are two major domesticated jujubes, *Z. mauritiana* Lam. the Indian jujube or ber, and *Z. jujuba* Mill. The common jujube. These two species have been cultivated over vast areas of the world. The species has a wide range of morphologies from shrubs to small or medium sized trees which might be erect, semi-erect or spreading. Height can vary from 3-4 to 10-16 m or more although trees of 20 m are rare. Trees are semi deciduous and much branched. The bark has deep longitudinal furrows and is greyish brown or reddish in color. Usually the shrub or tree is spinous, but occasionally unarmed. Branchlets are densely white pubescent, especially when young and tend to be zigzag. Branches spread erect, becoming flexuous and dull brown grey. Fruiting branches are not deciduous. Leaf laminae are elliptic to ovate or nearly orbicular. The apex is rounded, obtuse or sub-acute to emarginated, the base rounded, sometimes cuneate, mostly symmetrical or nearly so. Margins are minutely seriate. There are 3 marked nerves almost to the apex, the nerves being depressed in the upper, light or dark green, glabrous surface. Lower surface is whitish due to persistent dense hairs but may be buff colored. Occasionally the lower surface is glabrous. Leaves are petiolate 1.1-5.8 mm long and stipules are mostly spines, in each pair one hooked and one straight, or both hooked, or more rarely not developed into a spine. Flowers have sepals which are dorsally tomentose, a disk about 3 mm in diameter and a 2-celled ovary, immersed in the disk. Styles are 2, 1 mm long and connate for half their length. Flowers tend to have an acrid smell. Flowers are borne in cymes or small axillary clusters. Cymes can be sessile or shortly pedunculate, peduncles 1-4 mm tomentose. Pedicels are also tomentose and are 2-4 mm at flowering and 3-6 mm at fruiting. Fruit is a glabrous globose or oval edible drupe varying greatly in size from (1-) 1.5 (-2) cm diameter but some oval varieties can reach 5 x 3 cm. The pulp is acidic and sweet, the fruit greenish yellow or sometimes reddish.[13]

Figure 1: Plant

Figure 2: Fruit

Vernacular Names

Rajabadari (Sanskrit); Beri (Punjabi); Kul (Bengali); Bogori (Assamese); Bodori (Uriya); Bordi (Gujarati); Ber (Hindi); Bor (Marathi); Badaram, (Malayalam); Bogari (Kannada); Vadari (Tamil); Renu (Telugu); Ber (Urdu); Jangri (Sindhi)

Taxonomical Classification

Kingdom: Plantae

Division: Magnoliophyta

Class: Magnoliopsida

Order: Rosales

Family: Rhamnaceae

Genus: *Ziziphus*

Species: *jujuba*

Medicinal Uses

There are large numbers of traditional medicinal uses that are not necessarily based on knowledge of the constituents. According to Ayurveda, the root of *Z. nummularia is* bitter and cooling, and cures coughs, biliousness and headache.[14] The bark cures boils and is good for the treatment of dysentery and diarrhea.[15] The leaves are antipyretic and reduce obesity. The fruit is cooling, digestible, tonic, aphrodisiac, laxative and removes biliousness, burning sensations, thirst, vomiting[16] and is also good in treating tuberculosis and blood diseases. The seeds cure eye diseases and are also useful in leucorrhoea.[17] The traditional workers of Chhattisgarh, India use fruit to treat common fevers and for vomiting use the seeds with bar sprouts *(Ficus benghalensis)* and sugar. The traditional healers of Bastar region use the dried leaves and powdered bark to dress wounds.[15] The fresh leaves are also used for the same purpose. The aqueous paste of the leaves is applied externally to relieve a burning sensation. Roots are used to treat dysentery; they are given with cow's milk until the patient is cured. Senior citizens used the fresh leaf juice with buffalo's milk to reduce the intensity of smallpox. Similarly, in the early days, the use of seeds to treat eye troubles was common. To treat hoarseness of the throat, traditional healers advise patients to keep the fresh roots of this plant inside their mouth. The traditional healers use the fresh leaves of this plant with cumin to treat urinary infections.[17] The fruit is employed as an antidote to aconite poisoning, abdominal pain in pregnancy and externally in poultice and applications for wounds. The kernels increase flesh and strength and are sedative in activity.[18]

Phytochemical Constituents

Alkaloids

Alkaloids are distributed in all parts of plant. Stem bark of *Ziziphus* species contain alkaloids.[19] A sapogenin, zizogenin has been isolated from Z. *mauritiana* stems.[20] The cyclic peptide alkaloids, mauritine-A, mucronine-D, amphibine-H, nummularine-A and -B, sativanine-A and sativanine-B, frangulanine, nummularine-B and mucronine were isolated from the bark of *Za jujuba* by.[21] The cyclic peptide alkaloids sativanine-C, sativanine-G, sativanine-E, sativanine-H, sativanine-F, sativanine-D and sativanine-K isolated from Z. *jujuba* stem bark.[22] The alkaloids coclaurine, isoboldine, norisoboldine, asimilobine, iusiphine and iusirine were isolated from *Z. jujuba* leaves by.[23] Cyclopeptide and peptide alkaloids from *Z. jujuba* were found to show sedative effects.[24] The seeds of *Z. jujuba* var. *spinosa* also contain cyclic peptide alkaloids sanjoinenine, franguloine and amphibine-D and four peptide alkaloids; sanjoinine-B-D-F and -G2.[25] The seeds are used in Chinese medicine as a sedative. Chemical studies of *Z. mauritiana* led to the isolation of the cyclopeptide alkaloids, mauritines A and B; C-F, G and H, frangufoline; amphibines D, E, B and F; hysodricanin-A, scutianin-F and aralionin-C.[21] The cyclopeptide alkaloid, mauritine J, was isolated from the root bark of *Z. mauritiana*.[26] For the first time[21] reported six Cyclopeptide alkaloids isolated from the stem bark of *Z.jujuba* are Mauritine-A; Amphibine-H; Jubanine-A; Jubanine-B; Mucronine-D and Nummularine-B. Latter[22] reported Sativanine-E. Antibacterial peptide alkaloid Frangufoline from Ziziphus species was reported.[27] Han and co-workers reported Melonovine-A; Franganine; Frangulanine; Daechuine-S3; Daechuine-S6; Nummularine-A and Nummularine-R, all are cyclopeptide alkaloids.[25] Four cyclopeptide alkaloids from the stem bark *Z.jujuba*, which are Scutianine-C; Scutianine-D; Jubanine-C and Ziziphine-A reported.[28] Two reports appeared in the literature on isolated ingredients from the root bark of *Z.jujuba*. Adouetine-X and Frangulanine which are active (sedative) ingredient cyclopeptide alkaloids isolated and characterized.[29]

Glycosides

The structure of spinosin (2"-O- beta -glucosylswertisin) extracted from *Z. jujuba* var. *spinosa* seed.[30] They later identified three acylated flavone-Cglycosides (6"'-sinapoylspinosin, 6"'-feruloylspinosin and 6"'p-coumaroylspinosin), pharmacologically they

have sedative activity in rats. Different parts of Z. jujube that is seeds, leafs and stem contain glycosides.

Saponins

The saponins isolated from the seeds of *Z .jujuba* include jujubosides A, B[31], A1 B1 and C and acetyljujuboside B[32] and the protojujubosides A, B and B1[33]. Kurihara *et al.* extracted the saponin, ziziphin, from the dried leaves of *Z. jujube.*[34] It has a structure, 3-O - a - L- rhamnopyranosyl (1-2) - a - arabinopyranosyl 20- O- (2,3)- di - O- acetyl - a - L - rhamnopyranosyl jujubogenin. Ikram *et al.* isolated a saponin from *Z .jujuba* leaves and stem. It was assigned the structure 3-O- ((2-O- alpha - D - furopyranosyl - 3-O- beta - D - glucopyranosyl) - alpha - L - arabinopyranosyl) jujubogenin.[35]

Flavonoids

Sedative flavonoids such as Swertish and spinosin were isolated and reported by Gong et al.,from fruit and seeds of *Z.jujuba.* Puerarin; 6'''-feruloylspinosin; Apigenin-6-*C*-b-D-glucopyranoside; 6'''-feruloylisospinosin; Isospinosin and Isovitexin-2''-*O*-b-D-glucopyranoside these flavonoids isolated and reported by Gong, et al.[36]. Ten flavonoids were reported by Pawlowska et al.,[37] are Quercetine 3-*O*0-robinobioside; Quercetine 3-*O*-rutinoside; Quercetine 3-*O*-α-L-arabinosyl-(1→2)- α -L-rhamnoside; Quercetine 3-*O*-b-D-xylosyl-(1→2)- α -L-rhamnoside; Quercetine 3-*O*-β-D-galactoside; Quercetine 3-*O*-β-D-glucoside; 3',5'-Di-C-β-D-glucosylphloretin; Quercetine 3-*O*-β-D-xylosyl-(1→2)- α -L- rhamnoside-4'-O-a-L-rhamnoside; Kaempferol 3-Orobinobioside and Kaempferol 3-O-rutinoside.

Some of the representative flavonoids are described by Gong et al.[36]. Discovered a new flavonoid, named zivulgarin, compound.

Terpenoids

The triterpenoic acids have been isolated from the fruits of Z. *jujuba:* some of them are colubrinic acid, alphitolic acid, 3-Ocis-p-coumaroylalphitolic acid, 3-O-transp-coumaroylalphitolic acid, 3-O-cis-p-coumaroylmaslinic acid, 3-O-trans-pcoumaroylmaslinic acid, oleanolic acid, betulonic acid, oleanonic acid, zizyberenalic acid and betulinic acid.[38] Triterpenoic acids have also been extracted from roots of Z. *mauritiana.*[39] Betulin; Betulinic acid; Ursolic acid; 2α-hydroxyursolic acid and Ceanothic acid are triterpenes reported by Shoei et al.[40]. Some of them have anticancer and anti-HIV properties. Sang et al.[41] demonstrated three triterpene esters viz. 2-*O*-protocatechuoyl alphitolic acid, Caffeoyl alphitolic acid and Ceanothic aciddimethyl ester.

Phenolic Compounds

Recently Pawlowska et al.,[37] reported phenolic compounds from the fruit of *Z. jujuba,* without citing any biological activity. Betulinic acid is widely distributed in all parts of plant. It is a naturally occurring pentacyclic triterpenoid which has demonstrated selective cytotoxicity against a number of specific tumour types. It has been found to selectively kill human melanoma cells while leaving healthy cells alive. In addition, betulinic acid has been found to have antiinflammatory activity[42] and antibacterial properties and inhibits the growth of both *Staphylococcus aureus* and *Eschericheria coli*[43].

Pharmacological Activities

Table 1: Report on pharmacological activities

Activity	Part Used	Result	Ref.
Hypnotic-sedative and Anxiolytic effect	Seed	The seeds extract of *Ziziphus* jujuba showed the significant anxiolytic effects. They are known to depress activity of the central nervous system which reduces anxiety and induces sleep. It was found that it produced sleep, but was not anticonvulsant or muscle relaxant.	44

Anti-Cancer Activity	Fruit	The *in vitro* cytotoxicities of the triterpenoic acids extracted from *Z. jujuba* were tested against tumour cell lines . The lupane-type triterpenes showed high cytotoxic activities. The cytotoxic activities of 3-O-p-coumaroylalphitolic acids were found to be better than those of non-coumaroic triterpenenoids. These results suggest that the coumaroyl moiety at the C-3 position of the lupane-type triterpene may play an important role in enhancing cytotoxic activity	38
Antioxidant Activity	Fruit	The results obtained in this investigation indicate that *Ziziphus Jujuba Mill*. peel is a rich source of many antioxidant compounds. The antioxidant activity of extracts was determined by DPPH and reducing power assay. Polyphenol and tannin contents were significantly ($p<0.05$) higher in the raw peel (1.67±0.07 and 7.69±0.09 g/100g respectively), while glutathione (GSH) content of cooked peel (125.75±5.04 µMol/100g) was significantly ($p<0.05$) higher than raw peel (99.49±8.84 µMol/100g).	45
Immunostimulant effects	Leaf	The leaf extract of *Z. jujuba* was found to stimulate chemo tactic, phagocytic and intracellular killing potency of human neutrophils (infection fighting white blood cells) at 5-50 micro g/ml	46
Wound healing activity	bark	The methanolic extract of Z.jujuba showed the wound healing activity at the high dose (10%w/w) then the low dose (5%w/w) by exercise wound model for the period of 24 days in albino rats.	47
Cardiovascular activity	leaf	A neo-lignan isolated from *Z. mauritiana* leaves was found to increase the release of endogenous prostaglandin I2 (the most potent natural inhibitor of platelet aggregation yet discovered and a powerful vasodilator) from the rat aorta by up to 25.3 % at 3 micro g/ml.	48
Antifertility/contraceptive property	Bark	The ethyl acetate extract of *Z. jujuba* bark was found to effect antisteroidogenic activity and hence fertility in adult female mice. It was found to arrest the normal estrus cycle of adult female mice at diestrus stage and reduced the wet weight of ovaries significantly. Antifertility activities of crude extracts were found to be reversible in rat.	49
Anti-inflammatory	Leaf	Ziziphus jujuba leaves extract possess significant anti-inflammatory activity against carrageenan-induced rat paw edema. The % inhibition of paw edema at 3 h after carrageenan administration produced by Ziziphus jujuba leaves extract at the dose of 200, 400 and 600 mg/kg was 44.5%, 62.2% and 81.8% respectively when compared to control.	50

Antiulcer activity	leaf	The results suggest that ZJE possesses significant and dose dependent antiulcer activity by pylorus ligation model in rats. The antiulcer activity of ZJE can be attributed to its cytoprotective and Anti-secretory action.	51
Sweetness inhibitors	Leaf, seed	Triterpenoid sweetness inhibitors were isolated from *Z. jujuba.* Extracts from the leaves of *Z. jujuba* have been found to suppress sweet taste sensation in fly *(Pharma regina),* rat and in hamster. Antisweet substances isolated from *Z.jujuba* included jujubasponins II, III, IV, V and VI and from the leaves, jujuboside B from the leaves and seeds and ziziphus saponins I-III from dried fruit. Ziziphin and jujubosaponins II and III, the only three of the anti-sweet saponins from this plant with acyl groups, were up to 4 times more active in suppressing the sweet taste of sucrose than the other anti-sweet constituents and thereby reducing obesity in diabetic or overweight people.	52
Anti-allergic activity	leaf	The anti-allergic activity of the aqueous extracts of leaves of Z. *jujuba* was studied by measuring its inhibitory effect on hyaluronidase (bovine testes) activation *in vitro. Z. jujuba* was shown to have strong anti-allergic activity.	53
Antifungal Activity	stones	Ethanolic extract shows good antifungal activity against *Trichophyton rubrum* as compare with aqueous extract. The zone of inhibition of ethanolic extract (25mm) shows more than aqueous extract (19 mm) while taken 10 mg/ml extract.	54
Anti diarrhoeal activity	Leaf	In the castor oil-induced diarrhea experiment, the leaf extract of *Ziziphus jujuba* produced a significant inhibitory activity against castor oil and Mgso4 induced diarrhea in the rats.	55
Antipyretic Activity	Leaf	The experimental rats showed a marked increase in rectal temperature 18 hours after Brewer's Yeast injection. In the first hour, the antipyretic effect of *Zizyphus jujuba* (200 and 400 mg/kg) was significant (p<0.05 and p<0.01, respectively). *Zizyphus jujuba* at a dose of 200mg/kg caused a highly significant reduction at third hour (p<0.001). However, the effect increases significantly at the dose of 400 mg/kg having p<0.01 at first, second and fourth hour. The antipyretic effect was comparable with that of a standard paracetamol.	56
Hypoglycemic effect	Leaf	The analysis variance results indicated significant reduction (P = 0.001) of glucose–triglyceride–cholesterol and VLDL levels in group 3 in comparison with group 2. Z. Jujuba also increased HDL levels significantly (P=0.001) in comparison with group 2. Also, the extract reduced diabetic rats LDL level, but it wasn't significant (P=0.12) in comparison with group 2.	57

Anti-obese activity	Leaf	The results of the present study conclude that alcoholic extract of *Z. jujuba* leaves showed anti-obese property by decreasing the body weight, food intake, serum glucose and lipid levels and internal organs and fat pad weights in dietary obese rats. The effect produced was comparable with that produced by standard anti-obese drug, Sibutramine.	58

DISCUSSION AND CONCLUSION

Ziziphus jujuba is a widely traditionally used and potent medicinal plant amongst all the thousands of medicinal plants. The pharmacological activities reported in the present review confirm that the therapeutic value of *Ziziphus jujuba* is much more. It is an important source of compounds with theirs chemical structures as well as pharmacological properties. The presence of phytochemical constituents and pharmacological activities proved that the plant has a leading capacity for the development of new good efficacy drugs in future. Thus, a detailed and systematic medicinal study is required for identification, cataloguing and documentation of plants, which may provide a meaningful way for the promotion of the traditional knowledge of the herbal medicinal plants.

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