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Phyto-Pharmacology of *Ziziphus jujuba* Mill – A Plant Review

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ABSTRACT
Herbs have always been the natural form of medicine in India. Medicinal plants have curative properties due to presence of various complex chemical substances of different composition which contain secondary metabolites such as alkaloids, flavonoids, terpenoids, saponin and phenolic compounds distributed in different parts of the plants. *Ziziphus jujuba* Mill, a member of the family Rhamnaceae, commonly known as Bor, 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. It possesses allied compounds *viz.* Ascorbic acid, thiamine, riboflavin-bioflavonoids and Pectin A and various chemical substances like Mauritine-A; Amphibine-H; Jubanine-A; Jubanine-B; Mucronine-D and Nummularine-B. Sativanine-E. Frangufoline, Ziziphine-A to Q, betulinic acid colubrinic acid, alphitolic acid, 3-O-cis-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, jujubosides A, B, A1 B1 and C and acetyljujuboside B and the protojujubosides A, B and B1, saponin, ziziphin, from the dried leaves of *Z. jujube* - 3-O-a-L-rhamnopyranosyl (1-2)-a-arabinopyranosyl-20-O- (2,3)-di-O-acetyl-a-L-rhamnopyranosyl jujubogenin. Saponin from leaves and stem are 3-O- ((2-O- alpha – D – furopyranosyl – 3-O- beta – D –glucopyranosyl) – alpha – L – arabinopyranosyl) jujubogenin and (6'''-sinapoylspinosin, 6'''-feruloylspinosin and 6'''-p-coumaroylspinosin. The present review discusses photo-chemistry, pharmacology, medicinal properties and biological activities of *Z. jujuba* and its usage in different ailments.
Key words- Antioxidant, Antibacterial, Anticarcinogenic, Phytochemistry, *Ziziphus jujuba*
List of Abbreviations Used : m – meter ; mm – millimeter ; cm – centimeter ; mg – milligram; gm – gram; FAO- Food and Agriculture Organization; WHO- World Health Organization; % - percentage; Micro g – micro gram; ml – milliliter

INTRODUCTION

Traditional medicines are used by near about 60 per cent of the world's population. These are not only used for primary health care in rural areas but also in developing countries. In developed countries modern medicines are predominantly used. While the traditional medicines are derived from medicinal plants, minerals, and organic matter, the herbal drugs are prepared from medicinal plants only. Use of plants as a source of medicine has been inherited and is an important component of the health care system in India. In the Indian systems of medicine, most practitioners formulate and dispense their own recipes; hence this requires proper documentation and research. Public, academic and Government interest in traditional medicines is growing exponentially due to the increased incidence of the adverse drug reactions and economic burden of the modern system of medicine. There are about 45,000 plant species in India. India is the largest producer of medicinal herbs and is appropriately called the "Botanical garden of the world". In rural India, 70 per cent of the population is dependent on the traditional system of medicine (1). Seven members of the family *Rhamnaceae* occurred in Khandesh region *i.e.* North Maharashtra Region. Out of these three members are natives of the same. Various genera and species of the family Rhamnaceae are given below.

Rhamnaceae

Distribution of Species

***Ziziphus jujuba* Mill.**

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Rosales
Family: Rhamnaceae
Genus: *Ziziphus*
Species: *jujuba*

Taxonomic Description

Jujubes are species of the genus *Ziziphus* Tourn. ex L. *Ziziphus* 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 grayish 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.

Indian 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)

Historical evidences

Ber has been recognized as a useful edible fruit since mythology of Ram and Shabari in India and depicted in Ramayana. Researchers mention both *Z. mauritiana* and *Z. jujuba* and even the wild *Z.nummularia* (2). Deccan plateau area is one where ber is thought to have been truly wild. (3). Once cultivated, ber would be carried with historical migrations of people and their trade.

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 (4). The bark cures boils and is good for the treatment of dysentery and diarrhea (5). The leaves are antipyretic and reduce obesity. The fruit is cooling, digestible, tonic, aphrodisiac, laxative and removes biliousness, burning sensations, thirst, vomiting (1) and is also good in treating tuberculosis and blood diseases. The seeds cure eye diseases and are also useful in leucorrhoea (6). 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 (5). 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 (6). 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 (7). Here, some allied substances are described such as ascorbic acid, thiamine, riboflavin and bioflavonoids and pectin-A. *Ziziphus jujuba* fruits are very rich in vitamins C (188 to 544 mg per 100 gm pulp) and B1 (thiamine) and B2 (riboflavin) studied (8). 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 (354 to 888 mg per 100 gm pulp) (bioflavonoid) content. It enhances the action of Vitamin C. Antibacterial, anti inflammatory and antioxidant are some medicinal properties. It is also known to stimulate bile production, promote circulation and prevent allergies. Presence of Pectin-A in *Z. jujuba* fruit is also reported (9). Chemically it contains 2, 3, 6-tri-o-acetyl D lactose units. Pectin has a number of pharmaceutical properties such as binding bile acid, lowering plasma cholesterol and anti diarrhoeal properties (10).

Phytochemistry of *Z. jujuba*

Alkaloids

Alkaloids are distributed in all parts of plant. Stem bark of *Ziziphus* species contain alkaloids (3). A sapogenin, zizogenin has been isolated from Z. *mauritiana* stems (11). The cyclic peptide alkaloids, mauritine-A, mucronine-D, amphibine-H, nummularine-A and -B (12), sativanine-A and sativanine-B, frangulanine, nummularine-B and mucronine were isolated from the bark of *Z. jujuba* by (12). 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 (13). The alkaloids coclaurine, isoboldine, norisoboldine, asimilobine, iusiphine and iusirine were isolated from *Z. jujuba* leaves by (14). Cyclopeptide and peptide alkaloids from *Z. jujuba* were found to show sedative effects (15). 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 (16). 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 (12). The cyclopeptide alkaloid, mauritine J, was isolated from the root bark of *Z. mauritiana* (17). For the first time (12) 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 (13) reported Sativanine-E. Antibacterial peptide alkaloid Frangufoline from *Ziziphus* species was reported (18). Han and co-workers reported Melonovine-A; Franganine; Frangulanine; Daechuine-S3; Daechuine-S6; Nummularine-A and Nummularine-R, all are cyclopeptide alkaloids (16). Four cyclopeptide alkaloids from the stem bark *Z.jujuba,* which are Scutianine-C; Scutianine-D; Jubanine-C and Ziziphine-A reported (19). 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 (20). Some of the representative alkaloids are given in table 1 (21, 22).

Some cyclopeptide alkaloids of *Z. jujuba*

Glycosides

(i) Flavonoid glycosides/spinosins: The structure of spinosin (2"-O- beta –glucosylswertisin) extracted from *Z. jujuba* var. *spinosa* seed (23). They later identified three acylated flavone-C-glycosides (6"'-sinapoylspinosin, 6"'-feruloylspinosin and 6"'-p-coumaroylspinosin), pharmacologically they have sedative activity in rat.

(ii) Glycosides/saponins: Different parts of *Z. jujuba* that is seeds, leaf and stem contain glycosides. The saponins isolated from the seeds of *Z .jujuba* include jujubosides A, B (24), A1 B1 and C and acetyljujuboside B (25) and the protojujubosides A, B and B1 (26). Kurihara *et al.* extracted the saponin, ziziphin, from the dried leaves of *Z. jujuba* (27). 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 (28). They are being widely researched for cancer prevention and cholesterol control as mentioned by Ogihara (29). Same compound is also reported by Sharma and Kumar (30) in another species that is *Z. mauritiana*. Saponins showed adjuvant and hemolytic (31), sedative (32) anxiolytic and sweetness inhibiting properties (27). Jujuboside A (JuA), is also known to be a noncompetitive inhibitor of calmodulin and is thought to be linked to its sedative properties (33).

Flavonoids

Sedative flavonoids such as Swertish and spinosin were isolated and reported by Gong et al., (34) from fruit and seeds of *Z.jujuba.* Puerarin; 6"'-feruloylspinosin; Apigenin-6-*C*- β-D-glucopyranoside; 6"'-feruloylisospinosin; Isospinosin and Isovitexin-2"-*O*-β-D-glucopyranoside these flavonoids isolated and reported by Gong, et al. (34). Ten flavonoids were reported by Pawlowska et al., (35) are Quercetine 3-*O*-robinobioside; Quercetine 3-*O*-rutinoside; Quercetine 3-*O*-α-L-arabinosyl-(1→2)- α-L-rhamnoside; Quercetine 3-*O*-β-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-O-robinobioside and Kaempferol 3-O-rutinoside. Some of the representative flavonoids are described by Gong et al., (34). Zeng *et al*., (24) discovered a new flavonoid, named zivulgarin, compound (4-beta-D-glycopyranosyl swetisin).

Terpenoids

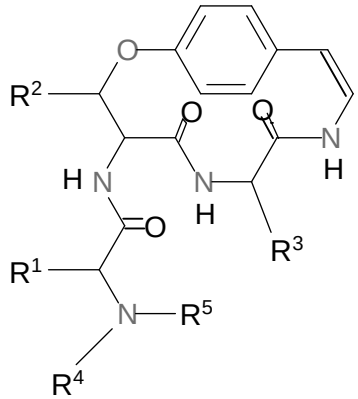
The triterpenoic acids have been isolated from the fruits of *Z. jujuba*: some of them are colubrinic acid, alphitolic acid, 3-O-cis-p-coumaroylalphitolic acid, 3-O-transp-coumaroylalphitolic acid, 3-O-cis-p-coumaroylmaslinic acid, 3-O-trans-pcoumaroylmaslinic acid, oleanolic acid, betulonic acid, oleanonic acid, zizyberenalic acid and betulinic acid (36). Triterpenoic acids have also been extracted from roots of *Z. mauritiana* (37). Betulin; Betulinic acid; Ursolic acid; 2α-hydroxyursolic acid and Ceanothic acid are triterpenes reported by Shoei et al., (38). Some of them have anticancer and anti-HIV properties. Sang et al., (39) demonstrated three triterpene esters *viz.* 2-*O*-protocatechuoyl alphitolic acid, Caffeoyl alphitolic acid and Ceanothic aciddimethyl ester.

Phenolic Compounds

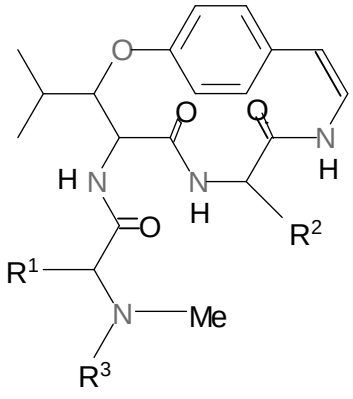
Recently Pawlowska et al., (35) reported phenolic compounds from the fruit of *Z. jujuba,* without citing any biological activity.

Table 1 Structures of various isolated secondary metabolites from various parts of *Z. Jujub*a

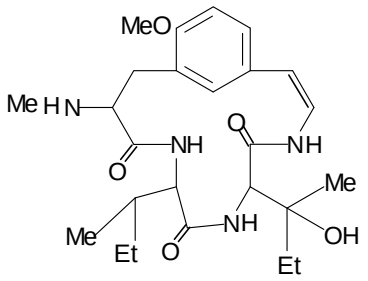
Alkaloids



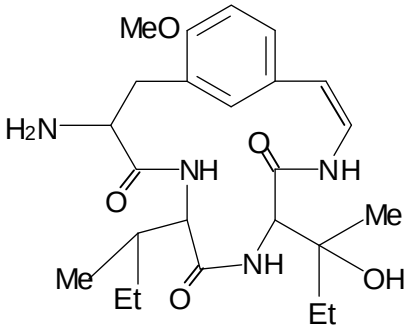
General Cyclopeptide alkaloid



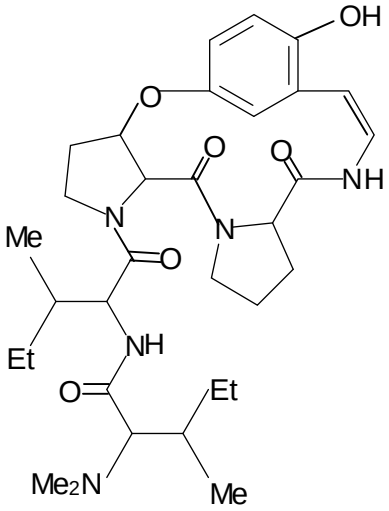
Frangulanine



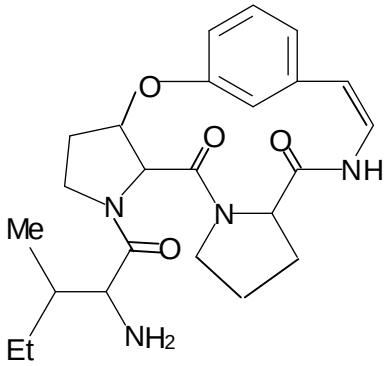
Zizyphine D



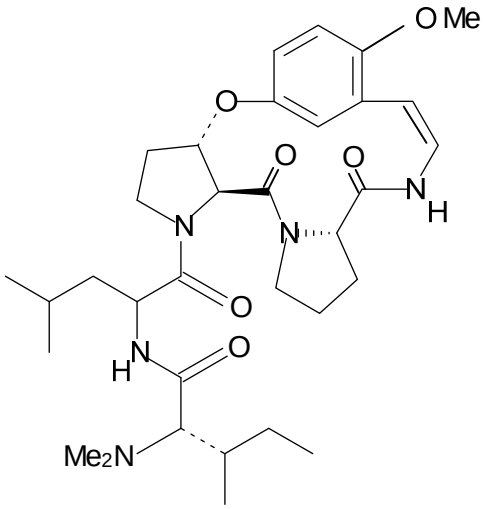
Zizyphine E



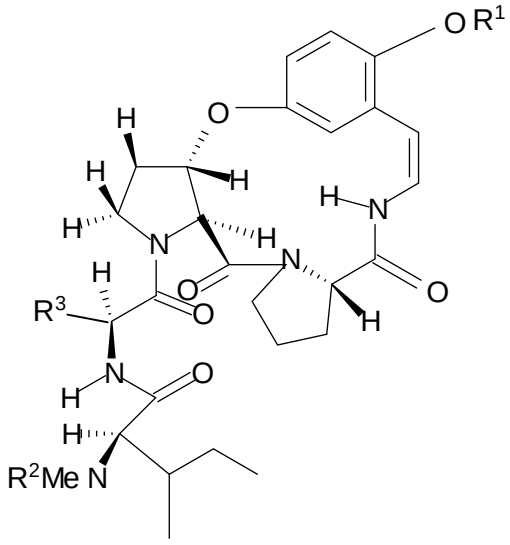
Zizyphine F



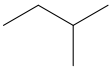
Zizyphine G



Zizyphine N

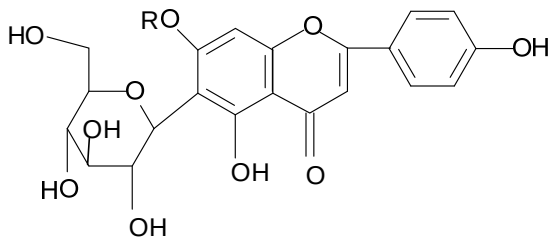


Zizyphine N, O, P, Q and A

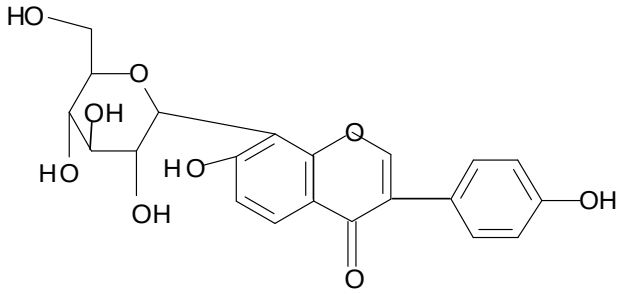
(1 Ziziphine N: $R^1 = R^2 = Me$, R^3 =  2

Ziziphine O: R^1= Me, R^2 = H, R^3 = CH_2 $CH(CH_3)_2$; 3 Ziziphine P: R^1=H, R^2 =Me, R^3 = CH_2 $CH(CH_3)_2$; 4 Ziziphine Q: R^1= R^2 = Me, R^3 = $CH(CH_3)_2$; 5 Zizyphine A: R^1= R^2 = Me, R^3 = $CH(CH_3)CH_2CH_3$)

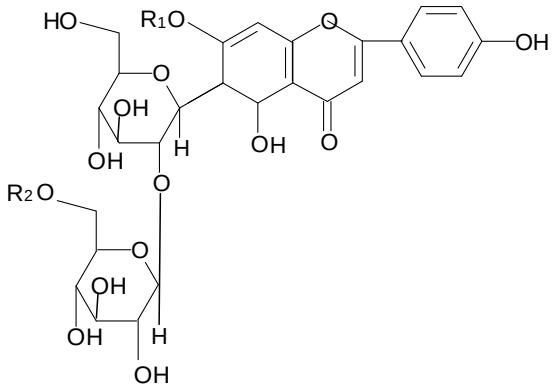
Flavonoids



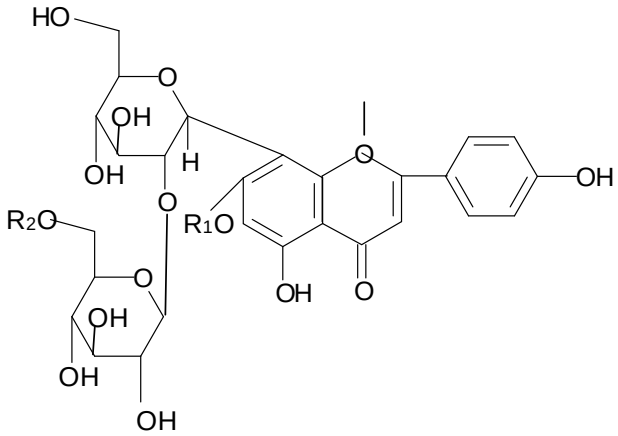
R= CH3 = Swertish, R=H = Apigenin-6-C-β-D-glc



Puerarin

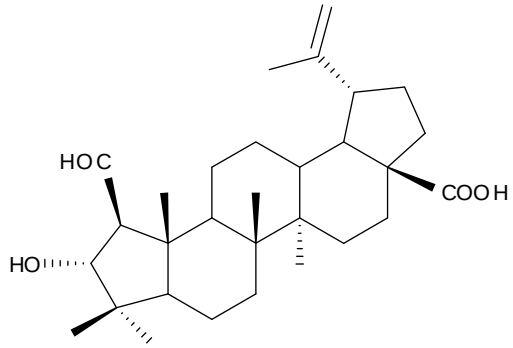


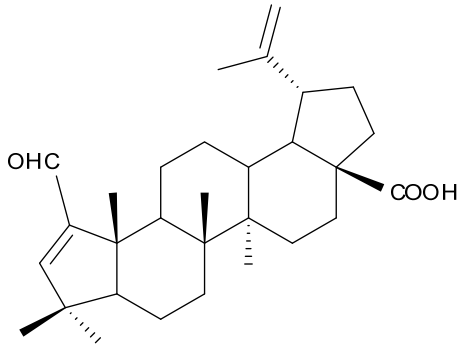
R1 = CH3, R2 = Feruloyl = 6'''-feruloylspinosin, R1 = CH3, R2 = H = Spinosin, R_1 = R_2 = H = Isovitexin-2''-0-β-D-glc



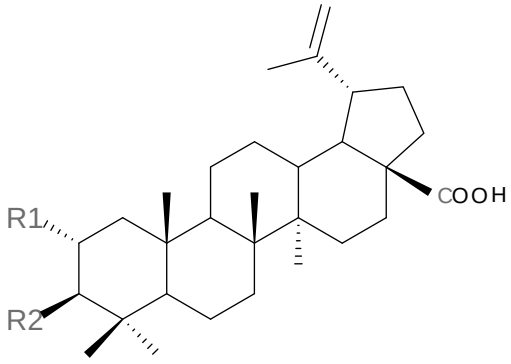
R1 = OCH3, R2 = Feruloyl = 6'''-feruloylisospinosin, R_1 = OCH_3, R_2 = H=isospinosin

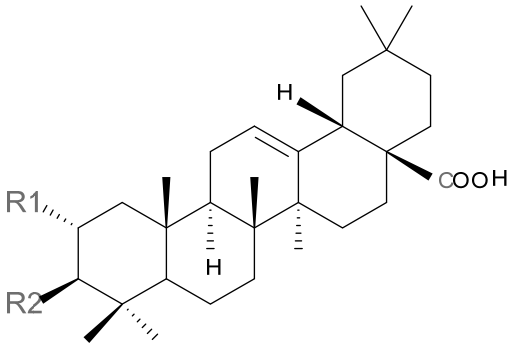
Triterpenoids



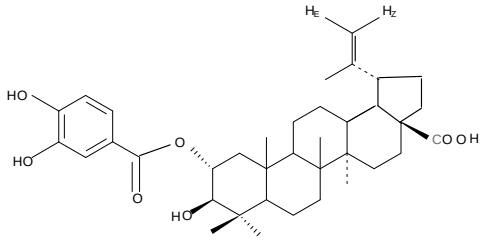


2 R1 = OH, R2 = OH
3 R1 = OH, R2 = *cis-p-coumaroyl*
4 R1 = OH, R2 = *trans-p-coumaroyl*
7 R1 = H, R2 = OH
9 R1 = H, R2 = O
5 R_1= OH, R2 = *cis-p-coumaroyl*
6 R_1= OH, R2 = *trans-p-coumaroyl*
8 R_1= H, R2 = OH
10 R_1= H, R2 = O

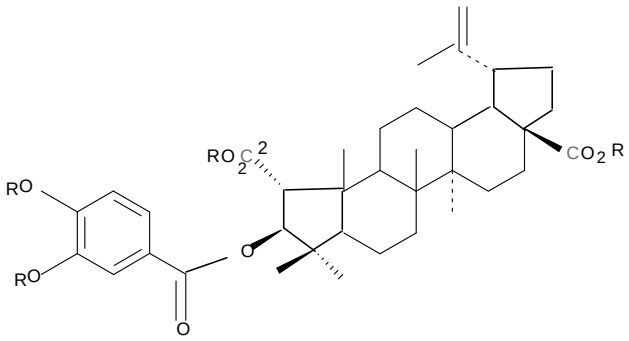




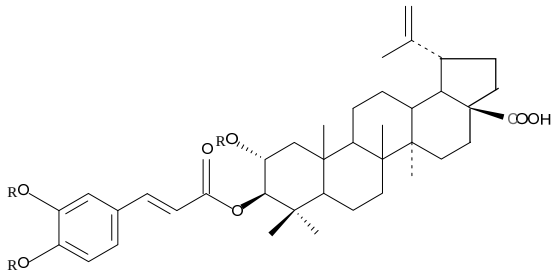
Triterpene esters



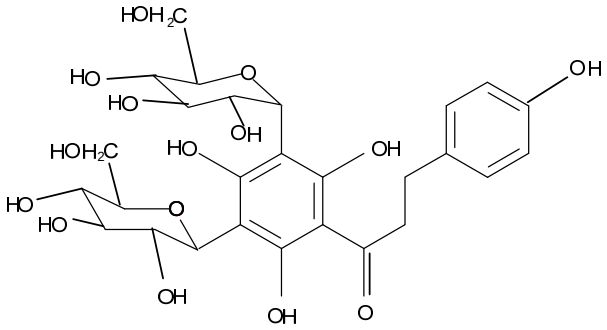
2-*O*-protocatechuoyl alphitolic acid



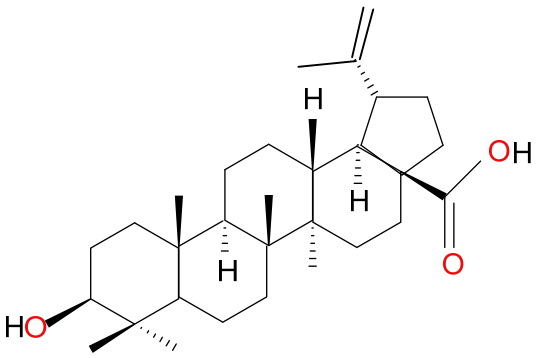
Caffeoyl alphitolic acid, 3. R=H, 3a. R= Me



Ceanothic aciddimethyl ester, 2. R=H, 2a. R=Ac



Phenolic compound



Betulinic acid

Chemical structure of Phenolic compound of the fruit of *Z.jujuba*

Betulinic acid

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 anti-inflammatory activity (40) and antibacterial properties and inhibits the growth of both *Staphylococcus aureus* and *Eschericheria coli* (41).

Pharmacological properties of *Z. jujba*

Hypnotic-sedative and Anxiolytic effect

The seeds and leaves of many *Ziziphus* species have been found to have anxiolytic and hypnotic-sedative 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 (42). The inhibitory effect of Jujuboside A (JuA) on rat hippocampus is demonstrated by Feng and Zheng, (43). Anxiolytic effects in mice of a polyherbal substance containing seed extract of *Z. jujuba* reported by Lin *et al.*, (44). Both sanjoinine A and nuciferine, alkaloids obtained from fruit, prolonged the sleeping time produced by hexobarbital. When sanjoinine was heated it was found to produce an isomer of even greater sedative effect (15).

Sweetness inhibitors

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 (45). The saponin, ziziphin extracted by Kurihara *et al.* (27) suppressed the sweetness induced by D-glucose, D-fructose, stevioside, glycine, sodium saccharin, aspartame and naringin dihydrochalcone. It however showed no suppressive effect on the sour taste of hydrochloric acid and the bitter taste of quinine indicating that ziziphin is highly specific to sweet taste (46). Ziziphin was found to inhibit the sweet taste receptors in humans (47). The mechanism which ziziphin used was identified as taste modification. On comparison with known gymnemic acids, effects suggest that net dissociation of ziziphins from taste receptor membranes and/or inactivation in the membrane may be much faster than with gymnemic acids.

Cancer (chemotherapy)

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 (36). The triterponic acid, betulinic acid, extracted from *Z. jujuba* and *Z. mauritiana*, showed selective toxicity against cultured human melanoma cells (40). Betulinic acid is currently undergoing preclinical development (48). It is thought that betulinic acid may also be effective against other types of cancer. Recently, considerable *in vitro* evidence has demonstrated that betulinic acid is effective against small- and non-small-cell lung, ovarian, cervical, and head and neck carcinomas (48). Published data suggest that betulinic acid induces apoptosis (40, 49) in sensitive cells in a p53- and CD95-independent fashion (41).

Antimicrobial activity

Sarfaraz *et al.*, (50) reported antifungal effects of *Z. jujuba.* Ethanol extract of the root showed significant inhibitory activity on fungi *Candida albicans*, *C. tropicalis*, *Aspergillus flavus*, *A. niger* and *Malassezia furfur* (strains 1374 and 1765). Additionally, extract of root bark of *Z. jujuba* exhibited antibacterial activity against 20 bacteria (51). Leaf extracts of *Z. mauritiana* were found to show antibacterial effects against *Escherichia coli*, *Klebsiella* spp., *Pseudomonas* spp., *Proteus vulgaris* and *Bacillus subtilis* when methanol and acetone extracts were

used (52). Betulinic acid isolated from stem bark of *Z. jujuba* has also been found to retard the progression of HIV 1 infection that is antiviral activity (53).

Antiulcer activity

An antiulcer property of *Z. mauritiana* leaf extracts (ZJE) was reported by Ganachari and shiv (54) in rat. This extract possesses significant and dose-dependent antiulcer activity. The antiulcer activity of ZJE can be attributed to its cytoprotective and antisecretory action (54).

Anti-inflammatory and antispastic effect

The compound prescription Huangqin Tang which contains the fruit of *Z. jujuba* showed marked anti-inflammatory and significant antispastic or antispasmodic effect (55). *Z.mauritiana* leaf extracts were found to possess significant anti-inflammatory activity against carrageenan-induced rat paw edema (56).

Antiallergic

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 (57).

Permeability enhancement activity

Delivery of certain classes of drugs such as peptides creates problems in transportation across cell membranes and subsequent diminished bioavailability. To overcome this barrier, permeability enhancers can be used to aid the passage of drugs across cell membranes. To assess the permeability enhancing activity of *Z. jujuba*, an aqueous extract of seeds was compared to two members of a known series of permeability enhancement agents belonging to the alkyl glycosides (58).

Cognitive activities

Heo *et al.* (59) suggested that oleamide, a component of *Z. jujuba* extract, could be a useful chemo-preventative agent against Alzheimer's disease. They found that methanolic *Z. jujuba* showed 34.1 % activation effect on choline acetyltransferase *in vitro*, an enzyme that controls the production of acetylcholine which appears to be depleted in the brains of Alzheimer patients. Using sequential fractionation the active ingredient was found to be cis-9-octadecenoamide (oleamide) which showed 65% activation effect.

Antifertility/contraceptive property

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. Hematological profiles, biochemical estimations of whole blood and serum remained unaltered in extract-treated mice. Normal estrus cycle and ovarian steroidogenisis were restored after withdrawal of treatment. Antifertility activities of crude extracts were found to be reversible in rat (60).

Hypotensive and Antinephritic effect

Ziziphus jujuba has been found to stimulate nitric oxide release *in vitro*, in cultured endothelial cells and *in vivo*, in the kidney tissues of rats (61). They believed that *Z. jujuba* may contribute to its hypotensive (reduction of blood pressure) and antinephritic (reduction of inflammation of the kidney) action, possibly by increasing renal blood flow.

Cardiovascular activity

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 (62).

Immunostimulant effects

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 (63).

Antioxidant effects

Recently, a comprehensive and an exhaustive account on 70 antioxidant Korean medicinal plants have been reported by Seong et al., (64) and they confirmed antioxidant effect of *Z. jujuba* (*in vitro*) as reported by Na *et al.* (65).

Wound healing activity

Recently, Ansari et al., (66) mentioned the root of *Z.jujuba* as a wound healer in their book entitled Herbal Drugs. The experimental data on wound healing activity of the root of Z. *jujuba* is not available in literature in laboratory animals (67). Very recently we confirmed the wound healing activity of the root of *Z.jujuba* in experimental animal, rat model, in an ointment form at a dose 0.5% and 1% on topical application (68) and this confirms the validity of claim made by Ansari et al., (66)

SUMMARY

Z. jujuba, an indigenous plant possesses terrific medicinal properties, attributed by a diverse group of secondary metabolites. Phyto-chemically 64 alkaloids, 16 glycosides and flavonoids, 14 terpenoids and others are present in this plant. Each ingredient has unique and multifactorial properties. The importance of such constituents in health products and food supplements is ignored. Although there is a range of potentially useful medicinal substances in plant, the research in this area is scanty. Commercial industries neglected the use of such constituents in pharmaceutical and neutraceutical companies. The benefit of the hardy nature of *Z. jujuba* and its wide geographical distribution gave an opportunity to agro and pharma industries. Thus, this article provides excellent accessible source of active compounds for traditional medicine and allied applications.

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