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Ziziphus jujuba: A Review on Pharmacological Aspects

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Herbal medicine is the oldest medical practice known to man. Since the dawn of mankind, various plant resources are used to cure different diseases and also for a long and healthy life. This review focuses on the detailed phytochemical composition, medicinal uses, along with pharmacological properties of different parts of this multipurpose tree. The ancient knowledge of plant based medicine has transferred from generations to generations and accumulated as ethno-pharmacological knowledge among different ethnic groups. India is the spanning bed of traditional phytomedicinal system where Ayurveda was born out of the knowledge of traditional medicine. A great number of people rely primarily on phytomedicines for the treatment of diseases. In the complementary and alternative medicinal systems, Ziziphus jujuba is one such plant which is well-known for its therapeutic efficiency in different diseases globally.

INTRODUCTION

Traditional medicine is a main part of the cultural heritage of a society and it has developed in accordance with the lifestyle and ancient practices of the society. During practical experiences of herbal remedies the therapeutic results of the various traditional medicinal systems around the world. Indian, Chinese, and Arabian traditional medicinal systems are highly developed (Akerlee,1996). Traditional Indian medicinal systems have reached to various other countries such as Malaysia and America. According to a WHO report, around 80% of the world's population primarily relies on traditional medicines. Ayurveda (the knowledge for long life), originated in India in the mid-second millennium BCE, known as the Vedic period. Susruta Samhita and Charaka Samhita is the core of the Ayurvedic medicinal systems which have describe the therapeutic usage of thousands of plants. One such plant mentioned in Ayurveda (Pullaiah, 2002). *Ziziphus* is a genus of family Rhamnaceaecomprising of about 40 species. The leaves are alternate, entire, with three prominent basal veins, and 2-7 cm long; some species are deciduous, others evergreen. The flowers are small, inconspicuous yellow green. The fruit is an edible drupe, yellow-brown, red, or black, globose or oblong, 1-5 cm long, often very sweet and sugary, reminiscent of a date in texture and flavor(Majumadar,1954; Azam,2006). Plants of this genus are widely distributed in Europe and South-Eastern Asia. In India the plant is found throughout North-Western region, it is commonly known as Baer and used traditionally as tonic and aphrodisiac and sometimes as hypnotic-sedative, It also possess anxiolytic, anticancer, antifungal, antibacterial, antiulcer, anti-inflammatory, antispastic, and wound healing properties. Their pounded leaves are applied as a dressing to wounds (Nadkarni,1986). So far only few numbers of comprehensive reviews has been compiled from the literature encompassing the therapeutics uses of *Ziziphus jujuba*. Thus objectives of the present review are to provide an overview of the recent status on phytoconstituents and pharmacological uses of plants Ziziphus jujuba.

COMMON NAME:

Jujab (Hindi); 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 (Majumadar,1954). Deccan plateau area is one where ber is thought to have been truly wild. (Azam,2006). Once cultivated, ber would be carried with historical migrations of people and their trade

CLASSIFICATION:

- Domain : Eukaryota – eukaryotes
- Kingdom : Plantae Haeckel
- Subkingdom : Viridaeplantae
- Phylum : Magnoliophyta
- Subphylum : Euphyllophytina
- Infraphylum : Radiatopses
- Class : Magnoliopsida
- Subclass : Rosidae
- Superorder : Rhamnanae
- Order : Rhamnales
- Family : Rhamnaceae
- Genus : Ziziphus
- Specific : jujuba(Nadkarni,1986)

Leaves **Fruit** **Flower**

Fig.1: Various part of Zizyphus jujuba

CHEMICAL CONSTITUENTS

The major chemical constituents found in this plant are:

i. The leaves contain Quercetin and Quercitrin (Anonymous, 1989; Kuliev, 1974; Tomoda, 1985).

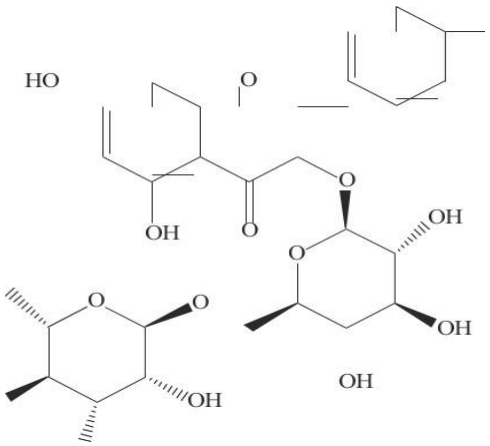
ii. Flowers has shown to have E-4-hydroxy cinnamic acid: p-coumaric acid, (E)-4- hydmxy - 3-methoxy cinnamic acid: ferulic acid, 5,7,3',4'-tetra hydroxy-3-0-aL-rhamnosyl flavone: quercitrin, 5,7,3',4'-tetrahydroxy 3-O-P-D-galactosyl flavone: hyperoside, kaempferol 3-O-rutinoside and Rutin which were isolated with the help of column chromatography (Kuliev, 1974).

iii. Bark contains Tannins, d-7, 3', 4'-trihydroxyflavan-3, 4-diol and oleanolic acid (Tschesche,1989; Srivastava, 1979). It also contains Cyclopeptide alkaloids namely Amphibine H, Nummularine- K**,** (Srivastava, 1979). Two new 13-membered cyclopeptide alkaloids, xylopyrine-A and xylopyrine-B also have been isolated from the bark of Zizyphus xylopyra (Shah,1985)**.** Root Bark reported to contain two flavonoids namely Kempferol-4'-methylether and Kempferol The bark and wood of ZX was found to contain Betulinic acid (1%) (Ziyaev, 1977)**.**

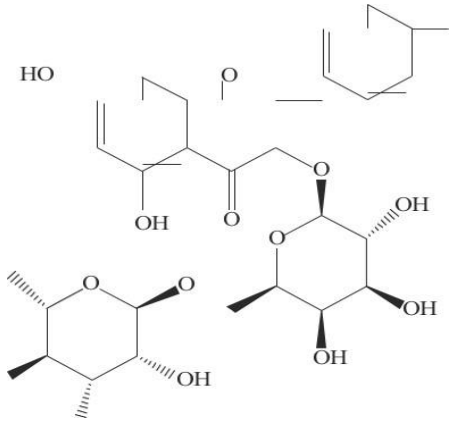
iv. Fruit contains Catechol-type of tannins (8-12%). Fruits were also reported to have Oleanolic acid, (Han, 1986; Han, 1990). l-leucocyanidin, 3, 3', 4-tri-O-methyl-ellagic acid (Tschesche,1989; Srivastava, 1979). The pulp of the fruit contains reducing sugars, sucrose, citric acid, carotene, vitamin C and tannins (Nadkarni,1986). Seeds consists of unsaponifiable matter (0.8%) a Sterol, insoluble mixed fatty acid found to contain Myristic, Linoleic and Oleic acid (Jossang, 1996). Stem wood is reported to have triterpenoids, lupeol, betulinic acid and a new triterpenoid designated as isoceanothic acid(Devi, 1987).

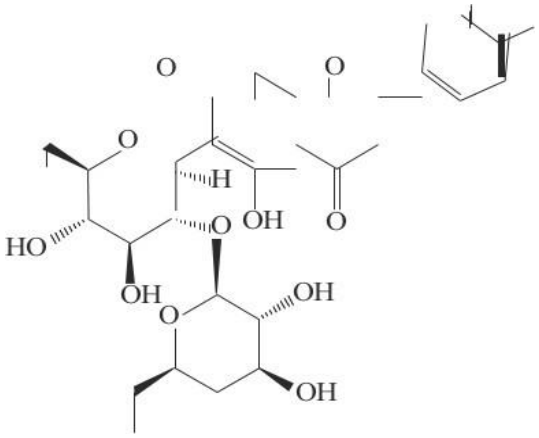
It contains three flavones-Cglucosides-6" sinapoylspinosin, 6"-feruloylspinisin and 6-"p-coumaroylspinosin. The leaves and stems of genus ziziyphus contain saponins 3-o- [2-α-L-fucopyrnosyl-3-o-β-Dglucopyranosyl-α-Larabinopyranosyl] jujubogenin (Zaher, 2005).

Kaempferol 3-*O*- rutinoside

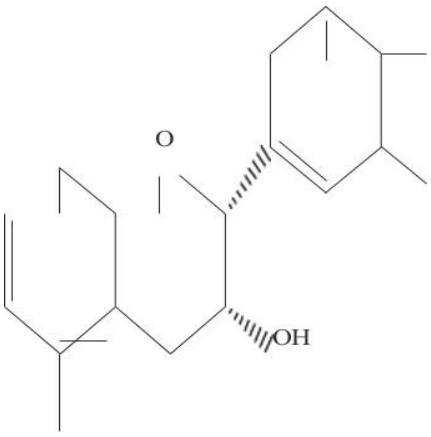


Quercetin 3-*O*- rutinoside

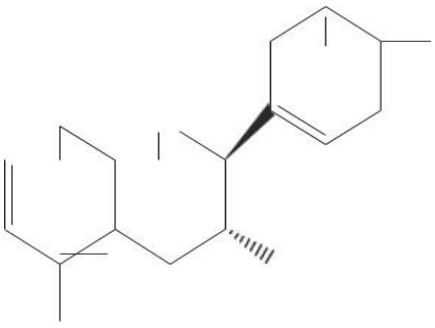




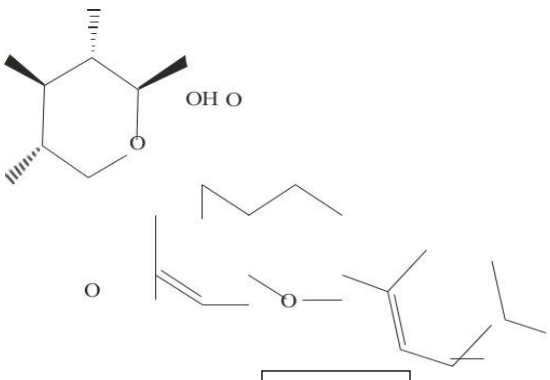
Spinosin



(−)-Epicatechin



(−)-Catechin



Swertish

PHYTOCONSTITUTENTS

Isolate two new 13-membered cyclopeptide alkaloids, xylopyrine-A and xylopyrine-B from Zizyphus xylopyra, and their structures established by spectral and chemical evidences. (Singh, 2007)

Alkaloids

Alkaloids are distributed in all parts of plant. Stem bark of Ziziphus species contain alkaloids. A sapogenin, zizogenin has been isolated from Z. mauritiana stems (Srivastava, 1979). The cyclic peptide alkaloids, mauritine A, mucronine D, amphibine H, nummularine A and B, sativanine A and sativanineB, frangulanine, nummularineB and mucronine were isolated from the bark of Za jujuba by (Tschesche,1989) . The cyclic peptide alkaloids sativanine C, sativanine G, sativanine E, sativanine H, sativanine F, sativanine D and sativanineK isolated from Z. jujuba stem bark (Ziyaev, 1977). The alkaloids coclaurine, isoboldine, norisoboldine, asimilobine, iusiphine and iusirine were isolated from Z. jujuba leaves by (Han, 1986). Cyclopeptide and peptide alkaloids from Z. jujuba were found to show sedative effects (Han, 1990). The seeds of Z. jujuba var. spinosa also contain cyclic peptide alkaloids sanjoinenine, franguloine and amphibineD and four peptide alkaloids; sanjoinine BDF and G2 (Jossang, 1996) . 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; CF, G and H, frangufoline; amphibines D, E, B and F;hysodricanin A, scutianin F and aralioninC (Tschesche,1989). The cyclopeptide alkaloid, mauritine J, was isolated from the root bark of Z. mauritiana (Devi, 1987). For the first time (Tschesche,1989) 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 (Ziyaev, 1977) reported Sativanine E. Antibacterial peptide alkaloid Frangufoline from Ziziphus species was reported (Zaher, 2005). Han and coworkers reported Melonovine A; Franganine; Frangulanine; Daechuine S3; Daechuine S6; Nummularine A and Nummularine R, all are cyclopeptide alkaloids (Jossang, 1996). Four cyclopeptide alkaloids from the stem bark Z.jujuba, which are ScutianineC; ScutianineD; JubanineC and ZiziphineA reported (Tripathi, 2001). Two reports appeared in the literature on isolated ingredients from the root bark of Z.jujuba. AdouetineX and Frangulanine which are active (sedative) ingredient cyclopeptide alkaloids isolated and characterized (Otsuka, 2016).

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 (Woo, 1979). They later identified three acylated flavone C-glycosides (6'''-sinapoylspinosin, 6'''feruloylspinosin and 6'''pcoumaroylspinosin), 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 (Zeng, 1987), A1 B1 and C and acetyljujuboside B (Yoshikawa, 1997) and the protojujubosides A, B and B1 (Matsuda, 1999) . Kurihara et al. extracted the saponin, ziziphin, from the dried leaves of Z. jujuba (Kurihara, 1988). It has a structure, 3O a L rhamnopyranosyl (12) 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 3O ((2O alpha D furopyranosyl 3-O beta D glucopyranosyl) (alpha L-arabinopyranosyl) jujubogenin (Ikram, 1981). They are being widely researched for cancer prevention and cholesterol control as mentioned by (Ogihara, 1976). Same compound is also reported by Sharma and Kumar (Sharma, 1982) in another species that is Z. mauritiana. Saponinsshowed adjuvant and hemolytic (Oda, 2000), sedative (Shou, 2002) anxiolytic and sweetness inhibiting properties (Kurihara, 1988).Jujuboside A (JuA), is also known to be a noncompetitive inhibitor of calmodulin and is thought to belinked to its sedative properties (Zhou, 1994).

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; Apigenin6CbDglucopyranoside; 6"'feruloylisospinosin; Isospinosin and Isovitexin2"ObDglucopyranoside these flavonoids isolated and reported by (Gong, 2000). Ten flavonoids were reported by (Pawlowska, 2000) are Quercetine 3-O0-robinobioside; Quercetine 3-O-rutinoside; Quercetine 3-O-α-Larabinosyl-(1→2)-α-Lrhamnoside; Quercetine 3-O-b-Dxylosyl-(1→2)-α-L-rhamnoside; Quercetine 3-O-β-Dgalactoside; Quercetine 3-O-β-D-glucoside; 3',5'Di-C-β-D-glucosylphloretin;

Quercetine 3-O-β-Dxylosyl-(1→2)-α-L rhamnoside-4'O-a-Lrhamnoside; Kaempferol 3-O-robinobioside and Kaempferol 3-O-rutinoside. Some of the representative flavonoids are described by Gong et al., (Gong, 2000), Zeng et al., (Zeng , 1987) discovered a new flavonoid, named zivulgarin, compound (4beta 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-cispcoumaroylalphitolic acid, 3-O-transpcoumaroylalphitolic acid, 3-O-cisp-coumaroylmaslinic acid, 3Otranspcoumaroylmaslinic acid, oleanolic acid, betulonic acid, oleanonic acid, zizyberenalic acid and betulinic acid (Lee, 2003). Triterpenoic acids have also been extracted from roots of Z. mauritiana (Kundu, 1989). Betulin; Betulinic acid; Ursolic acid; 2αhydroxyursolic acid and Ceanothic acid are triterpenes reported by Shoei et al., (Shoei, 1996). Some of them have anticancer and antiHIV properties. Sang et al.,(Sang, 2004) demonstrated three triterpene esters viz. 2Oprotocatechuoyl alphitolic acid, Caffeoyl alphitolic acid and Ceanothic aciddimethyl ester. Phenolic Compounds Recently Pawlowska et al., ((Pawlowska, 2000)) reported phenolic compounds from the fruit of Z. jujuba, without citing any biological activity. 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 antiinflammatory activity (Kim, 1998) and antibacterial properties and inhibits the growth of both Staphylococcus aureus and Eschericheria coli (Eiznhamer, 2004).

PHARMACOLOGICAL ACTIVITES

Antidiabetic effect

Ethanolic leaf extract of ziziphus jujuba was used to treat alloxan induced diabetic rats. 100mg/kg of extract was given to diabetic rats for five days alternately. The analysis variance results indicated significant reduction (P = 0.001) of glucose– triglyceride– cholesterol and VLDL levels in diabetic in comparison with no diabetic. Z. Jujuba also increased HDL levels significantly (P=0.001). Also, the extract reduced diabetic rats LDL level, but it wasn't significant (P=0.12). According to the results obtained, it was concluded that, Z. Jujuba leaves can be used in diabetics for the purpose of glucose and lipid reduction. (Sherdil, 2009).

Clinical trials were done on Root extracts of ziziphus jojoba.100mg/kg extract was used to treat diabetic rats orally. Fasting serum glucose was measured every week and the period of the treatment continued for 2 weeks. Serum insulin lipid profiles, liver and kidney functions were measured at the end of experiment. In diabetic rats extract significantly reduced fasting serum glucose level ($p<0.001$) and markedly increase serum insulin level($p<0.001$).the data reveled that extract of Z. Jujuba have beneficial effects on diabetic rats. It reduce hyperglycemia, hyperlipidemia and peroxidates that associate diabetes. Its save towards liver and kidney function also. (Hussein, 2006)

Nephrotoxic effect

Evaluated the therapeutic effect of Z. jujuba fruit aqueous extract (ZE) on nephrotoxicity induced by ibuprofen (IBP) in rats. Male Sprague-Dawley rats were grouped as normal saline (control), ZE (500 mg/kg), IBP (400 mg/kg) and ZEþIBP-treated groups. After five days of oral administration, rats were sacrificed. The protective effect of ZE was evaluated by measuring kidney biomarkers, and histopathological changes of kidney were observed. Kidney antioxidant enzymes such as superoxide dismutase, catalase (CAT), glutathione S-transferase (GST) and lipid peroxidase were investigated. The results indicated that Z. jujuba aqueous extract could have a therapeutic role in reducing nephrotoxicity induced by ibuprofen.(Dalal, 2014)

In this study, they aimed to investigate the protective effects of Ziziphus jujube (ZE), a species of Ziziphus (L) in the buckthorn family Rhamnaceae, on cisplatin-induced nephrotoxicity. Twenty Sprague Dawley rats were divided into four groups and received different drug combinations orally. Group I was regarded as control group and received normal saline. Group II received cisplatin at 5mg/kg, group III received ZE at 500mg/kg, and group IV received both cisplatin and ZE. All animals were decapitated 6 days after cisplatin administration. Results revealed that cisplatin induced nephrotoxicity as indicated by a significant increase

in plasma creatinine and lipid peroxidation. This increase was significantly inhibited in animals pretreated with ZE. Histopathological observations were in correlation with the biochemical parameters in that ZE minimized cisplatin-induced renal tubular damage. Accordingly, ZE provides protection against cisplatin-induced nephrotoxicity in terms of oxidative stress(Faisal, 2019).

Antiviral activity

In this study investigate the antiviral activity on influenza A/PR/8 virus infected A549 human lung adenocarcinoma epithelial cell line and C57BL/6 mice. Betulinic acid showed the anti-influenza viral activity at a concentration of 50 μM without a significant cytotoxicity in influenza A/PR/8 virus infected A549 cells. Also, betulinic acid significantly attenuated pulmonary pathology including increased necrosis, numbers of inflammatory cells and pulmonary edema induced by influenza A/PR/8 virus infection compared with vehicle- or oseltamivir-treated mice in vivo model.(Hong, 2015)

This study aimed to determine the effect of jujube lotion on the recovery of breast fissure. This double-blind clinical trial recruited 100 primiparous lactating women who were randomly divided into two groups. In Jujube group, mothers used 0.5 mL of Fruit Lotion, and in control group mothers applied 4-5 drops of their breast milk five times a day, after breastfeeding. Both groups were examined on the 7th and 14th days after childbirth. The damage severity was assessed using the Amir scale and the presence or absence of nipple discharge was recorded. A significant difference was observed between the two groups in the extent of nipple damage before intervention on the 3rd day after childbirth and after intervention on the 7th and 14th days after childbirth (P = 0/02 ،P = 0/000). No significant difference was observed in sore nipple discharge between the two groups before the study and on the 7th day, while a statistically significant difference was observed between the two groups on the 14th day (P = 0/1, P = 0/01). The finding of this study revealed that the Ziziphus jujube fruits lotion heals nipple fissure faster and better than breast milk (Shahrahmani, 2018).

Neuroprotective effect

Investigated the neuro protective effect of fruit aqueous extract of Ziziphus jujuba Lam on glucose-induced neurotoxicity in PC12 cells as an appropriate in vitro model of diabetic neuropathy. Cell viability was determined by the MTT assay. Cellular reactive oxygen species (ROS) generation was measured by DCFH-DA analysis. Cleaved caspase-3, a biochemical parameter of cellular apoptosis, was measured by western blot analysis & they concluded that the aqueous extract of Z. jujuba protects against hyperglycaemia-induced cellular toxicity. This could be associated with the prevention of ROS generation and neural apoptosis. Moreover, the results suggest that the ZJF has a therapeutic potential to attenuate diabetes complications such as neuropathy(Taati, 2011).

The neuroprotective effect of fruit aqueous extract of *Ziziphus jujuba* Lam on glucose-induced neurotoxicity in PC12 cells as an appropriate *in vitro* model of diabetic neuropathy was investigated, Cell viability was determined by the MTT assay. Cellular reactive oxygen species (ROS) generation was measured by DCFH-DA analysis. Cleaved caspase-3, a biochemical parameter of cellular apoptosis, was measured by western blot analysis. The data showed that a 4-fold elevation in glucose levels within the medium significantly reduced cell viability, increased intracellular ROS and caspase-3 activation in PC12 cells after 24 hr. Incubation of the high glucose medium cells with 300-μg/ml *Z. jujuba* fruit (ZJF) extract decreased the high glucose-induced cell toxicity and prevented caspase-3 activation and excited ROS generation (Kaeidi, 2015).

Gastro protective effect

Evaluated the gastro protective effects of standardized aqueous extract of Ziziphus jujuba (Z. jujuba) stem bark against acidified ethanol- induced gastric ulcers as well as anti -helicobacter pylori activity of the plant extract in rats. Five groups of rats were orally pre-treated with normal saline (0.9%) as ulcer group, 150 mg/kg of ranitidine as positive control group, 100, 200 and 400 mg of standardized extract solution as the experimental groups. Two hours later, acidified ethanol solution was given by gavages in order to induce of gastric ulcer. The antibacterial effect of extract against clinical strains of Helicobacter pylori (H. pylori) was evaluated through disc diffusion test. The study indicates that Z. jujuba stem bark extract had a potential antiulcer activity which might be due to its protective effect on the gastric mucosa. Our study showed that anti-H. Pylori activity was not among gastro protective mechanism of Z. jujuba (Hamedi, 2016).

Evaluate the antiulcer activity of Ziziphus jujuba leaves extract (ZJE) at various doses using different experimentally induced gastric ulcer models in rats. Gastric ulcers were induced in rats by Pylorus ligation, 80% ethanol (1ml/rat) and aspirin (200mg/kg). In pylorus ligation induced ulcer model the parameters studied were gastric volume, free acidity, total acidity and ulcer index. Lesion index and gastric mucus content were determined in ethanol induced ulcer model and in aspirin induced ulcer model the ulcer index was determined. In pylorus ligation model, ZJE pretreatment caused significant reduction in gastric volume, free acidity, total acidity and ulcer index as compared to control group. In ethanol-induced ulcers, ZJE was effective in reducing lesion index and increasing the gastric mucus content. It was also effective in decreasing ulcer index in aspirin-induced ulcers. All the results obtained with ZJE were dose dependent. The antiulcer activity of ZJE can be attributed to its cytoprotective and antisecretory action (Ganachari, 2004).

Anti-inflammatory activity

In this study chloroform and methanol extracts of Ziziphus xylopyrus stem barks were tested for analgesic (Hot plate, Tail immersion and Acetic acid- induced writhing method) and anti-inflammatory activity (paw edema induced by carrageenan) in mice and rats, respectively. In the Hot plate and Tail immersion models, methanolic extract in the above doses increased the pain threshold significantly after 30 min, 1, 2 and 3h of administration. Methanolic extract showed dose-dependent action in all the experimental models in different doses whereas chloroform extract was not able to show such remarkable significant activities (Tripathi, 2001).

A dried ethanolic extract, obtained from Ziziphus jujuba Mill. (Rhamnaceae) leaves, was tested in order to evaluate the effects on plant cell division, its acute oral toxicity and anti-inflammatory properties. Two inflammation experimental models on rats, with carrageenan and kaolin as inflammatory agents, were used. The experimental group was treated by gavage for 7 days with 5 % aqueous suspension of the extract (500 mg/kg b.w.) and the control group with 1 mL/100 g b.w. distilled water. The reference group, in the 7th day, was treated with 0.1 % indomethacin solution (10 mg/kg b.w.). No toxic symptoms or mortality were observed in any animals. In both inflammation models a very weak anti-inflammatory effect was detected, a little better in the kaolin model but generally inferior to indomethacin. A statistically significant inhibitory effect on the growth of Triticum radicles was observed at 0.5% and 1% concentrations, accompanied by microscopic signs of cytotoxicity (Oana, 2016).

The study is conduct to determine the in vivo antidiarrhoeal, antibacterial and anti-inflammatory activities of Z. jujuba fruit ethanolic extract. The fruit was macerated and extracted by 95% (v/v) ethanol. The antidiarrhoeal activity was evaluated using castor oil and Escherichia coli induced diarrhoea mouse model. The antidiarrhoeal and antibacterial activity was investigated at graded doses (400-1200 mg/kg). The anti-inflammatory effects were tested using the carrageenan-induced paw oedema in female Wistar rats. Rat's treatment groups received tragacanth, 100 mg/kg diclofenac sodium, 800 mg/kg, 1200 mg/kg or 1600 mg/kg of an ethanolic extract of Z. jujuba (EEZJ). All treatment groups were fed with the compounds one hour before carrageenan injection at of rat's paw. EEZJ different doses did not show inhibitory activity against castor oil induced diarrhoea except for the higher (1200 mg/kg) dose. However, the frequency of defecation of stools and watery stool were reduced significantly when compared to control group ($P \leq 0.05$ and $P \leq 0.01$ respectively), resulted in overall 67% inhibition of diarrhoea. Our anti-inflammatory results demonstrated that EEZJ was able to inhibit the carrageenan-induced paw oedema in rats to a significant degree ($p \leq 0.05$) and the paw volume and thickness of both left and right paw were affected compared to the negative control group (Mesaik, 2018).

Wound healing activity

Studied the angiogenic activity of ethanolic extract of Z. xylopyrus Willd. stem bark by using chorioallantoic membrane (CAM) model (in-vitro) in 9 days old fertilized chick eggs. They also investigated the wound healing activity of the test extract by using excision and incision wound model (in-vivo) in Swiss Albino rats. The experimental data demonstrated that Z. xylopyrus Wild. stem bark extract displayed remarkable wound healing activity. The results of histological examination supported the outcome of linear incision and excision wound model as well (Jena, 2012). A dry ethanolic extract was obtained from Ziziphus jujuba Mill. leaves. The extract embedded in simple ointment (10% w/w) was evaluated in rat for wound healing

activity by topical application for a period of 12 days. The animal experiment was carried out using Cicatrizin (a known commercial ointment) as a positive control. The animals treated with Z. jujuba leaf extract showed a healing of 82.25% compared to the beginning of the experiment. The healing effect was similar to Cicatrizin (83.10%) and slightly higher, but not statistically significant from the one seen in the negative control group (76.2%, p=0.259) at the end of the study. Complete healing occurred after 18 days in both groups, without obvious scars and after 20 days in the control group (Marilena, 2016).

CONFLICTS OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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