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Jujube, a super-fruit in traditional Chinese medicine, heading for modern pharmacological science

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Abstract
Chinese jujube (*Zizyphus jujube* Mill.) and Indian jujube (*Ziziphus mauritiana* Lamk.) are largely use in traditional Asian medicine because of high nutritional composition. Its fruit is an edible oval drupe 1.5-3 cm long, varying from round to elongate and from cherry-size to plum-size depending on cultivar. The immature fruit is green in color and the fully mature fruit is entirely red. Under dry conditions, jujubes lose moisture, shrivel and become spongy inside. Jujube trees have stronger adaption to various biotic and abiotic stresses, especially salinity and drought. Chinese jujube is grown in temperate regions while Indian jujube is cultivated in hot arid regions of India. Jujube is cultivated from ancient time in China and reported that cultivated for last 5000 years. Chinese jujube is found in subtropics of Asia and largely in China. The jujube leaf, which is the main byproduct of jujube, has also been used in TCM for thousands of year to improve sleep, to nourish the heart and soothe the nerves, and to reduce hemorrhaging and diarrhea. Jujube contains 23 types of amino acids that are not found in most other kinds of fruits, and it has numerous health beneficial so it has famous as traditional and functional Chinese food. The major minerals in jujube is phosphorus, potassium, calcium and manganese. Also, there are also high amounts of sodium, zinc, copper and iron. It has also contains vitamin C, riboflavin and thiamine. Jujube usage in combination with other medicinal herbs and fruits have been used safely and effectively in traditional Chinese medicine for many years for various indications. What is necessary is more and better education on traditional Chinese medicine, fruits and herbs by experts and researchers as well as reasonable regulation by responsible government agencies. The development of a jujube industry will be beneficial in managing salinity and drought which are main challenges facing sustainability of production of this ancient Chinese fruit in the world. Jujube has numerous important pharmacological activities and it can be considered as a valuable source of nutraceuticals.

Keywords: Jujube, pharmacological science, traditional Asian medicine, super-fruit

Introduction

Jujube occurrence

In order for Chinese medicine, and in particular, Traditional Chinese medicine to become more integrated into medical practice in the world, there is a need to bridge the many conceptual and practical differences between western medicine and Chinese medicine [1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11]. The Chinese jujube (*Ziziphus jujube* Mill.) which originates from China with a history of over 4000 years is recognized as the most important fruit species belongings to the Rhamnaceae family (60) [12]. It was first described scientifically by Carlous Linnaeus as *Rhamnus zizyphus*, in *Species Plantarum* in 1753. Later in 1768, Philip Miller concluded it was sufficiently distinct from *Rhamnus* to merit separation into a new genus, in which he named it *Ziziphus jujube*, using Linnaeus species name for the genus but with a probably accidental single letter spelling difference, i for y; for the species name he used a different name, as tautonyms (Repetition of exactly the same name in the genus and species) are not permitted in botanical naming. However, because of Miller's slightly different spelling, the combination correctly using the earliest species name (from Linnaeus) with the new genus, *Ziziphus zizyphus*, is not a tautonym, and was therefore permitted as a botanical name; this combination was made by Hermann Karsten in 1882 [13]. Chinese jujube (*Zizyphus jujuba* Mill.) and Indian jujube (*Ziziphus mauritiana* Lamk.) are largely use in traditional Asian medicine as super fruit. Indian jujube (*Ziziphus mauritiana* Lamk.) is known as ber, desert apple or Indian plum, and it also belongs to family Rhamnaceae; it is a tropical/subtropical fruit native to the northern

hemisphere [14]. Li *et al*. [15] discovered that the Chinese jujube (*Ziziphus jujuba* Mill.) originates from sour jujube (*Ziziphus acidojujuba* Mill.) and is an economically important genus in the Rhamnaceae family. They also concluded that most jujube cultivars have a certain correlation with their origin, and there are obvious gene exchanges between sour jujube and jujube cultivars. Its pulp is eaten mostly fresh, but may be dried or processed into confectionary recipes in bread, cakes, compotes, and candy [16].

Description of flower, fruit and trunk, branches, culture and other characteristics of jujube is shown in Table 1. World distribution of Chinese jujube is shown in Table 2.

Table 1: Description of flower, fruit and trunk, branches, culture and other characteristics of jujube.

Height	**457 to 1070 cm**
Spread	305 to 915 cm
Crown uniformity	Irregular outline or silhouette
Crown shape	Oval, round
Crown density	Open
Growth rate	Medium
Texture	Fine
Foliage	
Leaf arrangement	Alternate
Leaf type	Simple
Leaf margin	Crenate, serrulate
Leaf shape	Lanceloate, ovate
Leaf venation	Bowed
Leaf type and persistence	Deciduous
Leaf blade length	5 to 10.5 cm, less than 5.5 cm
Leaf color	Green
Fall color	Yellow
Fall characteristic	Showy
Flower	
Flower color	Yellow
Flower characteristics	Inconspicuous and not showy; spring flower
Fruit	
Fruit shape	Oval, Round
Fruit length	2.5 to 12.5 cm
Fruit covering	Fleshy
Fruit color	Black, red
Fruit Characteristics	It attracts squirrels and other mammals; fruit, twigs, or foliar cause significant litter, showy
Trunk and Branches	
Trunk/bark/branches	Grow mostly upright and will not droop, not particularly showy, should be grown with a single leader, thorns are present on the trunk or branches
Breakage	Resistant
Current year twig color	Brown
Current year twig thickness	Medium
Culture	
Light requirement	Tree grows in part shade/part sun; and also grows in full sun
Soil tolerances	Clay, loam, sand, slightly alkaline, acidic, well-drained
Drought tolerance	High
Other characteristics	
Roots	Surface roots are usually not a problem

Table 2: World distribution of Chinese jujube.

Region	**Country**
Asia	Afghanistan, Armenia, Azerbaijan, bengla, Burma, China, Cyprus, India, Iraq, Iran, Israel, Japan, Kyrguzstan, Lebanon, Malaysia, Mongolia, Pakistan, Palestine, South Korea, Syria, Thailand, Turkey, Turkmenistan, Uzbekistan
Europe	Bulgaria, England, France, Germany, Greece, Italy, Czech, Macedonia, Portugal, Romania, Russia, Slovenia, Spain, Ukraine, Yugoslavia
Africa	Egypt, Tanzania, Tunisia
North America	Canada, USA
Oceania	Australia, New Zealand

Jujube nutritional composition and chemical constituents

Kader *et al*. [17] stated that relative to most other fresh fruits, Chinese jujubes are lower in water content and titratable acidity, and higher in total sugars (Mostly reducing sugars) and phenolics. Chinese jujubes are very rich in ascorbic acid (Vitamin C) content which increased with maturation to 559 mg/100 g fresh weight. Fruits held at 0º for 26 days exhibited sheet pitting due to chilling injury. Li *et al*. [18] provided the proximate composition of five cultivars of Chinese jujube. In their experiment, total phenols, minerals and vitamins were also determined for fruits of Jinsixiaozao, Yazao, Jianzao, Junzao, Sanbianhong cultivars. Significant variations were recorded for moisture (17.38-22.52%), carbohydrate (80.86-85.63%), proteins (4.75%-6.86%), lipids (0.37-1.02%), soluble (0.57-2.79%), and insoluble (5.24-7.18%) fibers, reducing sugar (57.61-77.93%) and ash (2.26-3.01%). Glucose and fructose were identified as major soluble sugar in all the five cultivars, while rhamnose, sorbitol and sucrose

contribute in lesser amount. They have also found that vitamin C content is very high in Chinese jujube. Yan *et al*. [19] found that five essential elements and two toxic elements (Except cadmium) varied widely in their contents in the four jujube fruits. They announced that knowledge of the contents of these elements would provide consumers with information on the quality of jujube fruits. Chen *et al*. [20] reported the Junzao cultivar contained relatively low level on the total dietary fiber, protein, total sugar, and total titratable acids. The Huizao cultivar possessed the mediate level of the sugar-to-acid ration and ascorbic acid. The Dazao cultivar showed high level of the total dietary fiber, protein, sugar, and total acids. In their experiment, principal components analysis indicated that the parameters that differentiated these jujube cultivars appeared to be the total dietary fiber, protein, total sugar, fructose, glucose, sucrose, and total titratable acids. Rahman *et al*. [21] noted that Chinese jujubes consist of 51.99-71.75% edible part, 82.35-89.63% carbohydrates, 4.43-6.01% protein, 0.48-0.63% lipid, 2.80-4.80% polysaccharide, 45.64-88.97 mg/100 g ascorbic acid, 132.16-196.58 mg/100 g phenolics and 101.17-132.04 mg/100 g flavonoids in dry matter. Ertop and Atasoy [22] found that the jujube fruit is rich in mineral content, fiber and a good source of food for direct consumption and maybe a good additive for different foods when dried. In their study, they found that jujube fruit, especially in dried and powder form can be valorized in future studies as fortifying and hydrocolloid ingredient due to its high carbohydrate content in a different type of products. Huang *et al*. [23] also found that the fruits are nutritious, being high in flavonoids and vitamins C, B1, and B2, and because of that it can be considered as a so-called functional food, having nutritional as well as medicinal uses. Islam *et al*. [24] found that jujube as a nutritious fruit is important especially for low-income group people because of it, s cheaper value of cost than other available fruits. Besides, it is grown successfully in unfertile land and drought prone areas. It is also a less perishable fruit and cultivating this fruit with large scale famers can be economically benefits and also helpful for maintaining national economic level.

Proximate composition of *Ziziphus mauritiana* seeds is shown in Table 3. Mineral composition of seeds of *Ziziphus mauritiana* is shown in Table 4.

Table 3: Proximate composition (g/100 g dry weight) of *Ziziphus mauritiana* seeds [25].

Content	Dry weight (g/100 g)
Mositure	4.21±0.30
Ash	2.79±0.27
Protein	36.10±0.57
Crude fiber	11.04±0.88
Lipids	27.40±0.11
Carbohydrate	21.26±0.63

Carbohydrates were estimated by difference. The values are means and standard deviation (SD) for those determinations.

Table 4: Mineral composition of the seeds of *Ziziphus mauritiana* (in mg/100 g) [25].

Content	Dry weight (mg/100g)
Sodium (Na)	154.79±10.50
Magnesium (Mg)	6.23±0.12
Potassium (K)	589.08±10.69
Zinc (Zn)	3.52±0.05
Manganese (Mn)	1.15±0.14
Iron (Fe)	1.21±0.15
Phosphorus (P)	585.43±41.29

The values are means a standard deviations for three determinations.

Traditional medicinal uses and potential health benefits of jujube in modern medicine industry

The jujube leaf, which is the main byproduct of jujube, has also been used in TCM for thousands of year to improve sleep, to nourish the heart and soothe the nerves, and to reduce hemorrhaging and diarrhea [26]. On the basis of Iranian traditional medicine, local traditional healers [27] used powders of stem bark and leaves of jujube to cure wounds and oral wounds as aphthous. Hamedi *et al*. [27] also discovered that fruits are widely used in Iranian folk medicine as antitussive, laxative agent and blood pressure reducer. Jujube has also been used as a traditional Chinese medicine (TCM) for many years with its various and numerous health benefits such as anti-inflammatory [28], anti-cancer [29], gastrointertinal protective, anti-oxidant, anti-insomnia, and neuroprotective [30]. Mill Goetz [31] reported that the fruits and seeds of Jujuba are used in Chinese and Korean traditional medicine, where they are believed to alleviate stress. In Persian traditional medicine, it is used in combination with other herbal medicines to treat colds, flu and coughing. Jujube fruit contains flavonoids, vitamins, amino acids, organic acids, polysaccharides, and microelement, which found useful in spleen diseases and nourishment of blood in Chinese system of medicine [32]. Tahergorabi *et al*. [33] stated that different parts of jujube can be used for curing different kinds of illness such as diabetes, diarrhea, skin infections, liver complaints, urinary disorders, obesity, fever, pharyngitis, bronchitis, anemia, cancer, insomnia, and of course for blood purification and tonification of the gastrointestinal tract. Hemmati *et al*. [34] reported that jujube causes a decrease in the blood levels of glucose and lipids and it has been reported to make a significant decline in triglyceride, LDL and cholesterol levels. Mahajan & Chopda [35] found that roots and the bark are used to treat dysentery, and the bark cures boil is good for the treatment of diarrhea. They have also considered the aqueous paste of the leaves is applied externally to relieve a burning sensation. Furthermore, they did report that seeds cure eye diseases and are also useful in leucorrhoea, and the kernels increase flesh and strength and are sedative in activity. Beavo & Brunton [36] found that jujube fruits contain a certain amount of cyclic adenosine monophosphate (cAMP) which has positive effect on the heart muscle, nutritional myocardium, diastolic blood vessels, anti-arrhythmia, and anti-platelet aggregation. Recent phytochemical researches of jujube fruits have revealed their effects, such as the anticancer, anti-inflammatory, antiobesity, immunostimulating, antioxidant, hepatoprotective, and gastrointestinal protective activities and inhibition of foam cell formation in macrophages [37]. Cosmulescu *et al*. [38] noted that the impact of maturity stage was significant on organic acid distribution of jujube extracts, and ascorbic acid is the major organic acid found in jujube fruits, followed by malic acid and lactic acid. They have also mentioned that jujube fruits are rich in bioactive compounds and can be complement in human, s healthy eating. Shi *et al*. [39] indicated that the skin color of jujube fruit during maturation is due to changes in the levels of flavonoids, cartenoids, and anthocyanins. They concluded that the color changes are also associated with changes in antioxidant activity. Hoshyar *et al*. [40] indicated that the *Z. jujube* ameliorates the adverse effects of NMU carcinogenesis and could be useful for treating mammary tumours in humans. Betulinic acid and jujuboside B could be the active components showing beneficial effects on cardiovascular system [41]. Motevali *et al*. [42] stated that jujube is a valuable medicinal plant, is consumed either as fresh fruit

or dried product in Iran. Drying jujube guarantees a longer shelf time while preserving its quality to be used in medical and pharmaceutical industries. Ivanisova *et al*. [43] reported that jujube fruit is rich in bioactive compounds and can be used in food, medicine and pharmacy industry. Taechakulwanijya *et al*. [44] have found that all jujube seed extracts were not toxic to Vero cells, all jujubes cultivars tested are promising candidates for more elaborate study of their anticancer mechanisms. Vafaei and Abdollahzadeh [45] indicated that the jujube fruit extract could accelerate burn wound healing among Balb/c mice. It has been reported that triterpenic acids were considered as active ingredients for the effect on anti-inflammatory and anti-cancer activities [46]. The aqueous ethanol extract of the jujube leaf were used as energetic constituent for hepatosis and wound healing in animal trials [47]. Shahrahmani *et al*. [48] showed that *Zizuphus Jujube* Fruit lotion can treat sore nipples faster than breast milk over a period of 10 days. Also, nipple pain in the jujube lotion group was less than the breast milk group. Gheibi *et al*. [49] found that the accessibility and affordability of jujube fruit and the side effects of routine drugs, taking a combination of jujube fruit with low doses of routine pharmaceutical drugs can improve and cure ulcerative colitis disease. Neuronal beneficial properties of jujube are shown in Table 5. Safizadeh *et al*. [50] concluded that BUN, cratinine, urate and liver enzymes in all extracts increased. They have suggested that administration of high doses of jujube (up 5000 mg/kg) is nearly safe and did not exert hepato and nephrotoxicity in rats. Combination of *Zizyhpus jujube* and green tea extracts exerts excellent cytotoxic activity in HepG2 cells via reducing the expression of APRIL; also, jujuba extract and green tea extract mixture might provide a lead to a new drug design to treat hepatocellular carcinoma in the future APRIL [51]. Dahiru and Obidoa [52] reported that pretreatment of rats with aqueous leave extract of *Ziziphus jujube* inhibited alcohol induced increase in cholesterol and triglyceride levels in rats serum. Anbarasi and Brindha [53] found that methanolic extract of dried bark of *Ziziphus jujube* was found to cause a significant decrease in the levels of total cholesterol, triglycerides and LDL-cholesterol, and glucose levels in streptozotocin-induced diabetes in rats. *Z. Jujube* powder possesses hypolipidemic and anti-obesity properties and did not show any negative impact on liver function as measured by ALT and AST [54]. Gao *et al*. [55] mentioned that Chinese jujube polysaccharides are anecdotally reputed to be useful in amerliorating intestine oxidative injury resulting from ischemia and reperfusion in rabbits. The jujube polysaccharides composed of glucose (23%), xylose (31.3%), mannose (12.9%), and fructose (21.6%) possess antioxidant effects, and this may have contributed to the observed effects (Wang 2011). Varghese and Patil [56] revealed that jujube leaves have insecticide action against *Helicoverpa armigera* and *Tribolium confusum*, respectively. It has been proven that jujube leaves' insecticide actions is done by inhibiting the digestive and mitochondrial enzymes which lead to growth retarding of the larvae. The most important pharmacological properties of jujube is shown in Table 5.

Conclusion

The most important pharmacological properties of jujube are anti-diabetic effects, hypnotic-sedative and anxiolytic effect, neuroprotective activity, sweetness inhibitor, anti-cancer activity, anti-ulcer activity, anti-inflammatory effect, anti-spastic effect, anti-allergic activity, permeability enhancement activity, cognitive activities, anti-fertility, hyptensive and anti-nephritic effect, cardiovascular activity, immunostimulant effects, anti-oxidant effects and wound healing activity. Traditional Chinese Medicine included fruits and herbs are increasingly and extensively used by a substantial part of the population. Jujube has numerous important pharmacological activities and it can be considered as a valuable source of nutraceuticals.

Table 5: The most important pharmacological properties of jujube.

1- Anti-diabetic effects
2- Hypnotic-sedative and anxiolytic effect
3- Neuroprotective activity
4- Sweetness inhibitor
5- Anti-cancer activity
6- Antimicrobial activity
7- Anti-ulcer activity
8- Anti-inflammatory and anti-spastic effect
9- Anti-allergic activity
10- Permeability enhancement activity
11- Cognitive activities
12- Anti-fertility/contraceptive property
13- Hypotensive and anti-nephritic effect
14- Cardiovascular activity
15- Immunostimulant effects
16- Anti-oxidant effects
17- Wound healing activity

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