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Health Promoting Effects of *Ziziphus mauritiana* : An Overview

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Abstract

Natural products are the main source for an alternative system of medicine. *Ziziphus mauritiana*, commonly known as jujubes, belongs to the family Rhamnaceae and is majorly found in the Indian subcontinent. They are traditionally used to treat chronic bronchitis, insomnia, diabetes, diarrhoea, abscesses, wounds, liver diseases, fever, sleeplessness, constipation, urinary diseases, and abdominal pains. Over the course of many years, various parts of *Ziziphus mauritiana* has been found to possess hair growth stimulating, anti-platelet aggregating, anti-inflammation, wound-healing, anti-obesity, antibacterial, and antioxidant effects. Various peer-reviewed research articles were collected from SCOPUS, PubMed, Google, Research Gate, and Web of Science databases. A total of 26 papers were selected based on their relevance. Acetyljujuboside B, Mauritine A, and Jujuboside A are some of the numerous chemical constituents present in *Ziziphus mauritiana.* The present review is an effort to provide a comprehensive review of the literature on the health-promoting effects of *Ziziphus mauritiana*.

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INTRODUCTION

Ziziphus mauritiana (ZM), also known as jujubes, Boroi, or Kul, is widely cultivated in India and other states of the Indian subcontinent. It is a spiny, evergreen shrub/ small tropical fruit tree species, belonging to the Rhamnaceae family. The synonyms, vernacular names, and scientific classification are mentioned in Tables 1 and 2 and Table 3 respectively. It grows up to 15 m high with a 40 cm or more trunk diameter, spreading crown, stipular spines, and many drooping branches. Depending on the variety, the fruit can be obovate, oval, or round with white and crisp flesh and can be 1 - 2.5 inches long. The leaves are either alternate and spiralling or opposite. The plant has symmetrical flowers that have 5 separate sepals and petals. The petals are isomerous, with 5 stemens. The plant also has 2 or 3 ovules (Macwan *et al.*, 2012). ZM has shown to possess many different activities, and the family Rhamnaceae have shown to have high nutritional values. This paper hopes to explain in detail the health-promoting effects of ZM.

MATERIALS AND METHODS

The articles for this review was carried out systematically by surveying peer-reviewed research articles from SCOPUS, PubMed, Google, Research Gate, and Web of Science databases. The online search involved the use of keywords such as *Ziziphus mauritiana*, *Ziziphus jujuba*, phytochemical screening, antioxidant, anti-diabetic, anti-obesity, antibacterial, wound healing, hepatoprotective, anti-inflammatory, anti-platelet aggregating, hair

growth-promoting activity. Research articles of Non-English origin were not included in the study. This screening narrowed the article count to 26, and this was used in the study.

RESULTS AND DISCUSSION

Traditional uses

ZM has been widely used as a medicinal plant in Asian countries. Ancient Chinese books, *Huangdi* Neijing (475 – 221 BC) and *Shennong Bencao Jing* (300 BC – 200 AD), states *ZM* as one of the most valuable and superior herbal medicines in China (Chen *et al.*, 2014). They are traditionally used to treat chronic bronchitis, insomnia (Afroz *et al.*, 2014), diabetes, diarrhoea, abscesses, wounds, liver diseases, asthma, fever, sleeplessness, constipation, urinary diseases, gastrointestinal disorders and abdominal pains (Jarald *et al.*, 2009). They are used on cuts, treat ulcer, and to treat pulmonary ailments (Abalaka *et al.*, 2010). The roots are used against skin diseases while the leaves are used to treat sores, used in the treatment of typhoid, and have antimicrobial, antioxidant, and hepatoprotective effects. When taken with buttermilk, the seeds can stop vomiting and abdominal pains during pregnancy. They are also used as sedatives (Abalaka *et al.*, 2010; Jain *et al.*, 2019).

Ethnobotany

Two ethnobotany surveys were conducted in Lesser Himalayas – Pakistan (Abbasi *et al.*, 2013) and Burkina Faso (Sop *et al.*, 2012) in West Africa. Both of the studies were focused on the species that are most used in the respective communities. The studies in Pakistan yielded a total of 35 wild edible fruits belonging to 21 genera and 17 families, which were used for the treatment of various ailments and consumed. Out of the 17 families, Rhamnaceae (5 spp.) was considered to be one of the most dominating species behind Rosaceae (8 spp.) and Moraceae (6 spp.). *ZM* was also found to be the most significant species within top fruit plants on the basis of cultural importance index (Abbasi *et al.*, 2013).

3 ethnic groups were subjected to a survey to identify the most important species of their region, Burkina Faso. The survey also shed light on the conservation priorities from the informant's perspective. *ZM* was ranked 4^{th} and 5^{th} in the Most Important Species (MIS) and species for conservation priority (SCP), respectively. *ZM* was also considered as one of the food species with a high socioeconomic value in Burkina Faso (Sop *et al.*, 2012). These data suggest that *ZM* has significant importance in the livelihood in local communities.

Phytochemistry

Extensive phytochemical investigations on Ziziphus species have proven it to be a rich source of many chemically unique and biologically interesting compounds. The constituents are cyclopeptide alkaloids (Table 4), sedative flavonoids (Table 5), Terpenoids (Table 6), and glycosides (Table 7).

Pharmacological activities

Antioxidant

The antioxidant properties of ZM has been well-documented. Traditional names for ZM are Apple Kul and Bau Kul. Different concentrations of methanolic extract of Apple kul and Bau Kul from Dhaka, Bangladesh was found to increase its inhibitory potential with increasing concentration when tested for DPPH radical scavenging activities. The 50% inhibitory concentration (IC_{50}) was 0.73 mg/mL for Apple Kul which was significantly higher than the standards, catechin (3.30μg/mL), ascorbic acid (2.80 μg/mL) and gallic acid (3.00 μg/mL) but much lower than the IC_{50} of an Indian jujube variety (ZM*)* (6.15 μg/mL) and IC_{50} values was 1.34 mg/ml for Bau Kul (Tanvir *et al.*, 2015).

Apple kul also showed promising activity, when tested using Ferric-Reducing Antioxidant Power Assay (FRAP) and compared with 15 other promising jujube genotypes from the Mediterranean regions in Turkey and Indian jujube genotype, while Bau Kul showed appreciable FRAP value. Apple kul and Bau Kul also has the ability to scavenge H_2O_2 in a concentration-dependent manner in H_2O_2 scavenging activity carried out by the titration method (Afroz *et al.*, 2014).

Researchers from Burkina Faso have also performed antioxidant studies on leaf extracts of ZM collected from Loumbila, BF. Out of the 5 FRAP fractions used for the study, ethyl acetate extract showed highest inhibition on DPPH radical (8.20 μg/mL) followed by aqueous (9.15 μg/mL), ethanol (9.80 μg/mL) and dichloromethane (12.70 μg/mL) when compared to standard quercetin (6.90 μg/mL). FRAP assay of the extracts were also investigated. The order of FRAP activity was: aqueous (85.58 mg AAE/ 100 mg) > ethyl acetate (82.84 mg AAE/ 100 mg) > ethanol (41.74 mg AAE/ 100 mg) > dichloromethane (26.36 mg AAE/ 100 mg) > hexane (7.50 mg AAE/ 100 mg) (Youl *et al.*, 2019).

The above evidences suggest that different parts of *the ZM* plant can be a potent antioxidant. Among the different plant parts used in the above studies, leaf extracts possess better antioxidant properties when compared to the fruit and bark extracts. The antioxidant property has been largely related

Table 1: Synonyms

Paliurus mairei H. Lév.	Rhamnus jujuba L.	Ziziphus jujuba (L.) Gaertn.
Ziziphus mairei (H. Lév.) K. Browicz & Lauener	Ziziphus mauritiana var. muratiana (Maire) A. Chev.	Ziziphus mauritiana var. orthacantha (DC.) A. Chev.
Ziziphus mauritiana Maire	Ziziphus orthacantha DC.	Ziziphus rotunda DC.

*The synonyms were obtained from (India Biodiversity, 2019)

Table 2: Vernacular names

English	Jujube tree, jujube, common jujube, Chinese date
Assamese	Bogori, Bagari
Tamil	Yellande, Ilantha, Ilanthai
Hindi	Ber
Irula	Elanthai, Elasi
Kannada	Yelchi
Karbi	Thakri
Malayalam	Perimthudali, Lanthapazham, Badari, Elentha,
Arabic	annab, aunnabe-hindi, aunnabehindi, nabig, nabiq,
Persian	kanar, kunar, nabik, sinpo-i-jilani
Tibetan	gya-sug, ko la, rgya sug
Urdu	annab, baer, ber, unab, unnab

*The vernacular names were obtained from (ENVIS, 2019; India Biodiversity, 2019)

Table 3: Scientific Classification

Kingdom	Plantae	Order	Rhamnales
Subkingdom	Tracheobionta	Family	Rhamnaceae
Superdivision	Spermatophyta	Tribe	Paliureae
Division	Magnoliophyta	Genus	Ziziphus
Class	Magnoliopsida	Species	Ziziphus mauritiana
Subclass	Rosidae		

*The scientific classification were obtained from (India Biodiversity, 2019; USDA, 2019)

Table 4: Cyclopeptide alkaloids

Melonovine A	Sativanine F	mauritines A-H, J-M	amphibines B, D-F	Scutianine C-D
Nummularine H, B	Sativanine C-E	Ziziphine A	Daechuine S6	Nummularine R
Sanjoinenine	Franguloine	Amphibine B	Amphibine D-E	Sativanine G
Daechuine S3	Hysodricanin A	Aralionin C	Jubanine A-B	Frangulanine
Mucronine D	Nummularine A	Franganine	Sativanine K	Sativanine H

*Some of the cyclopeptide alkaloids present in ZM (Hossain *et al.*, 2015; Mahajan and Chopda, 2009).

Table 5: Sedative flavonoids

Swertish	spinosin	puerarin (6'''-feruloylspinosin)	apigenin-6-C-D-glucopyranoside	,6'''feruloylisospinosin
isospinosin	γ-fagarine	, β-sitosterol	stigmasterol,	α and β-amyrin,

* Some of the sedative flavonoids present in ZM (Mahajan and Chopda, 2009)

Table 6: Terpenoids

Betulin	Betulinic acid	colubrinic acid	3-O-cis-p-coumaroylmaslinic acid	2α-hydroxyursonic acid
alphi-tolic acid	3-Ocis-p-coumaroylalphitolic acid	3-O-transpcoumaroylalphitoilic acid	ursolic acid	3-o-trans-pcoumaroylmaslinic acid

*Some of the terpenoids present in ZM (Mahajan and Chopda, 2009).

Table 7: Glycosides

protojujuboside B. Jujuboside C	Jujuboside A acetyljujuboside B,	Jujuboside B protojujuboside A	Jujuboside A1, protojujuboside B1	Jujuboside B1,

* Some of the glycosides present in ZM (Mahajan and Chopda, 2009)

to the polyphenol content present in the plant extracts (Youl *et al.*, 2019). States that plant polyphenols are mostly antioxidants. Polyphenols were responsible for 98.63% reduction of DPPH and play a major role in mediating antioxidant effect by scavenging free radicals and/or by chelating metal ions.

Anti-Obesity

Bark powders of *ZM* (ZMBP) have shown to exert good anti-obesity activity (Deshpande *et al.*, 2013). Performed an anti-obesity study on Wistar rats. The obese rats were administered with 250 and 500 mg/kg dose of ZMBP. ZMBP induced rats showed a significant reduction in the weight of the peritoneal fat pad when compared to the Standard drug Sibutramine after 90 days of treatment. MRI scans of the DEXA analysis also showed 68.99 % and 72.84 % reduction in body fat mass at 250 and 500 mg/kg dose, respectively, when compared to the obese control group. The mechanism of reduction in body fat has been found to be through the excretion of fat through the fecal matter. Fecal fat analysis shows that obese rats treated with 250 mg/kg and 500 mg/kg ZMBP showed an increasing weight of fecal matter when compared to the standard. This shows that ZMBP have far more superior activity when compared to the standard drug. Another study performed by (Deepak and Anurekha, 2018) also showed a dose-dependent reduction of body weight of obese Wistar rats when treated with aqueous extracts of *ZM.* 200 and 400 mg/kg/day dose of extracts of *ZM* showed a significant reduction of body weight during a period of 14 days. The polyphenolic compounds that are abundant in ZMBP has be speculated to be responsible for the property of anti-obesity.

Wound-healing activity

Wound healing activity has been established in different parts of the *Ziziphus* plant. (Sumanth and Bhargavi, 2014) Performed exclusion and inclusion wound models to assess the wound-healing activity of ethanolic extracts of *ZM* leaf. The study was performed over a period of 20 days on albino strains of Wistar strains, and the rate of wound contraction and epithelisation period was calculated. *ZM* aqueous extract of 300 mg/kg dose showed considerable 20 days wound contraction activity but was overshadowed by gel of ethanol extract of *ZM* 100 mg/cm^2 (EEZM) and standard Framycetin skin cream (FSC) 100 mg/cm^2. It also showed a similar period of epithelisation when compared to EEZM gel and standard FSC. The similar wound-healing activity was performed by (Kumar *et al.*, 2012) on albino rats using 5% and 10% of *Z. jujube* methanolic bark extracts to assess their excision wound surface area, wound concentration and wound protein concentration. The 10% methanolic extracts showed similar wound surface area (0 mm^2 at 24th day) and comparable wound contraction results to that of standard (10% Povidine iodine) and wound protein concentration. The presence of tannins, saponins, flavonoids, and triterpenoids are said to be responsible for promoted wound contraction and decreased the period of epithelisation in the excision wound model (Sumanth and Bhargavi, 2014).

Anti-platelet aggregating activity

The seeds of *Z. jujuba* (SZJ) has been used in this study. The ethanolic extract of SZJ (ESZJ) and Jujuboside A and B were assessed for their antiplatelet effects using 3 different models: collagen-, thrombin- and arachidonic acid (AA)-induced platelet aggregation model. Results showed that 300 μg/ml of aspirin (standard antiplatelet drug) and ESZJ showed the same activity at collagen

and AA models, but ESZJ showed better activity than aspirin in the thrombin-induced platelet aggregation model with IC_{50} of 181.3 $\pm$ 1.6 and 325.9 $\pm$ 2.2 respectively. Studies further performed on Jujuboside A, and B showed that Jujuboside B showed better activity comparatively in all the 3 models. ESZJ treated mice also showed an increase in bleeding time and protection against acute pulmonary thromboembolism, further solidifying its activity against platelet aggregation (Al-Reza *et al.*, 2009).

Hair growth-promoting effect

The essential oils of seeds of Z. jujuba showed hair grow*th-promoti*ng activity by an in-vivo method. Investigations on BALB/c mice showed that 1% and 10% essential oils show better hair length, hair weight, hair thickness, and relative area of hair follicle when compared to treatment. On comparison within oils, 1% essential oil showed better activity than 10% essential oil (Yoon *et al.*, 2010).

CONCLUSIONS

With the recent global concern regarding the change of lifestyle choices, herbal remedies are gaining more traction, importance, and relevance. ZM has been well-documented and used as a remedy in many cultures. With this review article, we have concluded that ZM contains many different constituents such as alkaloids, glycosides, and terpenoids of different nature and are used to treat diabetes, wounds, liver diseases, asthma, fever, constipation, urinary diseases, and gastrointestinal diseases. ZM has also shown to have potent properties of hair growth, anti-platelet aggregation, myocardial ischemia, antidiabetic, anti-inflammation, hepatoprotection, wound-healing, anti-obesity, antibacterial and antioxidant effects. By understanding the health-promoting properties of ZM, it can help provide better solutions to diseases that do not have a comprehensive treatment with the constituents that are less researched.

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