

Potential therapeutic applications for Terminalia chebula in Iranian traditional medicine

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Abstract

Terminalia chebula (family: Combretaceae) is widely used in the traditional medicine of India and Iran to treat diseases that include dementia, constipation, and diabetes. This tree is known in Iranian traditional medicine (ITM) as halileh or halilaj and the fruit is used to develop treatments. It is described in ITM as an astringent that has a "cold" and "dry" temperament. References to the medicinal properties of *Terminalia chebula* were collected from important ITM sources and from modern medical databases (PubMed, Scirus, ScienceDirect, and Scopus). The medicinal properties described for this

tree in ITM were compared with those reported in studies of modern phytotherapy. The results confirm that the tree referred to as halileh in traditional books is the *Terminalia chebula* used in present-day studies. Treatments that have not been evaluated in modern phytotherapy but have been traditionally treated with *Terminalia chebula* include fever, and psychological and psychiatric issues. This article confirms the medicinal uses of *Terminalia chebula*.

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Key words: Fructus chebula; Phytochemicals; Pharmacology; Iranian traditional medicine

INTRODUCTION

Terminalia chebula (myrobalan) is a commonly consumed herb used in Indian traditional medicine that has been adopted for use in Iranian traditional medicine (ITM). Traditional Iranian physicians have used the herb to treat many diseases. Myrobalan is referred to as halileh in ITM textbooks in Farsi, ah-halilaj in Arabic, and harharu in Hindi.^{1,2}

Myrobalan has a well-documented history of use in traditional medicines to treat disease. ITM bases the use of medications on the temperament of the substance. These temperaments cannot be defined using laboratory criteria, so myrobalan was assessed according to modern scientific standards to allow comparison of traditional and modern scientific findings.

In both ITM and modern phytotherapy, the main medicinal part of myrobalan is the fruit. The pharmacologically active compounds of myrobalan are total phenols (tannins). ITM states that all things are composed of four elements and the differences between objects can be attributed to the ratios of these four elements in each object. Thus, every object has a specific quality

based on its dominant element (s). This specific quality is known as temperament (midzaj).^{3,5} Belief in the temperament of objects is common to many types of traditional medicine, including Greek, Arabic, Roman, Indian, European, and Traditional Chinese Medicine.⁶ Plants are also thought to be composed of the four elements and adhere to specific rules.

Myrobalan is believed to have a cold and dry nature in ITM. The present study reviewed and compared the pharmacological uses of myrobalan in ITM and modern phytotherapy. ITM and modern phytotherapy recommendations about the safety and acceptable dosages for the medicines made from this plant are discussed.

METHODS AND MATERIALS

Major ancient sources of information about ITM were consulted. The following sources were searched for information about halileh for the treatment of disease: the Avicenna's Canon, Al-Igraz, At-Tibbieh, Al-Mabalahis, Al-Alaieh, Axirazam, Sharhe-Asbab, Akbari medicine, and Kholasat-Al-Hekmaa. The habitat, appearance, and properties of this herb as described in ITM were recorded.

The following modern botanical sources and databases were searched for the key words "Terminalia chebula" and myrobalan: ScienceDirect, Google Scholar, Iranmedex, PubMed, Scirus, and Scopus. These key words were combined with the terms "phytochemistry" and "pharmacology" to search for phytochemical and pharmacological properties of myrobalan. The articles were selected based on academic and scientific journal. The results were compared with the findings from ITM sources. This method of data collection was used to control for possible publication bias.

RESULTS

Shape and structure

Terminalia chebula is a traditional plant belonging to the genus *Terminalia*, family *Combretaceae*. It is native to India and Southeast Asia and is commonly known as myrobalan in English.⁷⁻⁹ It is extensively cultivated in Taiwan and India.^{8,10} The fruit of the tree is the most important part. If unripe fruit is picked from the tree and dried, it becomes black in color and is then called black myrobalan. The fruit is yellow when it is fully ripe. When the yellow fruit has dried, it becomes very hard and is known as yellow myrobalan. The tannin content of the fruit increases as it ripens.⁹ The best myrobalan fruit for use in ITM is stiff, heavy, free from decay, and sinks in water.^{4,11}

ITM and myrobalan

ITM physicians believe that the fruit of the myrobalan tree has a water component that is called an extract and an earth component that is called scum. Addition-

ally, it contains moisture (rotoobat fazliyye) that is resinous. The earthy components comprise two parts: cool components, and burnt and hot components. Cool components are acrid and astringent. Burnt and hot components are bitter and tender. Moisture can contain air components that make the fruit oily in appearance. The interaction of these basic components forms the temperament of myrobalan, which is cold and dry.¹¹

Phytochemistry of myrobalan

Steroids/sapogenins, saponins, anthraquinone derivatives, flavonoids, and tannins were detected in the fruit of myrobalan.⁸ The most important component in the fruit is tannin. *Terminalia chebula* has a tannin content of 32%–45% that includes gallic acid, ellagic acid, chebulic acid, chebulinic acid, punicalagin, and tannic acid. The flavonoids quercetin, catechin, and kaempferol have been detected. Monosaccharides/oligosaccharides (9%) detected are D-glucose, D-fructose, and saccharose. The fruit acids include quinic acid (1.5%), shikimic acid (2%), and fatty oil (from seeds; 40%). The high tannin content of myrobalan makes it popular for use as an astringent.^{8,12,13}

Psychological and psychiatric uses

ITM sources report that myrobalan strengthens memory retention and brain activity. It is reported useful for confusion, headache, melancholy, depression, obsession, amnesia, facial paralysis, misanthropy, dizziness, and insomnia. Traditional texts report that it helps to prevent stomach vapors from ascending into the brain and evacuates phlegmatic excreta from the brain.^{1,3,4}

Ophthalmic effects

Myrobalan aids visual acuity and drainage from the eyes;⁴ it is an eye tonic, a desiccant of moisture in the eye, and is useful for epiphoria and eye irritation when soaked in rosewater.^{11,14}

Cardiopulmonary effects

Myrobalan refreshes the heart and is useful in treating palpitations and tachycardia.¹¹

Gastrointestinal effects

A myrobalan tonic for the stomach controls vomiting and diarrhea (roasted), absorbs stomach moisture, and increases stomach retention and appetite. It is a digestive, laxative (soaked), and decreases hemorrhoidal bleeding (burnt powder).^{1-4,11,14}

Hepatic, splenic, and urinary effects

A liver tonic (jam) of myrobalan moderates liver temperament and is used to treat generalized dropsy and spleen pain, as a diuretic, and for treatment of polyus.^{1,3,11}

Dermatologic effects

Myrobalan improves paleness, decreases greying of the hair, and is a hair tonic (when sucked). It is also effective in the treatment of leprosy.^{1-3,11,14}

Dental and oral cavity effects

Myrobalan strengthens the gums and teeth and is beneficial in treating mouth ulcers, aphthous, and milk fever.^{1-3,11,14}

General effects

General effects of myrobalan include opening of blockages, quenching bile heat, and preventing the development of burning black bile. It is effective for treating combined fever, diluting phlegm, and as a bile laxative (squeezed), to dry humidity (sprinkling powder), as a phlegm solvent, for joint pain, and for relief of boiling humors.^{1-3,11} It is harmful in irritable bowel disease and irritable bowel syndrome.^{1,3}

Pharmacological effects

Animal experiments show that the fruit has remarkable effects in decreasing blood sugar levels and improving diabetes. Research shows a significant antidiabetic and renoprotective effect from a chloroform extract of myrobalan, which enhanced insulin secretion from the β -cells in the islets of Langerhans, or by an extra pancreatic mechanism, which supports its traditional usage.^{10,15} The cardiotoxic activity of myrobalan fruits has been demonstrated. Myrobalan increases the force of contractions and cardiac output without altering heart rate.¹⁶ The benefits of myrobalan for the skin have also been shown. It is effective for healing wounds and treats wounds quickly, as indicated by the increased rates of contraction and decreased periods of epithelialization. Biochemical studies show a significant increase in total protein, DNA, and collagen content in the granulation tissues of treated wounds. In addition, myrobalan has antimicrobial and antioxidant properties. These results confirm the beneficial effects of myrobalan on the acceleration of healing.¹⁷

Myrobalan has antiulcerative properties on the gastric mucosa. The gastroprotective and antisecretory mechanisms of chebulinic acid isolated from myrobalan fruit have been demonstrated. Chebulinic acid significantly decreases free acidity, total acidity, and upregulated mucin secretion, and inhibits H⁺K⁺-ATPase activity. It is employed to treat gastrointestinal ailments against *Helicobacter pylori*.^{18,19}

The fruit of myrobalan contains antioxidant agents, including quercetin and vitamin C, which work against oxidative stress-induced neurodegeneration. It can decrease the risk of neurodegenerative disorders such as dementia and Parkinson's disease.^{11,12,20} As myrobalan contains a large percentage of tannin, it is beneficial for decreasing gingival bleeding, aphthous, and other inflammatory mouth diseases. It is a potent antimicrobial against microorganisms that form dental caries.^{21,22}

Myrobalan has antiarthritic properties that can be beneficial for the treatment of rheumatoid arthritis by decreasing serum tumor necrosis factor- α levels.²³ It offers antibacterial, antiviral, and antifungal effects. The ethanolic extract of myrobalan fruit has been found effective

against both gram-positive and gram-negative bacteria such as *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Pseudomonas aeruginosa*. It is also effective against *Helicobacter pylori*. Ellagic acid exerts a potent inhibitory effect against *C. perfringens* and *E. coli*. An aqueous extract of myrobalan has been reported to show antifungal activity against a number of dermatophytes.^{24,25} A hot water extract of myrobalan shows antiherpes simplex virus activity, anticytomegalovirus activity, and antiHIV-1 activity.²⁶⁻²⁹

Hepatoprotective compounds have been isolated from the extract of myrobalan fruits. Chebulic acid has an antioxidant effect and exhibits free radical scavenging activity *in vitro* and ferric-reducing antioxidant activity. The treatment of hepatocytes with chebulic acid significantly reduces cell cytotoxicity.³⁰ Myrobalan is also retinoprotective,³¹ cytoprotective,^{18,32} and offers antiaging,^{32,33} antinociceptive,³⁴ antianaphylactic,³⁵ and radio protective²⁵ activities.

Mode of application in ITM

The fruit should not be finely powdered, but should be partially pounded. The fruit is more effective when first soaked in water than as a decoction or powder. Eating the dry fruit can cause colic. ITM uses Myrobalan in different forms: dry fruit, decoction, and soaked fruit. It is more effective when combined with jujube, almond oil, fresh cow oil, sugar, manna, and honey (These material are corrector. In ITM, There is an Idiom: Corrector that it help to reduce the side effect of plants for example ancient physician were believed half crushed Myrobalan sticks in the bowel and fresh cow oil can prevent.).^{1,11} The mode of administration is whole herb preparations for internal and external use. Daily dosage ranges from 3 to 9 g. A study on acute toxicity showed that the oral LD₅₀ dose for myrobalan is >2000 mg/kg. Chronic administration to rats did not produce significant physiological changes when compared with control rats.²⁶

DISCUSSION

This study of traditional medicine texts shows that myrobalan has been an important plant in traditional medicine. It was shown that halileh in ITM is equivalent to the myrobalan tree with the scientific name *Terminalia chebula*. Some pharmacological properties documented for this plant in ITM have been confirmed by studies of modern phytotherapy.

The morphology of this plant recorded in traditional texts includes details about habitat and therapeutic activity that match those of modern findings. These properties include the use of the fruit for its gastroprotective effects and its use for Alzheimer's disease treatment, gingival bleeding, and wound healing.

The therapeutic dosages in modern phytotherapy range from 3 to 9 g, while therapeutic dosages in ITM

range from 15 to 30 g. The higher therapeutic dose in ITM may be because myrobalan fruit is decocted or soaked, and because ITM is a holistic therapeutic system and the nature of the patient is considered before treatment. Its records show that the most serious adverse effects of myrobalan are observed in people with a cool temperament; thus, it is not prescribed for such patients. Modern medicine does not consider the nature of patients before treatment; however, it is recommended to avoid the administration of high doses until adequate studies confirm their safety and quality. However, no serious toxicity or adverse effects have been recorded after ingestion of myrobalan.

The morphology and habitat indicate that myrobalan is the plant described in traditional books. Some of the remedies used may be derived from traditional applications. The ITM medicinal properties described for this plant have been demonstrated in modern phytotherapy. Its abundant tannin content produces high astringency and it has a cold and dry temperament.²⁹ Its astringent nature makes it an effective tonic for organs such as the stomach, heart, and liver. Although modern pharmacological mechanisms are different from the mechanisms described in traditional documents, the results of both approaches are similar.^{8,26}

The results of this study confirm the use of Myrobalan. As the main sources of study are Iranian medical texts, researchers and medical experts can use these findings as a basis for further study. Myrobalan has been used to treat disease for hundreds of years, so the probability of bias is very low and the results have been confirmed by recent research. Physicians can base their treatments on this confirmation of indications, dosage, toxicity, and patient and drug temperament.

ITM uses roasted myrobalan fruit in the treatment of diarrhea because of its high tannin content, and uses soaked myrobalan fruit as a laxative because of its anthraquinone derivative content. This indicates that different forms of the drug can be applied for different or contradictory effects. Myrobalan is a tonic for the stomach and heart and has a cold temperament. Its tonic effects in ITM are the result of its cold temperament. These effects cannot be found in substances with hot temperaments.

ITM's comprehensive knowledge of the temperament of substances (plants, animals, and minerals) is helpful in understanding the function of a substance. Myrobalan has extensive therapeutic applications in ITM, some of which have been confirmed by modern medicine. Future study could focus on previously untested therapeutic applications of myrobalan.

This review provides a basis for researchers to use ITM information about *Terminalia chebula*. It is an efficacious natural drug and its safety and acceptable dosage have been determined. Further preclinical and clinical studies for adequate evaluation of its safety and therapeutic efficacy are recommended.

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