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Khan Asma Mohd Anis
PG Scholar, Department of Ilmul Advia, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, Telangana, India

Sultan Ul Haque
PG Scholar, Department of Moalajat, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, Telangana, India

Mariya Fatema
PG Scholar, Department of Ilmul Qabalat-Wa-Amraz-e-Niswan, Ayurvedic and Unani Tibbia College, Karol Bagh, New Delhi, Delhi, India

Corresponding Author:
Khan Asma Mohd Anis
PG Scholar, Department of Ilmul Advia, National Research Institute of Unani Medicine for Skin Disorders, Hyderabad, Telangana, India

Mastagi (*Pistacia lentiscus* Linn.): Plant origin drug of Unani medicine: A review

Khan Asma Mohd Anis, Sultan Ul Haque and Mariya Fatema

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Abstract
Since the dawn of time, people have employed plants as medicines, and many common and significant treatments still have their roots in plants. Traditional medicine has long employed *Pistacia lentiscus* L. Treatment of gastrointestinal disorders, wound healing, skin inflammation, lowering of plasma lipid and blood sugar levels, and oral care have all shown it to have positive effects. It is used as *Muhallil-i-Riyah* (Carminative), *Muqawwi-i-Mi'da* (Stomachic), *Muqawwī-i-Kulya* (Renal tonic), *Qābid* (Constipative), *Mushtahī* (Appetizer), *Mudir* (Diuretics), *Nafkh al-Mi'da* (Flatulence) in Unani system of medicine.

Keywords: *Pistacia lentiscus* L., *Mastagi*, phytochemicals, Unani medicine

Introduction
About a thousand years ago, the Muslims brought the Unani medicinal system to India, where it has since been ingrained [1]. Greek in origin, Unani medicine is an antiquated Greek medicinal system based on the characteristics of the four temperaments and four humors [2]. Mastic is a naturally occurring resin that comes from mastic trees and is a semi-transparent, white colour. The mastic tree is an evergreen bush that grows throughout the Eastern Mediterranean region, but it only produces resin that congeals in the southern section of the Greek island of Chios [3]. Mastic comes in peppercorn-sized, rigid, microscopic rips. Most are pear-shaped, avoid globular, or almost globular, and occasionally, but infrequently, they are elongated. The medicine has a mildly acceptable taste and an agreeable, slightly aromatic odour, both of which are characteristics [4].

Collection and preparation
Collection: When a little tool resembling a chisel is used to make a small hole in the tree's bark, which has a circle of oleo-resin ducts in the phloem, the oleo-resin seeps in the form of tiny tears that in a few days become dry and hard. Then it is gathered, with the material plucked directly from the tree having the highest properties and the material that has fallen to the ground having poorer attributes [5].
Preparation: In cavities found in the inner bark, the resinous juice gathers. The larger branches and the trunk both have relatively long wounds through which resin pours. Finally, little tears on the outside begin to collect the resin. These are hand-selected and kept in a dry environment [6].

Morphology: Mastic is a resinous substance. It is achieved by cracking the branches of *P. lentiscus* or spontaneous dripping. A good tree yields more mastic approximate 4.5 to 5.5 kg. Its gum is in the form of irregular small granules, it's colour is yellowish white and transparent. Its pulp is sweet and fragrant. By chewing its seeds in the mouth, become soft and sticky. Mastic is not soluble in water but also soluble in alcohol and chloroform. It cannot be thinned by rubbing it hard, because it sticks, but by rubbing it lightly in mortar, it becomes thin.
The best mastic is found in Rome. But it is also found in Syria, Morocco, Spain, West Africa and Greece. It's not found in India [7].

Description

Mastic is a dioecious enduring woody plant. This plant is an evergreen that grows up to 1 to 5 m tall with a potent resin scent, the plant grows in rocky, arid regions of North Africa and Mediterranean Europe. The leaves have five or six pairs of deep-green leaflets and are alternating, leathery, compound paripinnate (No terminal leaflet). It displays very tiny blooms, each with three parts and five stamens on the male and five on the female. The fruit is a drupe that has a diameter of around 4 mm and turns from scarlet to black when ripe. The fruit has a sour, raisin-like flavor and is edible, despite not being very popular.

RESIN: There is aromatic, ivory colour resin called as mastic and it is produced like spices. Initially it's like liquid but as the weather gets colder it hardens. On chewing, the resin becomes soft, white and cloudy [7].

- ***Miqdar-i-Khurak* (Dose):** It can be used in the dose of 1-3 gm [8].
- ***Mazarrat* (adverse effects):** *Mastagi* has been said to have negative impacts on urinary system [8].
- ***Muslih* (Corrective):** *Sirka* or *Ab-i Morad* [9].
- ***Badal* (Alternative):** *Kundur* (*Boswellia serrata*) and *Izkhar Makki* (*Cymbopogon schoenanthus* L.) [8].

Selected local names

Mastagi (Arabic) [10, 14], *Mastiche* (English) [9, 10], *Mastic*, [7, 9], *Kundur Rumi* (Persian), *Alk Rumi* (Arabic) [10], *Mastio*, *Mumlik Rumi* [11], *Mulk Rumi* [12], *Mastakha* [13, 14], *Alandar Rumi* [13], *Sakhees*, *Sakheenas* [15], *Pistacia lentiscus* [16], *Mastix Lentisk* (Common name), *Ruma Mastakee* (Marathi), *Rumi Mastagee* (Gujrati) [7].

Chemical constituents

Pistacia lentiscus is well-known for producing resin, and it also includes anthocyanins including cyanidin 3-0-arabinoside and delphinidin 3-o-glucoside. There are 250 components in the chemical makeup of the essential oil derived from mastic gum, leaves, and unripe and ripe fruit. Alpha-pinene, limonene, germacrene D, terpinen-4-ol, p-cymene, Beta pinene, sabinene, c-terpinene, and alpha-terpineol were the main compounds in this oil composition during flowering, followed by oxygenated monoterpenes (13.3-23.1%) and sesquiterpene hydrocarbons (9.2-28.1%) [17].

Mastic acid, isomastic acid, and oleanolic acid are the main components of resin triterpenes [7]. Palmitoleic, oleic, Gondoic, palmitelaidic, vaccenic, and paullinic acids are among the monosaturated fatty acids found in mastic.

Polysaturated Acids: Linoleic acid, linolenic acid, eicosadienoic acid.

Saturated Acid: Palmitic acid, stearic acid, Arachidic acid [18]. It contains resin, Essential Oil. [19], Volatile Oil, Bicyclic-terpinoid, Fatty acids [20], Flavonoids, alkaloids, saponins Glycosides and steroids [21]. A novel bicyclic triterpenoid (1) isolated from gum mastic [22], Masticadienonic, dihydromasticadienonic, oleanonic, masticadienolic, dihydromasticadienolic, oleanolic, 3-epimasticadienolic, dihydro-3-epimasticadienolic and epioleanolic acids isolated as methyl esters; Beta-amyrin, Beta-amyrone, oleanolic aldehyde, 28-hydroxy-beta-amyrone, dammarenediol, erythrodiol and masticadiendiol also isolated from galls [23].

Temperament: The *Mizaj* of *Mastagi* (*P. Lentiscus* L.) was described by Unani clinicians as Harr[2] and Yabis[2] [24, 25, 26, 27].

Pharmacological actions: *Mudirr-i-bawl* (Diuretics), *Muharrik* (Stimulant) [28], *Munaffith- i-balgham* (expectorant), *Qābid* (astringent, styptic, anastaltic) [29]. *Mohallil* (Resolvent), *Tajfeef* (Siccative, desiccative) [30], *Jāli* (Detergent), *Hādim* (Digestive), *dāfi-i-ta'affun* (Antiseptic) [31], *Hābis* (Haemostatic), *Muqawwī-i-mi'da* (Stomachic), *Muqawwī-i-jigar* (Hepatic tonic) [9].

Pharmacological Studies

Anti-Oxidant Properties

Andrikopoulos *et al*. found that *Mastiha* was the most effective in reducing human LDL oxidation after studying the antioxidant capacity of various gums and resins *in vitro* [32]. *Mastiha's* hydromethanolic component was primarily responsible for this effect, however triterpenes and hydroxynaphthoquinones also showed LDL protective efficacy. Again highlighting the tight relationship between inflammation and oxidative stress, *Mastiha* reduces cellular superoxide generation by downregulating NADPH oxidase through the suppression of protein kinase C pathways. TNF-a may be involved in this process, further demonstrating the strong relationship between oxidative stress and inflammation [33]. Given its distinctive structural characteristic that is vulnerable to oxidative alteration, protein kinase C is well recognized to play a significant role in a number of cellular signaling pathways and is reversibly controlled by ROS [34]. Macrophages intracellular antioxidant glutathione levels rise as a result of *Mastiha's* triterpenes, which also inhibit these pathways, while CD36 expression is downregulated [35]. These latter molecules are known as the oxLDL receptors in macrophages and maintain a crucial position in the development of foam cells during atherogenesis, where they are increased in the presence of oxLDL and interleukin-4 [36].

Anti-Atherogenic Properties

Chios mastic's anti-inflammatory and antioxidant qualities are linked to its anti-atherogenic actions. Beyond the enhancement of the intracellular antioxidant glutathione, it has been proposed that mastic triterpenes exert their antioxidant effect by suppressing the expression of CD36 in macrophages, preventing the uptake of ox-LDL, which promotes the formation and accumulation of foam cells at sites of vascular endothelial dysfunction in both the early and late stages of atherosclerosis. Mastic therapy has been discovered to have anti-ischemic characteristics in animal experimental models, resulting in a decrease in infarct size [37].

Anticancer Properties

Mastic reduces androgen receptor expression and activity, which is crucial for the initiation and development of prostate cancer [38]. Mastic also prevents the advancement of the cell cycle in prostate cancer cells by inhibiting NF-B activity and the NF-kB signaling pathway [39]. Mastic oil was also shown to have an antiproliferative and proapoptotic effect on human K562 leukemia cells in a lab setting [40]. Additionally, it was discovered to inhibit vascular endothelial growth factor, reducing the production of micro-

vessels from mouse melanoma cells both *in vitro* and *in vivo* [40].

Antibacterial Properties

Most thoroughly studied, both *in vitro* and in clinical trials, is undoubtedly the antibacterial activity of mastic resin against Helicobacter Pylori (H. Pylori). Treatment for H. Pylori infection is critical for the management and prevention of common digestive illnesses, as it is known to be one of the primary causes of gastritis, peptic ulcer disease, and stomach cancer [41]. Clarithromycin, along with either amoxicillin or metronidazole and a proton pump inhibitor, is typically used to treat H. Pylori for 7–14 days [42]. There is an urgent need for alternative medicines that could effectively contribute to the management of infectious diseases, as eradication is only accomplished in less than 85% of treated patients due to antibiotic resistance [43]. The New England Journal of Medicine published the first evidence indicating that mastic had antibacterial activity against H. Pylori in 1998, offering a potential pathogenetic interpretation of the therapeutic effects of mastic on gastric and duodenal ulcers that were earlier recognized [44].

Therapeutic uses: It is useful in *sozāk* (Gonorrhoea), *Sayalan al-rahim* (Leucorrhoea), *Amrād-i- Ri'a* (respiratory complaints) [45]. The oleoresin is useful in chronic diarrhea and fruit is an excellent emulsion for irritation of the urethra [29]. It is also useful in bed wetting [11]. Its *sunoon* (tooth powder) is beneficial for bad breath and tooth cleaning. Due to the action of expectorant, it dissolves mucus. It prevents the wound from growing. The inverted hair of the eyelid becomes straight with its use. It is also useful in stomach ulcer. It dissolves mucus. Apart from this, it increases appetite and causes belching [25].

Table 1: Compound formulation

S. No.	Name	Pharmacological action	Therapeutic uses
1.	Jawarish-e-Mastagi Sada	Kāsir-i-Riyāh (Carminative) [46, 47]	Nafakh-e-shikam (Flatulence)
2.	Jawarish-e-Mastagi Murakkab	Kāsir-i-Riyāh (Carminative) [46].	Ishāl (Diarrhoea)
3.	Jawarish-e-Jalinoos	Muqawwī-i-Bāh (aphrodisiac) Kāsir-i-Riyāh (Carminative),	Du'f-i-Mi'da (indigestion), Bawāsīr (hemorrhoids),
		Muqawwī-i-Jigar (Hepato tonic)	Hasāh al-kulya (renal- stone) [48], Qay' (vomiting) [49]
4.	Roghan-e-Mastagi	Muqawwī-i-A'sāb (Nervine tonic) [50] Muhallil-i-waram (Anti-inflammatory) [46]	Thiql-i-sar (Heaviness of head)
5.	Jawarish-e- tabasheer	Muqawwī-i-Mi'da (Stomachic) [51] Sū'Mizāj-i-Safrā (impaired bilious temperament)	Ishāl (Diarrhoea) Qay' (vomiting) [52]
6.	Jawarish-e-Zarishk	Hādim (Digestive), Mushtahī (Appetizing) [53]	Du'f-i-Ishtihā (Anorexia), Du'f-i-Hadm (delayed digestion)
7.	Jawarish-e-Ood	Muqawwī-i-Mi'da (Stomachic) Hādim (Digestive) and Munaffith (Expectorant) [54]	Du'f-i-Hadm (Poor digestion), Qay' (Vomiting)
8.	Jawarish-e-Muqil	Waja'al-Maq'ad (Rectal pain and piles) [53].	Bawāsīr (Hemorrhoids) Du'f-i-Mi'da (Indigestion)
9.	Jawarish-e-Zarooni sada	Muqawwī-i-Kulya (Renal tonic), Muqawwī-i-Mi'da (stomachic), Muqawwī-i-Bāh (Aphrodisiac) [55].	Hasāh al-kulya (Renal- stone), Du'f-i Bāh (Sexual debility)
10.	Zimad-e- Feesaghorus	Muhallil-i-wram (Anti- inflammatory), Mudirr-i-Bawl (Diuretic)	Istisqā (ascites) [56]
11.	MajunDabid-ul ward [57]	Muhallil-i-wram (anti- inflammatory), Mudirr-i-Bawl (Diuretic)	Waja'al-Mi'da (Gastralgia) Waja'al-Kabid (Hepatic pain)
12.	Habb-e-	Muqawwī-i-Mi'da (Stomachic),	Nafkh-e-Shikam
	Mastagi [58]	Kāsir-i-Riyāh (Carminative)	(Flatulence)
13.	Jawarish-e-Anarain	Qābid (constipative) Muqawwī-i-Mi'da (stomachic)	Du'f-al-Mi'da (Weakness of stomach) Qay' (Vomiting) [59]

Clinical studies of *P. lentiscus*

1. A clinical study was conducted on 10 patients of active CD and 8 healthy controls with 2.2gm of mastic daily for 4 weeks. The results showed that CD activity index decreases, IL-6 and CRP also decreases but there was no effect on plasma TNF-alpha [60].
2. In another study where 2.2gm of mastic was used in 10 pts of active CD and 8 healthy control. The result was reduction of TNF-a secretion by mononuclear cells and increase in macrophage migration inhibitory factor [61].
3. In other clinical study was done on 60 patients with IBD randomized to either 2.8 g of mastic daily for 3 months or placebo. The outcome of these patients was that IBDQ had improved. And decrease in oxLDL and also decrease in plasma cysteine and faecal lysozyme [62, 63].
4. In a study of 68 patients with randomized to either 2.8 g of mastic daily for 6 months or placebo. The result was no impact on serum IL-6, Faecal calprotectin and faecal lactoferrin [64].
5. A clinical study that was done on 129 patients. They were divided by two groups. The first group was 68 randomized to mastic group (2.8 g daily for 6 months for pts in remission and for 3 months for pts in relapse) and second group of patients were on placebo. The results was increase in IL-17A [65].
6. In a study of 148 patients with functional dyspepsia randomized to either mastic 350 mg tid or placebo for 3 weeks. The results showed that significant improvement of symptoms (Stomach pain in general, stomach pain when anxious, dull ache in the upper abdomen and heartburn [66].
7. In other study of 98 patients with obesity (BMI greater than or equals to 30kg/m2) and NAFLD. They randomized to either mastic 2.1 g/day or placebo for 6 months. The outcome was improvement in total antioxidant status of NAFLD pts and interaction of

mastic with cytokines and antioxidant biomarkers implicated in NAFLD pathogenesis [67].

8. In a study of 147 postpartum women. They randomized to topical application of 15 g mastic for 3 days on episiotomy wound or to placebo. The results showed that higher healing rates of episiotomy wound but no effect on episiotomy pain [68].
9. In a clinical study of 133 subjects were randomized to either 5 g mastic powder (higher dose) or mastic solution for 18 months. The outcome was decrease in serum total cholesterol, LDL, total lipoprotein (a), apolipoprotien A-1, apolipoprotein B, SGOT, SGPT and Gama-GT levels [69].
10. In a clinical study of 156 subjects received different dose of mastic for 8 weeks. The outcome was reduction in TC in subjects receiving crude mastic 1g/day (highest dose). But there was no effect on LDL, HDL, triglycerides, uric acid and CRP [70].
11. In a study of 27 subjects in which 13 patients was hypertensive. All were randomized to receive one dose of 2.8 g mastic. The result was acute decrease in peripheral and aortic SBP in hypertensive pts and also found that there was no change in normotensive patients [71].
12. The clinical study conducted on 8 patients with H. pylori. They treated by 1gm mastic four times daily for 14 days. The results showed that no effect on H. pylori status [72].

Conclusion

The Unani system's foundational ideas, diagnostic techniques, and therapeutic approaches, rooted on rational scientific thinking and holistic notions of health and healing. Unani system of medicine (USM) uses all three natural sources of drugs (Mawalid-i-Thalatha) i.e. plants, animals and minerals in different dosage forms. It advocates therapeutic uses of herbal, mineral and metallic preparations in many diseases since century in clinical practice. Mastagi (*Pistacia lentiscus* L.), is a key component of the Unani medicinal system. It has a number of significant pharmacological effects i.e, *Muqawwi-i-Mi'da* (stomachic), *Kāsir-i-Riyāh* (Carminative), *Muqawwī-i-Jigar* (Hepato tonic) and *Qābiḍ* (astringent). It demonstrates a variety of actions including those that are anti-atherogenic, anti-cancer, anti-inflammatory and anti- oxidant.

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