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Review

Traditional Hepatoprotective Unani Formulation *Jawarish-e-Utraj*

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Abstract

Traditional system of medicine is being practiced since Greek ages. Among the traditional system of medicine Unani is one of the well-known traditional systems of medicine. Among the formulations in unani system of medicine *jawarish-e-utraj (majoon)* is being prescribed for its hepatoprotective effect. In this formulation, 10 ingredients are present which are as follows: *Muraba-e-turanj - Citrus medica ,Zanja beel-Zingiber officlane, Filfil daraz-Piper longnum, Darchini-Cinanmomum zeylanicum, Mastagi-Pistacia lentiscus, Bisbasa-Myristica fragrans, Barg-e-tambol-Piper bettle, Qaranful-Syzgium aromaticum, Ood hindi-Aquilaria agallocha, Sumbal-ut-teeb-Nardostachys jatamansi* and among these 10 ingredients, this review will provide a compiled data on two plants *Pistacia lentiscus* and *Aquilaria agalloacha* as the other ingredients are commonly known. This review provides updated information on taxonomical, phytochemical, pharmacological aspects and the detailed profiling of phytoconstituents from the two plants showed structural diversity of phytoconstituents that may provide a lead molecule against hepatotoxic effect. In addition to this, this review will provide a way for researchers to unlock the different targeted molecular mechanisms involved in pathogenesis of hepatotoxicity.

Keywords: Unani, hepatoprotective effect, *jawarish-e-utraj*, taxonomical, phytochemical, pharmacology.

Introduction

Traditional system of medicine is being practiced worldwide for combating human disorders and aliments. Among the traditional system of medicine, World Health Organization (WHO) recognized Unani system of medicine (Greeco-Arabic) as an alternative system of medicine to cater health care needs of human population (Ishtiyaq, 1983). In Unani system of medicine, the drugs are used in four forms and these drugs are used orally. Types of drug formulations used in Unani system of medicine are *Solid formulations:* Powder, tablets and pills etc., Semi Solid formulations: Electuaries, Aperients, Jwarish, Khamerajat etc., Liquid formulations: Syrups, decoctions, linctuses, eye and nasal drops etc. and Gaseous formulations: Snuffs, Shamoom, notukh, lakhlakha etc. In addition to oral drugs, Unani physicians also prescribe drugs administration locally and they are Haqna (Enema) Shief (Suppositories), Firzahah (Pessaries) and Thiala (Liniments). In Unani system of medicine, if the formulation contains single drug it is called as mufradad (single drug) and if it contains compound formulation it is called as murakabat (Sina *et al*., 2002). The liver performs a vital role in metabolism, secretion, storage and detoxification of exogenous and endogenous substances and drugs are an important cause of liver injury, more than 900 drug toxins and herbs have been reported to cause liver injury and drugs account for 20-40% of all instances of hepatic failure, 2000 cases of acute liver failure occur annually and the pathogenesis has remained unknown (Wiegand and Berg, 2013). In Unani system of medicine, there are various formulations are being prescribed for Hepatoprotectives, one such formulation is *jawarish-e-utraj,* a semi-solid (majoon) compound formulation. Among the 10 medicinal herbs used for the foemulation, this review highlights the taxonomical, phytochemical and pharmacological aspects of *Pistacia lentiscus* and *Aquillaria agallocah* as the other ingredients are well known.

Pistacia lentiscus

Botanical description: *Pistacia lentiscus* is widely distributed in Mediterranean countries and it belongs to Kingdom: Plantae, Division: Mangnoliophyta, Order: Sapindales, Family: Anacardiaceae, Genus: Pistacia, Species: *Pistacia lentiscus* and Botanical name: *Pistacia lentiscus* L. The vernacular name of *Pistacia lentiscus* in English is Mastic tree. In Unani it is called as Mastagi, Roomi Mastagi, Mastaki and in Siddha/Tamil t is called as Ponnuikan kungiliyam (Khare, 2013).

Description of the plant: *Pistacia lentiscus* is a shrub or tree with separate male and female plants evergreen 1 to 5 m height with pinnate leaves and small (4-5 mm dia) globose black drupes (Fig. 1 and 2).

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Ethnobotany: Mastic is widely used especially in the Mediterranean countries as a masticator, mouth fresheners and to preserve teeth and gums. At present it is used in preparation of chewing gum, it is also being used as flavoring agent for alcoholic beverages and cordials mastic. It is also used as a temporary filling of caries teeth as a protective covering for wounds. It is also suitable for microscopical mounting. The principal use of mastic is in the manufacture of high grade transparent varnishes employed for coating valuable art paintings and retouching negatives and metals for lithographic processes.

Ethnopharmacology: Mastic (rumi-mastaki) has been considered as carminative, stimulant and diuretic, and used in the preparation of various pharmaceutical products, perfumes and incenses (The Wealth Of India, 1983).

Phytochemistry: The different classes of phytomolecules are volatile oils, resins, polyphenols, falvonol glycoside, flavanone and anthocyanin glycoside, tannins and fatty oils are found to be present in *Pistacia lentiscus*. The various essential oils isolated from leaves by super critical fluid technology by carbon dioxide method are beta carophyllin, germaerin, gamma cadinin (Raffaele *et al.,* 2002) and by hydrodistillation method alpha pinene, beta phellandrene, gama terpene, terpene -4-ol (Romano *et al.,* 2002), poly phenols like gallic acid, galloyl derivatives (Abdelwahed *et al.,* 2007) flavanol and anthocyanins derivatives were obtained. Delphinia diene-3-o glycoside and cyanadine-3-o glycoside, myricitin derivatives like Tanins-cathechin (Kıvcak *et al.,*2005) and tocopherols are reported from the leaf part of *Pistacia lentiscus* (Boelens *et al.,* 1991). The resin part of *Pistacia lentiscus* contains alpha pinene and gas chromatographic studies are reported for the presence of monoterpene hydrocarbons, alphapinene and beta merecine from the gum oil. The comparative phytochemical studies showed different percentages of phytomolecules and they are 23% pinene and 54% merecine in unripe fruit and 11% alpha piene and 72% beta myricine from the ripe fruit. Volatile oils viz., alpha piene, merecine, limonine, sesquiterpenes, aliphatic esters, phenolic esters (thymol and carbacrol) di merecine and alpha phellandrene is reported in fruit oil (Wyllie *et al.,* 1991) Verbeone, alpha terpeneol and linolol (Marner *et al.,* 1991). Novel nor-terpenoid and arabino galactone protein from gum mastagi has been reported for its activity against *Helicobacter pylori* (Berg *et al.,* 1998), polymer of mono terpene–1,4 poly–beta-merecene is reported in Mastagi resin (Kottakis *et al.,* 1998).

Pharmacological studies on *Pistacia lentiscus*

Antiatherogenic activity: It is reported that triterpenoid fractions of *Pistacia lentiscus*is is helpful in the treatment of atherogenesis (Kordali *et al.,* 2003).

Fig. 1. Habitat of *Pistacia lentiscus.*

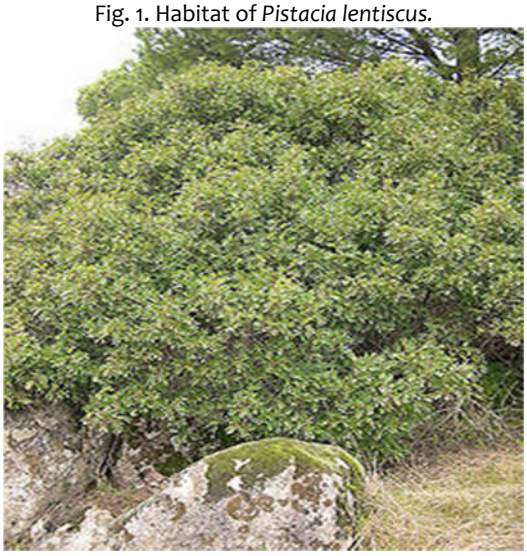
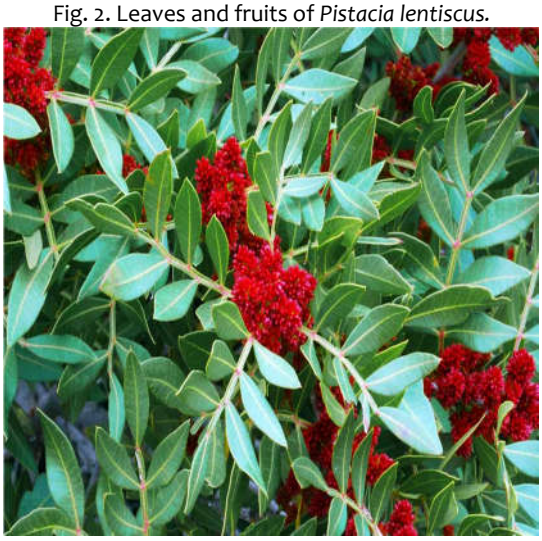


Fig. 2. Leaves and fruits of *Pistacia lentiscus.*



Antimicrobial activity: Antimicrobial activity against *Phytium ultimum* and *Rhizoctonia solani* for petroleum ether extract, chloroform extract, ethyl acetate extract and ethanol extract of *Pistacia lentiscus* showed minimum inhibitory concentration of 0.62 to 40 mg/mL. The leaf extract of *Pistacia lentiscus* has been reported for antimicrobial property, strong antifungal property and weak antibacterial property. The whole plant *Pistacia lentiscus* was screened for antimycotic activity, the essential oils are extracted from the leaves of mastic tree by steam distillation method showed its activity against *Rhizoctania solani*. The aqueous extract and the flavonoid enriched extract of essential oil from the leaf part showed remarkable inhibitory effect against bacteria, the acetone extract of mastic tree showed significant activity against *Mutans streptococci in vitro* and *in vivo* showed its uses in prevention of caries in clinical studies on 25 healthy pre-odontial healthy volunteers (Liubuncic *et al.,* 2005).

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Antioxidant activity: The essential oil collected at the flowering stage contains larger amounts of mono terpenes, hydro carbon fraction, resins and triterpenes. It is reported for remarkable antioxidant action. Digallic acid, gallic acid, 1,2,3,4,6 pentagalloyl glucose is screened by ABTS method and is reported for its antioxidant activity. Alloyl quinic acid isolated from leaves showed free radical scavenging activity (Janakat *et al.,* 2002).

Lipid lowering activity: The gums and resins of *Pistacia lentiscus* was reported for its inhibition on LDL oxidation at the minimum dose of 2.5 mg and maximum dose of 50 mg (Mansoor *et al.,* 2001).

Hepatoprotective activity: The aqueous extract of *Pistacia lentiscus* is reported for its hepatoprotective action against carbon tetra chloride induced animal model. The resin exudate of *Pistcia lentiscus* is reported for its beneficial effectiveness in gastric ulcer treatment and mastic tree is reported for its cytoprotective effect (Berboucha *et al.*, 2009).

Antigout and Antiarthritic activity: Digallic acid isolated from fruits of *Pistacia lentiscus*is was reported for its inhibitory action against xanthone oxidase which is reported for its treatment in gout (Abdelwahed *et al.,* 2007).

Wound healing activity: Topical application of fatty oils from the fruits of *Pistacia lentiscus* and its unsaponifiable fraction is reported for wound healing property (Balan *et al.,* 2007).

Anti-cancer activity: About 50% ethanolic extract of mastig gum of *Pistacia lentiscus* is reported for its inhibition on proliferation of HCT116 human colon cancer cells *in vitro* and in addition to this, it is reported for its apoptosis activity by DNA damage. The Hexane extract of mastig gum is reported for its treatment on colon rectum tumour. Gum mastig is reported for its inhibitory effect on proliferation on LNCAP cells (prostate cancer cell lines) (Dimas *et al*., 2009).

Aquilaria agallocha

Botanical description: *Auilaria agallocha* is widely distributed in Himalayan regions and it belongs to *Kingdom*: Plantae, Subphylum: Euphyllophytina, Subclass: Magnolidae, Order: Malvales, Family: Malvaceae, Genus: Aquillarieae, Species: Aquilaria, Binomial name: *Aquilaria agallocha.* The vernacular name for *Aquilaria agallocha* is as follows: English: Aloe wood, Eagle wood, Agar wood. Ayurvedic name: Aguru, Krimij, Krishnaaguru, Jongaka, Maaliyaka, Loha, Kaalaloha, Asitaka. Unani: Ood-ulHindi, OodGharqi. Siddha/Tamil: Akil kattai, Agil (Khare, 2007).

Fig. 3. Habitat of *Aquilaria agallocha.*

Description of plant: A large evergreen tree of 18-21 m sometimes up to 40 m in height, 1.5 -2.5 m in girth with a moderately straight and often fluted stem, leaves 5-9 cm long, thin curvaceous, oblong–lanceolate flowers white or green or dirty yellow in terminal, sessile or shortly peduncle umbellate cymes (Fig. 3).

Ethnobotany: The wood is not durable and is used to make bows, walking sticks and occasionally for dugouts. It is also used for making beads, rosaries, and small jewel cases and it is rated as third class timber. In Malaysia the wood is used for pencil making and it is also used in the production of writing and printing paper (The wealth of India, 1983).

Phytochemistry: Fungal infected plant of *Aquillaria agallocha* contains sesquiterpenic furanoids of the selinane group are agarospirol (sesquiterpene alcohol) Sesquiterpene dihydroagarofuran isodihydroagarofuran (Nagashima *et al.*, 2007), Sesquiterpene alcohol jinkohol II and jinkoheremol from the Indonesian Agarwood oil (Tamuli *et al.,* 2000). The comparative phytochemical studies were done between healthy plant and infected plant and the infected plant contains Valerianol (3.0%) and tetradecanoic acid (7.1%), dodecanoic acid (3.1%), pentedecanoic acid (6.2%), hexadecanoic acid (31.5%) and octadecanoic acid Pentedecanoic acid Valerianol 0.1%) and tetradecanoic acid (0.7%), dodecanoic acid (3.1%), hexadecanoic acid (31.5%) and octadecanoic acid Pentedecanoic acid in healthy plants were reported.

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The major sesquiterpenes reported are agarofuran (0.6%), norketoagarofuran (0.6%), agarspirol (4.7%), jinkoeremol (4.0%), kusunol (2.9%), dihydrokaranone (2.4%) and oxoagarospirol (5.8%) and also isolated agarofuran, agarospirol (7.2%), jinkohol (5.2%), jinkoeremol (3.7%), kusunol (3.4%) and oxoagarospirol (3.1%) (Pant *et al.,* 1980), Agarol and agarospirol together with α and β-agarofuran, β-agarofuran, vetispira-2(11), 6(14)-dien-7-ol, dihydrokaranone and valeriano 2-(2-phenylethyl)4H-chromen-4-one derivatives Agarospirol, Baimuxinal, Baimuxinic Agarospirol, Baimuxinal, Baimuxinicacid,I (Bhattacharyya *et al.,* 1938), Vetaspira-2(11), 6(14)-dien-7-ol, Vetaspira-2(11), 6-dien-14-al, 2, 14-Epoxyvestispir-6-ene, 2, 14- Epoxyvestipir-6(14),7-diene 11- Hydroxyspirovetiv-1(10)-en-2-one, Agarofurans (sesquiterpines) Baimuxifuranic acid, Norketoagarofuran Dihyro-3,4-dihydroxyagaro furan, Dihydroagarofuran, Dihydro-4-hydroxyagarofuran, α-agarofuran, β-agarofuran, Epoxy-β-agarofuran Selina 3,11dien14al, Selina4,11dien14oic acid, Dehydrojinkoheremol, neopetasane. Presence of coumarrino lignine is reported in *Aquillaria agallocha* (Alkhathlan *et al.,* 2005) from the phytochemical studies the major constituent sesquiterpene is found in agarwood oil and also fatty acids are found in addition to this diterpenoids compound is also reported (Meier *et al.,* 2003).

Pharmacological aspects of *Aquilaria agallocha*

Antioxidant activity: Ethylacetate extract of *Aqularia agallocha* leaves were analyzed for its antioxidant action at different concentrations and were reported for having significant antioxidant actions at lower concentrations. Free radicals scavenging activity of *A. agallocha* using DPPH methods is screened and the IC50 value is reported. *In vitro* antioxidant is done for ethylacetate extract of *A. agallocha* by nitrite induced oxidation of haemoglobin in human blood heamolysate method showed strong antioxidant effects (Ishihara *et al.,* 2006).

Antidiabetic activity: *In vitro* antioxidant activity is done by alpha glucosidase and amylase inhibitory methods for methanol and aqueous extracts of *Aquilaria agallocha,* antidiabetic activity of methanol, water and hexane crude extracts of *Aquilaria agallocha* leaves is done in streptozocin induced hyperglycaemic diabetic rats (Miniyar *et al.,* 2008).

Hepatoprotective activity: Ethanolic extracts of *Aguilaria agallocha* leaves were evaluated for its hepatoprotective effects on carbon tetra chloride induced hepatotoxicty in rats (Omar *et al.,* 2013).

Antiinflammatory activity: Antiinflammatory activity from the aqueous extract of *Aquilaria agallocha* leaves is done by using carrageenan induced inflammation method (Aromdee *et al.,* 2011).

Analgesic activity: Ethanolic extract of *Aquilaria agallocha* is reported for analgesic activity in mice using acetic acid induced writhing method, analgesic activity of ethyl acetate extract of *Aquilaria agallocha* by formalin induced paw licking in mice was reported (Hanskaar *et al.,* 1983).

Antihistaminic activity: The effect of the aqueous extract of *Aquilaria agallocha* leaves on the immediate hypersensitivity reactions was reported (Hara *et al.,* 2003).

Laxative effect and Antimicrobial activity: Laxative effect of acetone extract of *Aquilaria agallocha* leaves is reported (Khalil *et al.,* 2013). Antibacterial activity is reported for *A. agallocha* oil by agar well diffusion method against *Escherichia coli, Enterococcus faecalis, Staphylococcus aureus, Pseudomonas aeruginosa* (Iyer *et al*., 2001). Aqueous extract of *Aquilaria agallocha* leaves inhibited the growth of *Pseudomonas aeruginosa and Staphylococcus aureus* (Manasi *et al*., 2008).

Conclusion

Jawarish–e–utraj is a semisolid poly herbal formulation containing ten ingredients. This review focused on *Pistacia lentiscus* and *Aquilaria agallocha* as the other ingredients are well known. The data on *Pistacia lentiscus* showed different classes of phytomolecules and their biological properties. The phytochemical studies on *Aquilaria agallocha* revealed the presences of biological compounds screened for antioxidant activity, antidiabetic activity, hepatoprotective and antiinflammatory activity. The review on these two plants will give detailed updated information for the researchers to unlock the different targeted mechanism for the drug discovery process.

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