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The therapeutic potential of Mazu (*Quercus infectoria*) in the Unani system of medicine: A comprehensive review

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Abstract
Mazu (*Quercus infectoria*) is a species of oak native to the Mediterranean region and parts of Asia. In the Unani system of medicine, Mazu has been extensively utilized for its medicinal properties for centuries. This review aims to compile and analyse the traditional uses, phytochemical constituents, pharmacological activities, and potential therapeutic applications of Mazu according to the principles of the Unani system of medicine. Various traditional Unani formulations containing Mazu and their indications in the management of different ailments are discussed. Additionally, modern scientific evidence supporting the pharmacological activities attributed to Mazu, such as antimicrobial, anti-inflammatory, antioxidant, wound healing, and gastroprotective effects, are reviewed. The synergistic effects of Mazu in polyherbal formulations commonly used in the Unani system are also explored. Furthermore, the safety profile, dosage forms, and future perspectives for research and development of Mazu-based Unani formulations are discussed. This comprehensive review provides valuable insights into the therapeutic potential of Mazu in the Unani system of medicine and highlights its importance as a promising natural remedy for various health conditions.

Keywords: Mazu, *Quercus infectoria*, Unani medicine, traditional medicine, therapeutic potential

Introduction
Quercus infectoria, commonly known as Mazu or Aleppo oak, Galls in local speech mean swelling, Kobak, growth or gallnut. These excrescences arise in consequence of the deposition of an egg by a small insect, Alderia gallectinctoriae Olivier, family cynipidae, often known as the gall, belongs to the family Fagaceae and is indigenous to the Mediterranean region and parts of Asia, including Iran, Turkey, Greece, and India. In the Unani system of medicine, Mazu holds a significant position due to its diverse medicinal properties and therapeutic applications. The Unani system, which originated from the teachings of Greek physician Hippocrates and later enriched by Arab scholars such as Ibn Sina (Avicenna), emphasizes the balance of bodily humors and the use of natural remedies derived from plants, minerals, and animal sources for maintaining health and treating diseases.
According to Hakim Najmul Ghani, it has been written in Ganjbadaward that the Mazu of best variety is green in colour and its inner tissue is soft**.** While in Minhajuddukan, it has been written that Mazu of best variety has rough surface while low grade is smooth**.** The plant, from which Mazu obtained, is not found in India**.** It is imported from Greece, Minor Asia and Syria.

Fig 1: Plant of Mazu

Fig 2: Fruits of Mazu

Ethnobotany
Oak galls (Turkish galls; Mazu) are an outgrowth formed on the young twigs of the dyer's oak, *Quercus infectoria* (Family - Fagaceae), as a result of the deposition of the eggs of the nocturnes the bark of young twigs and lays the eggs on or in the cambium of a young shoot. The egg develops into a larva and gets surrounded by the tissues of the developing gall.

Vernaculars
The Gall is known by different vernacular names: Ifas, Uffes, Swadul Quzat (Arabic); Maayaaphala (Ayurvedic); Majuphala, Majuphal (Bengali); Gall Nut, Oak Galls, Magic Nuts, Galls, Aleppo Galls, Mecca Gall (English); Mazyan, Mai phala (Gujrati); Majuphul, Majuphal, Mazu, Muphal (Hindi); Gala (Latin); Mai Phal, Majuphala (Maharashtra); Manja Kani, Mashikkay, Majakani (Malyalam); Mazu (Persian); Machkam, Majuphul, Keetavasa (Sanskrit); Mochakai, Mashikkai (Siddha); Aafsi (Siryani); Machakai, Mashikai (Tamil); Mashikaya, Machikaya (Telgu); Maaju phal, Maazu, Feetus, Falees, Maaphala, Iqaqualees (Unani) and Mazu.

Temperament *(Mizaj)*
The Unani physicians have unanimously described the *Mizaj* of the drug as cold and dry. But they differ regarding its degree of cold and dryness. It is cold in first degree**.** But according to others it is cold in second degree. It is Dry in second degree**.** While some says it is Dry in third degree.

Traditional uses of mazu in the unani system
According to classical Unani texts, Mazu has been used in various formulations to treat a wide range of ailments, including gastrointestinal disorders, respiratory conditions, skin diseases, and wounds. It is commonly employed as an astringent, styptic, anti-inflammatory, antimicrobial, and wound healing agent. Traditional Unani formulations such as Majoon Muqawwi Dimagh, Majoon Ushba, and Safoof Mohazzil contain Mazu as a key ingredient for their therapeutic effects on the brain, liver, and gastrointestinal tract.

Phytochemical constituents of mazu
Mazu contains a diverse array of phytochemical constituents, including tannins, gallic acid, ellagic acid, flavonoids, and quercetin derivatives. These bioactive compounds contribute to its pharmacological activities and therapeutic potential.

Phytochemical constituents
Galls contain 50-70% of the tannic acid, gallic and ellagic acid [9] besides starch, sugars, essential oil, and anthocyanins. They were also found to contain beta-sitosterol, amenoflavone, hexamethyl ether, isocryptomerin, calcium oxalate, methyl oleanolate.

Pharmacological studies
Antibacterial activity
The passage provided highlights the efficacy of ethanol extract from certain sources, such as *Quercus infectoria* nutgalls, in inhibiting the growth of urobacterial species, particularly gram-negative bacteria, which can help prevent urinary tract infections (UTIs). This inhibitory effect is attributed to compounds like tannins, which mimic bacterial binding receptors on the surface of urinary tract cells, thus preventing bacterial adherence to these cells.
Furthermore, the ethanol extract from *Quercus infectoria* nutgalls has been investigated for its potential against methicillin-resistant Staphylococcus aureus (MRSA). The extract induces changes in the bacteria, leading to the formation of pseudomulticellular structures. Additionally, there appears to be a synergistic effect between the extract and beta-lactamase-susceptible penicillins, suggesting that the extract might interfere with staphylococcal enzymes, including wall autolysins and beta-lactamase. This interference could contribute to its antimicrobial activity against MRSA.

Anti-microbial activity
Active compounds present in crude ethanol extract shows antibacterial activity with dose dependent manner. Their mode of antimicrobial action may be related to their ability to inactivate microbial adhesions, enzymes, cell envelope transport proteins, complex with polysaccharides etc. The antimicrobial activity of *Quercus infectoria* was examined using different solvents of varying polarity and efficacy were compared. The results obtained from this study reveal that *Quercus infectoria* galls have antimicrobial activity against Gram positive Bacillus subtilis, and Staphylococcus aureus and Gram-negative bacteria Escherichia coli. All extracts from the galls inhibited the Gram-positive bacteria better than Gram negative bacteria.

Anti-inflammatory activity
Effect of alcoholic extract of Quercus infetoria galls was evaluated on various experimental models of inflammation. Oral administration of gall extract significantly inhibited carrageenan, histamine, serotonin and prostaglandin E2 induced paw oedemas, exile topical application of gall extract inhibited phorbol-12-myrisate-13-acetate induced ear inflammation. Proposed pathophysiology the anti-inflammatory activity of the galls may be related to inhibition in functions of macrophages and neutrophils wherein the extract inhibits the release of inflammatory mediators, *viz.* PGE2, NO, O2 -and lytic enzymes from these cells.

Hepatoprotective action
The alcoholic extract of fruits can offer 36% liver protection against carbon tetrachloride induced toxicity at a dose of 800 mg/kg). Patel *et al*, Indian drugs, 1988, 25,244 in a study, galls of *Quercus infectoria* were evaluated for their hepatoprotective effect against carbon tetra chloride (CCl4) induced hepatotoxicity in rats. Subcutaneous injection of CCl4, administered twice a week, produced a mark elevation in the serum levels of aspartate transaminase (AST), alanine transaminase (ALT) and tumour necrosis factor (TNF-alpha). Daily oral administration of aqueous ethanolic extract of

Quercus infectoria galls at 200, 400 and 600 mg/kg doses produced a dose dependent reduction in the serum levels of liver enzymes and inflammatory mediators and attenuated the necro inflammatory changes in the liver. *Quercus infectoria* acts as a potent chemo preventive agent and suppresses Fe-NTA induced renal carcinogenesis and oxidative and inflammatory response in wistar rats. Oral administration of *Quercus infectoria* at doses of 75 and 150 mg/kg b wt. effectively suppressed renal oxidative stress, inflammation and tumour incidence .Chemo preventive effects were associated with up-regulation of xenobiotic metabolizing enzyme activities and down regulation of serum toxicity markers.

Wound healing property

In an experimental trial, ethanol extract of the shaded dried leaves of *Quercus infectoria* were studied for its effect on wound healing in rats, using incision, excision and dead space wound models, at two different dose levels of 400 and 800 mg/kg. The plant showed a definitive, positive effect on wound healing, with a significant increase in the levels of the antioxidant enzymes, superoxidase dismutase and catalase, in the granuloma tissue. These wounds healing potential may be due to its action on antioxidant enzymes.

Anti-diabetic activity

R.Saini *et al* tested the methanolic extract of roots of *Quercus infectoria* Olivier at a dose of 250 mg/kg and 500 mg/kg body weight respectively for anti-diabetic activity compared with glibenclamide, an oral hypoglycemic agent (3mg/kg) in alloxan induced hyperglycemic rats. The blood glucose levels were measured at 0, 2h, 4h and 6h after the treatment. This reduced the blood glucose from 282.52 to 206.57mg/dl after oral administration of extract ($p<0.01$).

Larvicidal activity

An effort to assay Anopheles Stephens larvae with gall extracts of *Quercus infectoria* was made under laboratory conditions. Ethyl-acetate extract was found to be most effective for larvicidal activity against the fourth instar larvae, followed by gallotonin, n-butanol, acetone, and methanol respectively.

Anti-candida activity

Methanol and aqueous extracts of *Q. infectoria* galls were tested for anti-candida activity against *Candida albicans*, Candida krusei, Candida glabrat, *Candida parapsilosis* and Candida tropicalis. Results showed that both methanol and aqueous extracts displayed substantial anticandida activity and pyrogallol was the major component of both crude extracts. Pyrogallol has been reported to have various biological activities such as candidicidal and fungicidal activities.

Anti-oxidant activity

Ethanol, acetone and water extract of *Quercus infectoria* were evaluated for antioxidant activity via DPPH radical scavenging and metal chelating assays .Ethanolic extract have the highest antioxidant activity with 94 0.05 using DPPH assay, other extracts had less activity. Potent antioxidant activities may be due to high presence of flavonoid and tannins.

CNS depressive activity

The methanolic fractions of the galls of *Quercus infectoria* exhibited neuropharmacological activity in laboratory animals. Chemical characterization of the CNS active component identified it as syringic acid. Isolated and pure syringic acid was studied and it suggest significant local anesthetic and sedative activity of the compound.

Pharmacological activities of mazu in the unani system

Modern pharmacological studies have validated several traditional uses of Mazu in the Unani system. Mazu exhibits potent antimicrobial activity against various bacterial and fungal pathogens, making it effective in the treatment of infectious diseases. Its anti-inflammatory and antioxidant properties contribute to its efficacy in managing inflammatory conditions and oxidative stress-related disorders. Additionally, Mazu promotes wound healing by accelerating the formation of granulation tissue and epithelialization. Moreover, it has shown gastroprotective effects against experimentally induced gastric ulcers, highlighting its potential in the management of gastrointestinal disorders.

Safety profile and dosage forms

Mazu is generally considered safe when used in appropriate doses (1-3 gm). However, prolonged or excessive consumption may lead to adverse effects such as gastric irritation. In the Unani system, Mazu is commonly administered orally as powder, decoction, or paste, or topically as a paste or ointment for external applications.

Conclusion

Mazu (*Quercus infectoria*) is a valuable medicinal plant in the Unani system of medicine, possessing diverse pharmacological activities and therapeutic potential. Its traditional uses in treating various ailments are supported by modern scientific evidence, making it a promising natural remedy for integration into mainstream healthcare practices. Further research is warranted to explore its mechanisms of action, optimize dosage forms, and evaluate its efficacy in clinical settings. Overall, Mazu represents a prime example of the rich heritage of traditional medicine and its relevance in contemporary healthcare.

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