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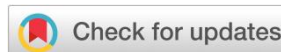
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Review Article

Zūfā (*Hyssopus officinalis* L.): Unani Temperament, Traditional Therapeutic Uses, Phytochemistry, Pharmacological Actions, and Clinical Potential: A Comprehensive Review

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Abstract

Background: *Hyssopus officinalis* L. (Zūfā), a medicinal herb in the family Lamiaceae, has been extensively used in Unani medicine and other traditional systems for respiratory, gastrointestinal, and inflammatory disorders. Traditional uses focus on cough, dyspnoea, digestive disturbances, and inflammation. It has attracted modern scientific interest due to its phytochemical constituents (essential oils, terpenoids, flavonoids, phenolic acids, and other bioactive compounds). Experimental studies (in vitro and in vivo) have reported antioxidant, antimicrobial, anti-inflammatory, antispasmodic, and cytotoxic activities. Its aromatic properties also support applications in food, flavour, fragrance, and aroma industries. The authors note that existing information remains dispersed and that an integrated assessment of its traditional uses, phytochemistry, pharmacological activities, and contemporary applications is needed. **Objective:** To comprehensively summarize the Unani perspective, botanical characteristics, phytochemical constituents, pharmacological activities, and clinical potential of *H. officinalis*, while highlighting its relevance as a promising medicinal plant for future research. **Material and Methods:** The authors have gone through a comprehensive literature review was conducted to identify and document the medicinal uses of *Hyssopus officinalis* L. (Zūfā) as described in classical Unani medical texts, including *Al-Qanoon fi'l-Tibb* (Canon of Medicine), *Khazain-ul-Adviyah*, *Makhzan-ul-Mufradat*, the Unani Pharmacopoeia of India, and Pharmacographia Indica. Contemporary published literature was also reviewed using electronic databases and peer-reviewed journals to gather updated information on its taxonomy, morphology, *Mizāj* (temperament), traditional therapeutic uses, phytochemical composition, and experimental pharmacological studies. The information obtained was systematically compiled, compared, and analysed to provide an integrative understanding of the classical foundations and modern scientific perspectives on *H. officinalis*. **Results:** Rich phytochemical profile: essential oils, flavonoids (luteolin, apigenin, quercetin, diosmin), phenolic acids (chlorogenic, caffeic, ferulic, protocatechuic acids), terpenoids, and triterpenoids. Demonstrated activities: significant antioxidant, antimicrobial, antifungal, anti-inflammatory, gastroprotective, smooth muscle-relaxant, antiplatelet, and xanthine oxidase inhibitory effects. **Conclusion:** Current evidence largely supports many of the traditional therapeutic claims associated with *H. officinalis*. However, well-designed clinical trials, standardized phytochemical profiling, and safety evaluations are needed to establish its efficacy and facilitate its integration into evidence-based clinical practice.

Keywords: *Mizāj*; phytochemistry; pharmacological activities; Unani medicine; Zūfā (*Hyssopus officinalis* L.)

1. Introduction

Medicinal herbs have long been recognized for their ability to treat and prevent a wide range of health conditions, with records of their use dating back to ancient civilizations. In recent years, both developing and developed nations have shown increasing interest in medicinal plants and herbal preparations, largely because of their proven effectiveness and relatively favourable safety profiles. Traditional herbal medicine continues to serve as the foundation of primary healthcare for roughly 75% of the global population, particularly in less developed and developing regions. Among the various forms of traditional medicine, herbal

therapies remain the most widely practiced and continue to experience strong worldwide demand. Moreover, medicinal plants supply approximately 80% of the raw materials required for the manufacture of pharmaceutical products.¹ *Hyssopus officinalis* L. (Family: Lamiaceae) is a valuable aromatic and medicinal perennial herb or subshrub renowned for its diverse therapeutic benefits. It is widely used in modern herbal medicine and also serves as a spice and flavouring agent in the food industry.² The genus *Hyssopus* comprises several species that are widely cultivated across Asia, Europe, and the temperate regions of the Americas for culinary, medicinal, and commercial importance.³ In India, *H. officinalis* is

distributed in the Western Himalayan region, from Kashmir to Kumaon, at elevations ranging from 8,000 to 11,000 ft. It naturally grows on dry, rocky slopes, banks, and ruins, attaining a height of approximately 50–120 cm.⁴ Traditionally, *H. officinalis* has been employed in various systems of medicine for the management of numerous ailments. However, despite its long-standing medicinal use, many of its therapeutic claims remain inadequately supported by rigorous scientific evidence. Consequently, a comprehensive synthesis of the available literature on its phytochemical constituents, traditional and ethnomedicinal uses, and pharmacological activities reported in recent scientific studies is warranted to critically evaluate its therapeutic potential and identify future research directions.³

S. No	Taxonomic Rank ⁵	Classifications
1	Kingdom	<i>Plantae</i> - Plants
2	Subkingdom	<i>Tracheobionta</i> - Vascular plants
3	Superdivision	<i>Spermatophyta</i> - Seed plants
4	Division	<i>Magnoliophyta</i> - Flowering plants
5	Class	<i>Magnoliopsida</i> - Dicotyledons
6	Subclass	<i>Asteridae</i>
7	Order	<i>Lamiales</i>
8	Family	<i>Lamiaceae</i> Martinov - Mint family
9	Genus	<i>Hyssopus</i> L. - hyssopus
10	Species	<i>Hyssopus officinalis</i> L. - hyssop

According to Pharmacographia Indica, *Zūfā-i-Yābis* is a small woody herb, approximately 6–8 inches tall, with a four-angled purplish stem, numerous oblong flower spikes, and pale-brown, three-angled seeds. The commercial drug is usually found in fragmented form with a pleasant sweet-hay aroma and a bitter taste. Traditional Unani authorities describe it as a stimulant, anthelmintic, and deobstruent. Although it has generally been attributed to *Hyssopus officinalis*, its spike-like inflorescence suggests that the commercial Persian drug may not exactly correspond to this species.⁶

Vernacular names ⁷		
S.No	Language	Vernacular Names
1	English	Hyssope
2	French	Hyssope
3	German	Ysop
4	Italian	Issopo
5	Spanish	Hisopo
6	Sanskrit	Jufa, zupha ⁷
7	Indian	Jufa
8	Arabic	Az-zufa
9	Persian	Zufa, Ushnan-e-Dawood ⁷
10	Hindi	Zufah-yabis, zupha ⁷
11	Urdu	Zufah, Zufa Khushk ⁷

2. Morphology

Macroscopic examination: The leaves are opposite, dark green, glossy, entire, and lanceolate to oblong, measuring 2–4 cm in length and 0.5–1.0 cm wide, with an obtuse to acuminate apex. The plant has a strongly branched, multi-headed taproot and erect to decumbent, woody, highly branched stems reaching 0.5–0.7 m in height. The inflorescence is a 20–25 cm long terminal false spike composed of 4–10-flowered pseudoverticillasters. Flowers are pedicellate, complete, and hypogynous. The calyx is 15-nerved and five-toothed, while the corolla is bilabiate. There are four exserted, divergent stamens, with the lower pair longer than the upper; the anther cells are linear and spreading, and the style bears two subequal, subulate lobes.^{2,8}

Microscopy: The transverse section (T.S.) of the pedicel shows a solid central stele surrounded by a single-layered epidermis of rectangular, cuticularized cells and a multi-layered parenchymatous cortex. The stele is enclosed by a sclerenchymatous pericycle, followed by a continuous phloem, while the xylem consists of vessels, tracheids, fibres, and xylem parenchyma. Calcium oxalate crystals are present in the cortical cells, and characteristic uniseriate, unicellular trichomes occur on the epidermis. The T.S. of the sepal comprises upper and lower epidermis enclosing 3–4 layers of parenchymatous mesophyll with intercellular spaces, 4–5 vascular bundles, and calcium oxalate crystals. The petal has a similar structure but with smaller cells and 3–4 vascular bundles. The anther is tetrasporangiate with four pollen sacs, a single-layered epidermis, and an endothecium showing characteristic lignified radial and tangential wall thickenings.⁸

Powder Microscopy: The powder is brownish-green, odourless, and contains fragments of the pedicel, calyx, corolla, anther epidermis, endothecium, pollen grains, tracheids, xylem parenchyma, and characteristic uniseriate, unicellular trichomes. These features serve as reliable diagnostic markers for the authentication of the crude drug.⁸

The genus *Hyssopus* is naturally distributed across Europe, Asia, and North Africa. Additionally, introduced species have been observed in North America.⁹

Parts Used: Leaves, Roots, flowers, Whole Plants.^{8,10,11}

Temperament (Mizāj): Hot 3° and dry 3°^{8,10}

Pharmacological Actions (Af'āl): *Mulattif*: Attenuant; softens and dilutes thick humours, *Munaffith-i-Balgham*: Expectorant; facilitates the expulsion of phlegm from the respiratory tract. *Muhallil-i-Waram*: Anti-inflammatory; resolves inflammatory swellings. *Kāsir-i-Riyāh*: Carminative; disperses and relieves flatulence. *Dāfi'-i-Dīdān-i-Am'ā*: Anthelmintic; expels intestinal worms. *Mu'arriq*: Diaphoretic; promotes perspiration.⁸

Munaffith-i-Balgham: Expectorant; facilitates the expulsion of phlegm from the respiratory tract. *Muhallil-i-Riyāh*: Carminative; disperses thick and accumulated flatulence.

Qātil-i-Dīdān: Anthelmintic; expels intestinal worms. *Muhallil-i-Awrām*: Anti-inflammatory; resolves inflammatory swellings. *Muhallil-i-Dam-i-Ghalīz*: Resolves thick or congested blood. *Muqawwī-i-A'sāb*: Nervine tonic; strengthens the nerves. *Mufattiḥ-i-Sud*: Deobstruent; helps remove bodily obstructions.^[12,13]

3. Classical Unani Therapeutic Uses (*Mawāqī'i-Isti'māl*)

According to classical Unani literature, *Zūfā* (*Hyssopus officinalis* L.) is valued for its diverse therapeutic applications. Oral administration is believed to improve complexion, while topical application helps reduce facial blemishes and discoloration. It is particularly recommended for chest and lung ailments, including asthma, chronic cough, and orthopneic breathing. A decoction prepared with fig and honey is traditionally used to relieve respiratory complaints and resolve hard swellings. As a gargle, it is considered beneficial in inflammatory conditions of the throat associated with suffocation. Beyond respiratory uses, *Zūfā* is also described as a remedy for hard swellings, especially when taken with wine. A decoction with vinegar is traditionally employed to alleviate toothache, while the vapour of its decoction, particularly when combined with its stalks and figs, is directed into the ear to relieve tinnitus. For ocular conditions, the decocted herb is applied as a poultice to reduce ecchymosis and sub palpebral blood spots, reflecting its broad therapeutic significance in classical Unani medicine.¹⁰

Zo'f-i-Ishtihā: Loss of appetite. *Nafkh-i-Shikam*: Abdominal flatulence and distension. *Su'āl*: Cough. *Nazla*: Coryza/catarrh (common cold with nasal discharge). *Ḍiq al-Nafas*: Breathlessness/asthma. *Khushūnat-i-Halq*: Roughness or irritation of the throat.⁸

Su'āl Muzmin: Chronic cough. *Ḍiq al-Nafas*: Breathlessness and respiratory congestion. *Waja' al-Ṣadr*: Chest pain. *Dhāt al-Janb*: Pleuritic pain and pleurisy. *Qūlanj*: Colitis and abdominal colic associated with flatulence. *Irq al-Nisā*: Sciatica. *Fālij*: Paralysis. *Dīdān-i-Am'ā*: Intestinal worm infestation.^{12,13}

4. Phytochemical constituents

The chemical composition of *Hyssopus officinalis* is highly diverse and varies based on its geographic origin and environmental growing conditions. Its primary components include essential oils, flavonoids, resins, mineral salts, and both oleanolic and ursolic acids, tannins, and organic acids.¹⁴ Various classes of chemicals were isolated from *Hyssopus officinalis* L. flower tips contain ursolic acid and the glucoside diosmin. The main components of the essential oil are bicyclic monoterpenes (L-pinocamphene, cis-pinocamphone, pinocarvone, β-pinene), depending on the chemotype of the plant. The major components of *H. officinalis* include apigenin, quercetin, diosmin, luteolin and their glycosides, as well as chlorogenic, protocatechuic, ferulic, syringic, p-hydroxybenzoic, caffeic and other acids.⁹ Subsp. *angustifolius* revealed that the aqueous leaf extract contained the highest total phenolic and flavonoid contents, measuring 1.3% (gallic acid equivalents, GAE) and 4.7%, respectively.

Proanthocyanidins were detected in high concentrations in the aqueous, chloroform, and hexane leaf extracts, with the chloroform extract exhibiting the highest level (10,250 mg/L). High-performance liquid chromatography (HPLC) analysis further confirmed the presence of major antioxidant phenolic compounds, including chlorogenic acid (166.21 µg/g) and caffeic acid (111.09 µg/g) in the methanolic leaf extract, highlighting the plant's rich antioxidant phytochemical profile.^[3,15] The major phytoconstituents of *Hyssopus officinalis* include a diverse range of polyphenolic compounds, predominantly flavonoids such as luteolin, diosmin, quercetin, apigenin, and their glycosides, together with phenolic acids including caffeic, p-hydroxybenzoic, syringic, ferulic, protocatechuic, and chlorogenic acids. In addition, the essential oil obtained from the aerial parts is rich in terpenoids, with β-pinene, isopinocampheol, and Pino camphene identified as the principal volatile constituents.^{3,2}

5. Pharmacological Properties

Hyssopus officinalis L. exhibits a broad spectrum of pharmacological activities that support both its long-standing traditional use and its emerging therapeutic potential. Traditionally, it has been employed as an expectorant, antispasmodic, digestive aid, antifungal, and antimicrobial herb for the management of respiratory and gastrointestinal disorders. Its aerial parts are widely employed for respiratory ailments, including asthma, bronchitis, and cough. It has also been used to treat rheumatic pain, bruises, wounds, blood pressure fluctuations, and neurological disorders such as anxiety and depression.^{16, 17,18} The ethanolic extract of *Hyssopus officinalis* has demonstrated gastroprotective, anticoagulant, and antioxidant activities. Its gastroprotective effect is attributed to enhanced adhesion of the gastric mucosal barrier, while its antioxidant action reduces free radical generation, thereby helping to protect tissues from oxidative damage.^{16,19}

Modern pharmacological studies have substantiated many of these traditional claims, demonstrating significant antioxidant, antimicrobial, anti-inflammatory, and smooth muscle-relaxant activities.^{14,20} The ethyl acetate fractions of its leaves and stems exhibit potent free-radical scavenging activity in DPPH and ABTS assays, along with strong ferric-reducing antioxidant power, effects largely attributed to its rich content of phenolic compounds and flavonoids, including quercetin, hesperidin, and esculin. These bioactive constituents also contribute to its ability to suppress cough, combat microbial infections, reduce inflammation, and promote gastrointestinal health by relaxing the smooth muscles of the digestive tract and alleviating painful spasms, thereby supporting its therapeutic applications in both respiratory and digestive ailments.^{14,21} Its also exhibits moderate antioxidant activity and antimicrobial effects against both Gram-positive and Gram-negative bacteria. In vitro studies have also demonstrated pronounced antifungal, insecticidal, and antiviral properties. Animal model

research has revealed muscle-relaxant and antiplatelet effects.⁹

Xanthine Oxidase (XO) Inhibitory Activity

Microwave-assisted extracts (MAE), selected for their high phenolic content and antioxidant activity, exhibited notable xanthine oxidase (XO) inhibitory effects, with inhibition ranging from 50–88%, compared with 90% for allopurinol. Among the tested Unani medicinal plants, *Hyssopus officinalis* showed the highest inhibition (88%), followed by *Portulaca oleracea* (85%), *Origanum vulgare* (82%), and *Rubia cordifolia* (80%), whereas *Cichorium intybus* (58%) and *Achyranthes aspera* (50%) showed comparatively lower activity. These findings suggest that *H. officinalis* is a promising natural XO inhibitor and may have potential in managing hyperuricemia and gout. Given the adverse effects associated with allopurinol, plant-derived XO inhibitors warrant further investigation as safer therapeutic alternatives.²²

Superoxide dismutase (SOD) Inhibitory Activity

is a highly thermostable antioxidant enzyme and a key indicator of cellular defence against oxidative stress, ranking among the most heat-stable enzymes (after ascorbate peroxidase) involved in reducing reactive oxygen species. Most plant extracts inhibited SOD activity (38.5–70.2%), with effectiveness ranked by extraction method as microwave-assisted extraction (MAE) > ultrasound-assisted extraction (UAE) > Soxhlet extraction (SE) > maceration (MC). These results were compared against vitamin C (75.2% inhibition) as the standard. The highest inhibition (>60%) was observed for *Hyssopus officinalis* (70.2%), *Origanum vulgare* (65.5%), *Portulaca oleracea* (63.3%), and *Rubia cordifolia* (60.1%).^{22,23}

Antimicrobial, Antifungal, and Antiviral Activity

The essential oil of *Hyssopus officinalis* exhibits broad-spectrum antimicrobial activity, largely attributed to bioactive constituents such as β -pinene, pinocamphone, isopinocampone, pinocarvone, terpinen-4-ol, carvacrol, and p-cymene. It has demonstrated inhibitory effects against several pathogenic bacteria, including *Staphylococcus aureus*, *Escherichia coli*, *Bacillus cereus*, *Proteus hauseri*, *Listeria monocytogenes*, *L. ivanovii*, *Salmonella enteritidis*, and *Enterococcus faecalis*. The essential oil also possesses notable antifungal activity against *Candida albicans*, *C. krusei*, and *C. tropicalis*, with minimum inhibitory concentrations (MICs) ranging from 0.15–0.3% in liquid media and 15.625–250 μ L/mL against various yeasts and fungi. Additionally, it has been reported to inhibit the mushroom pathogen *Mycogoneperniciosa*, highlighting its potential as a natural antimicrobial and antifungal agent for therapeutic and agricultural applications.^{24,25,26,27}

Hyssopus officinalis essential oil reveal notable antifungal activity. It showed a MIC of approximately 5 μ L/mL and minimal fungicidal activity at 15–20 μ L/mL against *Mycogoneperniciosa*. The oil also demonstrated weak-to-moderate activity against *Penicillium italicum*, *Botrytis cinerea*, *Rhizopus stolonifer*, and *Phytophthora*

citrophthora, suggesting potential as a natural food preservative. Moreover, complete inhibition of *Aspergillus niger* growth was observed at 0.5–1.5% concentrations. In addition, dried leaf extract of *H. officinalis* showed inhibitory activity against HIV replication, indicating potential antiviral properties. These findings support the traditional medicinal relevance of Zūfā and its potential as a source of natural antifungal and antiviral agents.^{24,28,29,30}

6. Conclusion

Hyssopus officinalis L. (Zūfā) represents an important medicinal plant with a long history of use in Unani medicine, particularly for the management of respiratory disorders such as cough and dyspnoea, as well as gastrointestinal and inflammatory conditions. Contemporary phytochemical investigations have identified a wide range of bioactive constituents, including essential oils, flavonoids, phenolic acids, and terpenoids, which contribute to its diverse pharmacological properties. Evidence from in vitro and in vivo studies supports its antioxidant, antimicrobial, anti-inflammatory, antispasmodic, and cytotoxic activities, while its aromatic characteristics have also established its value in the food, flavour, and fragrance industries.

Despite these promising findings, most available evidence is derived from experimental studies, and well-designed clinical trials remain limited. Standardization of extracts, comprehensive safety and toxicity assessments, and rigorous clinical investigations are necessary to validate its therapeutic efficacy and establish appropriate dosage and quality-control parameters. Integrating traditional Unani knowledge with modern scientific research may facilitate the development of evidence-based herbal formulations and expand the therapeutic potential of *H. officinalis* in contemporary healthcare.

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