



Clinical efficacy of *Hyssopus officinalis* (Zufa-e-Yaabis) in Bronchial Asthma (DĪQ Al-Nafas) -A Review Article

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Abstract:

The *Hyssopus officinalis*, has been demonstrated to affect the levels of a number of cytokines in asthmatic mice, including interleukin-4, -6 and -17 and interferon- γ . In the present study, the effect of *Hyssopus officinalis* L. on airway immune regulation and airway inflammation was investigated in a mouse model of chronic asthma. A total of 32 BALB/c mice were randomly divided into four groups, which included the normal, chronic asthmatic, dexamethasone treatment and *Hyssopus officinalis* L. treatment groups. Mice were sensitized and challenged with ovalbumin to establish an asthma model and the ratio of eosinophils (EOS) in the broncho alveolar lavage fluid (BALF) was determined. In addition, the levels of immunoglobulin (Ig)E and IgG were detected using an enzyme-linked immuno sorbent assay. The degree of airway mucus secretion was observed using the periodic acid-Schiff stain method. It has been proved that Uygur herb *Hyssopus officinalis* L. could affect the levels of some cytokines in asthmatic mice. By detection of the expressions of MMP-9 and TIMP-1 and the morphological changes, the aim of this research is to reveal the mechanism of Uygur herb *Hyssopus officinalis* L. in the process of airway remodeling. It was observed that the expressions of MMP-9 and TIMP-1 increased, but the ratio of MMP-9/TIMP-1 decreased in airway remodeling group. However, the expression of both MMP-9 and TIMP-1 decreased after being treated with dexamethasone and *Hyssopus officinalis*, accompanied by the relieved pathological changes, including collagen deposition, mucus secretion, and smooth muscle proliferation. It is suggested that Uygur herb

Hyssopus officinalis L. could inhibit airway remodeling by correcting imbalance of MMP-9/TIMP-1 ratio.

Keywords: Asthma, *Hyssopus officinalis*, airway inflammation, immune regulation, Anti Asthaminic activity of Hyssop,

I. Introduction

The word "asthma" originates from the Greek meaning short of breath, meaning that any patient with breathlessness was asthmatic. The term was refined in the latter part of the 19th Century with the publication of a treatise by Henry Hyde Salter entitled "On Asthma and its Treatment". In this scholarly work Salter defined asthma as "Paroxysmal dyspnoea of a peculiar character with intervals of healthy respiration between attacks", a description that captures his concept of a disease in which the airways narrow due to contraction of their smooth muscle.¹ His book contains remarkably accurate illustrations of the airways in asthma and bronchitis as well as the cellular appearance of asthmatic sputum some 30 years before Paul Ehrlich described aniline stains for eosinophils (eosin) and mast cells (toluidine blue). He also described black coffee as a treatment for asthmatic spasms, a drink with a high content of theobromine, a derivative of theophylline and theophylline itself. This extraordinary insight into asthma stems from Dr. Salter himself suffering from asthma himself. Thus, by the late nineteenth century, physicians adopted the view that asthma was a distinct disease which had a specific set of causes, clinical consequences, and requirements for treatment.

The father of modern medicine in the Western World, Sir William Osler (one of the three founders of the John Hopkins Medical School in Baltimore, US) described asthma in his first (1892) edition of the textbook Principles and Practice of Medicine in the following terms:

1. Spasm of the bronchial muscles
2. Swelling of the bronchial mucous membrane
3. A special form of inflammation of the smaller bronchioles
4. Having many resemblances to hay fever
5. The affection running in families.
6. Often beginning in childhood and sometimes lasting into old age.
7. Bizarre and extraordinary variety of circumstances which at times induce a paroxysm:
 - a. Climate and atmosphere e.g. hay, dust, cat
 - b. Fright or violent emotion
 - c. Diet (overloading of the stomach) or certain foods
 - d. Cold infection
8. Sputum is distinctive: rounded gelatinous masses ("perles") and Curschmann spirals & octahedral crystals of Leyden

The primary functions of the lungs are oxygenation of the blood and the elimination of carbon dioxide. The lungs and heart may be seen as physiologically related dual organs whose combined function is to supply the tissues with oxygen and venous carbon dioxide. Asthma is a condition of airways characterized by heightened reactivity of the tracheobronchial tree to various stimuli resulting in extensive spasmodic constriction of the air route, which may be alleviated spontaneously or by therapy. Asthma is an episodic

condition seemed to clinically by paroxysms of dyspnea, cough, and wheezing. However, a severe and constant type of sickness described as "status asthmaticus" may prove fatal. Asthma is a significant global health problem that affects people of all ages. It is becoming more prevalent in several countries, particularly among children. Asthma places an unacceptably high burden on the health care system and society. It is a common and potentially serious chronic condition that causes respiratory symptoms, activity restrictions, and flare-ups that occasionally require immediate medical attention and maybe fatal.

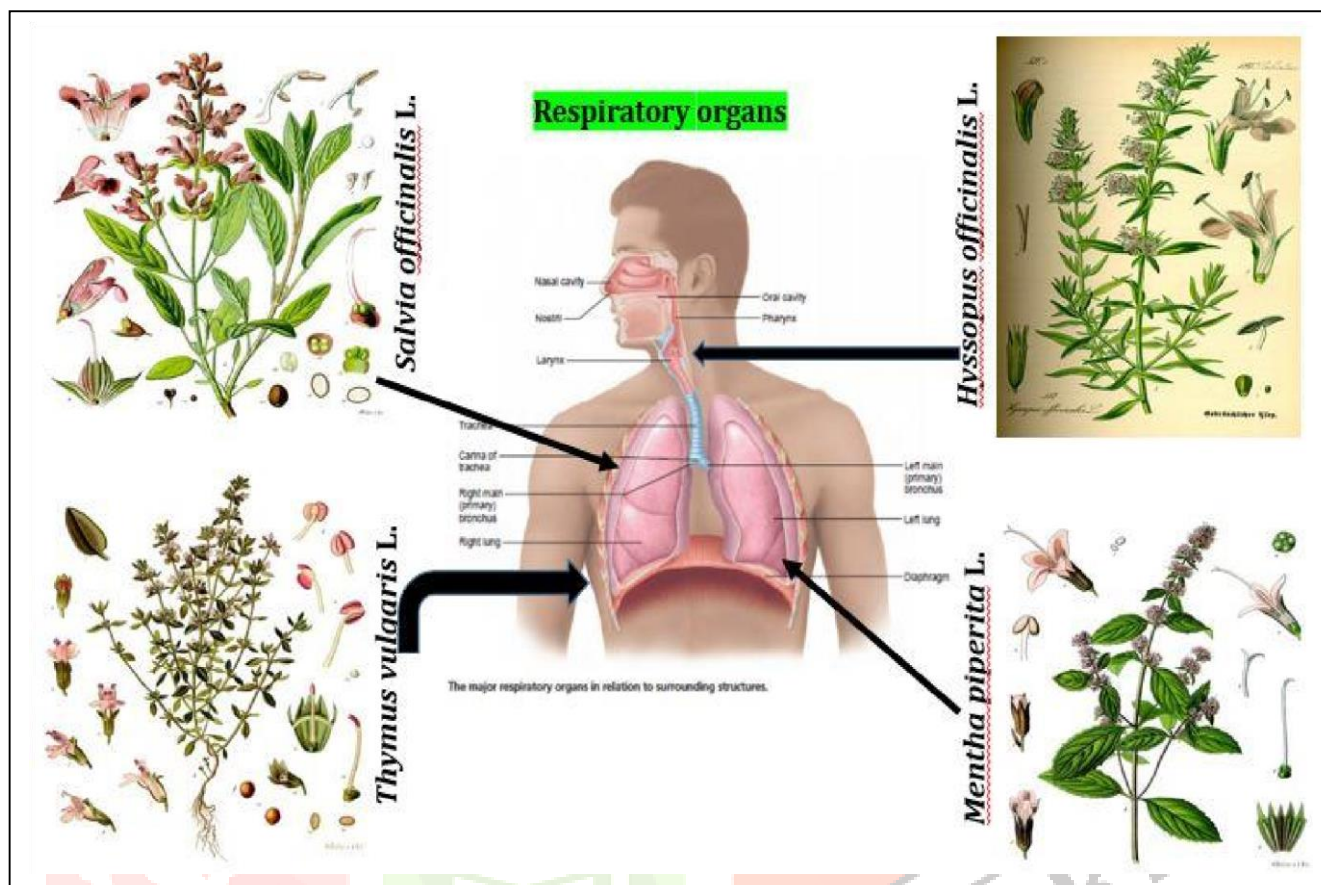


Fig. 1 Respiratory Organ and Herbal drugs used for various respiratory Diseases

Asthma is a chronic condition that affects both children and adults. Asthma impacted an estimated 262 million individuals in 2019 and resulted in around 461000 deaths. Nearly 80% of deaths from asthma occur in low- and lower- middle-income countries, where underdiagnosis and under treatment are common. Inflammation and narrowing of the tiny airways in the lungs contribute to the development of asthmatic symptoms: cough, wheeze, chest tightness, and shortness of breath. In India, the total prevalence of asthma is 2.38%, while it is 2.28% in

Chandigarh, 1.69% in Delhi, 2.05% in Kanpur, and 3.47% in Bangalore. Asthma is a serious disease of the airways and bronchial tree that has been known to humans since the time of Hippocrates but was defined by its unusual traits. Hippocrates was the first to coin the term 'panting,' which translates as "breathlessness". Later on, numerous Unani scholars diligently examined and detailed asthma in their works. Asthma is derived from the Greek word "aazein," which means to exhale via an open mouth, pant, and take a quick breath. In ancient Rome, physicians described asthma as gasping and an inability to breathe without making a noise, which is now referred to as wheezing.

II. Unani Concept about Asthma (Dīq al-Nafas):

In the Unani system of medicine, asthma is referred to by a variety of terms, including Dhīq al-Nafas, Dama, Rabw, Buhr, and Intisāb al-Nafas. Although there is no distinction between these synonyms, they all refer to respiratory difficulties.

According to Majūsī, Dhīq al-Nafas, Rabw, Buhr, and Intisāb al-Nafas are all respiratory illnesses caused by constriction of the arteries and venulose of the lungs; hence, when the difficulty develops in the arteries of the lungs, Rabwand Buhr occur. It creates Dīq al-Nafas and Intisāb al-Nafas when it develops in the bronchi and bronchioles.

The father of medicine, Hippocrates, was the first to link asthma symptoms and environmental triggers and specific trades and occupations. Ibn Sina, a great Unani scholar, characterized Asthma (Dīq al-Nafas) in his classic work "Al-Qanun fi'l Tibb" as a chronic respiratory ailment in which the patient continually breathes, and its episodes are incredibly rapid and intense. According to Zakariyya Razi, asthma (Rabw) is mainly caused by thick mucus clogging the trachea (Qasaba al-Ri'a), resulting in bronchospasm, wheezing, and shortness of breath. Asthma is a purely pulmonary condition in which the patient repeatedly breathes despite being comfortable. The time interval between two breaths is decreased while the expiratory phase is lengthened. This is because the need for cold air is greater, and it cannot reach the heart due to the pathways' narrowness and congestion. As a result, breathing becomes extremely rapid and frequent during this sickness. Hakim Ajmal Khan, a famous Unani scholar, stated that asthma is a severe disease that cannot be readily healed or treated. This condition is distinguished by episodic breathlessness and wheezing.

In Dīq al-Nafas, a condition in which breathing becomes difficult due to a narrowing of the airways induced by the accumulation of Balgham Lazij (vitreous phlegm) in Urūq Khashna (bronchioles). Additionally, it is referred to as Intisāb al-Nafas (orthopnoea), a mix of the two terms 'Intisāb' meaning 'to stand' and 'Nafas' meaning 'breath.' At times, the patient may be unable to breathe or may feel uneasy in a sitting or lying position. As a result, he stands to take a breath and feel relaxed (Kabir, 1960). Rabw is a term that refers to a type of lung ailment in which the patient's breathing becomes irregular and also in breathing trouble in which the patient breathes like a very weary person.

III. Etio-pathogenesis of Asthma (Ḍīq al-Nafas):

Asthma is a disorder in which the body does not receive the needed amount of oxygen for Tarvih al-Qalb (sufficient supply of oxygen to the heart), resulting in patient discomfort due to breathlessness. Asthma is most frequently caused by an accumulation of thick mucus secreted within the bronchi and alveoli.

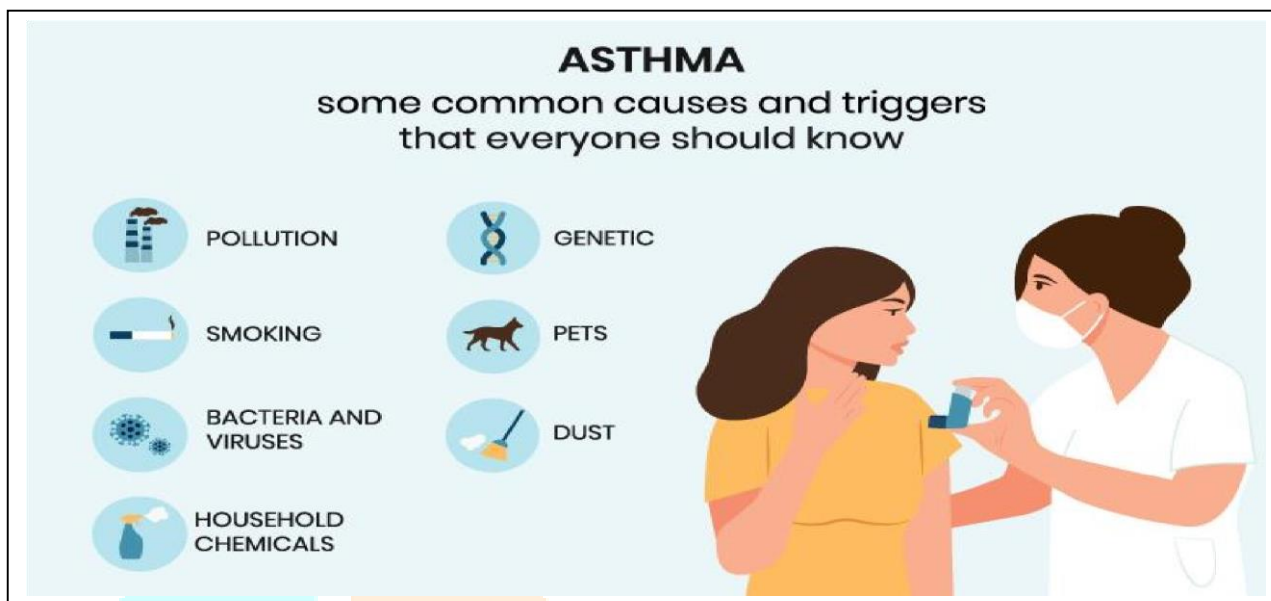


Fig. 2 Asthma, common causes and Triggers

The primary cause of Dama or Ḍīq al-Nafas is narrowing of Urūq Khashna (bronchioles) that may be due to various causes such as Accumulation of Balgham Lazij (vitreous phlegm) in the air passages, Inṣībāb-i Mawād-i-Nazla (exudation of catarrhal fluid) and Warm (inflammation) of the respiratory tract. Accumulation of Ghalīz Rutūbat (thick secretions) in the bronchi and alveoli, Imtilā' sadr (thoracic congestion) and surrounding organ pressure, gaseous collection in the chest, creating pressure and bronchial constriction and genetic (Ibn Hubul, 2004). Accumulation of pus and blood surrounding the lungs prevents them from expelling. The flow of catarrhal fluids from the brain may cause Asthma. Colds and coughs occasionally cause a buildup of Balgham (phlegm) in the lungs, making breathing difficult; rarely, it occurs as a result of pulmonary dryness and may end in breathing cessation; and rarely, it develops as a result of smallpox.

Asthma is a reversible chronic airway disease usually brought on by an immunological reaction. Asthma is characterized by an overactive TH2 response to normally harmless antigens in the environment. Inflammatory signals, such as cytokines, are produced by TH2 cells, prompting B cells to generate IgE and other antibodies. IL-4, which enhances IgE production, and IL-13, which modulates mucus release from bronchial submucosal glands while simultaneously boosting IgE synthesis from B cells, are two cytokines. Asthma has traditionally been divided into extrinsic (allergic, atopic) and intrinsic (idiosyncratic, non-atopic). Extrinsic asthma is the most common type. It usually starts in infancy or early adulthood. Most people with this kind have a family history of allergies or asthma. Adults with no personal or familial history of asthma develop intrinsic asthma later. Bronchospasm episodes of any sort can be caused by several reasons, including respiratory infection, smoking, fumes, cold air, and exercise. Asthma is further categorized based on the agents

that produce bronchoconstriction, such as seasonal, exercise-induced, drug-induced (aspirin-induced), and occupational asthma.

IV. Classification of Asthma (Ḍīq al-Nafas) in Unani Medicine:

Asthma is a chronic inflammatory illness that can quickly deteriorate into a life-threatening and severe condition. Hakim Ajmal Khan, a renowned Unani scholar, classified asthma

Components of Severity		Classification of Asthma Severity (Youths ≥12 years of age and adults)			
		Intermittent	Mild	Persistent	
Impairment	Symptoms	≤2 days/week	>2 days/week but not daily	Daily	Throughout the day
	Nighttime awakenings	≤2x/month	3–4x/month	>1x/week but not nightly	Often 7x/week
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)	≤2 days/week	>2 days/week but not >1x/day	Daily	Several times per day
	Interference with normal activity	None	Minor limitation	Some limitation	Extremely limited
	Lung function	<ul style="list-style-type: none"> Normal FEV₁ between exacerbations FEV₁ >80% predicted FEV₁/FVC normal 	<ul style="list-style-type: none"> FEV₁ ≥80% predicted FEV₁/FVC normal 	<ul style="list-style-type: none"> FEV₁ >60% but <80% predicted FEV₁/FVC reduced 5% 	<ul style="list-style-type: none"> FEV₁ <60% predicted FEV₁/FVC reduced >5%
Risk	Exacerbations requiring oral systemic corticosteroids	0–1/year (see note)	≥2/year (see note) →		

← Consider severity and interval since last exacerbation. Frequency and severity may fluctuate over time for patients in any severity category. →

Relative annual risk of exacerbations may be related to FEV₁

Fig. 3 Classification of Asthma and Serverity

According to its difficulties: Ḍīq al-Nafas Yabis and Ḍīq al-Nafas Ratab. In Ḍīq al-Nafas Yabis, spasmodic narrowing of the airway and respiratory muscle results in trouble breathing; in Ḍīq al-Nafas Ratab, does not only spasmodic narrowing of the airway result in breathlessness but also mucus accumulation. Rabban Tabri stated various forms of Ḍīq al-Nafas, which are listed below.

1. Ḍīq al-Nafas Qasir (short respiration caused by weakness of the respiratory muscle)
2. Ḍīq al-Nafas Mutatabae (
3. Ḍīq al-Nafas Mustaqeem (straight respiration caused by weakness of respiratory muscles)
4. Ḍīq al-Nafas Qawi (strong respiration caused by Iltehāb-i Harārat)
5. Ḍīq al-Nafas Zaef (weak respiration caused by coldness (burūdat)).
6. Ḍīq al-Nafas Aseer (dyspnea caused by the accumulation of viscid secretion in the bronchial tree or gaseous collection in the chest putting pressure on the bronchial tree externally).

According to Kabir al-din, there are three forms of Rabw:

The first form, Haqiqi Rabw (true asthma), is characterized by the closure of the bronchial branches by a sort of thick cold mucus. In Haqiqi Rabw, Intisāb al-Nafas (orthopnea) is occasionally discovered or not. The second type is when the lining of the lungs narrows owing to inflammation, but no pus is observed, and it is caused by hot black bile (Khilt Sawda Harr). The distinction between the two types is that the first does not

have thirst but occasionally coughs, discharges, and wheezing. The second form is characterized by fever, thirst, and agitation.

The third form is caused by flaccidity or atonicity of the bronchial muscles; in this type, Intisāb alNafas (orthopnea) is primarily present, and breathing is occasionally stopped.

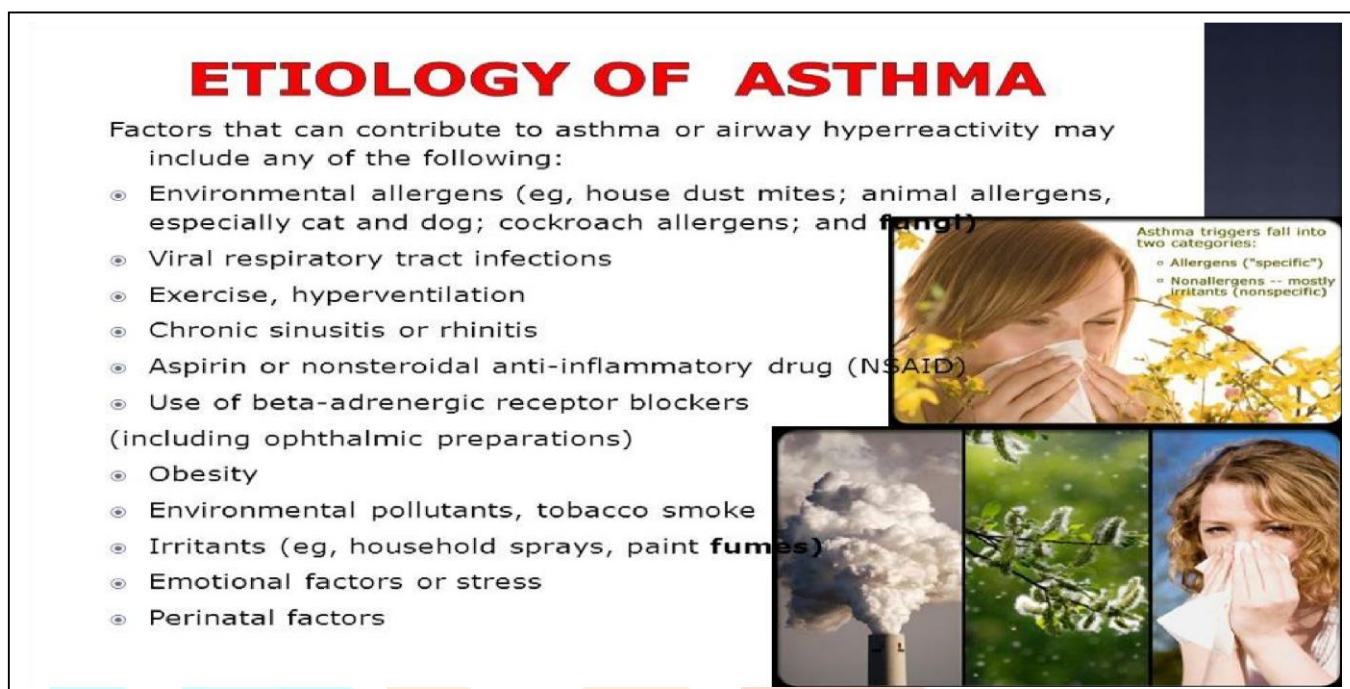


Fig. 4 Etiologies of Asthma

V. Signs and symptoms of Asthma (Ḍīq al-Nafas):

The symptoms of Ḍīq al-Nafas differ from person to person. Patients may present with wheezing, shortness of breath, and coughing, most common at night and early morning. Wheezing and nocturnal dyspnea is strongly linked to asthma diagnosis. The signs and symptoms of Ḍīq al-Nafas are primarily present in episodic and non-episodic phases, with pre-episodic constipation and bloating. A mild cough is followed by breathing difficulties. A sudden episode occurs, and the patient feels suffocated, restless, and weak; the face turns red, then a tiny bit of mucus comes out, and the entire body sweats away. During the resting period, the patient appears to be in good health without discomfort. The pulse becomes Azīm (magnus), Sari (rapid), and Mutwātir (frequent). When asthmatic patients have asthma symptoms, they may feel as if they are inhaling through a straw and hear a whistling or squeaking noise. During an asthma episode, the patient's breathing is exceptionally rapid. Coughing, wheezing, and pressure in the chest can make you feel anxious or scared.

VI. Principle of treatment and preventive measures (Usool-e Ilaj wa Tadābīr):

According to Unani philosophy, Mizāj (temperament) plays a significant factor in asthma management. The patient's temperament and the disease are the essential criteria per 'Ilaj bi'l Didd (heteropathy).

A. Preventive measures (Taḥaffuzī Tadābīr):

The patients should be kept in a tidy and clean environment free of contamination and pollution. The modification of the temperament (Ta'dīl-e Mizāj) should be done. Dust and allergens should be avoided. The patient should be advised to do regular physical exercise.

Cold waves and cold conditions should be avoided. Excessive sleep should be avoided. **B.**

Recommended diet:

The hot and dry food(Harr Yābis Aghdhiya) such as meat of Titer (grey francolin), chukar partridge as well as the meat of dear, and rabbit, as well as Mā'al-lahm (meat soup) are recommended(Ibn Hubul, 2004). Chicken and mutton soup, pumpkin, beetroot, sponge gourd, and pigeon pea are suggested. Mā' al-Sha'ir (barley water) is recommended (Ibn Sina, 2010). Halfboiled eggs yellow portion may also be given.

The phytochemicals, including phenolics, flavonoids, and carotenoids from fruits and vegetables, may play a key role in reducing chronic disease risk, e.g., apples and bananas decrease wheezing due to their antioxidant property and presence of potassium contents, which could improve the lung function. The pomegranates have antioxidant actions that reduce lung inflammation.

VII. Plant Description of Hyssop (*Hyssopus officinalis*)

Hyssopus officinalis or **hyssop** is a shrub in the Lamiaceae or mint family native to Southern Europe, the Middle East, and the region surrounding the Caspian Sea. Due to its purported properties as an antiseptic, cough reliever, and expectorant, it has been used in traditional herbal medicine. Hyssop is a brightly coloured shrub or subshrub that ranges from 30 to 60 cm in height. The stem is woody at the base, from which grow a number of upright branches. Its leaves are lanceolate, dark green, and from 2 to 2.5 cm ($\frac{3}{4}$ to 1 in) long. During the summer, hyssop produces pink, blue, or, more rarely, white fragrant (ssp. f. *albus*) flowers. These give rise to small oblong tetra-achenes. Under optimal weather conditions, herb hyssop is harvested twice yearly, once at the end of spring and once more at the beginning of autumn. The plants are

preferably harvested when flowering in order to collect the flowering tips. Once the stalks are cut, they are collected and dried either stacked on pallets to allow for draining or hung to dry. The actual drying process takes place in a cool, dry, well-ventilated area, where the materials are mixed several times to ensure even drying. Drying herbs are kept from exposure to the sun to prevent discoloration and oxidation. The drying process takes approximately six days in its entirety. Once dried, the leaves are removed and both components,



Fig. 5 Herbs of Hyssop



Fig. 6 Flowers of Hyssop

leaves and flowers, are chopped finely. The final dried product weighs a third of the initial fresh weight and can be stored for up to 18 months. The essential oil includes the chemicals thujone and phenol, which give it antiseptic properties. Its high concentrations of thujone and chemicals that stimulate the central nervous system, including pinocamphone and cineole, can provoke epileptic reactions. The oil of hyssop can cause seizures and even low doses (2–3 drops) can cause convulsions in children.

The fresh herb is commonly used in cooking. Za'atar is a famous Middle Eastern herbal mixture, some versions of which include dried hyssop leaves. Essence of hyssop can be obtained by steaming, and is used in cooking to a lesser extent. The plant is commonly used by beekeepers to produce nectar from which western honey bees make a rich and aromatic honey. Herb hyssop leaves are used as an aromatic condiment. The leaves have a lightly bitter taste due to its tannins, and an intense minty aroma. Due to its intensity, it is used moderately in cooking. The herb is also used to flavor liqueur, and is part of the official formulation of Chartreuse. It is also a key ingredient in many formulations of absinthe, where it is the main source of the green colour.

In herbal medicine hyssop is believed to have soothing, expectorant, and cough suppressant properties. Hyssop has been used for centuries in traditional medicine in order to increase circulation and to treat multiple conditions such as coughing and sore throat. Hyssop can stimulate the gastrointestinal system.

Hyssop (*Hyssopus officinalis*) is an herb that has been claimed to treat various ailments, including ulcers, herpes, and cancer. However, there is not enough scientific evidence to prove that hyssop is safe and effective for these or any other medical uses. Hyssop is native to southern Europe and central Asia, but can also be found growing in gardens throughout North America. This article will look at the potential benefits of hyssop, as well as side effects, precautions, dosage, and what to look for. Dietary supplements are not regulated in the United States, meaning the Food and Drug Administration (FDA) does not approve them for safety and effectiveness before products are marketed. When possible, choose a supplement that has been tested by a trusted third party, such as USP, Consumer Labs, or NSF. However, third-party testing does not mean a supplement is safe and effective for everyone. It is important to talk to your healthcare provider about any supplements you plan to take and to check in about any potential interactions with other supplements or medications. Supplement Facts

- **Active Ingredient(s):** Hyssop leaf, hyssop flower
- **Alternate Name(s):** *Hyssopus officinalis*
- **Legal Status:** Legal in the US. Sold over-the-counter.
- **Suggested Dose:** There is no evidence-backed suggested dose for hyssop.
- **Safety Considerations:** Using hyssop may cause side effects like upset stomach, anxiety, and tremors.

A. Uses of Hyssop

Supplement use should be individualized and vetted by a healthcare professional, such as a registered dietitian, pharmacist, or doctor. No supplement is intended to treat, cure, or prevent disease. Hyssop is said to have a variety of health benefits. While supplements rarely get extensive research done on them, we do have some scientific literature on hyssop's potential benefits. Research on hyssop is in the early stages still, but much of it is promising. And this could give researchers an incentive to keep studying it.

A 2018 review of the literature on Lamiaceae plants against the retrovirus HIV showed promising preliminary results from in vitro studies. Researchers said the plants, including hyssop, appear to target structures that allow the virus to infect cells. Hyssop may also destroy key enzymes that HIV relies on for its life cycle. Despite these positive results, researchers agree that human trials are needed to strengthen these claims. Hyssop has been used for centuries in a variety of ways. Other traditional uses of hyssop include treatment of:

- Poor circulation
- Upper respiratory illness
- Asthma
- Cough
- Sore throat
- Intestinal infections
- Upset stomach
- Gallbladder disease
- Poor appetite
- Urinary tract infections (UTI)
- Dysmenorrhea

Hyssop may also have anti-microbial properties, as evidenced by in vitro studies. It's always best to talk with your healthcare provider before starting hyssop or any other supplement. They can walk you through the potential benefits and the supplement and help you decide if it is right for you.

Even natural treatments can have unwanted side effects, and hyssop is no exception. The herb is believed to be relatively safe at levels commonly. However, at high doses, hyssop can be dangerous. And some people should avoid hyssop entirely. Some side effects associated with taking hyssop are more common than others. Common hyssop side effects include:

- **Upset stomach**
- **Anxiety**
- **Tremor**

These side effects are typically reported as mild. If you notice these or other side effects then stop use and ask your healthcare provider if you should continue taking hyssop. Severe side effects are also possible while taking hyssop. Severe side effects possible while taking hyssop include:

- **Seizure:** Hyssop oil is a known convulsant and should not be given to children or to people with seizure disorders. In healthy adults, hyssop may elevate seizure risk, especially at high doses.
- **Miscarriage:** Do not take this herb while you're pregnant. Hyssop oil may cause uterine contractions and trigger menstruation, which may cause miscarriage.
- **Allergic reaction:** Do not use hyssop if you've ever had an allergic reaction to hyssop-containing products, the hyssop plant itself, or other plants in the Lamiaceae family (also known as the mint or deadnettle family).

It's important to seek medical attention if you experience severe side effects when taking hyssop. Some populations should take precautions and avoid using hyssop.

People who are pregnant or nursing should avoid hyssop. Miscarriage is possible while taking hyssop. And there is not enough information to know if it is safe to take while nursing. It is also recommended that children avoid taking hyssop. This is because seizures are a possible, severe side effect that can occur when taking hyssop. The risk of seizures also means people with a history of epilepsy and other seizure disorders should avoid hyssop. Only use hyssop supplements and oils as directed to avoid side effects or other adverse reactions. Always speak with a healthcare provider to learn how to safely use a new supplement. We don't have enough information to say whether hyssop is safe to use while breastfeeding, so it is best to avoid it if you are nursing. Children shouldn't use hyssop due to the increased risk of seizure.

C. Dosage of Hyssop

Always speak with a healthcare provider before taking a supplement to ensure that the supplement and dosage are appropriate for your individual needs. No standard, safe dosage has been determined for hyssop. The right dose for you may depend on your age, health, and other conditions. Most studies done on hyssop have been performed on animal models or in lab settings. Without adequate human testing, it is not safe to recommend a standard dose for hyssop. Remember that you increase your risk of side effects when you take more hyssop than recommended. Therefore, it's important to use hyssop only as directed.

You should only take hyssop as recommended either by your healthcare provider or as listed on the supplement packaging. Hyssop has the potential to become toxic if taken incorrectly. Taking too much hyssop can result in severe side effects, including seizures. Hyssop extracts contain oils that are classified as volatile. One of these, pinocamphone, has been found to be neurotoxic in certain settings. Be aware of how much hyssop you take each time you use it. You may have taken too much hyssop if you experience side effects.

Interactions

Medication, food, and supplement interactions have not been reported for hyssop. However, it is possible that interactions exist but have not been properly reported. Regardless, it is still recommended that you speak with your healthcare provider about any medications or supplements you plan to use at the same time as hyssop. They may be able to tell you whether hyssop will interact with anything else you are taking. It is essential to carefully read the ingredient list and nutrition facts panel of hyssop and other supplements to know which ingredients and how much of each ingredient is included. Please review this supplement label with your healthcare provider to discuss any potential interactions with foods, other supplements, and medications.

Hyssop supplements should be stored properly to avoid spoiling. Keep hyssop leaves, teas, capsules, and oils in a cool, dry place that is not directly hit by the sun at any time of the day. It's also best to store hyssop in its original packaging. Loose hyssop leaves and teas should be kept in an airtight container. Store hyssop in a place that children cannot access to prevent accidental consumption. Discard hyssop supplements once the expiration date listed on the packaging has been reached.

D. Mechanism of Action

The main constituents of *Hyssopus officinalis* L. include polyphenolic compounds and essential oils generally known to have antimicrobial and antioxidant properties. Essential oils can also act as expectorants and antispasmodics. They are aromatic and generally impart the characteristic odor of a plant because of their volatility. Polyphenols generally taste bitter, are astringent, or both.

Of the different types of polyphenols in *Hyssopus* the most abundant phenolic acids were ferulic acid (13.2 mg/100 g) and caffeic acid (6.5 mg/100 g). Three flavonoid glycosides, isoquercitrin, rutin, and quercitrin, and two flavonoid aglycones, quercetin and luteolin, were also found. Isoquercitrin was the flavonoid found in the largest amount ($32.78 \pm 0.23 \mu\text{g/g}$). Many of the polyphenols in *Hyssopus* have significant antioxidant and antimicrobial properties.

A detailed examination of the essential oil of *H. officinalis* (var. *decumbens*) revealed linalool (49.6%); 1,8-cineole (13.3%); limonene (5.4%); β -caryophyllene (2.8%); β -pinene (3.0%); and α -pinene (2.4%); however, climate, environmental factors, species subtypes, and extraction methods can considerably affect the plant's essential oil profile.² For example, *Hyssopus* from Italy has been shown to differ in its essential oil compounds from that found in France (*H. officinalis* var. *decumbens*). The Italian form contains pinocamphone and isopinocamphone (4.4% and 43.3%, respectively), whereas the French species do not; instead, linalool, 1, 8-cineole, and limonene are predominant.

The essential oils in both varieties significantly inhibited yeasts (seven strains of *Candida albicans*, *Candida krusei*, and *Candida tropicalis*), but only *H. officinalis* var. *decumbens* showed inhibition of both gram-positive and gram-negative bacteria. Comparatively, this variety is also thought to have greater antimicrobial activity because of its linalool, and to a lesser extent, 1, 8-cineole contents. Limonene is present in both varieties of hyssop and may also be responsible for inhibition of the yeasts.

Of the various constituents of the essential oil, linalool seems to have the strongest antispasmodic action.

E. Evidenced-Based Research

The effect of *Hyssopus officinalis* on respiratory immune regulation and respiratory inflammation was investigated in a mouse model of chronic asthma. In total, 32 BALB/c mice were randomly divided into four groups: normal, chronic asthmatic, dexamethasone (anti-inflammatory drug) treatment, and *H. officinalis* treatment. Ovalbumin is commonly used in studies to stimulate an allergic reaction; and in this study, it was used to establish an asthma model. The mice were sensitized and challenged with ovalbumin, and the ratio of eosinophils (EOSs) in the broncho alveolar lavage fluid (BALF) was recorded. In addition, an enzyme-linked immuno sorbent assay was used to measure levels of immunoglobulin (Ig) E and Ig G, and the periodic acid-Schiff stain method was used to observe the degree of airway mucus secretion. The results showed that the ratio of EOS in the BALF and the level of serum IgE in the chronic asthmatic and dexamethasone treatment

groups increased, whereas the level of serum IgG decreased compared with the normal group. Excessive secretion of airway mucus was also observed in these two groups.

F. Safety in Pregnancy and Breastfeeding

In traditional herbal literature, Hyssopus is listed as an emmenagogue and abortifacient. Although research on the subject is lacking, use during pregnancy is cautioned. There is insufficient information about the safety of Hyssopus in breastfeeding. Hyssopus has generally recognized as safe status in the United States. This means that there is a consensus of expert opinion regarding the safety of its use. Hyssopus is generally considered safe at doses of the powdered herb up to 2–3 g/day. Typical doses are taken alone as 450–900 mg up to three times daily; and when combined in a formula with other respiratory herbs, 100–300 mg is used up to three times daily.

G. Traditional Uses

Going back to ancient Greece, Hippocrates prescribed Hyssopus for pleurisy. Dioscorides recommended it in a formula along with rue, fig, and honey to treat pleurisy, respiratory congestion, asthma, and chronic cough. In traditional and modern literature, hyssop is often included as an important expectorant to increase the fluidity of the mucus in the lungs and gently promote its expulsion from the body.

H. Health Benefits of Hyssop

There are a wide variety of plants known by the name “hyssop,” from hedge hyssop to capers to anise hyssop. However, true hyssop, *Hyssopus officinalis*, is an edible member of the mint family that’s been used in a wide variety of foods, drinks, folk remedies, and even perfumes. Compared to other plants known as hyssops, true hyssop is safe to eat and is found in a variety of spice mixes and foods. Hyssop plants look like a smaller form of lavender, with spikes of blue flowers that smell slightly minty. Tea made from true hyssop has been used to help treat coughs, earaches, asthma, and bloating. Today, studies are beginning to back up some of these age-old folk remedies, showing that hyssop offers some impressive health benefits. The nutrients and essential oils in hyssop can offer some helpful health effects. For example, hyssop is rich in flavonoids, flavorful compounds that can act as antioxidants. Eating foods rich in flavonoids may help reduce your risk of age-related conditions like cataracts, heart disease, and strokes. In addition, true hyssop may provide health benefits.

○ Reduced Risk of Ulcers

Ulcers have a number of causes, but there are two particular chemicals linked to ulcer creation: urease and α -chymotrypsin. Studies have shown that hyssop extracts seem to inhibit these chemicals, or stop them from forming ulcers. By adding small amounts of hyssop to your diet, you may be able to reduce your risk of developing uncomfortable stomach ulcers.

○ May Help with Asthma

Several studies have suggested that hyssop’s traditional use for treating symptoms of asthma and head colds may actually have an effect. These studies have compared hyssop to other herbal and non-herbal methods of treating asthma symptoms and found that hyssop was one of the most effective natural substances. This may be because hyssop contains pinocamphone, which is a slightly toxic chemical related to camphor that is known to help open airways. However, in case of an asthma attack, always take your prescribed medications first.

○ Reduced Risk of Cancer

The antioxidants in hyssop aren't just good for reducing your risk of age-related conditions. They may also help lower your risk of cancer. Eating foods rich in antioxidants is connected to a lower risk of certain forms of cancer, as antioxidants help your body remove the free radicals that can trigger cells to become cancerous.

○ May Reduce Inflammation

Asthma involves a significant inflammation of the airways. Hyssop's effect on asthma may also extend to other types of inflammation. While more studies need to be done to determine hyssop's effectiveness treating inflammation in people, early animal trials suggest that hyssop may help reduce inflammation, lowering your risk of problems like heart disease, arthritis, and diabetes.

VIII. Marketed Preparation of *Hyssopus officinalis*

A. Formulations of Sharbat (Syrup) for *Zeeq-un-Nafas* (Bronchial Asthma)

Sharbat e- Irsa: - very effective in Ribw [10]

Sharbat e- Habb-e-Balsan: Beneficial in Orthopnoea [10]

Sharbat-e- Zarawand Mudahraj- Beneficial in Ribw with qatiryun akbar root water [10]

Sharbat-e Zufa Sazaj [19]

Methods: Taken the *Zufa Khushk* (dry hyssop) and keep it cleans with wood then Soak in 2500 ml of warm water for a day and night, after that cleaned and prepare Sharbat by adding 2000gram sugar and honey.

Indication: Beneficent to *Zeeq-un-Nafas* (Asthma) and Cough.

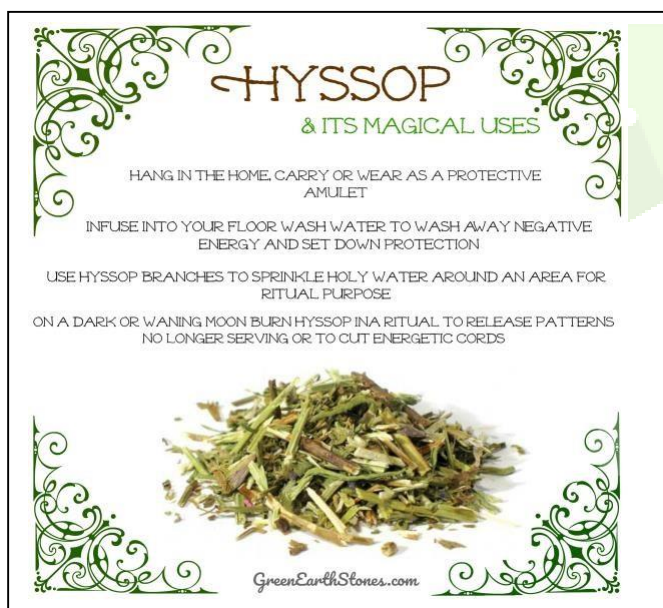


Fig. 7 Hyssop Dry Leaf



Fig. 8 Hyssop Herbal Tea

B. Sharb-e-Zufa Mudabbar [19]**Ingredients**

1. Tukhm-e- Karafs (celery seeds) – 17 grams
2. Zufa Khushk (*Hyssopus officinalis*, Dry hyssop) - 25 grams
3. Anjeer (*Ficus carica*, fig)- 10 piece
4. Maweez (*Vitis vinifera*, large raising) – 30 pieces
5. Hulba(*Trigonella foenum*) – 15 grams
6. Tukhm-e-Khatmi (*Althaea officinalis*, Marsh Mallow seeds)-10.5 gm
7. Asl-us-soos (*Glycyrrhiza glabra*, liquorice)-10.5 gm
8. Irsa (*Iris ensata*, orris root)-10.5 gm
9. Parshiaoshan (*Adiantum capillus*, Maiden hair fern) -21 grams.
10. Maghz-e Badam Talkh (*Prunus amygdalus*, Bitter almond kernels) - 3.50 grams

Method: Prepare Sharbat with all ingredients.

Indication: Given complete Nuz to the phlegm which are present in respiratory tract. Due this region it is effective to cough and Asthma.



Fig. 9 Hussop Syrup



Fig. 10 Hyssop Herb

C. Sikanjabeen Unsuli Degar [19]**Ingredients:**

1. Piyaz Unsul (*Urginea scilla*, Onion)-17.5 gm
2. Zufa Khushk (*Hyssopus officinalis*, Dry Hyssop)-17.5 gm
3. Asl-us-Soos (*Glycyrrhiza glabra*, Licorice)-17.5 gm
4. Gaozaban (*Borage officinalis*)-17.5 gm
5. Parshiosaon (*Adiantum capillus*, Maiden hair fern)- 17.5 gm
6. Ustukhuddus (*Lavendula steochas*)-17.5 gm

7. Ghariqoon (*Agaricus albus*)-17.5 gm
8. Naana (*Mentha piperatta*, peppermint)-17.5 gm
9. Razyana (*Foeniculum vulgare*, fennel seeds)-10.5 gm
10. Beekh sosan (*Iris ensata*, Orris root)-10.5 gm
11. Kabud-10.5 gm
12. Qardmana-10.5 gm

Methods: Soak all ingredients in 500 ml vinegar and 1530 ml water for 2 days and nights, then boiled. When half of total remain, cleaned and prepare qiwan by adding 950 grams sugar. Dose- 17.5 -35 grams daily with Joshanda Parsiaoshan

Indication: It is very effective in chronic cough, *Zeeq-un-Nafas*.

D. Nuskha Joshanda Zufa Kabeer [19]

Ingredients

1. Anjeer (*Ficus carica*, Fig) -5 gm
2. Methi (*Trigonella foenum*, fenugreek)-5gm
3. Mulethi (*Glycyrrhiza glabra* or liquorice) -5 gm
4. Zufa Khushk (*Hyssopus officinalis* Hyssop)-5gm
5. Parsiaoshan (*Adiantum capillus* or maiden hair fern)-5gm
6. Beekh-e-Sosan (*Iris ensata* or Orris root)-5gm
7. Beekh-e-Badyan (*Foeniculum vulgare*, fennel root)-5 gm
8. Beekh-e-Karafs (*Apium graveolens*, celery)-5 gm
9. Tukhm-e-Badyan (*Foeniculum vulgare*, Fennel seeds)-5 gm
10. Tukhm-e-Anjra (*Anjra seeds*)-5 gm
11. Frasiyun (*Marrubium vulgare*) -5 gm

Method: Boil or cook all ingredient in 3 ratal water (1.5 litter), when remained 420 gm lift it. Take 3 auqiah water (1 litter) and drink with murabba Banafsha.

Indication: Effective for Ribw & viscous humours of chest.

Discussion.

Asthma is a type I allergic disease, and IgE has an important role in the development of asthma. Previous studies have demonstrated that there are various levels of inflammatory responses in patients who suffer from asthma, and allergic airway inflammation with increasing EOS is the main pathological feature of asthma. Numerous studies have identified a correlation between the infiltrate level of EOS and the severity of airway inflammation. The variety of cell types present in BALF may reflect the degree of inflammation in the peripheral airways, which is also the main factor causing bronchial hyper responsiveness in asthma.

Therefore, airway inflammation is the basic condition of reversible airway inhibition, as well as non-special hyper responsiveness of the bronchus. In the present study, the percentage of EOS in the BALF and the levels of IgE in the chronic asthma group were higher compared with the normal group ($P < 0.05$). PAS staining revealed that mucus secretion was elevated in the chronic asthma group. Furthermore, the level of IgG was

observed to decrease in the chronic asthma group. These results indicated that the immune reaction in individuals suffering chronic asthma is restrained.

Hormonal nebulizer inhalation has become a common clinical treatment for non-special airway inflammation; however, this suppresses the immune system. Due to the geography and climate of the Autonomous region of Xinjiang, the incidence of asthma is increasing. There are a number of effective strategies and medicines for treating asthma in Uygur medicine. *Hyssopus officinalis* L. is medicine used for the treatment of a number of conditions, including asthma, coughing, fever and rheumatism. In a number of previous studies, *Hyssopus officinalis* L. has been demonstrated to affect the expression of a number of cytokines. In the present study, mice treated with *Hyssopus officinalis* L. and dexamethasone were shown to have decreased levels of EOS in the BALF when compared with mice in the chronic asthma group. In addition, the level of IgE and the secretion of airway mucus were reduced. Mice treated with *Hyssopus officinalis* L. were also shown to have higher levels of IgG when compared with the dexamethasone and asthma groups. These observations indicate that *Hyssopus officinalis* L. may exhibit an anti-inflammatory effect by inhibiting the infiltration of EOS and reducing the level of IgE in the lung tissue; thus, regulating immunity.

In conclusion, the results of the present study demonstrate the effect of *Hyssopus officinalis* L. on chronic asthma, and may provide a novel therapeutic strategy for the treatment of chronic asthma. However, further investigation is required to determine the specific mechanism.

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