

# Herbal Treatment of COPD and Asthma According to Persian Medicine: a Review of Current Evidence

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common pulmonary disease that is harmful to human health. COPD was the fourth leading cause of death worldwide which increased to the 3<sup>rd</sup> rank in 2020 (1). Recurrent acute exacerbations of COPD affect patients

**Background:** Chronic obstructive pulmonary disease (COPD) is one of the most common pulmonary diseases. The current therapeutic outcomes are not satisfactory and may cause adverse events such as cardiovascular complications. In this study, we aimed to discuss some effective medicinal herbs for the management of COPD.

**Materials and Methods:** In this review, we looked for effective medicinal herbs for productive cough with thick and sticky mucus in Persian medicine sources such as Qanoon fi al-Teb, Exir Azam, and Zakhire Kharazmshahi. Then, to find relevant evidence about them, the data sources (PubMed and Google Scholar) were searched in the English language without time restriction from inception up to March 2022.

**Results:** We found that *Zataria multiflora*, *Thymus vulgaris* L., *Glycyrrhiza glabra* L., *Crocus sativus* L., *Nepeta bracteata* Benth., and *Hyssopus officinalis* have beneficial effects on COPD due to their properties including anti-inflammatory and antioxidant activity. In addition, considering asthma COPD overlap (ACO), medicinal herbs including *Cordia myxa*, *Adiantum capillus-veneris*, *Cinnamomum verum*, *Viola odorata*, *Borago officinalis*, *Linum usitatissimum* and *Vitis vinifera* L. were found to have useful effects on asthma.

**Conclusion:** Considering the mentioned beneficial mechanisms of action of these medicinal herbs, they could be used as a complementary therapy in COPD and asthma. However, more experimental and clinical research should be done to confirm their clinical effects.

**Keywords:** Asthma; Chronic Obstructive Pulmonary Disease; Lung Diseases; Persian Medicine; Medicinal Herb

leading to a faster decrease in pulmonary function and an increase in the risk of death. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), reducing the risk of future exacerbations and relieving symptoms are the major treatment goals for stable COPD. Thus, successful prevention of exacerbations is vital to

manage COPD (2). The available pharmacotherapy for stable COPD control disease progression includes bronchodilators as well as anti-inflammatory drugs such as  $\beta_2$  receptor agonists, corticosteroids, and muscarinic receptor blockers (2,3). Nonetheless, on one hand, the results are not satisfactory enough and on the other, they may cause adverse events such as oropharyngeal candidiasis, cardiovascular events, and pneumonia (3).

Complementary and alternative medicine (CAM) is used for stable COPD patients. A study in Australia reported that 41% of the subjects had used some type of CAM for improving their health, counteract the adverse effects of drugs, and compensate for dietary deficiencies (4). Complementary and traditional drugs include new and commonly natural medicines. Persian Medicine has been in use for thousands of years. The Iranian Muslim physicians' books, such as *Qanoon fi al-Teb* (Canon of Medicine) by Avicenna, contain natural treatments with at least 800 years of supporting experience (5).

There is no exact equivalent term for COPD in the pulmonary diseases section of Persian Medicine sources. However, having chronic productive cough, it is classified in the group of pulmonary diseases with cough as a sign that is caused by the production of thick and sticky secretions in which COPD and asthma are common (6–8). Both COPD and asthma are respiratory diseases that are recognized as common complex inflammatory and heterogeneous diseases that often require treatment with multiple drug classes. As airway obstruction is common in COPD and asthma, they are identified by functional abnormalities and characteristic symptoms. So, asthma COPD overlap (ACO) is a descriptive term for clinical use that includes several overlapping clinical phenotypes of chronic airway disease with different underlying mechanisms and does not define a single disease (9, 10).

In this study, we aimed to review medicinal herbs which have been recommended for the management of COPD and asthma in Persian Medicine sources. It is obvious that according to ACO, some mentioned medicinal herbs are common between COPD and asthma.

## **MATERIALS AND METHODS**

In order to explore the beneficial effects of medicinal herbs on COPD and asthma, we looked for effective medicinal herbs for productive cough with thick and sticky mucus in Persian medical sources such as *Qanoon fi al-Teb*, *Zakhire-Kharazmshahi*, and *Exir Azam*. Then, herbs that were more commonly recommended were selected. In the next step, to find evidence about the mentioned herbs in COPD and related pulmonary disorders such as asthma, data sources such as PubMed and Google Scholar were searched without time restriction from inception up to March 2022 using the scientific names of the herbs, COPD, and asthma as keywords.

## **RESULTS**

### **Pathophysiology of COPD**

The triggering factors of COPD include infectious and noninfectious precipitants. However, up to 30% of COPD is of unknown etiology (11). The COPD pathogenesis is based on the innate and adaptive inflammatory immune reaction against the inhalation of gases and toxic particles. Tobacco smoking is the main cause of this inhalation injury, but several other occupational and environmental exposures are involved in COPD pathology. The immune inflammatory alterations associated with COPD are associated with a tissue repair as well as remodeling process resulting in an increase in mucus formation and emphysematous destruction of the lung gas-exchanging surface. The common type of emphysema found in smokers starts in the respiratory bronchioles close to the thickened and narrowed small bronchioles becoming the main site of obstruction in COPD. Little is known about the mechanism(s) allowing small airways to thicken near the lung tissue subjected to emphysematous destruction which should be addressed (12).

### **Medicinal herbs used in COPD**

Although prescribing medications has not been shown conclusively for modifying the long-term decline in lung function, they can manage COPD. Medications like bronchodilators and corticosteroids, used orally or by inhalation, can minimize COPD exacerbations, control symptoms, increase health status, and improve exercise

tolerance. Vaccinations against influenza every year, whooping cough, and other disorders can prevent infections resulting in serious complications in cases with COPD (CDC, 2015). However, several side effects were reported for COPD medications, such as dry mouth, tremor, headache, elevated heart rate, and nausea. Serious side effects can increase the risk of cardiac arrhythmias, fatal and non-fatal cardiovascular events, and pneumonia. It is not known whether there is an association between long-acting bronchodilators and cardiovascular events (13).

Some plants have anti-inflammatory activities, and can increase immune functions and assist in expelling sticky and thick secretions (3). Miedema et al. reported the protective impact of flavonoids against chronic lung disease. They reported that the association between 25-yr incidence of asthma and COPD found for solid fruits (apples and pears) compared to other types of fruits can be because of the high levels of flavonoids in apples (14). Flavonoids are polyphenols that are found in plant foods. They are highly found in tea, fruits, and vegetables (15,16). Flavonoids have both anti-inflammatory and antioxidative activities. Through the inhibition of lipoxygenase and cyclooxygenase, these enzymes play a role in arachidonic acid metabolism. In addition, flavonoids can reduce the generation of two classes of proinflammatory factors (leukotrienes and prostaglandins) which can be associated with the pathogenesis of COPD (15,17–20). Also, consuming other dietary antioxidants such as vitamin C is beneficially associated with COPD-related outcomes (15,21). Thus, nutraceuticals with strong anti-inflammatory and antioxidant effects can be used for the treatment of COPD (22).

In the following, we have reviewed the current evidence of the most commonly recommended medicinal herbs for COPD and asthma management in Persian medicine literature (Table 1).

#### **Zataria multiflora Boiss.**

Iran has 14 perennial species of *Thymus* L., but all of the species are known as thyme. However, the genus *Zataria* Boiss that grows in southern Iran has one species namely *Z. multiflora*, and is called thyme. An aromatic essential oil of all *Thymus* spp. and *Z. multiflora* have main components including

carvacrol, thymol, and *para*-cymene and the geographical location of plants affects the constituents of their essential oils. Sometimes according to the similarity of biological actions of thyme essential oils, it is possible to use one species instead of another due to their antimicrobial effects. The biological activities of thyme essential oils are different and include anti-inflammatory, antipyretic, analgesic, and immune-stimulation effects. (39).

*Zataria multiflora* Boiss belongs to the Lamiaceae family (23) and is a perennial plant characterized by fibrous root, woody, small leaves, and height of 40–80 cm, which has highly narrow branches (40). *Z. multiflora* has a limited global distribution and only grows in Pakistan, Iran, and Afghanistan (41). It contains different compounds, such as bioactive chemicals, especially terpenes, like carvacrol and thymol. It also has luteolin, apigenin, and 6-hydroxyluteolin glycosides, and also di-, tri-, and tetra-methoxylated, which are involved in the therapeutic effects of *Z. multiflora* (40). It has long been used for pharmaceutical uses that indicated antioxidant, anti-inflammatory, antibacterial, antidiarrheal, smooth muscle relaxant, and antitussive impacts. This plant has many pharmacological effects including the effects on respiratory system conditions such as cough, respiratory disorders of chemical war victims, bronchitis, lung inflammation, pathological alterations, and emphysema in animal models (23). *Z. multiflora* and carvacrol as its major constituent have reduced airway inflammation in an animal model of asthma and COPD. Treatment with *Z. multiflora* and carvacrol reduced oxidative stress, inflammatory cells, and mediators and also lung pathological alterations (42–47). One study showed that a two-month treatment with this plant could improve clinical symptoms, oxidative stress, lung function tests, and C-reactive protein (CRP) in COPD patients (23). Boskabadi and Gholami indicated a preventive impact of hydro-ethanolic extract from *Z. multiflora* on all assessed factors in the COPD animal model which is comparable to or even higher (in the highest concentration) than the impact of dexamethasone at the used doses (44). Gholami et al. reported a preventive effect of carvacrol and *Z. multiflora* extract on tracheal responsiveness as well as pathological changes in the lung (48).

**Table 1.** Pharmacological effects of the effective medicinal herbs on COPD and asthma

Scientific name	Common name	Persian name	Family name	Persian medicine effects	Scientific studies
<b>Medicinal herbs used in COPD</b>					
<i>Zataria multiflora</i>	Shirazi Thyme	Avishan-e-Shirazi	Lamiaceae	Helping the clearance of airways (7).	Improving clinical symptoms, lung function tests and reducing oxidative stress (23).
<i>Thymus vulgaris</i>	Thyme	Avishan	Lamiaceae	Helping the clearance of airways (7).	Decreasing extracellular Ca <sup>2+</sup> concentrations and increasing the cilia beat frequency in airway epithelia (24).
<i>Glycyrrhiza glabra</i>	Licorice	Shirinbayan	Fabaceae	Helping the clearance of airways, is an emollient for bronchial tree (7).	Modulation of airway inflammation in combination with some other medicinal herbs (25).
<i>Crocus sativus</i>	Saffron	Za'faran	Iridaceae	Improving breathing and the state of respiratory system (7).	Protection against lung injury due to COPD and resulted cardiac dysfunction by Crocin co-treatment (26).
<i>Nepeta bracteata</i>	Zoofa	Zoofa	Lamiaceae	Effective on chronic cough and dyspnea (7)	Improving the COPD Assessment Test (CAT) score, FEV1 and FEV1/FVC (27).
<i>Hyssopus officinalis</i>	Hyssop	Zoofa	Lamiaceae	Effective on chronic cough and dyspnea (7).	Reducing the IL-4 and IL-17 level and increasing the IFN-λ and IL-10 level (28)
<b>Medicinal herbs used in asthma</b>					
<i>Cordia myxa</i>	Lasura (Assyrian plum)	Sepestan	Boraginaceae	Emollient effect on respiratory system and nasopharynx (7).	Inducing tracheal smooth muscle relaxation in sheep (29)
<i>Adiantum capillus-veneris</i>	Maidenhair fern	Parsiavoshan	Pteridaceae	Helping the clearance of airways and improving cough (7).	Reduction of coughs and nocturnal awakenings in the asthmatic children in combination with some other medicinal herbs (30).
<i>Cinnamomum verum</i>	Cinnamon	Darchin	Lauraceae	Helping the clearance of airways and is effective on cough (7).	Improving night and morning symptoms, activity tolerance, chest tightness, shortness of breath, the amount of short-acting inhaler bronchodilator consumption and the overall score of the ACQ in combination with some other medicinal herbs (31).
<i>Viola odorata</i>	Sweat violet	Banafsheh	Violaceae	Effective on cough and pneumonia and possessing emollient effect on respiratory system (7).	Enhancing the cough suppression in children with intermittent asthma by the adjuvant use of violet syrup with short-acting β-agonist (32)
<i>Borago officinalis</i>	Borage	Gavzaban	Boraginaceae	Effective on cough (7).	Reducing cough, dyspnea, wheezing, nocturnal symptoms, airway hyper-responsiveness and flare up of asthma and emergency department visits, and improving ACT scores (33), altering 20–22 carbon PUFA levels, attenuating leukotriene production, and reduction in inflammation in combination with one another herbal oil (34).
<i>Linum usitassimum</i>	Flaxseed	Bazr-e-Katan	Lineaceae	Effective on cough with thick and sticky secretions and rhinitis (7).	Reducing the levels of TGF-β, IL-13 in blood and BALF and hydroxyproline content in lung homogenates, attenuating effect on inflammatory cells infiltration, goblet cell hyperplasia and sub-epithelial fibrosis in combination with some other medicinal herbs (35).
<i>Vitis vinifera</i>	Grape	Angoor	Vitaceae	Possessing beneficial effects on respiratory system (36)	Inhibiting recruitment of inflammatory cytokines, IgE, nitrites and circulating cells particularly eosinophils in blood/serum and bronchoalveolar fluid, normalizing lung functions and histamine levels (37). Decreasing the level of IgE, cytokines, nitrites and influx of eosinophils and neutrophils in blood and BALF, improving lung functions, suppressing degranulation of mast cells in combination with some other medicinal herbs (38).

COPD: Chronic Pulmonary Obstructive Disease; CAT: COPD Assessment Test; FEV1: Forced expiratory volume in the first second; FVC: Forced vital capacity; IL: Interleukin; IFN-λ: lambda interferon; ACQ: Asthma Control Questionnaire; PUFA: Poly Unsaturated Fatty Acid; TGF-β: Transforming growth factor beta; BALF: Broncho-alveolar lavage fluid; IgE: Immunoglobulin E.

Khazdair et al. showed that treatment with *Z. multiflora* for two months improved cytokine levels, respiratory symptom, and FEV1 values in sulfur mustard-exposed patients (49).

### ***Thymus vulgaris* L.**

*Thymus vulgaris* L. belongs to the Lamiaceae family which is usually grown wild in the Mediterranean region including Spain, Italy, France, and in Caribbean countries. It is a source of the essential oil (thyme oil) and flavanoid, thymol, labiatic acid and caffeic acid which are derived from its different parts. Its extracts especially the essential oils have been evaluated and afforded several industrial (as food additive) as well as medical uses. *Thymus vulgaris* and its essential oil are used in pharmacy and medicine. Its oil has antimicrobial (against bacteria and fungi), expectorant and carminative activities. These properties are mediated by carvacrol and thymol, as the phenolic components (50). Nabissi et al. indicated that thyme extract can increase cAMP concentrations starting from 12 h post-treatment, decrease extracellular Ca<sup>2+</sup> concentrations and increase the cilia beat frequency in airway epithelia of COPD patients. Thyme extract was effective to stimulate cilia beat frequency through increasing cAMP and Ca<sup>2+</sup> levels suggesting its therapeutic use for the treatment of COPD (24). Al-Khalaf showed that thymol and thyme elevated the levels of antioxidants in the body, as well as the subjects' ability to get rid of oxidative compounds and free radicals produced inside the body or caused by the polluted environment. Thus, the potential therapeutic effects of thyme and thymol on asthma were confirmed (50).

### ***Glycyrrhiza glabra* L.**

*Glycyrrhiza glabra* L. (licorice) is one of the most popular medicinal plants belonging to the Fabaceae family (51). Licorice has long been employed as antidote, demulcent, antioxidant, expectorant, flavoring and sweetening agents, and for treatment of inflammation in Europe and Asia (52). It is an important and popular herbal medicine worldwide

which has been applied as a cough reliever as well as an immunomodulatory, anti-inflammatory, and detoxifying agent. Different compounds have been derived from licorice like flavonoids and triterpene saponins. Glycyrrhizic acid (GA), as a triterpenoid saponin, is considered as the main component of licorice. It has several pharmacological effects such as anti-allergy, anti-inflammatory, and the immune-system-activating effects (53). Licorice includes oleanane triterpenoids, glycyrrhizin, glucose, and flavonoids. Its flavonoids have many biological activities such as enzyme inhibiting activity, antioxidant, and anti-inflammatory properties (52). One study showed that intravenous injection of glycyrrhizin reduces lipopolysaccharide (LPS)-related acute respiratory distress syndrome (ARDS) mortality in BALB/c mice (54). Study by Kim et al. showed that the herbal combinational mixture of *Glycyrrhiza glabra* and *Agastache rugosa* could more effectively inhibit neutrophilic airway inflammation through regulation of the CXCL-2 and inflammatory cytokines expression via blocking the IL-17/STAT3 pathway (53). In addition, study by Wu et al. revealed that the combination of licorice root and some other herbs could modulate airway inflammation and may enhance the anti-inflammatory effect of glucocorticoid through the upregulation of HADC2 expression in a rat model of COPD (25).

### ***Crocus sativus* L.**

*Crocus sativus* L. (saffron) is from Iridaceae family which has been long used as spice, herbal medicine, flavoring agent and food coloring (55). It is cultivated in Turkey, Europe, Central Asia, China, India, Algeria and especially in Iran. It has long been cultivated in the south Khorasan province, Iran (56). Saffron has four main pharmacologically active compounds including crocetin, picrocrocin, safranal and crocin. It is a water-soluble carotenoid and is the main active compound of saffron. In pharmacological investigations, it was found with anti-inflammatory, anticonvulsant and anti-tumor properties. It has radical scavenging activity, learning and memory

improving effects in addition to promoting the diffusivity of oxygen in indifferent tissues. Crocin has protective effects against genotoxins-related oxidative stress in Swiss albino mice. Also, it has cardio protective effects and modulates endogenous antioxidant enzymatic activities (26).

Kaempferol as a flavonoid is extracted in good quantities from the *C. sativa* petals. Kaempferol has several pharmacological properties such as antioxidant, anticancer, and anti-inflammatory effects. Its smooth muscle relaxant and anti-inflammatory effects (anti-asthmatic activity) has been reported (55). Various effects of saffron and its constituents on the respiratory tract include antitussive effects (57), relaxant effects on tracheal smooth muscle, inhibitory effects on histamine H1 receptors of tracheal smooth muscle and stimulatory effects on  $\beta$ 2-adrenoceptors (58,59) as well as anti-inflammatory and immune-modulatory activity in lung diseases (60). The relaxant effects of saffron and its derivatives on tracheal smooth muscle as well as their possible underlying mechanisms have been reported. Boskabadi et al. indicated the bronchodilatory effect of saffron and its derivatives on obstructive pulmonary disorders. Saffron and its derivatives have an effect on lung inflammation, lung pathological alterations, and tracheal response to methacholine and ovalbumin and also affect Th1/Th2 cytokines in animal models of asthma (56). Kianmehr and Khazdair showed that *C. sativus* and kaempferol as its petal flavonoid have relatively strong therapeutic effects on respiratory diseases through the relaxation of tracheal smooth muscles by stimulatory or blocking impacts on muscarinic receptors and  $\beta$ 2-adrenoceptor, respectively. Kaempferol and Saffron could decrease the generation of NO, chemokines and inflammatory cytokines in respiratory systems (55). Mahmoudabady et al. showed that the *C. sativus* extract alleviated lung inflammatory cells, particularly eosinophils in lung lavage of sensitized animals indicating its preventive effect on lung inflammation in asthma (61). Dianat et al. showed that Crocin co-treatment by modulating of nuclear erythroid-

related factor 2 pathway could protect lung injury due to COPD and resulted cardiac dysfunction (26).

### ***Nepeta bracteata* Benth.**

*Nepeta bracteata* Benth. (*Zoofa*) is a member of Lamiaceae family (62) and grows in the Northeast regions of Iran, Khorasan (27). The main constituents of *N. bracteata* are spathulenol, caryophyllene oxide, bicyclogermacrene and  $\beta$ -caryophyllene (63). *N. bracteata* has antibacterial effects (64), antioxidant activities (62), and could relieve the symptoms of allergic rhinitis (65). Abdolahinia et al. showed that complementary therapy with syrup of *N. bracteata* in COPD patients leads to a significant improvement in the COPD Assessment Test (CAT) score, FEV1, and FEV1/FVC (27).

### ***Hyssopus officinalis* L.**

*Hyssopus officinalis* L., commonly known as hyssop, is a flowering plant that belongs to Lamiaceae family (66) and widely grown in Iran (67). Flavonoids are known as a group of secondary plant metabolites with important effects on plant growth and development, and a protective effect against immune and inflammatory reactions (68). Hyssop includes several polyphenolic compounds primarily the flavonoids such as quercetin, diosmin, apigenin, and luteolin as the main constituents (69). It also possesses antimicrobial (69) and anti-inflammatory activity (70-73). Using *Hyssopus officinalis* L. in COPD mice model leads to a reduction of the IL-4 and IL-17 levels and an increase of the IFN- $\lambda$  and IL-10 levels (28). One study showed that the use of Unani compound formulation (combination of *Piper longum*, *Adhatoda vasica*, *Picrorhiza kuroa*, *Hyssopus officinalis*, and *Linum usitatissimum* lead to an improvement of Peak Expiratory Flow Rate (PEFR) and FEV1 after the treatment in asthmatic patients (74).

### **Medicinal herbs used in asthma**

There are some medicinal herbs which have been recommended for cough with thick secretion in Persian medicine sources. Although some studies have done to



investigate their effects on asthma, their effect on COPD has not been evaluated.

### ***Cordia myxa* L.**

*Cordia myxa* L. (lasura) belongs to Boraginaceae family. *Cordia myxa* fruit extract contains oil, flavonoids, glycosides, saponins, terpenoids, sterols, alkaloids, saponins, phenolic acids, coumarins, tannins, resins, gums, and mucilage (75). The *Cordia myxa* fruit has been used for the prophylaxis treatment of asthma. It has been reported that *Cordia myxa* fruit has significant analgesic, anti-inflammatory, and tracheal smooth muscle relaxant properties due to flavinoids contents. One animal study on sheep showed that relaxation induced by *Cordia myxa* extract may be due to NO from exogenously administered L-arginine as well as endogenous NO donors such as amino acid and arginine derivatives (29).

### ***Adiantum capillus-veneris* L.**

*Adiantum capillus-veneris* Linn., commonly known as maidenhair, is a member of Pteridaceae family. Warm temperature to tropical regions with high amounts of moisture is the regions where maidenhair fern is widely grown. It has various biological effects possessing different chemical constituents such as tannins, terpenoids, alkaloids, flavonoids, and steroids. An animal study on ethanolic extract of maidenhair fern revealed its antioxidant, anti-asthmatic, and anti-inflammatory effects in histamine aerosol-induced asthma in guinea pigs (76). Another study showed that a syrup containing *Matricaria chamomilla*, *Glycyrrhiza glabra*, *Malva sylvestris*, *Althaea officinalis*, *Adiantum capillus-veneris*, *Hyssopus officinalis*, *Glycyrrhiza glabra*, and *Ziziphus jujube*, has a significant effect on the nocturnal awakenings and severity of coughs in asthmatic children (30). In a clinical study, formulation consisting *Adiantum capillus veresis*, *Glycyrrhiza glabra*, *Hyssopus officinalis*, and *Cordia dichotoma* significantly improved cough, sputum production, breathlessness, wheezes, chest X-Ray findings, and spirometric measures including predicted FEV1%, FEV1/FVC, and PEF in patients with chronic bronchitis (77).

### ***Cinnamomum verum* J.S. Presl**

Cinnamon (*Cinnamomum verum* formerly *C. zeylanicum*) belongs to Lauraceae family. It is grown in Sri Lanka, East and Middle Asia (78,79), it has anticholinergic, antimicrobial, anti-inflammatory (80,81), and anti-bacterial effects (82-84). A study showed that type-A procyanidine polyphenols (TAPP) isolated from Cinnamon (*Cinnamomum zeylanicum* Syn *C. verum*) bark the anti-asthmatic potential against ovalbumin (OVA)-induced airway hyper-responsiveness (AHR) in laboratory animals (85). Another study conducted to evaluate the effect of compound honey syrup (cinnamon is one of its ingredients) on patients with asthma, showed that this syrup is effective on night and morning symptoms, activity tolerance, chest tightness, shortness of breath, the amount of short-acting inhaled bronchodilator consumption and the overall score of the Asthma Control Questionnaire (ACQ) (31).

### ***Viola odorata* L.**

*Viola odorata* L. belongs to the Violaceae family. It has different compounds such as flavonoids, saponins, glycosides, methyl salicylate, mucilage, tannins, coumarin, alkaloids, and vitamin C (86). Expectorant agents of *Viola* contribute to the reduction of pulmonary inflammation and edema of the mucous membrane. *Viola* anti-cough effect leads to improve respiration for asthmatic patients. Also, *viola* is effective in sore throat, whooping cough, acute bronchitis, pneumonia, and chest discomfort (87). One study in children with intermittent asthma showed that short-acting  $\beta$ -agonists with the adjuvant use of violet syrup can reduce cough (32).

### ***Borago officinalis* L.**

*Borago officinalis* L. and *Echium amoenum* as its Iranian species (88) belong to the Boraginaceae family (34). It contains several fatty acids including stearic, linoleic, palmitic, stearic, and  $\gamma$ -linolenic acids (88). *Borago officinalis* has antioxidant, and anti-inflammatory activity in addition to beneficial effects on the gastrointestinal, respiratory and cardiovascular systems (89). One study showed that using

*Borago officinalis* extract in patients with moderate persistent asthma significantly reduces dyspnea, cough, wheezing, airway hyper-responsiveness, nocturnal symptoms, flare-up of asthma, and emergency department visits. It also improved asthma control test (ACT) scores significantly. (33). Another study revealed that dietary supplementation with *Borago officinalis* oil and *Echium plantagineum* seed oil (BO/EO) alters 20-22 carbon Poly Unsaturated Fatty Acid (PUFA) levels and attenuates leukotriene production in a manner consistent with a reduction in inflammation in patients with mild asthma (34).

#### ***Linum usitatissimum* L.**

*Linum usitatissimum* L. (flaxseed) belongs to the Lineaceae family (90). It is a medicinal herb, any part of which is used for a certain medical purpose (91,92). Flaxseed is the ingredient of a wide range of food products. Natural food products containing flaxseed are becoming increasingly popular due to their high content of soluble fiber, polyunsaturated fatty acids, protein, and phytochemicals. Alpha linolenic acid as the major ingredient of flaxseed is the exclusive source of omega-3 fatty acid in vegetarian diets (93). One study showed that UNIM-352 formulation contains six different herbal ingredients (*Linum usitatissimum*, *Allium sativum*, *Trigonella foenum-graecum*, *Strychnos potatorum*, *Pongamia glabra*, and *Caesalpinia bonducella*) markedly reduces the levels of IL-13, TGF- $\beta$  in blood and broncho-alveolar lavage (BAL) fluid and hydroxyproline content in lung homogenates. Histopathological examination of lung tissue showed that the polyherbal agent had an attenuating effect on goblet cell hyperplasia, inflammatory cells infiltration, and sub-epithelial fibrosis in an experimental model of bronchial asthma (35).

#### ***Vitis vinifera* L.**

*Vitis vinifera* L. (grapes) belongs to Vitaceae family. Grape has high nutritional value and unique phytochemical composition that makes it a natural dietary

supplement. Fruits are a good source of polyphenols, phenolic acids, flavanols, anthocyanins, stilbenes (resveratrol), fats, proteins, fibers, and vitamins (C and A). According to its medicinal properties, it has long been recognized in folklore medicine. Documented evidence has reported antioxidant and anti-inflammatory properties of fruits and seeds of *V. vinifera*. A study showed that treatment of ovalbumin-induced animal model of bronchial asthma with *V. vinifera* fruits extract inhibited recruitment of nitrites, IgE, inflammatory cytokines, and circulating cells, particularly eosinophils in blood/serum and bronchoalveolar fluid and also normalizes the lung functions and histamine level (37). Another study showed that treating allergen (ovalbumin, 40 mg/rat+aluminum hydroxide, 2.0 mg/rat)-sensitized male wistar rats with Kanakasava -an Indian traditional Ayurvedic formulation containing *Datura metel*, *Vasaca (Adhatoda vasica)*, *Dhataki (Woodfordia fruticosa)* and *Grape (Vitis vinifera)* extracts- significantly reverses elevated levels of cytokines, IgE, nitrites, and influx of eosinophils and neutrophils in blood and BALF in addition to significant improvement of lung functions and suppression of degranulation of mast cells (38).

### **CONCLUSION**

Persian medicine sources classify COPD as a pulmonary disease that primarily involves coughing. This is caused by the production of thick and sticky secretions, which can lead to inflammation and infection. In the present study, we showed that medicinal herbs including *Zataria multiflora*, *Thymus vulgaris*, *Glycyrrhiza glabra*, *Crocus sativus*, *Nepeta bracteata* Benth., and *Hyssopus officinalis* L. have beneficial effects on COPD due to their anti-inflammatory, anti-oxidant and anti-microbial properties. Also, considering ACO, *Cordia myxa*, *Adiantum capillus-veneris*, *Viola odorata*, *Borago officinalis*, *Linum usitatissimum* and *Vitis vinifera* L. have shown beneficial effects on asthma. Regarding the mentioned beneficial mechanisms of action and potential therapeutic effects of these medicinal herbs, they could be used as complementary



therapy in COPD and asthma. However, more experimental and clinical investigations should be conducted to confirm their effects.

### Conflict of interest disclosure

The authors have no conflict of interests to be declared.

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