

Remedies in asthma treatment: Introduce a new remedy from perspective of Persian medicine

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RESEARCH

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ABSTRACT

Background

Asthma is a chronic inflammatory disease of the airways. Mucus plug formation, oxidative stress, swelling of the airway walls, inflammatory process and vascular changes are important events in asthma pathogenesis.

Aims

Although bronchodilators and steroids are two main drugs in asthma treatment, many adults and children still use complementary and alternative (CAM) medicine. This study was conducted to determine the most popular remedies in asthma treatment from perspective of Traditional Persian medicine (TPM) manuscripts.

Methods

The main Traditional Persian textbooks from the 9th to 18th

centuries AD were collected and analysed. Thereafter, the most listed plants in asthma treatment were gathered. The plants in this list were searched and compared in recent studies.

Results

Some of these plants have anti-inflammatory and antioxidant effects; a few of them have undergone animal or human researches in conventional medicine.

Conclusion

According to long history of medicine in Persia the collected list of remedies could be helpful in selecting plants for future studies in asthma treatment.

Key Words

Asthma, traditional Persian medicine, *Trigonella graecum* L., antioxidant, complementary and alternative medicine, fenugreek

What this study adds:

1. What is known about this subject?

Although bronchodilators and steroids are two main drugs in asthma treatment, many adults and children still use complementary and alternative (CAM) medicine.

2. What new information is offered in this study?

Based on TPM and recent studies, some remedies were determined to have useful effects in asthma treatment. One of the special remedies in asthma treatment from the TPM point of view is *Trigonella graecum* L.

3. What are the implications for research, policy, or practice?

According to long history of medicine in Persia the collected list of remedies could be helpful in selecting plants for future studies in asthma treatment.

Background

One of the famous pulmonary diseases is Asthma that characterized by airway hyper-responsiveness, airflow restriction, acute broncho-constriction, swelling of the airway walls, chronic mucus plug formation and airway wall remodelling.¹ Oxidative stress has been indicated as the main related mechanisms of asthma disease.² It is mentioned to be the most important event in inflammatory process.³ Increased oxidative stress is related to the severity of asthma.⁴ In animal research studies, H₂O₂ caused contraction of airway's smooth muscle and hyper responsiveness.⁵ Asthma as a major chronic respiratory disease has a prevalence of about 300 million in adults and children all over the world. In USA statistics show 15.7 million adults and 6.5 million children are suffering from asthma symptoms.¹ In westernized countries, asthma prevalence has increased to 50% in the past few decades. Although, recent anti-asthmatic drugs are effective in asthma treatment, there is still no cure for asthma. Drugs side effects in chronic usage are another concern especially in children. Non-adherence to medical regimens has been estimated to cost \$100 billion annually for health-care system in the United States. Hence, the result of this non-adherence could be the loss of chances for patients to amend their health and also loss of medication by health-care providers which results in increased morbidity.⁶ Because of the chronicity of asthma and lack of preventive principles and curative treatment the patients use complementary and alternative medicine (CAM) treatment, especially in western countries.^{7,8} It seems that up to 30% of adults and 60% of children in the US still use some form of CAM for asthma treatment.⁹ The Traditional Persian medicine (TPM) system is one of the ancient systems of CAM in the world. Although, more studies are required to find useful remedies with lesser side effects for asthma management; some remedies from Persian Traditional medicine textbooks could be recommended. Since medication prescriptions from TPM were used by ancient physicians and people over the years, it is very likely that these remedies will be selected for future studies. The aim of this study is to find a new hope with lesser side effects and better adherence in asthma treatment.

Method

The treatment principles of asthma and the remedies that have been used were collected and analysed from Persian Traditional Medicine (PTM) manuscripts. From 9th to 18th centuries AD, like Al- Mansuri- Fi- Teb(9th and 10th centuries), Canon of medicine(11th century), Mofarah- Al- Gholoub(18th century) and Exir- e- Azam(19th century), as

well as some pharmaceutical books like Makhzan- Al- Advieh, Alshamel and Moalejat – e-Aghili were collected and analysed. According to these analyses, a list of more frequent remedies was prepared. Up to September, 2017, electronic databases including Pub Med, Scopus, Web of Science, Google Scholar, and the Cochrane library were searched with scientific names of plants separately. English and Persian language publications were included. Some mentioned remedies had been proved in animal or human studies on asthma.^{13,14,23-25,29,32,41} Studies that exhibited apparent efficacy or indirect effectiveness on asthma pathogenesis were selected for this current research. Duplication was avoided by excluding multiple copies of the same article in different databases. The key words are the scientific name and common name of the plants in the whole text and the terms “asthma” or “flavonoid” or “anti-oxidant” or “anti-inflammation” in the title and abstract.

Results

Table 1: shows the remedies based on TPM manuscripts and their consumption instruction. Their efficacy in asthma treatment was compared with new studies.

Discussion

Treatment in TPM is based on humors theory.⁵⁹ From perspective of Persian Medicine the most common pathology for asthma disease is air way restriction and mucus formation due to phlegm [60-62]. So they consider plants which can clean and wash out this excessive phlegm.

As shown in Table 1 Many of these remedies are antioxidant and have anti-inflammatory effects like Honey, Pistacia terebinthus, Linum Usitatissimum, Ficus Carica [Table 1] some of them don't have any investigations in conventional medicine but a few of them have clinical trials like Glycyhiza glabra, Boswella sacra, Drimia maritime and Nigella sativa.^{13,14,23-25,29,32,41} Despite of the positive results, more studies with larger sample size and stronger study designs are recommended.

Through these remedies with regard to Persian scholars' point of view we selected the *Trigonella foenum graecum* for our future research. *T. foenum- graecum*L has the common name; Fenugreek which belongs to the family Leguminosae. All articles that made mention of this plant in their abstract and entire paper work were selected and analysed.

Fenugreek is an annual plant. This plant is used alone or in combination for relieving asthma symptoms in many TPM prescriptions.⁶⁰⁻⁶² Fenugreek seeds have been known as a

spice from ancient time and also had some medical uses, for example, appetizer, tonic, carminative, expectorant and etc.⁶⁰⁻⁶² In “Makhzanal- advieh” one of the famous Persian Traditional pharmacology books *T. foenum- graecum* L. (Fenugreek) was stated as the lung tonic.⁶³ In recent researches, fenugreek seeds were observed to have anti-diabetic,⁶⁴⁻⁶⁶ hypocholesterolaemic effects⁶⁷ and anti-oxidant properties. Also there is report that *T. foenum-graecum* L. could have anti-peptic ulcer actions.⁶⁸ Anti-bacterial, anti-worm effects,⁶⁹ immunomodulatory^{66,70} and anti-inflammatory effects are other features of *T. foenum-graecum* L.

Chemical analysis of fenugreek seeds

- Alkaloides:⁷¹ Trimethylamine, Neurin, Trigonelline, Choline, Gentianine, Carpaine and Betain. Saponins:⁷² Graecunins, fenugrin B, fenugreekine and trigofenosides A-G.

- Steroidal sapinogens: Yamogenin, diosgenin, smilagenin, sarsasapogenin, tigogenin, neotigogenin, gitogenin, neogitogenin, yuccagenin and saponaretin. - Fibers: Gum, neutral detergent and fiber.⁷³

- Flavonoids: Orientin, Vitexin and Quercetin.^{74,75}

- Amino acids: Isoleucine, 4-Hydroxyisoleucine, Histidine, Leucine, lysine, L-tryptophan and Arginine.

Other: Coumarin, lipids, vitamins, minerals. Mucilage (28%) and Proteins (22%).

Active ingredient helpful in asthma management

Many epidemiologic studies have reported beneficial effects of flavonoids on asthma.⁷⁶ Poly phenols are the most important low molecular weight of Flavonoids.^{77,78} Besides the anti-oxidative effects; flavonoids can inhibit the activation of basophiles and mast cells and thus prevent histamine and other preformed granule-associated mediators release that lead to granule-associated process.⁷⁹ One of the well-known flavonoids that inhibits the eosinophilic secretion of Charcot-Leyden crystal protein and eosinophil cationic protein is Quercetin.⁸⁰ Another major part of asthma pathogenesis is vascular changes.⁸¹ These changes consist of an increase in vascular permeability, vascular dilation, and vasculogenesis which is called angiogenesis.⁸¹ It has been shown that flavonoids and their certain compounds have demonstrated the ability to modulate the expression of HIF-1, VEGF, matrix metalloproteinase (MMPs), and epidermal growth factor receptor and also inhibit NF- κ B, PI3K/Akt, and ERK1/2 signalling pathways.^{82,83} Finding a drug which could balance between TH1/TH2 and avoid the inflammation and angiogenesis process and mucus formation, would be a major success in asthma treatment. As mentioned in the results, fenugreek seeds have anti-inflammatory effects and

possess acceptable flavonoids content. *T. foenum- graecum* L. showed anti-oxidant effects which could explain the anti-inflammatory activities by regulation of various inflammatory mediators that could have protective vascular effects. Saponins and flavonoids are two major compounds of fenugreek that can approximately explain the anti-inflammatory activity of this plant.⁸⁴ Despite these positive data on Fenugreek usage in asthmatic patients, there are still some conflicting findings of Fenugreek in some reports. Patients who have allergy to Fenugreek or chickpeas must take caution in using this herb, because of the possible reactions.⁸⁵ Studies have reported some side effects such as transient diarrhoea and distension⁸⁶ also dizziness.⁸⁷ Another theoretical risk is increase in prothrombin time (PT) or the international normalized ratio (INR), that could lead to increase bleeding risk.⁸⁸ In early animal researches, Fenugreek has the potential of stimulating the uterine, hence it should be avoided during pregnancy.⁸⁹

Conclusion

This study revealed some remedies that could be useful in asthma treatment from Traditional Persian Medicine (TPM) perspective. From the selected remedies, *Trigonella graecum* L. was widely searched. According to these findings one small randomized controlled trial is designed in Shahid Sadoughi School of Persian medicine in Yazd to compare the effect of Fenugreek seeds with placebo. Its results will be published as soon as the work is completed, but more studies in large trials which are designed for randomized controlled with placebo are still needed to observe the effectiveness of Fenugreek in asthma treatment cautiously.

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Not needed

Table1: Remedies in asthma treatment from perspective of Persian Traditional Medicine

Common name in TPM	Scientific name	The used part	Uses in conventional medicine
Assal	Honey	The hole liquid	- Antioxidant ^{10,11} - Anti-inflammatory ¹²
Shirin bian (soos)	<i>Glycyhiza glabra</i>	Rhizome	- Increase inFEV1 levels ¹³ - In ASHMA combination improve the lung function test and reduce the interlokin levels ¹⁴
Badam shirin (Looz al- holve)	<i>Prunus dulcin</i>	Fruit	- Contains polyphenols and has antioxidant activity ¹⁵ - Almond has high levels of monounsaturated fat ¹⁶
Kadoo (gharee)	<i>Cucurbita pepo L.</i>	Fruit and Seeds	- Antioxidant ¹⁷
Saghez	<i>Pistacia terebinthus</i>	Gum	- Antioxidant ¹⁸ and anti-inflammatory effects ¹⁹
Kondor	<i>Boswellia sacra</i>	Gum	- Anti-inflammatory ²⁰ - Improve the spirometry parameters ^{21,22}
Squill	<i>Drimia Maritima</i>	Vinegar	- Significantly improved spirometry parameters ²³ - Reduction mucus secretion of the airway ²⁴ - Useful in respiratory diseases including asthma ²⁵
Katan	<i>Linum Usitatissimum</i>	Seeds	- Antioxidant effects ^{26,27} - Using flaxseed oil reduce IL4 cells in layer near the base of epithelium in atopic dermatitis patients ²⁸
Siah Daneh (Shooniz)	<i>Nigella Sativa</i>	Seeds	- Nigella oil reduces eosinophilia and improves quality of life in asthma patients ²⁹ Anti-inflammatory and immunomodulatory effect on marine lung tissue ³⁰
Chinese Ravand	<i>Rheum Officinale</i>	Root and Bark	- Emodin isolated from barks and root has anti-inflammatory and antibacterial effects ³¹ - Emodin could delay airway inflammation process on non-infection asthma in mouses ³²
Anjir (Tin)	<i>Ficus Carica</i>	Fruit	- Antiinflammatory effects ³³ - Ficus is rich in polyphenoles and works as a strong antioxidant ^{34,35}
Onnab	<i>Ziziphus Jujuba</i>	Fruit	- Antioxidant effects ³⁶ - Immune-modulating effects ^{37,38}
Sir (Soom)	<i>Allium Sativum</i>	Cloves	- Anti-inflammatory ³⁹ and antioxidant ^{39,40} - Using 4gr raw garlic per day in asthmatic smokers show significant increase in spirometry parameters ⁴¹
Zoofa	<i>Hyssopus Officinalis</i>	Flower	- Anti-inflammatory effects and reduction of IgE levels ⁴² - Reduce the level of IL4, IL6, IL17 ⁴³⁻⁴⁵
Parsiavoshan	<i>Adiantum Capilus Veneris</i>	Leaf	- Antioxidant and anti-inflammatory effects ^{46,47}
Aftimoon	<i>Cuscuta Epithimum</i>	Aerial parts	- Anti-microbial effects ⁴⁸ - Contains flavonoids which can act as antioxidants ⁴⁹
Razianaj	<i>Foeniculum Vulgare Mill.</i>	Seeds	- Seeds contain flavonoids that are considers as important antioxidants ^{50,51} - Anti-inflammatory activity ⁵²
Banafsej	<i>Viola Odorata L.</i>	Flower	- Antimicrobial effect ⁵³ - Antioxidant ⁵⁴ - Lung tissue protection ⁵⁵ - Effective in controlling of cough among children with asthma ⁵⁶
Shanballileh (Holbeh)	<i>Trigonella Foenum Graecum L.</i>	Seeds	- Antioxidant ⁵⁷ - Anti-inflammatory effects ⁵⁸ seeds contain28% mucilage