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Efficacy and Safety of Iranian Poly Herbal Formulation (Compound Honey Syrup) in Pediatric Patients with Mild to Moderate Asthma: A Randomized Clinical Trial

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Abstract

Background: Asthma is a chronic relapsing airways disease that represents a major public health problem worldwide. With the high incidence of asthma, there has been a surge in the use of complementary therapies, such as compound honey syrup in Traditional Persian Medicine, in the treatment of asthma. The aim of this study was to evaluate the efficacy and safety of Iranian poly herbal formulation (compound honey syrup) in the treatment of mild to moderate pediatric asthma. **Materials and Methods:** The study was a randomized clinical trial that was conducted on 80 patients with mild to moderate asthma assigned to two groups (n=40 for each group) for eight weeks. Control and experimental groups received classical treatment of asthma with fluticasone spray; in case of worsening of symptoms, salbutamol spray was used for short term. The experimental group also received compound honey syrup (the combination of honey and an extract of the following five medicinal plants: ginger, cinnamon, saffron, cardamom, and galangal). Asthma Control Questionnaire (ACQ) items and total scores of ACQ were evaluated before and after treatment. **Results:** To this end, 72 patients completed this study. There was no significant difference between the experimental and the control groups in baseline data such as age, sex, body mass index, ACQ items, and ACQ scores. Total scores and all items of ACQ, with the exception of forced expiratory volume in one second (FEV1%), were significant between groups ($P<0.05$). No serious adverse effects were observed in the two groups. **Conclusions:** The results of this study reveal that compound honey syrup can be a safe and effective complementary drug for the treatment of pediatric asthma.
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Keywords: Asthma; Iranian Poly Herbal Formulation; Compound Honey Syrup; Asthma Control Questionnaire

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Introduction

Asthma, as one of the major causes of chronic airway disease, has affected 334 million people in 2014 across the globe [1]. The symptoms of asthma are experienced by 14% and 8.6% of the world's pediatric population and young adult population (aged 18-45 years), respectively. The burden of asthma is the greatest for children in the age group of 10 to 14 years and the elderly aged between 75 and 79 years [1]. Overall prevalence of asthma symptoms is 13.14% in children under the age of 18 years in Iran. This prevalence is variable, from 2.7% in Kerman Iran to 35.4% in Tehran Iran [2]. Its prevalence is increasing daily with increased pollution, with increased incidence of exacerbations being associated with the stress and strain of life [3, 4]. Symptoms of asthma include wheezing, cough, tightness of the chest, and shortness of breath, which are more frequent at night and early morning. In addition to the impairment of respiratory function, it can also affect the physical, social, and emotional life of the individual [5, 6]. Asthma's pathology includes hypertrophy of mucous glands, inflammation of the airways, and bronchoconstriction [6, 7]. Currently, asthma management focuses on the control of inflammatory process and improving the patient's comfort and quality of life [6, 8]. Inhalational corticosteroids and beta2-agonists are known as the treatment of choice, which provide relief from symptoms by controlling the inflammation and bronchial constriction [9].

Despite the continuous effort to discover a safe and efficient treatment for asthma, finding a drug that is free from local or systemic side effects has proved difficult [3, 6]. Conversely, the prolonged course of the disease and the absence of preventive and therapeutic measures have motivated asthma patients to opt for complementary and alternative medicine (CAM) [10]. In fact, there's a greater likelihood of patients living in developed countries using traditional medicine as either sole or complementary therapeutic plan [11]. A research conducted by the National Asthma Campaign established that 70% of the patients with severe asthma and 60% of those with moderate disease have tried CAM. Herbal medicine is regarded as the third most common type of CAM that is used by patients with asthma, in both adult (11%) and children (6%) groups [12, 13]. Traditional Persian Medicine (TPM) is also considered as a type of CAM. TPM is one of the oldest types of medicine. From the prehistoric era to 637 AD, the annals of ancient Iran date back to about 10,000 years ago, with the development of medicinal science being particularly remarkable. Prominent medieval scientists, such as Razi (Rhazes; 865-925 AD), Ali Ebn Abbas (Haly Abbas; 949-982 AD), Ibn Sina (Avicenna; 980-1037 AD), and Jorjani (Sorsanus; 1042-1137 AD), significantly influenced the improvement of Iranian medical science. The texts of *Al-Qanoon fi al-Tibb* (*The Canon of Medicine*) by Avicenna, *Al-Hawi* (The Continens) by Rhazes, *Zakhireh Kharazmshahi* (the Treasure of Kharazmshah) by Sorsanus, and *Kitab-al Maliki* (Liber Regius) by Haly-Abbas were central to western medical science from the 13th to the 19th century [14]. The TPM is a holistic medicine that relies heavily on the concept of temperament for maintaining health and treating diseases [15]. The TPM is used in Iran by practitioners for the treatment of various diseases, including asthma, either as monotherapy or as a complementary therapy to standard conventional medications. However, well-controlled clinical trials using TPM for asthma treatment are still not common. With a long history of several thousand years, TPM has specific classification and management strategy for asthma and provides effective treatments in this field with diet, lifestyle modification, and drugs of plant or animalistic origin. The use of Iranian poly herbal formulation (compound honey syrup) is one of the most common treatment for asthma in TPM [16, 17]. Compound honey syrup is the combination of honey and an extract of five medicinal plants, which include *Zingiber officinale Roscoe* (Zingiberaceae), *Cinnamomum verum* J Presl (Lauraceae), *Crocus sativus* L (Iridaceae), *Elettaria cardamomum* (L) Maton (Zingiberaceae), and *Alpinia galanga* (L) Willd (Zingiberaceae)—the common names of these plants being ginger, cinnamon, saffron, cardamom,

and galangal, respectively.

Each of the components of the compound honey syrup possesses properties that are useful in the treatment of asthma. Honey possesses anti-inflammatory, antibacterial [18, 19], and antitussive [20, 21] properties, and ginger has anti-inflammatory [22, 23], bronchodilator [24], and anticholinergic effects [25]. Cinnamon has anti-inflammatory [26], antimicrobial [27], and anti-asthmatic effects [28]. Saffron has antitussive [29], anti-inflammatory [30], and antioxidant properties [31]. Cardamom has a bronchodilator effect [32]. Galangal has shown antibacterial [33] and anti-inflammatory activities [34].The onset of asthma symptoms occurs because of an inflammatory process in the airways, which induces bronchospasm, bronchoconstriction and cholinergic stimulation; compound honey syrup with its component parts, including honey, ginger, cinnamon, saffron, cardamom, and galangal, can be effective in eliminating inflammation, bronchospasm, and asthma symptoms with its anti-inflammatory, anticholinergic, bronchodilator, and antitussive effects. However, to the best of our knowledge, no clinical trial has examined the efficacy of compound honey syrup on the clinical manifestation of pediatric asthma. The aim of this study that was conducted as a randomized clinical trial was to evaluate the efficacy and safety of compound honey syrup in child patients with mild to moderate asthma.

Materials and Methods

Patients

In this randomized clinical trial, the subjects were 80 patients with a diagnosis of mild to moderate asthma (56 male and 24 female, age: 6-16 years) who came to Mofid Children Hospital Pulmonology Clinic for follow-up treatment; they were recruited from October 2015 to May 2016. The 8-week study was conducted.

Sample Size Calculation

Based on statistical calculations with the default power (1- β) 0.95, type I error (α) 0.05, 20% improvement in drug efficacy variables ($\bar{X}_1$ - $\bar{X}_2$), and the group variance (S_1 and S_2) of about 25%, and with the overall sample size formula,

$$n = \frac{(S_1^2 + S_2^2)(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})2}{(\bar{X}_1 - \bar{X}_2)^2}$$

the estimated sample size was 60 subjects. A sample size of 80 patients (40 patients each in the experimental and the control group) was considered with a 30% possibility of withdrawal rate.

Inclusion and Exclusion Criteria

Inclusion criteria was as follows: being 6 to 16 years of age; having mild to moderate asthma that has been diagnosed by a pediatric pulmonologist (Children and adolescents with mild asthma have cough or wheeze more than twice per week, but less than daily. Nocturnal symptoms of cough or wheeze occur no more often than 3 to 4 times per month, and pulmonary function (forced expiratory volume in one second [FEV_1] and FEV_1/FVC [forced vital capacity]) is in the normal range. Patients with mild asthma may also have two or more exacerbations per year. Patients with moderate asthma have symptoms during most of the days and nocturnal symptoms at least weekly, and they may report frequent slowed play and missed school days. The FEV_1 and FEV_1/FVC measures are often in the range of mild obstructive lung disease (60%-80% of predicted). As with patients with mild asthma, those categorized as having moderate asthma may also have two or more serious exacerbations per year) [35, 36]; understanding the research protocol and consent to participate.

Exclusion criteria in this study included patients with severe asthma and require hospitalization or patients with an asthma attack; having underlying diseases such as cystic fibrosis, bronchopulmonary dysplasia, heart failure, tracheobronchomalacia, gastroesophageal reflux disease, bronchiectasis, pulmonary embolism, and sarcoidosis, allergy or intolerance to the individual herbs in compound honey syrup; use of medications such as aspirin, beta blockers and nonsteroidal anti-inflammatory drugs, other acute disease during the study, and patients who have decided to

leave the study at their personal request.

Drug Preparation

Compound honey syrup is a popular beverage in TPM that has been used for asthma for many years [16]. In our study, compound honey syrup was prepared according to documented pharmaceutical TPM manuscripts [16, 37, 38] but with slight modifications. Compound honey syrup is a TPM product that has a license from the Iranian Food and Drug Administration (IFDA) affiliated to The Ministry of Health of Iran (license number: S-94-0425). Plants used in compound honey syrup are considered as well-known medicinal plants that were prepared by Niak Company and were controlled using standard methods at quality control laboratory, Niak Company. Compound honey syrup with the batch number 94230, 10.08.2015 was given to each patient. This product has two years expiry date. As a syrup formulation, compound honey syrup is a mixture of honey, water and an extract of herbs of *Z. officinale* Roscoe (root), *C. verum* Presl (bark), *C. sativus* L (stigma), *E. cardamomum* (L) Maton (fruit), and *A. galanga* (L) Willd (root).Each 100 cm^3 of compound honey syrup consisted of ginger, saffron, and galangal (1 g), cinnamon and cardamom (2 g), and honey (40 g).

Study Design

Eligible subjects were randomly assigned into two groups (experimental and control groups, [n=40] in each group) that received classical treatment of asthma with two puffs of fluticasone spray 50 mcg (from Jaber pharmaceutical company, Iran) every 12 hours; in case of deterioration of symptoms, salbutamol spray (from Jaber Pharmaceutical Company, Iran) was used for short term. The experimental group, in addition to the usual treatment, received 5 cm^3 of compound honey syrup in 100 cm^3 of warm water, three times per day for 8 weeks as well. During the first visit for both groups, Asthma Control Questionnaire (ACQ) was completed by the investigator and FEV_1 was evaluated for all patients. In weeks 2, 4 and 6, patients were monitored for side effects and improvement of symptoms. At week 8, ACQ was completed by the investigator and FEV_1 was carried out for all patients. Furthermore, the questionnaire on drug's side effects was also completed. Then the findings before and after the intervention were compared within and between groups.

Clinical Evaluation

Personal data were collected by interview and physical examinations of subjects during their visits. In the first visit, the mode of application of each medication was explained to the subjects who met the inclusion criteria. To establish a baseline, average symptoms scores were evaluated at the beginning of the study. The effect of treatment was evaluated by analyzing average ACQ items in weeks 1 and 8 of treatment on the basis of seven categories (questions) about the following: (1) night symptoms, (2) morning symptoms, (3) activity limitation, (4) shortness of breath, (5) wheeze, 6) use of short-acting bronchodilator (SABA), and (7) FEV_1 %. Each category was scored from 0 to 6, whereby score 0 denotes no symptoms and score 6 denotes very severe symptoms.The evaluation of lung function and FEV_1 measurements was carried out by using an HI-701 spirometer (Chest Co Ltd, Tokyo, Japan). Lung function measurements were recorded in the first visit before the initiation of treatment and after the discontinuation of the treatment.

Ethical Issue

The experiment was explained to potential subjects, and they were asked to provide written informed consent before participating in the study. The study protocol was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.REC.1394.88: 172) and registered in the Iranian Registry of Clinical Trials (IRCT2015083123834N1).

Statistical Analysis

All analyses of baseline and treatment effects were performed by using the Statistical Package for the Social Sciences (SPSS), version 22. A $P<0.05$ was considered statistically significant, and all tests were two-tailed. The Kolmogorov-Smirnov test of normality of data was employed. On the basis of the

nature of the results, we used nonparametric methods (descriptive statistics, Wilcoxon, and Mann-Whitney test) for symptom scores and numbers of puffs of SABA were used per day. For all other variables, we tested the assumptions of equal variances and normality used in the analysis of differences between groups with respect to changes from baseline. We employed the independent sample t test to analyze these changes if these assumptions were satisfied, and the Mann-Whitney test if otherwise. Analysis of within-group differences from baseline was usually not a problem because the results were very obvious, and our policy was to use the paired t test if the analysis of differences between groups (which involved an examination of assumptions) was based on the independent sample *t* test.

Results

Patient Enrollment and Exclusion

A total of 80 patients participated in the study from October 2015 to May 2016, and 40 patients each were randomized in both the control and the experimental group. During the 8-week study, eight patients (four patients in each group) were excluded from the study population. The number of patients who completed the study and were analyzed was 72 (90%),

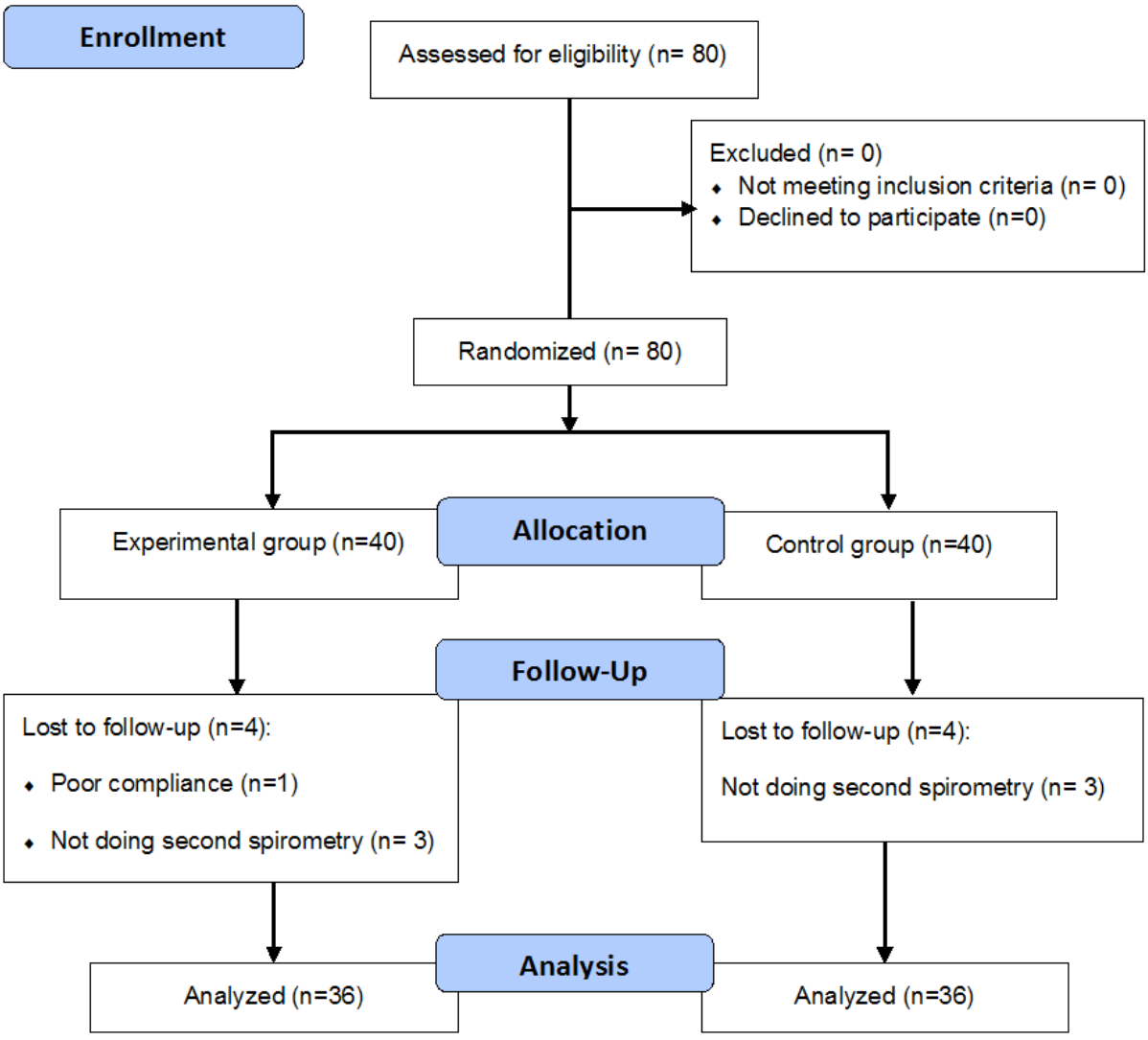

Figure 1. Consolidated standards of reporting trials (CONSORT) flowchart of study

with 36 patients in each group (Figure-1).

Baseline Data

There was no significant difference between the experimental and the control groups in terms of age, sex, and body mass index and at baseline in terms of FEV_1 and ACQ scores (Table-1).

Efficacy

The efficacy results are presented in Table-2. At the end of the 8 weeks of study, night symptoms, morning symptoms, activity limitation, shortness of breath, wheeze, use of SABA, and total scores of ACQ were significantly reduced in both groups, and all mentioned variables in the experimental group were significant (P<0.001) (Table-3); in the control group, night symptoms, shortness of breath, and total scores of ACQ were significant (P<0.001), and morning symptoms, activity limitation, wheeze, and the use of SABA were significant (P<0.05) (Table-4). All variables mentioned above in the experimental group were significant compared with the control group (P<0.05). To a great extent, there was no significant difference in FEV_1% between the two groups (P=0.43), and within the experimental and the control group; there was significant improvement (P=0.004 and

Table 1. Baseline Characteristics of Patients

Variable	Experimental	Control	P-Value
Gender (male)*	27 (75%)	25 (69.4%)	0.60
Age (year)†	8.72 (1.83)	8.72 (2.72)	0.42
BMI†,‡	17.77 (5.01)	17.21 (2.79)	0.66
Night symptom scores†	1.38 (1.39)	1.94 (1.75)	0.21
Morning symptoms scores†	1.27 (1.32)	1.38 (1.53)	0.90
Activity limitation scores†	2.08 (2.11)	1.22 (1.72)	0.12
Shortness of breath scores†	1.02 (1.36)	1.22 (1.26)	0.37
Wheeze scores†	1.33 (1.24)	1.30 (1.26)	0.81
Short-acting bronchodilator scores†	2.11 (1.28)	1.94 (1.63)	0.62
FEV_1%†,§	99.77 (15.10)	103.01 (19.70)	0.15
Total score of ACQ†,‖	10.13 (4.22)	9.47 (5.56)	0.32

*Data presented as number of patients (percentage).
†Data presented as mean (standard deviation).
‡**BMI**: Body mass index
§**FEV_1**: Forced expiratory volume in one second
‖**ACQ**: Asthma control questionnaire

Table 2. Change in the Variables After Intervention

Variable	Experimental Mean (SD)	Control Mean (SD)	P-Value
Night symptom scores	0.08 (0.36)	0.50 (0.84)	0.002
Morning symptoms scores	0.16 (0.44)	0.58 (1.10)	0.04
Activity limitation scores	0.22 (0.54)	0.72 (1.30)	0.03
Shortness of breath scores	0.11 (0.31)	0.41 (1.69)	0.03
Wheeze scores	0.05 (0.23)	0.52 (0.73)	0.000
Short-acting bronchodilator scores	0.02 (0.16)	0.58 (1.22)	0.02
FEV_1%*	114.30 (25.47)	122.31 (31.57)	0.43
Total score of ACQ†	1 (1.30)	3.38 (3.78)	0.003

***FEV_1**: Forced expiratory volume in one second
†**ACQ**: Asthma control questionnaire

Table 3. Changes in the Variables in the Experimental Group Before and After Intervention

Experimental Group Variable	Before Intervention Mean (SD)	Post Intervention Mean (SD)	P-Value
Night symptom scores	1.38 (1.39)	0.08 (0.36)	0.000
Morning symptoms scores	1.27 (1.32)	0.16 (0.44)	0.000
Activity limitation scores	2.08 (2.11)	0.22 (0.54)	0.000
Shortness of breath scores	1.02 (1.36)	0.11 (0.31)	0.000
Wheeze scores	1.33 (1.24)	0.05 (0.23)	0.000
Short-acting bronchodilator scores	2.11 (1.28)	0.02 (0.16)	0.000
FEV_1%*	99.77 (15.10)	114.30 (25.47)	0.004
Total score of ACQ†	10.13 (4.22)	1 (1.30)	0.000

***FEV_1**: Forced expiratory volume in one second
†ACQ: Asthma control questionnaire

Table 4. Changes in the Variables in the Control Group Before and After Intervention

Control Group Variable	Before Intervention Mean (SD)	Post Intervention Mean (SD)	P-Value
Night symptom scores	1.94 (1.75)	0.50 (0.84)	0.000
Morning symptoms scores	1.38 (1.53)	0.58 (1.10)	0.007
Activity limitation scores	1.22 (1.72)	0.72 (1.30)	0.006
Shortness of breath scores	1.22 (1.26)	0.41 (1.69)	0.000
Wheeze scores	1.30 (1.26)	0.52 (0.73)	0.001
Short-acting bronchodilator scores	1.94 (1.63)	0.58 (1.22)	0.001
FEV_1%*	103.01 (19.70)	122.31 (31.57)	0.01
Total score of ACQ†	9.47 (5.56)	3.38 (3.78)	0.000

***FEV_1**: Forced expiratory volume in one second
†ACQ: Asthma control questionnaire

P=0.01, respectively). Total score of ACQ was significant between the two groups (P<0.05).

Safety
No serious adverse effects were observed in the two groups.

Discussion

This study demonstrated the prescription of compound honey syrup to cause significantly reduced symptom scores (night symptoms, morning symptoms, activity limitation, shortness of breath, and wheeze), reduced use of SABA, reduced total score of ACQ, and increased lung function as determined by increased FEV_1%. These variations were statistically significant for the experimental group and the control group. Comparisons of symptom scores, use of SABA, and total score of ACQ showed significant difference between the two groups, but there was no significant difference in FEV_1% between the two groups. It may be that more time is required to determine the spirometry finding before and after an intervention and the duration of 2 months was inadequate.Presently, asthma management focuses on the control of inflammatory process [6, 8]. Although the use of traditional medicines has been highly regarded in the treat-

ment of asthma and per TPM, compound honey syrup has been used for the improvement of clinical manifestation of asthma [16, 17], MEDLINE research did not offer any previous studies toward the assessment of the efficacy of these medicinal plants or drugs on clinical manifestation of asthma within the framework of a clinical trial. Nevertheless, there is little research on the effects of each component of compound honey syrup on asthma that could indicate the mechanism of action of this drug in improving the symptoms of asthma.Recent studies have revealed that honey is an effective natural remedy for nocturnal cough in children and sleep difficulty [20, 21]. Honey also has a better effect on nocturnal cough and sleep quality in children when compared with dextromethorphan and diphenhydramine [39]. Honey possesses anti-inflammatory [18)], antioxidant, and antibacterial [19] properties. This study demonstrated that nocturnal cough was reduced to a greater extent in the experimental group than in the control group.The effect of ginger (*Z officinale*) on respiratory airways has been investigated in recent studies by using crude ginger extract. The results revealed its bronchodilator activity, inhibition of acetylcholine-induced contraction and Ca^{2+} transients in guinea pigs, whereas intraperitoneal injections reduced lipopolysaccharide (LPS)-induced hyperresponsiveness in rat trachea [24].

A study showed the ability of ginger in preventing phthalate ester-associated asthma [40]. Another study suggested the anti-inflammatory effect of ginger in respiratory infections [22], whereas two other studies demonstrated that ginger suppressed Th2-mediated immune responses and could play a role in the management of allergic asthma [23, 41]. Furthermore, 6-gingerol, 8-gingerol, or 6-shogaol isolated components of ginger potentiate beta-agonist-induced relaxation in human airway smooth muscle (ASM). Together with beta-agonists, 6-gingerol, 8-gingerol, or 6-shogaol may augment existing asthma therapy, resulting in relief of symptoms through complementary intracellular pathways [42]. These novel data have indicated that ginger and its isolated active components, 6-gingerol, 8-gingerol, and 6-shogaol, relax ASM, and 8-gingerol attenuates airway hyperresponsiveness, partly by altering (Ca^{2+}) (i) regulation [43]. Ginger compounds also reduced the LPS-induced interleukin 8 (IL-8) secretion and could be used as anti-inflammatory drugs in respiratory diseases [22]. Furthermore, 6-gingerol, a major component of ginger, was sufficient to suppress eosinophilia, IL-4, IL-5, and eotaxin levels in the lungs as well as specific immunoglobulin E (IgE) titers in serum in mice model of inflammation. Hence, ginger can suppress Th2-mediated immune responses and might thus provide a probable therapeutic application in allergic asthma [23]. A study showed that honey-ginger powder extract mixtures have the potential to serve as cheap source of antibacterial agents, particularly for the drug-resistant bacteria strains [44]. Recent studies have revealed that cinnamon (*C. verum*) is used as a drug or spice. The essential oils and tannins present in cinnamon are responsible for its antimicrobial property [27].

One study indicated that cinnamon water extract (CWE) with anti-inflammatory property can reduce LPS-induced tumor necrosis factor (TNF)-α in serum, therefore it can be useful in the treatment of asthma [26]. Treatment with CWE decreased LPS-induced TNF-α and IL-6 in serum. In vitro inhibition of *TNF-α* gene by CWE may occur through the modulation of IκBα degradation and JNK, p38, and ERK1/2 activation [26]. Cinnamon also has anti-asthmatic effects [28]. From a pharmacological point of view, saffron (*C. sativus*) constituents have shown antitussive [29] and anti-inflammatory [30] activities. More recent investigations show that *C. sativus* extract can reduce the number of inflammatory cells and white blood cells including eosinophils and platelets in the blood, which may show its prophylactic effect on asthma [30, 45]. Safranal (the main constituent of saffron) can reduce the hyperresponsiveness of the airways, as well as inducible nitric oxide synthase (iNOS) production, apoptosis of the bronchial epithelial cells, and the production of Th2 type cytokine in the lungs [31]. Cardamom (*E. cardamomum*) is extensively used in traditional medicine for the treatment

of asthma. A study demonstrated that cardamom exhibits bronchodilator effect, mediated through Ca^{2+} antagonist mechanism, which offers sound mechanistic background for its medicinal use in asthma [32].Recent findings demonstrate the antibacterial properties of galangal (*A. galangal*), especially against *Bacillus subtilis*, *Escherichia coli, Staphylococcus aureus*, *Salmonella typhimurium* and *Vibrio cholerae* [33]. A component of galangal, 1′-acetoxychavicol acetate (ACA) can reduce the eosinophilic infiltration and the IgE level in the lungs of mice subjected to ovalbumin. In addition to that, ACA suppresses the airway remodeling, goblet-cell hyperplasia, and glycoprotein secretion. Furthermore, ACA can inhibit the expression of Th2 cytokines, IL-4 and IL-13 and Th1 cytokines, IL-12α and interferon gamma (IFN-γ). Thus, ACA appears to be a suitable candidate for asthma management as immunologic and inflammatory reactions play a vital role in asthma [34]. The mechanisms underlying the remarkable effects of compound honey syrup on asthma are somewhat unknown but are possibly a result of synergistic or additive effects of the complex nature of its constituents. It was suggested in this study that this drug can be used to improve clinical manifestation of asthma.

Conclusion

The results of this study demonstrate that compound honey syrup can be a safe and effective complementary drug for the treatment of pediatric asthma. Despite short-term prescription of the mentioned drug in this study, ACQ items were significantly altered in the experimental group. It was suggested that other controlled experiments over longer periods and with larger sample sizes should be conducted on the other parameters that are related to the assessment of the drug efficacy such as the effects of this drug on the clinical symptoms of asthma in adults, quality of life of the patients with asthma, serum IgE and serum cytokine levels, and the expression of genes associated with asthma.

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Conflicts of Interest

None declared.

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