Herbal medicines for asthma: a systematic review

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Abstract

Background—Asthma is one of the most common chronic diseases in modern society and there is increasing evidence to suggest that its incidence and severity are increasing. There is a high prevalence of usage of complementary medicine for asthma. Herbal preparations have been cited as the third most popular complementary treatment modality by British asthma sufferers. This study was undertaken to determine if there is any evidence for the clinical efficacy of herbal preparations for the treatment of asthma symptoms.

Methods—Four independent literature searches were performed on Medline, Pubmed, Cochrane Library, and Embase. Only randomised clinical trials were included. There were no restrictions on the language of publication. The data were extracted in a standardised, predefined manner and assessed critically.

Results—Seventeen randomised clinical trials were found, six of which concerned the use of traditional Chinese herbal medicine and eight described traditional Indian medicine, of which five investigated *Tylophora indica*. Three other randomised trials tested a Japanese Kampo medicine, marihuana, and dried ivy leaf extract. Nine of the 17 trials reported a clinically relevant improvement in lung function and/or symptom scores.

Conclusions—No definitive evidence for any of the herbal preparations emerged. Considering the popularity of herbal medicine with asthma patients, there is urgent need for stringently designed clinically relevant randomised clinical trials for herbal preparations in the treatment of asthma.

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Keywords: asthma; herbal medicine

A survey by the National Asthma Campaign found that 60% of people with moderate asthma and 70% with severe asthma have used complementary and alternative medicine to treat their condition.1 Herbal medicine is the third most popular choice of both adults (11%) and children (6%) suffering from asthma.1

The historical importance of herbal medicine in the treatment of asthma is indisputable. Four of the five classes of drugs currently used to treat asthma—namely, β, agonists, anticholinergics, methylxanthines and Cromones—have origins in herbal treatments going back at least 5000 years.2

There is a large archive of information on herbal medicine from many cultures for the treatment of asthma. However, a significant proportion of these reports is not based on adequately designed trials. This review provides a critical analysis of herbal medicinal products used in the treatment of asthma symptoms that have been the subject of randomised clinical trials.

Methods

Computerised literature searches were performed to identify all published articles on the subject. The following databases were used: Medline, Pubmed, Cochrane Library, and Embase, all from their inception to December 1999. Search terms used were “asthma”, “herb*”, “Ayurvedic”, and “traditional Chinese medicine”, as well as any individual herb name cited in the asthma literature. In addition, other researchers in this field were asked for further papers and our own files were searched. The bibliographies of all papers thus located were searched for further relevant articles. Only randomised clinical trials (parallel and crossover) were included. There were no restrictions regarding publication language. All articles were read in full and data extracted in a predefined fashion by the first author. All trials were rated according to methodological rigour using the Jadad score (table 1).3

There are 5 or more symptoms that have been the subject of experimentally induced asthma or patients suffering from other medical conditions in addition to their asthma were excluded. The outcome measures considered were lung function parameters, symptom diaries, medication usage, and asthma events (unscheduled visits to doctors, antibiotics, prednisolone, or days missed from school/work). Immunological studies were not included. This paper concen-
trated on the lung function tests, forced expiratory volume in one second (FEV$_1$), and airway resistance (Raw). Only a change in lung function of 15% or more was considered clinically relevant.

**Results**

Seventeen randomised clinical trials of herbal preparations for the treatment of asthma were found. Six of the trials involved the use of traditional Chinese herbal medicine and eight investigated traditional Indian preparations, five of which described the use of *Tylophora indica*. One trial related to a traditional Japanese (Kampo) herbal preparation, TJ-96. Two further trials involved the use of marianhuana and dried ivy extract.

The overall methodological quality of the trials was poor. Five of the trials included both children and adults (three papers did not state the age or age range of the participants). In none of the studies did the investigators perform a sample size calculation. Only one paper explained the method of randomisation. Dropouts and withdrawals were described in just two papers. Only nine of the trials were double blind. Thus, 14 of the 17 trials scored 3 or less of a maximum of 5 on the Jadad score.'

**TRADITIONAL CHINESE HERBAL MEDICINE**

These studies are listed in table 2. Interpretation of the validity of trials with Chinese herbal medicines is quite difficult because of various confounding factors. The theories behind the causes of asthma and the classification of asthma into heat and cold type make representation of their results problematic. Although adverse effects were described in two of the studies, no dropouts or withdrawals were mentioned in any of the six trials. Moreover, none of the trials was blinded and no explicit description of the randomisation methods was provided. Thus, all six trials with Chinese herbal medicine had a score of 1 on the Jadad scale.

*Ginkgo biloba*

Concentrated ginkgo leaf liquor (15 g thrice daily) was used by Li and co-workers to treat 61 asthmatic patients aged 13–48 years. FEV$_1$ was significantly increased (10%) in the treatment group at four weeks and reached a clinically relevant improvement (15%) at eight weeks (p<0.05). This increase was significantly greater than placebo (p<0.05). The authors suggest that the ginkgolides in the extract act as anti-inflammatory agents and reduce airway hyperresponsiveness and bronchospasm.

*Ligusticum wallichii (L wallichii)*

Shao et al$^9$ performed a randomised controlled trial of *L wallichii* (10 ml thrice daily) in 150 adult patients with moderate or severe asthma. FEV$_1$ was significantly increased in the *L. wallichii* group compared with baseline after one month, although only by 13% (p<0.01). Subjective symptoms were reported to improve with treatment but no details were given. No significant changes were seen in the control group. Parallel studies on guinea pigs in the same paper showed *L. wallichii* to relax tracheal smooth muscle and decrease levels of thromboxane B$_2$.

**Strengthening body resistance method (SBR)**

The effect of the SBR method (20 ml thrice daily) on 117 adult asthmatics was evaluated by Xu and co-workers.$^7$ FEV$_1$ showed a 11% increase in the test group (p<0.05) compared with baseline after a two week period. There were no significant changes in the control group. The SBR herbal decoctions in this study contained mahuang (*Ephedra sinica*) so the effects of this treatment were at least partially due to a bronchodilator mechanism.

**Reinforcing kidney and invigorating spleen principle (RKISP)**

In a second study by Xu et al the effect of RKISP in conjunction with conventional steroid treatment was investigated in 41 severe asthmatic adults in a 4–6 month study.$^7$ FEV$_1$ was significantly increased compared with baseline in both the treatment (15%) and control (steroid treatment alone) (11%) groups (p<0.05). The authors suggest that the RKISP treatment increased the activity of suppressor T cells, decreasing the production of IgE. They conclude that RKISP produces additional benefit to steroid treatment.

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**Table 2 Chinese traditional medicine and asthma**

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. definition, duration of trial</th>
<th>Treatment (n)</th>
<th>Control (n)</th>
<th>Primary measures</th>
<th>Results</th>
<th>Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al$^9$</td>
<td>61 asthmatics, 8 weeks</td>
<td>Ginkgo leaf liquor (39)</td>
<td>Placebo (22)</td>
<td>Lung function tests</td>
<td>Clinically relevant increase in FEV$_1$, at 8 weeks (p&lt;0.05), significantly greater than control (p&lt;0.05)</td>
<td>1</td>
</tr>
<tr>
<td>Shao et al$^9$</td>
<td>150 bronchial asthmatics (moderate to severe), 1 month</td>
<td>L. wallichii mixture (100)</td>
<td>Control tea (50)</td>
<td>Lung function tests; subjective symptoms</td>
<td>Increase in FEV$_1$, with treatment but not clinically significant. Improvement in subjective symptoms with treatment but no criteria or statistics</td>
<td>1</td>
</tr>
<tr>
<td>Xu et al$^6$</td>
<td>117 cold and heat type asthmatics, 2 weeks</td>
<td>SBR decoction (58)</td>
<td>Control herbal tea (59)</td>
<td>Lung function tests</td>
<td>Increase in FEV$_1$, with treatment but not clinically relevant</td>
<td>1</td>
</tr>
<tr>
<td>Xu et al$^5$</td>
<td>41 severe asthmatics, 4–6 months</td>
<td>RKISP decoction and steroid aerosol (21)</td>
<td>Steroid aerosol (20)</td>
<td>Lung function tests</td>
<td>Clinically relevant increase in FEV$_1$, (p&lt;0.05) but not greater than control</td>
<td>1</td>
</tr>
<tr>
<td>Xu and Xu$^7$</td>
<td>57 seasonal asthmatics, 3 months</td>
<td>IKPA tablets and inhaled BDP (32)</td>
<td>Inhaled BDP only (25)</td>
<td>Lung function tests</td>
<td>Clinically relevant increase in FEV$_1$, with treatment (p&lt;0.001), significantly greater than control (p&lt;0.05)</td>
<td>1</td>
</tr>
<tr>
<td>Zou et al$^8$</td>
<td>68 asthmatics of ‘cold type’, 8 weeks</td>
<td>Wenyang Tongluo mixture (34)</td>
<td>Oral salbutamol and aerosol BCP (34)</td>
<td>Lung function tests</td>
<td>Clinically relevant increase in FEV$_1$, with treatment (p&lt;0.05), significantly greater than control (p&lt;0.05)</td>
<td>1</td>
</tr>
</tbody>
</table>

SBR = strengthening body resistance; IKPA = invigorating kidney for preventing asthma; RKISP = reinforcing kidney and invigorating spleen principle; FEV$_1$ = forced expiratory volume in one second; BCP = beclomethasone dipropionate.
Table 3  Traditional Indian medicine and asthma

<table>
<thead>
<tr>
<th>Reference</th>
<th>No, definition, duration of trial</th>
<th>Treatment (n)</th>
<th>Control (n)</th>
<th>Primary measures</th>
<th>Results</th>
<th>Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doshi et al</td>
<td>72 bronchial asthmatics, 14 weeks</td>
<td>(a) 2 wks placebo, 3 wks P kurroa (26) (b) 2 wks placebo, 3-6 wks P kurroa (22)</td>
<td>Lung function tests; daily diary</td>
<td>No significant differences between treatment and placebo</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Govindan et al</td>
<td>60 bronchial asthmatics, 2 hours</td>
<td>S xanthocarpum (20) or S trilobatum (20)</td>
<td>Salbutamol (10) or deriphylline (10)</td>
<td>Lung function tests</td>
<td>Significant increase in FEV1, in both herb preparation groups (p&lt;0.01) but less than standard drugs</td>
<td>1</td>
</tr>
<tr>
<td>Gupta et al</td>
<td>135 bronchial asthmatics, 3 weeks</td>
<td>Encapsulated powdered B serrata gum resin (40)</td>
<td>Encapsulated lactose (40)</td>
<td>Lung function tests</td>
<td>FEV1, significantly increased with treatment vs. control (p&lt;0.0001) but % increase could not be calculated from data given</td>
<td>2</td>
</tr>
<tr>
<td>Gupta et al</td>
<td>80 bronchial asthmatics, 6 weeks</td>
<td>Alkaloid extract from T indica in glucose</td>
<td>Glucose coloured with spinach</td>
<td>Lung function tests; symptom score</td>
<td>% patients with &gt;15% increase in FEV1 : test &gt; control at all times peaking at 4 wks (p&lt;0.01); symptom score: test &gt; control at all times (p&lt;0.05)</td>
<td>4</td>
</tr>
<tr>
<td>Mathew and</td>
<td>123 bronchial asthmatics, 12 weeks</td>
<td>(a) 2 wks placebo, 3 day break, placebo/7 days, 2 day break, T indica/7 days</td>
<td>Lung function tests; symptom score</td>
<td>Daily diary</td>
<td>Symptom relief at 6 days: test 62%, control 28%; at 12 wks: test 16%, control 0% (no statistics)</td>
<td>2</td>
</tr>
<tr>
<td>Shiv puri et al</td>
<td>110 bronchial asthmatics, 12 weeks</td>
<td>T indica leaves chewed and swallowed (53)</td>
<td>Spinach leaves chewed and swallowed (57)</td>
<td>Diary of symptom scores</td>
<td>Complete to moderate relief at 1 wk: test 56%, control 31% (p&lt;0.01); 12 wk: test 14.8%, placebo 7.8% (NS)</td>
<td>3</td>
</tr>
<tr>
<td>Shiv puri et al</td>
<td>195 bronchial asthmatics, 12 weeks</td>
<td>T indica powder (179)</td>
<td>Placebo powder (166)</td>
<td>Daily diary</td>
<td>No significant differences between treatment and placebo</td>
<td>3</td>
</tr>
<tr>
<td>Thiruvengadam et al</td>
<td>30 bronchial asthmatics, 16 days</td>
<td>(a) T indica’7 days, 2 day break, placebo/7 days, 2 day break, T indica/7 days</td>
<td>Lung function tests; symptom score</td>
<td>No statistics given for lung function; nocturnal dyspnoea significantly better with T indica than placebo (p&lt;0.01)</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

FEV1 = forced expiratory volume in one second; NS = not statistically significant.

Invigorating kidney for preventing asthma (IKPA) tablets

Xu and co-workers also investigated the prevention and treatment of seasonal asthma in 57 patients aged 15-45 years with IKPA tablets (five thrice daily) and beclomethasone dipropionate (800 µg daily). The FEV1 of both groups improved significantly over the three month trial period (p<0.001). The test group improved by 30% which was significantly higher than the 17% improvement seen in the control group (p<0.05). The authors suggest an anti-inflammatory, anti-hyperresponsive mode of action.

Wenyang Tonglulo mixture (WTM)

In a study by Zou et al WTM (30 ml twice daily) containing roasted mahuang was compared with oral salbutamol and inhaled beclomethasone in 68 adult asthmatic patients. Both groups improved throughout the eight week study. In the WTM group FEV1 improved by 30% (p<0.01) and in the control group by 16% (p<0.05) over the baseline values. The improvement in the WTM group was significantly greater than in the control group (p<0.05).

TRADITIONAL INDIAN HERBAL (AYURVEDIC) MEDICINE

These are listed in table 3.

Picrorrhiza kurroa (P kurroa)

P kurroa is a small herb with tuberous roots that is used in Ayurvedic medicine for the treatment of various conditions including lung diseases such as asthma and bronchitis.

In a randomised, crossover, double blind trial Doshi et al used P kurroa to treat 72 patients aged 14-60 years suffering from bronchial asthma over a 14 week period. Patients were given either P kurroa root powder (300 mg thrice daily) or an identical placebo in a three arm study (table 3). The main outcome parameters were lung function tests including FEV1 and daily diary symptom scores. There was no significant change in any of the parameters measured.

Solanium xanthocarpum/trilobatum

S xanthocarpum and S trilobatum as a powder of the whole dried plant or decoction are widely used to treat respiratory disorders by practitioners of the Sidda system of medicine in Southern India.

Sixty adult patients with bronchial asthma were randomised in a four-arm study (table 3). Lung function tests were performed before and two hours after drug administration. FEV1 was significantly increased above baseline levels in all groups (p<0.01). S xanthocarpum and S trilobatum increased FEV1 by 65% and 67%, respectively, at two hours but this effect was less than with conventional drugs. Subjective relief was reported after one hour and this effect lasted 6–8 hours. The authors suggest that the mechanism may involve bronchodilation, reduction of bronchial mucosal oedema, and/or reduction of airway secretions.

Boswellia serrata (B serrata)

The gum resin of B serrata is known in the Indian Ayurvedic system of medicine as Salai guggal and contains boswellic acids which have been shown to inhibit leukotriene biosynthesis.

In a six week, double blind, randomised clinical trial of 80 adult patients with bronchial asthma Gupta and co-workers compared the effect of B serrata gum resin with placebo (lactose). The authors reported a significant increase in FEV1 in the B serrata group compared with placebo (p<0.0001). However, the data were presented in such a way that a percentage increase could not be calculated.
Table 4  Other herbal treatments and asthma

<table>
<thead>
<tr>
<th>Reference</th>
<th>No., definition, duration of trial</th>
<th>Treatment (n)</th>
<th>Control (n)</th>
<th>Primary measures</th>
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<th>Jadad score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Egashiri and Nagano26</td>
<td>120 steroid dependent bronchial asthmatics, 12 weeks</td>
<td>TJ-96 (23.6%) vs. placebo (p=0.0361)</td>
<td>Conventional drugs (48)</td>
<td>Lung function tests; symptom diary</td>
<td>No data given on lung function; symptom improvement and perceptions greater in test than control group (p&lt;0.01)</td>
<td>2</td>
</tr>
<tr>
<td>Taskin et al24</td>
<td>10 bronchial asthmatics (stable to moderate) defined by ATS criteria, 2 hours</td>
<td>Smoking marihuana (2% THC) (10)</td>
<td>Smoking marihuana (0% THC) (10)</td>
<td>Lung function tests</td>
<td>Smoking and ingestion of marihuana resulted in lower Raw but not clinically relevant</td>
<td>3</td>
</tr>
<tr>
<td>Mansfeld et al23</td>
<td>24 bronchial asthmatics, 3 days</td>
<td>Dried ivy extract (24)</td>
<td>Placebo (24)</td>
<td>Lung function tests</td>
<td>Raw significantly better with ivy extract (23.6%) vs. placebo (p=0.0361)</td>
<td>4</td>
</tr>
</tbody>
</table>

THC = tetrahydrocannabinol; Raw = airway resistance.

*Tulsiophora indica (T indica)*

*T. indica* is a plant indigenous to India and reputed to be able to provide relief to patients with bronchial asthma. Five randomised clinical trials have been published on the use of *T. indica* in the treatment of asthmatic symptoms. A substantial amount of work was carried out on *T. indica* in asthma by Shippuri and co-workers in the late 1960s and early 1970s including three randomised clinical trials.

The first was a double blind, crossover study in 110 patients aged 10–44+ years with bronchial asthma who ate one *T. indica* leaf daily. At the end of one week 62% of the *T. indica* group had complete to moderate relief of symptoms compared with 28% in the placebo (spinach) group. After crossover, at the end of week 1, 50% of the *T. indica* group had improved compared with 11% of the placebo group. At 12 weeks the improvements in the two groups were 16% and 0%, respectively. No statistical analysis was performed.

The second trial reported by this group involved the use of an alcoholic tincture of *T. indica*. In this study 195 patients (no ages given) with bronchial asthma were recruited into a double blind, crossover trial. After one week 56.3% of patients in the *T. indica* group had complete to moderate relief of symptoms compared with 31.6% in the placebo group. After the crossover 34.2% had improved with *T. indica* and 13.5% with placebo (both statistically significant, p<0.01). After 12 weeks the results were 14.8% and 7.2%, respectively (p<0.02).

In the third double blind trial by the same research group 123 patients (no ages given) with bronchial asthma were treated with alkaloids extracted from *T. indica*. The percentage of patients in whom FEV1 improved by more than 15% was significantly higher in the treated group than in the placebo group at one, two, four, eight and 12 weeks, peaking at four weeks (p<0.01). In addition, symptom scores and medication usage were also significantly improved in the test group compared with the placebo group at all time points, both being greatest at one week (p<0.05 and p<0.01, respectively).

In the study by Thiruvengadam et al 30 patients (no ages given) with bronchial asthma were enrolled into a four-arm, double blind, randomised clinical trial for 16 days. Dried *T. indica* in capsules was compared with standard drugs and a placebo (table 3). The main outcome measures were lung function testing and symptom scores. Nocturnal dyspnoea was the only parameter that significantly improved with *T. indica* compared with placebo (p<0.01).

Gupta and co-workers performed a double blind study of 135 bronchial asthma patients aged 14–60 years in whom powdered *T. indica* was compared with placebo over six days with a follow up of two weeks. The authors found no statistically significant change in symptom score or lung function parameters with either *T. indica* or the placebo and no differences were seen between the groups.

From these five trials the efficacy of *T. indica* in the treatment of asthma symptoms is thus inconclusive.

**TRADITIONAL JAPANESE (KAMPO) HERBAL MEDICINE**

These are listed in table 4.

*Tsumura saiboku-to (TJ-96)*

TJ-96 is the one of the most popular and best studied anti-asthmatic Kampo herbal medicines and is used both in Japan and China. It is a combination of two herbal preparations containing 10 herbs and has been used in China for steroid dependent asthma resulting in a steroid sparing effect. Despite its intensive use, there is only one randomised clinical trial in the literature from Japan. This 12 week study involved 112 adults with steroid dependent bronchial asthma. The main outcome measures were pulmonary function tests and asthma attacks and symptom scores calculated from symptom diaries. Unfortunately no results of the pulmonary function tests were reported and there was no description of drop-out or withdrawal rates. Symptomatic improvement and patient perceptions were reported to be significantly better in the treatment group than in the control group (both p<0.01).

**Marihuana**

Marihuana was used for the treatment of asthma in the last century. The effects of its principal psychoactive ingredient (∆9-tetrahydrocannabinol, THC) on pulmonary function have been investigated in normal healthy subjects. Only one randomised clinical trial with marihuana appears in the literature concerning its use (THC % predetermined by gas liquid chromatography) in 10 adult patients with bronchial asthma. Airway resistance (Raw) decreased compared with placebo and baseline after smoking the 2% THC preparation for approximately two hours, but the difference was not significant. Raw was
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significantly reduced by 10–13% (p<0.05) compared with placebo 1–4 hours after ingesting the 2% THC capsule. The authors suggest that the significant decrease in airway resistance (and increase in conductance) indicate that THC has a systematically active bronchodilator effect in asthmatic subjects.

DRIED IVY LEAF EXTRACT

In a double blind, crossover, randomised clinical trial dried ivy extract (∼35 mg) was investigated in the treatment of bronchial asthma in 24 children over three days. Although there was no significant improvement in FEV₁, there was a significant decrease in Raw (23.6%) compared with placebo (p=0.0361). The authors suggest that ivy extract may work in a secretolytic and bronchospasmodic manner.

Discussion

Seventeen randomised clinical trials on the use of herbal medicinal products in the treatment of asthma were found in the literature. Most had significant methodological flaws and the majority were not conducted with products of standardised quality.

Trials with Ginkgo liquor,1 IKPA tablets,2 WTM,3 and dried ivy extract4 produced clinically relevant improvements in lung function, significantly better than placebo or control treatment. Four of the trials with T indica5–7 and the TJ-96 study8 resulted in a significant improvement in asthma symptoms. L tuallichii,9 SBR and RKISP decoctions,10 P kurroa,11 Solanum sp.,12 one trial with T indica,13 and marianhua14 did not produce any clinically relevant or statistically significant improvement in lung function or asthma symptoms compared with the control. Two trials, one with T indica15 and the other with B serrata16 reported a clinically significant improvement in FEV₁, but the data were presented in such a way that the percentage change could not be calculated.

There is no fully convincing evidence for any of the herbal preparations described in this paper. Lack of blinding, description of adverse effects, and dropout/withdrawal rates were frequent limitations. Outcome measures were variable and, in several cases, of doubtful relevance. Although some trials yielded positive results, their flaws mean that further meticulous investigations are required before positive recommendations can be made.

None of the herbal medicinal products discussed here are likely to be free from adverse effects or interactions with prescribed drugs. For example, it is known that Ginkgo biloba, which is generally considered as one of the safest herbal medicinal products on the market, has a list of adverse reactions ranging from headaches and nausea to bleeding and seizure.17 Ginkgo also has potential interactions with anticoagulant and antipiletmedicines because of its effect on platelet activating factor.18 Uncertainty therefore pertains as to the efficacy and safety of these products and it is not possible to conduct adequate risk-benefit assessments.

It is concluded that herbal medicinal products, even though in prevalent use, are of uncertain value in the treatment of asthma. For some there are promising data which warrant further investigation.

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