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.

(Thorax 2000;55:925–929)

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

Table 1 Scoring system to measure the likelihood of bias (Jadad)

<table>
<thead>
<tr>
<th>Question</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Study described as randomised (this includes the use of words such as “random”, “randomly” and “randomisation”)</td>
<td>1</td>
</tr>
<tr>
<td>2. Study described as double blind?</td>
<td>1</td>
</tr>
<tr>
<td>3. Description of withdrawals and dropouts?</td>
<td>1</td>
</tr>
<tr>
<td>4. Method to generate the sequence of randomisation described and appropriate (table of random numbers, computer generated, etc)?</td>
<td>1</td>
</tr>
<tr>
<td>5. Method of double blinding described and appropriate (identical placebo, active placebo, dummy etc)?</td>
<td>1</td>
</tr>
<tr>
<td>6. Method to generate the sequence of randomisation described and inappropriate (patients were allocated alternately or according to their date of birth, hospital number, etc).</td>
<td>1</td>
</tr>
<tr>
<td>7. Method of double blinding described and inappropriate (e.g. comparison of tablet vs. injection with no double dummy).</td>
<td>1</td>
</tr>
</tbody>
</table>

For questions 1–5 Y es = 1 point and No = 0 points. Deduct 1 point if questions 6 or 7 apply.

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

Asthmatic subjects were preferably defined by ATS criteria. If this was not possible they were defined as those who had reversible airway constriction. Any studies involving 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 mahuang 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 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. FEV$_1$, showed a 11% increase in the test group (p<0.05) compared with baseline over 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. 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$^a$</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$^b$</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$^c$</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$^d$</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$^e$</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$^f$</td>
<td>68 asthmatics of ‘cold type’, 8 weeks</td>
<td>Wenyang Tonglulo 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.
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 FEV\(_1\), 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 FEV\(_1\), 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 FEV\(_1\), 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. FEV\(_1\), was significantly increased above baseline levels in all groups (p<0.01). *S xanthocarpum* and *S trilobatum* increased FEV\(_1\), 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 FEV\(_1\), 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.

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**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(^{a})</td>
<td>72 bronchial asthmatics, 14 weeks</td>
<td>2 wks of placebo followed by 12 wks of <em>P kurroa</em> (24)</td>
<td>2 wks placebo, 3 wks <em>P kurroa</em> (26)</td>
<td>Lung function tests; daily diary</td>
<td>No significant differences between treatment and placebo</td>
<td>3</td>
</tr>
<tr>
<td>Govindan et al(^{a})</td>
<td>60 bronchial asthmatics, 2 hours</td>
<td><em>S xanthocarpum</em> (20) or <em>S trilobatum</em> (20)</td>
<td><em>Salbutamol</em> (10) or dextrophine (10)</td>
<td>Lung function tests</td>
<td>Significant increase in FEV(_1),; in both herb preparation groups (p&lt;0.001) but less then standard drugs</td>
<td>1</td>
</tr>
<tr>
<td>Gupta et al(^{a})</td>
<td>135 bronchial asthmatics, 3 weeks</td>
<td>Powdered <em>T indica</em> (71)</td>
<td>Powdered placebo (64)</td>
<td>Lung function tests; symptom score</td>
<td>No differences between treatment and placebo</td>
<td>4</td>
</tr>
<tr>
<td>Gupta et al(^{a})</td>
<td>80 bronchial asthmatics, 6 weeks</td>
<td>Encapsulated powdered <em>B serrata</em> gum resin (40)</td>
<td>Encapsulated lactose (40)</td>
<td>Lung function tests</td>
<td>FEV(_1), 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>Mathew and Shivppuri(^{a})</td>
<td>123 bronchial asthmatics, 12 weeks</td>
<td>Alkaloid extract from <em>T indica</em> in glucose</td>
<td>Glucose coloured with spinach</td>
<td>Lung function tests; symptom score</td>
<td>% patients with &gt;15% increase in FEV(_1), at test&gt; control at all times peaking at 4 wks (p&lt;0.0001); symptom score: test &gt; control at all times (p&lt;0.05)</td>
<td>4</td>
</tr>
<tr>
<td>Shivppuri et al(^{a})</td>
<td>110 bronchial asthmatics, 12 weeks</td>
<td><em>T indica</em> leaves chewed and swallowed (53)</td>
<td>Spinach leaves chewed and swallowed (57)</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>Shivppuri et al(^{a})</td>
<td>195 bronchial asthmatics, 12 weeks</td>
<td><em>T indica</em> powder (179)</td>
<td>Placebo powder (166)</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>Thiruvengadam et al(^{a})</td>
<td>30 bronchial asthmatics, 16 days</td>
<td>(a) <em>T indica</em>’s days, 2 day break, placebo’7 days (b) placebo’7 days, 2 day break, <em>T indica</em>’s days</td>
<td>(c) <em>T indica</em>’s days, 2 day break, standard drugs’7 days (d) standard drugs’7 days, 2 day break, <em>T indica</em>’s days</td>
<td>Lung function tests; symptom score</td>
<td>No statistics given for lung function; nocturnal dyspnoea significantly better with <em>T indica</em> than placebo (p&lt;0.01)</td>
<td>3</td>
</tr>
</tbody>
</table>

FEV\(_1\), = forced expiratory volume in one second; NS = not statistically significant.
Table 4 Other herbal treatments and asthma

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of patients</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>Egashiri and Nagano²⁰</td>
<td>112</td>
<td>TBJ-96 plus conventional drugs (64)</td>
<td>Conventional drugs only (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 al²²</td>
<td>10 bronchial asthmatics (stable to moderate) defined by ATS criteria, 2 hours</td>
<td>(a) Smoking marihuana (2% THC), (10)</td>
<td>(b) Ingestion of placebo capsules (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>Mansfield 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.

TBJ-96 is 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).

Tsumura saiboku-to (TBJ-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 (Δ⁹-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 decreased compared with placebo and baseline after smoking the 2% THC preparation for approximately two hours, but the difference was not significant. Raw was...
Herbal medicines for asthma

For example, it is known that herbal medicines for asthma can significantly reduce symptoms and improve respiratory function. However, the quality of evidence supporting these claims is often limited by small sample sizes, lack of blinding, and inadequate reporting of adverse effects.

**Dried Ivy Leaf Extract**

In a double-blind, crossover, randomised clinical trial, dried ivy leaf 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 bronchospasmylic 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, IKPA tablets, WTM, and dried ivy extract produced clinically relevant improvements in lung function, significantly better than placebo, or control treatment. Four of the trials with *T indica* and the TJ-96 study resulted in a significant improvement in asthma symptoms. *L. tschuktschi*, SBR and RKISP decoctions, *P. kurroa*, *Solanum sp.*, one trial with *T indica*, and marianhua 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 indica* and the other with *B serrata*, 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 means fail to 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. *Ginkgo* also has potential interactions with anticoagulant and antiplatelet medicines because of its effect on platelet activating factor. 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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