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_2 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 (Jadad³)

1. Study described as randomised (this includes the use of words such as "random", "randomly" and "randomisation")
2. Study described as double blind?
3. Description of withdrawals and dropouts?
4. Method to generate the sequence of randomisation described and appropriate (table of random numbers, computer generated, etc)?
5. Method of double blinding described and appropriate (identical placebo, active placebo, dummy etc)?
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).
7. Method of double blinding described and inappropriate (e.g. comparison of tablet vs. injection with no double dummy).

For questions 1-5 Yes = 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-

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Table 2 Chinese traditional medicine and asthma

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

SBR = strengthening body resistance; IKPA = invigorating kidney for preventing asthma; RKISP = reinforcing kidney and invigorating spleen principle; FEV₁ = forced expiratory volume in one second; BCP = beclomethasone dipropionate.

trated on the lung function tests, forced expiratory volume in one second (FEV₁), 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 marihuana 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.³

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.⁴ FEV₁

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*^b performed a randomised controlled trial of *L wallichii* (10 ml thrice daily) in 150 adult patients with moderate or severe asthma. FEV₁ 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 B₂.

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.⁶ FEV₁ 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.⁷ FEV₁ 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.

Table 3 Traditional Indian medicine and asthma

Reference	No, definition, duration of trial	Treatment (n)	Control (n)	Primary measures	Results	Jadad score
Doshi <i>et al</i> ¹⁰	72 bronchial asthmatics, 14 weeks	2 wks of placebo followed by 12 weeks of <i>P kurroa</i> (24)	(a) 2 wks placebo, 3 wks <i>P kurroa</i> , 9 wks placebo (26) (b) 2 wks placebo, 3–6 wks <i>P kurroa</i> , 9–12 wks placebo (22)	Lung function tests; daily diary	No significant differences between treatment and placebo	3
Govindan <i>et al</i> ¹¹	60 bronchial asthmatics, 2 hours	<i>S xanthocarpum</i> (20) or <i>S trilobatum</i> (20)	Salbutamol (10) or deriphylline (10)	Lung function tests	Significant increase in FEV ₁ in both herb preparation groups ($p \leq 0.01$) but less than standard drugs	1
Gupta <i>et al</i> ¹⁸	135 bronchial asthmatics, 3 weeks	Powdered <i>T indica</i> (71)	Powdered placebo (64)	Lung function tests; symptom score	No differences between treatment and placebo	4
Gupta <i>et al</i> ¹³	80 bronchial asthmatics, 6 weeks	Encapsulated powdered <i>B serrata</i> gum resin (40)	Encapsulated lactose (40)	Lung function tests	FEV ₁ significantly increased with treatment vs. control ($p < 0.0001$) but % increase could not be calculated from data given	2
Mathew and Shivpuri ¹⁶	123 bronchial asthmatics, 12 weeks	Alkaloid extract from <i>T indica</i> in glucose	Glucose coloured with spinach	Lung function tests; symptom score	% patients with >15% increase in FEV ₁ : test > control at all times peaking at 4 wks ($p < 0.01$); symptom score: test > control at all times ($p < 0.05$)	4
Shivpuri <i>et al</i> ¹⁴	110 bronchial asthmatics, 12 weeks	<i>T indica</i> leaves chewed and swallowed (53)	Spinach leaves chewed and swallowed (57)	Daily diary	Symptom relief at 6 days: test 62%, control 28%; at 12 wks: test 16%, control 0% (no statistics)	2
Shivpuri <i>et al</i> ¹⁵	195 bronchial asthmatics, 12 weeks	<i>T indica</i> powder (179)	Placebo powder (166)	Diary of symptom scores	Complete to moderate relief at 1 wk: test 56%, control 31% ($p \leq 0.01$), 12 wk: test 14.8%, placebo 7.8% (NS)	3
Thiruvengadam <i>et al</i> ¹⁷	30 bronchial asthmatics, 16 days	(a) <i>T indica</i> /7 days, 2 day break, placebo/7 days (b) placebo/7 days, 2 day break, <i>T indica</i> /7 days	(c) <i>T indica</i> /7 days, 2 day break, standard drugs/7 days (d) standard drugs/7 days, 2 day break, <i>T indica</i> /7 days	Lung function tests; symptom score	No statistics given for lung function; nocturnal dyspnoea significantly better with <i>T indica</i> than placebo ($p < 0.01$)	3

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).⁸ 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 Tonghulo 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.⁹ 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.²

In a randomised, crossover, double blind trial Doshi *et al*¹⁰ 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.

Solanum 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).¹¹ 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.¹²

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).¹³ 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

Reference	No, definition, duration of trial	Treatment (n)	Control (n)	Primary measures	Results	Jadad score
Egashiri and Nagano ²⁰	112 steroid dependent bronchial asthmatics, 12 weeks	TJ-96 plus conventional drugs (64)	Conventional drugs only (48)	Lung function tests; symptom diary	No data given on lung function; symptom improvement and perceptions greater in test than control group (p<0.01)	2
Taskin <i>et al</i> ²⁴	10 bronchial asthmatics (stable to moderate) defined by ATS criteria, 2 hours	(a) Smoking marihuana (2% THC), (10) (b) Ingestion of 2% THC capsules (10)	(a) Smoking marihuana (0% THC), (10) (b) Ingestion of placebo capsules (10)	Lung function tests	Smoking and ingestion of marihuana resulted in lower Raw but not clinically relevant	3
Mansfield <i>et al</i> ²⁵	24 bronchial asthmatics, 3 days	Dried ivy extract (24)	Placebo (24)	Lung function tests	Raw significantly better with ivy extract (23.6%) vs. placebo (p=0.0361)	4

THC = tetrahydrocannabinol; Raw = airway resistance.

Tylophora 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.¹⁴⁻¹⁸ A substantial amount of work was carried out on *T indica* in asthma by Shivpuri and co-workers in the late 1960s and early 1970s including three randomised clinical trials.¹⁴⁻¹⁶

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.¹⁴ 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*.¹⁵ 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 improvement in 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<0.2).

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*.¹⁶ 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).¹⁷ 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.¹⁸ 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.² It is a combination of two herbal preparations containing 10 herbs¹⁹ 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.²⁰ 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.²¹ The effects of its principal psychoactive ingredient (Δ^9 -tetrahydrocannabinol, THC) on pulmonary function have been investigated in normal healthy subjects.²²⁻²³ 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.²⁴ 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

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.²⁵ 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 bronchospasmolytic 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,⁴ IKPA tablets,⁸ WTM,⁹ and dried ivy extract²⁵ produced clinically relevant improvements in lung function, significantly better than placebo or control treatment. Four of the trials with *T. indica*^{14–17} and the TJ-96 study²⁰ resulted in a significant improvement in asthma symptoms. *L. wallichii*,⁵ SBR and RKISP decoctions,^{6–7} *P. kurroa*,¹⁰ *Solanum* sp.,¹¹ one trial with *T. indica*,¹⁸ and marihuana²⁴ 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*¹⁶ and the other with *B. serrata*,¹³ 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.²⁶ Ginkgo also has potential interactions with anticoagulant and antiplatelet medicines because of its effect on platelet activating factor.²⁶ 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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- Ernst E. Complementary therapies in asthma: what patients use. *J Asthma* 1998;35:667–71.
- Bielory L, Lupoli K. Review article: herbal interventions in asthma and allergy. *J Asthma* 1999;36:1–65.
- Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomised clinical trials: is blinding necessary? *Controlled Clin Trials* 1996;17:1–12.
- Li M, Zhang H, Yang B. Effects of Ginkgo leaf concentrated oral liquor in treating asthma. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1997;17:216–8.
- Shao C, Chen F, Tang Y, et al. Clinical and experimental study on *Ligusticum wallichii* mixture in preventing and treating bronchial asthma. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1994;14:465–8.
- Xu DS, Shen ZY, Wang WJ, et al. Study on effect of strengthening body resistance method on asthmatic attack. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1996;16:198–200.
- Xu D, Shen Z, Wang W, et al. Study on effect of reinforcing kidney and invigorating spleen principle on severe asthma. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1997;17:584–6.
- Xu D, Xu RH. Prevention and treatment of seasonal asthmatic patients by combined invigorating kidney for preventing asthma tablets and beclomethasone dipropionate. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1997;17:721–3.
- Zou JP, Gu FQ, Liao WJ. Clinical study on treating asthma of cold type with Wenyang Tonglulo mixture. *Chung Kuo Ching Hsi I Chieh Ho Tsa Chih* 1996;16:529–32.
- Doshi VB, Shetye M, Mahashur AA, et al. *Picrorrhiza kurroa* in bronchial asthma. *J Postgrad Med* 1983;29:89–95.
- Govindan S, Viswanathan S, Vijayasekaran V, et al. A pilot study on the clinical efficacy of *Solanum xanthocarpum* and *Solanum trilobatum* in bronchial asthma. *J Ethnopharmacology* 1999;66:205–10.
- Ammon HPT, Mack T, Singh GB, et al. Inhibition of LTB₄-formation in rat peritoneal neutrophils by an ethanolic extract of the gum resin extract of *Boswellia serrata*. *Planta Med* 1999;57:203–7.
- Gupta I, Gupta V, Parihar A, et al. Effects of *Boswellia serrata* gum resin in patients with bronchial asthma: results of a double-blind, placebo-controlled, 6-week clinical study. *Eur J Med Res* 1998;3:511–4.
- Shivpuri DN, Menon MPS, Parkash D. Preliminary studies in *Tylophora indica* in the treatment of asthma and allergic rhinitis. *J Assoc Physicians* 1968;16:9–15.
- Shivpuri DN, Singal SC, Parkash D. Treatment of asthma with an alcoholic extract of *Tylophora indica*: a cross-over, double blind study. *Ann Allergy* 1972;30:407–12.
- Mathew KK, Shivpuri DN. Treatment of asthma with alkaloids of *Tylophora indica*: a double-blind study. *Aspects Allergy Appl Immunol* 1974;7:166–79.
- Thiruvengadam KV, Haranath K, Sudarsan S, et al. *Tylophora indica* in bronchial asthma. *J Indian Med Assoc* 1978;71:172–7.
- Gupta S, George P, Gupta V, et al. *Tylophora indica* in bronchial asthma: a double-blind study. *Indian J Med Res* 1979;69:981–9.
- Toda S, Kimura M, Ohnishi M, et al. Effects of the Chinese herbal medicine "saiboku-to" on histamine release from and the degranulation of mouse peritoneal mast cells induced by compound 48/80. *J Ethnopharmacol* 1988;24:303–9.
- Egashira Y, Nagano H. A multicenter clinical trial of TJ-96 in patients with steroid-dependent bronchial asthma. *Ann NY Acad Sci* 1993;685:580–3.
- Grinspoon L. Marijuana. *Sci Am* 1969;221:17–25.
- Vachon L, Fitzgerald MX, Solliday NH, et al. Single-dose effect of marijuana smoke. Bronchial dynamics and respiratory-center sensitivity in normal subjects. *N Engl J Med* 1973;288:985.
- Tashkin DP, Shapiro BJ, Frank IM. Acute pulmonary physiological effects of smoked marijuana and oral tetrahydrocannabinol in healthy young men. *N Engl J Med* 1973;289:336.
- Tashkin DP, Shapiro BJ, Frank IM. Acute effects of marihuana on airway dynamics in spontaneous and experimentally induced bronchial asthma. In: Braude MC, Szara S, eds. *The pharmacology of marihuana*. New York: Raven Press, 1976: 785–801.
- Mansfeld HJ, Hohre H, Repges R, et al. Therapy of bronchial asthma with dried ivy leaf. *Munch Med Wschr* 1998;140:26–30.
- Fetrow CW, Avila JR. *Professional's handbook of complementary and alternative medicines*. 1st ed. Pennsylvania: Springhouse Corporation, 1999: 278–87.