



Herbal medicines, probiotics and functional foods for allergic rhinitis

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Many of the studies that show herbal medicines, probiotics and functional foods can improve the symptoms of allergic rhinitis are small, and the results should be interpreted with caution.

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Patients with allergic rhinitis frequently use complementary medicines.^{1,2} In this article, the clinical research on herbal medicines (including extracts), probiotics and other functional foods is reviewed to provide a summary of the evidence for the efficacy and safety of these products and assist readers in locating relevant studies so they can form their own conclusions. The review excludes studies concerning vitamin or mineral supplements, homeopathy and manual therapies.

Of 29 studies included in this review, 24 provided quality control data and 14 used a specific commercial product (Tables 1 to 3). Some of the products currently marketed under the name Aller-7 have ingredients in addition to the seven herbs used in the studies mentioned here.

SINGLE HERB PREPARATIONS

Of the single herb preparations used by patients with allergic rhinitis, extracts prepared from butterbur (*Petasites hybridus*) have received considerable preclinical and clinical research attention in Switzerland and Germany (Table 1). The plant contains toxic pyrrolizidine alkaloids, but these have been removed from the commercial extracts, so the results from clinical studies do not apply to the crude herb. In a systematic review based on six double-blind studies published up to 2005, the results of the clinical studies on butterbur extracts were described as 'encouraging'.³

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TABLE 1. SUMMARY OF CLINICAL STUDIES OF SINGLE HERBS AND EXTRACTS FOR ALLERGIC RHINITIS

Intervention	Ref	QC	Study type	Comparison	Duration of treatment (location)	n	AR type	Summary of effects
Butterbur extract Ze339	5	Y, CP	RCT, multicentre, double blind, parallel groups	Cetirizine 10 mg	2 weeks (Switzerland, Germany)	131	Seasonal	Similar to cetirizine on global symptoms
Butterbur extract Ze339 (high v. low dose)	4	Y, CP	RCT, multicentre, double blind, parallel groups	Placebo	2 weeks (Switzerland, Germany)	186	Intermittent	Superior to placebo on global symptoms, dose dependent
Butterbur extract Ze339	6	Y, CP	RCT, multicentre, double blind, parallel groups	Fexofenadine 180 mg, placebo	2 weeks (Switzerland, Germany)	330	Intermittent	Superior to placebo and similar to fexofenadine on global symptoms
<i>Perilla frutescens</i> extract (2 dosages)	7	Y	RCT, double blind, parallel groups	Placebo	21 days (Japan)	29	Seasonal	Superior to placebo on global symptoms
Stinging nettle (<i>Urtica dioica</i>)	8	N, CP	RCT, double blind, parallel groups	Placebo	1 week (USA)	98	AR (in peak season)	Slightly superior to placebo on global assessment
<i>Tinospora cordifolia</i> extract	9	Y, CP	RCT, double blind, parallel groups	Placebo	8 weeks (India)	75	AR	Superior to placebo on global symptoms
Grape seed extract	10	N, CP	RCT, double blind, parallel groups	Placebo	8 weeks (USA)	54	Seasonal	No difference in rhinitis QoL assessments or symptom diary scores
<i>Astragalus membranaceus</i> extract	11	Y	RCT, double blind, parallel groups	Placebo	6 weeks (Croatia)	48	Seasonal	Superior to placebo on rhinorrhoea
<i>Rubus suavissimus</i> extract	12	N, CP	RCT, multicentre, double blind, parallel groups	Placebo	4 weeks (Japan)	89	Dust mite	Nonsignificant trend for symptom scores
Red ginseng (<i>Panax ginseng</i>)	13	Y	RCT, double blind, parallel groups	Placebo	4 weeks (Korea)	59	Perennial	No difference in total nasal symptoms, but better for congestion and QoL
'Benifuuki' Japanese green tea (before v. during pollen season)	14	Y	Open label, randomised, parallel groups	Other green tea	1.5 months (Japan)	38	Seasonal	Superior to other teas on symptom scores, activities of daily living and medication use when taken prior to pollen season
Isoquercitrin (enzymatically modified)	16	Y	RCT, double blind, parallel groups, pilot	Placebo	8 weeks (Japan)	20	Seasonal	Superior to placebo on ocular symptoms
Isoquercitrin (enzymatically modified)	17	Y	RCT, double blind, parallel groups	Placebo	8 weeks (Japan)	24	Seasonal	Superior to placebo on ocular symptom, but not serum IgE levels
Silymarin (extract from <i>Silybum marianum</i>)	18	N	RCT, parallel groups, pilot	Placebo plus cetirizine 10 mg	1 month (Iran)	60	Persistent	Superior to control on symptom scores, rise in serum IgE levels, no difference in IL4, IL5 or IFN-gamma

ABBREVIATIONS: AR = allergic rhinitis; CP = commercial product; IFN = interferon; IgE = immunoglobulin E; IL = interleukin; n = number of participants; N = no; QoL = quality of life; QC = quality control specified (yes/no); RCT = randomised controlled trial; Y = yes.

TABLE 2. SUMMARY OF CLINICAL STUDIES OF MULTI-HERB FORMULATIONS FOR ALLERGIC RHINITIS

Intervention	Ref	QC	Study type	Comparison	Duration of treatment (location)	n	AR type	Summary of effects
Aller-7 (extracts of 7 herbs)	22	Y, CP	Open label, multicentre		12 weeks (India)	374	Chronic	Improvement in symptom scores over baseline
Aller-7 (extracts of 7 herbs)	22	Y, CP	RCT, multicentre, double blind, parallel groups	Placebo	12 weeks (India)	171	Chronic	Superior to placebo on symptom scores, but not on serum IgE
CHM (18 herbs including astragalus and magnolia)	25	Y	RCT, double blind, parallel groups	Placebo	8 weeks (Australia)	55	Seasonal	Superior to placebo on symptom scores and patient rating of overall response
CHM: Biminne (11 herbs including astragalus)	26	Y, CP	RCT, double blind, parallel groups	Placebo	12 weeks (Australia)	58	Perennial	Superior to placebo on sneezing, global QoL and serum IgE levels, trend for other symptom scores
CHM: Shi-Bi-Lin (6 herbs including magnolia)	29	Y	RCT, double blind, parallel groups	Placebo	4 weeks (Hong Kong)	126	Perennial	Superior to placebo on rhinorrhoea, sneezing, some QoL domains, but not on serum IgE levels
CHM: Xin-yi-san (9 herbs including magnolia)	30	Y, CP	RCT, double blind, parallel groups	Placebo	3 months (Taiwan)	100	Perennial	Superior to placebo on nasal symptoms, nasal airflow resistance and serum dust mite-specific IgE levels
CHM: Bu-zhong-yi-qi-tang (10 herbs including astragalus)	31	Y, CP	RCT, parallel groups	Nonspecific CHM	3 months (Taiwan)	60	Perennial	Superior to control on nasal symptoms, serum IgE levels
CHM nasal drops (11 herbs)	35	Y, CP	RCT, double blind, cross-over	Placebo of 2 nonspecific CHMs	2+2 weeks (Hong Kong)	35	Perennial	Superior to placebo on nasal symptoms

ABBREVIATIONS: AR = allergic rhinitis; CHM = chinese herbal medicines; CP = commercial product; IgE = immunoglobulin E; n = number of participants; N = no; QoL = quality of life; QC = quality control specified (yes/no); RCT = randomised controlled trial; Y = yes.

In multicentre studies, the butterbur extract Ze339 was found to be superior to placebo in patients with intermittent allergic rhinitis (n = 186) and similar to the antihistamine cetirizine (n = 131) in patients with seasonal allergic rhinitis.^{4,5} In another study of patients with intermittent allergic rhinitis (n = 330) Ze339 was found to be superior to placebo and as effective as the antihistamine fexofenadine.⁶

The same review identified randomised controlled trials of three other single herb extracts: *Perilla frutescens* used in patients with seasonal allergic rhinitis (n = 29), stinging nettles (*Urtica dioica*) (n = 98) and *Tinospora cordifolia* (n = 75), both of which were used in patients with allergic rhinitis.⁷⁻⁹ All these single herbs were reported to be superior to placebo in relation to at least some symp-

toms.³ However, a randomised controlled trial of grape seed extract (n = 54) found no benefit over placebo in patients with seasonal allergic rhinitis.¹⁰ No subsequent studies of these plants could be located.

More recently, a Croatian study (n = 48) of an extract of *Astragalus membranaceus* root found significant improvements in rhinorrhoea in patients with seasonal allergic rhinitis after six weeks compared

TABLE 3. SUMMARY OF CLINICAL STUDIES OF PROBIOTICS AND OTHER FUNCTIONAL FOODS FOR ALLERGIC RHINITIS

Intervention	Ref	QC	Study type	Comparison	Duration of treatment (location)	n	AR type	Summary of effects
<i>Bifidobacterium longum</i> (BB536) in yoghurt	42	Y	RCT, double blind, parallel groups	Placebo yoghurt	14 weeks (Japan)	40	Seasonal	Superior to placebo on ocular symptoms, trend for nasal symptoms
<i>Lactobacillus paracasei</i> (KW3110) powder	43	Y	RCT, double blind, parallel groups	Placebo	12 weeks (Japan)	126	Seasonal	Superior to placebo on nasal discharge (confirmed by examination), trend for other symptoms, improved QoL for outdoor activities, lower eosinophil count
<i>Lactobacillus plantarum</i> (HSK201) in milk	44	Y	RCT, single blind, parallel groups, pilot	Placebo milk	8 weeks (Japan)	19	Seasonal	Superior to placebo on sneezing and runny nose, trend for ocular symptoms
<i>Lactobacillus gasseri</i> (OLL2809) tablets	45	Y	RCT, double blind, parallel groups	Placebo	8 weeks (Japan)	107	Seasonal	Superior to placebo on nasal symptoms in high CAP-RAST subgroup
<i>Lactobacillus johnsonii</i> (EM1) plus levocetirizine 5 mg	46	Y	Open label, randomised, cross-over	Levocetirizine alone	12+12 weeks (Taiwan)	63	Perennial	Superior to control on total symptoms in first 12 weeks, no difference in second 12 weeks
<i>Spirulina platensis</i> tablets	49	Y	RCT, double blind, parallel groups	Placebo	6 months (Turkey)	129	AR (not in season)	Superior to placebo on nasal symptoms.
<i>Saccharomyces cerevisiae</i> (EpiCor)	50	N, CP	RCT, double blind, parallel groups	Placebo	12 weeks (USA)	96	Seasonal	Superior to placebo on nasal congestion and rhinorrhoea when pollen counts were high, trend for serum IgE levels

ABBREVIATIONS: AR = allergic rhinitis; CAP-RAST = CAP-radioallergosorbent test; CP = commercial product; IgE = immunoglobulin E; n = number of participants; N = no; QoL = quality of life; QC = quality control specified (yes/no); RCT = randomised controlled trial; Y = yes.

with placebo.¹¹ A study of *Rubus suavis-simus*, which is an ingredient in teas popularly used by patients with allergic rhinitis in Japan, compared an extract with placebo in patients with allergic rhinitis triggered by dust mite allergy (n = 89). Although not significantly superior

to placebo, improvement in symptoms was greater in the group given the extract of *R. suavis-simus*. The authors concluded that, at the dose given, the benefits of this extract were small and not comparable with mast cell stabilising medications.¹²

Red ginseng capsules have been found

to reduce nasal congestion and improve some aspects of quality of life after four weeks compared with placebo (n = 59).¹³ Subsequent to a series of experimental and clinical studies, an open-label study (n = 38) of a Japanese green tea (Benifuuki), which is high in O-methylated

catechin, found that it reduced the symptoms of seasonal allergic rhinitis, especially in the group that consumed it in the months before the pollen season.¹⁴

The flavonoid isoquercitrin, which is present in tea and some other plants,¹⁵ has been the subject of two randomised controlled trials in patients with seasonal allergic rhinitis in Japan. The first was a pilot randomised controlled trial (n = 20) in which a reduction in symptom scores was observed in the test group during the pollen season but was significant only for ocular symptoms.¹⁶ In a subsequent trial (n = 24), a similar result was again found but in neither study was there a significant difference in serum inflammatory cytokines between the treatment and placebo groups.¹⁷

The polyphenol silymarin has been evaluated as an add-on therapy to cetirizine in patients with persistent allergic rhinitis (n = 60) and showed an improvement in total symptoms. However, no difference in inflammatory cytokines was seen, and serum immunoglobulin (Ig) E level rose, for which no explanation was apparent.¹⁸

In all but the butterbur studies, the evidence for efficacy of these herbal medicines is based on single or small-sized studies. Moreover, the lack of an active comparator in most studies means that the magnitude of any effect is difficult to determine.

MULTI-HERB FORMULATIONS

Numerous multi-herb formulations have been subjected to clinical trials (Table 2). A commercial ayurvedic preparation of seven herbs called Aller-7 has undergone a series of preclinical evaluations.¹⁹⁻²¹ In addition, an open-label study (n = 374) and a double-blind placebo-controlled randomised trial (n = 171) both reported symptom improvements in patients with allergic rhinitis.²² However, some methodological issues with these trials have been identified, and the magnitude of any effect remains unclear.³

Reviews of randomised controlled trials have found that orally administered Chinese multi-herb formulations showed improvements in symptom scores compared with placebo.^{3,23,24} Two of the better designed trials, which studied perennial allergic rhinitis (n = 58) and seasonal allergic rhinitis, respectively, in patients in Australia (n = 55), reported improvements

in nasal symptoms and quality of life.^{25,26} The anti-inflammatory actions of some of the constituents of multi-herb formulations may at least partially explain these effects.²³ For example, magnolia flower buds (called xin yi in Chinese) have demonstrated anti-inflammatory effects in animal models.^{27,28}

Magnolia buds were a principal ingredient in formulas used in two more recent studies. In Hong Kong, 126 participants were administered either the six-herb formula Shi-Bi-Lin or placebo to treat perennial allergic rhinitis over four weeks, resulting in symptom improvements in both groups but greater benefits in the treatment group.²⁹ In Taiwan, a nine-herb formula called Xin-yi-san was compared with placebo over three months in 100 patients with perennial allergic rhinitis. Improvements were evident in nasal symptoms, nasal airflow resistance and

serum levels of IgE antibodies specific to house dust mites.³⁰

The same research group compared a herbal medicine specific for allergic rhinitis, called Bu-zhong-yi-qi-tang, with a non-specific herbal medicine control in patients with perennial allergic rhinitis (n = 60) and found improvements in symptom scores, total serum IgE and COX-2 mRNA expression.³¹ One of the components of this formula was *Astragalus membranaceus* root, which was also an ingredient in the herbal medicines used in two earlier randomised controlled trials.^{25,26} It has been found to have anti-inflammatory effects and to improve immune tolerance in experimental studies.³²⁻³⁴

In addition to the above studies of oral herbal medicines, a recent placebo-controlled cross-over study (n = 35) in Hong Kong reported that multi-herb nasal drops improved the symptoms of perennial allergic rhinitis after two weeks.³⁵

Safety of herb preparations

Concerns over the safety of herbal medicines have been frequently raised.^{1,36,37} In the case of butterbur, the extract used in the trials (Ze339) did not include the toxic compounds found in the crude herb, and a postmarketing survey found only minor adverse events.³⁸ However, similar efficacy and safety cannot be assumed for butterbur in general. The safety of Aller-7 has been evaluated via a series of animal studies^{20,21} and in clinical trials. Liver and kidney function were not adversely affected by the preparation, although there were considerably more adverse events in the trial group than in the group receiving placebo.²² In most of the other studies discussed above, adverse events were reported to be minor or absent.^{7-12,25,26,29-31,35}

PROBIOTICS AND OTHER FUNCTIONAL FOODS

Probiotics have received research attention for treating patients with allergic

diseases (Table 3). Reviews reported that nine of 12 randomised controlled trials showed positive effects of probiotics in patients with allergic rhinitis.^{39,40} In Japan, seasonal allergic rhinitis primarily due to tree pollens is prevalent⁴¹ and has been the subject of a number of recent studies on the effects of probiotics. In a placebo-controlled randomised trial (n = 40), yoghurt containing *Bifidobacterium longum* (BB536) reduced symptoms of allergic rhinitis, especially ocular symptoms, and some differences in serological measures of immune response were evident.⁴²

Another randomised controlled trial (n = 126) found *Lactobacillus paracasei* (KW3110) powder produced a significant reduction in nasal discharge, but the reductions in other symptoms and medication usage did not reach significance. A significantly lower degree of interference with outdoor activities was evident in the test group. Of the serological parameters measured, only eosinophil count was significantly lower in the KW3110 group. The authors' interpretation was that when this probiotic was administered from four weeks before pollen dispersal, it had a limited clinical effect that was most evident when pollen counts were lower.⁴³ Similar results were found in a small study (n = 19) of *Lactobacillus plantarum*.⁴⁴

A larger study (n = 107) of heat-killed *Lactobacillus gasseri* (OLL2809) found no significant differences in symptoms or serological parameters between OLL2809 and placebo. However, in the subgroup of participants with high CAP-radio-allergosorbent test (RAST) scores (i.e. four or five), there was a significant improvement in nasal symptoms and a reduction in pollen-specific IgE levels, suggesting that the effect of this probiotic was most pronounced in highly sensitised people.⁴⁵

In Taiwan, a randomised open-label cross-over study of children with perennial allergic rhinitis (n = 63) found a greater improvement in total symptoms,

but not in quality of life, when *Lactobacillus johnsonii* (EM1) was combined with levocetirizine compared with levocetirizine alone.⁴⁶ Serum IgE did not vary significantly in either group.

A popular functional food is the blue-green algae spirulina. Its immunomodulatory effects have received research attention,^{47,48} and a recent Turkish randomised controlled trial of 129 patients with allergic rhinitis found significant improvement in nasal symptoms over placebo.⁴⁹

A US study (n = 96) of a yeast-based fermentation product (*Saccharomyces cerevisiae*) found nasal symptoms were improved, compared with placebo, and the effect was more pronounced when pollen counts were high.⁵⁰ However, no further randomised controlled trials of spirulina or yeast products for allergic rhinitis could be located.

Safety of probiotics

None of the studies of probiotics and other functional foods reported serious adverse events. Overall, the evidence suggests these products are relatively safe but any effects on allergic rhinitis may be small. Although several probiotics have been studied, the trials have not been replicated, so firm conclusions cannot be drawn.

CONCLUSION

The herbal medicines, probiotics and functional foods discussed for use in

patients with allergic rhinitis appear to be generally safe, at least when manufactured to defined standards. The same cannot be said for products of unclear quality obtained via sources such as the internet. So products of the same name may vary in their constituents and quality.

Although the evidence tends to be based on single clinical studies, a number of these are well designed, some are supported by experimental studies, and there are some areas of converging evidence. It appears that some of the mentioned products could reduce symptom severity, but the results reported for serological tests are difficult to interpret, especially as many trials were of short duration. Moreover, it is not possible to determine how well most of these products compare with antihistamines, intranasal corticosteroids and specific immunotherapy.⁵¹ In two of the butterbur studies, a direct comparison with an antihistamine was made, but in the others any benefit found was in comparison with placebo. Also, it is notable that participants in a number of the randomised controlled trials were also using 'rescue' medications when needed.

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