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Original article

Efficacy of a novel food supplement in the relief of the signs and symptoms of seasonal allergic rhinitis and in the reduction of the consumption of anti-allergic drugs

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Summary. *Background:* Seasonal Allergic rhinitis (SAR) is characterized by runny nose, congestion, sneezing and sinus pressure. A clinical study was performed to demonstrate the efficacy of Lertal®, an innovative food supplement containing Quercetin, *Perilla frutescens* and Vitamin D_3 formulated in a double layer "fast-slow" release tablet form, in the relief of symptoms of seasonal allergic rhinitis and in the reduction of consumption of anti-allergic drugs. *Patients and methods:* 23 subjects enrolled in the open clinical study had at least one year history of allergic rhinitis and positive skin prick test or RAST to *Parietaria officinalis* pollen. At baseline, the subjects had symptoms of nasal and/or ocular seasonal allergic rhinitis. The activity of the food supplement was evaluated using the Total Symptoms Score at first (baseline) and second (final) visit, after one month of supplementation. The consumption of anti-allergic drugs was also evaluated. *Results:* All subjects enrolled completed the study. The comparison of the scores obtained in the two visits (baseline and final) showed a highly significant reduction of the overall symptoms: approximately 70% for symptom scores and 73% in use of anti-allergic drugs. Sneezing, rhinorrhea, nasal obstruction, ocular itching, lacrimation and congestion of the conjunctiva, all showed a highly significant reduction. No noteworthy side effect was recorded and all patients finished the study with good compliance. *Conclusions:* The results showed a clear efficacy of the food supplement Lertal® in reducing nasal and/or eye symptoms. This activity was objectively confirmed by the reduction in the consumption of anti-allergic drugs used to relieve symptoms. (www.actabiomedica.it)

Key words: seasonal allergic rhinitis, Quercetin, Perilla, *Parietaria*, vitamin D_3

Introduction

Allergic rhinitis (AR) is a highly prevalent, chronic disease, with incidence rates of up to 40% in some populations. Furthermore, the prevalence is increasing in many "westernized" countries (1). Its disease burden is considerable with negative impacts on sleep, mood, social functioning, work/school performance and health-related quality of life.

Seasonal Allergic Rhinitis (SAR; commonly called hay fever) is characterized by runny nose, congestion, sneezing and sinus pressure. SAR is caused by an allergic response to outdoor allergens, such as pollens. SAR is not a life-threatening disease but it is classified as a major chronic respiratory disease because of its high prevalence and impact on quality of life. SAR and asthma frequently co-exist and, moreover, SAR is a significant risk factor for asthma (1).

Diagnosis of SAR is typically performed in the primary care setting, with an examination of the patient's history of typical nasal and ocular symptoms used to make a successful diagnosis.

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Further clarification of the cause of the allergy can be achieved through a skin test in which the patient is injected with small amounts of common allergens to identify triggers. Testing is done to determine the presence of allergen-specific IgE and also to confirm which allergens are relevant to the symptoms.

First-line treatment for SAR consists in the identification and avoidance of provoking allergens, together with the use of decongestants and second-generation antihistamines, while second-line therapy includes corticosteroids (intranasal/oral/injected), anti-leukotriens (LTAs) and anticholinergics. Immunotherapy constitutes the third line treatment for SAR but it is seldom prescribed due to its cost. It is well know that antihistamines may cause side effects like drowsiness, dizziness, headache, loss of appetite, stomach upset, vision changes, irritability, dry mouth and nose.

A clinical study was performed to demonstrate the efficacy of Lertal®, a novel food supplement, for the relief of nasal and/or ocular symptoms of seasonal allergic rhinitis and the reduction of consumption of anti-allergic drugs. Lertal® supplement contains Quercetin, *Perilla frutescens* and Vitamin D_3 formulated in a double layer "fast-slow" release tablet form.

Rationale for the choice of the ingredients of Lertal® natural product

Quercetin is a flavonoid that has been shown to inhibit the release of histamine, leukotrienes, PGD2, IL (IL-6 , IL-8 , TNF-alpha) (2) and in cultured human mast cell tryptase, with a strength greater than cromolyn sodium.

The dry extract of the seeds of *Perilla frutescens*, which includes, in addition to rosmarinic acid also other flavonoids, such as luteolin, apigenin and crysoeriol, has shown in vivo and in vitro anti-allergic activity mediated by inhibition of the release of histamine and expression of interleukins (IL-6, TNF-alpha) (3-6). This activity was demonstrated in a clinical study that showed the significant reduction in the clinical symptoms and in the number of neutrophils and eosinophils in the nasal fluid of seasonal allergic rhinoconjunctivitis compared to placebo.

Vitamin D_3 is very important for its contribution to the normal function of immune system (7,8) as shown in numerous studies. One recent study demonstrated significant associations between low vitamin D_3 status and markers of inflammation (including the ratio of IL-6 to IL-10) within elderly adults. These findings suggest that an adequate vitamin D_3 level may be required for optimal immune function (9).

In particular another recent study provides a mechanistic explanation for the anti-inflammatory effects of Vitamin D_3 on mast cell function by demonstrating that mast cells can actively metabolize $25OHD_3$ to dampen IgE-mediated mast cell activation in vitro and in vivo (10).

Based on these data, a food supplement containing Quercetin, dry extract of *Perilla frutescens* and Vitamin D_3 was formulated in bilayer tablets (Lertal®, PH&T SpA).

These tablets are formulated with a fast-release layer and a lipidic slow-release layer. Fast-release layer allows rapid antihistaminic activity of *Perilla frutescens*. Sustained-release layer enhances Quercetin and Vitamin D_3 bioavailability, thanks to its lipidic matrix, and exerts anti-allergic activity spread over time.

Moreover, it is known that oral quercetin normally has a limited bioavailability; in this formulation it is increased by medium chain triglycerides (MCT) (11).

As there are no human studies available on the combination of these ingredients in a controlled release formulation, the present observational open study was conducted to investigate whether the combination of *Perilla frutescens* and bioavailable Quercetin is capable of relieving nasal and/or ocular symptoms in patients after administration of two tablets per day (morning and evening) of the food supplement. In addition, its activity on the severity and occurrence of allergic symptoms was evaluated quantifying the consumption of anti-allergic drugs.

Materials and methods

The subjects enrolled were 23 (16 women, mean age of 44 years and 7 men, mean age 46 years).

The 23 subjects enrolled in this open clinical study had a history of allergic rhinitis for at least one

year and had positive skin prick test or RAST to *Parietaria officinalis* pollen, the allergen prevalent in the geographic area in which the study was carried out. At baseline, the subjects had symptoms of nasal and/or ocular SAR. The activity of the food supplement was assessed using an evaluation scale, the Total Symptoms Score (TSS), which included six parameters related to symptoms, assessed with a numerical score from 0 to 3 (Evaluation scale: 0 = no episodes; 1 = 1-5 episodes/day; 2 = 6-10 episodes/day; 3 = ≥ 11 episodes/day). It is noteworthy that this score is the preferred one in clinical trials on Allergic Rhinitis (12).

Subjects performed two visits, an initial at baseline (Visit 1) and a second final after one month of supplementation (Visit 2).

The subjects recorded their symptoms at both visits; the consumption of anti-allergic drugs was also evaluated.

All subjects were adult patients and signed an informed consent.

Women who were pregnant or nursing or those who wished to become pregnant during the study, were excluded; patients with bacterial or viral infections of the upper or lower respiratory tract, sinus or ear in the thirty days prior to enrollment were also excluded.

During the first visit the following information were collected: informed consent, demographic characteristics, medical history especially in relation to the onset of the allergic disease, the assessment of nasal and/or eye symptoms, the evaluation of the consumption of anti-allergic drug, the inclusion or exclusion criteria. The use of other concomitant medications administered in the three weeks prior to the first visit with any side effects was also recorded.

The food supplement was given to the patients together with indications of its use: to be taken twice a day, morning and evening, during or after meal, for 30 consecutive days.

In the final visit the following parameters were assessed: nasal and/or eye symptoms, the consumption of anti-allergic drugs and possible side effects which occurred during the period of administration of the food supplement.

The pollen count of *Parietaria officinalis* in the atmosphere was carried out during the study period.

Results

All the 23 subjects enrolled completed the study. The comparison between the scores obtained in the two visits (initial and final) shows a reduction of approximately 70% for symptom scores and 73% with respect to the use of anti-allergic drugs.

Analyzing the data according to gender, there is a more positive trend for female (-72% for symptoms and -76% for the consumption of drugs) compared to males (-68% for symptoms and -67% for the consumption of drugs) (Table 1).

Looking at the average TSS, there was a highly significant reduction ($p<0.001$) of the overall symptoms (Figure 1).

Looking at the different individual symptoms: sneezing, rhinorrhea, nasal obstruction, ocular itching, lacrimation, congestion of the conjunctiva, all of them showed a highly significant reduction of at least $p<0,0001$ (Figure 2 and Table 2).

There were no noteworthy side effects during the administration of the food supplement and all of the patients enrolled finished the study with good com-

Table 1. Reduction of symptoms and consumption of anti-allergic drugs by gender

	Females (n = 16)	Males (n = 7)
Average age (years)	44	46
Symptom score reduction	72%	68%
Consumption of anti-allergic drugs	- 76%	- 67%

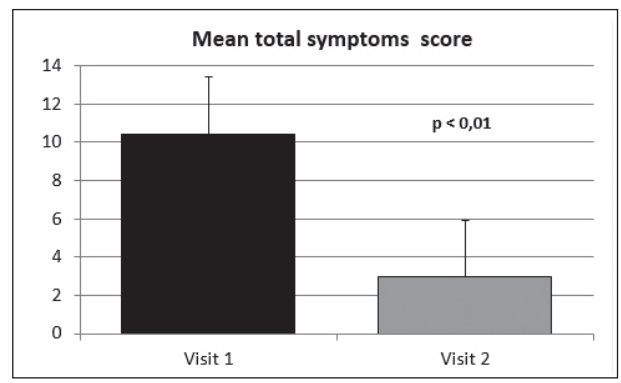

Figure 1. Reduction of the average of total symptoms evaluation score

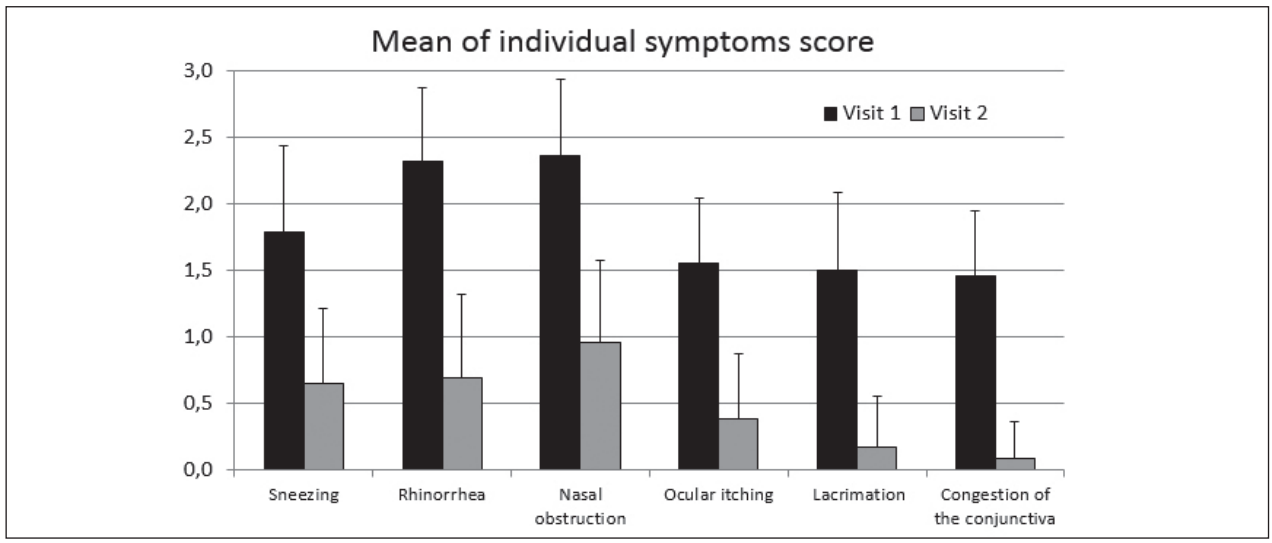

Figure 2. Reduction of the average of individual symptom's evaluation score. Evaluation scale: 0 = no episodes; 1 = 1-5 episodes/day; 2 = 6-10 episodes/day; 3 = ≥ 11 episodes/day.

Table 2. Percentage reduction of individual symptoms' evaluation score

Symptoms	Delta % V_1 vs V_2	p value
Sneezing	-69%	<0,00001
Rhinorrea	-72%	<0,00001
Nasal obstruciton	-72%	<0,00001
Ocular itching	-64%	<0,00001
Lacrimation	-74%	<0,00001
Congestion of the conjunctiva	-80%	<0,00001

pliance. During the study *Parietaria officinalis* pollens count was always present at high levels in the atmosphere, as shown in Figure 3 where the data collected daily by the "Centro di Monitoraggio Aerobiologico ed Allergologico" of Bordighera related to the aerodispersed *Parietaria officinalis* pollens during the period of the Study (March – April 2014) are displayed.

Looking at the individual patients' answer, it is possible to note that only one patient was a non-responder, while all the others had a noteworthy improvement of their symptoms score, as shown in Figure 4.

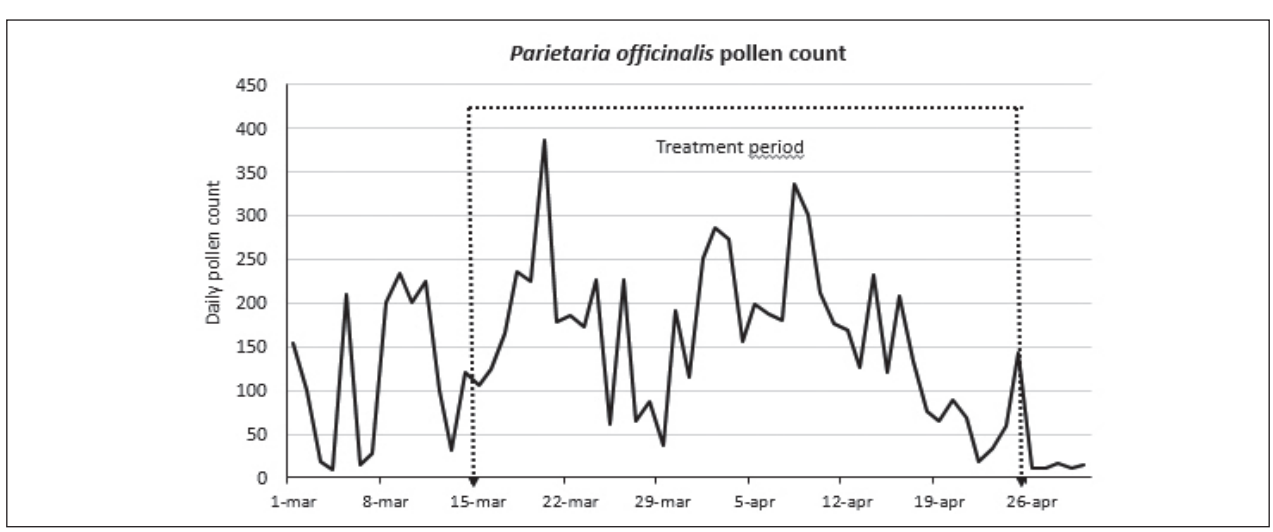

Figure 3. *Parietaria officinalis* pollens count 2014

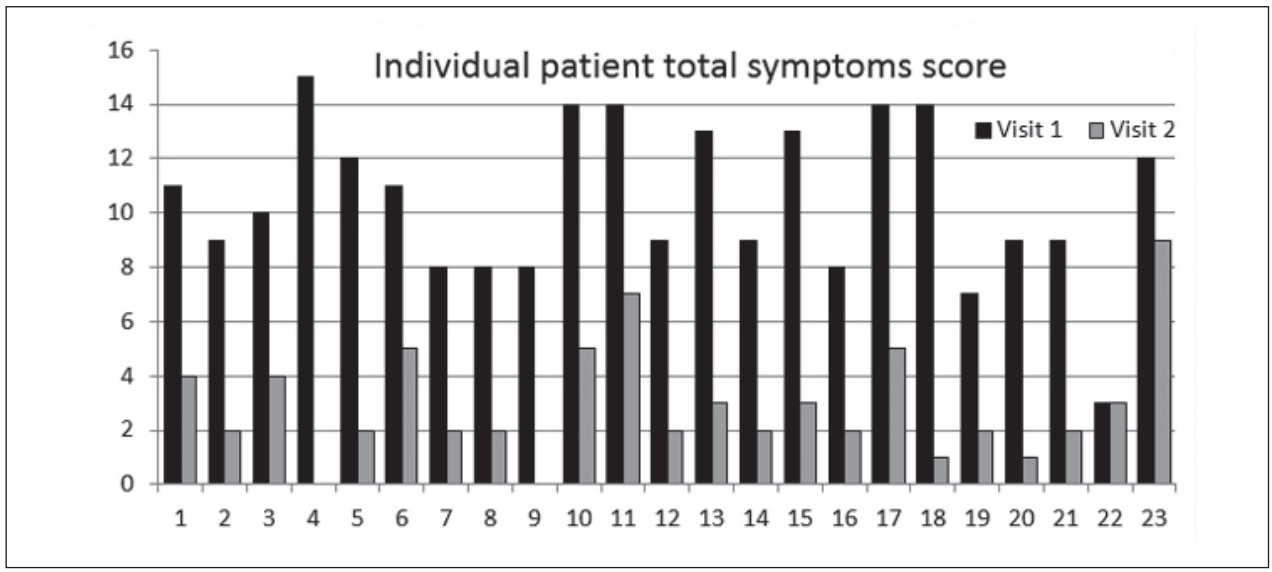

Figure 4. Individual patient total symptom score before and after supplementation

Conclusions

Parietaria officinalis allergy is characterized by persistent symptoms as the pollination period is usually prolonged in the Mediterranean area. In addition, *Parietaria officinalis* pollen sustains intense mucosal inflammation that induces severe complaints, seldom refractory to common antihistaminic medications.

Although this is an open study, the results show a clear evidence of efficacy of Lertal®, a novel food supplement containing Quercetin, *Perilla frutescens* and Vitamin D_3, in statistically reducing nasal and/or eye symptoms in subjects with seasonal allergic rhinitis to *Parietaria officinalis*.

Moreover, this activity is objectively confirmed by the reduction in the consumption of anti-allergic drugs in the pollinic period, in which these patients take relieve medication more frequently. The food supplement was very well tolerated with no side effects recorded.

In view of the results of this clinical study, Lertal® can be considered a good natural way to control nasal and/or eye symptoms due to seasonal allergy to pollen and to considerably reduce the need for drugs, even if these results should be confirmed by other in vivo studies.

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