



**ALLERGY**  
**Nasaleze**  
natural allergy prevention

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# Clinical Trial Data 2003-2012



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# Clinical research on Nasaleze

Study	Description	Population	Measurements and results	Page
<b>Prevention and treatment of Seasonal Allergic Rhinitis</b>	Josling P, Steadman S. Use of cellulose powder for the treatment of seasonal allergic rhinitis Adv Ther. 2003 Jul-Aug;20(4):213-9. Open Clinical Trial.	102 participants (66 female and 36 male)	Utilized a questionnaire format with 5 point rating scale (score of 5 represents no symptoms and complete control.) Overall average daily score was reported as 3.85 for men and women combined indicating a minimum 77% success rate, in chronic hay fever sufferers. Only 12% of volunteers recorded a daily average score under 2.9 revealing a total control of symptoms score of 88%. Cellulose powder earned on average a higher score than all pharmaceutical alternatives. Relief was obtained within 0.1-3 hours. Rarely, an uncomfortable sensation in the back of the throat was the only side effect reported (10%).	7
<b>Clinical study of Nasaleze for relief of allergy symptoms including sneezing, runny nose, itchy and watery eyes</b>	Vlahtis K. Clinical Study Results Summary. Presented at the Pan-Hellenic Conference of ENT Specialists on 19th March 2004 in Thessaloniki, Greece. Open Clinical Trial.	40 participants	All participants were using a pharmaceutical treatment (decongestant 35%, corticosteroids 42.5%, antihistamines 2.5%, corticosteroid/antihistamine combination 20%) at the beginning of the study. Participants were asked to discontinue use of this medication during the study. After 3 weeks of use, 85% of participants realized improvement in their allergy symptoms. After 6 weeks of use, 90% of participants realized improvement in their symptoms.	15
<b>Measure of improvement in nasal muco-ciliary clearance and PNIFR (peak inspiratory flow rate) in children with allergic rhinitis.</b>	Aivazis V, Bourli E, Maratou E et al. Study of Mucociliary Clearance and Peak Nasal Inspiratory Flow Rate in Children Before and After Therapy with Natural Cellulose Powder. University of Thessaloniki, Greece. Presented at World Allergy Congress in Munich, Germany June 2005, also published in Nea Paediatrica Chronica, June 2005, Vol 5 no 2. Open Clinical Trial.	100 children with allergic rhinitis (age 1.5-18, mean 8.2 years)	Significant improvement in Nasal Mucous Clearance (reduced from 39 minutes to 18.15 minutes) and PNIFR value (increased up to 25.7%) was reported. The improvement in the Nasal Mucous Clearance and PNIFR values were due to the regeneration and normalization of the ciliary's epithelium. Cellulose allows the filtration of the inhaled air and protects the nasal mucosa from irritants such as allergens, pollutants, and viruses. Mucociliary Clearance and PNIFR improve since allergic inflammation and edema are avoided.	17
<b>Effect of Nasaleze on symptoms of hayfever in adults and the difference in amount of and type of rescue medication required for adult hayfever sufferers to control their symptoms during grass pollen season.</b>	Emberlin JC, Lewis RA. A double blind placebo controlled trial of inert cellulose powder for the relief of symptoms of Hay fever in adults. Current Medical Research Opinion 2006;22(2):275-85.	97 hay fever sufferers (aged 18 years and older)	The amount of rescue medication used by the placebo group (over all and in individual categories e.g. antihistamines, nasal sprays and eye drops) was significantly greater than that used by the active (Nasaleze) group. Few differences in the symptom scores during the trial for the two groups were reported. Nasaleze significantly reduced the need for rescue medication. No adverse effects were reported.	19
<b>Efficacy of Nasaleze for use in hayfever via pollen provocation tests</b>	Emberlin JC, Lewis RA. A double blind, placebo controlled cross-over trial of inert cellulose powder, by nasal provocation with grass pollen to assess efficacy of the product in controlling the symptoms of hay fever. Presented as a Poster at EAACI, Vienna June 2006.	11 volunteers	Significant differences ( $p < 0.05$ and $p < 0.01$ ) occurred in the data at various times from challenge in peak nasal expiratory flow between placebo and active treatments, and also in nasal PIF, in sneezing and in itching eyes. The results for other lung function tests and symptoms were slightly under the level for significance. The results for the nasal secretions were significantly different at $p < 0.05$ . No adverse reactions occurred. Conclusion - The results of the trial show that the inert cellulose powder can have significant effects in reducing symptoms of sneezing and itchy eyes due to grass pollen allergy. It can also have significant effects in reducing nasal inflammation, as measured as nasal PEF, PIF and as ECP in secretions. The results indicate that the use of inert cellulose powder can help to alleviate symptoms of hay fever.	33

# Clinical research on Nasaleze (continued)

Study	Description	Population	Measurements and results	Page
<b>Double blind placebo controlled dust mite challenge study</b>	Emberlin JC, Lewis RA. Double blind placebo controlled cross-over trial of Nasaleze by nasal provocation tests with Der p1 and Der fl. Presented as a Poster EAACI, Gothenburg June 2007. Current Medical Research Opinion; Vol 23; No 10; 2007, 2423-2431.	15 volunteer adults (aged 18 years and older)	The results show significant differences ( $p < 0.05$ ) for sneezing, itchy nose, runny nose and ECPs in nasal secretions. The results were also significant at this level for peak nasal expiratory and inspiratory flow but there was considerable variation. The results for other symptoms were not significantly different between the cellulose powder and the placebo. There were no adverse reactions.  Conclusion - the inert cellulose powder can have significant effects in reducing some symptoms of persistent rhinitis due to house dust mite allergy.	35
<b>Nasaleze cellulose powder delays house dust mite allergen (Der p1) diffusion in vitro</b>	Purpose of the study was to investigate this theory about the mechanism of action of the gel in relation to house dust mite allergen (Der p1). Presented as a Poster at EAACI XXVII Congress, Barcelona, Spain 7-11 June 2008. Bernadette Diethart and Professor Jean Emberlin of University of Worcester, UK; Richard Lewis, Worcestershire Royal Hospital, UK. Published in Natural Science Vol.2, No.2, 79-84 (2010)	In vitro	The diffusion of the allergen through Nasaleze showed a significant reduction in all points of time. After 15 minutes only 0.76% of baseline amount had diffused through. After 360 minutes only 14% had diffused through. With the control 100% had diffused through.	47
<b>A meta-analysis of the Efficacy and Safety of Nasaleze in the Prevention and Management of AR</b>	A meta-analysis paper by Professor Patrick JD Bouic, Division of Medical Microbiology, Dept of Pathology, University of Stellenbosch, South Africa. Published in The Open Allergy Journal, 2008, 1, 1-4.	N/A	This meta-analysis reviews the clinical data conducted on Nasaleze between 2004 and 2008.	49
<b>Efficacy and safety of Nasaleze in prevention and treatment of persistent allergic rhinitis in adults and children.</b>	This paper describes the findings of an open non-comparative clinical study of efficacy and safety of an ultra-disperse cellulose preparation in prevention and treatment of persistent allergic rhinitis (AR). The volunteers were administered Nasaleze 3 times per day over the course of 4 weeks. Study was presented Moscow XVI Congress for Man and Drug April 06-10, 2009.	25 adults and 23 children, 48 total.	The volunteers visited the investigator weekly, i.e. 4 times during the study period. The severity of AR symptoms and the tolerability of the product were assessed during each visit. The results showed that Nasaleze reduces the severity of AR symptoms already in the first week of treatment and overall there was significant improvement in symptom reduction as the study progressed over the 4 weeks. A twofold improvement in the quality of life of the AR patients was recorded. Therefore proving Nasaleze is an effective and safe method of prevention and treatment of allergic rhinitis both in adults and children.	55
<b>Clinical study in children suffering from allergic rhinitis.</b>	Åberg N and Benson M. A nasally applied cellulose powder reduces symptoms of seasonal allergic rhinitis (SAR). A double blind, placebo controlled trial in children and adolescents. Conducted at The Queen Silvia Children's Hospital, Gothenburg, Sweden. Presented EAACI London 2010. Published Pediatric Allergy and Immunology 22 (2011) 594-599 (2011)	53 children with allergic rhinitis aged 8-18 years	A very good compliance was obtained. Intention to treat analysis showed a significant reduction of total symptom scores from the nose (P 7.29, A 6.07, $p=0.033$ ) and specifically for running nose (P 2.56, A 2.03, $p=0.017$ ). All symptoms from the nose, eyes and lower airways were lower in the active group but reached significance only as above. The cellulose powder reduces symptoms of SAR in children and adolescents.	65
<b>Intranasal Inert Cellulose Powder in Prevention and Management of Seasonal Allergic Rhinitis (SAR) in Children.</b>	Geppe N.A., Snegotskaya M.N.; Kolosova N.G.; Konopelko, O.U. Conducted at the Clinic of Child Diseases at The I.M. Sechenov Moscow Medical Academy. An open comparative randomized study in order to evaluate the efficacy and safety of intranasal inert cellulose powder in preventing seasonal allergic rhinitis (SAR) in children. The study was conducted between April and June 2009 and presented as a Poster in EAACI London 2010.	50 children aged 4-14 with seasonal allergic rhinitis were selected	26 patients (86.4%) demonstrated positive results from the very first application of cellulose powder therapy. After six weeks treatment, Group 1 demonstrated a steady decrease of all SAR symptoms: rhinorrhea - from 1.8 to 0.6 ( $p < 0.001$ ); sneezing - from 1.5 to 0.5 ( $p < 0.001$ ); nasal blockage - from 1.8 to 0.5 ( $p < 0.001$ ); nasal itching - from 1.2 to 0.4 ( $p < 0.001$ ); eye itching - from 0.8 to 0.4 ( $p < 0.001$ ); nasopharyngeal itching - from 0.8 to 0.2 ( $p < 0.001$ ). Conclusion: Children that received inert cellulose powder throughout the study period demonstrated a significant decrease of SAR symptoms. Inert cellulose powder may be used as part of standard SAR therapy.	73

Study	Description	Population	Measurements and results	Page
<p><b>Open non-comparative study to evaluate the effectiveness of nasaleze for patients with allergic rhinitis.</b></p>	<p>Conducted at the Russian Federal Medical Biological Agency by Chief clinical physician, professor, Doctor of medical sciences NI Ilina.</p> <p>An open study to determine the effectiveness of Nasaleze at treating allergic rhinitis by nasal provocation test with significantly causative aeroallergens.</p> <p>To be published in Russian Allergy Journal in No. 2 (March-April 2011)</p>	<p>Study included 30 patients (40% men and 60% women) suffering from AR and meeting the criteria for inclusion/exclusion. The mean age of the patients was 28.5.</p>	<p>A total of 30 patients (100%) completed the study in accordance with the protocol. Of the 30 patients who completed the study, the therapy using Nasaleze was found to be effective in 28 (99.6%) of the patients, which showed a statistically valid decrease in nasal reactivity to a significantly causative allergen. The best results were obtained in patients with isolated dust sensitivity and a mild period of rhinitis.</p>	75
<p><b>Nasal mucociliary clearance and mucoadhesion of hydroxypropylmethylcellulose powder used for alleviation of allergic rhinitis</b></p>	<p>A study to prove whether the attachment of HPMC to nasal mucus (mucoadhesion) slows down nasal clearance, thus enabling a longer period of cellulose residence in the nose acting as a protective barrier against airborne allergens.</p> <p>Bernadette Diethart of School of Human and Health Sciences, Swansea University, Jean Emberlin of National Pollen and Aerobiology Research Unit, University of Worcester and Richard Lewis, Worcestershire Royal Hospital. Poster presented at EAACI XXVIII, London 2010. Published in Natural Science Vol.2, No.2, 79-84 (2020).</p>	<p>Twelve volunteers were tested after the end of the grass pollen season 2008.</p>	<p>The mean mucociliary clearance time at baseline was 11.14 minutes. This base-line MCT significantly increased to 35.45 minutes when 10 mg of HPMC were applied to the nostril prior to the test (<math>p &lt; 0.0005</math>). Application of 20 mg resulted in a mean MCT of 50.37 minutes and thus a further increase &gt;120 % (&gt;420 % longer MCT compared to baseline). This elongation of MCT was statistically significant when compared to baseline and 10 mg HPMC (<math>p &lt; 0.0005</math>).</p>	81
<p><b>Efficacy of cellulose powder as part of a complex therapy for patients with seasonal allergic rhinitis</b></p>	<p>E.M.Penechko, L.P.Sizyakina. The patients were divided into 2 groups. Group one received standard therapy (second generation cetirizine antihistamine, sorbents and topical glucocorticosteroids. Group two received cellulose powder three times a day in addition to the basic therapy. The quality of life and symptom control of both groups was analysed and compared. The observation period was 4 weeks with the patients visiting the clinic once a week.</p>	<p>30 subjects aged between 18 and 33</p>	<p>A comparative analysis of the effectiveness of including the cellulose powder in the complex treatment of intermittent allergic rhinitis has shown that it leads to a faster alleviation of the symptoms of allergic rhinitis and improves the quality of life of patients. The information presented in this study allows the conclusion to be drawn that including the cellulose powder as part of the complex treatment for intermittent allergic rhinitis is beneficial.</p>	83

## Nasaleze patented delivery system



3 The nozzle delivers a fine mist of powder

2 The air and powder travel up the hollow delivery tube to the nozzle

1 When the bottle is squeezed, air forces Nasaleze powder up the hollow tube

**ALLERGY**  
**Nasaleze**<sup>®</sup>  
natural hayfever and allergy prevention





# Prevention and treatment of Seasonal Allergic Rhinitis

Josling P, Steadman S. Use of cellulose powder for  
the treatment of seasonal allergic rhinitis.

Adv Ther. 2003 Jul-Aug;20(4):213-9.  
Open Clinical Trial.



# Use of Cellulose Powder for the Treatment of Seasonal Allergic Rhinitis

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S. Steadman  
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## ABSTRACT

Our study was designed to determine whether a unique cellulose powder extract could prevent the classic hay fever attack from occurring among volunteers who have suffered for some years. Nasaleze enhances nasal mucus, which allows the filtration of allergens, to ensure that only clean air reaches the lungs. One hundred and two volunteers were recruited and, using a simple five-point scoring system to grade their general well-being and severity of any hay fever attacks, the overall average score was 3.85, indicating that Nasaleze was able to control hay fever very well. Rapid relief of symptoms was also demonstrated, sometimes within minutes after inhalation. Overall, 77% of volunteers reported a significant reduction in the number of challenges throughout the study period and most graded Nasaleze as more effective and reported fewer side effects than with a wide range of chemical treatments.

**Keywords:** | cellulose; seasonal allergic rhinitis; allergen

## INTRODUCTION

Approximately 12 million people in the United Kingdom<sup>1</sup> and more than 60 million in the United States<sup>2</sup> have seasonal allergic rhinitis. Symptoms vary from mild discomfort to activity-limiting.

Seasonal allergic rhinitis is characterized by a relatively dry nasal tract, without adequate mucus to absorb airborne dust, animal dander, pollens, and spores and prevent these irritants from reaching the lungs. Each day, up to 20 billion particles enter the nasal passages<sup>3</sup> and are swept to the back of the throat, swallowed, and ultimately destroyed by stomach acid. This process, accomplished by the on going wave action of the nasal hair cells.



The rising prevalence of seasonal allergic rhinitis parallels the increase in environmental allergens whose presence in the nose trigger the release of histamine and other compounds into the bloodstream.

## **CAUSES AND SYMPTOMS**

An allergic reaction may result when the immune system mistakenly identifies a normally harmless substance as a threat, the filtration system of the nasal tract becomes overloaded from excessive pollution, or the nasal tract dries out. The precise mechanism is unknown but may be genetic.

An allergic reaction is triggered when mast cells found in or near the nose, lungs, skin, eyes, and blood vessels release high concentrations of histamine in response to stimulation by the body's immune defenses.

Histamine, in turn, induces the classic symptoms of seasonal allergic rhinitis, including nasal congestion and itching; runny nose; itchy, watery eyes; swollen, itchy eyelids; difficulty breathing; loss of taste and hearing; dry cough; and headache.

The severity of symptoms varies among individuals and in response to pollen counts and local weather conditions.

## **TREATMENTS**

In the United Kingdom, the allergy market is currently worth about £67.9 million sterling and is growing by about 5.5% each year according to the OTC Bulletin published in June 2003.

### **Antihistamines**

Antihistamines prevent the release of histamine from mast cells or diminish its effect after release. Oral antihistamines are probably the most convenient chemical treatment for most people, although a number of natural alternatives are available.

Older antihistamines cause substantial drowsiness because they can cross the blood-brain barrier; newer, nonsedating antihistamines are longer-acting and better tolerated but still elicit adverse effects.

### **Topical Agents**

The effectiveness of eyedrops and nasal sprays depends, to a considerable degree, on frequent application. Sodium cromoglycate, the most widely used topical treatment, acts by preventing the release of histamine. Instillation is not recommended in the presence of contact lenses or glaucoma.

Nasal sprays, like beclomethasone, reduce inflammation and mucus production. These products are not used in cases of nasal infection and are not licensed for sale over the counter to patients younger than 18 years of age, in the UK.

A number of herbal or plant-based compounds, including garlic, goldenseal, and feverfew, are also available for oral use.

Cellulose powder is used as a thickener in many liquid nasal sprays and is generally regarded as safe. The special proprietary grade of micronized cellulose in this study\* used a patented method that ensures delivery into the nose of a suitable amount of material drawn from the container. Compared with liquid nasal sprays, which require preservatives, powdered cellulose inhibits bacterial growth. While not a medicine, it is classified as a medical device that is safe to use throughout the year. The powdered cellulose product addresses the cause of allergic reactions, rather than the symptoms, because it works as a facial mask in preventing inhaled pollen, dirt, and allergens from reaching the lungs. In a healthy individual, the nose and nasal tract extract these materials from the inhaled air, including air that has been exposed to mucus membranes and therefore been stripped of allergens. Mucus has a low surface tension and can easily absorb allergens from air as it passes down into the lungs.

Uniquely, the cellulose powder described herein turns into a gel on contact with the moisture always present in the nasal cavity. This gel is similar to normal mucus and helps to maintain delivery of a supply of clean air to the lungs.

## METHODS

Following recruitment through local and national press releases, 102 volunteers (66 female, 36 male; mean age, 44 years), who had previously used products for seasonal allergic rhinitis, were enrolled in the early spring of 2003. Each participant completed a pretrial questionnaire designed to assess the severity and range of symptoms experienced and the months when they were most distressing (Table 1). Pharmaceutical treatments used in the past were identified, and their effectiveness was rated on a five-point scale (1 = not effective at all to 5 = very effective). General well-being during the study was recorded daily in a take-home diary and graded on a five-point scale (5 = well, no problems; 4 = quite well with occasional sneeze; 3 = can feel an attack coming on, some minor symptoms; 2 = feeling low and definitely suffering; 1 = full hay fever attack with symptoms listed). Also listed were the number and variety of symptoms, the day or time elapsed when recovery began, and the time until symptoms resolved. A global assessment of the cellular powder was provided at the end of the 6-week study.

Participants were instructed to place one puff of the inert cellulose powder into each nostril according to the manufacturer's recommendations. If a full-scale hay fever attack occurred, drug treatment was allowed but was to be recorded in the diary.

The pollen count, obtained from both local and national sources, was monitored and recorded every day throughout the study. A large number of volunteers rode horses and admitted to symptoms throughout the year mainly as a result of daily exposure to hay and horse hair.

The average time to symptom relief in minutes, hours, or days and the total number of days when symptoms occurred were recorded and compared with the predicted onset of action of previously used pharmaceutical alternatives<sup>4</sup> and with the volunteer's own subjective assessment of the efficacy of these products. Data were analyzed by means of a Student's *t* test to gain a probability coefficient that allowed for the calculated number of degrees of freedom.

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\*Nasaleze, a registered trademark of Kisska International Ltd, Keighley, West Yorkshire BD21 3ND UK  
www.nasaleze.com

**Table 1. Time of Hay Fever Symptoms**

Month	Volunteers, no.	
	Male	Female
January	6	18
February	14	19
March	24	45
April	36	66
May	36	66
June	36	66
July	34	66
August	26	58
September	12	27
October	6	14
November	5	13
December	7	19

## RESULTS

A wide range of pharmaceutical treatments had been used in the past to alleviate hay fever symptoms, but most of these products were rated as not very effective (Table 2). When exceptions were noted (as with beclomethasone), side effects were often recorded. In contrast, the natural cellulose powder earned, on average, a higher score than all the pharmaceutical alternatives. The scores of 3.8 for men and 3.9 for women represent a minimum 77% success rate, because a rating of 5 equals no symptoms and complete control. The average daily score with the cellulose powder was in excess of 4.0 in over 35% of volunteers and above 3.0 in over 70%, indicating an occasional sneeze but no hay fever symptoms. In only 12% of volunteers was the average daily score less than 2.9. A total symptom-control score of nearly 88% with the cellulose product is therefore warranted. At the end of 6 weeks, more than 70% of volunteers rated the cellulose powder as good or excellent (Table 3). Either of these ratings was more likely in women than in men.

Volunteers were statistically likely ( $P < 0.005$ ) to gain relief from symptoms within 0.1 to 3 hours of using the cellulose powder—a rapid onset of action suggesting value in the relief of the most chronic hay fever symptoms.<sup>5</sup>

A comparison of the weekly average scores for volunteers and the reported pollen count in the United Kingdom indicates a small reduction in quality-of-life scores as pollen increased in weeks 3 and 4 of this study (Figure 1); however, high scores throughout the 6-week trial indicated considerable benefit from the test substance.

The single treatment failure occurred in a woman who could not record a score above 1 at any time throughout the study. She reported a wide range of symptoms and a number of concomitant diseases. Her removal from the calculations would result in a slightly higher average score for women.

**Table 2. Use of Pharmaceutical Treatments**

<b>Treatment</b>	<b>Average Efficacy Score</b>	
	<b>Male</b>	<b>Female</b>
	<b>Volunteers</b>	<b>Volunteers</b>
Beconase®(steroid nasal inhaler) Glaxo Smith Kline, UK	3.0	3.1
Sodium cromoglycate (antihistamine nasal inhaler) - Various generic manufacturers	1.3	2.1
Opticrom® (eyedrops) Aventis Pharma, UK	1.5	2.0
Clarityn® (oral tablets) Schering Plough, UK	2.0	2.2
Zirtek® (oral tablets) Glaxo Smith Kline, UK	1.1	1.8
Piriton® (oral tablets and liquid) Stafford Miller, UK	1.3	1.8
Telfast® (oral caplet) HMR, UK	2.0	1.8
<b>Natural cellulose powder</b>	<b>3.8</b>	<b>3.9</b>

Scale from 1 (not effective at all) to 5 (very effective).

Other products used regularly in the past by volunteers included Benadryl, Otrivine, Flixonase, Triludan, Sudafed, New Era, Rhinocourt, Atarax, Phenergan, Vallergran, Semprex, and Zaditen.

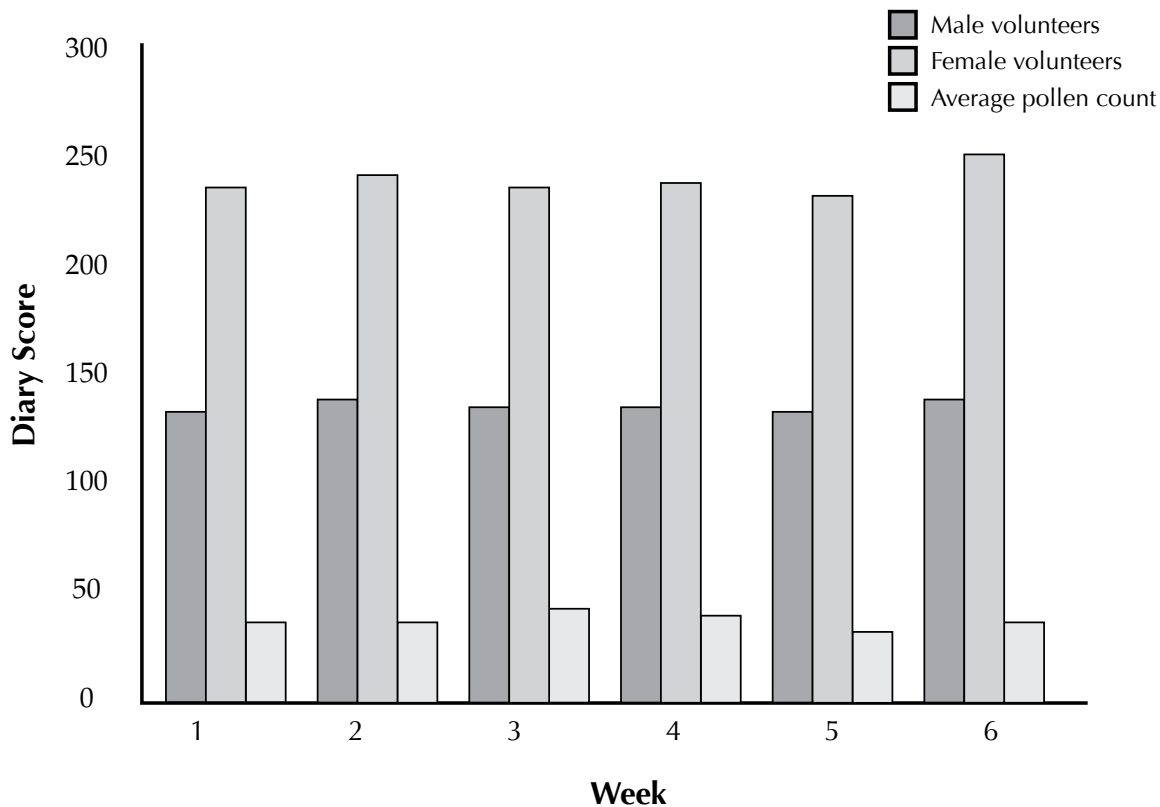
**Table 3. Global Assessment of Efficacy of Cellulose Powder**

<b>Volunteers</b>	<b>Overall Impression, %</b>	
	<b>Good</b>	<b>Excellent</b>
Male	76	69
Female	80	75
Total	78	72

Side effects were infrequently reported, but in week 1, 10% of volunteers noted that it was easy to inhale a large amount of powder, which caused an uncomfortable sensation at the back of the throat. One person reported itchy eyes, and another mentioned a sore throat; both symptoms may have been related to hay fever. Difficulty gauging how much powder remained in the bottle (opaque white plastic) was a common complaint, and in one case when the powder ran out, serious hay fever symptoms occurred immediately. Nine volunteers reported being able to smell the powder on inhalation, but this was not regarded as a problem.

Six women and two men required additional treatment with pharmaceutical products; however, volunteers who took more than the recommended one puff in each nostril per day could derive increased and accelerated relief of symptoms.

**Figure 1 Average Weekly diary scores\***



\* Maximum score: 180 for men, 330 for women

## DISCUSSION

In this pilot investigation, an inert cellulose powder placed into a novel, patented delivery system relieved classic hay fever symptoms, sometimes within minutes but usually within 3 hours of inhalation. The volunteers selected had a long history of multiple symptoms requiring chemical treatments that were, at best, only moderately effective. Of the 102 volunteers, 78 volunteers reported no hay fever episode during the study and experienced their first season free of sore throat, runny nose, sneezing, and watery eyes. The cellulose powder was easy to take and effective; the overall success rate exceeded 77%.

Although a short period of experimentation appears to be necessary before effective use of the product, adequate instructions are provided in patient leaflets supplied by the manufacturer (not used in this study). A metered-dose delivery system is under consideration that would allow more frequent use of the product (when the pollen count is especially high) and easier identification of the need for a new supply. The ability to filter air in the nasal passages appears to be superior to air purifiers and room air-conditioning filters.



Most volunteers observed that previous drug treatment had never alleviated all symptoms, whereas resolution of symptoms was complete with the cellulose powder.

This pilot investigation demonstrated that inert cellulose powder, delivered into the nasal cavity, prevents allergic reaction to pollen and other irritants and represents a safe and natural alternative to pharmaceutical preparations. Treatment with cellulose powder should be started as early as possible and continued throughout the pollen season, with the number of applications per day increased as appropriate. This product is suitable for use by individuals with diabetes and asthma, pregnant women, and children.

Further work should be done to ascertain the exact degree of efficacy, perhaps by adopting a double-blind placebo-controlled design for future evaluations, but in the meantime, Nasaleze treatment represents a real opportunity to significantly improve the quality of life for hay fever sufferers everywhere.

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# **Clinical study of Nasaleze for relief of allergy symptoms including sneezing, runny nose, itchy and watery eyes**

Vlahtis K. Clinical Study Results Summary.

Presented at the Pan-Hellenic Conference of ENT  
Specialists on 19th March 2004 in Thessaloniki,  
Greece. Open Clinical Trial.



# Clinical Study Results Summary

## Dr. Konstantinos Vlahtsis

External Co-operator American Hellenic Educational Progressive Association (AHEPA) Hospital, Aristotelian University of Thessaloniki, Greece

### Product Use:

- Used once daily, mainly in the morning or shortly before the known time of day when symptoms usually appear.
- One application per each nostril.
- Symptoms measured were sneezing, runny nose, itchy and watery eyes.
- Scale used to measure symptoms
- 5 - complete relief, without symptoms
- 4 - major relief, casual sneezing
- 3 - light, but noticeable allergy symptoms
- 2 - allergy symptoms apparent with periodic flare ups
- 1 - allergic rhinitis with complete symptoms

### Time period:

- December 2003 through March 2004; this time period does not represent seasonal sufferers, but rather perennial or chronic allergy sufferers. This means they could suffer from a variety of triggers including but not limited to dust mites, pet dander, and/or smoke in addition to pollen.
- Duration of 6 weeks with evaluation at time zero, 3 weeks (21st day after start of treatment), and 6 weeks (42nd day after start of treatment).

### Study participants:

- Suffer from diagnosed allergic rhinitis as diagnosed by a radioallergosorbent test (RAST) which is an allergy test that involves collecting blood or by traditional dermal skin tests.
- Currently use a pharmaceutical treatment (either over-the-counter or prescription); participants were asked to discontinue use of their current medications during the study.
- Total of 40 participants (16 men, 24 women)
- Summary of previous treatments used by participants:
- Decongestant - 35%
- Corticosteroids - 42.5%
- Antihistamines - 2.5%
- Corticosteroid/Antihistamine combination - 20%

**Table 1**

	Scale 1	Scale 2	Scale 3	Scale 4	Scale 5	% scoring complete or major relief (4,5)
Baseline - before treatment	4 (10%)	16 (40%)	14 (35%)	6 (15%)	0 (0%)	15%
3 weeks	1 (2.5%)	5 (12.5%)	16 (40%)	13 (32.5%)	5 (12.5%)	45%
6 weeks	1 (2.5%)	2 (5%)	6 (15%)	20 (50%)	11 (27.5%)	77.5%

Table 1 shows number of patients during each time period and their reported score (percent of total participants in parenthesis).

**Table 2**

	3 scale improvement	2 scale improvement	1 scale improvement	0 scale improvement	Mean improvement
3 weeks	0%	5%	80%	15%	0.9 scales
6 weeks	7.5%	35%	47.5%	10%	1.4 scales

Table 2 shows the percent of participants that experienced improvement. After 3 weeks of use, 85% of participants realized improvement in their allergy symptoms. After 6 weeks of use, 90% of participants realized improvement in their symptoms.

### Side Effects

- There were no reported side effects from any participants.
- Participants reported that the product was simple and easy to use.

Presented at the Pan-Hellenic Conference of ENT Specialists on 19th March 2004 in Thessaloniki, Greece. Open Clinical Trial

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# **Measure of improvement in nasal muco-ciliary clearance and PNIFR (peak inspiratory flow rate) in children with allergic rhinitis.**

Aivazis V, Bourli E, Maratou E et al. Study of Mucociliary Clearance and Peak Nasal Inspiratory Flow Rate in Children Before and After Therapy with Natural Cellulose Powder.

University of Thessaloniki, Greece.

Presented at World Allergy Congress  
in Munich, Germany June 2005.

Published in Nea Paediatrica Chronica,  
June 2005, Vol 5 no 2. Open Clinical Trial.



# Clinical Study Results Summary

Aivazis V, Bourli E, Maratou E, Mavroudi A, Aivazi D, Foutzila E and Ilonidis G  
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## Study of mucociliary clearance in children with allergic rhinitis, before and after a six week therapy with natural cellulose powder

**Background:** The aim of the study was to estimate the nasal mucus clearance before and after monotherapy with natural cellulose administered in the form of inhaled powder in children with allergic rhinitis.

**Method:** One hundred (100) children: 53 boys and 47 girls were selected. Mean age of the study group was 7.96 years (range 1.5 - 8 years). All children had a positive medical history for allergic rhinitis. Seventy eight out of 93 children (83.8%) who were subjected to allergological investigation had high serum total IgE immunoglobulin, specific IgE antibodies or positive skin prick tests. Mucociliary clearance was determined in vivo by means of a simple non invasive dye method (Edicol Orange 3%+ CaHPO<sub>4</sub>·2H<sub>2</sub>O 97%). Mucociliary clearance was measured once before starting therapy and one more time 2 days after the child had received a six week therapy.

**Results:** The clearance reduced from 39 minutes measured before therapy to 18.15 minutes after therapy. The reduction was statistically significant (p<0.001). In the beginning of the clinical trial 51

out of 100 children had abnormally prolonged clearance with a mean value 55.23 min (range 31-80 min) which became 21.1 min after treatment. Only 5 children did not improve and mucociliary clearance remained abnormally long above 37 minutes.

**Conclusion:** The significant decrease of clearance observed in children of our study after treatment, especially in those with mean value above 31 minutes is due to the effect of cellulose, since the children received no other therapy. It is apparent that the improvement in clearance may be attributed to regeneration and normalization of the ciliary epithelium. Mucociliary clearance is the first line of defense of ciliated nasal epithelium against inhaled particles such as allergens, pollutants and viruses. Cellulose enhances nasal mucus, which allows the filtration of allergens, to ensure that only clean air reaches the lungs.

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**Effect of Nasaleze on symptoms  
of hayfever in adults and the  
difference in amount of and type of  
rescue medication required for adult  
hayfever sufferers to control their  
symptoms during grass  
pollen season.**

Emberlin JC, Lewis RA. A double blind placebo controlled trial of inert cellulose powder for the relief of symptoms of Hay fever in adults.

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Poster presented at World Allergy Congress,  
Munich 2005



# A double blind placebo controlled trial of inert cellulose powder for the relief of symptoms of hayfever in adults

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## Background

Seasonal allergic rhinitis due to pollen allergy occurs in 15 to 37% of the population of Europe depending on age group and region resulting in notable social and economic costs. An inert cellulose powder (Nasaleze) has been on sale in the UK since 1994 as a remedy for hay fever but no scientific trials have been conducted previously. The principal aim was to determine if there is a significant difference in the amount and type of rescue medication required for adult hay fever sufferers to control their symptoms in the grass pollen season while using either Nasaleze or a placebo. The second objective was to see whether Nasaleze resulted in an improvement in symptom control.

## Methods

A double blind placebo controlled study was conducted of 106 adult hay fever sufferers, over the grass pollen season of 2004. Participants were allowed to take any medications they wished in addition to the Nasaleze or placebo.

## Results

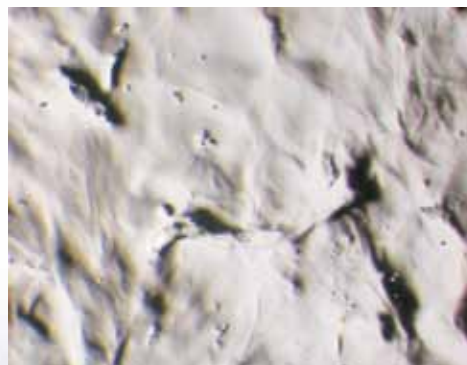
No significant differences were found ( $p < 0.01$ ) between the active and placebo groups in Likert scores for any of the rhinitis nasal symptoms or in the total Likert symptom daily scores (Fig 1). Significant differences were found in the amounts of rescue medication taken by the active and placebo groups ( $p < 0.05$ ) (Fig 2). More people in the placebo group took rescue treatments than those in the active group.

## Conclusion

The amount of rescue medication taken by the placebo group was significantly more than that taken by the active group both overall, considering all types of medication, and also in the individual cases of antihistamines (Fig 3), nasal sprays and eye drops. These results provide strong evidence that Nasaleze reduces the need to take rescue medication for the symptoms of hay fever.



Nasaleze powder dry (taken from 100 x magnification)



Nasaleze powder after exposure to damp surface (taken from 100 x magnification)

Fig 1

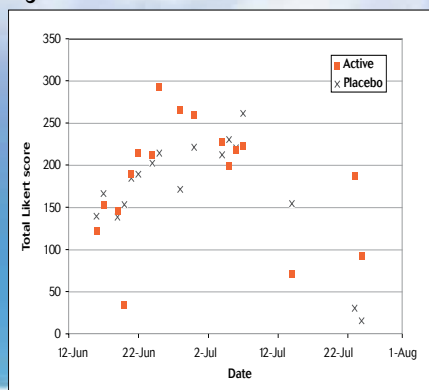


Fig 2

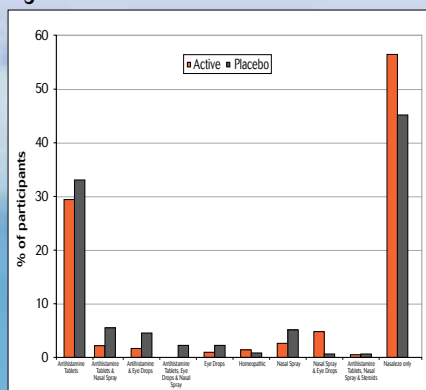
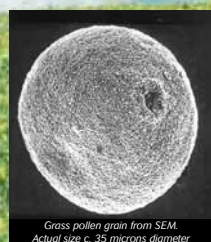
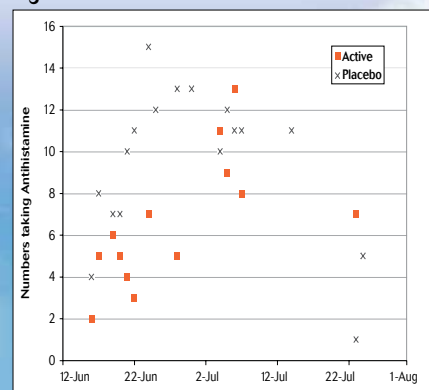


Fig 3



Acknowledgement - This study was funded by Kisska International Ltd makers of Nasaleze

ORIGINAL ARTICLE

# A double blind, placebo controlled trial of inert cellulose powder for the relief of symptoms of hay fever in adults\*

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**Key words:** Hay fever – Inert cellulose powder – Seasonal allergic rhinitis

## ABSTRACT

**Objective:** An inert cellulose powder has been on sale in the UK since 1994 as a remedy for hay fever but no scientific trials have been conducted previously. It is applied to the inside of the nose where it forms a gelatinous coating. The principal aim was to determine if there is a significant difference in the amount and type of rescue medication required for adult hay fever sufferers to control their symptoms while using either the inert cellulose powder or a placebo. The second objective was to see whether the cellulose powder resulted in an improvement in symptom control.

**Research design:** A double blind, placebo controlled study was conducted of 97 adult hay fever sufferers, over the grass pollen season of 2004. Participants (selectively recruited to be living within the catchment area of a 50-km radius from Worcester, UK) were assigned randomly to two groups (A, Active and B, Placebo) matched by age by decades and gender. Of those completing the trial, group A had 19 males and 28 females and group B had 21 males and 29 females. There were no significant differences between the groups in age distributions, severity of symptoms over the last 2 years or in medication taken. They completed

daily symptom diary score cards and were allowed to take any medications they wished in addition to the inert cellulose powder or placebo because medication use was taken as an outcome measure. Results were analysed in relation to pollen counts.

**Results:** Significant differences were found in the amounts of rescue medication taken by the active and placebo groups ( $p < 0.05$ ). More people in the placebo group took rescue treatments than those in the active group.

No significant differences were found ( $p < 0.01$ ) between the active and placebo groups in Likert scores for any of the rhinitis nasal symptoms or in the total Likert symptom daily scores. No adverse events were reported during the study.

**Conclusions:** The amount of rescue medication taken by the placebo group was significantly more than that taken by the active group both overall, considering all types of medication, and also in the individual cases of antihistamines, nasal sprays and eye drops. These results provide evidence that the inert cellulose powder reduces the need to take rescue medication for the symptoms of hay fever.

## Introduction

Seasonal allergic rhinitis due to pollen allergy occurs in 15–35% of the population of Europe depending on

age group and region<sup>1–3</sup>. In the UK hay fever affects at least 10% of the general population<sup>4</sup> and in teenagers (12–14 year olds) lifetime prevalence increased from 34.8% in 1995 to 37.4% in 2002<sup>5</sup>, resulting in notable

\* Selected material from this paper was presented as a poster at the World Allergy Congress, Munich, 26th June–1st July 2005

social and economic costs. A wide range of remedies and treatments is available both on prescription and for sale over the counter but many of these can have side effects and some sufferers are reluctant to take them. An inert cellulose powder (Nasaleze†) has been registered as a class one medical device with the Medical Devices Agency (MDA) since 1994 and is on sale in many countries, including the UK, as a remedy for hay fever. It is applied to the inside of the nose by a simple puffer device. The mechanism of action of the cellulose is unclear although it is likely that the cellulose reacts with moisture within the airway to produce a protective barrier over the nasal mucosa, preventing binding of inhaled allergen with receptors. Evidence for the efficacy of this device in the management of rhinitis has been almost entirely anecdotal as no scientific trials have been conducted previously. The popularity of the product has been increasing steadily over the last 10 years with numerous unsolicited testimonials being cited by the manufacturers.

In the UK, and the majority of Europe, the most important allergenic pollen type is grass, with approximately 95% of hay fever sufferers being allergic to this taxon, whereas only about 25% are allergic to tree pollen and about 20% to weed pollen<sup>6</sup>.

The UK grass pollen season typically starts in late May and continues through to mid-August, with the main peak occurring in June and a second smaller peak typically occurring in early July. This period overlaps with the flowering times for some weeds, such as Nettle (*Urtica* spp.), certain trees such as Lime (*Tilia* spp.) and pollen from some crops (such as Oil seed rape, *Brassica napus*).

A trial was conducted with the principal objective of determining if there is a significant difference in the amount of and type of rescue medication required for adult hay fever sufferers to control their symptoms in the main grass pollen season while using either the inert cellulose powder or a placebo. The secondary objective was to establish whether the inert cellulose powder has a significant effect in the control of the symptoms of hay fever in adults during the grass pollen season.

## Patients and methods

### Patients and their selection

Subjects were recruited via local general practitioners, leaflets in libraries and other public places and via the National Pollen and Aerobiology Research Unit (NPARU) web site. Informed consent was obtained from potential volunteers who then completed a baseline questionnaire which supplied the following types of information: age range, name and address

of doctor, occurrence and timing of hay fever in the previous two summers, qualitative assessment of symptoms (as none, slight, moderate or severe for frequent sneezing, itchy eyes, blocked nose, running eyes, headache/tiredness, itchy throat/mouth). Subjects were also asked if they took medication or other treatments (if so, were these bought over the counter or on prescription) and the generic types e.g. eye drops (choices to tick plus 'other'). They were also asked about asthma in the summer months and whether this required treatment with steroids.

The criteria for inclusion were as follows:

1. Subjects must be 18 years or over.
2. Subjects must have had symptoms of seasonal allergic rhinitis during June and July for at least the previous 2 years.
3. Subjects must have had symptoms sufficiently severe to need treatment by medication either from a pharmacy or on prescription.
4. Subjects must be residing and spending the majority of time within 50 km of Worcester during the trial period.

Criteria for exclusion were as follows:

1. Subjects who did not understand English clearly. This was because the relevant documents need to be completed in English.
2. Subjects with a history of severe grass pollen associated asthma who were likely to require steroid treatment for asthma symptoms during the hay fever season.
3. Subjects who were likely to be spending more than 2 weeks at a time away from the region during June and July.
4. Subjects who had rhinitis outside of the grass pollen season.

These criteria ensured that recruits were highly likely to suffer symptoms of seasonal allergic rhinitis due to grass pollen allergy. The baseline questionnaire specifically asked about the occurrence of symptoms in relation to calendar month. Only those people who had clear seasonal rhinitis during the grass pollen season were included. People who had symptoms at other times of the year were excluded. If people were sensitized to other allergens such as dogs, cats, house dust mites or mould, it is highly likely that they would have symptoms outside of the grass pollen season.

The catchment area was a 50-km radius from Worcester so that symptoms could be related to pollen count data at the National Network pollen-monitoring site at the National Pollen and Aerobiology Research

† Nasaleze is a registered trade mark, Kisska International Ltd, Keighley, UK

Unit, Worcester. Previous research has demonstrated that it is acceptable to use the results from a standard roof top pollen monitoring site to indicate the pollen counts prevailing in a region of about 50 km radius from the site<sup>7-9</sup>. Throughout the duration of the trial the daily average pollen counts for all allergenic pollen types were taken from the Worcester site which uses the standard techniques of the British Aerobiology Federation<sup>10</sup>.

## Study design

A double blind, placebo controlled study was conducted on adult hay fever sufferers (aged 18 years and over) who had experienced symptoms of hay fever in June and July in the previous 2 years that were sufficiently severe to require treatment. A pilot study was conducted in the summer of 2003 in one GP practice in Worcester, which indicated a high efficacy for the inert cellulose powder. This indicated the power of the study and the sample size required. The pilot indicated that with 100 patients in this two treatment study, the probability is 90% that the study will detect a treatment difference at a two-sided 1.000% significance level, if the true difference between the treatments is 0.555 units. This is based on the assumption that the within patient standard deviation of the response variable is 1.000.

The trial was planned for the main grass pollen season (June and July) in 2004 with the intention of recruiting 120 hay fever sufferers (sample size of 100, plus 20% over-recruitment to allow for 'dropout').

Suitable volunteers were assigned randomly to two groups matched by gender and age within decades from 18 to 57 years, then to the groups as people 58 years and over to give stratified random samples (Table 1). Recruits were given a participant number and were grouped by gender and age range. Within these categories they were assigned to group A or B by alternate random draw of sealed shuffled envelopes. There were no significant differences at the 95% level

in the occurrence or severity of symptoms experienced by the people in the two groups over the previous 2 years (Table 2). Similarly there were no significant differences at the 95% level in the numbers taking different types of medication (Table 3). Participants who were recruited but did not complete the trial are not included in the tables.

## Ethical considerations

Ethical approval was obtained from the Hereford and Worcestershire NHS Local Research Ethics Committee. The study complies with the Declaration of Helsinki.

## Collection and analysis of data

In early June those recruited were given daily diary cards to cover 4 weeks together with detailed instructions, prepaid envelopes for returns and nasal powder type A or B. They were given the opportunity to discuss the project and to ask any questions. They were also given a phone number to contact if they had any questions during the trial period. The diary cards included reports on symptoms as Likert scores. These are widely used as a qualitative assessment of the severity of symptoms. The Likert technique presents a set of statements. Subjects are asked to express agreement or disagreement of a five-point scale (in relation to having symptoms). Each degree of agreement is

**Table 1.** The age and gender of participants completing the trial

Age range	Active group		Placebo group	
	Male	Female	Male	Female
18-27 years	3	6	2	7
28-37 years	7	8	8	7
38-47 years	3	9	3	9
48-57 years	5	3	6	3
58+ years	1	2	2	3
Totals for analysis	19	28	21	29

**Table 2.** Results from the baseline questionnaire. Occurrence and severity of symptoms over the last 2 years

	Sneezing	Itchy eyes	Blocked nose	Running nose	Running eyes	Headaches/tiredness	Itchy throat/mouth
Active group							
Severe	19	21	15	23	14	11	10
Moderate	25	19	16	15	15	16	17
Slight	3	7	10	5	10	10	10
None			5	4	8	8	8
Placebo group							
Severe	20	27	18	24	17	15	10
Moderate	26	17	17	16	13	16	16
Slight	4	6	8	9	11	9	13
None			5	1	9	10	9



**Table 3.** Results from the baseline questionnaire. Medication taken regularly during grass pollen season over the last 2 years

	Active group	Placebo group
Antihistamines only	20	21
Antihistamines with nasal spray	4	4
Antihistamines with eye drops	4	5
Antihistamines with eye drops and nasal spray	9	10
Antihistamines with eye drops, nasal spray and steroids	1	1
Nasal spray only	1	2
Nasal spray and eye drops	2	3
Eye drops only	1	1
Eye drops and herbal	1	0
Eye drops, nasal spray and herbal	1	0
Steroids only	1	0
Herbal only	2	0
Antihistamines with nasal spray and herbal	0	1
Antihistamines with eye drops, nasal spray and herbal	0	1
Antihistamines with eye drops, nasal spray, herbal and steroids	0	1

given a numerical value from one to five. Thus a total numerical value can be calculated from all the responses.

The daily diary cards requested the following information:

- Likert scores for each of four individual categories of symptoms of hay fever over the last 24 h.
- How many times the nasal powder was used that day.
- Whether they had taken any hay fever medication or treatment today, if so what type and how much.
- Visits to GP or nurse related to allergy.
- Whether they had cold or flu like symptoms. If so what were these?
- If they had been away from the Worcester area (more than 50 km radius) during the day.

Subjects were told that they could use any hay fever treatments or remedies they felt they needed during the trial. This was done because use of medication was to be taken as an outcome measure. Also if it was overtly allowed and monitored it could be taken into account. Restrictions on the use of rescue remedies and medication in a field trial could have resulted in non-compliance. If this was not recorded it could have distorted the results considerably.

One group was given the active product and the other the placebo, which was a lactose powder with the same particle size and appearance as the inert cellulose powder and supplied in an identical container (the containers were labelled A and B). The codes for the active and placebo products were not revealed until the data had been analysed at the end of the study. The nasal powders were supplied in plastic containers which delivered the powder from a nozzle when squeezed. The exact amount delivered is not

standardized and the variation of patterns of deposition in the nose are not known. These are topics of ongoing product development and research.

In total 116 subjects were recruited to the study, but 19 did not complete the 4 weeks. The analysis of results has been based only on those subjects who completed the whole trial. Analysis was done anonymously and in accordance with the data protection act. After the study was completed all participants were informed whether they had taken the active or placebo product and they were sent a summary of the results.

### Statistical methodology

Diary card data have been analysed for differences between the active and placebo groups both for individual aspects and combinations taking only those days with grass pollen counts at moderate, high or very high levels. Non-parametric tests have been used as follows: Chi<sup>2</sup> to test for differences in the distributions of the actual frequencies of scores, Mann–Whitney U-test of medians and correlations. Statistical significance was applied at the 95% level or above.

## Results

### Features of the two sample groups at the start of the study

The demographic features of age and gender showed no significant differences between the active and placebo groups at the start of the trial (Table 1). Similarly the occurrence and severity of individual hay fever symptoms (Table 2) reported from the previous 2 years also showed no significant differences between the groups. With 2 degrees of freedom, no values were within 1%, or 5% of significance levels. No significant differences were found between the active and placebo

groups in the use of different types of medication for hay fever in the previous two summers (at 1% significance level) (Table 3). Based on these results the two groups can be taken as being drawn from the same population for the study.

### Diary card results

No significant differences were found at the 1% level in differences in the distribution frequencies of Likert scores for any of the individual symptoms. However, some significant differences were found at the 5% level (Table 4). These differences were such that symptom scores were higher in the placebo group than in the active group.

No significant differences occurred between the total Likert symptom daily scores for the active and placebo

groups (Figure 1 and Table 4), using a non parametric test of difference in central tendency.

The number of times that the inert cellulose powder was taken by the active group compared to the placebo group (Figure 2) was similar. On most days a few people in each of the groups forgot to take their powder, or did not take it for various other reasons such as having a cold.

Very few visits to GPs for allergy related symptoms were recorded for either group. No significant differences were detected in the number of people in each group reporting symptoms of colds or flu. No adverse reactions were reported by any of the participants in the study. Of the 19 people who did not complete the 4 weeks of trial, 4 said that they did not like the feel of powder in the nose, 1 went on holiday and 14 gave no reason for giving up.

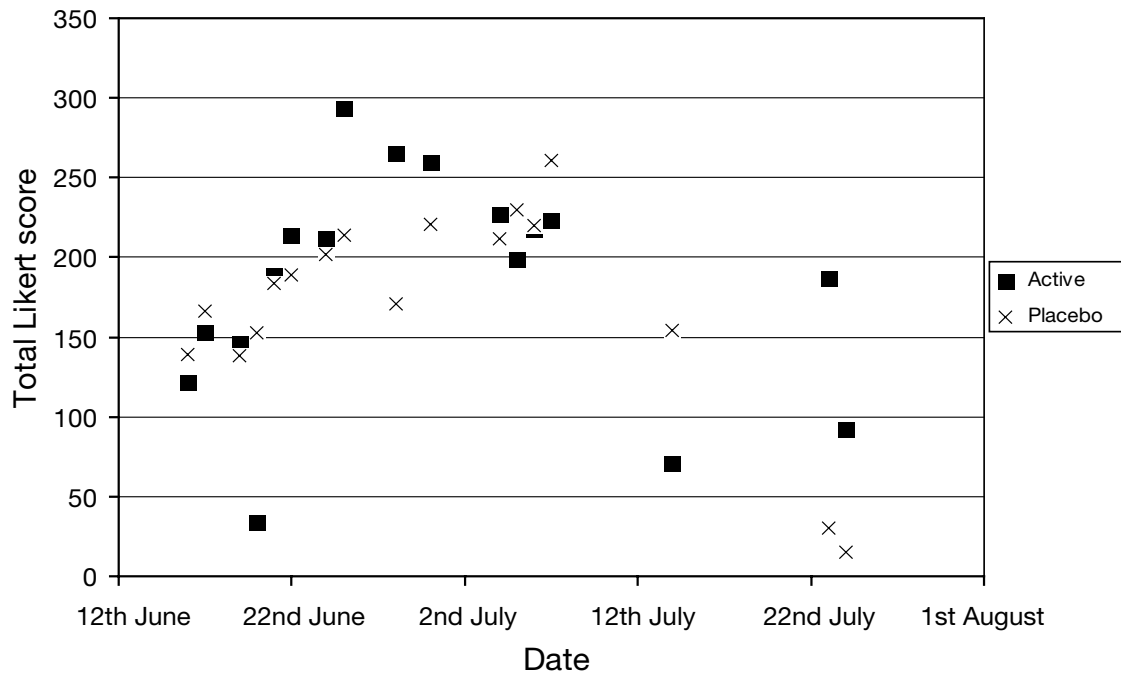


Figure 1. Total Likert scores for active and placebo groups on days with very high, high or moderate pollen counts

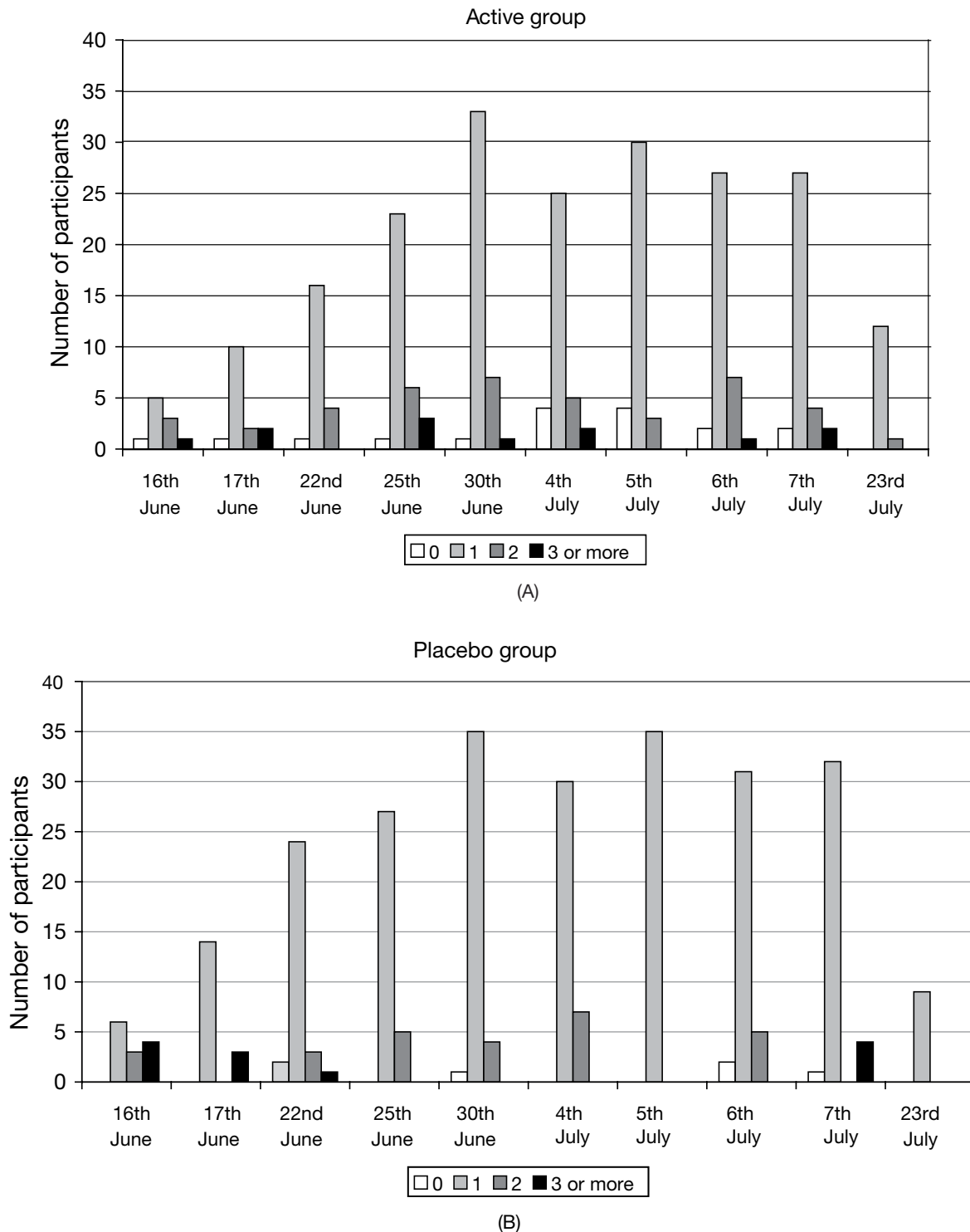
Table 4. The differences in symptom scores between active and placebo groups over the study period

	Chi <sup>2</sup> value	Significance	Degrees of freedom (n – 1), based on number of classes for frequency
Sneezing			
Moderate pollen count days	6.31	Not significant	4
Running nose			
Moderate pollen count days	10.05	Significant at 5%	5
High and very high pollen count days	8.04	Not significant	5
Blocked nose			
Moderate pollen count days	8.17	Not significant	5
High and very high pollen count days	12.16	Significant at 5%	5
Watering eyes			
Moderate pollen count days	5.78	Not significant	4
High and very high pollen count days	5.92	Not significant	5

## Rescue medication

Significant differences were found in the overall amounts of rescue medication taken by the active and placebo groups (Figure 3 and Table 5). For simplicity, in Table 5, both the inert cellulose powder and the placebo are referred to as 'Nasal powder' as the subjects did not know what they were taking. Almost all of the treatments are 'once a day', the exceptions being some herbal remedies. The results are analysed on a daily basis so there is a measure of the amounts taken.

Considering individual types and combinations of remedies, the predominant pattern was such that more people in the placebo group took treatments than those in the active group. This was apparent for all the types and combinations with the exception of homeopathic remedies and a combination of nasal sprays and eye drops. Antihistamines were by far the most frequently used type of medication (Figure 3). In the active group, 29% of people took only antihistamines compared with 33% in the placebo group (Figure 4). There was no significant difference between these groups, but when



**Figure 2.** The number of times each day the nasal powder was taken by (A) the active and (B) placebo groups on days with high or very high pollen counts

overall use of antihistamines is considered (i.e. people using antihistamine whether or not it is in combination with other medication), the percentage in the active group was 34% compared with 48% in the placebo group (significantly different at  $p < 0.05$ ). Taking into

account all days with grass pollen counts at high or very high only, the figures are 34% for the active group and 45% for the placebo group (significantly different at  $p < 0.05$ ). The Mann–Whitney U-tests are reinforced by results from correlation (d.f. = 15, Rho statistic =

**Table 5.** Summary of statistical tests on medication taken by the active and placebo groups during the study period

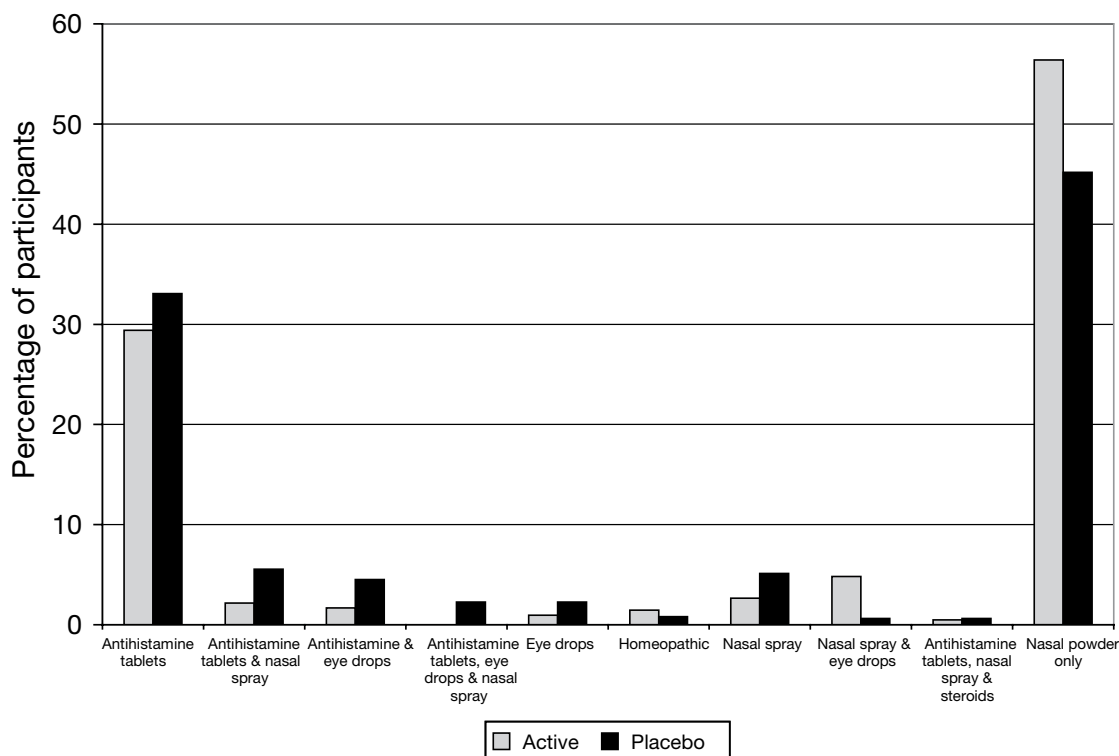
Overall medication taken	Chi <sup>2</sup> value significant at $p \leq 0.1$	Degrees of freedom ( $n - 1$ )
Very high, high and moderate pollen days	51.32	–
Very high and high pollen days	20.73	–

Mann–Whitney U-test results on medication categories	$p$ values (< 0.05 = significant)	Degrees of freedom ( $n - 1$ )	Means		SD	
			A	P	A	P
High and very high pollen days, medication – nasal powder only	0.288	9	15.6	13.7	7.62	6.2
Combined pollen days, antihistamine (+ nasal powder)	0.000	16	8.23	31.4	3.9	12.1
High and very high pollen days, antihistamine (+ nasal powder)	0.048	9	9.4	33.2	4.17	12.32
Combined pollen days, nasal spray (+ nasal powder)	0.037	16	2.47	4.06	1.66	2.19
Very high and high pollen days, nasal spray (+ nasal powder)	0.179	9	3.2	4.5	1.33	2.17
Combined pollen days, eye drops (+ nasal powder)	0.103	16	1.8	2.76	1.07	1.6
Very high and high pollen days, eye drops (+ nasal powder)	0.050	9	2.1	3.1	0.88	1.85

Combined pollen days are those with very high, high or moderate grass pollen counts

A = active group

P = placebo group



**Figure 3.** Percentage of participants in the active and placebo groups taking different types of hay fever treatments over the study period

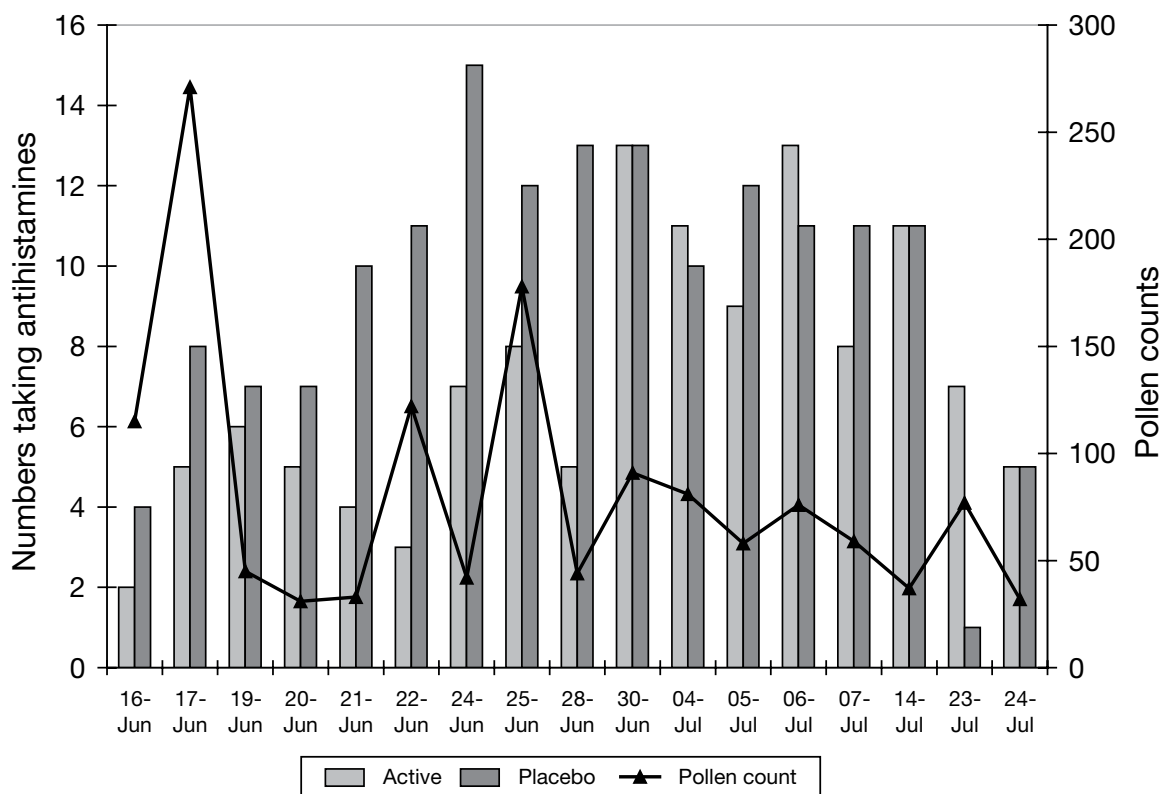


Figure 4. Numbers of people taking antihistamines in the active and placebo groups on days with very high, high or moderate pollen counts over the study period

1.91) which is not significant at 1% or 5% levels of probability. This indicated that there was no significant relationship between the data sets for the two groups and that they were different.

Nasal sprays were the second most frequent type of medication used. Taking all the days with grass pollen counts at moderate or above, 10% of the active group took nasal sprays compared to 14% of the placebo group (significantly different at  $p < 0.05$ ). In the case of eye drops, there is no significant difference between the results for the two groups in the data for days combined but considering only high and very high grass pollen count days, 7.5% of subjects in the active group used eye drops compared to 11.3% in the placebo group (significantly different at  $p < 0.05$ ).

The placebo group participants took a wider range of medication combinations than those in the active group. Very few subjects in either group took steroids or homeopathic remedies. Fifty-seven per cent of subjects in the active group took the inert cellulose powder only, with no rescue medication, on days with counts at moderate or over, compared with 44% in the placebo group (Figure 5).

## Discussion

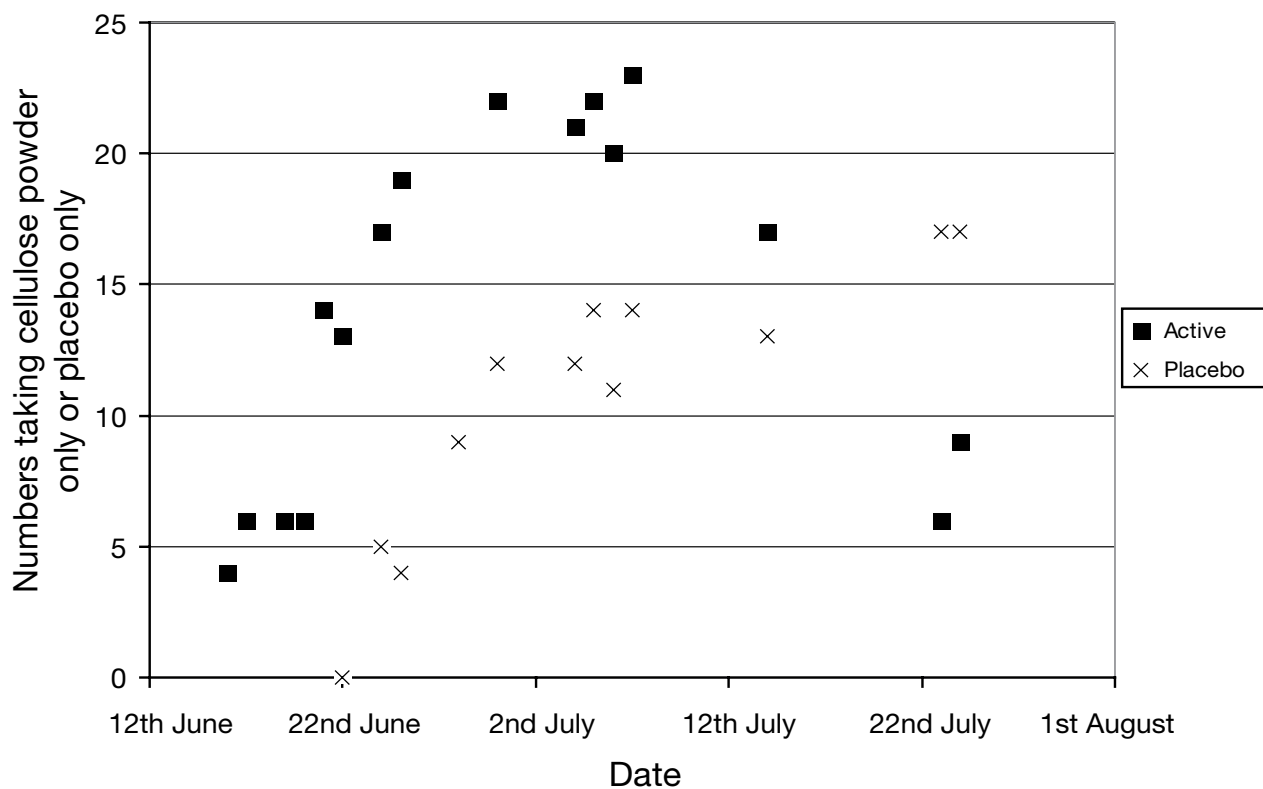
The main differences in the results between the two groups occurred in the amounts of rescue medication taken. This measure is widely used in research on

allergy and related areas, for example by Rolinck-Werninghaus *et al.*<sup>11</sup>, Miller *et al.*<sup>12</sup> and Roefaro and Daryanari<sup>13</sup>. The overall significant difference in the amounts of medication taken is reinforced by the results of tests on individual types. The significantly different results in the amounts of medication taken by the active and placebo groups show similarities across three types of hay fever medication i.e. antihistamines, nasal sprays and eye drops. This constancy of outcome helps to confirm the results. The only case in which more rescue medication was taken by the active group than the placebo group, was in the group taking nasal sprays and eye drops without antihistamines. This suggests that the inert cellulose powder may not have an effect on eye symptoms but the sample size is small and this aspect would have to be investigated further.

The results show that there are few significant differences in the symptom scores during the trial for the two groups in the cases of individual symptoms (sneezing, runny nose, blocked nose, watering eyes). The subjects did not all experience each of the symptoms that were monitored. They were also taking medication if they wanted to. Consequently, the total Likert scores are not high and this is not unexpected.

The amount of rescue medication taken by the placebo group was significantly more than that taken by the active group, both overall considering all types of medication and also in the individual cases of antihistamines, nasal sprays and eye drops. There were no significant differences in the demographic profiles of





**Figure 5.** Numbers of people taking cellulose powder only or placebo powder only on days with very high, high or moderate pollen counts over the study period

the two sample groups or in the severity of their reported symptoms in previous grass pollen seasons. This indicates that the inert cellulose powder was operating to reduce the symptoms of hay fever in the active group.

### The 2004 grass pollen season

The 2004 Worcester grass pollen season was less severe than average. The first 2 weeks of June followed a typical pattern of many days with high counts but after this, rainfall was above average (108% of long term norm). Despite the unusually low severity of the grass pollen season overall, there were sufficient moderate, high and very high days during the trial to provide an adequate sample (pollen count categories for grass are moderate 30–49 grains per cubic metre, 50–149 high, 150 or over very high). Due to the season being below average severity, the results were analysed for those days with moderate, high or very high grass pollen counts only. Once inflammation is established some symptoms can persist on days when pollen counts are lower. However, in this study use of medication is an outcome measure and this is more likely to be related to the days with pollen counts above the threshold. In a season which is markedly below average severity the inclusion of substantial periods with low pollen counts could distort the results.

Apart from grass pollen, the other main pollen types in the air during the trial were Nettle (*Urtica* spp.), with minor amounts of oil seed rape (*Brassica napus*) and

weeds such as Plantain (*Plantago* spp.) and Mugwort (*Artemisia* spp.). The thresholds of response to these taxa are not well established due to lack of clinical evidence but the days when moderate, high or very high pollen counts occurred for these other types coincided with those for grass, due to the overriding influence of weather conditions on pollen release and dispersal.

### Discussion of results

The data generated from this study were from self reporting by volunteers who had been admitted to the trial on the basis of a baseline questionnaire. These aspects could produce some bias and subjectivity in the data which needs to be considered. For example, in some of the participants the diagnosis of hay fever in the peak grass pollen season was based on their description of the symptoms and the timing of them. However, the application of the exclusion and inclusion criteria was designed to eliminate those with perennial rhinitis which could be caused by indoor allergens or by non-allergic rhinitis.

The scale of severity of symptoms is relative and may be applied differently by individuals. However, the use of Likert scores is a well established and accepted methodology and the relatively large sample size would reduce any bias. The results from the baseline questionnaire have shown no significant differences in the severity of the symptoms reported by the two groups at the start of the study.

In the trial itself it is possible that the use of the placebo powder could have caused some 'wash out effect'. If this was the case, then the outcome would be to decrease the differences between the results for the two groups, whereas certain significant differences have been detected.

Towards the end of the season there are 2 days (July 6th and July 23rd) on which more people in the active group took antihistamines than those in the placebo group (Figure 4). Similarly there are 2 days (July 23rd and 24th) when the total Likert scores for the active group are higher than those for the placebo group (Figure 1). These differences are not statistically significant due to the small sample sizes (2 days in each case). The subjects did not report irritation from the powder. It is possible that the active group took less anti-inflammatory medication earlier in the season and may have suffered more nasal infiltration by inflammatory cells which will take longer to settle down.

It is reasonable to suppose that the few significant differences in the symptom scores shown between the two groups in the data from the diary cards, reflect a real difference due to the action of the cellulose powder combined with the amounts of rescue medication taken. Exposure to a large amount of grass pollen on days with very high counts would present a severe challenge to hay fever sufferers and could result in all hay fever sufferers, who are allergic to grass pollen, having some symptoms despite taking treatments<sup>14</sup>.

Although it is very likely that someone who had hay fever in June and July would be allergic to grass pollen, it is possible that they were allergic to other types such as weeds and summer flowering trees either in addition to grass or on their own. All types of pollen released in June and July tend to have high counts during the same sort of weather as grass pollen due to the influence of variables such as temperature, rainfall and wind. It is extremely unlikely that pollen counts for weeds and the few summer flowering trees would be low on days when the grass pollen count was moderate or high. This factor would tend to produce synchronisation of symptoms for hay fever sufferers at this time of year.

These results provide evidence that the inert cellulose powder reduces the need to take rescue medication for the symptoms of hay fever. Further research is needed to explore the effects of the cellulose powder in controlling symptoms of hay fever when the subject is not taking any medication and also to determine the degrees of protection conferred in different pollen concentrations (moderate through to very high). It would also be useful to run comparative studies between the cellulose powder and conventional medications. In addition, research is needed to investigate how the cellulose powder works because an

understanding of the mechanisms is likely to help in the development of the product and in the extension of its applications.

Both of these aspects will be addressed by challenge tests planned to take place outside of the pollen season. Known amounts of grass pollen allergen will be introduced to the noses of subjects under controlled conditions when they are not taking medication for hay fever and the response will be monitored both for expression of symptoms and physiological reactions. The outcome of these experiments will help the design of further trials. In particular, it would be useful to determine whether the inert cellulose powder can be employed to reduce or even eliminate the use of steroids in pollen allergy, including some cases of asthma.

Although the mechanism of action is unknown, the fact that cellulose is an inert substance which develops a gel-like consistency on contact with moisture indicates that it is likely that the primary mechanism of action of the product is to produce a simple mechanical barrier to the allergenic component of the pollen grains preventing them from triggering an inflammatory response on the mucosal membrane. The benefit of this product is that it has the potential ability to reduce the need for the use of other medication such as decongestants and intranasal steroids which are known to have significant side effects. There is also an economic benefit as the over the counter cost of the cellulose powder works out at less than 50% of the daily cost of antihistamines. It is about the same cost as or slightly less than the daily dose for most nasal sprays.

## Acknowledgements

**Declaration of interest:** The study was sponsored by Kisska International Ltd.

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# **Efficacy of Nasaleze for use in hayfever via pollen provocation tests**

Emberlin JC, Lewis RA. A double blind, placebo controlled cross-over trial of inert cellulose powder, by nasal provocation with grass pollen to assess efficacy of the product in controlling the symptoms of hay fever.

Poster presented at EAACI, Vienna  
June 2006.





# Double blind placebo controlled cross over trial of inert cellulose powder, by nasal provocation with grass pollen to assess efficacy of the product in controlling symptoms of hay fever

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## Introduction

Inert cellulose powder has been on sale in the UK as a remedy for hay fever since 1994. It is applied to the inside of the nose where it forms a gelatinous coating. The results of a double blind placebo controlled study which the authors conducted on 98 hay fever sufferers over the 2004 grass pollen season showed that the active product group used significantly less rescue medication than that using the placebo (Current Medical Research and Opinion 2006;22:2:275-285). The aim of this study was to explore the effects of the cellulose powder in controlling symptoms when subjects are not taking any medication.

## Method

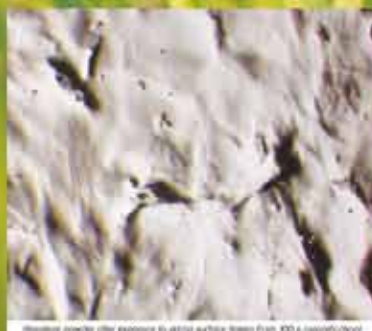
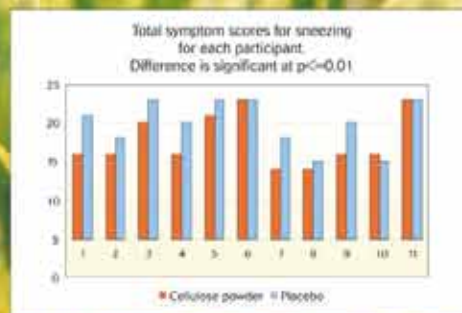
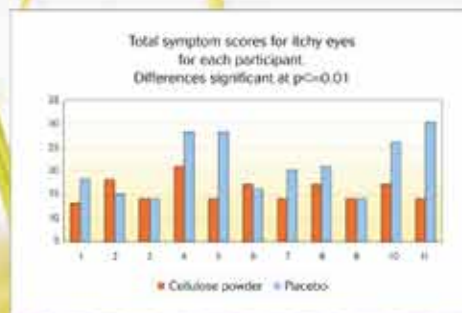
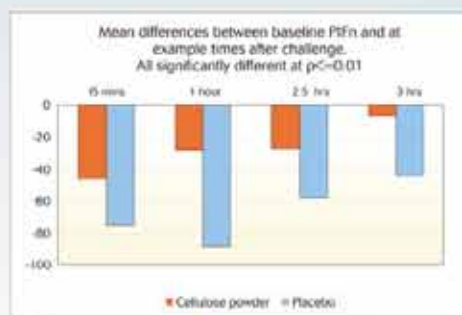
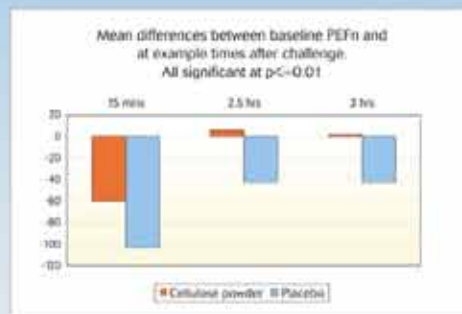
A double blind placebo controlled cross over trial was conducted on 11 adult hay fever sufferers (diagnosed to be allergic to grass pollen but not to tree pollen by SPT and who had symptoms in the previous two summers). The sample size was set by a power calculation. The trials were in the spring before the grass pollen season. The placebo was lactose powder. Exclusion criteria were applied e.g. those with perennial rhinitis or asthma. Ethical approval was given by the National system of research ethics committees. Powder (real or placebo, order randomised) was put into the nose, followed by grass pollen equivalent to 350 grains per cubic metre air. At baseline and at regular intervals after challenge, scores were taken for 6 symptom categories, nasal secretions were sampled for ECP, and measures were taken of nasal peak inspiratory and expiratory flow. All measurements were continued in the clinic for 4.5 hours, then symptom scores and basic lung function were repeated at 6.5 hours and at 24 hours after challenge.

## Results

Significant differences ( $p < 0.05$  and  $p < 0.01$ ) occurred in the data at various times from challenge in peak nasal expiratory flow between placebo and active treatments, and also in nasal PIF, in sneezing and in itching eyes. The results for other lung function tests and symptoms were slightly under the level for significance. The results for the nasal secretions were significantly different at  $p < 0.05$ . No adverse reactions occurred.

## Conclusion

The results of the trial show that the inert cellulose powder can have significant effects in reducing symptoms of sneezing and itchy eyes due to grass pollen allergy. It can also have significant effects in reducing nasal inflammation, as measured as nasal PEF, PIF and as ECP in secretions. The results indicate that the use of inert cellulose powder can help to alleviate symptoms of hay fever.



Acknowledgement - This study was funded by Kisska International Ltd makers of Nasaleze



# **Double blind placebo controlled dust mite challenge study**

Emberlin JC, Lewis RA. Double blind placebo controlled cross-over trial of Nasaleze by nasal provocation tests with Der p1 and Der f1.

Presented as a Poster EAACI,  
Gothenburg June 2007.

Current Medical Research Opinion; Vol 23;  
No 10; 2007, 2423-2431.





# A double blind placebo controlled trial of cellulose powder as a remedy for persistent allergic rhinitis, by nasal provocation with Der p1 and Der f1

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## Background

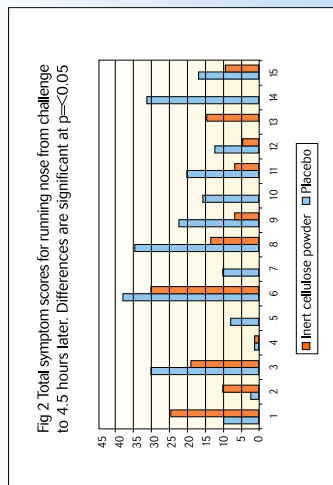
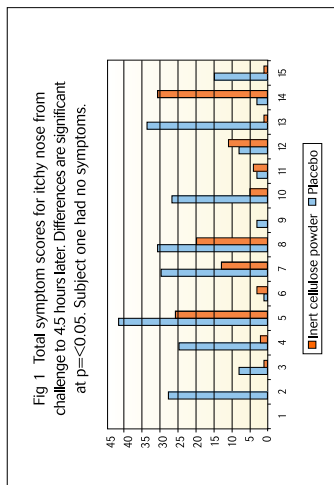
The study aimed to investigate the efficacy of inert cellulose powder applied to the nose for the control of persistent allergic rhinitis in adults due to house dust mite allergy. The powder has been registered as a medical device in the UK since 1994 and is on sale in many countries as a remedy for hay fever.

Two previous trials by the authors have demonstrated the efficacy of the powder in the control of some symptoms of hay fever.

## Method

A double blind placebo controlled cross over trial was conducted on 15 adult persistent rhinitis sufferers (male and female, diagnosed positive to Der p1 and/or Der f1 by SPT) and with symptoms over the previous two years, the placebo was lactose powder. Base line measurements were taken. Subjects were symptom free at the start of each trial. Challenge was a 0.01 µg dose delivered to each nostril, of homogenised dust containing 5 µg of Der p1 and 5 µg of Der f1 per g.

The study took place in the spring before the main pollen seasons. The primary outcome measures were observed severity scores for symptoms (sneezing, nasal secretion and runny eyes) and amount of ECP in nasal secretions. The secondary outcome measures were symptom scores by subject report (nasal blockage, itching of nose, throat and eyes), nasal peak inspiratory and expiratory flow. Observations and measurements were taken 5 mins after challenge then at every 15 mins for the first hour, then at 30 min intervals until 4



Adult *Dermatophagoides farinae* taken from SEM at 3,500 times magnification. Actual size about 0.33mm long.



Adult male of *Dermatophagoides pteronyssinus* taken from 400 times magnification.

hours, then at 6 hours and at 24 hours to observe any late phase reactions. The second trial for each subject was at least 7 days after the first visit. The order of treatments was randomised. Ethical approval was given by the NHS local ethics committee REC no 05/Q2801/104.

## Results

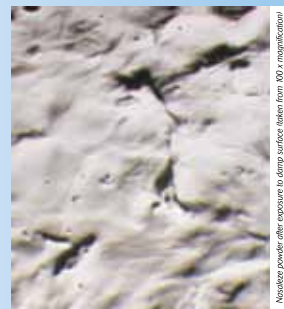
The results show significant differences ( $p < 0.05$ ) for sneezing, itchy nose, runny nose and ECPs in nasal secretions. The results were also significant at this level for peak nasal expiratory and inspiratory flow but there was considerable variation. The results for other symptoms were not significantly different between the cellulose powder and the placebo. There were no adverse reactions.

## Conclusions

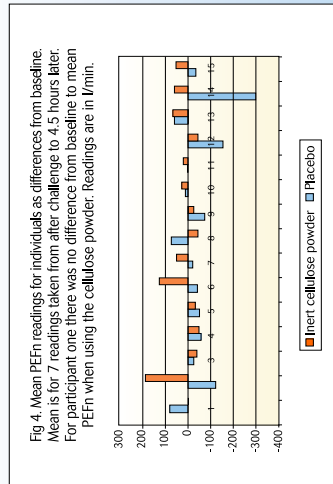
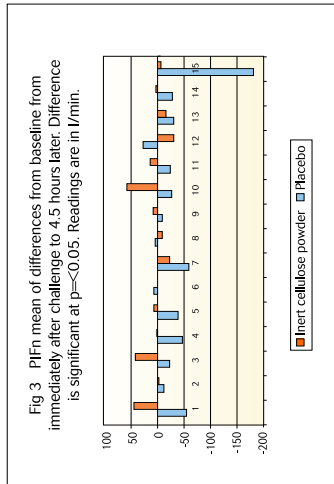
The inert cellulose powder can have significant effects in reducing some symptoms of persistent rhinitis due to house dust mite allergy.



Nasal mucus after exposure to inert cellulose powder taken from 100 x magnification



Nasaleze powder after exposure to damp surface taken from 100 x magnification



Acknowledgement - this study was funded by Kisska International Ltd makers of Nasaleze



ORIGINAL ARTICLE

# A double blind, placebo-controlled cross over trial of cellulose powder by nasal provocation with Der p1 and Der f1

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**Key words:** Cellulose – House dust mite – Provocation test – Rhinitis

## ABSTRACT

**Objective:** The purpose of this study was to assess whether inert cellulose powder would reduce the response to nasal challenge with house dust mite antigens. The study aimed to investigate the efficacy of inert cellulose powder applied to the nose for the control of persistent allergic rhinitis in adults due to house dust mite allergy. The powder has been registered as a medical device since 1994 and is available in many countries as a remedy for hay fever. Anecdotal evidence reported that it reduced symptoms of persistent rhinitis but no scientific evidence exists for this.

**Research design and methods:** A double blind, placebo-controlled cross over trial was conducted on 15 adult persistent rhinitis sufferers (diagnosed positive to Der p1 and/or Der f1 by SPT) and who had symptoms over the previous 2 years. The placebo was lactose powder. Challenge was by measured dose of homogenised allergenic dust. The study took place in the spring of 2006 before

the main pollen seasons.

**Main outcome measures:** The primary outcome measures were observed severity scores for 3 symptom categories and the amount of ECP in nasal secretions. The secondary outcome measures were symptom scores by subject report (nasal blockage, itching of nose, throat and eyes), nasal peak inspiratory (PIFn) and expiratory flow (PEFn).

**Results:** The results show significant differences for sneezing, itchy nose, runny nose and ECPs in nasal secretions. Some results are also significantly different between placebo and active for PIFn and for PEFn (all at  $p = 0.05$ ). There were no adverse reactions.

**Conclusions:** The inert cellulose powder can have significant effects in reducing some symptoms of persistent rhinitis due to house dust mite allergy.

## Introduction

The trial reported in this paper aimed to investigate the efficacy of inert cellulose powder applied to the nose for the control of symptoms of persistent allergic rhinitis in

adults due to house dust mite allergy. Allergic rhinitis is a heterogeneous disorder that has high prevalence but is often undiagnosed<sup>1</sup>. Symptoms include one or more of sneezing, itching, nasal congestion and rhinorrhoea and can have a notable impact on quality of life as

well as exerting a high economic cost. In a two step cross-sectional population based study in 6 European countries the prevalence of subjects with clinically confirmable allergic rhinitis ranged from 17% in Italy to 29% in Belgium with an overall value of 23%<sup>2</sup>. This large scale study confirmed that allergic rhinitis has a high prevalence in Western Europe and is frequently undiagnosed. In addition, within the population with allergic rhinitis, 29% had persistent rhinitis. Bauchau and Durham report that this group had more severe symptoms and a greater self awareness<sup>3</sup>. In the USA, allergic rhinitis affects approximately 20–40 million people<sup>4</sup> of whom 20% are intermittent, 40% persistent and 40% of cases are mixed<sup>5</sup>.

Inert cellulose powder (Nasaleze\*) has been registered with the Medicines and Healthcare Products Regulatory Agency (formerly Medical Devices Agency) since 1994 and is on sale in many countries, including the UK, as a remedy for hay fever. It is applied to the inside of the nose where it forms a gelatinous coating. It is thought that this layer prevents the allergens from reaching the mast cells in the nasal mucosa. Two previous trials have been conducted by the authors to investigate the efficacy of the powder in the control of hay fever<sup>6,7</sup>. The results showed that the product reduces some symptoms. No adverse reactions were reported and the trials confirmed the powder as a low cost remedy with no known side effects.

Anecdotal evidence suggested that the powder also reduces symptoms of persistent rhinitis but scientific evidence was lacking. The principal objective of the current trial was to determine if the inert cellulose powder has a significant effect in the control of symptoms of persistent allergic rhinitis due to house dust mite allergy when no other medication was being taken.

## Patients and methods

### Basic study design

A double blind placebo controlled cross over trial with allergen provocation was conducted on 15 adult persistent rhinitis sufferers who had symptoms over the previous 2 years. The placebo was lactose powder. The study took place in the spring of 2006 before the main pollen seasons.

### Ethical considerations

Ethical approval was given by NHS Hereford and Worcester local ethics committee REC number

05/Q2801/104. The study complies with the declaration of Helsinki.

### Patients

Fifteen adult patients were recruited both male and female during the month before the trial. The sample size was set by a power calculation which indicated that the probability was 90% that the study would detect a treatment difference at a two sided 1.00% significance level if the true difference between the treatments is 1.609 units. This is based on the assumption that the within patient standard deviation of the response variable is 1.000.

Potential volunteers were sent a Baseline questionnaire 1–2 months before the trial which included questions on monthly occurrence and severity of symptoms, treatments used etc. People who seemed to be suitable were invited for a skin allergy test if they had not had one in the previous year. Selection was then based on the following. Inclusion criteria were subjects who have had a positive skin prick test for house dust mite allergen (Der p1 and/or Der f1) performed within the previous 12 months (wheal diameter at least 75% as large as histamine control), subjects who have had persistent rhinitis symptoms for a minimum of 2 years and were being treated by a doctor for this and who have no history of asthma. Principal exclusion criteria were people with asthma, upper respiratory viral infections, nasal deformities, pregnant women and people who have any other adverse medical conditions. Subjects must not have taken antihistamines in the preceding week or have used corticosteroids within the preceding 30 days.

### Study design

Before the start of each trial the subjects were interviewed to explain the procedures in detail and to check for the presence of the symptoms that would be monitored, namely, sneezing, runny nose, itchy eyes, running eyes, itchy nose, itchy throat and itchy throat/palate. The symptoms were assessed by observation and by questionnaire which took approximately 30 min. If the subject had these symptoms that day they were excluded from the trial and another appointment was made. No medication was permitted to be taken by the subjects during the trial.

A pre wash (2.5 mL sterile saline) was given to each nostril and allowed to dry for 15 min. The saline wash was retained for analysis for ECPs (Eosinophil cationic proteins)<sup>8</sup>. Baseline PIFn (Nasal peak inspiratory flow) and PEFn (Nasal peak expiratory flow) were taken

\* Nasalez is a registered trade mark of Nasaleze International Ltd

(best of three noted) using a computerised system (Vitalograph 2120 operated with the Vitalograph Spirotrac 4.20 software). Baseline symptom scores were also recorded.

Powder (real or placebo labelled as A or B, order randomised by blind draw) was put into each nostril as two applications per nostril from a plastic bottle with a patented valve applicator and was allowed to settle for 15 min. During the application the subjects were asked to breathe in but were told not to sniff. The powder was applied by a trained member of staff (either a nurse or a post doctorate researcher). The placebo was a lactose powder of similar particle size to the cellulose and in identical plastic bottles. New bottles were used for each application.

An allergen challenge was delivered to the nostrils by a Morrow Brown microspoon<sup>9</sup>, equivalent to 5 µg of Der p1 and 5 µg Der f1 per g of inert carrier fine particle dust (particles 15–100 µm). The dust was prepared in house and the allergen content was checked by 3 separate repeats of ELISA for Der p1 and for Der f1 each with 5 replicates at 4 serial dilutions. The dose given was 0.01 µg of homogenised dust mix in each nostril.

At baseline and at regular intervals after challenge, scores were taken for sneezing, itchy eyes, running eyes, itchy nose, running nose, itchy throat and itchy throat/palate graded as symptoms 0 = absent, 1 = very mild, symptoms hardly noticeable, 2 = mild, symptoms noticeable intermittently but do not interfere with any normal daily activities, 3 = moderate, symptoms noticeable all the time but do not interfere with any normal daily activities, 4 = severe, symptoms interfere with normal activities some of the time, 5 = very severe, symptoms interfere with normal everyday activities constantly. They were taken 5 min after challenge, every 15 min for the first hour after challenge then at 30 min intervals until 4 h after challenge, then at 6 h and at 24 h to observe any late phase reactions.

Nasal secretions were sampled for ECPs and measures were taken of PIFn and PEFn at 5 min after challenge, 15 min later, then at 30 min intervals for a further 2 h, then again at 4 h. At 6 h and 24 h after challenge peak flow readings were taken.

Nasal secretions were taken by inserting pre-weighed Whatman number 1 filter strips (Whatman Ltd, England) into the nostrils (left and right separately) following the methodology described by Knowles *et al.*<sup>10</sup> which is acceptable to subjects and minimises stimulation that could lead to extra sneezing or secretions. The strips were stored in eppendorf tubes (pre-weighed), re-weighed then frozen until analysis. Any with blood stains were discarded. The nasal wash taken at baseline before the start of each session and the samples of nasal secretions taken through the trials

were analysed for ECPs using the Pharmacia Unicap system by the Department of Immunology, Northern General Hospital, Sheffield.

The second visit for each subject for the trial with the alternative powder was at least 7 days after the first visit.

The primary outcome measures were observed severity scores for symptoms (sneezing, nasal secretion and runny eyes) and the amount of ECP present in nasal secretions. The secondary outcome measures were symptom scores by subject report (nasal blockage, itching of nose, itching of throat, itching of eyes), PIFn and PEFn.

The participants and researchers did not know the identity of the powders until after the analysis was completed.

## Subjects

Seven female and eight male subjects were recruited ranging in age from 18 to 60 years (modal age range 38–47 years). All had consulted their doctors about 'year round' symptoms of rhinitis. The recruits were selected on the basis of replies to a baseline questionnaire, an interview covering the baseline questions and the results of a skin allergy test. The baseline questionnaire and interview included questions designed to investigate whether patients had symptoms due to their house dust mite allergy. For example, subjects were questioned with regards to the severity of their symptoms and when and where they experienced these symptoms. Only those patients who had a suitable symptom history were recruited. The possibility of sensitisation to other allergens which may have been present in the home during the time the trial was undertaken was not taken into account. Subjects were symptom free at the start of the trial.

Some differences in the severity of rhinitis symptoms experienced over the previous 2 years were noted in the recruitment questionnaire (Table 1) but all of the recruits had persistent symptoms of frequent sneezing and runny nose to some degree. All of the subjects were allergic to Der p1 and 10 were also allergic to Der f1. The differences in subject profile were considered in the interpretation of the results. For example, the results of the skin allergy tests and the range and severity of symptoms reported in the baseline questionnaire were considered.

## Statistical analysis

In most cases nonparametric tests of significant difference (Mann–Whitney and Wilcoxon tests) were applied as these do not assume normality and can be used to test ordinal variables. Student *t*-tests were used where possible

**Table 1. Profile of the 15 participants**

(a) Age, gender and symptom severity reported on recruitment questionnaire for the 15 participants															
Participant No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Gender M/F	F	M	F	F	M	M	M	M	F	F	F	F	M	M	M
Age range	38-47	58+	38-47	38-47	58+	28-37	58+	58+	38-47	58+	28-37	18-27	58+	48-57	38-47
Symptom scores as estimate for severity over the last 2 years; symptoms 0 = none, 1 = slight, 2 = moderate, 3 = severe															
Sneezing	2	2	3	2	3	3	1	2	2	1	3	2	3	3	3
Itchy eyes	2	0	3	2	2	3	1	3	2	0	2	1	1	3	2
Running eyes	0	1	2	2	3	1	1	2	0	2	2	0	1	3	3
Running nose	2	2	2	2	3	2	2	2	1	2	3	1	3	3	3
Blocked nose	0	2	2	3	3	3	0	3	3	0	3	2	0	3	3
Headache/tiredness	0	1	2	2	2	3	0	3	2	2	1	1	1	2	3
Itchy throat/mouth	2	2	2	2	2	1	0	2	2	0	2	0	3	3	2
Total symptom score	8	10	16	15	18	16	5	17	12	7	16	7	12	20	19
Seasonality of symptoms over last 2 years															
All year	All	All	All	All	All	All	All	All	All	All	All	All	All	All	All
but less in winter	year	year	year	year	year	year	year	year	year	year	year	year	year	year	year
	but											Any time of year but not constantly			

**(b) Skin test results and medication used routinely for rhinitis**

Participant No	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Skin test result*	No	No	4.0	4.0	No	No	4.0	7.0	6.0	No	5.5	6.5	6.0	5.0	3.5
Der f1 (mm)	6.0	4.0	5.0	5.0	3.5	5.5	5.0	6.0	5.0	5.5	5.5	6.5	4.0	7.5	5.6
Medication used for symptoms of rhinitis**															
NS, A, S	P	A	A	NS	NS	N	N	N	ST	N	A	N	A	NS	NS, A

\*Y = yes then diameter of wheal (all at least 75% diameter of histamine control)

No = negative test result

Medication used\*\*: A = antihistamine tablets; NS = nasal spray; P = pseudoephedrine hydrochloride; S = steroids; ST = sudafed tablets; NS = not specified; N = none

in cases of interval scale data. The level of probability was set at 0.05 or higher for acceptance. In many cases the data sets were highly skewed so descriptive statistics such as standard deviation are not useful. However, these have been included for comparison in some cases.

## Results

No adverse reactions occurred. All 15 participants completed both stages of the trial.

In the cases of several of the symptom categories the scores were low or zero for many of the subjects. This may have been because the patients did not have allergic sensitivity to house dust mite. The low scores or absence of some symptoms could have been due to the relatively low amount of the challenge given and to the subjects' tendency to get only certain types of symptoms rather than all of the ones being monitored.

### Primary outcome measures

#### Symptom scores

In the results for symptoms of runny nose (Figure 1), the differences overall are significant at the  $p \leq 0.05$  level. Means are 8.8 cellulose powder and 15 placebo with SD 8.4 and 11.5, respectively. The confidence intervals of the means are 4.0 and 6.1 at  $p \leq 0.05$ .

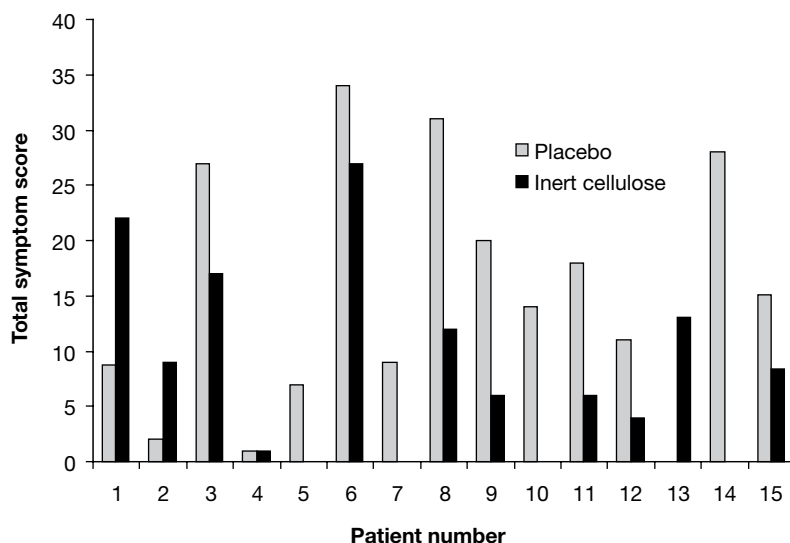
In the case of sneezing, the difference in symptom scores is significant at  $p \leq 0.05$  (means were 3.5 cellulose powder and 9.5 placebo, SD 3.6 and 10.2, confidence interval of the mean 1.4 and 5.2, respectively at  $p \leq 0.05$ ). However, 4 subjects did not have symptoms.

Six subjects did not have any symptoms of running eyes on either stage of the study. A further 5 had only

very low scores and spasmodic symptoms. Of the other 4, three had zero scores with the cellulose powder but had total scores for the placebo of 17, 10 and 10, and one subject had a total score of 6 with the placebo against 1 with the cellulose powder.

#### Eosinophil cationic proteins

The results show a wide variance between ECP; however, there is a general trend towards the presence of larger amounts of ECP after the first 20 min following challenge (Table 2). In the samples taken 5 min after challenge (numbers 1–15), 7 of the participants had higher levels of ECP when the placebo was used than when the cellulose powder was used. This is compared with 3 subjects who had lower levels of ECP when on placebo than when on cellulose powder. The remaining 5 subjects had negligible differences. The same pattern is evident in the next set of readings, taken at 20 min after challenge. At 60 min after challenge, the level of ECP in some of the samples increased notably. Eight of the subjects had higher ECP levels with the placebo and in 5 cases, the differences were very large (over 100%). In 3 cases this difference occurred the opposite way round (results for cellulose powder were > 100% more than placebo). In the other four cases the results for the two wings were similar. Considering the magnitude of readings, for those at or over 2000  $\mu\text{g/L}$ , 13 are with the placebo and 9 with the cellulose powder. For those at or over 4000  $\mu\text{g/L}$  seven are with the placebo and 4 with the cellulose. For readings at or over 6000  $\mu\text{g/L}$  four are with the placebo and only 1 is with the cellulose. The readings for the placebo are significantly different from those for the cellulose powder ( $p \leq 0.5$ ), for the readings taken at 60 min and at 90 min after challenge.



**Figure 1.** Total symptom scores for running nose from challenge to 4.5 h later. Means are 15 for placebo, SD 11.5 and 8.8 for cellulose powder, SD 8.4. Differences are significant at  $p \leq 0.05$ . Vertical axis is total symptom score, horizontal axis is patient number

**Table 2.** ECP results per participant at 5 min, 20 min, 60 min and 90 min after challenge

Time after challenge in min	5		20		60		90	
	C	P	C	P	C	P	C	P
Participant								
1	64	1174	250	240	250	940	2072	487
2	136	80	77	304	288	303	54	200
3	271	278	59	64	825	315	220	500
4	1020	546	943	1212	2033	2313	1232	2548
5	250	100	375	645	176	120	250	863
6	284	304	902	111	833	946	1024	131
7	120	1008	300	1100	158	3540	300	249
8	860	675	N	307	5025	441	4085	185
9	968	2678	392	2033	3038	1050	736	1125
10	381	450	580	429	461	255	317	1011
11	3906	436	549	215	3061	10857	422	4500
12	248	5882	1606	2562	1916	7317	832	804
13	1025	1503	1954	710	7500	331	731	15575
14	1130	786	429	354	2919	284	1000	895
15	1136	990	1622	6383	4110	952	1485	5000
Totals	11799	16891	10038*	16667	32592	29966	14760	34072

C: cellulose powder; P: placebo; N: no data; \*One missing reading

ECP shown as  $\mu\text{g/L}$ . Differences are significant at  $p \leq 0.05$  between placebo and cellulose treatments for the readings taken at 60 min and at 90 min after challenge

## Secondary outcome measures

For symptoms of itchy nose (Figure 2) the difference in the results overall is significant at  $p \leq 0.05$ . Means are 17.2 with placebo and 7.8 with cellulose powder with SD 14.1 and 10.2, respectively. Confidence intervals of the means are 7.1 and 5.2 at  $p \leq 0.05$ . However, one subject had no symptoms and in 4 cases the total symptom scores were higher with the cellulose powder than with the placebo. In three of these cases the differences are not large but in one case there is a very marked difference.

For the other two symptom categories there are no significant results. For itchy mouth/palate, eight of the subjects had zero scores on both stages of the trial. For itchy throat, 5 subjects did not have any symptoms on either stage of the trial. The results for the other ten subjects are very similar for placebo and cellulose powder apart from one subject who had a total symptom score of 36 for the placebo and 24 for the cellulose powder.

## Nasal flow readings

In the majority of cases mean PIFn readings were notably better compared to baseline, after challenge when the inert cellulose powder was used, compared to the results when the placebo was used (Figure 3). The mean difference is significant at  $p \leq 0.05$ . Means are  $-25$  (placebo) and  $-3$  (cellulose powder) with SD

$-7$  and  $-29$ . The confidence intervals of the means are 50 and 14.7, respectively.

The mean peak PEFn results were significantly better ( $p \leq 0.05$ ) after challenge when the inert cellulose powder was used compared with when the placebo was used (Figure 4). However, in three cases (numbered 1, 3 and 8 on the figure) the results were better with the placebo than with the inert cellulose powder. The means were  $-43$  (placebo) and 22 (cellulose) with SD 96 and 95. The confidence intervals of the means were 48 and 47, respectively.

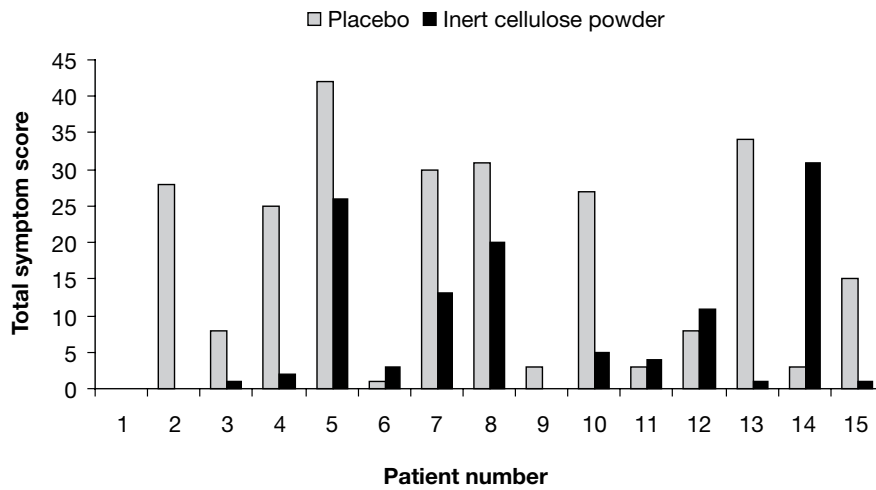
In several subjects there were marked differences with a clear pattern of decreased PEFn when using the placebo. These general patterns both for overall results and for individual subjects were apparent through the time course of the study.

## Discussion

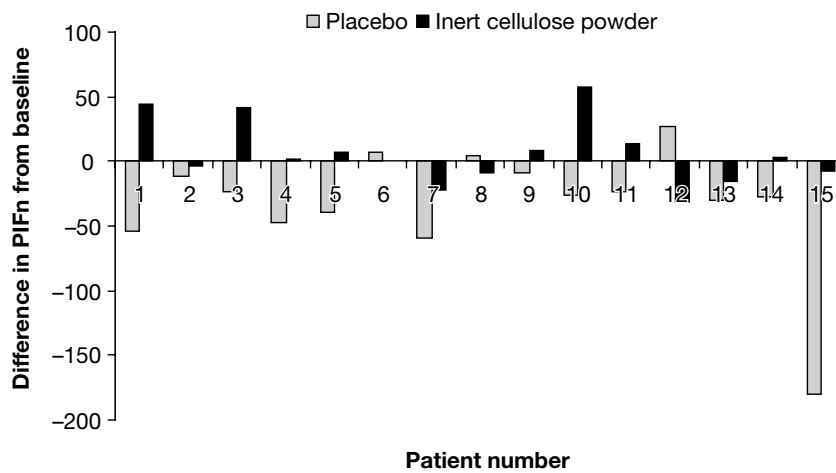
Although there was only a 1 week wash out period, no order effect was noted between wash out with active and placebo treatment. Also Baseline nasal resistance was noted to have returned to baseline after a minimum of a 1 week wash out period.

The results display considerable variance but this is not unexpected in trials such as this. A lot of factors may influence the outcomes, including thresholds of

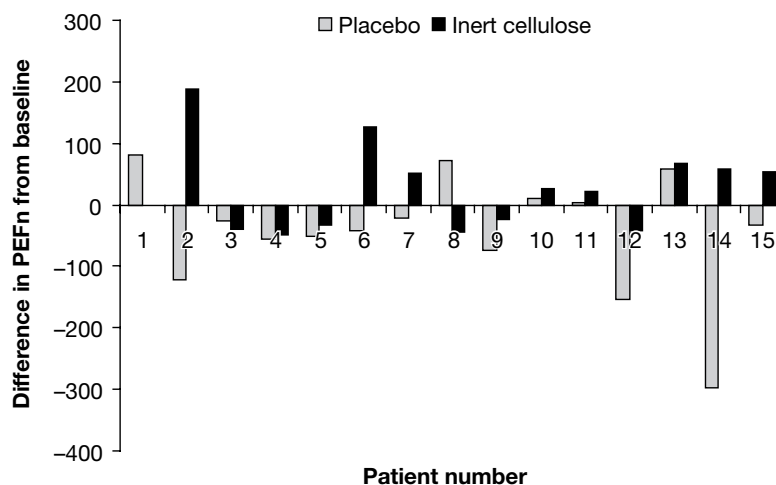




**Figure 2.** Total symptom scores for itchy nose from challenge to 4.5 h later. Mean for placebo scores =17.2, SD 14.2, mean for cellulose powder scores is 7.8, SD 10.2. Differences are significant at  $p \leq 0.05$ . Subject one had no symptoms. Vertical axis is total symptom score, horizontal axis is patient number



**Figure 3.** PIFn mean of differences from baseline from immediately after challenge to 4.5 h later. Overall mean for placebo is -25, SD 47, overall mean for cellulose powder is -3, SD 25. Difference is significant at  $p \leq 0.05$ . Readings are in L/min. Vertical axis is difference in PIFn from baseline, horizontal axis is patient number



**Figure 4.** Mean PEFn readings for individuals as differences from baseline. Mean is for 7 readings taken from after challenge to 4.5 h later. Overall mean for placebo is -43, SD 96. Overall mean for cellulose powder is 24, SD 69. For participant one there was no difference from baseline to mean PEFn when using the cellulose powder. Readings are in L/min. Vertical axis is difference in PEFn from baseline, horizontal axis is patient number

sensitivity. Although all of the subjects had positive skin prick tests results to Der p1 and 10 were also positive to Der f1, the reaction to the challenge could differ notably. The challenge was set at a fairly low level even though the subjects had no history of asthma. Crude reference points for risk levels for asthma due to Der p1 and Der f1 exposure have been cited as for sensitisation  $> 2 \mu\text{g/g}$  dust, and for symptoms  $> 10 \mu\text{g/g}$  dust<sup>11,12</sup>, but comparable figures for rhinitis are lacking. These thresholds would apply to a continuous exposure and little information is available to predict reactions when the allergen is applied in one dose. Previous studies have indicated that nasal provocation by house dust mite allergens may also provoke concomitant asthmatic symptoms during the late phase reaction<sup>12</sup>. This is not exclusive to people with a history of asthma and we wanted to minimise the risk of this complication in the study whilst having the possibility of invoking some symptoms of rhinitis.

Some previous research projects have used nasal spray with phosphate buffered saline (PBS) with concentrations of house dust mite allergen extracts<sup>13</sup>. This approach was not considered suitable for this trial as we were interested in achieving conditions which were as close as possible to those in real life. The challenge was, therefore, delivered as a homogenised and standardised dust rather than as a spray.

Currently the powder is supplied in plastic containers and is dispensed through a patented valve system by a squeezing action. The amount of powder delivered per puff is approximately the same but it may not be constant. This aspect was minimised by having a standard technique and only two people making the applications.

The challenge was given as one delivery of allergen to the nose. Other work has examined the effect of continuous allergen challenge on clinical symptoms and mediator release in dust mite allergic patients<sup>14</sup> over 8 h. In this double blind placebo controlled cross over study the whole sample population showed a rise of nasal and ocular symptoms which were perceptibly but not significantly attenuated by active drug treatment. ECPs exhibited a constant level over the whole provocation period.

The study was designed to detect both early and late phase reactions. Early phase response occurs within minutes of the allergen challenge and tends to produce sneezing, itching and clear rhinorrhoea. Late phase response occurs 4–8 h after allergen challenge and is characterised by congestion, fatigue, malaise, irritability and possibly neurocognitive deficits. However, in this study the development of late phase

reactions was not evident, possibly due to the low level of the challenge.

Eosinophil cationic proteins in nasal fluid have been used frequently as a marker for local inflammation<sup>15,16</sup>. Previous research has established that this marker is an effective measure of degranulation and thus activation of the eosinophils<sup>17</sup>. In order to maintain the blind nature of the trial the collation and analysis of the results was done by different people from those who assisted with the challenge tests.

## Conclusion

The results of the trial indicate that the inert cellulose powder can have significant effects in reducing some symptoms of rhinitis due to house dust mite allergy. The results show significant differences between the placebo and active treatments for sneezing, itchy nose and runny nose, and ECPs in nasal secretions. Also the results indicate that when the inert cellulose powder is used the mean peak nasal expiratory and inspiratory flows are higher than when the placebo is used.

Further research is in progress to determine the mode of action of the cellulose powder, particularly its capacity to act as a barrier to the passage of allergens.

## Acknowledgement

This study was sponsored by Nasaleze (International) Ltd. The authors are grateful to the Department of Immunology, Northern General Hospital, Sheffield for the analysis of the ECPs and to Rachael Marks for help with the administration of the trial.

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# **Nasaleze cellulose powder delays house dust mite allergen (Der p1) diffusion in vitro**

Purpose of the study was to investigate this theory about the mechanism of action of the gel in relation to house dust mite allergen (Der p1). Bernadette Diethart and Professor Jean Emberlin of University of Worcester, UK; Richard Lewis, Worcestershire Royal Hospital, UK

Presented as a Poster at EAACI XXVII Congress, Barcelona, Spain 7-11 June 2008.





## **Nasaleze cellulose powder delays house dust mite allergen (Der p1) diffusion in vitro**

Bernadette Diethart is studying under the guidance of Professor Jean Emberlin of the National Pollen and Aerobiology Research Unit at Worcester University [www.pollenuk.com](http://www.pollenuk.com)

This study was recently poster presented at the XXVII Congress of the European Academy of Allergology and Clinical Immunology Barcelona, Spain 7-11 June 2008 ([www.eaaci2008.com](http://www.eaaci2008.com))

**Background:** An inert cellulose powder (Nasaleze®) has been used since 1994 in the alleviation of allergic rhinitis. The powder is applied to the nose where it absorbs water and forms a gel which is thought to act as a mechanical barrier against allergens. The purpose of the study was to investigate this theory about the mechanism of action of the gel in relation to house dust mite allergen (Der p1).

**Methods:** The amount of Der p1 which diffused through the cellulose gel and an agar gel, which was used as a reference, were measured by ELISA and compared to the baseline allergen content of the solution applied to the gels. The allergen portion that passed the gels was measured at 15, 30, 45, 60, 180 and 300 minutes after application of the standard allergen solution.

**Results:** The diffusion of Der p1 was delayed by both gel layers. The amount of allergen diffused through the agar gel was not significantly different from the baseline values. After 15 minutes of incubation 69% of the baseline allergen amount had diffused through the agar gel which did not give a significant difference in the one-way ANOVA ( $p = 0.15$ ). The amount of allergen that passed the agar then steadily increased until it reached baseline level after 180 minutes. Diffusion of Der p1 through Nasaleze cellulose powder showed a significant reduction of diffused allergen in all tests ( $p = 0.001$  to  $0.008$ ). After 15 minutes of diffusion only 1.9% of the baseline amount had diffused through the cellulose gel. After 300 minutes 44.8% of the baseline Der p1 crossed the cellulose gel while 100% had diffused through the agar layer.

**Conclusion:** Allergens are small, water-soluble molecules that are able to diffuse through gels. However, the mesh size of the polymer chains in the gel determines the size of the molecules that can pass through and the speed of their diffusion. The mesh size in the Nasaleze cellulose powder is smaller than in agar gel.

Nasaleze cellulose powder does delay the diffusion of Der p1 significantly but due to the small size of allergenic proteins it is not able to act as an impermeable barrier. Therefore regular re-application of the powder to the nostrils has to be suggested for optimum efficacy of the product in the prevention and alleviation of allergic rhinitis.

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<sup>1</sup>University of Worcester, United Kingdom;

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# **A meta-analysis of the Efficacy and Safety of Nasaleze in the Prevention and Management of Allergic Rhinitis**

A meta-analysis paper by Professor  
Patrick JD Bouic, Division of Medical Microbiology,  
Dept of Pathology, University of Stellenbosch,  
South Africa.

Published in The Open Allergy Journal, 2008, 1, 1-4.





# A Review of the Efficacy and Safety of Nasaleze™ in the Prevention and Management of Allergic Rhinitis

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*Synexa Life Sciences (Pty) Ltd., and Dept. of Pathology, Faculty of Health Sciences, University of Stellenbosch, South Africa*

**Abstract:** Nasaleze™ is an inert cellulose powder which has been on sale in the UK since 1994 and is used as a remedy for hay fever. It is applied to the nasal passage where it forms a gelatinous coating, thereby trapping aero-allergens and preventing the initial allergic response. Some limited clinical studies have been conducted in predominantly adults but also in children: outcome measures included the reporting of symptoms by volunteers (sneezing, itching, blocked nose, etc) using questionnaires; prevention of symptoms when challenged to aerosolized allergens; concomitant use of rescue medication and the measurement of inspiratory air flow across the mucosa as well as the release of ECP in nasal washings. The product has been reported to be safe and well tolerated by all volunteers and warrant further investigation in larger studies.

## INTRODUCTION

Seasonal and/or perennial allergic rhinitis is on the increase world wide, having increased two- or three fold over the last 15 years and current prevalence studies indicate that almost 15 million individuals are affected in the UK and 50-60 million people having been diagnosed in the USA alone [1]. It is often left undiagnosed due to the heterogeneity of the presenting symptoms, notably sneezing, itching, nasal congestion and very often, rhinorrhoea. Rhinitis is possibly one of the most debilitating conditions for sufferers due to the fact that the symptoms are often so severe that medications used during such crises are not fast-acting enough to provide relief and almost always induce side-effects which prevent the users from participating in normal day-to-day activities.

Nasaleze™, is an inert, micronized cellulose powder delivered in a patented delivery system. This proprietary grade powder is registered since 1994 and is currently on sale in many countries, including the UK. It is applied to the nasal mucosa where it forms a gelatinous coating, thereby preventing the airborne allergens from triggering the release of vasoactive substances from the mast cells lining the mucosa. It can therefore be considered not only as an effective measure to prevent the initial immunological reaction but also as a management strategy for reducing the symptoms of the allergic rhinitis once triggered.

This product has recently been commercialized in South Africa and is sold mostly through health store outlets or through some prescribing clinicians. It is relatively unknown although it has been available in the UK and some European countries. A mini-review of its properties and clinical benefits was therefore necessitated and this is presented herein:

no other reviews of this product have been previously conducted.

## METHODS

A computerized literature search using the National Library of Medicine's Medline database and ScienceDirect journal access was conducted and any relevant articles referring to the product was extracted. Key words used for the search included: rhinitis & cellulose powder, Nasaleze, allergen challenge & powder, inert powder & rhinitis. This search yielded 5 published papers [2-6] and 4 poster presentations at congresses. They all referred to the work conducted using Nasaleze™, the product containing an inert cellulose powder. The congress poster presentations were often abstracts of the full articles and for this reason, they were excluded from this analysis: only the data of the published literature were extracted and is presented under the following categories:

- Study designs and patient population studied
- Study outcome measures, safety and product acceptability
- Possibilities of product development

This review is no attempt to represent a meta-analysis of the published data since the literature is too limited and the study outcomes are too varied to conduct such an analysis.

## RESULTS

### A. Study Designs and Patient Populations Studied

Most of the published works deal with patients recruited by means of advertisements placed in national and local press media. The patients were required to complete pretrial questionnaires which pre-selected the patients based on pre-defined criteria for eligibility such as range of rhinitis symptoms, severity (requiring medication for management), time of the year when symptoms were at their worst, etc. The self-reporting questionnaire graded the patients on a point scale

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system (1 for severe uncontrolled symptoms to 5 for an indication of well-being, no symptoms): changes in any of the scores could be used to determine the eventual outcome of the interventional study.

In some studies, recruited patients participating in the study had recourse to rescue medication and this was recorded in daily journals since the use of concomitant medication was an indirect measurement of the efficacy of the Nasaleze™ product in the control of the patients' symptoms. In other studies, a new formulation (Nasaleze™ Travel) was compared to the routine preparation in the prevention of airborne infections which could have been acquired whilst traveling. Yet another study challenged volunteers to house-dust mite allergens and determined the efficacy of the Nasaleze™ product in preventing the allergic reaction. The studies are summarized hereunder in Table 1.

All of the above studies made use of selected patient population either recruited *via* the general practitioners who referred their patients to the study sites or volunteers who responded to recruitment advertisements *via* the local press. The respondents were screened for participation in the studies and the criteria used included severity of symptoms based on allergy medication history, seasonality of symptoms (pollen counts also used to determine whether the symptoms corresponded to high allergenic challenge), accessibility for follow up, etc. In most studies, compliance was never compromised and fall out from the study was minimal since most volunteers benefited from the intervention. This in itself was an indication of the efficacy of the product in controlling the symptoms. The intervention periods were relatively short (4-8 weeks) and yet, efficacy outcomes were achieved and these were reported by the authors.

Although questionnaires were used to determine study outcomes (these could be considered as biased tools to measure efficacy), some studies made use of biomarkers which provided unbiased, quantitative laboratory data to corroborate the clinical outcome measures. These are reported in the following section.

## B. Study Outcome Measures, Safety and Product Acceptability

The studies made use of questionnaires which was scored by the volunteers and these recorded their sense of well-being. Some limited laboratory biomarkers of successful intervention were also recorded in some studies. Furthermore, accessibility to rescue medication during some of the studies was considered as an unbiased measurement of the ability of the product being investigated to manage the symptoms of the patients. These results are summarized hereunder (Table 2).

All of the studies clearly showed efficacy of the cellulose powder in reducing symptoms associated with either seasonal or chronic rhinitis without the need of the patient to make use of pharmaceutical drugs (although very few patients had such recourse). The most significant findings are that the product is well tolerated, safe and easy to apply. The independent measurements of efficacy included measurements of improved inspiration and expiration air flow implying that the use of the product lead to less inflammation and oedema at the mucosal surfaces. The use of the inert powder by children (and possibly pregnant women) is an added advantage: not many drugs can be used by these target populations without medical advice and warning.

The lack of significant difference in the symptoms scores between the placebo and active group in the study by Emberlin & Lewis [4] deserves some discussion: the authors reported that at the 1% significance level, no differences existed between the groups. However, at the 5% level, differences were reported by the volunteers for some symptoms such as "running nose" or "blocked nose" and this tended to correspond to days with lower pollen count days. However, these significant differences were lost when the total Likert score was compared between the groups.

## C. Possibilities of Product Development

The study conducted using the cellulose powder as a carrier of bioactive molecules, in this case, an extract of garlic,

**Table 1. Summary of Published Studies Making Use of Nasaleze™**

Authors	Number of Patients Recruited	Patient Population	Type of Study	Duration of Study Period
Josling & Steadman (2003)	102 (66 females, 36 males).	Adults (mean age = 44 yrs): reporting seasonal rhinitis.	Open labeled: volunteers compared present product to previously used drugs.	6 weeks.
Aivazis W <i>et al.</i> (2005)	100 (47 girls, 53 boys).	Children (age range 1.5 – 18 years, mean age = 7.96 years).	Open labeled: measurement of mucociliary clearance in allergic rhinitis pre- and post therapy with Nasaleze™	6 weeks.
Emberlin & Lewis (2006)	97 (57 females, 40 males).	Adults (mean age = not reported): hay fever sufferers.	Randomised, double blind, placebo-controlled. Patients recorded symptoms including Likert scores. Rescue medication permitted.	4 weeks.
Emberlin & Lewis (2007)	15 (7 females, 8 males).	Adults (modal age range 38-47 yrs): selected specifically for house dust mite allergy.	Double blind, cross over challenge study using Der p1 and Der f1 sensitivity.	1 month recruitment and 2 week actual study at clinic.
Hiltunen <i>et al.</i> (2007)	52 (gender distribution not stated)	Adults (mean ages not reported).	Randomised, double-blind study of Nasaleze™ vs Nasaleze™ Travel (with garlic extract) to determine prevention of airborne infections.	8 weeks.

Table 2. Outcomes, safety and Product Acceptability

Study	Significant Findings	Compliance and Safety	Conclusions Drawn by Authors
Josling & Steadman (2003):	77% of volunteers reported success (either good or excellent) by end of 6 weeks; average scores of 3.8 by men and 3.9 by women (5 indicating symptom free) were achieved: this was better when compared to pharmaceutical drugs used in the past; symptoms controlled within 0.1 – 3 hours after use.	No major problem: some volunteers reported some discomfort in throat due to powder. Only 8 patients required additional treatments.	Pilot study which clearly indicated that further investigations were warranted. Inert powder not medicated hence no side-effects with added advantage. Product well tolerated and provided fast relief.
Aivazis <i>et al.</i> (2005):	Only study conducted in children: statistically significant improvement in mucociliary clearance (39 mins. to 18.15 mins and this was directly related to improved peak nasal inspiratory flow rate (114.9 L/min to 144.4 L/min) implying less oedema and inflammation following use of product.	Excellent tolerance to product: no safety issues raised by volunteers.	The results imply the regeneration of ciliary epithelium. Product can be used by children.
Emberlin & Lewis (2006):	Blinded study in hay fever sufferers with significant differences in outcomes between groups: placebo used more rescue medication ( $p < 0.05$ ) although Likert scores showed no differences.	No adverse effects reported during trial: both powders well tolerated. The placebo powder (lactose) may have provided some protection to the users.	The inert cellulose powder provides safe and effective protection thereby obviating the need for anti-histamine and other pharmaceutical drugs for the symptoms.
Emberlin & Lewis (2007)	Allergen challenge in house dust mite allergic individuals: significant decrease in biomarker ECP ( $p < 0.05$ ) in nasal secretions as well as significant increase in measurements of nasal air flow ( $p < 0.05$ ) when placebos compared to active. Cross over period of study proves efficacy of cellulose powder in preventing allergic reaction.	No adverse effects reported by any volunteer.	Nasaleze™ has ability to significantly reduce symptoms of persistent rhinitis due to house dust mite and possibly provides effective barrier to inhaled allergens.
Hiltunen <i>et al.</i> (2007):	Significantly less infections (all combined) reported by volunteers using powder enriched with garlic extract compared to users of powder alone ( $p < 0.001$ ) and days affected by airborne pathogens also different between groups (less days reported ill, $p < 0.05$ ).	Volunteers continued with their daily travel plans and this study (albeit small) shows that garlic extract enriched cellulose powder provided effective barrier to airborne pathogens. No adverse effects reported by volunteers.	Cellulose powder can be used as effective carrier of bioactive molecules to prevent airborne pathogens during traveling.

presents exciting novel applications of the technology to address other important medical challenges. This trial showed that the active could be absorbed *via* a well vascularized mucosa and provide the efficacy sought (prevention of airborne infections). Numerous studies are currently searching for ways to deliver small amounts of antigenic peptides for immunization purposes since the immune cells of these surfaces are extremely powerful antigen presenting cells and are thus able to induce an immune response in the draining lymphoid organs. Also, the delivery of other natural molecules which have been described as effective anti-inflammatory compounds [7] for the management of chronic conditions affecting the mucosal surfaces is another area of research which warrants investigation by the manufacturers of the product.

## CONCLUSIONS

The treatment of allergic rhinitis to date has relied heavily on drugs that act either as membrane stabilizers thereby preventing the degranulation of the immune cells lining the nasal mucosae and which contain vasoactive peptides (steroid based drugs) or on drugs that neutralize the release of histamines (generic anti-histamines). Most of these drugs are not without side effects: they cause drowsiness and cannot be used by pregnant women. The novel product Nasaleze™

represents a new management strategy in the control and management of allergic rhinitis: this inert cellulose powder is administered into the nasal passages and forms an impervious barrier to the aero-allergens to which the individual may be sensitized. It is a natural and safe product, does not contain any drugs and above-all, has shown itself to be effective under trial conditions (albeit small studies).

The powder was tested not only as a preventative approach to attacks of hay fever but also as a treatment to the symptoms of allergic reactions, it stops the sneezing within minutes (response within 0.3 hours) and allows the improvement of air flow into and out of the nasal passages, thereby implying that it decreases the degree of on-going inflammation and oedema which normally accompanies an allergic reaction. These findings were corroborated by the laboratory measurement of decreases in the nasal washings of released ECP (Eosinophilic Cationic Protein), a biomarker of cellular degranulation.

The use of the inert powder as a carrier medium for bioactive molecules such as garlic extract to prevent travel-associated infections showed interesting results: fewer infections were reported by the volunteers who applied this enriched powder during their travels locally and even internationally. The study however is not clearly defined due to the fact that some patients traveled internationally using air

travel while others may have been using local train travel. The study implies that other molecules could be tested using this safe carrier. Further studies using larger patient groups are certainly warranted and these should include other immune biomarkers of efficacy, such as IgE levels, specific IgE titers to offending allergens, etc.

#### DISCLOSURE

The author would hereby like to declare that he has no vested interest (financial or otherwise) in the product being reviewed in this article. The need for such a review was necessitated by the fact that the product was unknown at the time of its launch in South Africa.

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# **Efficacy and safety of Nasaleze in prevention and treatment of persistent allergic rhinitis in adults and children.**

This paper describes the findings of an open non-comparative clinical study of efficacy and safety of an ultra-disperse cellulose preparation in prevention and treatment of persistent allergic rhinitis (AR). The volunteers were administered Nasaleze 3 times per day over the course of 4 weeks.

This study was presented at Moscow XVI Congress for Man and Drugs April 06-10, 2009.



# **Efficacy and safety of medical device Nasaleze in prevention and treatment of persistent allergic rhinitis in adults and children**

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This was presented at Moscow XVI Congress for Men and drug April 06-10, 2009.

*Keywords:* persistent allergic rhinitis, Nasaleze, ultra-disperse cellulose powder, clinical trial

## **Summary**

This paper describes the findings of an open non-comparative clinical study of efficacy and safety of an ultra-disperse cellulose preparation in prevention and treatment of persistent allergic rhinitis (AR).

## **Introduction**

Allergic rhinitis is a condition characterized by allergic inflammation, resulting from contact of allergens with nasal mucosa and associated with one or more of the following symptoms:

1. Nasal congestion
2. Nasal discharge
3. Sneezing
4. Nasal itching (1)

AR is one the most widespread allergic diseases. Not infrequently, it precedes other allergic disease, such as atopic dermatitis and bronchial asthma. Active manifestations of AR have a significant impact on the patient's quality of life, interfere with sleep and rest, and decrease capacity for work.

Methods of preventing and treating AR, which are currently available in an allergist's armamentarium, are not completely effective, are time-consuming, costly and associated with a number of side effects. The challenge of finding adequate means to prevent and treat AR is further aggravated in children and pregnant women, due to the lack of evidence confirming the safety of such medications in these categories of patients.

The usage of ultra-disperse cellulose may become a method of choice to prevent and treat AR.

After the registration and approval of micro-cellulose powder for medical application in Russian Federation, this open non-comparative study was conducted in 2009 to investigate the effectiveness and safety of medical device Nasaleze in prevention and treatment of allergic rhinitis.

## **Study design**

Forty-eight patients with persistent allergic rhinitis were included into the study. The group consisted of 25 adults and 23 children of both genders, aged 2 to 62 years. The patients were examined weekly over the observation period of 4 weeks. Children were accompanied by their parents during their visits to the trial centre. At study enrollment, the patients were asked for their verbal and written informed consent, according to a form developed for this study in accordance with the Helsinki Declaration. One of the parents was requested to sign the consent form for an under-aged child.



In accordance with the study protocol, an individual record form was filled out for each patient and included passport data, initial case history and examination findings as well as the findings of follow up visits during the course of the study.

- The patients received one puff Nasaleze into each nostril 3 times a day over the course of 4 weeks. In case of insufficient effect they were allowed to use the preparation more frequently.
- The patients visited the investigator weekly, i.e. 4 times during the study period. The severity of AR symptoms and the tolerability of the product were assessed during each visit.
- The patients filled out a quality of life questionnaire and a visual analogue scale during initial and final visits.
- The effectiveness of treatment was assessed by investigator together with the patient (in case of children together with the parents) during the final visit.
- The patients were maintaining a diary with daily records of severity of AR symptoms, any side effects and need for other medications.

## Subjects

Patients, who were enrolled into the study, came to the initial visits with a confirmed diagnosis of AR, supported by the findings of allergen tests and rhinoscopy.

*Figure 1. Characteristics of the study group.*

<b>Parameter</b>	<b>Adults n=25</b>	<b>Children n=23</b>
<b>Age</b>	<b>18 to 62 years Mean - 40.2 years.</b>	<b>2 to 18 years Mean - 10.8 years</b>
<b>Duration of AR</b>	<b>13.8 years (2-40)</b>	<b>5.75 years (1-15)</b>
<b>Bronchial asthma</b>	<b>68%</b>	<b>24%</b>
<b>Atopic dermatitis</b>	<b>-</b>	<b>8%</b>
<b>Pollenosis</b>	<b>64%</b>	<b>79%</b>
<b>Epidermal allergy</b>	<b>82%</b>	<b>79%</b>
<b>Nutritional allergy</b>	<b>36%</b>	<b>33%</b>
<b>Family history of allergy</b>	<b>68%</b>	<b>92%</b>
<b>Drug allergy</b>	<b>23%</b>	<b>12%</b>

Figure 1 demonstrates that most of the subjects had several concomitant types of allergy. Household and epidermal types of sensitization were most common. The presence of various allergy types was revealed by history taking and allergen tests. Concomitant bronchial asthma, nutritional or drug allergy was observed in many of the subjects. Nutritional and medicamentous types of sensitization were commonly manifesting as nettle rash, and sometimes as asthmatic attacks. Most of the subjects had a family history of allergy. Therefore, AR was associated with other atopic conditions in most subjects of the study group. The sensitization spectrum of the study group is presented in Figure 2.

Figure 2. Forms of sensitization found in study subjects during allergen tests.

Types of allergens	Adults (n=25), %	Children, (n=23), %
<i>Dermatophag. Pteron.</i> <i>Dermatophag. Farine</i>	100	100
<b>Pollen</b>	64	79
<b>Thereof:</b>		
<b>Trees</b>	79	89
<b>Cereals</b>	43	74
<b>Weeds</b>	21	52
<b>Allergy to 2 or 3 types of pollen:</b>	57	68
<b>Epidermal allergy</b>	82	79
<b>Thereof:</b>		
<b>Cat</b>	94	89
<b>Dog</b>	50	79
<b>Horse</b>	11	21
<b>Hamster</b>		5
<b>Allergy to 2 or more epidermal allergens:</b>	50	68

With regard to the data in Figure 2, the following conclusions may be drawn. Firstly, all subjects enrolled in the study were sensitized to house dust mite allergens. Secondly, house dust mite allergy was frequently concomitant with epidermal and pollen allergies. The structure of sensitization types was virtually similar in children and adults. A combination of household allergy with sensitization to cat epidermis and tree pollen was very frequent in all age groups.

When interviewed, all patients participating in the study complained of the symptoms of actively manifesting AR of various severity grades: sneezing, nasal and nasopharyngeal itching, eyelid itching, nasal discharge, impaired nasal breathing. All symptoms were assessed for severity grading:

0. Absent (no symptoms)
1. Mild (symptoms do not influence the lifestyle)
2. Moderate (symptoms have a moderate impact on everyday lifestyle)
3. Severe (symptoms have a significant impact on the patient's lifestyle and interfere with normal everyday activities).

## Findings

Figures 3 and 4 demonstrate the improvement of AR symptoms in both adults and children in the course of regular administration of disperse cellulose powder.

Figure 3. Evolution of AR symptoms in the course of 4 week treatment with Nasaleze in adults.

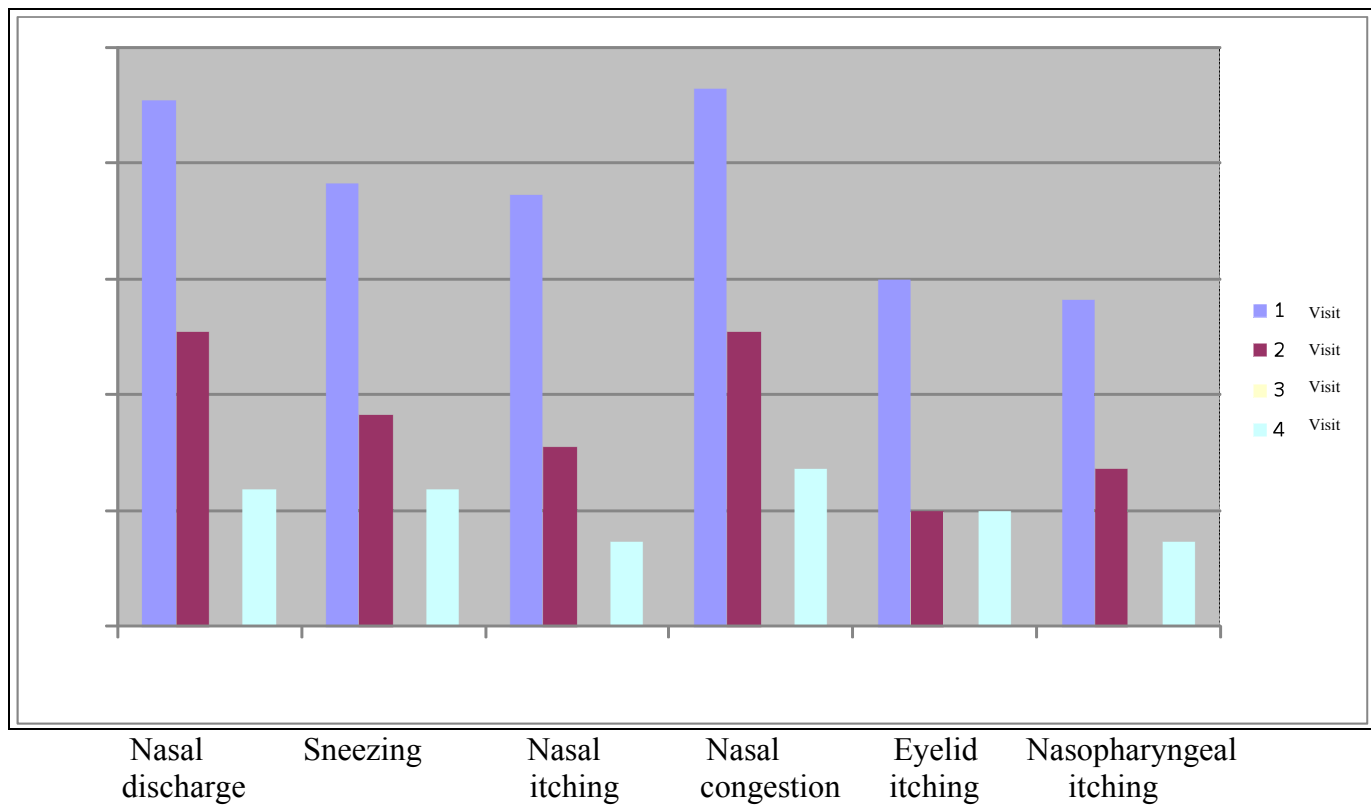
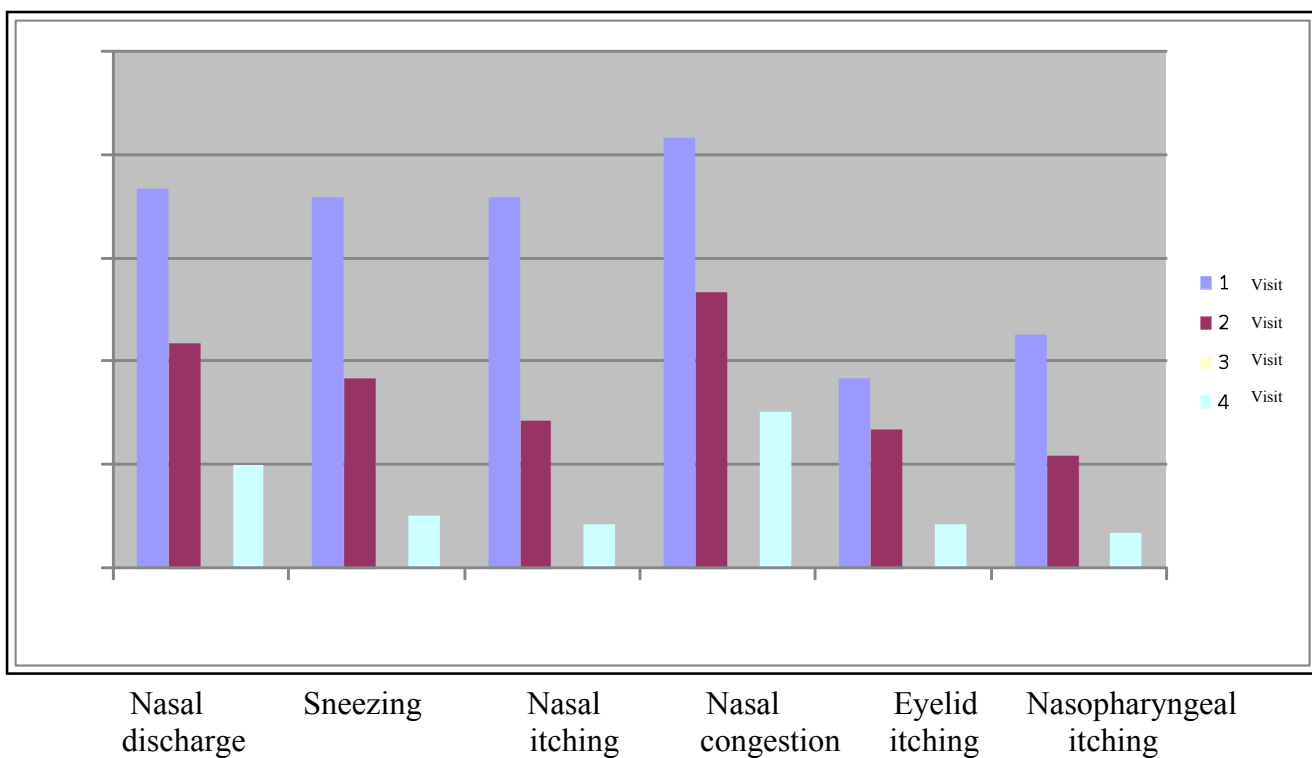


Figure 4. Evolution of AR symptoms in the course of 4 week treatment with Nasaleze in children.



Analysis of the data presented in Figures 3 and 4 demonstrates that the effects of micro-cellulose had an early onset. Improvement of all AR symptoms was observed already in the first week of therapy, and was especially significant by the end of the study period, both in children and in adults.

The following case record illustrates this trend: A 25-year old woman was diagnosed with perennial moderate allergic rhinitis 20 years ago. Allergy tests confirmed allergy to house dust mite and pollen of cereals and weeds. Family history includes allergic rhinitis in father and brother. Improvement of AR symptoms in the course of 4-week therapy with micro-cellulose powder is presented in Figure 5.

Figure 5. Effects of Nasaleze therapy on symptom scores in a 25-year-old patient.

	<b>Nasal discharge</b>	<b>Sneezing</b>	<b>Nasal itching</b>	<b>Nasal congestion</b>	<b>Ocular itching</b>	<b>Nasopharyngeal Itching</b>
<b>Initial symptoms</b>	<b>3</b>	<b>2</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>0</b>
<b>Study week 1</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>0</b>
<b>Study week 2</b>	<b>1</b>	<b>1</b>	<b>2</b>	<b>1</b>	<b>0</b>	<b>0</b>
<b>Study week 4</b>	<b>1</b>	<b>0</b>	<b>0</b>	<b>1</b>	<b>0</b>	<b>0</b>

0. Absent (no symptoms)  
 1. Mild (symptoms do not influence the lifestyle)  
 2. Moderate (symptoms have a moderate impact on everyday lifestyle)  
 3. Severe (symptoms have a significant impact on the patient’s lifestyle and interfere with normal everyday activities).

Overall assessment of the outcomes of 4-week therapy with Nasaleze was conducted during the final visit. The investigator assessed the overall efficacy of cellulose micropowder together with the patient. The patients’ judgement was based on their sensation of the symptoms, while the investigators analyzed the evolution of AR symptoms, visual scale scores, and the findings of the quality of life questionnaires. The results are summarized in Figure 6.

Figure 6. Assessment of the efficacy of Nasaleze.

Effectiveness	Adults (% of all adult subjects)	Children (% of all pediatric subjects)	Total (% of all subjects)
Very good	45	38	41
Good	50	62	57
Moderate	5	-	2
No effect	-	-	-

As it can be noted from the data in Figure 6, therapy with micro-cellulose powder was effective in varying degrees in all patients participating in the study. The majority of both adults and children (in the latter case the feedback was as a rule collected from the parents) assessed the efficacy of the product as good or very good.

Effectiveness of treatment is further confirmed by the improvement in quality of life of the patients treated with Nasaleze. The questionnaire, which was used to assess quality of life of AR patients before and after 4 weeks of treatment with cellulose powder is presented in Figure 7.

Figure 7. AR patient quality of life questionnaire.

<u>Types of activity</u>	1. Usual activities at home and at work; 2. Communication; 3. Outdoor activities
<u>Sleep</u>	4. Difficult to fall asleep 5. Awaking during the night 6. Difficult to wake up
<u>General symptoms</u>	7. Fatigue 8. Thirst/dryness in the mouth 9. Decreased capacity for work 10. Sluggishness 11. Concentration problems 12. Headache 13. Depression
<u>Practical problems</u>	14. Must always carry tissues 15. Must rub nose and eyes 16. Must blow the nose all the time
<u>Nasal symptoms</u>	17. Nasal congestion 18. Nasal discharge 19. Sneezing 20. Postnasal drip
<u>Ocular symptoms</u>	21. Itching in the eyes 22. Epiphora 23. Pain 24. Swelling around the eyes
<u>Emotional condition</u>	25. Frustration, anger 26. Impatience, anxiety. 27. Irritation 28. Uneasiness.

Assessment scale:

0 – not disturbing

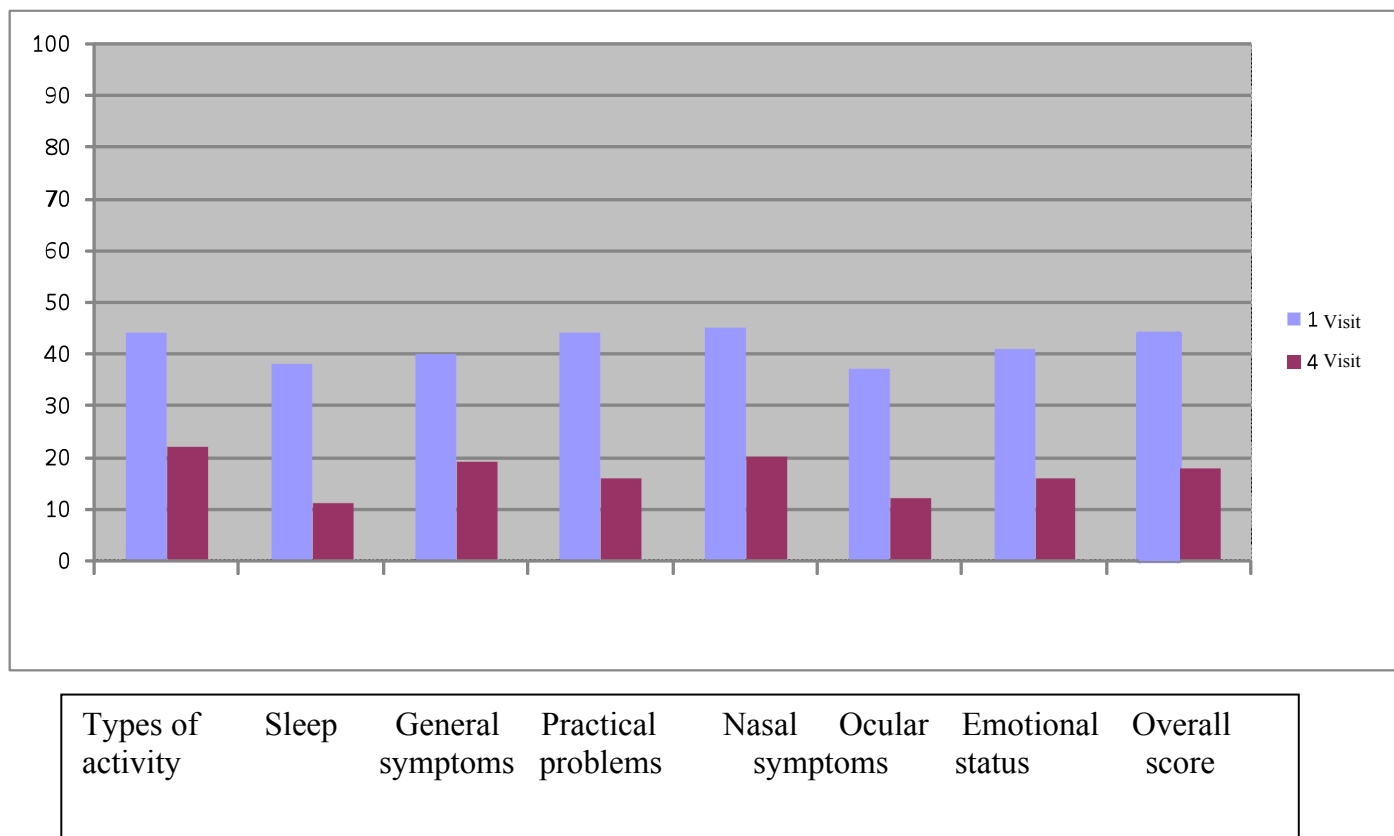
1 – almost undisturbing      3 – moderately disturbing      5 – very significantly disturbing

2 – slightly disturbing      4 – significantly disturbing      6 – extremely disturbing

The questionnaire covers various aspects of the patient's life, his/her physical and emotional condition and other factors, which may be negatively affected by AR.

The findings of the questionnaires are analyzed in Figure 8.

Figure 8. Assessment of quality of life by the patients before and after therapy with Nasaleze. (Scale of assessment: 100 % - Maximal impact of the disease on quality of life.)



It can be observed from the data in Figure 8, that quality of life of AR patients improved more than twofold in the course of treatment with micro-cellulose powder.

Both patients and investigators assessed the tolerability of Nasaleze. This assessment is summarized in Figure 9.

Figure 9. Tolerability of Nasaleze

Tolerability	Adults (% of total adult subjects)	Children (% of total pediatric subjects)
Very good	95	87
Good	5	9
Moderate	-	4
Poor	-	-
Description of unwanted effects	<ul style="list-style-type: none"> <li>• Formation of crusts in the nose during 4 first days of therapy – 2 patients;</li> <li>• Burning in the nose – 1 patient</li> </ul>	<ul style="list-style-type: none"> <li>• Burning in the nose – 1 patient</li> <li>• Itching in the nose, sneezing for 1 hour after administration – 1 patient</li> </ul>

As a rule, both children and adults reported good or very good tolerability of micro-cellulose powder. Occasional unwanted effects included: formation of crusts in the nose, burning in the nose, sneezing. These symptoms occurred in isolated cases and did not lead to discontinuation of therapy.

### **Conclusions**

1. Nasaleze reduces the severity of AR symptoms already in the first week of treatment.
2. Nasaleze therapy is associated with a more than twofold improvement in the quality of life of AR patients.
3. Therefore, Nasaleze is an effective and safe method of prevention and treatment of allergic rhinitis both in adults and children.
4. Micro-cellulose powder is capable of creating a natural safe barrier protecting the airways from contact with allergens and oxidating pollutants.

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**ALLERGY**  
**Nasaleze**<sup>®</sup>  
natural hayfever and allergy prevention



# **Clinical study in children suffering from allergic rhinitis.**

Åberg N and Benson M. A nasally applied cellulose powder reduces symptoms of seasonal allergic rhinitis (SAR). A double blind, placebo controlled trial in children and adolescents. Conducted at The Queen Silvia Children's Hospital, Gothenburg, Sweden.

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# A nasally applied cellulose powder in seasonal allergic rhinitis (SAR) in children and adolescents; reduction of symptoms and relation to pollen load

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## Keywords:

allergic rhinitis; clinical trial; barrier protection; children; adolescents; pollen concentration

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## Abstract

**Background:** A nasally applied cellulose powder is increasingly used in many countries as a remedy for allergic rhinitis. The absence of side effects makes the treatment particularly attractive in children. The efficacy in pollen allergic children, however, is not studied, nor is the relation to various pollen exposures.

**Methods:** During the birch pollen season in 2009, a double blind, placebo-controlled study was conducted in 53 subjects, aged 8–18 yr, with allergic rhinitis attributed to birch pollen. All children were on daily oral antihistamine. Reminders and reporting of symptom scores were made by SMS on mobile phones. Pollen was collected in a volumetric trap from which figures of pollen concentrations from 1979 to 2009 were available.

**Results:** There was a significant reduction in total symptom scores from the nose (active 7.29, placebo 6.07,  $p = 0.033$ ) and specifically for running nose (active 2.03, placebo 2.56,  $p = 0.017$ ). All symptoms from the nose, eyes and lower airways were lower in the active group but reached significance only as earlier. The best effect was seen after days with low or moderate pollen counts ( $\leq 100/m^3$ ), the predominating pollen load over 31 yr in the area. No clinically significant adverse effects were seen.

**Conclusions:** The product reduces symptoms of SAR in children and adolescents. Original data on pollen concentrations over 31 yr are presented with levels mainly in the low range favouring the observed efficacy profile. SMS communication on mobile phone for reminders and recording symptom scores was an excellent logistics tool.

Allergic rhinitis appears to have increased in Sweden as well as in most affluent societies over the twentieth century [1, 2]. During childhood and adolescence, the prevalence of allergic rhinitis increases with age [3]. In school children, allergy to pollen is a predominant cause [4]. Apart from notable economic costs, many school children experience an adverse impact on their educational career [5]. A range of remedies and treatments are available on prescription and over the counter (OTC). Some of these may have adverse effects, and the relief is very often insufficient. Nasal steroid sprays are considered most efficacious but many sufferers are reluctant to take them because of fear of adverse effects.

An inert cellulose powder (Nasaleze<sup>®</sup>) has been on sale as a medical device against hay fever in Europe since 1994. It is applied in the nostrils by a simple puffer device. The mechanism of action of the cellulose is likely to be a reaction with

moisture on the mucous membrane. A protective barrier on the nasal mucosa may prevent contact between inhaled allergen and mucosal cells. One placebo-controlled clinical trial in adults with grass pollen allergy showed a reduced need of rescue medication but no significant symptom relief [6]. The inert substance has been virtually free from adverse effects, making it a particularly attractive treatment option for children. Still, no controlled clinical studies in children have been performed. Our aim was to assess the efficacy in a common clinical setting along with an oral antihistamine. In Sweden, birch pollen allergy is the most common cause of seasonal allergic rhinitis (SAR). Furthermore, the birch pollen occurs during a school term and yearly examinations with high risks of interference between symptoms of SAR and school results [5]. Therefore, we found it particularly important to study the efficacy in birch pollen-induced SAR in children.

The studied product has been generally held to be most efficacious in slight and moderately severe allergic disease. This context also includes the load of pollen exposure. Therefore, the approach to pollen exposure was not only a daily monitoring during the study period; by a presentation of available data on local pollen occurrence over 31 yr, we infer our findings in a wider perspective.

## Methods

### Research design

Patients 8–18 yr old were recruited by newspaper advertising during February–April 2009. They all had a history of typical symptoms of SAR during springtime. They should not have used nasal steroids. At an appointment, the history was scrutinized and an assessment of the severity excluded a current need for nasal steroids. They were tested with a finger prick blood sample for ImmunoCap Rapid (Phadia). ImmunoCap Rapid is an *in vitro* system with immediate results for the most common respiratory allergies with a high accuracy regarding both sensitivity and specificity [7, 8]. Fifty-two children tested positive for birch pollen allergy. One child tested negative in the blood sample but with a strongly positive history and a positive skin prick test for birch pollen allergy during the same month the child was also included in the study. The patients were randomly assigned to active or placebo treatment three times daily from an identical container. The nasal powders were supplied in patent approved plastic containers, which deliver the powder from a nozzle when squeezed. The exact amount delivered is not standardized, and the variations of patterns of deposition in the nose are not known. The placebo was a lactose powder with the same particle size, appearance and the same tinge of mint taste as the cellulose powder. The containers were labelled with serial numbers. The randomisation codes for active and placebo products were not revealed until the reported scores had been locked in a clean file at the end of the study. After the study was completed, all participants were informed whether they had taken the active or placebo products.

All children were given one orally soluble desloratadine tablet in a dose appropriate for age once daily during the treatment period. Each child was supplied with a mobile phone for instructions, reminders and reporting of symptoms, all by SMS. The medication and reporting lasted for 4 wk following the first increase in local birch pollen counts.

Three times a day, the patients were reminded by SMS to take their treatment including the nasal puffs and were asked to confirm the intake by a response SMS. At the evening reminder, they were asked about the severity of symptoms during the preceding day from the nose, eyes and lower airways and to answer with a figure 1–6. The figure 1 corresponded to 1 'no trouble at all', 2 'little trouble', 3 'moderate trouble', 4 'rather much trouble', 5 'much trouble' and 6 'very much trouble', respectively. From the nose, scoring of sneezing, running nose and blocked nose was reported. For the eyes and lower airways, respectively, only a concluding figure

was used. Otherwise, the SMS procedure was assumed to be too complicated and time consuming for the children.

For pollen monitoring, a Burkard 7-day volumetric spore trap situated close to the study centre, at the roof top of the Central Clinic at Östra sjukhuset, at the eastern border of Gothenburg (57°72'N, 12°05'E) was used. The trap has been on the same location since 1979. The counts are representative for a wide area with a radius of ca. 50 km from the trap, encompassing the residence of all subjects in the study.

In the presentation of the pollen load in the study area, we have chosen the Threshold 30 method to identify the main pollen period [9] whereby the start and end of the pollen season are defined as the first and last days when the pollen count is greater than or equal to 30 grains/m<sup>3</sup>. This method excludes the long tails of lower values at the start and the end of the season, which are likely to have less clinical significance. In addition, the first date must fall into a period when the pollen type in question was registered during ten consecutive days, to exclude isolated episodes of long distance transport.

Two threshold values that denote the likely severity of symptoms were used. Thus, the term 'high levels' describes a situation when pollen levels are within the range 101–1000 birch pollen/m<sup>3</sup> and 51–100 grass pollen/m<sup>3</sup> [10, 11], whereas 'very high levels' denotes birch pollen counts >1000 pollen/air and grass pollen counts >100 pollen/m<sup>3</sup>, respectively. The thresholds for high levels represent the levels when most or all patients studied react with symptoms. The study by Davies & Smith [11], concerning grass pollen, was undertaken in Britain, and these levels may vary geographically. However, the corresponding data from South Scandinavia were not available.

### Statistical methods

For each question, the mean score was calculated for the whole 28 days period for every child. Mean values for the sum of all scores as well as the sum of the nasal scores were also calculated. The two treatment groups were then compared using t tests. All results were based on intention to treat analyses. p values below 5% were considered significant. Days with a pollen count above and below 100/m<sup>3</sup> and day, respectively, were separated and analysed in the same way as the whole period. The study was approved by the ethics committee at the Sahlgren's Academy of the University of Gothenburg.

## Results

An excellent compliance was obtained. Only 6% of all possible SMS-replies were missing, including one boy who withdrew because of throat irritation. One girl used nasal steroid as rescue medication for one day. Both belonged to the placebo group and are included in the intention to treat analyses. There were 25 children in the active and 28 in the placebo group. The gender distribution was 3/2 in favour of boys in both groups. The mean age was 11 in both groups. No clinically significant adverse effects were reported. A total

of eight children evenly distributed between the groups experienced some irritation in nose or throat following treatment.

Over the entire 4 wk, there was a general tendency to a reduction of all symptoms from nose, eyes and lower airways in the active group. The mean scoring for nose and eyes ranged between 2 ('little trouble') and 3 ('moderate trouble'). There was a significant reduction in total symptom scores from the nose (active 7.29, placebo 6.07,  $p = 0.033$ ) and specifically for running nose (active 2.03, placebo 2.56,  $p = 0.017$ ).

In Table 1, the efficacy is further elaborated and shows a general trend to an increased difference in mean scores between the groups with low and moderate pollen counts ( $\leq 100$  pollen/ $m^3$ /day) as compared with when the pollen counts are high. During a situation with low or moderate pollen counts, there is a significant reduction not only in total nasal symptoms and running nose, but also in sneezing severity.

### Pollen concentrations

The birch pollen season 2009 was intense but not a record high. The pollen index, i.e. the annual pollen sum, in

**Table 1** Sum of symptoms scored retrospectively at night. Figures with significant reduction of scores are marked in bold.

Question	Treatment	n	Mean	p-value
<i>(a) 2 days after pollen counts <math>\leq 100/m^3</math></i>				
Sneezing	Placebo	27	<b>2.19</b>	<b>0.023</b>
	Active	25	<b>1.65</b>	
Running nose	Placebo	27	<b>2.35</b>	<b>0.019</b>
	Active	25	<b>1.79</b>	
Blocked nose	Placebo	27	2.21	0.23
	Active	25	1.88	
Eye symptoms	Placebo	27	1.79	0.84
	Active	25	1.75	
Lower airways	Placebo	27	1.59	0.51
	Active	25	1.45	
Sum of all symptoms	Placebo	27	10.14	0.081
	Active	25	8.50	
Sum of nasal symptoms	Placebo	27	<b>6.75</b>	<b>0.025</b>
	Active	25	<b>5.32</b>	
<i>(b) 2 days after pollen counts <math>&gt; 100/m^3</math></i>				
Sneezing	Placebo	28	2.39	0.15
	Active	25	2.08	
Running nose	Placebo	28	<b>2.67</b>	<b>0.038</b>
	Active	25	<b>2.19</b>	
Blocked nose	Placebo	28	2.56	0.29
	Active	25	2.27	
Eye symptoms	Placebo	28	2.50	0.52
	Active	25	2.33	
Lower airways	Placebo	28	1.63	0.54
	Active	25	1.50	
Sum of all symptoms	Placebo	28	11.75	0.15
	Active	25	10.37	
Sum of nasal symptoms	Placebo	28	7.62	0.074
	Active	25	6.54	

Gothenburg 2009 was 152% of the mean of the period 1979–2009. The local birch flowering started 1 wk before the study beginning on April 21 with a maximum of 3700 pollen/ $m^3$ /day on April 25.

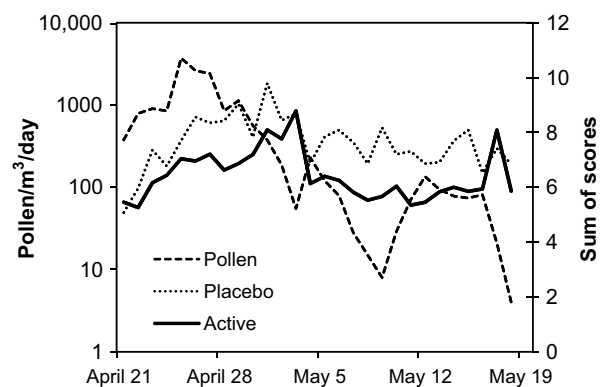
Figure 1 illustrates further the relation between symptom scores and pollen counts. Visually, there was a lag of 2 days between changes in pollen counts and subsequent symptoms. After the beginning of treatment, the symptoms intensified slower in the active group than in the group treated with placebo, and maximum of the score, which was lower in the former group, was reached about 2 days later. The decline of the pollen counts after the peak of pollen release was accelerated by rain during 1 wk beginning on May 3. In this case, the rain was associated with a more pronounced decline in the symptom scores of the active group than in the placebo group.

Figure 2 describes the pollen background in terms of a 31-yr survey of the pollen counts in the area. There were large variations in both the duration of pollen periods and the partition of days with low and moderate counts. For birch pollen (Fig. 2a), the percentage of days with low and moderate levels varied between 100% and 15%, mean  $48 \pm 20\%$  ( $\pm$ SD = standard variation). If the pollen season instead is defined as the period when fresh birch pollen (locally produced or long-distance transported) is registered in a regular manner, i.e. from March 1 to June 30, the percentage of days with low or moderate levels varied between 73% and 100%, mean  $90 \pm 6\%$ .

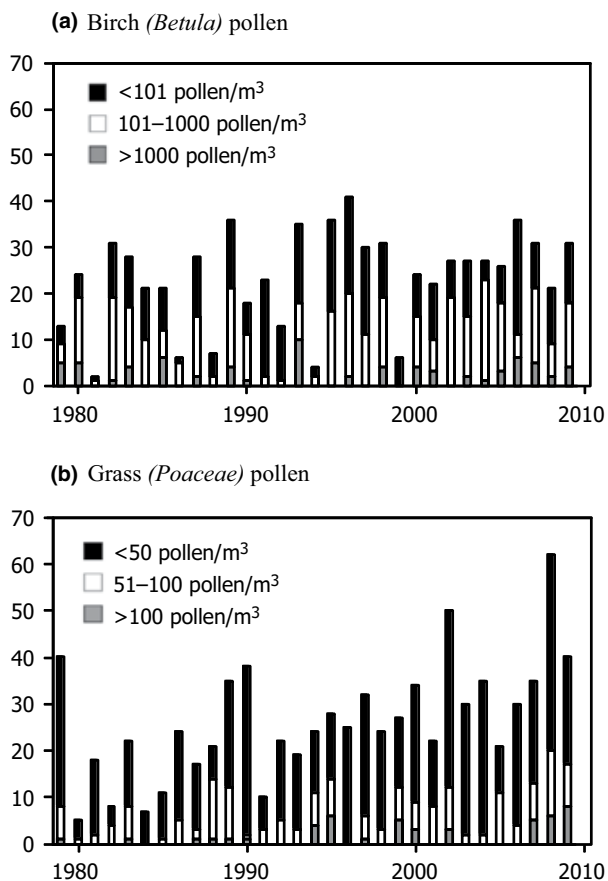
When the main grass pollen season is defined according to the Threshold 30 method (Fig. 2b), the total percentage of days with pollen levels with low and moderate levels varied between 100% and 33, mean  $74 \pm 17\%$ . The period when grass pollen is registered more or less daily lasts from April 20 until September. We chose September 7 as an end date for calculations. The total percentage of days with low and moderate levels during this longer period varied between 88% and 100%, mean  $95 \pm 4\%$ .

### Discussion

Since 1994, this British remedy for hay fever has been on sale as a medical device, and it has been increasingly used in



**Figure 1** Sum of nasal symptoms day by day in respective groups. Daily pollen concentrations in log scale.



**Figure 2** The number of days with different birch and grass pollen concentration levels in Gothenburg, Sweden during the years 1979–2009 and during the main pollen seasons, defined according to the Threshold30 method [9]. (a) Concentrations of birch pollen during the period March 1st–June 30th. (b). Concentrations of grass pollen during the period April 21st and September 7th.

many parts of the world. The inert cellulose powder has in various previous studies, mainly in adults, been free from clinically significant adverse effects [6, 12, 13]. The safety aspect of the product makes it particularly attractive for the treatment of children. This is the first placebo-controlled study in children in a clinical setting. It is also the first placebo-controlled study of the product proving a reduction in symptoms of SAR. In adults with grass pollen rhinitis, there was a reduction in rescue medication but no decrease in symptom scores [6]. We wanted to avoid that variable use of other treatments would confound the efficacy of the trial product. Therefore, we chose a fixed oral antihistamine dose throughout the study period, which is a common clinical context.

The inclusion of previously not published original data on the partitioning of days during the main pollen period into low, moderate, high and very high levels over the period 1979–2009 made it possible to assess our observed relation between pollen exposure and clinical symptoms in a wider perspective.

Another original feature with the study was the use of SMS on mobile phones for reminders and reporting of symptom scores. There are clear benefits of e-diaries as compared with paper records in terms of compliance and data safety [14]. The use of mobile phone logistics is a further development of the methodology that probably explains the unusually high compliance in this age group. The logistics also allow a continuous supervision of the study progress on an individual level. Some concern from the study staff regarding the SMS skill of the children (asking for SMS interest in the advertisement) was rudely mocked by the children at the first appointment.

### Population

The main weakness of the study is the relatively small number of patients. Consequently, most of the general reduction in all symptoms did not reach statistical significance. The study population was quite homogenous with a laboratory confirmed allergy to birch pollen and a narrow range of severity; a history of asthmatic or other perennial symptoms was not allowed at inclusion, nor was a previous use or assessed need of nasal steroids. This background ought to minimize the risk of significant baseline group differences.

### Dosage

We appraised a fixed dosage of three times daily to be both convenient and necessary to maintain controlled circumstances in our trial design as well as to reach a statistically significant reduction of symptoms. Still, it may not have been an optimal setting to prove the real efficacy of the product, particularly during a period of high pollen counts. It should be noted that most of birch pollen season in Sweden may be considered intense, as compared with grass pollen exposure, (Fig. 2). In clinical praxis, the dosage is usually 2–3 times daily basally during pollen season but with a possibility to increase the doses as needed to control symptoms. The inert nature of the product imposes no more than a practical upper limit of the dosage. The concurrent fixed antihistamine dosage may have hampered the breakthrough of pollen peak symptoms, but may also have constricted the range of scoring available for reduction after lower pollen counts. Given the aim of extensive symptom relief, our impression still is that the antihistamine treatment alone left a substantial need for further aid.

The optimal frequency of puffing the powder into the nostrils to obtain a 24-h protection of mucous membranes remains unknown and, as discussed earlier, may vary with the amount of allergen exposure. The ordinary clearance time of the nasal mucosa of <30 min is prolonged for cellulose products, a fact that may be used for certain treatment purposes [15]. Another gel formulation from seawater was efficacious against allergic rhinitis in a four times daily regimen in a recent study [16]. The higher efficacy in the lower pollen range may indicate that a three times daily dose may be sufficient as a basic clinical regimen which might need to be adjusted according to the intensity of symptoms.

### Efficacy

The profile of the effects with the predominating and statistically significant reduction of nasal symptoms is suggestive of a real biological effect. A less pronounced relief of ocular and bronchial symptoms may be secondary to the nasal effects in line with the concept of 'united airways' [17]. The number of patients, however, did not allow for statistical significance of the reduction of non-nasal symptoms.

The magnitude of reduction of nasal symptoms in the trial of about 20% was less than might have been expected from the clinical experience of the authors. Still, it corresponded to the cautious power calculations preceding the clinical part of the study and is not an uncommon mean effect in clinical trials, particularly in a probing phase. Given the background discussed earlier, the average symptom scores in the treatment group can be assumed to result from quite a wide scope of effects from very good to complete absence of effects.

The assumed mode of action of the cellulose powder is to form a gelatinous barrier preventing contact between pollen and the mucous membrane. It may be a matter of course that intense exposure may result in breakthrough of sneezing and running nose with blowing out of the powder/gel and a subsequent local absence of powder and effect. Such a sequence may be part of a dose–response relationship between the frequency of doses and efficacy. In the previous grass pollen study on the product [14], the dose was mainly once daily and this low dose may explain to the shortage of symptom reduction.

Nasal steroid sprays are recommended as the first choice in the international (ARIA) guidelines [18]. The guidelines do not discuss non-pharmacological products, probably because of the scarcity of studies of acceptable scientific quality in this context. In Sweden, however, the new intranasal corticosteroids with the profile of high efficacy and low bioavailability are not accessible OTC. Moreover, many parents still prefer to try non-pharmacological products for their children by other reasons.

### Pollen exposure

The choice of birch pollen rhinitis in the study was firstly that it is the most common cause of SAR in Swedish children [4]. Secondly, for children with multiple pollen allergies, birch pollen symptoms usually are the first of the total season. In severe birch pollen allergy, patients often have a crossreaction to hazel and alder earlier in the spring. Already at recruitment, however, we excluded children with perennial allergic symptoms or seasonal symptoms in the months preceding birch flowering. We believe that absence of all symptoms previously in the same year may have contributed to a narrow range of severity. Most children in Sweden with grass pollen

allergy also have a birch pollen allergy [4], and the baseline condition in a study of grass pollen allergy would have been more heterogeneous.

There was a general pattern with a variation of symptoms proportionally to a log scale of pollen concentrations with a lag of about 2 days. Lower pollen concentration caused milder symptoms as well as an amelioration of the protective effect of the cellulose powder. This is coherent with the discussion about sufficient dosage above and likewise the generally held opinion that the cellulose powder primarily protects against slight and moderate symptoms.

A pollen load of 100 birch pollen/m<sup>3</sup>/day, the upper limit for moderate levels, appears to constitute a threshold with relevance for the efficacy of the product.

In fact, low or moderate levels, when the product thus appears to subdue symptoms, predominate during the birch pollen season, as illustrated by the retrospective statistics from 31 yr (Fig. 2a). Although these levels differ between grass and birch pollen [10, 11], the method also appears to be applicable to birch pollen. In practice, the method cuts off the long tails with very low pollen amounts and irregular pollen occurrence at the beginning and the end of the season.

The predominance of low or moderate values is still more pronounced with respect to grass pollen than birch pollen (Fig. 2b). Therefore, it is quite possible that the product in the given dosage should be even more efficacious in grass pollinosis, a more common condition in a global perspective.

### Conclusions

We demonstrated that an inert cellulose powder (Nasaleze®) causes a significant alleviation of nasal symptoms in SAR in children. The best efficacy was seen after a low–moderate birch pollen load, a concentration representing major parts of the Swedish pollen season. The product could be effectively combined with oral antihistamine, the most common treatment of SAR [6].

### Acknowledgments

Kisska International Ltd and Green Medicine AB sponsored the study in terms of supplying test products, support of the logistics including mobile phones and funding for the nursing staff. We are grateful to the registered nurses Kerstin Sandstedt and Mainor Åmark for skill patient contact and testing and to the senior lecturer Lars Wahlgren, University of Lund, for statistical analyses. We want to thank Dr. S.O. Strandhede, former leader of the Pollen Laboratory at the University of Gothenburg, and all pollen analysts throughout the years.

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# **Intranasal Inert Cellulose Powder in Prevention and Management of Seasonal Allergic Rhinitis (SAR) in Children.**

Geppe N.A., Snegotskaya M.N.; Kolosova N.G.;  
Konopelko, O.U. Conducted at the Clinic of Child  
Diseases at The I.M. Sechenov Moscow Medical  
Academy. An open comparative randomized study  
in order to evaluate the efficacy and safety of  
intranasal inert cellulose powder in preventing  
seasonal allergic rhinitis (SAR) in children.

The study was conducted between April and June  
2009 and presented as a Poster in EACCI  
London 2010.



## Intranasal Inert Cellulose Powder in Prevention and Management of Seasonal Allergic Rhinitis in Children.

Gepe N.A., Snegotskaya M.N., Kolosova N.G., Konopelko O.U.

### Purpose:

To study the efficacy and safety of the intranasal inert cellulose powder (Nasaleze®) in the UK, Nasaval®) in Russia) to prevent seasonal exacerbation of allergic rhinitis (AR) in children. The Study was throughout 6 weeks between April and June 2009.

### Materials and Methods:

Open randomized study in order to evaluate the efficacy and safety of the intranasal inert cellulose powder to prevent exacerbation of seasonal allergic rhinitis (AR) in children. Depending on the treatment all children were divided into the following groups: in Group 1 (Main Group), the inert cellulose powder in a special device was administrated to 30 children twice a day; in Group 2, 30 children received Montelukast 5 mg a day; in Group 3, 20 children received Sodium Cromoglicate 2 doses of 50 mg x 2 times a day; in Group 4, 30 children received Budesonide 50 mg 3-4 times a day. AR symptoms were assessed in the case monitoring timetable for the patients per visit. (Table 1.) Comparative description of the surveyed patients are in Table 2.

Table 1.

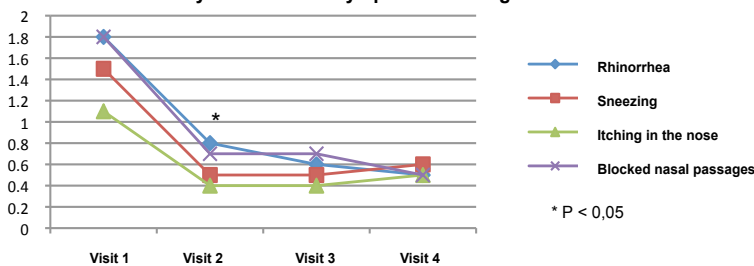
Study	Visit 1	Visit 2	Visit 3	Visit 4
Informed consent	X			
Questionnaire	X			
Collection of medical records	X			
Patient examination	X	X	X	X
Criteria for inclusion and exclusion	X			
Number Randomization	X			
Inert Cellulose Powder Issue	X			
Symptoms of seasonal allergic rhinitis (on a point scale: 0 - no symptoms, 1 - low level of intensity, 2 - moderate level of intensity, 3 - severe)	X	X	X	X
Treatment adjustment		X	X	X
Assessment of adverse events		X	X	X
General doctor and patient assessment		X	X	X

Table 2.

	Inert Cellulose Powder (N=30)	Montelukast (N=30)	Sodium cromoglicate (N=20)	Budesonide (N=30)
The average age of the patients (years)	8,3	8,9	7,9	8,5
Minimum age of the patients (years)	4,0	6,0	2,0	6,0
Average duration of the illness (years)	3,1	4	3,5	3,8
Sensitization to pollen allergens	50%	52%	49%	56%
Mild AR	22 (73,3%)	20 (66,7%)	15 (75,5%)	20 (66,7%)
Moderate and severe AR	8 (26,6%)	10 (33,3%)	5 (25%)	10 (33,3%)
AR and BA	5 (16,7%)	8 (26,7%)	4 (20%)	9 (30%)
Allergic conjunctivitis	50%	53%	48%	57%
Family history of allergic illnesses	20 (66,7%)	22 (73,3%)	15 (75,5%)	20 (66,7%)

### Results:

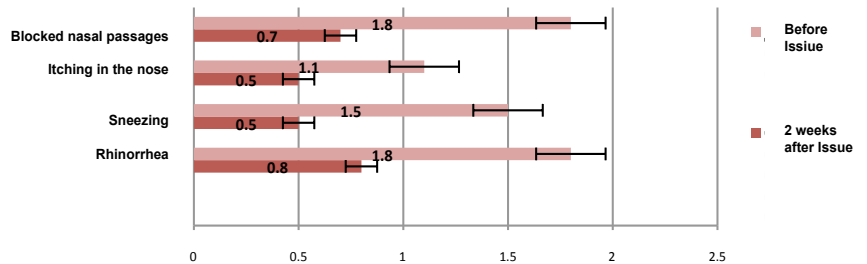
#### Dynamics of the symptoms of allergic rhinitis in scores within 6 weeks in Group 1 (the Inert Cellulose Powder).



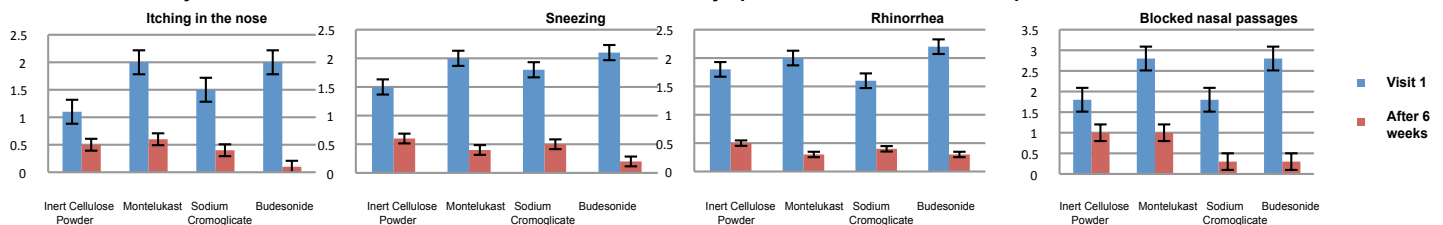
- ▶ The majority of patients (73%) noticed a distinct improvement in their condition by the fifth day.
- ▶ During the next 2 weeks, 12 children's (40%) symptoms disappeared completely.

#### Evaluating the efficacy of the Inert Cellulose Powder in children with AR during the first two weeks (p<0,05)

- ▶ Definite decrease of all SAR symptoms more than twice.
- ▶ 75% of patients before the prescription regularly received decongestants. During the Study 26,9% of patients occasionally received decongestants.



#### Efficacy of the Inert Cellulose Powder in children with seasonal symptoms AR within 6 weeks compared with other variants of treatment.



In the Main Group (Group 1) 9 children (34,6%) were receiving antihistamines occasionally, 7 children (26,9%) - decongestants, 3 children (10%) – nasal topical steroids. Comparing showed a significant improvement in symptoms of AR in all groups.

Side effects: 2 children (6,7%) in the Group 1 had increased sneezing, followed by removal of the drug. In the Budesonide group, two children was a slight nasal bleeding and burning of the nasal mucosa (6,7%).

**Conclusion:** The Inert Cellulose Powder reduces symptoms of AR, as well as other medicines. The children who received the Inert Cellulose Powder during pollen season, decreased frequency of use of antihistamines, decongestants and topical steroids. Preventative application of the Inert Cellulose Powder before contact with known allergens (pets, pollen allergens, house dust, etc.) reduces the symptoms of allergy. Using of the Inert Cellulose Powder for prevention of seasonal allergic rhinitis was proved. The Inert Cellulose Powder has minimal side effects and can be used in children from an early age.

**Open non-comparative study  
to evaluate the effectiveness of  
Nasaleze for patients  
with allergic rhinitis.**

Conducted at the Russian Federal Medical Biological  
Agency by Chief clinical physician, professor,  
Doctor of Medical Sciences NI Ilina.

An open study to determine the effectiveness  
of Nasaleze at treating allergic rhinitis by nasal  
provocation test with significantly causative  
aeroallergens.

To be published in Russian Allergy Journal in  
No. 2 (March-April 2011)



# REPORT ON AN OPEN NON-COMPARATIVE STUDY TO EVALUATE THE EFFECTIVENESS OF NASALEZE PREPARATION FOR PATIENTS WITH ALLERGIC RHINITIS

**Investigated preparation:** Nasaleze (vegetable cellulose in a spray dispenser).

**Manufacturer of the preparation:** Nasaleze Ltd, Great Britain

**Location where the study was conducted:** Federal State Budget Establishment Immunology Institute State Science Centre, Russian Federal Medical Biological Agency, building 24, Kashirskiy Highway, Moscow.

**Study director:** Chief clinical physician, professor, doctor of medical sciences. N.I. Ilina

## **Introduction. Basis of the study.**

Nasaleze, a micro-dispersed cellulose powder in a spray dispenser, is designed to protect the nasal mucous membrane from contact with pollutants and aeroallergens, as well as other micro-particles, which enter the nasal cavity during breathing. Nasaleze is used to prevent the development of the symptoms of allergic rhinitis (AR): nasal pruritis, swelling of nasal mucus and disruption of nasal breathing, prolific clear liquid discharges from the nose, sneezing attacks, etc. When the cellulose powder from the spray dispenser contacts the nasal mucus, it binds with the mucus of the nasal cavity lining and forms a strong gel-like film that covers the nasal cavity and serves as a natural barrier against aeroallergens.

Nasaleze is made up exclusively of natural components. It is an inert, natural, finely dispersed cellulose powder. It does not contain any systemic or locally active substances. Therefore, it is suitable for children and pregnant women.

Previous studies to evaluate the effectiveness of Nasaleze were based on the patient's subjective evaluation of the severity of AR symptoms under conditions of natural exposure to significantly causative aeroallergens. A study involving nasal provocation tests with measured doses of significantly causative aeroallergens on a backdrop of using the Nasaleze preparation with an evaluation of the changes in nasal obstruction and inspiratory nasal resistance will enable an objective evaluation of the effectiveness of the preparation for AR patients as a means of elimination therapy.

**The goal of the study** is to evaluate the effectiveness of Nasaleze preparation (vegetable cellulose) for patients with allergic rhinitis (AR).

## **Materials and methods.**

**Study Design.** Prospective open non-comparative study.

The study included 30 patients, of both sexes (12 men (40%) and 18 women (60%)), suffering from allergic rhinitis and meeting the criteria for inclusion/exclusion. The mean age of the patients was  $28.5 \pm 2.9$  years. The mean duration of illness was  $10.7 \pm 2.5$  years (from 3 to 24 years).

The duration of the study was 3 months (selection of patients) and 7 days for testing and active observation.

***Criteria for including patients in the study:***

- the existence of the patient's informed consent to participate in the study;
- aged between 18 and 65 years;
- patients with a history of allergic rhinitis for no less than 2 years
- positive skin tests for dust and household or epidermal allergens
- absence of clinical symptoms of allergic rhinitis at the time of the study
- ability to adequately participate in the study process

***Criteria for excluding patients from the study:***

- pregnancy, lactation
- presence of infections in air paths or nasal sinus cavities
- presence of anatomical anomalies of the nose (polyposis of the nose and paranasal sinuses, hypertrophy of nasal mucus, structural changes of the nasal cavity) that could significantly disrupt nasal breathing
- hypersensitivity to any of the components of the investigated preparation
- lesions of the mucous lining of the nose
- recent surgical interventions in the nasal cavity
- recent injuries to the nose
- smoking less than 4 hours before the testing
- clinical symptoms of rhinal conjunctivitis or bronchial asthma at the time of the study
- indicators of pulmonary function: FVC, FEV<sub>1</sub>, PEF < 85% of normal values, FVC/ FEV<sub>1</sub> < 70% of normal values
- dermatological diseases in the developed stage (psoriasis, atopic dermatitis, contact dermatitis)
- occurrence of acute respiratory disease less than 2 weeks before or at the time of the study
- occurrence of decompensated diseases or acute conditions that could significantly affect the results of the study
- alcoholism, drug addiction, mental unbalance
- probable inability to meet the demands of the clinical study
- participation in any other clinical testing during the last 28 days
- simultaneous use of preparations that could influence the dynamics of the indicators used to evaluate the effectiveness of the therapy (**Table 1**)

**Table 1. List of preparations prohibited during the study**

Patients were not allowed to participate in the study if they had taken any of the preparations listed below during the period preceding the start of the study or during the study.
Ketotifen (72 hours)
Systemic decongestants (48 hours)
Nasal decongestants (48 hours)
Systemic and/or nasal glucocorticoids (2 weeks)
Antihistamine preparations (14 days)
Antileukotriene preparations (14 days)
Cromoglycates (14 days)
Adrenaline (24 hours)
Non-steroid anti-inflammatory medications (7 days)
Tricyclic psychotropic preparations (21 days)

***Brief description of the programme.***

During the introductory period, the patients were evaluated according to the criteria for inclusion/exclusion. During visit 1 (after the patient was accepted onto the study) the initial condition of the patient was determined and the peak nasal inspiratory flow (PNIF) was measured. Then a series of nasal provocation tests were conducted: first with a test reference liquid and, in the case of a negative reaction, with measured doses of significantly causative aeroallergens (without the use of Nasaleze), beginning with a minimum dilution of 1/512 with a gradual increase in the allergen dose (in the case of a negative result). The PNIF was measured after the application of each allergen dose. In the case of a positive result, the test was ended and the dilution of allergen at which a reaction was observed was noted. During visit 2 (3±1 days after the first visit) the patient's initial condition was evaluated and the PNIF was measured. Then the research physician sprayed a single dose of Nasaleze into each nasal passage of each patient. After 20 minutes following the application of Nasaleze, a series of nasal provocation tests were conducted with the specific allergen, until a positive result was obtained (using the method described above), after which the PNIF was measured.

***The effectiveness of the preparation*** was evaluated based on a comparison of the nasal provocation test results obtained before and after the use of Nasaleze.

**Results of the study.*****Description of the group of patients in the study.***

30 patients, of both sexes (12 men (40%) and 18 women (60%)), suffering from allergic rhinitis and meeting the criteria for inclusion/exclusion took part in the study. The mean age of the patients was 28.5 ± 2.9 years. The mean duration of illness was 10.7 ± 2.5 years (from 3 to 24 years).

The distribution of patients by severity of illness is shown in **Table 2**.

**Table 2. Distribution of patients by severity of allergic rhinitis.**

Total, n (%)	slight, n (%)	moderate, n (%)	severe, n (%)
30 (100%)	20 (66.7%)	10 (33.3%)	0 (0%)

The allergic nature of the illness was confirmed in all the patients. All patients had a sensitivity to dust, 10 patients (33.3%) were also sensitive to household and/or epidermal allergens.

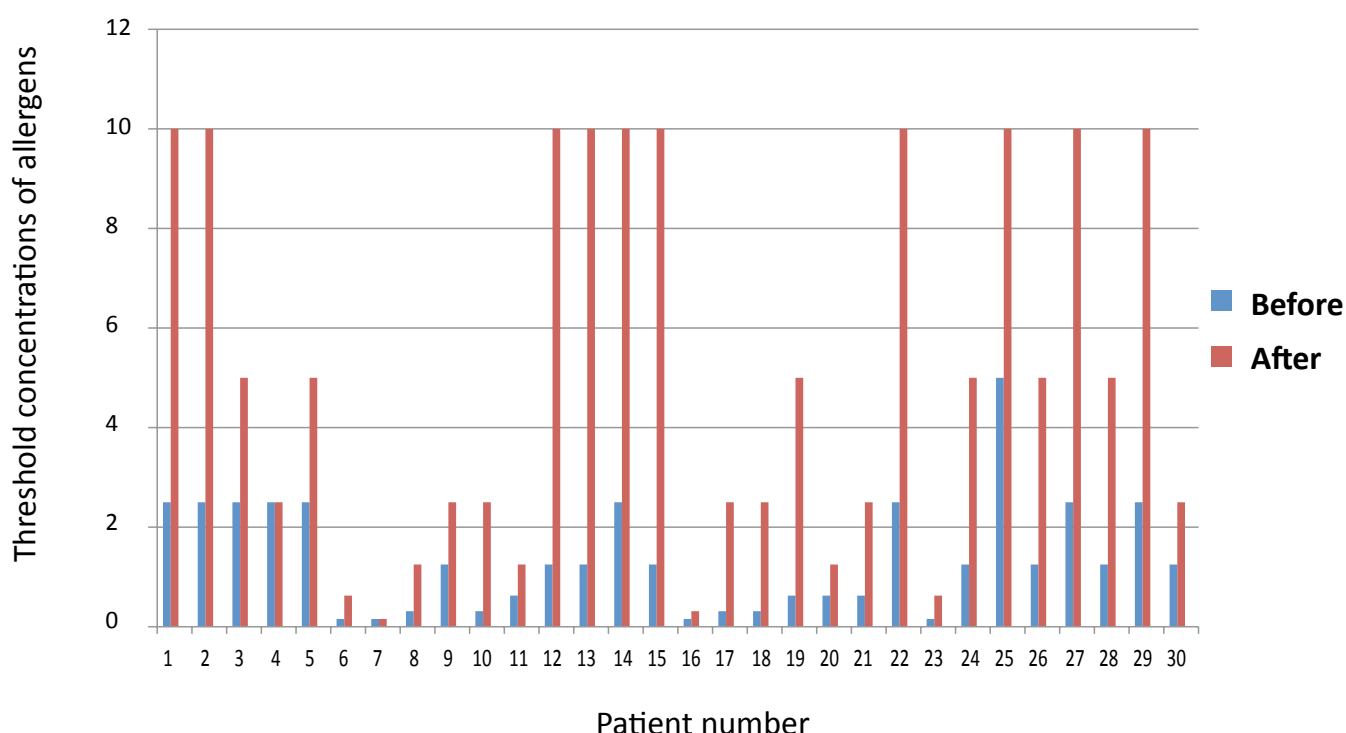
A total of 30 patients (100%) completed the study in accordance with the protocol.

***Evaluation of the effectiveness of the therapy.***

Of the 30 patients who completed the study, the therapy using Nasaleze was found to be effective in 28 (99.6%) of the patients, which showed a statistically valid decrease in nasal reactivity to a significantly causative allergen. Thus, the mean threshold concentration of allergen during the nasal provocation tests was initially 1250 PNU/ml, and after the application of Nasaleze, 5000 PNU/ml (Wilcoxon criterion  $z=4.694$ ,  $p<0,001$ ). However, in 4 patients, no development of symptoms was recorded, even with provocation by an allergen at the maximum concentration of 10,000 PNU/ml (**Table 3**). The best results were obtained in patients with isolated dust sensitivity and a mild period of rhinitis.

**Table 3 .Dynamics of threshold concentrations of allergens before and after the application of Nasaleze.**

**Threshold allergen concentration before and after application of Nasaleze**



Two patients for whom the preparation was not found to be effective had a combination of dust and household sensitivity. It is likely that the household sensitivity causes a persistent allergic inflammation of the nasal mucus and increased nasal hyper-reactivity, even though clinical manifestations of rhinitis are absent. Because Nasaleze does not have any anti-inflammatory or anti-allergic action, it is not expected that the preparation could affect the course of an allergic reaction that is already developed, but as part of a complex AR therapy, the preparation could stop the further uptake of allergen with inhaled air.

***Assessment of adverse reactions.***

During the entire period of observation, none of the patients taking part in the study showed any adverse reactions.

***Conclusion.*** Thus the study shows that:

1) Under conditions of allergen provocation, Nasaleze has a prophylactic action and prevents the development of an allergic reaction

2) The preparation is less effective in patients who have year-round allergic rhinitis

3) the use of Nasaleze will be effective if it is started before the beginning of contact and continues during the period of contact with a significantly causative allergen

4) it must be considered that after clearing the nose each time, the preparation must be applied again to renew the formation of the protective film

5) the advantage of Nasaleze is the high degree of safety, because it contains an inert, natural, finely dispersed cellulose powder and has no systemic action In connection with the above, Nasaleze can be used by children and by pregnant or breast-feeding women.



# **Nasal mucociliary clearance and mucoadhesion of hydroxypropylmethylcellulose powder used for alleviation of allergic rhinitis**

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# Nasal mucociliary clearance and mucoadhesion of hydroxypropylmethylcellulose powder used for alleviation of allergic rhinitis

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## Background:

An inert hydroxypropylmethylcellulose powder (Nasaleze<sup>®</sup>) has been used since 1994 in the alleviation of allergic rhinitis (AR). The powder is applied to the inside of the nose where the particles adhere to the nasal mucosa, absorb moisture and swell to form a gel. Its efficacy in reducing hay fever symptoms and its barrier function against Der p 1 allergen have been recently proven. Mucoadhesion and clearance of the gel influence the duration the barrier is efficient.

## Methods:

For the investigation of the effect of HPMC application on mucociliary clearance a modified Andersen saccharine test was applied. Twelve healthy volunteers were tested after the end of the grass pollen season 2008. In order to test the baseline mucociliary clearance time (MCT) of each participant, saccharine solution (3 %) was applied to the anterior tip of the inferior turbinate in one nostril of the subjects by means of rayon tip swabs. The subjects were instructed not to sniff or sneeze and to report a sweet taste as soon as it was noted and time was measured from the moment of solution application. After baseline measurements, 10 mg and 20 mg of HPMC was sniffed into the same nostril. After 5 minutes to allow gel formation the Andersen test procedure was repeated.

## Results:

The mean mucociliary clearance time at baseline was 11.14 minutes. This baseline MCT significantly increased to 35.45 minutes when 10 mg of HPMC were applied to the nostril prior to the test ( $p < 0.0005$ ). Application of 20 mg resulted in a mean MCT of 50.37 minutes and thus a further increase  $>120\%$  ( $>420\%$  longer MCT compared to baseline). This elongation of MCT was statistically significant when compared to baseline and 10 mg HPMC ( $p < 0.0005$ ).

## Conclusion:

Mucus maintains a hydrated layer over the epithelium which serves as a protective barrier against pathogens and noxious substances. However, the mesh spacing of mucus is too large to constitute a diffusion barrier to most allergens. HPMC gel applied to the nose has been proven to be a barrier to allergen entry. The attachment of HPMC to nasal mucus (mucoadhesion) slows down nasal clearance which enables longer residence time of HPMC in the nose and thus increases the time HPMC can be effective as a barrier before it is cleared. Also, dehydration of mucus while the HPMC gel forms increases mucus viscosity, which might decrease the diffusion coefficient through the mucus resulting in lower allergen diffusion.

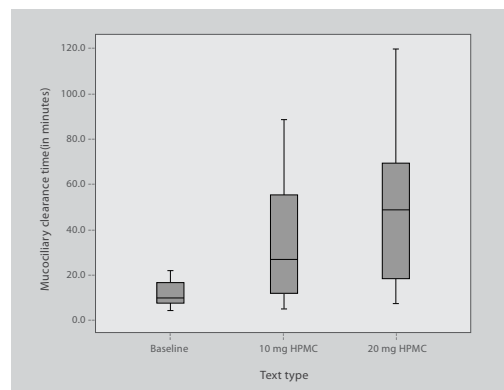


Figure 1: Boxplot of baseline MCT and MCT after nasal application of 10 mg and 20 mg of HPMC.

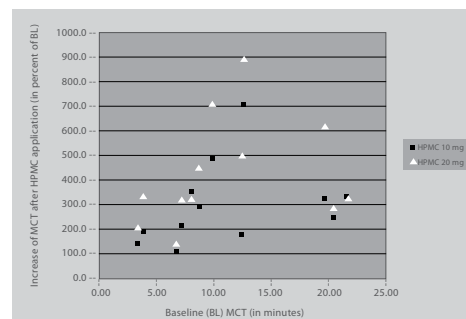


Figure 2: Relationship between initial MCT at baseline and degree of subsequent MCT increase after HPMC application.

	Women	Men
Number of participants	9	3
Mean age (in yrs)	32.8	37.0
Age range (in yrs)	25-40	25-60
Allergic rhinitis during last two yrs	3 (33.3 %)	1 (33.3 %)
Smoker	1	1

Table 1: Demographics of participants recruited for Andersen saccharine testing.

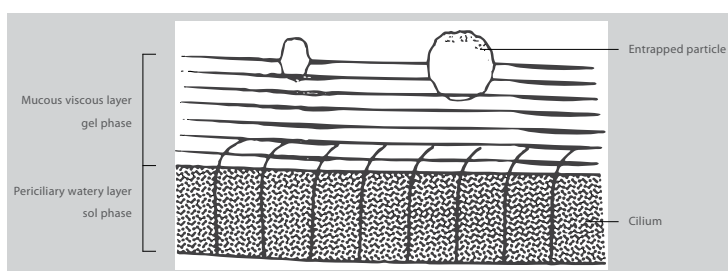


Figure 3: Viscous gel phase and periciliary fluid forming the mucus double layer (modified according to Quraishi et al. 1998).

# **Efficacy of cellulose powder as part of a complex therapy for patients with seasonal allergic rhinitis**

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Published in the Russian Allergy Journal, May 2011



# The efficiency of cellulose powder extract in complex therapy of patients with intermittent allergic rhinitis.

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Published in the Russian Allergy Journal, May 2011

*The dynamics of allergic and immunologic indices of patients with intermittent allergic rhinitis at the relapse stage have been analysed. The advisability to prescribe cellulose powder extract in complex therapy of patients with intermittent allergic rhinitis is substantiated.*

*Key words: intermittent allergic rhinitis, cellulose powder extract.*

Allergic rhinitis is related to a number of widespread diseases that affect between 10 and 20% of the population in various countries all over the world (1,3). This disease significantly impairs the quality of life of its sufferers, aggravates the course of bronchial asthma and promotes the development of other pathologies of the otorhinolaryngeal organs (sinusitis, otitis media and others) (2,4).

Modern approaches to treating allergic rhinitis include using elimination therapy, specific immunotherapy, pharmacotherapy and observing patients at an asthma school. In the case of both perennial (year-round) allergic rhinitis and seasonal rhinitis, it is not always possible to limit contact with allergens. For this reason, allergologists have always been interested by the idea of creating a barrier that can prevent allergens from acting on the nasopharyngeal mucous membrane. Topical medications play a significant role among the medicines used for this purpose (N.I. Ilyina, I.V. Sidorenko, 2003)

The purpose of this study was to evaluate the efficiency of a microdispersed cellulose powder in complex therapy of patients suffering from intermittent allergic rhinitis.

## Materials and methods.

The study included 30 subjects aged between 18 and 33 who were suffering from moderate intermittent allergic rhinitis in the relapse stage. According to the results of the skin test, all subjects had a sensitivity to weeds. In 95% of cases, the allergens mainly responsible were pollen, ragweed, sunflower and *Cyclachaena*. The patients were divided into 2 groups: Group I (10 people) received standard therapy, including: second generation antihistamine medications from the cetirizine group, sorbents, topical glucocorticosteroids, and Group II (20 people) received the microdispersed cellulose powder (Nasaleze) in one spray into each nasal passage three times a day in addition to the basic therapy.

Observation period — 4 weeks. The patients visited the clinic once a week. At both the beginning and the end of the study, each patient filled out a questionnaire regarding the quality of life of someone suffering from allergic rhinitis, which they assessed according to a seven-point scale:

- 0 - No adverse effects,
- 1 - Almost no adverse effects,
- 2 - Mild adverse effects,
- 3 - Moderate adverse effects,
- 4 - Strong adverse effects,
- 5 - Very strong adverse effects,
- 6 - Severe adverse effects, both before and after treatment.

In order to carry out the set tasks, a battery of clinical, immunological and statistical methods was used.

The general clinical study methods included: recording the patient's medical history with regard to allergies; evaluating the severity of the symptoms with a number of points (runny nose, sneezing, itchy nose, nasal congestion, conjunctivitis, tickle in throat) according to the severity:

- 0 - Absent (no symptoms),
- 1 - Mild (symptoms are present, but do not affect normal life),
- 2 - Moderate (symptom causes discomfort but does not interfere with normal daily activity or sleep),
- 3 - Medium severity (symptom causes significant discomfort, interferes with normal daily activity or sleep),
- 4 - Severe (symptom occurs so strongly that it is necessary to change the course of treatment and use stronger medications).

The dynamics of the symptoms were evaluated before the start of the treatment and also on the 7th, 14th and 21st days after treatment began.

The immunological examination of patients was carried out during visits to the clinic and one month following the end of the treatment. A blood specimen for analysis was collected from the cubital vein in the morning on an empty stomach.

The various types of immunocompetent cells were identified by the indirect immunofluorescence method using a range of monoclonal antibodies (JSC "Sorbent LTD", Russia): CD3, CD4, CD8, CD20, CD16, CD25, CD95 and HLA-DR. The results were analysed with a 'Cytomics FC 500' **laser flow cytometry system** (Becman Coulter, USA).

The content of immunoglobulin classes IgA, IgM and IgG in the blood serum was analysed using the radial immunodiffusion method developed by G. Mancini et al. (1965), with monospecific serum manufactured by "ImBio" (Russia).

The quantity of circulating immune complexes (CIC) in the blood serum was analysed by precipitation with polyethylene glycol, following the method by V.Yu. Klimov (1986).

The intensity of the neutrophils' oxygen-dependent metabolism was evaluated in a spontaneous and stimulated nitroblue tetrazolium (NBT) restoration test according to the methodology suggested by V.V. Menshikov et al. (1987). The NBT test stimulation coefficient was calculated with the aid of the following formula:

$$\text{Coeff. stim.} = \text{NBT stim.} / \text{NBT spont.}$$

The statistical processing of the data was carried out using the software programs “Microsoft Excel” and “Statistica 8.0”. The non-parametric significance criteria (Mann-Whitney-Wilcoxon criterion) were evaluated.

## Results and discussion.

During the first appointment, it was found that both groups of patients had clear symptoms of allergic rhinitis (Table 1). The clinical observation of the sufferers showed that among the group of patients receiving the standard treatment, a positive dynamic was observed in the course of the allergic rhinitis but, at the end of the study period, truly significant changes were only observed in symptoms such as runny nose (before  $3.1 \pm 0.3$  points, after  $1.7 \pm 0.5$  points) and stuffy nose (before  $3.5 \pm 0.8$  points, after  $1.5 \pm 0.3$  points).

An improvement in the condition of the second group was observed as early as the end of the first week following the first administration of the microdispersed cellulose powder (Fig. 1). Towards the end of the fourth week after the start of the study, the group of patients who had received the microdispersed cellulose powder were experiencing a statistically significant (for  $p < 0.05$ ) reduction in such symptoms as runny nose, from  $3.2 \pm 0.7$  points to  $0.7 \pm 0.1$  points, sneezing, from  $2.8 \pm 0.5$  points to  $0.7 \pm 0.3$  points, itchy nose, from  $1.9 \pm 0.2$  points to  $0.4 \pm 0.1$  points and stuffy nose, from  $3.3 \pm 0.5$  points to  $0.6 \pm 0.3$  points (Table 1).

In a comparison of the two study groups over the four weeks of observation, a real reduction in the severity of allergic rhinitis symptoms such as runny nose, sneezing, itchy nose and nasal congestion was observed in the second group of patients (Table 1).

The improvement in the quality of life of the patients serves as evidence of the effectiveness of the treatment. Thus, in the fourth week of the study, an analysis of the questionnaire results from the group who had received the microdispersed cellulose powder revealed a significant improvement in such subjective indices as: types of activity from  $5.5 \pm 0.3$  conventional units to  $1.5 \pm 0.2$  conventional units, sleep from  $4.6 \pm 0.3$  conventional units to  $1.1 \pm 0.1$  conventional units, general symptoms from  $3.5 \pm 0.4$  conventional units to  $1.1 \pm 0.1$  conventional units, practical problems from  $1.5 \pm 0.2$  conventional units to  $0.9 \pm 0.05$  conventional units, nasal symptoms from  $4.7 \pm 0.2$  conventional units to  $0.5 \pm 0.05$  conventional units, emotional state from  $5.8 \pm 0.2$  conventional units to  $0.8 \pm 0.07$  conventional units. ( $p < 0.05$  compared with original indices).

In contrast, in the group of patients who had received the standard therapy there were no diagnostically significant changes.

When the two study groups were compared after four weeks of observation, a real reduction was found in the severity of such subjective indices as: types of activity, sleep, general symptoms, practical problems, nasal symptoms, emotional state, in the group of patients who had received the microdispersed cellulose powder (Fig. 2).

All patients who took part in the study underwent a preliminary examination of their immune status before the start of the treatment. During this examination, elevated levels of secretory IgA and CICs were observed in both groups (Table 2). After completion of the treatment, the group of patients who had received the standard treatment did not show any essentially significant differences in the indices of their immune status, but in the group that received the microdispersed cellulose powder a marked reduction in CICs and normalisation of the secretory IgA content was observed (Table 2).

A comparative analysis of the effectiveness of including the microdispersed cellulose powder in the complex treatment of intermittent allergic rhinitis has shown that it leads to a faster alleviation of the symptoms of allergic rhinitis and improves the quality of life of patients.

Accordingly, the information presented in this study allows the conclusion to be drawn that including the microdispersed cellulose powder as part of the complex treatment for intermittent allergic rhinitis is beneficial.

**Table 1**  
**Dynamics of severity of allergic rhinitis symptoms**

Symptom (points)	Standard therapy before treatment	Standard therapy after treatment	Standard therapy + Nasaleze before treatment	Standard therapy + Nasaleze after treatment
Runny nose	3.1±0.3	1.7±0.5*	3.2±0.7	***0.7±0.1**
Sneezing	2.7±0.9	1.7±0.6	2.8±0.5	***0.7±0.3**
Itchy nose	1.5±0.1	0.8±0.1	1.9±0.2	***0.4±0.1**
Stuffy nose	3.5±0.8	1.5±0.3*	3.3±0.5	***0.6±0.3**
Itchy eyes	1.7±0.5	1.5±0.4	1.5±0.2	1.4±0.1
Tickle in throat	1.4±0.2	0.9±0.3	1.4±0.1	0.9±0.3

Notes:

\* - Statistically significant differences were noted in the patients who received the standard therapy compared with the results before the treatment ( $p < 0.05$ )

\*\* - Statistically significant differences were noted in the patients who received the standard therapy + Nasaleze compared with the results before the treatment ( $p < 0.05$ )

\*\*\* - Statistically significant differences were noted in the patients who received the standard therapy + Nasaleze compared with the results of the standard therapy ( $p < 0.05$ )

**Table 2****Dynamics of immune system indices among sufferers of intermittent allergic rhinitis**

	Standard therapy before treatment	Standard therapy after treatment	Standard therapy + Nasaleze before treatment	Standard therapy + Nasaleze after treatment
CD3 %	57.6±8.2	59.4±6.5	68±9.3	69±8.0
CD4 %	33.2±6.2	35.2±6.9	40±4.9	41.3±6.9
CD8 %	16.4±5.1	17.7±5.5	26.9±6.8	27.2±5.4
CD16 %	9.5±6.1	10.1±5.1	16.4±7.6	14.7±6.7
CD19 %	9.8±3.7	9.7±2.6	13.3±3.7	13.2±3.7
HLADR %	10.7±3.5	10.2±2.7	19.5±3.2	16±6.7
CD95 %	2.8±1.2	2.9±1.7	3.7±1.7	3.5±1.8
CD25 %	1.7±1.3	2.1±1.6	4.3±1.1	4.6±1.0
Ig A g/l	3.3±0.3	2.7±0.2	3.9±0.9	**1.9±0.5*
Ig M g/l	1.2±0.3	1.1±0.2	1.2±0.5	1.1±0.3
IgG g/l	11.8±1.1	10.8±1.1	12.4±2.1	12.2±1.5
CIC conventional units	81.3±18.2	77.3±11.2	103.3±34.9	54.8±16.9*
NBTspon.	103.8±21.4	106.7±17.4	123±21.7	134.5±22.9
NBTstim.	167.7±23.7	174.7±22.2	188.5±24.7	199.1±35.1
Coeff.stim.	1.5±0.1	1.4±0.1	1.6±0.2	1.5±0.1

**Notes:**

\* - Statistically significant differences were noted in the patients who received the standard therapy + Nasaleze compared with the results before the treatment ( $p < 0.05$ )

\*\* - Statistically significant differences were noted in the patients who received the standard therapy + Nasaleze compared with the results of the standard therapy ( $p < 0.05$ )



Figure 1. Dynamics of allergic rhinitis symptoms among patients who received Nasaleze

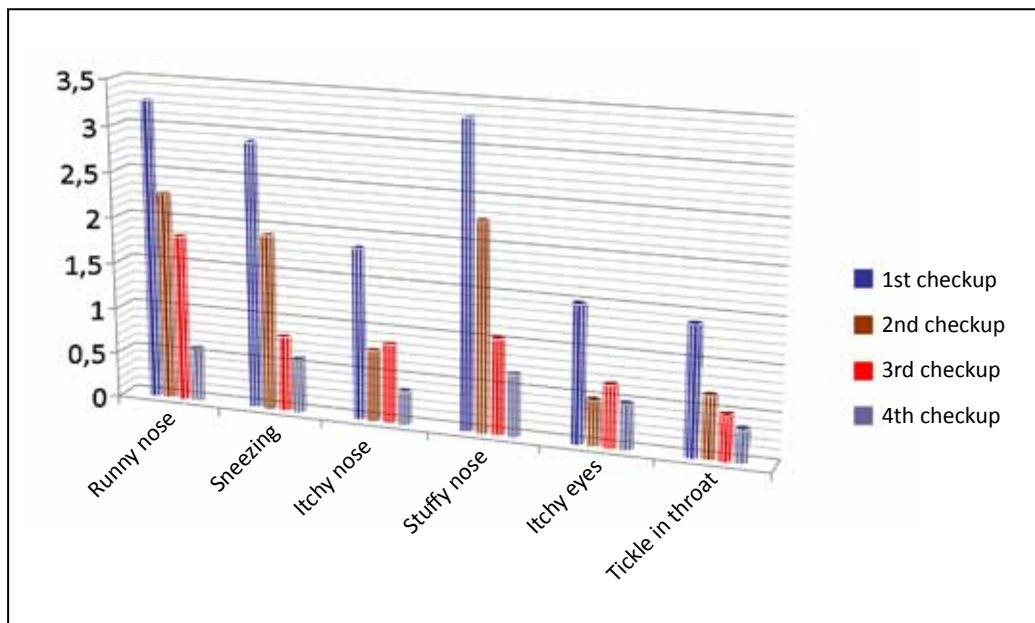
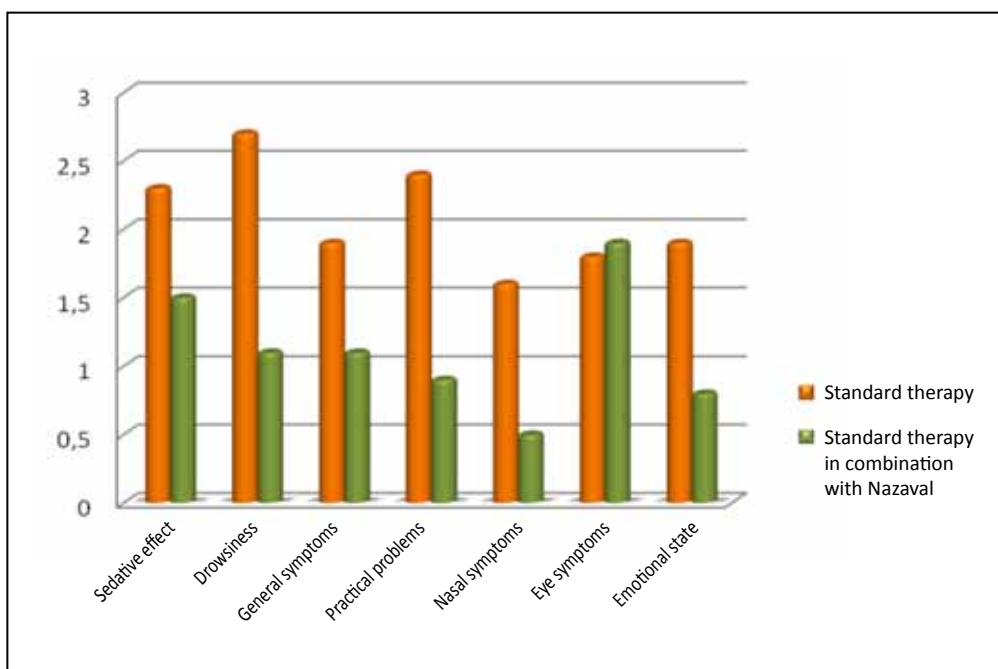


Figure 2. Evaluation of quality of life of a patient suffering from allergic rhinitis



Notes: Statistically significant differences were noted in the allergic rhinitis sufferers who received the standard therapy in combination with Nasaleze compared with the standard therapy group ( $p < 0.05$ )

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