

ORIGINAL PAPER

A randomized placebo-controlled pilot study of Cat saliva 9cH and Histaminum 9cH in cat allergic adults

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Background: Cat allergy is an abnormal immune response by the body to cat dander or saliva, leading to the development of a complex of symptoms which can negatively influence health. Cat saliva 9cH and Histaminum 9cH are indicated, according to isopathic principles, for the treatment of cat allergy, however no research has been done to date.

Aim: To determine the effect of Cat saliva 9cH and Histaminum 9cH (combined) on cat allergic adults.

Method: 30 Participants with a positive test result for a cat allergy skin prick test (SPT) were recruited to a double-blind, randomised, placebo controlled clinical trial. Participants took two tablets twice daily for 4 weeks, and attended a follow-up consultation at the end of weeks 2 and 4. The measurement tool used was the SPT, conducted at the beginning and at the end of the study.

Results: Cat saliva 9cH and Histaminum 9cH produced a highly statistically significant reduction in the wheal diameter of the cat allergen SPT at the end of week 4. The placebo group showed no statistically significant change.

Conclusion: The homeopathic medicine reduced the sensitivity reaction of cat allergic adults to cat allergen, according to the SPT. Future studies are warranted to further investigate the effect of Cat saliva and Histaminum and their role as a potential therapeutic option for this condition. *Homeopathy* (2013) 102, 123–129.

Keywords: Cat allergy; Homeopathy; Isopathy; Sarcodes; Complex; Cat saliva; Histaminum

Introduction

In urban areas cats are the most typical household pets, and an important source of indoor allergens.¹ Cat allergies are extremely prevalent, with the sensitization rate reaching up to 60% in western countries.² According to the Asthma and Allergy Foundation of America (AAFA) 15–30% of people in the USA are allergic to their pets,

with cat allergies being twice as common as dog allergies.³ Cat allergy is a type 1 hypersensitivity reaction by the body's immune system to cats. Symptoms are due to a histamine reaction to the cat glycoprotein cal Fel d1, which is secreted by the sebaceous glands of the cat and can be found in cat saliva and dander. Cat allergies may initiate or exacerbate conditions such as hayfever, asthma and atopic dermatitis. Symptoms of cat allergy range from mild rhinopharyngitis to potentially life-threatening acute asthmatic attacks and anaphylaxis.^{4,5}

Diagnosis of cat allergy can be made on clinical history and by the use of the RAST (radioallergosorbent test), MAST (multiple allergen simultaneous test) or the skin prick test (SPT). The SPT is cost effective and considered the most important diagnostic tool in clinical practice.⁶

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Skin prick testing involves introducing a tiny amount of allergen extract to the area of the skin which has been punctured. If the patient is allergic to the substance an inflammatory reaction will be visible within 15 minutes. The diameter of the wheal that forms is measured.^{7,8} Adverse effects from the SPT may include urticaria, and in very rare cases, anaphylaxis.⁶ Skin prick testing with domestic pet allergens shows good correlation with blood specific IgE testing.^{7,8} The SPT was chosen for this study as it is reliable, simple to use and a cost effective form of allergy testing.⁹

Avoidance of known offending allergens remains the most effective means of managing allergic conditions; however this may often prove impossible, as many people with cat allergies continue to own cats as pets. Conventional treatment for allergies comprises pharmacotherapy and immunotherapy. Pharmacological agents such as anti-histamines and decongestants are commonly prescribed, although these are merely palliative, may have adverse effects; tolerance develops in many patients.¹⁰

Specific immunotherapy is a process of reducing sensitivity to a specific allergen, whereby the patient is gradually vaccinated with increasingly larger doses of that allergen.¹¹ Immunotherapy requires a 3–5 year period of injections¹² and although helpful for many allergy sufferers when prescribed in the correct therapeutic dosage range, it is ineffective or only partially effective for some allergy patients.^{13–16} Side effects include local pain, redness and swelling of the injection site, and systemic reactions such as hives, sneezing and congestion, and in severe cases anaphylaxis.¹⁷ Sublingual immunotherapy (SLIT) is the oral version of specific immunotherapy. While SLIT is considered a much safer option with fewer side effects,^{11,18} one major disadvantage is that it is more expensive.¹⁷ SLIT therapy for cat allergy desensitization is not yet available in South Africa.

Various studies have been conducted on the use of homeopathic remedies in the treatment of allergies, many of which yielded positive findings.¹⁹ In 1986, Reilly et al. conducted a randomised controlled trial (RCT) involving 144 patients suffering from hayfever. This compared the effects of a homeopathic preparation of mixed grass pollens with a placebo. The treatment group had a statistically significant improvement in hayfever symptoms when compared to the placebo group, and a greater decrease in the need for anti-histamines.²⁰ In 1994, Reilly et al. examined the use of potentised allergens in the treatment of asthma. In this double-blind, placebo-controlled RCT, the homeopathic group again had a better outcome than the placebo group, with a greater reduction in bronchial reactivity, and a median 53% increase in histamine resistance (placebo group median 7%).²¹ In another RCT with crossover conducted by Taylor et al. on 51 patients with perennial allergic rhinitis, participants in the treatment group received a 30C potency of their main aeroallergen. While both groups showed a reduction in symptoms, the treatment group had greater improvements in nasal airflow from baseline. There was however no statistically significant difference in symptom improvement between the two groups.²²

Lewith et al. (2002) conducted a 16-week study on the use of potentised house dust mite in the treatment of asthmatic people with a predominant house dust mite allergy. No statistical difference was found between the homeopathic and placebo groups with regards to their forced expiratory volume (FEV₁) in 1 s, their mood or quality of life. The effect of the remedy on the SPT or IgE levels was however not assessed.²³ Kim et al. conducted a 4-week, double-blind clinical trial on adults with seasonal allergic rhinitis. A homeopathic preparation (6×) of the common aeroallergens in the geographical area was administered. The treatment group showed statistically significant improvement of quality of life, and a reduction in work productivity and activity impairment. No adverse effects were reported.²⁴

A comparative study was conducted between specific SLIT (grass pollens, house dust mite or cockroach) and homeopathic therapy (Poumon Histaminum and Apis mellifica) on 74 children with allergic rhinitis. Participants with persistent allergic rhinitis were treated for 12 months, and those with intermittent allergic rhinitis for 5 months. Measurement tools included a symptom diary, a paediatric rhino-conjunctivitis quality of life questionnaire, SPTs, specific IgE antibodies tests and nasal eosinophilia tests. Both methods were associated with symptomatic improvements, it was concluded that the homeopathic treatment was generally more effective and better tolerated than the SLIT.²⁵

Histaminum is a sarcode made from histamine and is believed to reduce allergic reactions by countering the effect of histamine on the body.²⁶ The effect of Histaminum on basophils has been explored in several in vitro studies. Basophils play a key role in the immediate allergic response, releasing inflammatory chemical mediators in response to antigen exposure. Many of these studies found that Histaminum appears to have a significant inhibitory effect on basophil activation; however the results are not yet conclusive.

Two recent studies have confirmed that Histamine in high dilutions inhibits histamine release.^{19,27,28} Heteroisopathy is a type of iso-therapeutics whereby a substance is taken from the patients' surroundings that is believed to play a role in the aetiology of their allergy.²⁹ Cat saliva in potency was therefore chosen based on isopathic principles, i.e. 'same cures same'. It was hypothesized that these two remedies in combination would possibly have a desensitizing effect to cat allergen, as seen on the SPT.

The purpose of this double-blind placebo-controlled pilot study was to determine the effect of Cat saliva 9cH and Histaminum 9cH on cat allergic adults, by means of a SPT.

Material and methods

This research study was approved by The Faculty of Health Sciences Academic Ethics Committee (AEC44/02-2010) and Higher Degrees Committee (HDC44/02-2010) at the University of Johannesburg. The study was conducted at the Homeopathic Health Training

Centre, at the Doornfontein campus, University of Johannesburg (UJ), South Africa and at Weleda pharmacy (Fourways, Johannesburg) under the supervision of a qualified homeopathic practitioner. All participants gave informed consent, and were free to withdraw from the study at any stage.

Research sample and inclusion criteria

Advertisements were placed at the UJ Homeopathic Health Training Centre and Weleda pharmacy, with relevant permission granted. Participants were recruited by means of purposive sampling. The study included thirty volunteers, both male and female, between the ages of 18 and 45. Participants had to have a positive SPT, to be living with a cat for a period of 6 months or more and be suffering from allergy-like symptoms (i.e. sneezing, red itchy eyes, skin rash, runny itchy stuffy nose, scratchy throat, wheezing and redness of the skin where a cat has scratched, licked or bitten) when in the presence of a cat or when exposed to cat dander.

Individuals that were pregnant or lactating, using any other medication or intervention for allergies (including previous immunotherapy for cat allergy), or who were immuno-compromised were excluded from the study.

Research design and procedure

This was a 4-week, double-blind placebo-controlled pilot study. Potential participants attended an initial interview where informed consent was obtained. They then reported to Ampath laboratories to undergo a SPT to validate and diagnose the presence of a cat allergy, and the results were forwarded directly to the researcher. The participants that yielded a positive SPT result were requested to attend an initial consultation with the researcher, consisting of a brief case history, presenting symptoms, vital signs and focused physical examination of the ears, nose, throat and eyes.

The participants were then divided into two groups, with 15 in the experimental group and 15 in the placebo group. The medication was randomized by Natura Laboratories, using the simple random sampling method, and the participants accordingly received the Cat Saliva 9cH and Histaminum 9cH (combined in a single tablet) on lactose tablets, or placebo (unmedicated lactose tablets).

Participants attended a follow-up consultation at the end of week 2 (where they received a second bottle of medication) and at the end of week 4. At these follow-up consultations, the researcher followed up on the initial case history and repeated the physical examination.

Participants reported to Ampath laboratories for their final SPT, immediately prior to the final consultation (Figure 1). Although not the primary outcome measure, the extent of the flare reaction and degree of itchiness of the SPT were also noted and analysed.

Measurement tools

The measurement tool used was the SPT. The SPT (conducted at the beginning and at the end of the study)

requires the use of three test serums: a positive control (histamine dihydrochloride), a negative control (saline), and cat allergen (a mixture of cat hair and cat saliva). The results of skin prick testing are read at 10 min (for the positive control) and 15 min (for the allergen), and the diameter of the resulting wheal is recorded in two dimensions. The results are interpreted on a 4-point scale of severity i.e. +1 meaning mild reaction or no reaction and +4 representing a major reaction. The diameter of the wheal that forms and the extent of the flare reaction are measured in millimetres, and the degree of itchiness is also noted. The positive control reaction scores +4. The specific allergen wheal is then measured with a perspex allergen ruler and compared to the control.

By convention, a positive test is one in which the mean of the two wheal diameters is at least 3 mm greater than the negative control. Positive and negative controls are critical to enable interpretation of test results. All allergic individuals should react to the positive control; a lack of reaction could indicate that he/she is taking medication with immune inhibitory activity. All participants in the study reacted to the positive control and the cat allergen. When performed correctly, skin prick testing with aeroallergens (such as domestic pet allergens) shows good correlation with blood specific IgE testing.^{7–9,30,31}

Medication administration

The medication was manufactured and randomised by Natura Laboratories (a registered homeopathic pharmaceutical laboratory), employing Good Manufacturing Procedures (GMPs), and dispensed in 25 mL bottles containing 56 tablets each. The placebo was manufactured to be identical in taste and appearance to the homeopathic complex. All bottles were labelled in the same manner. Participants were instructed to dissolve two tablets under the tongue twice daily, morning and night. Included with the medication bottle was an information leaflet explaining the dosage and storage conditions required.

Reliability and validity measures

The SPT is a valid and standardised tool for measuring the level of allergic reaction^{7,9} and was conducted by Ampath pathology laboratories to ensure quality control and safety of the participants. The vials of cat allergen were manufactured by STALLERGENES S.A., and one vial = 100 IR/ml of standardised allergen extract.^{30,31}

Data collection and analysis

Data collected from each participant was statistically analysed using non-parametric tests, due to the small sample size ($n = 30$). Comparison between groups was done using the Mann–Whitney Test and comparisons within groups over a period of time were done using the Wilcoxon Signed Ranks Test. For the purpose of this study, the p -values are interpreted as follows: $p < 0.05$ = statistically significant, $p < 0.001$ = highly statistically significant.

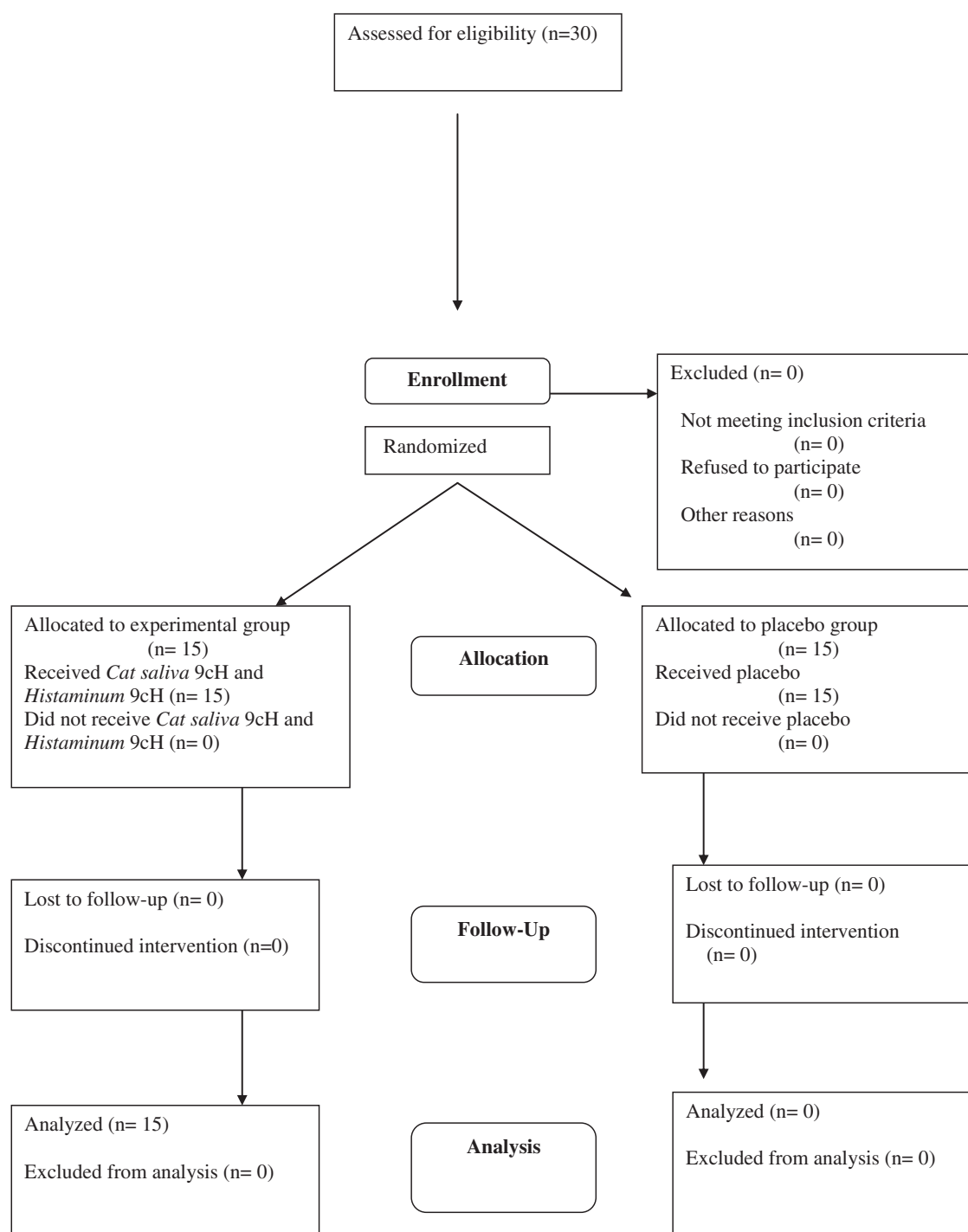


Figure 1 Flow of participants through study.

Results

Introduction

All 30 participants completed the study. Data collected from the SPT was analysed using SPSS version 13. Table 1 gives the baseline data for the wheal diameter of the SPT for cat allergen.

Analysis within groups showed that for the experimental group, there was a highly statistically significant improvement in the wheal diameter for the cat allergen, between day 0 and day 28, with $p = 0.001$ (Figure 2, Table 2). It was

noted that the flare reaction and degree of itchiness also showed a statistically significant improvement, with $p = 0.001$ for both variables (Table 2). There were no statistically significant differences found within the placebo group between day 0 and day 28, with $p = 0.177$ for the wheal diameter (Figure 3, Table 3), flare reaction and degree of itchiness (Table 3). Similar results were found for the positive control (histamine) test, with $p = 0.001$ for the wheal diameter of the experimental group, and $p = 0.715$ for the control group.

Analysis between groups for the cat allergen SPT revealed that the experimental group displayed a statistically

Table 1 Baseline wheal diameter data for the SPT cat allergen results

Experimental Group	Day 0 (mm)	Day 28 (mm)	Control Group	Day 0 (mm)	Day 28 (mm)
1	8	5	1	8	10
2	8	5	2	5	6
3	8	2	3	4	6
4	5	3	4	2	8
5	3	4	5	1	2
6	6	3	6	5	8
7	10	0	7	7	7
8	6	3	8	8	6
9	5	3	9	3	3
10	2	0	10	5	2
11	1	0	11	6	8
12	2	0	12	3	6
13	2	0	13	5	7
14	7	4	14	5	8
15	4	2	15	8	3

significant effect in reducing the wheal diameter ($p = 0.007$), flare reaction ($p = <0.001$) and degree of itchiness ($p = 0.002$) of the cat allergen SPT by day 28 (Table 4). Similar findings were seen for the positive control as well (Table 5).

Discussion

For this study, an objective measurement tool was employed, namely the SPT. The SPT is considered as a safe, effective, rapid, and cost-effective means of establishing the presence of an allergy. When the SPT is positive, it shows the presence of antibodies specific to cat allergen in sensitised individuals. The wheal that forms is due to the release of the chemical mediators of allergy, such as histamine, cytokines, platelet activating factor (PAF), leukotrienes and prostaglandins, all triggered by the antibody–antigen reaction.³⁰ SPTs cannot be performed in patients using drugs that inhibit the immune response, such as anti-histamines or corticosteroids, and this was an exclusion criterion for this study.

The results recorded for the cat allergen SPT showed that there was a highly statistically significant reduction in the wheal diameter in the experimental group. Five participants went from having a positive SPT for cat allergen at the beginning of the study to having no reaction to the

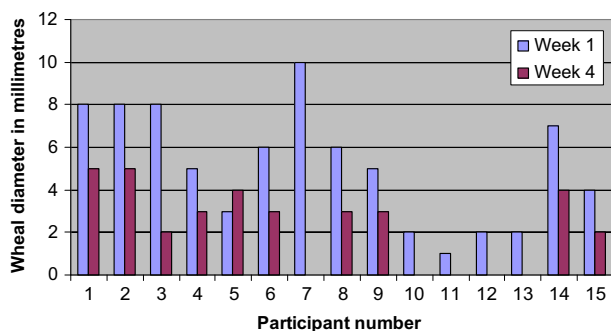


Figure 2 Frequency of wheal diameter in cat allergen SPT for experimental group.

Table 2 Comparison of the cat allergen SPT results between day 0 and day 28 in the experimental group

Cat allergen	Day	Mean	Standard deviation	p-Value
Wheal diameter scale	0	5.13	2.75	<0.001
	28	2.27	1.87	
Flare reaction scale	0	2.73	0.80	<0.001
	28	1.33	1.05	
Level of itchiness	0	3.67	1.29	<0.001
	28	1.07	0.88	

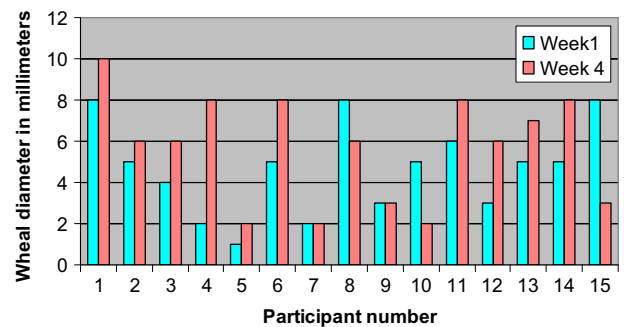


Figure 3 Frequency of wheal diameter in cat allergen SPT for control group.

same allergen at the end of the study. From this we deduce that the homoeopathic complex of Cat Saliva 9cH and Histaminum 9cH reduced the sensitivity of most of the participants in the experimental group to cat allergen, after a 4 week treatment period. In the placebo group, the results recorded for the cat allergen SPT showed that the wheal diameter had a mixed pattern of increased, decreased and status quo, with 10 of the 15 participants' in this group actually having a marked increase in wheal diameter at the end of the study. When comparing the groups, the experimental group displayed a statistically significant result in reducing the wheal diameter of the SPT, compared to the placebo group. Although not the main parameter of measurement, the flare reaction and degree of itchiness of the wheals were recorded, and similar results were seen.

Histaminum is believed to have an anti-histamine type of effect on the body, possibly by inhibiting the activation of basophils^{27,28} and therefore the results for the positive control (histamine) SPT were also recorded, to see whether the remedy inhibited the action of histamine. The results showed that the wheal diameter, flare reaction and degree of itchiness reduced significantly in the experimental group, as well as when compared to the placebo group on day 28. These findings provide further

Table 3 Comparison of the cat allergen SPT results between day 0 and day 28 in the control group

Cat allergen	Day	Mean	Standard deviation	p-Value
Wheal diameter scale	0	4.67	2.23	0.177
	28	5.67	2.64	
Flare reaction scale	0	2.93	1.16	0.499
	28	3.07	0.96	
Level of itchiness	0	3.53	1.25	0.264
	28	3.07	0.80	

Table 4 Comparison of the cat allergen SPT results between experimental and control groups

Cat skin prick	Group	Mean	Standard deviation	p-Value
Wheal diameter scale	Experimental	4.40	2.36	0.007
	Placebo	5.50	2.12	
Flare reaction scale	Experimental	2.22	1.09	0.000
	Placebo	3.07	0.88	
Level of itchiness	Experimental	2.57	1.68	0.002
	Placebo	3.43	1.03	

Table 5 Comparison of the positive SPT results between experimental and control groups

Cat skin prick	Group	Mean	Standard deviation	p-Value
Wheal diameter scale	Experimental	4.40	2.36	0.007
	Placebo	5.50	2.12	
Flare reaction scale	Experimental	2.22	1.09	0.000
	Placebo	3.07	0.88	
Level of Itchiness	Experimental	2.57	1.68	0.002
	Placebo	3.43	1.03	

evidence on the effects of Histaminum in allergy patients. There are many chemical mediators of allergy, of which histamine is just one. Further studies could investigate the effect of various potentised remedies made from these mediators, to identify their possible immune-modulating properties.

Low potencies were chosen for this study, in repeated doses, as it was believed that these would have more of a physiological effect on the body, and if any aggravations did occur, that these would be relatively short-lived once the remedy was discontinued. Other potencies of these remedies may however have different effects on the body, and these also need to be explored in future studies.

Internal validity of the study was ensured as this was a double-blind, placebo controlled randomized study. External validity could have been affected by the small sample size and the limited treatment time. Also, although each participant was given an information leaflet on medication dosage and storage instructions, it was not assessed if this was upheld. Participants were monitored for changes in exposure to cats, as well as if any new conventional allergy medicines were introduced. All participants in this study continued to keep cats as pets, and no new medications for allergies, conventional or otherwise, were introduced. Further future studies are warranted, and should be conducted on a larger sample group, which will improve statistical power. Other potencies and frequencies of administration could also be explored, as well as follow-up studies conducted after discontinuation of treatment in order to further determine the effects of these remedies.

Conclusion

This study has established that the complex of Cat Saliva 9cH and Histaminum 9cH has an effect on sensitivity to cat allergen in adults with cat allergies, according to the SPT. The remedies were well tolerated and no adverse effects were noted. Isopathic treatment may have a role in the

treatment of cat allergy, and possibly provide an alternative to conventional immunotherapy options. Further larger scale studies over longer time periods should be conducted to validate these results.

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