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## Local, Unpasteurized Honey as a Treatment for Allergic Rhinitis: A Systematic Review

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# Local, Unpasteurized Honey as a Treatment for Allergic Rhinitis: A Systematic Review

## Abstract

**Background:** Allergic rhinitis (AR) is a common disorder worldwide. Estimates show that 10% to 30% of the world population is affected by AR and that the prevalence of allergic diseases is drastically increasing in both developing and developed countries. Ingestion of honey is widely believed to be a natural remedy to reduce symptoms of allergic rhinitis. There are many theories addressing the mechanism(s) of action in which honey may treat AR symptoms. Many of these theories are postulated as a result of research evidence garnered from animal trials. This systematic review is to evaluate human studies looking at whether ingestion of honey can be used as a complementary or alternative form of therapy in treating allergic rhinitis.

**Methods:** An exhaustive literature search was conducted to identify relevant published papers using Medline-OVID, CINAHL, PubMed, and Web of Science using the keywords: *honey* and *allergic rhinitis*. Quality of relevant articles was assessed using the GRADE criteria.

**Results:** Two randomized control trials met the inclusion criteria. One randomized, double blinded study published in 2013 demonstrated a statistically significant reduction of symptoms in the local honey group when compared to the control group. Another randomized, double blinded study published in 2002 demonstrated no therapeutic effect for either local honey or commercial honey in reducing symptoms of allergic rhinitis when compared to the control group.

**Conclusion:** The results from each study were contradictory. Both studies had limitations in design and methodology which reduced their quality of evidence. Overall quality of evidence is low. A weak recommendation can be made in support of using oral ingestion of local honey as an adjunct in treating symptoms of allergic rhinitis. There was no evidence of effect using commercial honey when compared to placebo. Further research in the form of large population RCTs is needed to validate the results presented by these studies.

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## Keywords

allergic rhinitis, allergies, honey, pollen, rhinitis, seasonal allergies, honey therapy

## Subject Categories

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# Local, Unpasteurized Honey as a Treatment for Allergic Rhinitis: A Systematic Review

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*A Clinical Graduate Project Submitted to the Faculty of the*

*School of Physician Assistant Studies*

*Pacific University*

*Hillsboro, OR*

*For the Masters of Science Degree, August 9, 2014*

*Clinical Graduate Project Coordinator: Annjanette Sommers, PA-C, MS*

## **Biography**

[Redacted for privacy]

## Abstract

**Background:** Allergic rhinitis (AR) is a common disorder worldwide. Estimates show that 10% to 30% of the world population is affected by AR and that the prevalence of allergic diseases is drastically increasing in both developing and developed countries. Ingestion of honey is widely believed to be a natural remedy to reduce symptoms of allergic rhinitis. There are many theories addressing the mechanism(s) of action in which honey may treat AR symptoms. Many of these theories are postulated as a result of research evidence garnered from animal trials. This systematic review is to evaluate human studies looking at whether ingestion of honey can be used as a complementary or alternative form of therapy in treating allergic rhinitis.

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**Conclusion:** The results from each study were contradictory. Both studies had limitations in design and methodology which reduced their quality of evidence. Overall quality of evidence is low. A weak recommendation can be made in support of using oral ingestion of local honey as an adjunct in treating symptoms of allergic rhinitis. There was no evidence of effect using commercial honey when compared to placebo. Further research in the form of large population RCTs is needed to validate the results presented by these studies.

**Keywords:** honey, seasonal allergic rhinitis, perennial allergic rhinitis, allergic rhinitis

## **Acknowledgements**

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## List of Abbreviations

ANOVA	ANalysis Of Variance
AR	Allergic Rhinitis
ARIA	Allergic Rhinitis and its Impact on Asthma
GRADE	Grading of Recommendations, Assessment, Development and Evaluation
IgE	Immunoglobulin E
RCT	Randomized control trial

# Local, Unpasteurized Honey as a Treatment for Allergic Rhinitis: A Systematic Review

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## BACKGROUND

Allergic rhinitis (AR) is a common disorder worldwide. Estimates show that 10% to 30% of the world population is affected by AR and that the prevalence of allergic diseases is drastically increasing in both developing and developed countries.<sup>1</sup> The medical costs associated with AR are approximated at 6 billion annually in the United States alone.<sup>2</sup> A predisposed individual suffers from symptoms of AR when they are exposed to an allergen. Allergic rhinitis is a seasonal or perennial inflammatory disease that is classically characterized by inflammation of the nasal passages, rhinorrhea, nasal congestion and sneezing. Ocular symptoms are commonly seen as well.<sup>3</sup>

Those afflicted with AR have an assortment of current medical therapies and recommendations available for use which include intranasal corticosteroids, antihistamines, and allergen avoidance. Other adjunctive medical therapies and measures include: decongestants, cromolyn sodium, leukotriene modifiers, intranasal anticholinergic agents, and allergy immunotherapy. Many of these are sometimes ineffective or expensive and have various side effects.<sup>4-8</sup> Allergy immunotherapy by subcutaneous injection or sublingual route is more effective than placebo in treating patients who fail other medical therapies and has been shown to relieve symptoms of AR in up to 80% of patients. Current recommendations for immunotherapy are for those with severe AR which is refractory to medication.<sup>9-11</sup> A commonly considered drawback to

injection immunotherapy is the need to travel to a shot clinic on a regular basis to receive injections.<sup>12</sup> Additionally, immunotherapy has a high initial cost associated with it. However, research indicates that there may be significant cost savings recognized after 3 months of immunotherapy treatment for patients <18 years of age.<sup>13</sup>

As an alternative to medical therapy, ingestion of honey is widely believed to be a natural remedy to reduce symptoms of allergic rhinitis. There are many theories addressing the mechanism(s) of action in which honey may treat AR symptoms. Many of these theories are postulated as a result of research evidence garnered from animal trials. For instance, one component of honey, honeybee-collected pollen, has been shown to inhibit IgE-mediated mast cell activation from both in vivo and in vitro studies demonstrating a possible anti-allergic mechanism.<sup>14,15</sup> Another study<sup>16</sup> in mice demonstrated that ovalbumin-specific IgE responses elicited with a range of doses were completely suppressed by using different sources of commercially available honey. There is extensive evidence in human and animal studies which demonstrate that honey possesses anti-inflammatory properties.<sup>17-21</sup>

Perhaps the most widely believed theory is that ingestion of locally collected, unpasteurized honey works similar to immunotherapy. Bees play an important role by collecting pollen from flowering plants. In addition to floral pollen, bees collect windborne pollen during flight. It has been postulated that with sufficient pollen concentrations present in honey an oral low-dose tolerance to specific aeroallergens may be developed in a similar mechanism to sublingual immunotherapy.<sup>22</sup>

Few studies exist which evaluate whether honey has a therapeutic effect on symptoms of allergic rhinitis. This systematic review is to evaluate those studies and

grade the level of evidence to make recommendations on whether ingestion of local, unpasteurized honey can be used as a complementary or alternative form of therapy in treating allergic rhinitis.

## **METHODS**

An exhaustive literature search was conducted to identify relevant published articles using Medline-OVID, CINAHL, PubMed, and Web of Science using the keywords: *honey* and *allergic rhinitis*. Bibliographies from the discovered articles were cross-referenced for additional relevant sources. Inclusion criteria consisted of studies done on humans and studies published in the English language. Studies were excluded if researchers failed to perform allergen scratch testing on participants at study onset or if the honey was taken by any route other than orally. Quality of relevant articles was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) criteria.<sup>23</sup> A search of The National Institute of Health clinical trials website revealed no currently registered trials regarding the use of oral ingestion of honey in association with treatment for allergic rhinitis

## **RESULTS**

The initial search yielded a total of 54 articles for review. After removing duplicate articles there were two remaining studies which met the inclusion and exclusion criteria. Both studies are randomized control trials.<sup>22,24</sup> See Table I.

### **Asha'ari et al study**

This randomized, double-blinded, placebo-controlled trial<sup>24</sup> was conducted over a 1 year period from April 2010-April 2011. Participants in the study were recruited from an otolaryngology clinic in two tertiary referral centers located along the East coast of Peninsular Malaysia. The sample size was determined using power analysis software to an 80% power of study. Symptom history was gathered and subjects were tested by skin prick for common allergens in the area. Subjects whose skin prick test was negative were excluded from the study. Each subject was then graded using the Allergic Rhinitis and its Impact on Asthma (ARIA) classification.<sup>24,25</sup>

Forty participants between the ages of 20-50 years were divided into two equally-sized, prognostically balanced groups. All participants took 10 mg Loratadine (second-generation antihistamine) once daily for the first 4 weeks of the study, after which all participants discontinued use of the antihistamine. The case group received Tualong honey, a raw, unprocessed, and multifloral honey harvested from the Malaysian rainforest. The control group received honey-flavored corn syrup. All subjects were instructed to consume 1 gram per kilogram of body weight each day in separate doses for the first 4 weeks of the study period. In addition to this, all subjects were instructed to not consume any other products which included honey during the study period. Subjects were given a diary to fill out daily to record dosage taken and any possible side effects. Subjects were then instructed to mail each diary to the researchers on a weekly basis for the first 4 weeks of the study. The researchers make no mention regarding loss to follow-up.<sup>24</sup>

Seven symptoms were assessed to determine treatment effect (Table II). Symptom scores for each participant were recorded at study onset, week 4(day 28), and week 8(day

56). For the scoring, the participant evaluated the severity of individual symptoms using a 7-point visual analog scale which was published by The Joint Task Force on Practice Parameters on Allergy, Asthma, and Immunology.<sup>24,26</sup> Researchers regarded AR symptoms as present when a score of at least three was reported by the participant.<sup>24</sup>

On data analysis the researchers calculated the mean and the standard deviation for the total symptom score of the control and the case groups at the start of the study, at week 4, and again at week 8. Comparisons were completed using ANOVA and t test analysis techniques. Initial findings demonstrated no significant differences observed between the case and control group at study onset, week 4, and week 8. Post hoc comparisons were made between the weeks in the case group and control group using paired samples t tests. Statistically significant differences were observed within the case group between the mean total symptom scores of week 0 and week 4 (mean difference 3.05 ( $\pm$  4.76)  $P=0.010$ ), week 4 and week 8 (mean difference 2.30 ( $\pm$ 3.28)  $P=0.005$ ), and week 0 and week 8 (mean difference 5.35 ( $\pm$ 4.98)  $P=0.000$ ). In the control group, statistically significant differences were observed between the mean total symptom scores of week 0 and week 4 (mean difference 2.10 ( $\pm$ 4.15)  $P=0.036$ ) and week 0 and week 8 (mean difference 3.13 ( $\pm$ 4.10)  $P=0.003$ ), but not between week 4 and week 8 (mean difference 1.03 ( $\pm$ 3.54)  $P=0.209$ ). Based on the results of the study, the researchers determined that large doses of honey appear to improve the symptoms associated with AR over a short period and that there is indication that local honey could serve as an adjunct therapy for AR.<sup>24</sup> See Table III.

The researchers stated that the results of the study need to be considered preliminary as they identified various limitations of the study. The first limitation they

identified was that symptom scoring was determined using clinical criteria. They attempted to minimize this bias by using a validated scoring instrument and by having the same independent assessor conduct the symptom score for each patient throughout the study. Another limitation the researchers addressed is that the honey used in the study is a raw, unprocessed local honey and the results are only relevant to the lot of honey consumed in the study. Lastly, the researchers acknowledged a relatively small sample size for the study and stated that evidence from a larger randomized-control trial is needed to provide validation to the results of the study.<sup>24</sup>

### **Rajan et al study**

This randomized, double-blinded, placebo-controlled trial<sup>22</sup> was conducted at the University of Connecticut Health Center's Lowell P. Weicker General Clinical Research Center. Using a power analysis, the authors determined that at least 9 participants per group, 27 total, were needed for the study. Symptom history was gathered and participants were scratch tested for common seasonal allergens in the region upon entry into the study. Scratch test results were recorded and the patients' forearms were photographed; this data was stored for future blinded evaluation.<sup>22</sup>

Thirty-six participants between the ages of 20-70 years who complained of symptoms of allergic rhinoconjunctivitis were recruited and divided into three different cohorts. The first group (11 females, 2 males) received corn syrup with synthetic honey flavoring as a control. The second group (6 females, 5 males) received locally collected, unpasteurized and unfiltered honey. The third group (7 females, 5 males) received nationally collected, pasteurized and filtered honey. Participants were to consume one

tablespoon per day for 30 weeks and to record daily, in a diary provided, both nasal and ocular symptoms (Table IV) using a scale of 0 to 3, in addition to use of any allergy medication. Participants mailed their records to the researchers on a weekly basis. Twenty-three participants completed the study after loss to follow-up: seven participants remained in the placebo group, nine in the local honey group, and seven in the nationally collected honey group.<sup>22</sup>

On data analysis, the researchers divided the allergy season into 4 periods representing the common local aeroallergens. The researchers stated that it would be most clinically useful if subjects experienced no allergy symptoms, so they only evaluated each group by days with symptoms or days with no symptoms in a dichotomous format. The researchers combined the 10 subjective symptoms with the number of days participants used allergy medication and measured them across all four seasonal periods to result in 44 parameters. They found that the placebo group outperformed the other two groups in 19 of the 44 parameters, the local honey outperformed the other two groups in 18 of the 44 parameters and the national honey outperformed the other two groups in 7 of the 44 parameters. They noted there was no consistent improvement in symptoms for any group.<sup>22</sup>

Upon review of the scratch test results after completion of the study, the researchers found that only 14 of the 23 remaining participants demonstrated scratch test reactivity to the seasonal allergens which were tested. Of these 14 participants, 3 remained in the placebo group, 6 in the local honey group, and 5 in the national honey group. The researchers determined which participants were benefited by the treatment regimen based on their positive scratch test results correlated to their symptom reporting



during the relevant seasons. It was determined by the researchers that 2 of 3 participants in the placebo group, 2 of 6 participants in the local honey group, and 3 of 5 participants in the national honey group were benefitted by treatment (Table V). The authors state that the 7 patients who benefitted by treatment were comparably divided among the three groups ( $P=0.65$ ). Based on the results the researchers determined that the study did not support the belief that honey is effective at reducing the symptoms of rhinoconjunctivitis.<sup>22</sup>

The researchers reported that there were several possible limitations to the study. The first being that the dose of honey used could be inadequate to be effective. Another was the possibility that a longer treatment regimen might be required to reach adequate effect. They finally stated that the small size of the cohort would require that additional studies, using larger groups need to be conducted in order to confirm their findings.<sup>22</sup>

## **DISCUSSION**

Allergic rhinitis affects individuals from all age ranges around the world, and studies indicate an increasing prevalence of AR worldwide.<sup>1</sup> The annual medical costs associated with AR in the United States alone approach 6 billion.<sup>2</sup> There is a widely held belief that honey can be effective in managing symptoms of AR. The mechanisms postulated by which honey may reduce symptoms of AR include: anti-inflammatory properties, a possible immunosuppressive effect, and immunotherapy in the form of low-dose oral tolerance. Two randomized, double-blinded, placebo-controlled trials<sup>22,24</sup> were evaluated in this systematic review to determine if honey may play a role in the treatment of AR, and their results were contradictory. The researchers from the article by Asha'ari et al<sup>24</sup> determined that large doses of honey appear to improve the symptoms associated

with AR over a short period and that the results indicate it could serve as an adjunct therapy for AR. In the article by Rajan et al<sup>22</sup> the researchers stated that their study did not support the belief that honey is effective at reducing the symptoms of rhinoconjunctivitis. These studies varied from each other by design, methodology, environment, and study population. In light of the contradicting results from the respective studies, significant consideration was given regarding the quality of both studies (Table I). Specifically, the Asha'ari et al study<sup>24</sup> carries more validity than the Rajan et al study<sup>22</sup> in regards to limitations and consistency; therefore, their results should be favored. Additionally, when considering the low risk of side effects associated with honey and the ease of availability, it was determined that local honey may be a safe, effective adjunct therapy to reduce symptoms of allergic rhinitis. However, larger RCTs are needed to validate this conclusion and to provide further insight into the mechanisms by which honey affects the human body.

## **Limitations**

Both study<sup>22,24</sup> outcomes of interest were underpowered due to small population size. The study by Rajan et al<sup>22</sup> used a power analysis and determined that at least 9 participants per group (minimum of 27 participants) were needed for the duration of the study to indicate statistical significance. There were 36 participants at study onset and, after loss to follow-up, only 23 participants remained at study completion. Additionally, it appeared that the results from the allergen scratch testing performed upon entry into the study were not reviewed until study completion. After review, the authors determined that only 14 participants remained who demonstrated a positive reaction to the scratch

test. In contrast, the study by Asha'ari et al<sup>24</sup> excluded subjects who had a negative scratch test before entry into the study. This verified that all study participants were afflicted with AR. In the study by Asha'ari et al<sup>24</sup> the researchers calculated sample size using power analysis as well. Forty patients were recruited and study results ranged over an 8 week period. However, the authors did not address loss to follow-up in their paper and so it is unknown how many participants completed the study, although there may have been no loss to follow up in this study as implied by the Degree of Freedom reported. In both articles the authors state that further trials using a larger cohort are needed to confirm their findings.

A limitation of methodology that was present in both studies<sup>22,24</sup> was that clinical criteria were used to evaluate symptoms. Ideally, patient-reported outcomes will be validated with some form of objective data. In the context of these studies an immunologic test may serve best. Both studies were limited by the inability to standardize raw, unpasteurized, local honey and therefore the results of the respective studies can only apply to the lot of local honey used in that study. It should be noted that the Rajan et al study<sup>22</sup> also compared the use of pasteurized, filtered, commercially available honey.

A limitation of methodology that is singular to the Rajan et al study<sup>22</sup> is their choice of delineating that being symptom-free was the only clinically useful endpoint. Of interest to most clinicians is the symptom improvement at any level. This was measured in the Asha'ari et al study<sup>24</sup>; however, both studies<sup>22,24</sup> failed to report the percent of patients who had a remarkable level of improvement of AR symptoms.

An inconsistency demonstrated in the Rajan et al study<sup>22</sup> is that the three cohort groups were not prognostically balanced after randomization. The majority of the placebo group consisted of females (11 of 13), where females in the local honey group and the national honey group were more evenly balanced (6 of 11 and 7 of 12, respectively). Additionally, the only information concerning the patient characteristics upon entry to the study shared by the authors was the age ranges and the gender.

In consideration of these limitations the quality of the study by Asha'ari et al<sup>24</sup> has been downgraded to moderate and the quality of the study by Rajan et al<sup>22</sup> has been downgraded to very low. Further research is needed to validate the results presented by these studies.<sup>22,24</sup> Recommendations for future studies would include conducting several large-population, double-blinded randomized control trials in different regions of the world. It would be beneficial if the studies were to compare local honey to the region and commercial honey with a control group. Allergen scratch testing to confirm presence of seasonal versus perennial allergies performed as a requirement for study participation would increase the range of treatment effect; patients with both seasonal and perennial allergies should be included and evaluated for any benefit. As stated previously, any objective way to validate patient-reported symptoms would add more predictive value to the study.

## **CONCLUSION**

The results of the two studies<sup>22,24</sup> evaluated in this systematic review were contradictory. The overall quality of evidence is low. A weak recommendation can be made in support of using local, unpasteurized honey as an adjunct in treating symptoms of allergic rhinitis. There was no evidence of effect using national, pasteurized honey

when compared to placebo as assessed by the Rajan et al study.<sup>22</sup> Further research in the form of large population RCTs is needed to validate the results presented by these studies.<sup>22,24</sup> Additional studies formatted to provide further insight into the mechanisms by which ingested honey affects the human body would be beneficial as well.

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## Table I. Characteristics of Reviewed Studies

Quality Assessment							
		Downgrade Criteria					Quality
Number of Participants	Design	Limitations	Indirectness	Imprecision	Inconsistency	Publication bias likely	
<b>Ingestion of honey improves the symptoms of allergic rhinitis: evidence from a randomized placebo-controlled trial in the East Coast of Peninsular Malaysia (Asha'ari et al 2013)</b>							
40	Double blinded RCT	No serious limitations	No serious indirectness	Serious imprecision <sup>a</sup>	No serious inconsistencies	No bias likely	Moderate
<b>Effect of ingestion of honey on symptoms of rhinoconjunctivitis (Rajan et al 2002)</b>							
36	Double blinded RCT	Serious limitations <sup>b</sup>	No serious indirectness	Serious imprecision <sup>c,d</sup>	Serious inconsistencies <sup>d</sup>	No bias likely	Very low

<sup>a</sup> Small sample size

<sup>b</sup> Researchers failed to account for patients who demonstrated symptom improvement who did not completely reach symptom-free status

<sup>c</sup> Outcomes of interest are underpowered as a result of small final study population size. Authors stated they needed at least 9 participants per group (27 minimum) to have adequate determination of treatment effect, 13 patients dropped out of the study and scratch test results were unblinded after conclusion of study. Only 14 of the remaining participants demonstrated reactivity to seasonal allergen scratch testing.

<sup>d</sup> Study groups and control group were not prognostically balanced

Note: the local honey used in both studies is not standardized and therefore results from each study are only applicable to the batches of honey used during that trial

**Table II. Symptoms tracked by Asha'ari et al study<sup>24</sup>**

Symptoms
Hyposmia
Rhinorrhea
Nasal itchiness
Eye itchiness
Palatal itchiness
Nasal blockage
Sneezing

**Table III. Results of Asha'ari et al study<sup>24</sup>**

	Local honey	Placebo		Local Honey		Placebo	
Week	Mean total symptoms score	Mean total symptoms score	P value	Mean (SD) total symptoms score difference between weeks with <i>P</i> value		Mean (SD) total symptoms score difference between weeks with <i>P</i> value	
Week 0	17.2 (3.64)	16.3 (4.45)	0.464				
Week 4	14.2 (4.85)	14.2 (4.87)	1.000				
Week 8	11.9 (5.66)	13.1 (4.28)	0.428				
Week 0-4				3.05 (4.76)	<i>P</i> =0.010	2.10 (4.15)	<i>P</i> =0.036
Week 4-8				2.30 (3.28)	<i>P</i> =0.005	1.03 (3.54)	<i>P</i> =0.209
Week 0-8				5.35 (4.98)	<i>P</i> =0.000	3.13 (4.10)	<i>P</i> =0.003

**Table IV. Symptoms tracked by Rajan et al<sup>1</sup> study<sup>22</sup>**

Ocular Symptoms	Nasal symptoms
Itchy eyes	Itchy nose
Watery eyes	Runny nose
Headache	Sneezing
Swollen eyes	Stuffy/blocked nose
Sore eyes	Post-nasal drip

**Table V. Results of Rajan et al study<sup>22</sup>**

Group	Benefitted by treatment regimen*	Not benefitted by treatment regimen*
Placebo	2	1
Local honey	2	4
National honey	3	2

\*Participants who had positive scratch test results to seasonal allergens