

ORIGINAL ARTICLE

The Therapeutic Effect of Honey on Respiratory Infections: A Systematic Review

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Abstract

Background: In the context of complementary medicine, honey is a product used alongside conventional medical treatments or therapies to enhance their effectiveness or provide additional benefits. Honey has been used for centuries in traditional and complementary medicine for its various health-promoting properties.

Objectives: The aim of this systematic review was to analyze studies on the therapeutic use of honey in acute respiratory infections (ARI) and exacerbations of chronic diseases (ECD), and to compare the effect of honey with other traditional treatments/remedies.

Methods: literature searches on PubMed, Medline, Scopus, ScopeMed, and Google Scholar were performed to discover the current state of knowledge on the subject and recent publications. Variables were analysed using the full meta-analysis software, version 3 (Biostat, NJ, USA). Variables were analysed to calculate the odds ratio (OR) and standardised mean difference for dichotomous and continuous variables, respectively. Corresponding 95% confidence intervals for effect sizes were also calculated using a fixed-effects model. Mantel-Haenszelen random-effects models were used due to the large number of articles and the presence of significant heterogeneity. Heterogeneity was considered significant with an I^2 value greater than 50% or a P value less than 0.01.

Results: We found that honey seems to improve symptoms in both children and adults. Studies used from the literature search comprised 43% of pediatric studies; 26% were in an ambulatory setting; 9% were in surgical and 22% were medical. The results showed that honey was associated with a significantly greater reduction in the combined cough symptom score, frequency, and severity of acute infections, and an improvement in forced vital capacity, forced expiratory volume, peak expiratory flow, and respiratory symptoms for exacerbations of chronic diseases. Most of the studies reviewed were less than 10 years old; the comparison of the risk of bias between the studies showed that 48% of the studies on ARI had a low risk of bias, while this percentage was higher for the studies on ECD (68%).

Conclusion: Honey probably improves symptoms of respiratory infections, so it is recommended that honey may be a supplement to usual medicines and treatments.

Keywords: cough, honey, respiratory infections, respiratory symptoms, therapeutic effect.

1. INTRODUCTION

Over the last decade, there has been a worldwide increase in the use of traditional and complementary or natural medicine [1]. Alongside this public interest, there has been a renewed interest in these therapies in both the scientific and medical communities. While most research to date has focused on aromatherapy products, several other products show promise. One such resource is honey.

Honey plays a key role in human health, thanks to its high antioxidant and anti-inflammatory properties. Depending on its floral origin, honey has a variable therapeutic potential for all systems of the human body: growth; immune system; respiratory system; and digestive system. It mainly prevents oxidation of low-density lipoproteins in the respiratory system against asthma and infections. The current narrative review aimed to take stock of studies that have addressed the therapeutic potential of honey on acute respiratory infections as an adjuvant. [2][3].

Honey is produced from nectar collected from flowers; it was a source of immortality in ancient Egypt, had a great religious value during antiquity, and remains important in certain birth and death rituals in Africa [4]. It is also found in certain texts of the Bible and the Koran, which present it as a symbol of prosperity and abundance. Egyptian texts date back more than 2000 years and Chinese texts mention its medicinal properties (wound healing; digestive tract and kidney ailments; healing) [5]. Hippocrates and other doctors of the time recommended it for certain pathologies, as a tonic for the sight and sexual organs, in the treatment of coughs, wounds, angina, and this was the case throughout the different eras, whether it be the Middle Ages or the Renaissance. As a

subject of more than 2000 bibliographical references, honey has proven its therapeutic value [6][7].

In addition, antibacterial activity is one of the most widely reported biological properties, with numerous studies demonstrating that honey is active against clinically important pathogens. Therefore, in addition to its widespread use as a common food and flavoring agent, honey is an interesting natural antimicrobial agent [8]. Studies have demonstrated its nutritional value and its therapeutic properties, such as antioxidant; antimicrobial; antiparasitic; anti-inflammatory; antitumor; cardiovascular protective and mainly as a healing product [9][10].

Several scientific studies concern the protective activity of honey in the respiratory system. In developing countries, respiratory infections are one of the most common causes of death. It is a major public health problem: the leading cause of morbidity and mortality; 4-8 RI per child per year; the leading cause of consultation (50%); the leading cause of hospitalization (30%); the leading cause of drug use, especially antibiotics; and the risk of sequelae. Each year, nearly 4 million people die from respiratory infections, 98% of these deaths being due to lower respiratory tract infections. Mortality rates are particularly high among infants, children, and the elderly, especially in low- and middle-income countries [11].

It is indeed true that honey is considered as one of the therapeutic alternatives for managing symptoms of respiratory infections. The World Health Organization (WHO) recognizes honey as a potential treatment option, particularly for cough relief. However, it is important to note that while the WHO recommends honey for

cough relief, there was no systematic review available that specifically compared its use in different types of acute and exacerbations of chronic diseases. To this end, this systematic review was carried out to evaluate the use of honey for these two types of respiratory infections.

2. REVIEW METHODOLOGY

2.1 Research sources

A literature search was conducted on PubMed, Medline, Scopus, ScopeMed, and Google Scholar were performed to discover the current state of knowledge on the subject, and recent publications to identify the therapeutic use of honey on respiratory infections. Most of the studies reviewed were less than 10 years old; older studies and non-original articles were excluded (Figure 1).

The following search terms were used: [honey AND (acute respiratory infections) OR (Exacerbations of chronic diseases) OR (asthma) OR (upper respiratory infections) OR (lower respiratory infections) OR (therapeutic effect)] without language restriction. For further review according to the inclusion and exclusion criteria, four reviewers independently screened titles and abstracts to select potential full-text articles. The search commenced on 18 September 2022.

2.2 Study selection

We included 23 studies: 13 were randomized controlled trials; 4 were non-randomized studies, and 6 were observational clinical studies. The characteristics of these studies are summarised in Tables 2 and 3. The setting of these studies: 43% of the studies were pediatric studies; 26% were in an outpatient setting; 9% were surgical; and 22% were in medical. The comparator, standard care: 4 studies, Dextromethorphan (DM): 4 studies, placebo: 3 studies, Annas

Comosus: 1 study; Silan extract: 1 study; Ipratropium: 1 study; Carbocysteine: 1 study; coffee: 1 study; Honey alone: 3 studies and honey with other ingredients (*Nigella sativa*, *Vrisha Ghrita*): 5 studies. Whilst being aware that some studies used multiple means of comparison, for example, cots et al, (2019) used DM and ipratropium, and Shadkam (2010) used DM and diphenhydramine. These means of comparison are summarised in Table 1.

The most common measure was presenting symptoms of cough. 5 studies measured cough and sleep quality using a validated score; 3 studies measured cough symptoms only; 1 study used the Canadian Acute Respiratory and Influenza Scale (CARIS); and 2 studies worked with the validated respiratory symptoms score; 1 study used a questionnaire. For exacerbations of chronic diseases, the most commonly used measures were forced vital capacity, forced expiratory volume, and peak expiratory flow (7 studies). In addition to these measures, studies also included outcomes for (a) cough duration, (b) hoarseness, (c) sleep quality, (d) sore throat, (e) nasal obstruction, (f) quality of life, (g) endoscopic change score and (h) lung function.

Inclusion criteria: any article reporting the effect of honey on acute and exacerbations of chronic diseases, treatment of a patient of any age or sex, both inpatient and outpatient, with clinical or biological diagnoses.

Acute respiratory infections are defined as sudden, short-term infections of the respiratory system, impacting the airways including the nose, throat, bronchi, and lungs. On the other hand, exacerbations of chronic diseases refer to recurring or prolonged illnesses that affect the respiratory system. These conditions are characterized by persistent inflammation and enduring

respiratory symptoms. Common examples included asthma, chronic obstructive pulmonary disease (COPD), and cystic fibrosis.

Exclusion criteria: Case reports; animal studies; respiratory infections following an intervention; in vitro studies; unreliable data; non-original articles (reviews and analyses); research reports; articles without full text; repetition of information; containing irrelevant information; old references.

2.3 The statistic method

Variables were analysed using full meta-

analysis software, version 3 (Biostat, NJ, USA). Variables were analysed to calculate the odds ratio (OR) and standardised mean difference for dichotomous and continuous variables, respectively. Corresponding 95% confidence intervals for effect sizes were also calculated using a fixed-effects model. Mantel-Haenszelen random-effects models were used due to the large number of articles and the presence of significant heterogeneity. Heterogeneity was considered significant with an I^2 value greater than 50% or a P value less than 0.01.

Table 1: Comparison tools and products used

Comparison product	Authors
Usual care	Rajai N and al. (2022)/Nanda and al. (2017) Kaveh, S., (2022)/Muhamad, R., (2018) Zare, Z., (2016)
Dextromethorphan	Paul and al., (2007)/Shadkam (2010) J. M. Cots <i>et al.</i> , (2018)/ P. Ayazi and al. (2017)
Diphenhydramine	Shadkam (2010)
Honey/placebo	Y. Seçilmiş et S. Silici (2020)/Sulaiman and al. (2011)
Pineapple comosus extract	DM, Peixoto and al. (2016)
Silan extract	Cohen and al. (2012)
Ipratropium	Cots and al. (2019)
Carbocysteine	Cohen (2017)
Honey/prednisolone,coffe/ "honey + coffee"	Raieessi, MA. (2014)
Honey alone	Yasinyildiz, (2021)/Al moamary, M. S., (2008)lee, V. S., (2021).
Honey with other ingredients (NS, Vrisha Ghrita, celery seeds)	Ameen, N. M. A., (2011)/Reena, K., (2013) Abdelrahma, N. J. E., (2014)/ Abdelrahman, J. E., (2016)

2.4 Risk of bias

The table below summarizes the risk of bias assessments for the included studies. The comparison of the risk of bias between the studies showed that 48% of the studies on ARI had a low risk of bias, while this percentage was higher for the studies on CRI (68%); the high risk of bias represents 44.5%

for the studies on ARI; while for CRI, it was less important (28.5%). Regarding the unclear risk of bias, it was 7.5% and 9.5% for ARI and CRI respectively. Due to the limited number of studies, we were not able to use funnel plots to assess publication bias (Table 2).

Table 2: Risk of bias comparison between ARI and ECD studies

Types of studies	Acute respiratory infections (/12)			Exacerbations of chronic diseases (/11)		
	low risk of bias	high risk of bias	unclear risk of bias	low risk of bias	high risk of bias	unclear risk of bias
Random sequence generation (selection bias)	4	6	2	8	2	1
Allocation concealment (selection bias)	6	6	0	8	2	1
Blinding of participants and researchers (performance bias)	6	5	1	6	5	
Blinding of outcome assessment (detection bias)	5	6	1	10	1	
Incomplete outcome data (attrition bias)	2	8	2	2	6	3
Selective reporting (reporting bias)	6	6		6	4	1
Other bias	12			8	2	1
Total in %	48%	44.5%	7.5%	62%	28.5%	9.5%

3. RESULTS

3.1 acute respiratory infections

3.1.1 The effect of honey on children

The effect of combined honey

Acute respiratory infections (ARI) are infections of the respiratory system that can lead to breathing difficulties. These infections can affect both the upper and lower respiratory systems. While viruses are the most common cause of ARIs, bacteria can also be the cause of these respiratory illnesses [15]. Several studies have been conducted to explore the impact of honey on acute respiratory infections. A Turkish study that evaluated the efficacy of a mixture of bee products in acute respiratory infections in children was a prospective double randomized study; the authors divided the patients into 4 groups consisting of two viral groups treated with bee products or placebo. Of the two bacterial groups receiving

antibiotics or bee products plus antibiotics, the severity and duration of disease improvement were assessed using the Canadian acute respiratory illness and flu scale score.

This study showed significant results: patients with viral infection (n=54) receiving a combination of products showed improvement earlier, compared to the placebo group. The scores were significantly lower in the antibiotic (n=50) + combination group on day 2 and day 4, compared to the antibiotic alone group ($P < 0.05$).

The researchers concluded that bee products are effective in the symptomatic treatment of upper respiratory tract infections. They can be considered a good treatment option because drugs already used for symptomatic treatment are not cost-effective and may also have serious side effects in children [16].

In addition, another empirical, parallel-group study was conducted in a pediatric ward at Clinica Amaury Coutinho in Brazil. It aimed to evaluate the rate of immediate improvement of the irritative cough episode in patients treated with the combination of pineapple comosus extract in bee honey and compared it with the use of honey alone (placebo group). The study involved 26 children, aged between 2 and 15 years, with presenting symptoms of an irritating cough. The rate of immediate improvement of the irritant cough episode was similar in patients treated with the combination of pineapple comosus extract in bee honey and with the use of isolated honey (placebo group).

The researcher considered that the mucolytic for honey properties were responsible for the reduction in the cough score. This clinical trial suggests that, given the patent improvement in both groups, there was probably an effect of honey on mucus and cough characteristics, which may be difficult to identify the difference when honey is associated with pharmacological action. The hypothesis suggested in this study, was that the sweetness of honey itself promotes the production of salivation and secretions in the airways to the liquefaction of mucus, reducing cough due to irritation of the larynx and pharynx and, above all, without side effects [17].

In another study, Cohen (2017) compared the effects of honey and polysaccharide resin cough syrup and carbocysteine syrups on nocturnal and daytime cough associated with acute respiratory infection. The study enrolled 150 children aged 2 to 5 years from four pediatric wards. There was a better result for polysaccharide-resin-honey ($P < 0.05$) concerning all cough parameters (4 days).

Also, there was an improvement in all measured clinical cough symptoms from the first night of therapy, as well as the quality of sleep of children and parents.

In 2022, recent research in the form of a clinical trial to study the effect of gargling with honey and lemon water on cough, sore throat, and hoarseness after endotracheal tube extubation following surgery. It involved 110 patients undergoing surgery at Neyshabur Hospital.

The researchers found that there was no significant difference between the two groups in terms of sore throat and cough after 12 hours of extubation, but the hoarseness score was lower in the experimental group ($P = 0.05$). At 24 hours after extubation, cough ($P = 0.001$), hoarseness ($P = 0.006$), and sore throat ($P = 0.023$) were significantly lower in the experimental group. The study recommended the use of honey and lemon water gargle after extubation given its positive effects in reducing endotracheal tube complications and the absence of side effects [18].

Finally, a study comparing honey/prednisolone and coffee/honey with coffee in the treatment of persistent post-infectious cough (PPIC) involved 245 adult participants with PPIC over the period 2005 to 2013. Participants were asked to dissolve 25 grams of the prescribed product in 200 ml of warm water and drink it every eight hours for one week to measure the severity of their cough. Comparing the effectiveness of the 5 regimens, this study found that honey with coffee was the most effective treatment modality for PPIC. Honey and coffee can successfully treat PPIC over a short period [19]. See Table 3.

Table 3: Characteristics of treated studies for ARI

Authors	Study setting	Type of study	Population	Nature of Infection	Adults/children	Intervention product	Comparison	P-value
Seçilmiş and Silici, (2020)	Children's Hospital	Prospective randomised study	200	URIS	children	Propolis, royal jelly and honey	Placebo	0.152
DM, Peixoto and al. (2016)	A paediatric service Clinica	Randomised clinical trial	29	URIS	children	Honey and Pineapple comosus	Placebo	0.91
Paul (2007)	The paediatric outpatient setting	Prospective clinical study	130	URIS	children	Buckwheat/honey or Dextromethorphan/honey	No treatment	**
Shadkam (2010)	The paediatric hospital service	Randomised clinical trial	139	URIS	children	Honey, Dextromethorphan, the third Diphenhydramine	Other Medicines	**
Cohen (2012)	Community paediatrics Prospective	randomised study	300	URIS	children	Honey, silan extract	Placebo	**
J. M. Cots et al. (2019)	The ambulatory setting	Randomised clinical trial	668	Acute bronchitis	Adults	Dextromethorphan, ipratropium or Honey	Usual Care/ Other Medicines	
P. Ayazi, (2017)	The paediatric hospital service	Randomised clinical trial	87	URIS	children	Honey, Diphenhydramine	Other Medicines	*
Cohen (2017)	The paediatric hospital service	Randomised clinical trial	150	URIS	children	Polysaccharide-resin-honey preparation	Other Medicines	*
Sulaiman SA. et al, (2011)	The pilgrimage to Mecca	Non-randomised control trial	56	Rhinitis, sore throat	Adults	Honey	Honey alone	**
Nanda et al. (2017)	The medical college and the hospital	Randomised control trial	200	Sore throat	Adults	Honey	Usual Care	*
Rajai N. et al. (2022)	The surgery department	A clinical observational study	110	Hoarseness, and sore throat	Adults	Honey and lemon water	Usual Care	*
Raieessi MA. (2014)	The ambulatory setting	Randomised clinical trial	245	URIS	Adults	Honey, prednisolone, coffee, and "honey plus coffee"	Other Medicines	*

P-value: * $p < 0,05$; ** $p < 0,00$, URIS: upper respiratory infections

Four studies examined the treatment of presenting symptoms of cough with honey and other natural products, namely: a) a mixture of bee products, b) pineapple comosus extract, c) lemon water, and d) coffee. In addition, two studies used a combination of chemical products. The use of natural products gave better results in relieving the symptoms of acute respiratory infections.

The effect of honey used alone

Studies have also evaluated the use of honey alone. Paul and al (2007) conducted a study comparing the effects of one nightly dose of buckwheat honey or dextromethorphan (DM) on cough and sleep disturbances associated with upper respiratory tract infections in children. This study was conducted in a pediatric outpatient

setting and involved 105 children aged 2-15 years with nocturnal upper respiratory tract infections with illness duration of 7 days or less.

The authors found significant differences in symptom improvement between the prominent honey groups. In pairwise comparisons, honey was significantly better than no treatment for cough frequency and combined score, but DM was not better than any treatment for any outcome. A comparison of honey with DM revealed no significant difference.

According to the comparison made in the study, parents rated honey most favorably for providing symptomatic relief of their child's nocturnal cough and sleep difficulty caused by an upper respiratory tract infection. This suggests that honey may be a preferable treatment option for managing cough and sleep difficulties associated with childhood upper respiratory tract infections [12].

In addition, a German survey of parents compared the effects of a single nightly dose of three honey products (eucalyptus, citrus, or Labiatae) to a placebo (silan extract); the study population was 300 children aged 1-5 years with an acute respiratory infection; the study setting was community pediatrics. Eligible children received one dose of 10g of honey or a placebo administered 30 minutes before bedtime.

The results of the study showed a significant improvement in all groups (honey and placebo) compared with the night before treatment, but this improvement was greater in the honey groups compared with placebo for all the main endpoints. Generally, the parents noted that honey was more effective than silan extract in relieving cough symptoms and sleep difficulties. Honey may be a preferable treatment for symptoms associated with childhood acute upper

respiratory infections [13].

Moreover, an Iranian study aimed to compare the effect of honey, DM, and DPH on night cough and sleep quality of children and their parents. This was a clinical study involving 139 children aged 24-60 months with presenting symptoms of cough due to URI, divided into 4 groups. The first group received honey (HG), the second DM, and the third DPH; but the fourth group (control) received supportive treatment.

As a result, honey type 1 was superior to DPH in improving all aspects of cough except frequency, and honey type 2 was more effective than DPH in improving all aspects of cough except the child's sleep quality. There was no significant difference between honey type 1 and 2 in all aspects of cough relief. The results suggest that honey can provide relief to children's cough and improvement of sleep quality of children and their parents [20].

After this intervention of about 24 hours, the mean score for all variables in the honey group (night cough, sleep) was significantly higher than in the other groups. The results of the study showed that receiving a 2.5ml dose of honey before sleep had a more attenuating effect on URI-induced cough than did doses of DM and DPH [21].

3.1.1 The effect of honey on adults

The effect of combined honey

There have been limited studies conducted on the effect of honey specifically on acute respiratory infections in adults. The researchers attempted to compare the effectiveness of 3 symptomatic therapies (DM, ipratropium, or honey) combined with usual care in adults with acute bronchitis. This was a randomized open-label trial with a control group. Patients aged 18 years or older with acute uncomplicated bronchitis,

with a cough of fewer than three weeks duration as the main symptom. Patients were recommended to add honey to a cup of lemon or thyme juice, herbal tea with milk, yogurt, or herbal teas; the main outcome was a decrease in the number of days with cough for the honey group [14].

The effect of honey used alone

In addition, a Malaysian study in the form of a case-control trial was conducted among Hajj pilgrims in 2007. The intervention group was given two kilograms of honey, and the results were compared with those of the control group who did not received honey. No significant difference was observed in the symptoms of cough and fever. The difference in mean symptom score was greatest in the third week of the trip but was not statistically significant between the two groups. In conclusion, Madu Lebah Tualang - Agromas honey has been shown to reduce the respiratory symptom score of Malaysian Hajj pilgrims. It was very effective in reducing sore throat and rhinitis in the middle of the journey [22].

In another study on infection control and inflammation, several patients (n=200) suffering from sore throats were enrolled. Half (n=100) received a tablespoon of honey twice daily with anti-inflammatory drugs, antibiotics, and antiseptic gargle. The other patients (n=100) in the control group received other medications without honey. Patients were evaluated after 5, 10, and 15 days for throat congestion, fever, and pain. The results showed that relief of signs and symptoms of sore throat was faster in the study group than in the control group. In conclusion, honey is effective for faster recovery from signs and symptoms of sore throat having antibacterial and anti-inflammatory properties without causing any side effects [23].

3.2 Exacerbations of chronic diseases

3.2.1 The effect of honey adults

The effect of combined honey

In addition to acute respiratory infections, honey is also used for treatment of exacerbations of chronic diseases. These are recurrent or prolonged diseases affecting the respiratory system. These diseases are characterised by persistent inflammation and permanent respiratory symptoms. Asthma, chronic obstructive pulmonary disease (COPD) and cystic fibrosis are common examples [15].

Honey has a potential treatment for bronchial asthma, used alone or in combination with other ingredients. One study showed that the combination of honey and *Nigella sativa* (NS) showed significant improvement in lung function, including forced vital capacity (FVC) (MD = 0.55, $P = 0.002$); forced expiratory volume (FEV) (MD = 0.52, $P < 0.001$); and peak expiratory flow (PEF) (MD = 80.60, $P < 0.001$).

Due to the high incidence of asthma, some patients choose complementary therapies. Therefore, a randomized trial evaluated the effect of compound honey in improving clinical symptoms of asthma in adults (n=80). As a result, factors such as night and morning symptoms, breathlessness, activity limitation, and wheezing were reduced. There was also a significant decrease in the use of short-acting beta-agonists (SABA) in both groups, but more markedly in the intervention group. In addition, the difference in the asthma control test items and total scores was significant between the groups ($P < 0.05$). The results of this study demonstrate that compound honey can be a safe and effective adjuvant for the treatment of asthma in adults [24].

Furthermore, in a clinical study on the evaluation of the effect of honey and *Nigella*

sativa (NS) seeds in the treatment of asthma, a dose of 2 g of whole *N. sativa* seeds and 1 teaspoon of bee honey per day were taken by the subjects (27 patients) for three months. The researchers evaluated the effects of both products on lung function. There was a significant increase in FVC ($P = 0.023$) in the asthma group and PEF ($P = 0.049$) in the non-asthma group. This study showed that both *N. sativa* and BH appear to have some benefit for asthmatics without hepato-renal toxicity. [25]

In a Sudanese study, the adjuvant effect of combined honey (M) and normal saline (NS) was investigated. The study aimed to evaluate the effect of this combination along with inhaled corticosteroids (ICS) on respiratory rate (RR), blood pressure (BP), pulse rate (PR), oxygen saturation (SO₂), and wheeze symptoms in moderate and severe persistent asthmatics. A total of 30 asthma patients were included. At the end of the study (3 months), vital signs (RF, PS, diastolic BP, and systolic BP) were significantly decreased ($P < 0.05$); wheezing was significantly reduced in both asthma categories and SO₂ was increased. In conclusion, this combination of M as an adjuvant therapy to ICS has been shown to help control asthma symptoms and improve cardiopulmonary function [26].

Another study found that despite the use of ICS, a proportion of asthma patients still suffer from uncontrolled symptoms and may progress to irreducible airflow limitation. Researchers examined the therapeutic potential of M and NS on respiratory muscle power, lung function, and asthma in 30 patients. Indicators of respiratory muscle power (MEP, MIP) and the baseline asthma control test (ACT) score were measured initially as baseline data and monthly for 3 months. The finding was that there was a

statistically significant improvement in respiratory muscle power; lung function; and asthma control test score, in addition to a remarkable decrease in the need for β_2 agonists in both asthma groups [27].

The reduction of COPD symptoms may be another reason for the significant improvement in quality of life. COPD patients are at higher risk of recurrent acute and chronic airway infections, which are most clearly associated with increased COPD exacerbations and hospitalizations [28].

In Iran, a clinical study was conducted to investigate the effect of honey on cough relief in elderly COPD patients ($n=38$); the population consisted of 2 groups; the first group received M and routine treatment, and the other group received routine treatment. The severity of the cough was studied for 24 hours. As a result, cough severity decreased by 63.2% in 89.5% of cases in the M group, compared to the group receiving routine treatment only ($P < 0.03$) [29].

The effect of use of honey alone

In Saudi Arabia, a cross-sectional study of 200 asthma patients found that honey was the second most commonly used non-conventional therapy in 49 (24.5%) of patients. Honey used in controlled patients was 60.71% (CI = 41.99-76.74, $P = 0.261$), while 74.36% of asthmatic patients (CI = 58.56-85.61, $P = 0.004$) used honey. Their results showed no significant effect of honey use on disease control [30].

In addition to asthma, other studies have evaluated the efficacy of honey on COPD. Indeed, a study in Malaysia measured the effect of a 6-month regimen of "Tualang" honey supplementation in improving the quality of life of COPD patients. It was a

randomized controlled trial conducted on 34 patients (the honey group and the reference group) [28].

The study indicated that there were no significant differences between the two groups in terms of quality of life. The study also showed that lung cancer patients had a better quality of life at 6 months (22.91; 95% CI: 14.94, 30.87 VS 41.95; 95% CI: 31.17, 52.73). The researchers found that honey helped patients to engage better in their activities of daily living, with positive psychological and social impacts. In general, one tablespoon of honey provides 64 calories of energy to the muscles and body [28].

Another chronic disease that has been treated is cystic fibrosis. In a study to determine the feasibility of investigating Manuka honey as an irrigation treatment for cystic fibrosis sinusitis, 13 patients were recruited. The quality of life change score was clinically significant for honey (-9 [-14,-6]). Although the difference was not statistically significant ($P = 0.29$) for the endoscopic change score, it was significantly better for honey (-3 [-5,-3]) than for saline (0 [0.0]) ($P = 0.006$) [31] (Table 4).

3.1.1 The effect of honey on children

The effect of use of honey alone

A total of 26 children attending an outpatient department participated in the study. The evaluation showed that the effect was significant in the control of clinical manifestations ($P < 0.01$), reduction of episodes, school absenteeism, and several

unscheduled medical visits ($P < 0.01$). All these points indicate that this experimental combination is very effective in controlling recurrent asthma attacks and respiratory infections. However, the results of the lung function tests were not statistically significant. The study reduced the use of conventional antibiotic therapy and bronchodilators in children [32].

The effect of the use of combined honey

A study focused on the use of complementary medicine methods in children diagnosed with asthma. The study revealed that honey was one of the most preferred biological therapies for families, accounting for 36.6% of the choices. Molasses, derived from herbal and natural products, was the second most preferred therapy at 16.9%. However, this study did not yield significant results regarding the effectiveness of honey in treating asthma [33].

As a conclusion, two categories of studies treated the following parameters: a) SC: clinical score (fever, sleep), b) SR: respiratory score (cough, hoarseness, sore throat), c) Asthma score: forced vital capacity, forced expiratory volume, peak expiratory flow, indicators of respiratory muscle power, d) Quality of life. Honey is used either alone or in combination and association with other products (NS, bee products, DM, Ipratropium, DPH, polysaccharide, Resin, coffee, Vrisha Ghrita, celery seeds). See Table 4.

Table 4: Characteristics of studies treated for exacerbations of chronic diseases

Authors	Affection	Population	Type of study	P-value	Adults/children	Comparison	Results
Yasinyildiz, (2021)	Asthma	164	Observational study	*	children	Other Medicines	-
Alzhraa SA., (2019)	Asthma	Not specified	Observational study	**	Adults	placebo	+ FVC / FEV / PEF
Kaveh, S., (2022)	Asthma	80	Randomised, double-blind	*	Adults	placebo	- respiratory symptoms
Ameen, N. M. A., (2011)	Asthma	27	Prospective interventional trial	*	Adults/children	Usual Care	+ FVC / PEF
Al moamary, M. S., (2008)	Asthma	200	Cross-sectional study	*	Adults	placebo	-
Reena, K., 2013	Asthma	26	Randomised, double-blind	*	children	Other Medicines	-
Abdelrahma, N. J. E., (2014)	Asthma	30	Randomised, double-blind	*	Adults	Usual Care	++ Respiratory + cardiopulmonary symptoms
Muhamad, R., (2018).	COPD	34	Single-blind Randomised	*	Adults	Usual Care	-
Zare, Z., (2016)	COPD	38	Observational study	*	Adults	Usual Care	+ Cough
Abdelrahman, J. E., (2016).	Asthma	30	Randomized, double-blind	**	Adults	Other Medicines	+ Lung function / need for β_2 agonists / MIP/ control
lee, V. S., (2021).	Cystic Fibrosis	13	Randomised, double-blind	P = 1.0 0	Adults	Usual Care	+ Quality of life score/endoscopic change score.

FVC: forced vital capacity, FEV: forced expiratory volume, PEF: peak expiratory flow, MIP: FVC: forced vital capacity, FEV: forced expiratory volume, PEF: peak expiratory flow, MIP: respiratory muscle power indicators, P-value: * $p < 0.05$; ** $p < 0.001$, - : no effect; +: positive effect; ++: effect on control, FVC: forced vital.

4. DISCUSSION

Respiratory tract infections are an important health problem because of their high incidence and economic cost. The World Health Organization considers honey as an adjuvant treatment for coughs [34].

For the ARI studies (12/23), the methods of comparison and measures were different and limited. Ten studies reported an improvement in cough symptoms between the different reference groups and the honey group (P between < 0.001 and < 0.05). Four studies showed a significant effect on sleep quality, reducing the duration of night cough

and making it less severe. Two studies compared the effect of honey on sore throats with conventional care and found that honey was also effective in treating and preventing drug resistance. Honey improved respiratory scores; the average duration of infection was also reduced within two days.

The analysis included data from 12 trials involving 2,314 patients. These studies included virtually all conventional treatments, such as antibiotics and honey, as well as drugs for acute respiratory infections. The researchers found that honey was among the best of these treatments.

Honey improved respiratory scores, with significant improvements in cough frequency and severity compared to conventional treatments. In addition to being more effective in treating cough (44% better at reducing cough severity and 36% better at reducing cough frequency); the average duration of infection was also reduced within 2 days.

According to the researchers, honey can be used as a treatment for acute upper respiratory infections because it contains hydrogen peroxide, an effective bactericidal disinfectant which also allows it to be used as a topical treatment for other wounds, and because it has the right consistency to cover the mouth and throat and soothe irritation. The authors of these studies, therefore, suggest that clinicians might consider using honey as an adjunct to antibiotics when prescribing treatments for acute respiratory tract infections [16][35][36].

All authors stated that honey had no side effects on patients, but they did not include children under one year of age because of the potential risk of infant botulism. Only one study indicated a beneficial effect of a honey-based syrup on cough (the polysaccharide-resin-honey preparation). Three studies comparing honey to placebo indicated a benefit of honey, but those studies did not have a strong evidence base of comparisons between honey and matched placebo. Compared to usual care, honey was associated with a significantly greater reduction in respiratory scores [17].

The included meta-analysis studies (Table 5) aimed to evaluate the therapeutic effect of honey on acute respiratory infections, specifically comparing honey to various comparators and measuring different outcomes. Studies compared honey to a placebo and found a significant reduction in symptoms, as indicated by the combined

symptom score. However, there was a high level of heterogeneity ($I^2=91\%$), suggesting variations in study design or participant characteristics that may have influenced the results. [14][21][22].

Comparison between honey and dextromethorphan/diphenhydramine, silane extract/pineapple comosus extract, and ipratropium/prednisolone showed favorable effects of honey in terms of cough severity, combined symptom score and cough frequency. These results indicate that honey may be an effective alternative to these comparators in the management of acute respiratory infections. However, it should be noted that the comparator studies had lower levels of heterogeneity ($I^2=26\%$) than the honey-only studies [11][19].

Compared with usual care, honey demonstrated a beneficial effect by reducing the frequency and severity of cough, improving respiratory symptoms, and contributing to a better-combined symptom score. The lack of heterogeneity in these studies ($I^2=0\%$) suggests more consistent results across different patient populations and study designs [17][18].

Concerning the studies treating exacerbations of chronic diseases, 11 studies were included with 710 patients, aiming to evaluate the effect of the use of honey as an adjuvant treatment in patients with conditions such as asthma, COPD, and cystic fibrosis. Alone or in combination with other ingredients, the most commonly used combination is NS. Most studies that have used this combination have shown a clear improvement in lung function (FVC/VEF/DEP) and breathing (cough), muscle power tests (MEP, MIP), clinical control signs (wheezing), and quality of life scores.

The use of these associations (Honey/NS) can be explained by the anti-inflammatory, immunomodulatory, and anti-allergic

properties of honey and NS [12]. Nevertheless, for severe cases, there seems to be a need for synergistic therapeutic reinforcement of antitussives, bronchodilators, and other medicinal properties [37].

Patients with less severe asthma showed significantly positive responses in clinical parameters when using honey. The use of celery seed and honey was associated with improvements in respiratory parameters, lung function. Compared to baseline, a finding reinforced by several studies, honey alone has no strong evidence of efficacy in asthma control. However, when used in combination with other substances, it has shown relatively high efficacy in asthmatic patients. This finding could help control asthma with less expensive alternatives and better outcomes [38].

In pediatric studies, the use of honey did not give significant results for the effect on asthma [33]. However, for adults, the use of short-acting beta-agonists (SABA) was significantly reduced in the honey group [24].

Concerning the other chronic respiratory pathologies, we find few studies having treated the effect of honey (3/23). These studies showed that honey, associated with a routine treatment, relieves cough in patients suffering from COPD, and it has also demonstrated a clinically important difference in the score of quality of life and a significantly better endoscopic result for cystic fibrosis [28][30].

As for the positive effects of honey in the modality of combination with other products (NS, Vrisha Ghrita, celery seeds), the comparison did not show a statistically significant difference between IRA (33%) and IRC (26%), and the same observation for the use of honey alone: IRA (33%), IRC (29.9%). However, the Clinical/Quality of Life Score (RS) was more important for ARI 43%. This can be explained by the duration of the disease and the effect of other products used.

Studies on exacerbations of chronic diseases evaluated the effects of honey compared with placebo and standard care. Although the results are mixed, there were indications of potential benefits. Compared with a placebo, honey showed a trend toward improved lung function, respiratory muscle power, and quality of life. However, the level of heterogeneity was relatively high in these studies ($I^2 = 73\%$), indicating the need for further research to obtain more conclusive results [24][25].

Comparing honey to usual care in exacerbations of chronic diseases, the results suggested that honey may be more effective in reducing respiratory symptoms and improving quality of life. However, the effects on measures of lung function (FVC, FEV1, PEF, and PIM) were not uniform. The studies also showed varying levels of heterogeneity ($I^2 = 68\%$), suggesting differences in study characteristics or participant populations that may have influenced the results [25], [26].

Studies comparing honey with other drugs indicate that other drugs are also effective in improving lung function. Overall, studies into the therapeutic effect of honey on respiratory infections have produced promising results. Honey appeared to be a favorable therapeutic option compared with a placebo and certain comparators, particularly in terms of reducing cough severity, improving symptom scores, and relieving respiratory symptoms. However, the considerable heterogeneity observed in certain studies indicates the need for further research with standardized protocols and larger sample sizes to establish more solid conclusions [27][31][32].

It is important to take into account the limitations of the included studies, such as variations in honey types, dosages, and administration methods, as well as potential publication bias. In addition, individual patient

factors and underlying respiratory conditions may have influenced the response to honey treatment. In conclusion, the results of these

meta-analysis studies suggest that honey may have therapeutic benefits in the management of respiratory infections [29-31].

Table 5: Summary of results from meta-analyses studies evaluating the therapeutic effect of honey on respiratory infections

Type of infection	Comparator	Measuring results	Studies (n)	Estimated group effect (all studies)	Studies (n)	Estimates from studies of honey alone
Acute respiratory infections	Placebo	Combined Symptom score	2 (529)	SMD -0.594, 95%CI -1.41 to 0.16, $I^2 = 91\%$	1 (56)	SMD -0.99, 95%CI -1.23 to -0.68
	Dextromethorphan/ Diphenhydramine	Severity of The cough Combined Symptom score Frequency of Cough	5 (1024)	MD -0.51, 95%CI -1.32 to 0.30, $I^2 = 26\%$ MD -3.81, 95%CI -6.92 to 1.95 MD -0.40, 95%CI -1.02 to 0.23, $I^2 = 23\%$	2 (226)	NA NA SMD -0.20, 95%CI -0.35 to -0.7, $I^2 = 8\%$
	Silan extract/ Pineapple comosus extract	Severity of the cough Combined symptom score Frequency of cough	2 (329)	SMD -0.21, 95%CI -0.43 to -0.17, $I^2 = 0\%$ MD -2.96, 95%CI -3.50 to -1.98, $I^2 = 10\%$ SMD -0.18, 95%CI -0.25 to -0.11, $I^2 = 0\%$	1 (300)	NA MD -4.39, 95%CI -6.38 to -2.39, $I^2 = 0\%$ SMD -0.50, 95%CI -0.68 to -0.31, $I^2 = 0\%$
	Ipratropium/ Prednisolone, coffee	Severity of the cough Combined symptom score Frequency of cough	2 (913)	SMD -0.17, 95%CI -0.38 to -0.14, $I^2 = 0\%$ MD -32.96, 95%CI -2.48 to -1.86, $I^2 = 18\%$ SMD -0.24, 95%CI -0.30 to -0.19, $I^2 = 0\%$	1 (245)	NA SMD -0.9, 95%CI -0.30 to -0.6, $I^2 = 0\%$ SMD -0.63, 95%CI -0.82 to -0.43, $I^2 = 0\%$
	Usual Care	Frequency of cough Severity of the cough Respiratory symptom Combined symptom score	3 (978)	SMD -0.41, 95%CI -0.46 to -0.19, $I^2 = 0\%$ SMD -0.41, 95%CI -0.59, to -0.1 $I^2 = 17\%$ OR 0.98, 95%CI 0.43 to 2.19, $I^2 = 53\%$ MD -3.78, 95%CI -4.82 to -2.48, $I^2 = 0\%$	2 (310)	SMD -0.37, 95%CI -0.55 to -0.18, $I^2 = 0\%$ NA OR 0.70, 95%CI 0.39 to 1.24 MD -4.51, 95%CI -6.53 to -2.56, $I^2 = 0\%$
Exacerbations of chronic diseases	Placebo	FVC	3 (280)	SMD -0.63, 95%CI -1.79 to 0.28, $I^2 = 73\%$	1 (80)	SMD -0.21, 95%CI -1.19 to 0.08, $I^2 = 23\%$
		FEV		MD -3.52, 95%CI -5.81 to 0.84		MD -3.02, 95%CI -5.61 to 0.64
		PEF		MD -0.38, 95%CI -0.99 to 0.21, $I^2 = 16\%$		NA
		MIP		SMD -0.48, 95%CI -1.29 to 0.18, $I^2 = 71\%$		OR 0.57, 95%CI 0.29 to 0.66
		Quality of life		OR 0.65, 95%CI 0.32 to 0.74		OR 0.92, 95%CI 0.37 to 2.13, $I^2 = 50\%$

Type of infection	Comparator	Measuring results	Studies (n)	Estimated group effect (all studies)	Studies (n)	Estimates from studies of honey alone
	Usual care	Respiratory symptoms Quality of life FVC FEV PEF MIP	5 (142)	OR 0.74, 95%CI 0.51 to 0.81 OR 0.56, 95%CI 0.51 to 0.79 SMD -0.73, 95%CI -1.69 to 0.33, I ² =68% MD -2.65, 95%CI -4.32 to 0.79 MD -0.63, 95%CI -0.87 to 0.17, I ² =10% SMD -0.41, 95%CI -2.02 to 0.25, I ² =75%	3 (78)	NA OR 0.43, 95%CI 0.38 to 0.66 NA NA NA OR 0.38, 95%CI 0.33 to 0.50
	Other Medicines	Lung function	3 (220)	OR 0.32, 95%CI 0.29 to 0.49	1 (13)	OR 0.21, 95% CI 0.18 to 0.38

FVC: forced vital capacity, FEV: forced expiratory volume, MIP: respiratory muscle power, MD, Mean difference, NA: not applicable, PEF: peak expiratory flow, SMD, standard mean difference, I²: level of heterogeneity

5. CONCLUSION

The potential therapeutic properties of honey have been attributed to its complex composition, which gives this food antioxidant activity and free radical scavenging activities. Published studies suggest a beneficial action on the respiratory system.

Honey has multiple activities, including anti-inflammatory, antibacterial, metabolic, and antioxidant properties. Antibacterial activity is one of the most widely reported biological properties, with numerous studies demonstrating that honey is active against clinically important pathogens. Therefore, in addition to its widespread use as a common food and flavoring agent, honey is an interesting natural antimicrobial agent.

This systematic review found that honey probably improved symptoms of respiratory infections, with the strongest evidence in the context of cough severity and frequency, and respiratory and lung score in asthmatics. It is therefore advisable to use honey in addition

to the usual medicines and treatments. Honey is more effective and less harmful than the usual alternatives and avoids causing harm through antibiotic resistance; further trials with robust methodology are needed to confirm its therapeutic efficacy, especially in adults.

Abbreviations

ARI: acute respiratory infection

BP: blood pressure

COPD: chronic obstructive pulmonary disease

ECD: Exacerbations of chronic diseases

DM: Dextrometorphan

DPH: Diphenhydramine

FVC: forced vital capacity

FEV: forced expiratory volume

ICS: inhaled corticosteroids

MIP: respiratory muscle power indicators

PEF: peak expiratory flow

NS: nigella sativa

PPIC: persistent post-infectious cough

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التأثير العلاجي للعسل على التهابات الجهاز التنفسي مراجعة منهجية

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الملخص

الخلفية والأهداف: في إطار الطب التكميلي. العسل هو منتج طبيعي يتم استخدامه الى جانب العلاجات الطبية، لتعزيز فعاليتها وتوفير فوائد صحية تكميلية. وقد استعمل لقرون من طرف عدة حضارات. نظرا لخصائصه المختلفة التي تعزز الصحة. والهدف من هذا المقال هو استعراض منهجي وتحليل الدراسات حول الاستعمال العلاجي للعسل في التهابات الجهاز التنفسي وتقارن الأمراض المزمنة، إضافة الى مقارنة تأثير العسل مع العلاجات الأخرى.

منهجية الدراسة: تم اجراء عمليات البحث في عدة محركات علمية من اجل اكتشاف المعارف الجديدة حول الموضوع، (OR) تم تحليل المتغيرات لحساب نسبة الاحتمالات و (Biostat, NJ). تم تحليل البيانات والمتغيرات باستخدام برنامج للمتغيرات الثنائية والمتواصلة، على التوالي. كما تم حساب فترات الثقة المقابلة بنسبة 95%. اعثر عدم التجانس بقيمة أكبر من 50% مهما I^2 أو قيمة $P < 0.01$

النتائج: يبدو ان العسل يحسن الأعراض لدى كل من الأطفال والبالغين، وإعداد هذه الدراسات: أ) 43% من الدراسات هي دراسات للأطفال، ب) 26% في مراكز صحية متقلة، ج) 9% في الجناح الجراحي، و د) 22% في الجناح الطبي. أظهرت النتائج أن العسل كان مرتبطاً بانخفاض أكبر في درجة الاعراض التنفسية المجمعة، وتكرارها، وشدها بالنسبة للالتهابات التنفسية الحادة، وتحسن القدرة الحيوية الاجبارية، والحجم الزفيري القسري، وضيق التنفس، وأعراض الجهاز التنفسي بالنسبة للإمراض المزمنة المتفاقمة. تظهر مقارنة خطر التحيز بين الدراسات أن 48% من الدراسات حول التهاب لجهاز التنفسي الحادة لديها مخاطر منخفضة للتحيز.

الاستنتاج: العسل يحسن أعراض التهابات الجهاز التنفسي، لذلك يوصى بأن يكون العسل مكملاً للأدوية والعلاجات المعتادة.

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