

## Honey in Bronchial Asthma: From Folk Tales to Scientific Facts

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**ABSTRACT** Bronchial asthma is one of the most common chronic inflammatory diseases. Complementary and alternative medicine is increasingly used for treating bronchial asthma. Ten electronic databases were searched to investigate whether honey alone or in combination with other ingredients can be considered as the potential treatment for bronchial asthma. Combinations of honey and *Nigella sativa* (NS) showed significant improvement in all pulmonary functions, including forced expiratory volume (FEV1) (MD=0.52,  $P<.001$ ), forced vital capacity (FVC) (MD=0.55,  $P=.002$ ), and peak expiratory flow rate (PEFR) (MD=80.60,  $P<.001$ ), in both moderate and severe, uncontrolled persistent asthma compared with baseline. Asthma control test scores also improved significantly (MD=11.22,  $P<.001$ ) in patients using combinations of honey and NS compared with baseline. Patients with a less severe grade of asthma showed a significant positive response in clinical parameters upon using honey. One study showed that using celery seeds and honey was associated with clinical improvement of both lung functions, FEV1 (MD=18.09,  $P<.001$ ) and FVC (MD=24.23,  $P<.001$ ), and respiratory parameters compared with baseline. In conclusion, honey alone has no strong evidence of being effective in controlling asthma. However, when used in combination with other substances, it showed a relatively high efficacy in patients with asthma. This finding may help in asthma control with lower cost alternatives and better outcomes.

**KEYWORDS:** • asthma • efficacy • honey

## INTRODUCTION

**B**RONCHIAL ASTHMA IS one of the most common chronic inflammatory diseases affecting around 334 million people worldwide.<sup>1</sup> Prevalence of the disease varies widely between countries, ranging from 1 up to 18%, and is more common in developed countries.<sup>2</sup> It accounts for ~250,000 deaths per year with low- and middle-income countries

having more than 80% of the mortality rate.<sup>2,3</sup> Although asthma is two times more common in males than females, adult women have higher rates than men with severe asthma attacks occurring at an equal rate.<sup>2,4</sup>

Asthmatic patients present with recurrent episodes of wheezing, chest tightness, breathlessness, and coughing, worsening at night and early in the morning.<sup>5</sup> The disease is characterized by chronic inflammation of the airways with associated remodeling.<sup>6</sup> It is also associated with goblet cell hyperplasia and metaplasia, bronchial gland enlargement, increased smooth muscle mass, angiogenesis, and alteration of extracellular matrix components leading to airway mucus hypersecretion and obstruction.<sup>7,8</sup>

The most common treatments to manage asthma are mainly  $\beta$ -agonists and inhaled corticosteroids.<sup>9</sup> These drugs

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relieve asthmatic attacks by acting on the airway smooth muscles, causing relaxation.<sup>9</sup> Unfortunately, asthma attacks and exacerbation can reoccur as the underlying pathology still presents.<sup>10</sup> Additionally, prolonged use of these drugs can cause local and systemic side effects, including dysphonia, growth failure, elevated intraocular pressure, accelerated loss of bone mass, oral candidiasis, and mild tachyphylaxis.<sup>9</sup> These problems raise the need to find alternative treatments for asthma with fewer side effects; hence, the use of natural products is a promising approach.

Complementary and alternative medicine (CAM) is defined as a group of diverse medical practices and products that are not currently considered to be part of conventional medicine.<sup>11</sup> Lung complications, especially allergic diseases and asthma, rank in the top 15 most important diseases for which CAM is used for both children and adults.<sup>12,13</sup> In pediatric populations, some studies showed that CAM has been widely used in about 66% asthmatics, reaching 80% in some other diseases.<sup>14,15</sup> In the same context, honey (as a part of CAM) has been widely used as a treatment for cough, infections, fever, and inflammation.<sup>16</sup> It is reported to have anti-inflammatory, antibacterial, antioxidant, and anti-immunomodulatory effects.<sup>17,18</sup> It was suggested that honey nebulization is effective in treating upper acute asthma in pediatric patients.<sup>19</sup> Additionally, many studies have shown that oral honey intake was effective in decreasing both symptoms and frequency of asthma attacks.<sup>14,20–23</sup> This study aimed to review the efficacy and safety of honey (alone or combined) as an antiasthmatic remedy.

## METHODS

### *Search strategy and study selection*

This study was performed according to recommendations of the PRISMA statement, which is available as a supplementary PRISMA checklist.<sup>24</sup> In October 2016, 10 electronic databases were searched: PubMed, Scopus, ISI Web of Science, WHO Global Health Library (WHO GHL), Virtual Health Library (VHL), Google Scholar, POPLINE, New York Academy of Medicine Grey Literature report (NYAM), Controlled Trials (mRCT), WHO International Clinical Trials Registry Platform (ICTRP), and System for Information on Grey Literature Report in Europe (SIGLE). The following search terms were used: [honey AND (asthma OR (bronchial hypersensitivity) OR (bronchial hyper-reactivity) OR (respiratory hypersensitivity) OR (airway hypersensitivity) OR (airway hyperreactivity))] with no restrictions on language or publication date.

Three reviewers independently screened titles and abstracts to select potential full-text articles for further scrutiny according to inclusion and exclusion criteria. The inclusion criterion was any article that discussed the effect of honey on bronchial asthma, including animal and human studies.

All original articles were included without restriction to study design. No restriction of language, country, socioeconomic status, or time period was applied. Our exclusion

criteria were as follows: unreliably extracted data, overlapped data sets, books, conference articles, theses, case reports, nonoriginal articles (reviews and analyses), and articles without available full text (conference, editorial, and author response). Any disagreement was resolved through discussion and arbitrated with the senior authors. The study selection procedure is summarized in a systematic review flow chart (Fig. 1).

### *Data extraction*

Data were extracted independently by three reviewers using standard data extraction forms and any disagreement was resolved through discussion and consensus between reviewers and senior researchers was achieved. If there was one study with more than one publication report, they were compared and the publication with the most complete dataset was included. The data extraction sheet included the title of the article, name of authors, year of publication, characteristics of population, and country of recruitment, as well as data about sample size, study design, follow-up, and individual characteristics of participants. Confounders, form of honey, and outcome of the study were also recorded.

### *Quality assessment*

Two authors assessed the quality of studies independently without blinding to authorship or journal. Discrepancies were resolved by discussion with the senior authors. Three different quality assessment tools were utilized according to the study design of each article. Three included randomized controlled trials (RCTs) were assessed by Cochrane Collaboration's tool for assessing risk of bias in randomized trials.<sup>25</sup> Three cross-sectional studies were assessed by Australian Cancer Network's quality assessment tool for cross-sectional studies.<sup>26</sup> Two animal studies were assessed using SYRCLE's risk of bias tool for animal studies.<sup>27</sup>

The metrics used to assess the quality of RCTs included random sequence generation (selection bias), allocation concealment (selection bias), blinding, incomplete outcome data (attrition bias), selective reporting (reporting bias), and other sources of bias. The metrics used to assess the quality of cross-sectional studies included subject selection, comparability of groups analyzed on demographic characteristics, and participation rate. On the other hand, selection bias, performance bias, detection bias, and attrition bias were used to assess animal studies.

### *Analyses*

All data were analyzed using comprehensive meta-analysis software, version 3 (Biostat, NJ, USA). Whenever possible, dichotomous and continuous variables were analyzed to compute the pooled odds ratio (OR) and standardized mean difference, respectively. The corresponding 95% confidence intervals of pooled effect size were also calculated using a fixed-effects model. No heterogeneity was significant enough to use a random-effects model due to the relatively small number of articles. Heterogeneity was

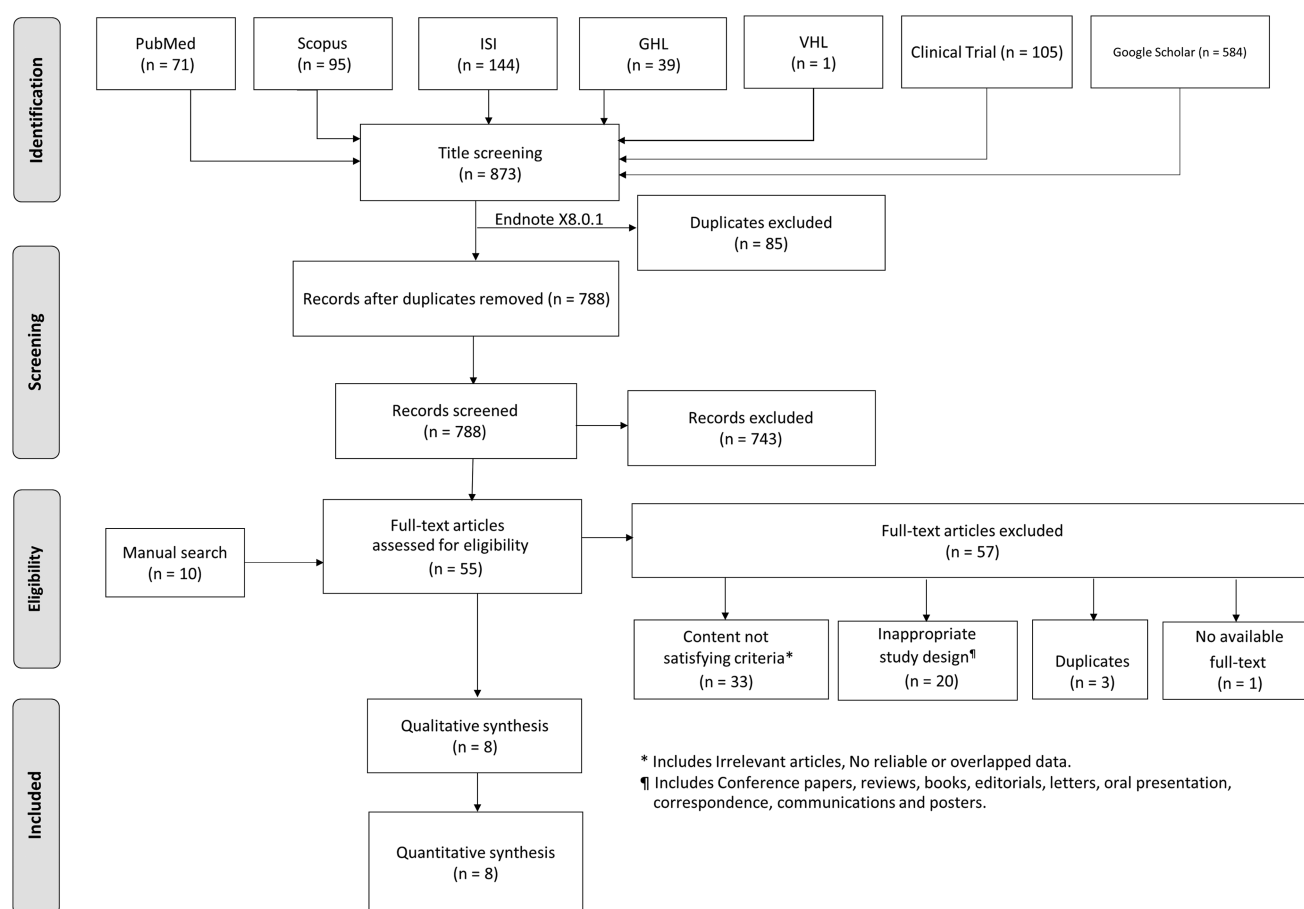


FIG. 1. Flow diagram of the search and review process.

assessed with Q statistics and  $I^2$  test considering it significant with  $I^2$  value  $>50\%$  or  $P$  value  $<.01$ .

## RESULT

### Study characteristics

A total of eight studies were included in the final analysis. Most of the studies were cross sectional ( $n=4$ ) and the rest were animal studies ( $n=2$ ) and RCTs ( $n=2$ ). These studies had been conducted in Sudan ( $n=3$ ), Egypt ( $n=2$ ), India ( $n=1$ ), Iraq ( $n=1$ ), Malaysia ( $n=1$ ), and Saudi Arabia ( $n=1$ ). Two studies assessing the effect of honey on asthmatic patients were conducted in Saudi Arabia and Iraq in 2008, followed by Sudan in 2011. The effect of honey alone was assessed in three studies (including animal), while the other five evaluated it as a combination with other therapies. Sample size in the included studies ranged from 27 to 60 patients. Most of the studies had patients with different degrees of asthma, ranging from mild to severe persistent asthma; only one study used human controls.<sup>28</sup> Three studies were performed using honey combinations with *Nigella sativa* (NS) and an RCT used a honey combination with *Vrisha ghrita* (VG).<sup>28–30</sup>

Most studies had both children and adults as participants with an age group ranging from 0 to 60 years. Statistics on

mean age with associated standard deviation (SD) and gender were not reported consistently in the included studies. Table 1 presents the summary characteristics of included studies.<sup>16,28–34</sup>

### Honey alone

A cross-sectional study done in Saudi Arabia interviewing 200 asthmatic patients demonstrated honey as the second most frequently used unconventional therapy in 49 (24.5%) patients.<sup>31</sup> Honey use among controlled patients was 60.71% (CI=41.99–76.74,  $P=.261$ ), whereas 74.36% of asthmatic patients (CI=58.56–85.61,  $P=.004$ ) used it. Their results found no significant effects of using honey for disease control.

Some animal studies have investigated honey effects with contradictory results. El-Aidy *et al.* tested the effect of using honey in a cobalamin-induced asthma model in mice.<sup>33</sup> It showed significant decrease in peripheral blood neutrophils in the sensitized honey group. Additionally, histopathological examination of lung tissues showed significant increase in inflammatory cells compared with the naive group. These results may be due to vasodilator and immunostimulatory effects leading to increased incidence of asthma cascade events. On the contrary, another study measured the effect

TABLE 1. SUMMARY CHARACTERISTICS OF INCLUDED STUDIES

| <i>First author<br/>(year<br/>published),<br/>country</i> | <i>Study design</i> | <i>Subjects<br/>of the<br/>study</i>            | <i>Number of participants</i>                | <i>Mean<br/>age<br/>(range)<br/>years</i> | <i>Male<br/>gender<br/>(%)</i> | <i>Risk<br/>of<br/>bias</i> | <i>Asthma severity</i>                            | <i>Measures<br/>of outcome</i>                                                | <i>Results</i>                                                                                                                                                                                                                                                                                  |
|-----------------------------------------------------------|---------------------|-------------------------------------------------|----------------------------------------------|-------------------------------------------|--------------------------------|-----------------------------|---------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ameen (2011),<br>Sudan <sup>28</sup>                      | RCT                 | Children<br>and adults                          | 27 patients used honey<br>and Nigella sativa | (8–40)                                    | 15                             | Low                         | 5 asthmatics and 22<br>controls                   | FEV <sub>1</sub> , FVC, and PEFR                                              | There was a significant increase<br>in FVC in the asthmatic group<br>and PEFR in the nonasthmatic<br>group.                                                                                                                                                                                     |
| Reena (2013),<br>India <sup>34</sup>                      | RCT                 | NA                                              | 26 patients used honey<br>and Vrisha ghrita  | NA                                        | 16                             | High                        | Chronic stable asthma                             | RR, wheezes, cough,<br>and chest expansion                                    | There was a significant decrease<br>noticed in the average<br>duration of sickness, severity<br>of each episode, and the<br>number of recurrent upper<br>respiratory tract infections.                                                                                                          |
| Al-bayati<br>(2008), Iraq <sup>32</sup>                   | Cross-sectional     | Children                                        | 60 patients used honey<br>and celery seeds   | NA                                        | (0–12)                         | High                        | Mild and moderate<br>asthma                       | FEV <sub>1</sub> and FVC                                                      | There was a significant increase<br>in FVC and FEV <sub>1</sub> .<br>Additionally, there was an<br>elevation in the serum zinc<br>level as well as Se level.                                                                                                                                    |
| Abdelrahman<br>(2014),<br>Sudan <sup>30</sup>             | Cross-sectional     | Children<br>and adults                          | 30 patients used honey<br>and Nigella sativa | 43.9<br>(16–50)                           | 16                             | Low                         | 13 severe and 17<br>moderate persistent<br>asthma | RR, wheezes, and<br>vesicular breathing                                       | RR was significantly decreased;<br>SPO <sub>2</sub> was increased, with<br>both wheezing and vesicular<br>breathing significantly<br>reduced in both asthma<br>categories.                                                                                                                      |
| Al Moamary<br>(2008), Saudi<br>Arabia <sup>31</sup>       | Cross-sectional     | Adults                                          | 200 (49 patients used<br>honey)              | 52.3                                      | 78                             | High                        | 47 mild, 43 moderate,<br>and 23 severe            | Disease control index                                                         | There was no significant<br>correlation between disease<br>control or FEV <sub>1</sub> and the use of<br>honey.                                                                                                                                                                                 |
| Abdelrahman<br>(2017),<br>Sudan <sup>29</sup>             | Cross-sectional     | Adults                                          | 30 patients used honey<br>and Nigella sativa | 43.9                                      | 16                             | Low                         | 13 severe and 17<br>moderate persistent<br>asthma | FEV <sub>1</sub> , FVC, MIP,<br>MEP, and ACT<br>score                         | There was statistically significant<br>improvement in lung function<br>and respiratory muscle power.<br>The need for asthma-relieving<br>$\beta_2$ agonists was remarkably<br>decreased and a significant<br>improvement in asthma control<br>test score in both asthma<br>groups was observed. |
| El-Aidy (2015),<br>Egypt <sup>33</sup>                    | Animal              | Albino<br>CD1 mice                              | 36 patients used honey                       | 6 weeks                                   | 36                             | High                        | NA                                                | Effect of using honey<br>in a cobalamin-<br>induced asthma<br>model in mice   | There was an increased<br>incidence of asthma cascade<br>events due to increased<br>inflammatory cells.                                                                                                                                                                                         |
| Kamaruzaman<br>(2014),<br>Malaysia <sup>16</sup>          | Animal              | Rabbits<br>( <i>Oryctolagus<br/>cuniculus</i> ) | 40 patients used honey                       | NA                                        | 37                             | High                        | NA                                                | Effect of aerosolized<br>honey in an<br>ovalbumin-induced<br>model in rabbits | Treatment with aerosolized<br>honey has reduced the number<br>of airway inflammatory cells<br>present in bronchoalveolar<br>lavage fluid and inhibited<br>goblet cell hyperplasia.                                                                                                              |

RCT, randomized controlled trial; NA, not applicable; FEV<sub>1</sub>, forced expiratory volume; FVC, forced vital capacity; PEFR, peak expiratory flow rate; RR, respiratory rate; SPO<sub>2</sub>, peripheral capillary oxygen saturation; MIP, maximal inspiratory pressure; MEP, maximal expiratory pressure; ACT, asthma control test.

of aerosolized honey in an ovalbumin (OVA)-induced model in rabbits and showed positive effects in inflammatory cell response, airway structures, and goblet cells.<sup>16</sup> Honey significantly decreased inflammatory cell infiltration with significant reduction in thickness of airway epithelial and mucosal regions following asthma induction with OVA. At the level of goblet cells, honey showed a significant reduction in all treatment groups.

### Honey and NS

Two Sudanese studies tested the effects of honey in combination with NS on lung functions.<sup>28,29</sup> Abdelrahman *et al.*<sup>29</sup> demonstrated a total significant improvement of all lung functions, including forced expiratory volume (FEV<sub>1</sub>) (MD=0.52,  $P>.001$ ), forced vital capacity (FVC) (MD=0.55,  $P=.002$ ), and peak expiratory flow rate (PEFR) (MD=80.60,  $P>.001$ ), in both moderate and severe persistent asthma compared with baseline.<sup>30</sup> Nevertheless, Ameen *et al.* showed only significant improvement at the level of FVC with no change of either FEV<sub>1</sub> or PEFR in five asthmatic patients.<sup>28</sup> Data from both studies could not be pooled together due to their different forms of presenting the results. Only one study showed a total significant improvement of all muscle power tests, including maximal inspiratory pressure (MIP) (MD=24.51,  $P>.001$ ) and maximal expiratory pressure (MEP) (MD=24.64,  $P>.001$ ), in 30 patients with both moderate and severe, uncontrolled persistent asthma compared with baseline.<sup>29</sup> Similarly, only one study found showing a significant improvement in asthma control test (ACT) scores (MD=11.22,  $P>.001$ ) in patients using the honey and NS combination compared with baseline.<sup>29</sup> In terms of clinical assessment, Abdelrahman *et al.* investigated clinical effects of honey and NS as an adjuvant therapy to inhaled corticosteroids in 30 patients with persistent asthma.<sup>30</sup> It showed a significant decrease in both the respiratory rate (MD=4.20,  $P=.087$ ) compared with baseline and wheezing percentage among patients in both severe (from 77.7% to 11.1%) and moderate (22.2% to 88.8%) asthma groups. Similarly, vesicular breathing showed a remarkable decrease among patients with moderate asthma (from 54.5% to 45.5%), although it was increased in patients with severe asthma (81.8% to 18.1%). This shows that a good optimal effect is obtained in less severe cases.

### Honey and celery seeds/Vrisha ghrita

One study demonstrated a total significant improvement of lung functions, including FEV<sub>1</sub>% (MD=18.09,  $P>.001$ ) and FVC % (MD=24.23,  $P>.001$ ), in 60 patients with bronchial asthma using celery seeds and honey compared with baseline.<sup>32</sup> A case-control study investigated the clinical effects of honey and VG as a treatment in children with asthma.<sup>34</sup> It showed a significant decrease in respiratory rate (MD=0.4,  $P=.05$ ), wheezes (MD=1.5,  $P=.01$ ), and cough (MD=1.5,  $P=.01$ ) compared with baseline. Additionally, it was associated with better chest expansion

(MD=1.3,  $P=.01$ ) and decreased breathlessness (MD=1.7,  $P=.01$ ) compared with baseline.

### Quality assessment

Quality of the included studies was assessed across several matrices. Overall, 5/8 studies had a high risk of bias, while the other three studies had low risk of bias.<sup>16,31-34</sup> The most common criteria unfulfilled or not reported by the included studies were allocation concealment ( $n=4$ ), blinding ( $n=3$ ), and subject selection for cross-sectional studies ( $n=2$ ) (Fig. 2).

## DISCUSSION

Our study aims to evaluate the effect of using honey as a treatment in asthmatic patients by itself or in combination with other therapies. The most popular combination in literature was honey and NS. All studies using this combination showed a significant improvement in all aspects of pulmonary functions (FVC, FEV<sub>1</sub>, and PEFR), muscle power tests (MIP and MEP), ACT, and clinical assessment (wheezes and vesicular breathing). This improvement in pulmonary functions could be explained by unique characteristics of the honey and NS combination, including anti-inflammatory/antiallergic and immunomodulatory characteristics.<sup>35</sup> The improvement in MIP and MEP can be possibly explained by the medicinal characteristics of honey.<sup>35-39</sup> However, more severe cases will need potentiation by the synergistic bronchodilator, antitussive, and other medicinal properties of NS.<sup>37,40-43</sup> Moreover, the significant improvement in ACT score was associated with an obvious reduction in the use of rapid reliever/rescue inhalers, which is consistent with the global strategy for asthma management and control.<sup>44</sup>

Other combinations mentioned in the literature were honey with either celery seeds or Vrisha ghrita. Both combinations were associated with significant improvement either in pulmonary functions (FEV<sub>1</sub> and FVC) or different aspects of clinical features. In addition to the aforementioned effect of honey, celery seeds contain limonene and antioxidant vitamins (A, E, and C).<sup>45</sup> These components increase the serum selenium level, which is an integral component of glutathione peroxidase,<sup>46,47</sup> part of the pulmonary antioxidant system, thus increasing stability and integrity of the cell membrane.<sup>46,47</sup>

Although honey alone has no significant advantage in controlling asthma in humans, animal studies showed positive results, which may be due to using different models (mice and rabbits) or different forms of honey. The positive effects obtained with rabbits are more reliable due to more phylogenetic similarity with humans and better understanding of lung structure than mice.<sup>36</sup> Additionally, using aerosolized honey ensures maximum deposition of honey on airway surfaces. In addition, the negative results shown in mouse models may be due to honey-induced vasodilatation and immunostimulatory effects leading to increased incidence of cascade events of asthma.

The most obvious limitation of our study is the small number of studies and population included. In addition,

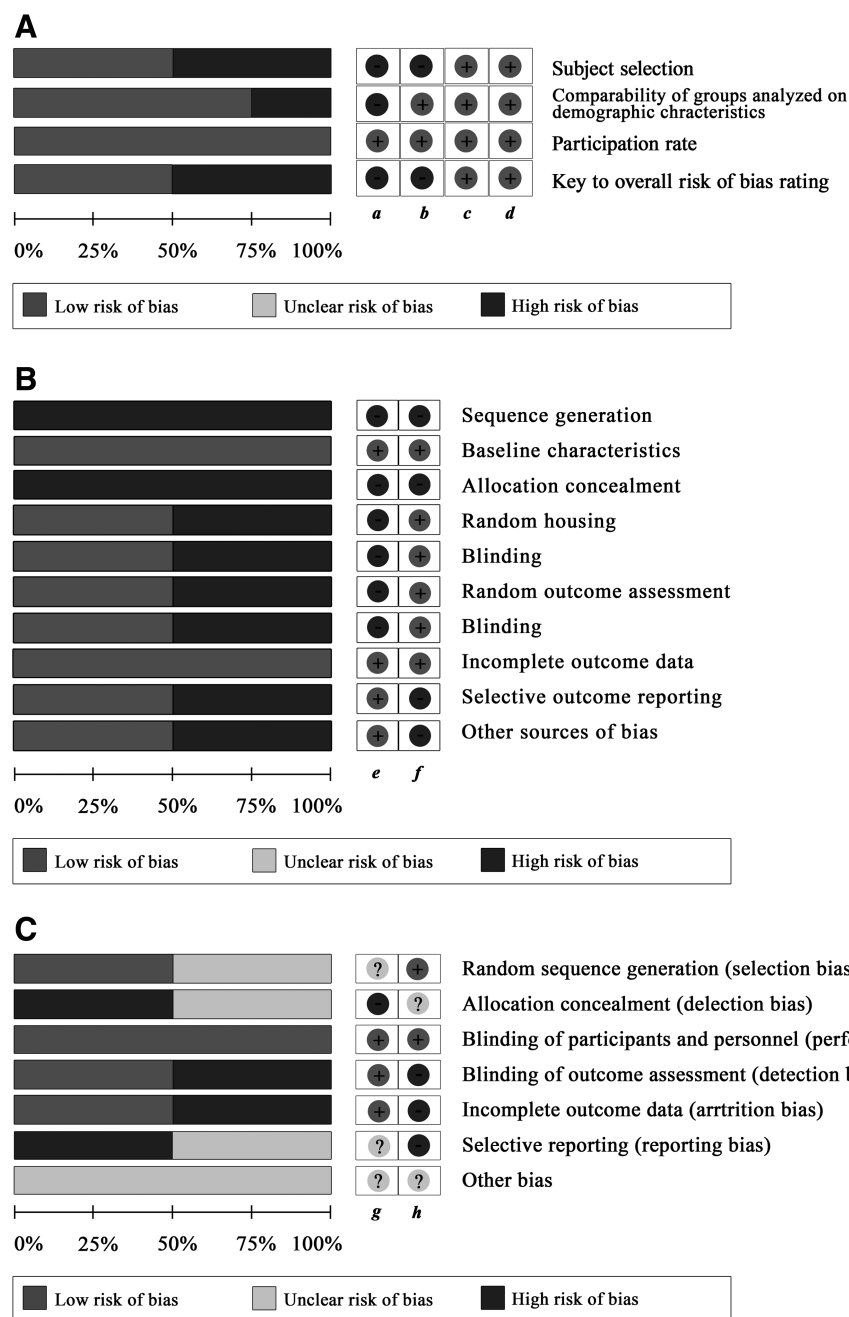


**FIG. 2.** Quality assessment. (A) QA of cross-sectional studies. (B) QA of animal studies. (C) QA of RCTs. Symbols: a, Abdelrahman *et al.*<sup>30</sup>; b, Abdelrahman *et al.*<sup>29</sup>; c, Al-bayati *et al.*<sup>32</sup>; d, Al Moamary *et al.*<sup>31</sup>; e, El-Aidy *et al.*<sup>33</sup>; f, Kamaruzaman *et al.*<sup>16</sup>; g, Al Ameen *et al.* (2011)<sup>28</sup>; and h, Reena and Ramachandran<sup>34</sup>. RCT, randomized controlled trial; QA, quality assessment.

many confounders were not taken into consideration such as different types of populations, ages, or severity of diseases. In addition, severe persistent disease, high education level, and congruence with the patient's own beliefs, values, or philosophical orientations toward health and life are established predictors of the use of CAM.<sup>48</sup> Another limitation is the different combinations studied. In those cases, it is unclear whether the positive/negative effect was due to honey alone, the combined element, or the synergistic effect of them together.

In conclusion, honey alone has no strong evidence to support its effectiveness in controlling asthma. However, when used in a combination with other substances, it showed

a relatively high efficacy in patients with asthma. Accordingly, these combinations can be used as adjuvant therapies to decrease asthma severity and hence the need for asthma-relieving drugs to improve the quality of life. This finding will help in asthma control with lower cost alternatives and better outcomes, which are consistent with the recent support of the World Health Organization (WHO) to integrate traditional medicine within health care systems.<sup>49</sup>

## AUTHOR CONTRIBUTIONS

N.T.H. and K.H. were responsible for the idea and study design. All authors determined the inclusion and exclusion

criteria under supervision of N.T.H. and K.H. S.G. and A.S.A. analyzed the data and interpreted them under supervision of N.T.H. and K.H. All authors were involved in manuscript writing and they approved the final version.

### AUTHOR DISCLOSURE STATEMENT

The authors declare that they have no competing interests.

### REFERENCES

1. Global asthma network. The global asthma report 2014. Auckland, New Zealand. [www.globalasthma-report.org/resources/Global\\_Asthma\\_Report\\_2014.pdf](http://www.globalasthma-report.org/resources/Global_Asthma_Report_2014.pdf) (accessed May 2018).
2. Global initiative for asthma-GINA. [https://web.archive.org/web/20121120205023/http://www.ginasthma.org/uploads/users/files/GINA\\_Report2011\\_May4.pdf](https://web.archive.org/web/20121120205023/http://www.ginasthma.org/uploads/users/files/GINA_Report2011_May4.pdf) (accessed May 2018).
3. World Health Organization. Asthma fact sheet 2017. <https://web.archive.org/web/20071215181927/http://www.who.int/media/centre/factsheets/fs307/en/> (accessed May 2018).
4. Bush A, Menzies-Gow A: Phenotypic differences between pediatric and adult asthma. *Proc Am Thorac Soc* 2009;6:712–719.
5. Balaha MF, Tanaka H, Yamashita H, *et al.*: Oral *Nigella sativa* oil ameliorates ovalbumin-induced bronchial asthma in mice. *Int Immunopharmacol* 2012;14:224–231.
6. Fahy JV, Corry DB, Boushey HA: Airway inflammation and remodeling in asthma. *Curr Opin Pulm Med* 2000;6:15–20.
7. Mauad T, Bel EH, Sterk PJ: Asthma therapy and airway remodeling. *J Allergy Clin Immunol* 2007;120:997–1009.
8. Jeffery P: Inflammation and remodeling in the adult and child with asthma. *Pediatr Pulmonol Suppl* 2001;32:3–16.
9. Fanta CH: Asthma. *N Engl J Med* 2009;360:1002–1014.
10. Kim DY, Yang WM: *Panax ginseng* ameliorates airway inflammation in an ovalbumin-sensitized mouse allergic asthma model. *J Ethnopharmacol* 2011;136:230–235.
11. National Center for Complementary and Alternative Medicine: Complementary, Alternative, or Integrative Health: What's in a Name? <https://nccih.nih.gov/health/integrative-health> (accessed June 25, 2018).
12. Shen J, Oraka E: Complementary and alternative medicine (CAM) use among children with current asthma. *Prev Med* 2012;54:27–31.
13. Barnes PM, Bloom B, Nahin RL: Complementary and alternative medicine use among adults and children: United States, 2007. *Natl Health Stat Reports* 2008;12:1–23.
14. Hocaoglu Babayigit A: High usage of complementary and alternative medicine among Turkish asthmatic children. *Iran J Allergy Asthma Immunol* 2015;14:410–415.
15. Reznik M, Ozuah PO, Franco K, *et al.*: Use of complementary therapy by adolescents with asthma. *Arch Pediatr Adolesc Med* 2002;156:1042–1044.
16. Kamaruzaman NA, Sulaiman SA, Kaur G, *et al.*: Inhalation of honey reduces airway inflammation and histopathological changes in a rabbit model of ovalbumin-induced chronic asthma. *BMC Complement Altern Med* 2014;14:176–176.
17. Tan HT, Rahman RA, Gan SH, *et al.*: The antibacterial properties of Malaysian tualang honey against wound and enteric microorganisms in comparison to manuka honey. *BMC Complement Altern Med* 2009;9:34–34.
18. Khalil MI, Sulaiman SA: The potential role of honey and its polyphenols in preventing heart diseases: A review. *Afr J Tradit Complement Altern Med* 2010;7:315–321.
19. Abdul Maksoud M, Abdul Rhman M: Bee honey nebulization as a non traditional treatment of acute bronchial asthma in infants and children. *Malays J Med Sci* 2007;14:115–115.
20. Orhan F, Sekerel BE, Kocabas CN, *et al.*: Complementary and alternative medicine in children with asthma. *Ann Allergy Asthma Immunol* 2003;90:611–615.
21. Aldahash FD, Marwa AMK: Attitude towards the use of complementary and alternative medicine by patients in Saudi Arabia. *Biomedica* 2012;28:1–6.
22. McQuaid EL, Fedele DA, Adams SK, *et al.*: Complementary and alternative medicine use and adherence to asthma medications among latino and non-latino white families. *Acad Pediatr* 2014;14:192–199.
23. Musaiger AO, Abahussain NA: Attitudes and practices of complementary and alternative medicine among adolescents in Saudi Arabia. *Global J Health Sci* 2015;7:173–179.
24. Liberati A, Altman DG, Tetzlaff J, *et al.*: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *PLoS Med* 2009;6:e1000100–e1000100.
25. Higgins JPT, Altman DG, Gotzsche PC, *et al.*: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *Br Med J* 2011;343:d5928–d5928.
26. Clinical guidelines network cancer council Australia. Development of clinical practice guidelines using cancer council Australia's cancer guidelines. *Handbook for section authors and the guideline working party*. Cancer Council Australia, Sydney, 2014.
27. Hooijmans CR, Rovers MM, Vries RBMD, *et al.*: SYRCLE's risk of bias tool for animal studies. *BMC Med Res Methodol* 2014;14:1–9.
28. Ameen NMAL, Altubaigy F, Jahangir T, *et al.*: Effect of *Nigella sativa* and bee honey on pulmonary, hepatic and renal function in Sudanese in Khartoum state. *J Med Plants Res* 2011;5:6857–6863.
29. Abdelrahman JE, Magzoub AA, Ibrahim RE, *et al.*: Effect of combination of *Nigella sativa* and bee's honey on lung function, respiratory muscle power, and asthma control in patients with persistent asthma. *Int J Res Med Sci* 2017;5:236–239.
30. Abdelrahman J, Magzoub A, Ibrahim R, *et al.*: Effect of *Nigella sativa* and bee's honey on cardiopulmonary functions in patients with persistent asthma. *Sudan Med Monitor* 2014;9:159–162.
31. Al Moamary MS: Unconventional therapy use among asthma patients in a tertiary care center in Riyadh, Saudi Arabia. *Ann Thorac Med* 2008;3:48–51.
32. Al-bayati NJ, Abdul Razzak AL, Al-Muktar EJ, *et al.*: The effect of celery seeds with honey in treatment of bronchial asthma. *Med J Babylon* 2008;5:162–165.
33. El-Aidy WK, Ebeid AA, Sallam AE-RM, *et al.*: Evaluation of propolis, honey, and royal jelly in amelioration of peripheral blood leukocytes and lung inflammation in mouse conalbumin-induced asthma model. *Saudi J Biol Sci* 2015;22:780–788.
34. Reena K, Ramachandran SK: Randomized controlled trial on the effect of *Vrisha ghrita* in childhood asthma management. *Int J Res Ayurveda Pharm* 2013;4:78–83.
35. Paul IM, Beiler J, McMonagle A, *et al.*: Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep

- quality for coughing children and their parents. *Arch Pediatr Adolesc Med* 2007;161:1140–1146.
36. Viuda-Martos M, Ruiz-Navajas Y, Fernandez-Lopez J, *et al.*: Functional properties of honey, propolis, and royal jelly. *J Food Sci* 2008;73:R117–R124.
  37. Mesaik MA, Azim MK, Mohiuddin S: Honey modulates oxidative burst of professional phagocytes. *Phytother Res* 2008;22:1404–1408.
  38. Olaitan PB, Adeleke OE, Ola IO: Honey: A reservoir for microorganisms and an inhibitory agent for microbes. *Afr Health Sci* 2007;7:159–165.
  39. Cooper R: Using honey to inhibit wound pathogens. *Nurs Times* 2008;104:46,48–49.
  40. Boskabady MH, Sheiravi N: Inhibitory effect of *Nigella sativa* on histamine (H1) receptors of isolated Guinea pig tracheal chains. *Pharm Biol* 2002;40:596–602.
  41. Boskabady M-H, Keyhanmanesh R, Khameneh S, *et al.*: Potential immunomodulation effect of the extract of *Nigella sativa* on ovalbumin sensitized guinea pigs. *J Zhejiang Univ Sci B* 2011;12:201–209.
  42. Keyhanmanesh R, Bagban H, Nazemiyeh H, *et al.*: The relaxant effects of different methanolic fractions of *Nigella sativa* on Guinea pig tracheal chains. *Iran J Basic Med Sci* 2013;16:123–128.
  43. Keyhanmanesh R, Boskabady MH, Eslamizadeh MJ, *et al.*: The effect of thymoquinone, the main constituent of *Nigella sativa* on tracheal responsiveness and white blood cell count in lung lavage of sensitized guinea pigs. *Planta Med* 2010;76:218–222.
  44. Global strategy for asthma management and prevention: Available at: <https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/> (accessed May 2018).
  45. Kotb FT: *Medicinal Plants in Libya*. Arab Encyclopedia House, Tripoli-Libya, 1985.
  46. Beasley R, Thompson C, Pearce N: Selenium, glutathione peroxidase and asthma. *Clin Exp Allergy* 1991;21:157–159.
  47. Misso NL, Powers KA, Gillon RL, *et al.*: Reduced platelet glutathione peroxidase activity and serum selenium concentration in atopic asthmatic patients. *Clin Exp Allergy* 1996;26:838–847.
  48. Astin JA: Why patients use alternative medicine: Results of a national study. *JAMA* 1998;279:1548–1553.
  49. World Health Organization: WHO Traditional Medicine Strategy: 2014–2023. [www.who.int/medicines/publications/traditional/trm\\_strategy14\\_23/en](http://www.who.int/medicines/publications/traditional/trm_strategy14_23/en) (accessed June 25, 2018).