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The Most Common Herb and Nutritional Supplements Used against Coronavirus in Saudi Arabia in 2020

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ABSTRACT

Background: The global outbreak of COVID-19, for which there are so far few effective vaccines or evidence-based treatments, has raised much concern among people around the world, leading to numerous attempts to go for alternatives, including hand washing, hand sanitizing, wearing face masks and social distancing strategies. Several dietary nutraceuticals and plant-based compounds derived from herbal extracts may be used to treat COVID-19. Additionally, natural products have been shown to improve the immune response.

Methods: This meta-analysis aimed to determine the most common herbs and nutritional supplements that were used as a treatment, prevention or both against COVID-19 in Saudi Arabia in 2020, a preliminary search on the PubMed, EBSCO, Science Direct, Web of Science and Google Scholar databases yielded 30 papers published in English between 2020 and 2022. Five studies were systematically reviewed and included in the final meta-analysis.

Results: The observed log odds ratios ranged from -1.1135 to -0.0852, with the majority of estimates being negative (100%). According to the Cook's distances, one study could be considered to be overly influential.

Conclusion: The most effective herb in most of studies was black seed mostly with 63%, which indicated positive effect on health during COVID-19 infection besides honey which is considered as natural supplement with 83.8% as most of the participants used it against COVID-19.

Keywords: Herbs; Nutritional supplements; Coronavirus; KSA; Plants; COVID-19; Respiratory infection; Incubation

INTRODUCTION

At the end of 2019, the world had witnessed the beginning of one of the biggest pandemics that is still occurring now, the outbreak of COVID-19 also known as SARS-CoV-2. The virus had emerged from China, Wuhan and did not take too long to spread around the whole world. Saudi Arabia reported the first case of COVID-19 in March 2020. The fast spread of the virus and the high mortality rate associated with it raised the anxiety and fear in the citizens

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leading them to use what they had in hand such as herbs and nutritional supplements as a prevention method to protect themselves from the infection and to treat themselves in case they were infected [1].

5000 years ago, the Sumerians wrote the first record of plant usage as medicine. It was the only available choice to counter, prevent and treat many infections and diseases. It was widely used due to its bioactive properties in enhancing the immune system. Nowadays, it is still widely used due to its beneficial effects and the ability to consume it without a prescription.

The use of alternative medicine in Saudi Arabia for either treating or preventing measurements is not novel; as it has been used since many generations for the treatment of chronic diseases such as diabetes miletus and common health symptoms including abdominal pain, cold and flu and cough. A range of studies provided clinical evidence of herbal medicine use in the treatment of SARS Coronavirus (SARS-CoV) which showed significant results and supported the idea of the herbal medicine use in the treatment and prevention of epidemic diseases [2].

Products from natural sources often have a safe profile. Although many of these products are harmless when used in the right way, some could be extremely harmful when they are misused, especially in elderly or chronically ill patients. The side effects may vary in severity from life threatening, such as herbal-drug interactions, to mild, such as diarrhea, abdominal pain and headaches.

In Saudi Arabia, the public still uses herbal medicines to treat various health conditions or support general health in both urban and rural areas. Studies have reported a high prevalence of using dietary or herbal supplements for therapeutic purposes among adults in Saudi Arabia, with the most reported reasons for the use of herbal medicines involving traditional beliefs in their efficacy and safety as well as their affordability compared with other pharmaceutical products. However, few studies have examined patients' use of dietary or herbal supplements during the COVID-19 pandemic.

The systemic review aims to determine the most common herbs and nutritional supplements that were used as a treatment, prevention or both against COVID-19 in Saudi Arabia in 2020 [3].

MATERIALS AND METHODS

Protocol and Registration

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Eligibility Criteria

Subjects: COVID-19 patients with no age restriction. All types of studies related to the topic were to be accepted in this review. However, five studies used a self-administrated cross-sectional questionnaire to obtain information regarding the use of herbs and nutritional supplements against COVID-19. The titles and abstracts were screened first then after the searching process ended; the studies were divided on the authors to scan the inner content of each literature to further check the eligibility [4].

Data Sources and Search Strategy

A systematic search was performed using the keywords the literatures search was done on February 1st of 2022. The authors searched the following databases: Google Scholar, Pubmed and Research Gate. The terms used for searching were the following: ("Herbal" or "herb") and ("therapy" or "treatment") and ("in Saudi Arabia" or "ksa"). ("Herbal" or "herb") and ("therapy" or "treatment") and ("in Saudi Arabia" or "ksa") and ("for COVID" or "coronavirus" or "corona various"). ("Herbal" or "herb" or "garlic" or "olive oil" or "vitamin c" or "orange" or "lemon" or "black seed" or "ginger" or "honey") and ("therapy" or "treatment") and ("in Saudi Arabia" or "ksa") and ("for "COVID-19" or "coronavirus" or "corona"). Various on PubMed, EBSCO, Web of Science and Google Scholar database. Between 2020 and 2022, a total of 30 articles were published in English. Abstract screening was performed to identify articles of interest. Full articles were obtained for all selected abstracts and reviewed for inclusion and exclusion criteria.

Inclusion and Exclusion Criteria

The inclusion criteria for this study were: (1) Published online questionnaire or survey, controlled trial, (2) study participants with active COVID-19 and (3) available outcome measures for treatment efficacy [5].

Risk of Bias Assessment

The Cochrane collaboration's tool for measuring risk of bias was used to assess the type of study quality.

Statistical Analysis

Methodological quality of the eligible clinical trials was appraised using the Cochrane collaboration's tool for assessing risk of bias. The primary outcome measure of interest is the log odds ratio in all studies. The secondary outcome is to measure presence of heterogeneity according to its scale. Estimates were pooled and where appropriate, 95% Confidence Intervals (95% CI) and p values were calculated. Heterogeneity amongst the different studies pooled was examined using the I2 statistic and Cochran's Q test. I2>50% indicates substantial heterogeneity. Jamovi 2.3.9 software was used in this meta-analysis (**Table 1**) [6].

Table 1: Summary of included studies.

Author	Year	Study design	Sample (n)	Herbs (Name) %	Natural supplement (%)
Sami, et al.	2021	Questionnaire	312	124 (Star anise) (39.7)	208 (Olive oil) (67)
Alotiby, et al.	2020	Questionnaire	494	311 (Black seed) (63)	414 (Honey) (83.8)
Alkharashi	2021	Cross-sectional online survey	1460	346 (Black seed) (23)	369 (Zinc) (25.3)
AlNajrany, et al.	2021	Cross-sectional online survey	1488	535 (Ginger) (36)	685 (Honey) (46)
Aldwihi, et al.	2021	Cross-sectional, questionnaire-based study	738	425 (Ginger) (57.6)	591 (Lemon) (80)

RESULTS

Study Selection and Characteristics

30 studies were identified in the literature search. Next 25 duplicate articles were excluded or ineligible. For eligibility, the remaining five studies were fully reviewed and met the meta-analysis inclusion criteria (**Figure 1**).

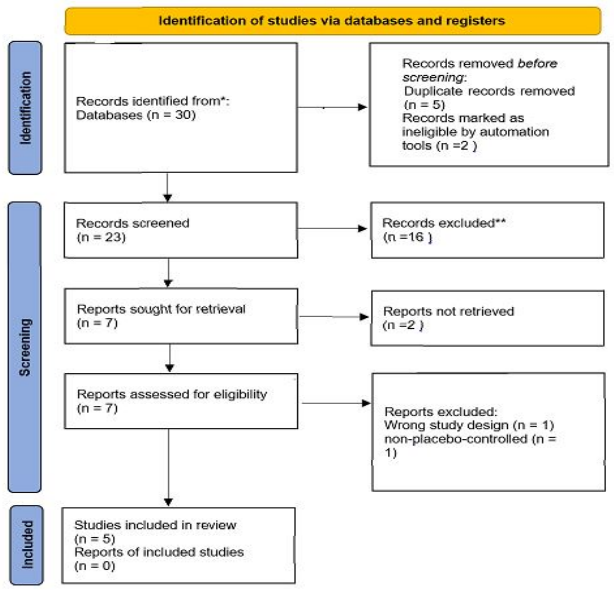

Figure 1: PRISMA 2020 flow diagram for updated systematic reviews, which included searches of databases, registers and other sources.

Statistical Outcome

The analysis was carried out using the log odds ratio as the outcome measure. A random-effects model was fitted to the data. The amount of heterogeneity (*i.e.,* tau^2), was estimated using the maximum-likelihood estimator. In addition to the estimate of tau^2, the Q-test for heterogeneity and the I^2 statistic are reported. In case any amount of heterogeneity is detected (*i.e.*, $tau^2>0$, regardless of the results of the Q-test), a prediction interval for the true outcomes is also provided. Studentized residuals and Cook's distances are used to examine whether studies may be outliers and/or influential in the context of the model. The rank correlation test and the regression test, using the standard error of the observed outcomes as predictor are used to check for funnel plot asymmetry (**Table 2**) [7].

Table 2: Funnel plot symmetry.

	Random-effects model (k=5)					
	Estimate	**se**	**Z**	**p**	**CI lower bound**	**CI upper bound**
Intercept	-0.746	0.195	-3.82	<0.001	-1.128	-0.364

Note. Tau² estimator: Maximum-likelihood

Heterogeneity statistics

Tau	Tau^2	I²	H²	df	Q	p
0.418	0.175 (SE=0.1202)	93.64%	15.734	4	77.31	<0.001

A total of k=5 studies with 4492 participants were included in the analysis. The observed log odds ratios ranged from -1.1135 to -0.0852, with the majority of estimates being negative (100%). The estimated average log odds ratio based on the random-effects model was=-0.7461 (95% CI: -1.1284 to -0.3637). Therefore, the average outcome differed significantly from zero (p=0.0001) which indicate a great significant effect of the use of those natural and herbal supplements during COVID-19 infection. According to the Q-test, the true outcomes appear to be heterogeneous (I^2=93.6445%) that shows high heterogeneity among selected studies and variation in outcome in this meta-analysis. Hence, although the average outcome is estimated to be negative, in some studies the true outcome may in fact be positive. According to the Cook's distances, one study could be considered to be overly influential and significant among the five studies (**Figures 2 and 3**) [8].

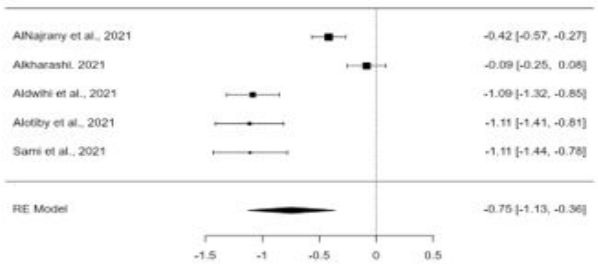

Figure 2: Forest plot.

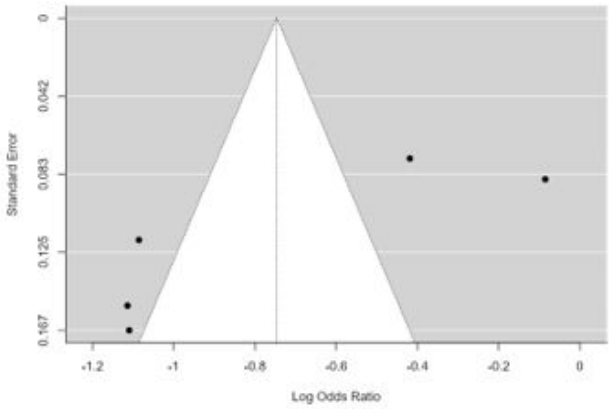

Figure 3: Funnel plot.

Publication Bias Assessment

The regression test indicated funnel plot asymmetry (p=0.0005) but not the rank correlation test (p=0.8167) (**Tables 3-5**).

Table 3: Fail-safe N analysis (File drawer analysis).

Fail-safe N	P
320	<0.001

Table 4: Rank correlation test for funnel plot asymmetry.

Kendall's Tau	P
-0.200	0.817

Table 5: Regression test for funnel plot asymmetry.

Z	P
-3.459	<0.001

Log OR

The log OR between the use of natural supplements and herbs is 0.75-folds thus most people prefer those natural over herbs based on daily life, routine, habit or even medical prescription besides natural herbal remedy. In addition, both had significant effect against COVID-19 [9].

DISCUSSION

This meta-analysis aims to illustrate the most common herbs and nutritional supplements that were utilized as a treatment, prevention or both against COVID-19 in Saudi Arabia in 2020.

Honey

Honeybees products are well known for their nutritional and medicinal values, they have been employed for ages for various therapeutic purposes. Products of honeybees that contain mixtures of potentially active chemicals, possess unique properties that might help to protect, fight and alleviate symptoms of COVID-19 infection [10].

Almost 1000 years ago, Avicenna, the great Iranian scientist and doctor, proposed honey as one of the best remedies for treatment of tuberculosis, evidence suggests that honey might have beneficial effects on health including as antioxidants, anti-inflammatory, antibacterial, antidiabetic, respiratory, gastrointestinal, cardiovascular and nervous system protective effects. Honey is more potent for suppression of cough than dextromethorphan and diphenhydramine. Some studies supported the use of honey to manage chronic bronchitis and asthmatic patients.

Honey in general, particularly Manuka honey, had potent inhibitory effects against the influenza virus. Potential anti COVID-19 effects of honeybees and other bee products will require further investigations, many studies suggest promising effects of bee pharmacy against COVID-19 either by direct antiviral effects of their bioactive peroxides, flavonoids and phenolics or indirect effects due to their immunomodulatory effect on the host immune system and interfering with host inflammatory response aroused by COVID-19 infection [11].

Honey has been recommended by the National Institute for Health and Care Excellence (NICE) and Public Health England (PHE) as a first line treatment for cough due to upper respiratory tract infection, which is the main well identified COVID-19 symptom.

Nigella sativa (Black seeds)

There is a direct association of the therapeutic effect of herbal medicine on its chemical compositions. *Nigella sativa* or black seed is a precious herbal medicine since it is traditionally used in treating many diseases. Its beneficial effect has been demonstrated by many studies and from long ago by Islam, as the beloved prophet Mohammed stated once “Abu Hurairah narrated that the messenger of Allah (s.a.w) said: Use this black seed. For indeed it contains a cure for every disease except As-Sam" and As-Sam is death [12].

Black seed (*N. sativa*) has been used in prophetic and traditional Arabic herbal medicine, especially in the middle east, for more than 2000 years to treat various diseases, including skin diseases, asthma, cough, bronchitis, headache, fever and influenza. The composition of black seed includes fixed oils, proteins, alkaloids, saponins and essential oils. However, most pharmacological activities of black seed are attributed to the presence of thymoquinone. The impact of black seed oil on patients who had Hepatitis C Virus (HCV) infection and who were not eligible for interferon therapy was assessed in a study conducted in Egypt. A dose of 450 mg of black seed oil was administered to these patients as soft gelatin capsules three times daily for three months and resulted in a significant reduction in the HCV viral load. In the current study, using black seed during infection with COVID-19 has significantly increased among the public by 83% [13].

CONCLUSION

The most effective herb in most of the studies was black seeds with 63%, which indicated positive effect on health during COVID-19 infection besides honey, which is considered as natural supplement with 83.8% as most of the participants, used it against COVID-19.

Most participants preferred natural supplement to herbs as they thought they would have a great effect against COVID-19 over herbs and even some other minerals and oils based on daily life, routine, habit or even medical prescription besides natural herbal remedy. This was indicated with an odds ratio of 0.75 over the use of herbs.

RECOMMENDATION

Based on the results this meta-analysis recommend honey as a potential compatible antiseptic prophylaxis to help protect against the virus. Honey might safely disinfect the throat and trap virus particles, beside a major advantage that it has no side effects and of great nutritional value. Next, it may even consider diluted solution of natural honey as a homemade antiseptic for hands, skin and mucous membranes or as a mouth gargle since honey is completely safe and widely used as sweetener in several pharmaceutical preparations.

More studies about RCTs should be applied irrespective making questionnaire or online survey as the prevalence of the pandemic is enclosed right now with the help of new boosters affecting the immunity system.

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DECLARATION OF COMPETING INTEREST

There are no conflicts of interest to disclose.

AUTHOR STATEMENT

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