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A Review On: A Natural Honey Is Treatment for Novel Coronavirus

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ABSTRACT: Present review is going on the globe shaking disease covid-19. This disease identified from December 2019. After identify the disease the world face the tremendous economic loss and unprecedented health crisis. So everyone to concentrate how to develop the medicine and cure the disease is at high speed, less attention and less effort for respiratory infectious disease. Although so far, a number of vaccine candidates have highly developed into clinical trials, limited data have been released regarding the vaccine efficacy and safety in human, not mention the long-term effectiveness of those vaccines remain as open question yet. Natural honey has been demonstrated as potent antimicrobial in many research investigations and has been considered a good alternative for antiviral drugs for the treatment of some viral infections. The main aim to study the efficacy of natural honey in the treatment of COVID-19 patients in this randomized, multicenter, controlled trial, comparing honey in one arm to standard care in the other arm. Natural honey has been historically used for acute respiratory infection and generally shows acceptable toxicity. Hereby, we summarized the most recent advance in SARS-CoV-2 prevention including vaccine development as well as experimental studies. Mainly, we reviewed the natural products showing increase the immunity and minimize the virus effect on human corona virus. We demonstrated that to fill in the response gap between appropriate treatment and commercially available vaccine, repurposing natural products will be a vigorous approach to stop or at least slow down SARS-CoV-2 transmission. In the interest of public health, this will lend health officials better control on the current pandemic.

Key words: SARS-COV-2. Natural honey, anti viral activity and Covid-19.

INTRODUCTION:

The novel corona virus disease 2019 (COVID-19) caused by severe acute respiratory syndrome corona virus 2 (SARS CoV-2) has been discovered recently in December 2019 from Wuhan city in China to spread in more than 40 countries all over the world. This disease has gain the attention of all nations after it has been stated as a pandemic by the World Health Organization (WHO) in March 12, 2020. Currently no treatment has been proved to be efficient in the treatment of infected patients by COVID-19. Natural honey has been demonstrated as potent antimicrobial in many research investigations and has been considered a good alternative for antiviral drugs for the treatment of some viral infections. The investigators aim to study the efficacy of natural honey in the treatment of COVID-19 patients in this randomized, multicenter, controlled trial, comparing honey in one arm to standard care in the other arm.

The (SARS CoV-2) virus is spreading globally, threatening all healthcare systems. Many healthcare systems and organizations are using different protocols and measures to fight the COVID-19. Hydroxychloroquine, lopinavir and other antiviral medications are currently under research investigations. Natural honey has been well known for its high health properties in diabetes, nutrition, dyslipidemia, skin lesions and it got FDA approval for topical wound treatment in 2007 as the most potent antimicrobial agent. Honey has been previously considered as an alternative for acyclovir in the treatment of herpes simplex virus 1 (HSV-1) and it also demonstrated for its significant antiviral effect against varicella zoster virus (VZV). Many studies have demonstrated the broad spectrum antimicrobial effect of honey as an antibacterial, anti fungal, antiviral and antimycobacterial. The National Institute for Health and Care Excellence (NICE) and the Public Health England (PHE) guidelines recommended honey as a first line of treatment for acute cough caused by upper respiratory tract infection which is currently a cornerstone symptom in COVID-19 infectious disease. Moreover, natural honey should no longer be used as "alternative" and deserves to gain more attention by scientists and researchers. The aim of

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this trial is to study the efficacy of natural honey in treatment of patients infected with COVID-19 in comparison with current standard care.

The use of chemo drugs comes with several problems including multidrug resistance and side effects which prompt us to think about other alternatives like natural products for reducing the unavoidable side effects Human has been using plant and its several derivatives as treatments for various types of diseases In recent years, honey has got the attraction of researchers for combating efficiently against these difficulties of chemo drugs Honey contains several compounds including sugars, organic acids, amino acids, phenolic compounds, vitamins, and minerals. This is the reason why honey has been studied for a long time in animal and human models to observe its antioxidant potency. It has proved its potency in several therapeutic properties including immunostimulatory, antibacterial, anti-inflammatory, and wound healing, antiulcer, antidiabetic, anticancer, antiviral, and antifungal. It reduces the level of triglycerides (TGs), very-low-density lipoprotein (VLDL), and systolic blood pressure in experimental animals. Reduced acute respiratory distress symptoms have been noticed when honey is ingested daily.

However, whether honey might be a therapeutic choice for controlling and/or treating the COVID-19, remained to be investigated. In this review, we summarized all promising beneficial roles of honey and its ingredients in the context of antimicrobial activities, numerous chronic diseases, and host immune signaling pathways and thereby tried to make a correlation of honey for the treatment of COVID-19.

Pharmacological effects of honey:

Several studies have observed honey and its active compound(s) on human physiological systems. Various in vivo or in vitro studies have also been performed to utilize its antimicrobial activities. However, the exact mechanism of protective effects of honey in case of viral infection has not been properly established yet. The recent studies on the protective effects of honey against immune dysfunction, anti-inflammatory effects, diabetes, hyperglycemia, cardiovascular disorders, and bacterial, fungal, and viral infections. We also tried to make a correlation of therapeutic effects of honey on COVID-19 as all of these above mentioned physiological disorders/comorbid conditions found to be associated with the high fatality rate of SARS-CoV-2 infected individuals.

Oxidative stress:

Honey has proved its antioxidant activity by preventing several acute and chronic diseases which include diseases related to inflammation, diabetes, cardiovascular, and cancer. Moreover, phenolic acids of honey protect humans from hydrogen peroxide-induced oxidative DNA damage in lymphocytes. Along with phenolic acids and flavonoids, several other compounds (such as sugars, proteins, amino acids, carotenes, organic acids, and other minor components) present in honey have shown antioxidant activity for a longer period. Consumption of 1200 mg/kg honey can increase both levels of antioxidants such as glutathione reductase, β-carotene, and vitamin C in healthy human subjects. While possible mechanism that could be involved in flavonoids substrate action for hydroxyl, metallic ion chelation, superoxide radical actions, hydrogen donation, free radical sequestration, is not known yet. Though the antioxidant effects of honey have been established in a structured manner, there are several unknown aspects yet to be found.

Immune responses and inflammation:

Human innate and adaptive immune systems might play protective roles against SARS-CoV-2, as no therapeutic intervention has been introduced. Angiotensin-converting enzyme-2 (ACE-2), a receptor of SARS-CoV-2 has been found on various cell surfaces including lungs, heart, kidney, and arteries. Stimulation of immune responsive cells occurs when a virus enters the body.

Honey may activate T-lymphocytes, B-lymphocytes, and neutrophils which ultimately produce cytokines such as interleukin-1 (IL-1), and interleukin-6 (IL-6), tumor necrosis factor- α (TNF-α). Honey also increases the serum levels of IFN-γ and IFN-γ receptor 1 (IFNGR1) in breast cancer in rats. As IFN-γ has an affinity to viral spike glycoprotein, nucleocapsid protein, and membrane protein, it may aid in targeting SARS-CoV-2. Honey has shown a cell dividing (mitosis) effect on both B- and T cells. This proves that it might have a role in inducing an adaptive immune response against SARS-CoV-2 infection. Nigerose, a sugar derived from honey is reported as immune stimulatory. In humans, honey provides beneficial effects by increasing the levels of ascorbic acid, glutathione reductase, minerals, and immune cells such as eosinophils, monocytes, and lymphocytes. At the same time, it decreases immunoglobulin E,

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ferritin, and enzymes including creatinine kinase, aspartate transaminase, lactate dehydrogenase, and alanine transaminase. It also decreases levels of different enzymes of liver and muscle and fasting blood sugars. These shreds of evidence suggest that honey may be able to give protection against SARS-CoV-2 but proper validation through in vitro and in vivo experiments is required.

Autophagy:

Autophagy is known as "self-degradation", is a highly conserved catabolic process that governs a cell to remove long-lived proteins, lipid, unwanted or damaged cells, and impurities, thereby helping to recover healthier cells, the process is aided by autophagosome formation and its merging with lysosomes to destroy the selected molecule. Natural honey is supplemented with flavonoids (kaempferol, catechin, and quercetin) and polyphenolic acid (caffeic acid and gallic acid) which have been found to show anticancer activity. One of the flavonoids present in honey i.e. quercetin has been found to inhibit proteasomal activity and mTOR signals, and promote substantial autophagy.

Antiviral properties:

The honey can suppress viral growth by inhibiting viral replication and/or virucidal activity. In some studies, honey has proved its potency against several RNA and DNA viruses i.e. influenza virus, varicella-zoster virus (VZV), rubella, herpes simplex virus (HSV), and has proved that it can be a potential antiviral agent. Another study reported that MGO, one of the major compounds of manuka honey, showed sensitivity against both influenza B and influenza A viruses proving its virucidal activity. Moreover, the synergistic effect of manuka honey with the anti-influenza A viral drugs zanamivir and oseltamivir has been reported and MGO is useful for the drug-resistant virus isolates. Therefore, these studies suggested that enveloped viruses might be sensitive to the virucidal ingredients of honey.

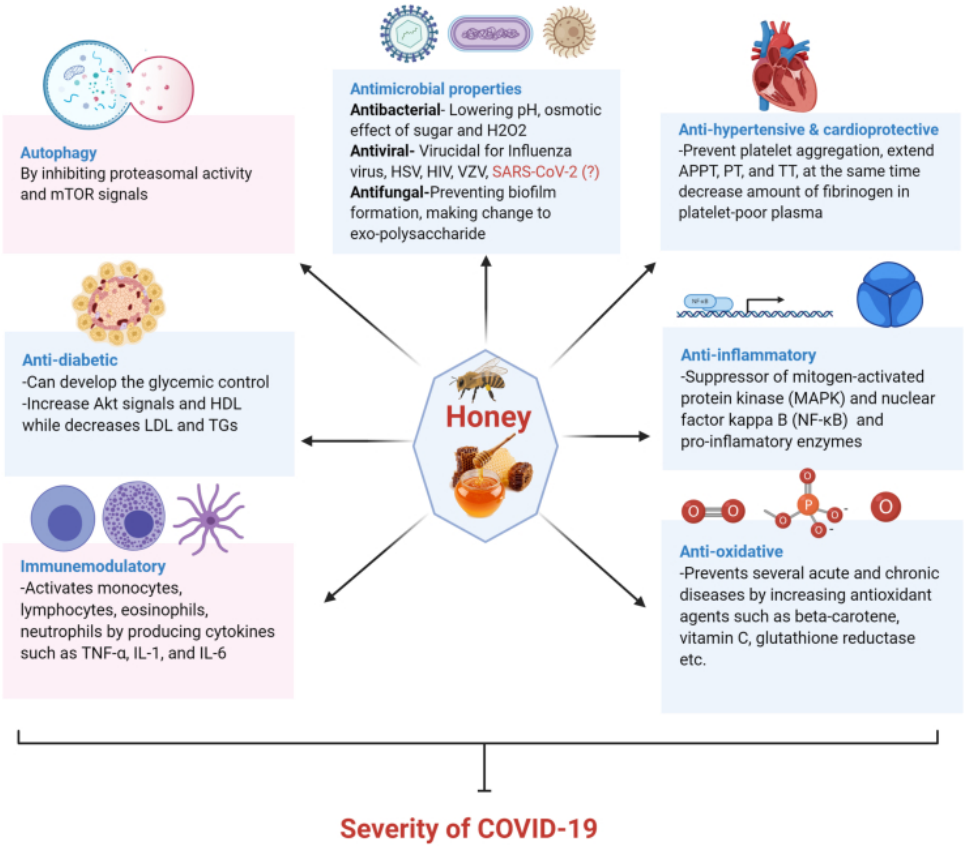

Fig no: 1. possible mechanisms involved in the pharmacological effects of honey on covid -19.

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Possible roles of honey against SARS-CoV-2 infection:

SARS-CoV-2 is an enveloped and positive-sense single-stranded RNA virus. As discussed above, several enveloped viruses might be killed by the virucidal ingredients of honey therefore it might also have a potent suppressive effect on SARS-CoV-2. Cell death is triggered by viral infection through draining lymphocytes which can be tackled by antioxidants. This proves that there is a relation between antiviral and antioxidant actions. Honey has a broad spectrum of antioxidant effects as described, it can be said that honey might act as protective agents for patients infected with viruses like influenza or corona. But to prove this, clinical trials and proper experiments are needed. The SARS-CoV-2 infected individual having a cytokine storm might be tackled with honey's antioxidant property along with increased IFN-γ level. Therefore, it is hypothesized that honey might be beneficial for SARS-CoV-2 infected patients through several major mechanisms such as direct virucidal properties, regulating/boosting host immune signaling pathways, and curing and/or improving comorbid conditions.

Current status and future directions:

The COVID-19 has been discovered at the end of 2021 and currently, it is a pandemic threat of international concern. Currently, there are no targeted therapies effective against COVID-19. However, many vaccines are undergoing clinical trials and a couple of drugs are going through re-purposing schemes. A phase-3 clinical trial of natural honey for the treatment of COVID-19 has also been started as mentioned by the National Institute of Health. It is already proved that honey plays a potential role against several enveloped viruses. Besides, honey acts as an antagonist of platelet-activating factor (PAF) which is involved in COVID-19. Therefore, we can say that honey may have a protective/beneficial effect on COVID-19. This review will be helpful to rethink the insights of possible potential therapeutic effects of honey in fighting against COVID-19 by strengthening the immune system. However, basic review on the effect of honey on SARS-CoV-2 replication and/or host immune system need to be investigated by in vitro and in vivo studies.

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