REVIEW ARTICLE

The SARS-CoV-2 Pandemic and the Role of Honey and its Products as an Emerging Therapeutic Regime: A Review

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ABSTRACT

The outbreak of pneumonia that broke out in Wuhan, in December 2019, later rapidly spread to the rest of the world. This was identified as Coronavirus disease 2019 (COVID-19) [officially renamed severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2)] caused by a zoonotic beta Coronavirus entitled 2019 novel Coronavirus (2019-nCoV). The aim of this study was to summarize the biological features of SARS-CoV-2, its clinical features and the possible antiviral effect of honey against SARS-CoV-2. For this purpose, recently published literature, official documents and selected up-to-date preprint studies were reviewed. The initial source of SARS-CoV-2 is still unknown but a possible animal-to-human transmission is indicated. Human spread of SARS-CoV-2 is due to droplet spread. The infected individual may present as symptomatic or asymptomatic, this varies from patient to patient mainly depending upon his/her immunity. To combat the current pandemic various modalities are under study, an important and harmless way of treatment might be the use of honey. Various studies have demonstrated antiviral effects of honey. Propolis and honey have shown promising anti-viral effect against SARS-CoV-2. Thus, the combined effect of honey and its products might open a door for developing a safe and highly efficient natural drug against COVID-19 infection.

KEYWORDS: SARS-CoV-2, COVID-19, Manuka honey, Propolis, Transmission, Droplets.

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INTRODUCTION

In December 2019, a novel Coronavirus emerged in the city of Wuhan, China that resulted in Coronavirus 2019 (COVID-19) pandemic. It then spread quickly nationwide. This novel Coronavirus was identified by the Chinese Centre for Disease Control and Prevention (CCDC). It is now named as Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).[1] After storming the Hubei province of China, the virus went beyond the international borders in no time and that's why World Health Organization (WHO) declared it as a pandemic.

SARS-CoV-2 is an enveloped positive sense RNA virus and is from the group of ß-Coronavirus of subgenus sarbecovirus (Subfamily: Orthocoronavirinae).[2] The further subgroups of Coronaviruse family are alpha (a), beta (b), gamma (c)and delta (d).[3] The alpha and beta Coronavirus are responsible for infecting mammals, however, gamma and delta infect birds. In humans, out of these, only six Coronaviruses have the etiology of infection. Among these strains, the alpha and beta strains have least infection capability and result in mild infection similar to common cold but the ß-

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CoV strains including SARS and MERS cause respiratory infections which are usually life-threatening.[4]

Structure of Coronavirus

Abulky non-structural poly protein is encoded by the genome of SARS-CoV-2. This protein is cleaved to generate 15/16 proteins. Out of which, four are structural proteins and five are accessory proteins.[5,6,7] The structural proteins include Spike (S) surface glycoprotein, membrane (M) protein, nucleocapsid (N) protein and envelope (E) protein. The N protein wraps around the genomic RNA. These structural proteins are fundamental for the assembly and infection of SARS-CoV-2. The spike or S surface glycoproteinis a transmembrane protein at the exterior of the virus with molecular weight of approximately 150 kDa. The attachment of the virus to the host cells is carried out by spike surface glycoproteins.[8]Angiotensin-converting enzyme 2 (ACE2) receptors expressed in lower respiratory tract cells are the main site where the S protein forms bond to the host cells. This glycoprotein is cleaved into two proteins, S1 and S2. S1 is in control for host virus range and S2 mediates the fusion of virus in the host.[9,10,11] M protein can attach itself to all of the structural proteins. Stabilization of nucleocapsid or N proteins is produced by its attachment with the M protein. It also promotes viral assembly by the stabilization of N protein-RNA complex. Envelop (E) protein in the SARS-CoV is obligatory for the production and maturation of this virus.[12]

Transmission

The original source of SARS-CoV-2 infection is till now unclear; however, the initial cases were reported in Wuhan city and were considered to be associated with the Huanan seafood market.[13] This indicated animal-to-human classical transmission. After few days, human-to human spread was indicated, as a large number of Corona patients were reported with no affiliation with the animal and seafood markets.[5,14,15,16] Human spread of SARS-CoV-2 was considered by droplets spread especially while coughing and sneezing. These droplets can remain suspended in air upto 3 hours and favor the virus spread.[10] The viral droplets, when acquired by the mucus membrane of the adjacent person can result in the infection of that person.[17] Indirect mode of spread of SARS-CoV-2 is also very important. This mainly occurs via shaking of hand of the infected person, contacting any objector any surface contaminated with the virus and afterward repeatedly touching of the eyes, nose or mouth. It has also been reported that the exposure to excreta of a Corona positive subject might be a possible indirect mode of SARS-CoV-2 infection. An important method of transmission also consists of "hidden transmission". It is defined as the unintentional spread of SARS-CoV-2 infection by asymptomatic virus carriers to his close contacts.[5]

Clinical Features

Malaise, fever, dry cough, body aches and shortness of breath are the main clinical features of SARS-CoV-2 infection. Nasal congestion or a runny nose, sore throat, vomiting and even diarrhea in some cases have also been observed. After one week of onset, severely infected patients frequently develop dyspnea and/or hypoxemia which may progress to septic shock. On the other hand, some patients may show mild/no fever with mild/no fatigue. Some asymptomatic patients have also been detected.[15,18]

Honey as a Medicine

To combat the current pandemic various modalities are under study, an important and harmless way of treatment can be the use of honey. It is a substance derived from the nectar of flowers, produced by bees. It is a unique mix of phenolics and sugars. It contains amino acids and other substances. The diverse types of honey obtained from various blossoming plants vary significantly in their capacity to eliminate microscopic organisms.[19,20] The inhibitory activity of honey to microbial growth is attributed to its increased level of sugars and low pH. The microbial inhibitory action of honey still remains when it is diluted to negligible levels. The sugar (glucose) is oxidized to produces hydrogen peroxide which has potent bactericidal activity. Hydrogen peroxide production is very little in manuka honey and might be optimized by catalase producing organisms, but the microbial inhibitory action still exists.[21,22]

Antiviral Effect of Honey

Honey's strong viricidal activity has been suggested by a number of studies.[23,24] A study reported that honey has a major anti-viral activity against rubella virus. The lesions of herpes simplex gingivostomatitis in children were also regressed by the use of honey.[25] Similarly, royal jelly was also established to possess potent antiviral effect against herpes simplex virus (HSV).[26,27] Royal jelly's viricidal activity has been attributed to 10-HAD (10-Hydroxy-2-Decenoic Acid).By the action of this compound, the activity of white blood cells (WBCs) is increased, especially against HSV and hepatitis viruses. Ultimately, causing increased viral destruction.[23] Pure clover and Manuka honey may have anti-Varicella Zoster virus (VZV) activities but its mechanism of actions still to be discovered.[28]The antiviral activity of honey was also observed against Respiratory Syncytial Virus (RSV).[29]

Now it has been well established by many studies that all types of honey, and more specifically manuka honey, has strong anti-viral activity against influenza virus. The range of inhibitory activity of honey against viral pathogenesis and its mechanism of actions are still unclear.[24]

Anti-Corona Effect of Honey

The antiviral effect of honey and its products against Coronavirus have also been observed in some studies. "Propolis" a bee product is the most well-known and old customary medication. It was firstly identified by the Hippocrates ("pro" for protection, and "polis" for beehive or city). This is made by extraction of a product from youthful buds of trees especially poplar and willow. This extract is blended by the honey bees with their saliva. The hexagonal beehive is made from this product for the protection of their larva from multiple microorganisms. For this reason, propolis is considered as "herbal" medicine. It has been demonstrated to hold inhibitory activities against a vast group of pathogens; therefore, it has dual antibacterial and antiviral activity.[30] A "Pathogenic" kinase (PAK1) atypical activation is the causative factor for a number of diseases. These diseases include inflammation, viral infection, cancers, immunosuppression and ageing.[31] Propolis contains caffeic acid (CA) and its ester (caffeic acid phenethyl ester = CAPE). This natural ingredient has shown inhibitory activity against RAC, which activates PAK.[32,33] PAK1is also responsible for infection with numerous viruses including influenza, HPV, HIV, and SARS-CoV-2 and causes immune-suppression. Studies have shown that propolis would be useful for boosting the immune system and would also block Coronavirus-induced fibrosis of lungs.[30]

In silico studies have shown antiviral activity of six compounds of honeybee and propolis against the COVID-19infection.This study noticed that the four compounds; Caffeic acid phenylethyl ester (CAPE), Galangin Chrysin and 3-phenyllactic acid have strong binding affinity with good glide score and might inhibit COVID-19 at the stage of protease activity and viral replication.[34] A number of studies have reported various ways of using honey as prophylaxis and treatment option for ongoing Corona pandemic.[35,36]

CONCLUSION

The cumulative effect of honey and its products has opened a new paradigm for developing a secure and an efficient natural drug against COVID-19 pandemic. Using honey as a treatment and prevention of Coronavirus disease might be very effective due to its no side effects and immune system boosting potential.

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CONFLICT OF INTEREST

None to declare.

FINANCIAL DISCLOSURE

None to disclose.

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Author's Contribution

FTZ: Acquisition of the published data, drafting of manuscript.
SS: Conception and design of study and final approval of the manuscript.
MI & AG: Critical revision of manuscript for important intellectual content.
UA: Drafting of manuscript.