Propolis anti-viral activity towards CODIV-19: is it effective?

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Propolis anti-viral activity towards CODIV-19: is it effective?

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ABSTRACT

The SARS-CoV-2 virus emerged in December 2019 and then spread rapidly worldwide, in March 2020, WHO raised the threat to COVID-19 epidemic to the "very high" level. Scientists are endeavoring to find antivirals specific to the virus., However, there is a need for the administration of a natural product that has antiviral activity for the protection from the rapidly-transmitted SARS-COV-2. Propolis as a natural safe product may has a protective antiviral activity against COVID-19, and gives the possibility of reducing COVID-19 reproduction number.

Introduction

According to the World Health Organization (WHO), viral diseases continue to emerge and represent a serious issue to public health. In the last twenty years, several viral epidemics such as the severe acute respiratory syndrome coronavirus (SARS-CoV) in 2002 to 2003, and H1N1 influenza in 2009, have been recorded. Most recently, the Middle East respiratory syndrome coronavirus (MERS-CoV) was first identified in Saudi Arabia in 2012 (1).

On February 11, 2020, the WHO Director-General, Dr. Tedros Adhanom Ghebreyesus, announced that a disease caused by a new CoV was "COVID-19," which is the acronym of "coronavirus disease 2019" (1).

As of March 16, 2020, a total of 167,511 confirmed cases of coronavirus disease 2019 (COVID-19) and 6,606 deaths have been reported globally (2). The data also showed that this novel epidemic doubled about every seven days, whereas the basic reproduction number (R0) is 2.2. In other words, on average, each patient transmits the infection to an additional 2.2 individuals (1). Thus, WHO raised the threat to the CoV epidemic to the "very high" level (2).

It is suggested that the COVID-19 is likely has a zoonotic origin. Person-to-person transmission of COVID-19 infection led to the isolation of patients that were subsequently administered a variety of treatments. Two main strategies were announced, the first is to find the most effective treatment for those who infected by the virus, the second is to reduce person-to-person transmission of COVID-19 (3,4). Lowering the susceptibility to COVID-19, thus lowering the replicability of the virus (for reducing the transmitted copies from a person to another thus allowing the time for the immune system to give a propriate response), may be the third intermediate strategy.

At the moment, the therapeutic strategies to deal with the infection are only supportive, and prevention aimed at reducing transmission in the community is our best weapon (1).

The immune system role

Of note, the fatal cases were primarily elderly patients, in particular those aged ≥ 80 years (about 15%), and 70 to 79 years (8.0%). Approximately half (49.0%) of the critical patients and affected by preexisting comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease, and oncological diseases, died. While 1% of patients were

aged 9 years or younger, no fatal cases occurred in this group (1). These data suggest that the immune system has a competent counter effect.

However, this competency depends on age. The competency of the adaptive immune function decreases with age, primarily because of the decline in production of naïve lymphocytes in the bone marrow and thymus as well as the expansion of incompetent memory lymphocytes (5).

Many diseases either communicable or non-communicable occur where the immune system go awry (6), and this condition is described by the term "Immunological chaos" that may lead to serious problems like in appropriate secretion of cytokine and chemokine and inflammatory molecules (7).

Significantly high blood levels of cytokines and chemokines were noted in patients with COVID-19 infection that included IL1-β, IL1RA, IL7, IL8, IL9, IL10, basic FGF2, GCSF, GMCSF, IFNγ, IP10, MCP1, MIP1α, MIP1β, PDGFB, TNFα, and VEGFA. Some of the severe cases that were admitted to the intensive care unit showed high levels of pro-inflammatory cytokines including IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1α, and TNFα that are reasoned to promote disease severity (8). The SARS-COV-2 obviously causes immunological chaos.

Treatments of COVID-19

Physicians and scientists around the world work tirelessly to mitigate the impact of this threat, especially in testing the drug's efficacy and safety in the treatment of coronavirus disease 2019 (9). Research has revealed more than 30 agents including Western medicines, natural products, and traditional Chinese medicines that may have potential efficacy against COVID-19. Some of these agents have been quickly tested in clinical studies and demonstrated preliminary efficacy against COVID-19. Antivirals including interferon-α (IFN-α), lopinavir/ritonavir, chloroquine phosphate, ribavirin, and arbidol In addition, Chinese herbal medicines such as Rhizoma Polygoni Cuspidati and Radix Sophorae Tonkinensis may contain active ingredients against SARS-COV-2 (10).

The suggestion of another natural products that may has antiviral activity against SARS-COV-2 may help both, treating the affecting people and immunizing the unaffected people (especially elderly), and may give a hand of safe and rapid strategy!

The anti-viral treatments mainly depend on two mechanisms. The first is by improving the immune response toward SARS-CoV-2 (e.g. IFN- α which enhances the proliferation and the activation of human immune cells). The second is by affecting on the viral RNA, thus its replicability. (e.g. Favipiravir which is a new type of RNA-dependent RNA polymerase inhibitors) (9). These two mechanisms may be introduced by our suggested natural product (Propolis), in addition to its predicted role in the suggested third strategy mentioned above.

What is propolis?

Propolis is a natural resinous mixture produced by honeybees from substances collected from parts of plants, buds, and exudates. The word propolis is derived from Greek, in which pro stands for "at the entrance to" and polis for "community", which means this natural product is used in hive defense. Another name of propolis is bee glue. Due to its waxy nature and mechanical properties, bees use propolis in the construction and repair of their hives for sealing openings and cracks and smoothing out the internal walls (11).

Since ancient times propolis has been extensively employed by man, especially in folk medicine to treat several maladies. Egyptians used bee glue to embalm their cadavers as they well knew about its putrefactive properties. Incas employed propolis as an antipyretic agent. Greek and Roman physicians used it as mouth disinfectant and as an antiseptic and healing product in wound treatment, prescribed for topical therapy of cutaneous and mucosal wounds (11).

Nowadays, propolis is a natural remedy found in many health food-stores in different forms for topical use. It is also used in cosmetics or as popular alternative medicine for self-treatment of various diseases. Due to its antimicrobial, antiviral and antioxidant properties, it is widely used in human and veterinary medicine, pharmacology (12).

The Immune and anti-viral roles of Propolis

Beside the antibacterial activity of propolis especially against Gram-positive (13), and the antifungal properties (14), the propolis shows many other useful characteristics (12), and most of these characteristics may be of a potential effect on COVID -19 as follow:

Lung enhancement

propolis was widely used due to its healing properties and in the Second World War it was

employed in several Soviet clinics for tuberculosis treatment, due to the observed decline of lung-problems (15). In addition, propolis-treated patients (from Asthma) showed a reduced incidence and severity of nocturnal attacks and improvement of ventilatory functions (16).

The immunomodulatory role

Propolis seems to has a role in the treatment of the Immunological chaos. Propolis-treated asthma was associated with decreased prostaglandins, leukotriene, and proinflammatory cytokines (TNF-, IL-6, and IL-8) and increased IL-10 (16).

Propolis is notable for its antioxidant properties. The antioxidants present in propolis play a great role in its immunomodulatory properties (12,17). The flavonoids concentrated in propolis are powerful antioxidants. It was reported that propolis increases the cellular immune response through the increase of mRNA for interferon-γ and activates the production of cytokines (18). It was observed that all propolis had strong antioxidant activity due to their contents of total phenols and flavonoids (19).

Propolis showed anti-inflammatory properties, where it has inhibitory effects on myeloperoxidase activity NADPH-oxidase ornithine decarboxylase, tirosine-proteinkinase, and hyaluronidase from guinea pig mast cells (20). An ethanol extract of propolis suppressed prostaglandin and leukotriene generation by mouse peritoneal macrophages in vitro and during zymosan-induced acute peritoneal inflammation in vivo (21).

In addition, the immunomodulatory effect by propolis was investigated, and the action of a water-soluble derivative (WSD) of natural Propolis was suggested to augment nonspecific host defense via macrophage activation (22).

The antiviral activity

Many studies showed that propolis shows antiviral activity. Aqueous and ethanol extracts of propolis were analyzed phytochemically and examined for their antiviral activity in vitro. Both propolis extracts exhibited high levels of antiviral activity against herpes simplex virus type 1 (HSV-1) However, the extracts containing many different components exhibited significantly higher antiherpetic effects as well as higher selectivity indices than single isolated constituents (23).

In addition, Hatay propolis samples was determined to have important antiviral effects compared with acyclovir. In particular, the synergy produced by antiviral activity of propolis and acyclovir combined had a stronger effect against HSV-1 and HSV-2 than acyclovir alone (24).

While the Brazilian propolis was indicated to possess anti-influenza virus activity and to ameliorate influenza symptoms in mice. AF-08 may be a possible candidate for an anti-influenza dietary supplement for humans (25).

Propolis samples from different geographic origins were investigated for their antiviral (against Avian influenza virus) activities. Most samples showed antiviral activity. And It seems that propolis has general pharmacological value as a natural safe mixture (26).

Propolis as Protective natural product

As a result of propolis protective and safe properties (either immunomodulatory or antiviral properties), it can be suggested for prescribed to unaffected people in general, and for people who are close to affected areas in specific. This may lower the predicted reproduction number.

Propolis potential effect for treatment of COVID-19

The guidelines recommend antivirals like IFN-α inhalation, ribavirin, Chloroquine phosphate and arbidol for treatment of COVID-19 (9). The administration of propolis with these agents may give promising synergetic effect. (e.g combining of propolis with IFN-α vapor inhalation).

Conclusion

Finding a potential natural agent may help in mitigating the impact of COVID-19 global threat. And Propolis may show a protective antiviral activity against COVID-19, and gives the possibility of reducing COVID-19 reproduction number.

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