



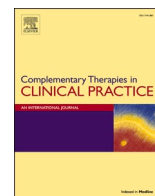
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Propolis and coronavirus disease 2019 (COVID-19): Lessons from nature

Always on the lookout for articles from the journal *Complementary Therapies in Clinical Practice* one in particular has attracted a lot of attention due the eminent clinical importance of this study. Very recent, Xu and Zhang published an excellent review article clearly demonstrating that the intervention of traditional Chinese medicine can reduce severe symptoms of patients with the new coronavirus (SARS-Cov-2) [1]. Considering that there is no standard therapy for SARS-Cov-2 prevention or treatment, we would like to add some thoughts that may open the debate about the possible viability of propolis in this situation.

SARS-Cov-2 which hit the central Chinese city of Wuhan in late December 2019, and subsequently spread rapidly to all provinces of China and all countries worldwide, has had a devastating impact on global public health [2]. SARS-Cov-2 is characterized by a high contagiousness. In 85% of cases it causes subclinical or mild disease, but compared to the flu it more easily causes respiratory complications (e.g., severe pneumonia (ground glass opacities) and interstitial pneumonia) in 10–15% of cases. 5% of infected patients require ICU admission [2]. During these worst-case scenarios, lethality is estimated at around 0.7–7% [2,3]. Compared to previous coronavirus epidemics, the contagiousness is higher, but the mortality decidedly lower compared to the *severe acute respiratory syndrome* (SARS) of 2002 and the *Middle East respiratory syndrome* (MERS) of 2012, both of them related with higher mortality (9.5% and 34.4%, respectively) [2,3]. Intensely, a series of translational studies for drug and vaccine development has been carried out worldwide with the aim of combating the SARS-Cov-2 [4]. In these lines, medicinal plants and the pure natural molecules isolated from plants has shown an important inhibitory antiviral activity against SARS-Cov-2 [4]. From this clinical reasoning, the use of propolis as a possible complementary treatment in patients with SARS-Cov-2 should play an important role in this scenario.

Although nature has served as a source of healing since evolution of mankind, nature is also inspiring the next generation of biomedical research and technology [5,6]. Despite this fact, it is also important to note that not all physicians and researchers are prepared to deepen their knowledge about biomimicry, probably because of a lack of exposure to biomimicry during training [7]. Biomimicry (from the Greek words *bios*, meaning “life,” and *mimesis*, meaning “to imitate”) it is an area of science that studies nature’s models and then emulates these forms, processes, systems, and strategies to solve human problems [5–8]. According to experts, biomimicry is based not on what we can extract from organisms and their ecosystems, but on what we can learn from them [6,7]. Regarding our proposal on propolis, it is already established in the literature that one of the ways that honey bees’ colonies maintain health and immunity is for the formation of a propolis envelope within the nest that acts as an important antimicrobial layer [9]. Following these reasonings, what would be the benefit of propolis in SARS-Cov-2?

Propolis is defined as a balsamic and resinous product composed of a

mixture of different plant parts and molecules secreted by bees [10]. Importantly, propolis is used by humans since ancient times for its medicinal properties [11]. As a natural compound with proven pharmacological and pharmaceutical properties, propolis has actually a wide application, with antioxidant, antimicrobial, antiviral, antiparasitic, antitumor, immunomodulatory, anti-inflammatory and hepatoprotective properties [10,12]. Thus, these different therapeutic effects of propolis justify its potential for the development of products for use in human and animal health [10]. Concerning the use of propolis in SARS-Cov-2-infected patients, some interesting considerations must be put forward.

Firstly, several experimental and clinical studies have clearly shown that propolis extracts from temperate climate presents a potent and broad-spectrum antiviral activity against a diverse panel of viruses, including HSV-1, HSV-2, Influenza virus type A and B, Parainfluenza virus, Adenovirus, HIV, infectious bursal disease virus and avian reovirus, Newcastle virus disease, bovine rotavirus, pseudorabies virus, feline calicivirus, canine adenovirus type 2, and bovine viral diarrhea virus [11]. The precise mechanisms of this antiviral activity is unknown, however, it is very likely that propolis inhibits the virus entry into the cells, and with that disrupt the viral replication machinery [11]. Concerning SARS-Cov-2, studies with propolis are still rare but those available are quite promising [11]. Three decades ago, *in vitro* studies evaluated the effect of propolis flavonoids on several DNA and RNA viruses, including coronavirus [11,13]. The authors found that chrysin and kaempferol were highly active in inhibiting viral replication [11, 13]. Another important propolis flavonoid applied in SARS research is quercetin [11,14]. In these terms, it has been demonstrated that quercetin in conjunction with vitamin C shows aminopeptidase inhibitor activity, interrupting the main proteases of SARS and MERS [11,14].

On the whole, due to the recent SARS-Cov-2 pandemic, studies with propolis can be considered very promising. Thus, our research group is totally convinced of the broad action of propolis in the various biological systems [15]. Finally, the safety, health effects, low cost, and easy use make propolis an intriguing supportive therapy for SARS-Cov-2.

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