Poplar brown propolis titrated in polyphenol and Covid-19 : Feedback from a retrospective field study

(Short version paper)

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Abstract

We report and discuss the interest, during the Covid-19 epidemic, of supplementation with poplar brown propolis titrated in polyphenol through a retrospective field study of people living in hospital for dependent elderly people. Propolis does not reduce the lethal risk but seems overall to promote asymptomatic clinical forms or the absence of contamination with Covid-19 ($p < 0.05$). Propolis appears to decrease the inflammation induced by Covid-19 and also boost the immune system. Polyphenols seem to play an essential role in the immunomodulation and anti-inflammatory and anti-viral actions of propolis. This confirms the interest of the use of a propolis characterized botanically and titrated in polyphenol for effective action.

1. Introduction

The Covid-2019 disease is responsible for the pandemic that is shaking the world. It is an emerging infectious disease that appeared in China at the end of 2019. The pathogen is coronavirus 2 (SARS-CoV-2). Global research is very active and lot of informations about this virus are disseminating. Thus, the Covid-19 viral genome is composed of RNA. In addition, the main viral mechanisms of human cell infection and virus replication now appear to be fairly well defined.

Based on this knowledge, various potentially interesting therapeutic targets are emerging. They are currently mainly four in number. These are 1) the inhibition of the activation of the crown of so-called "spike" proteins of the coronavirus, 2) the inhibition of the binding and fusion of the viral envelope with the membrane of the human cell, 3) inhibition of the replication of the viral genome, 4) inhibition of the exploitation by the virus of the synthesis machinery of the infected human cell. Others aim to counter major clinical complications due to the "cytokine storm" triggered by the virus.

Therapeutic molecules present on the market are under study. The results of these early studies appear chaotic and the public's hyper-information generated general confusion. Faced with the progression of the Covid-19 epidemic, and because propolis is known to the general public to stimulate immune defenses, a group of individuals living in hospital for dependent elderly people during the general confinement that occurred in France in the spring of 2020, decided to add propolis to diet. We report and discuss the retrospective results of this field study of propolis supplementation.

2. Feedback from a retrospective field study

Twenty four dependent elderly people supplemented their diet served in their hospital with brown poplar propolis titrating 400 milligrams / day of polyphenol, divided into two takes over four consecutive weeks in April 2020.
Thirty-five other people of the same profile and from the same hospital shared the same meals without supplementation.
During this period, 38% of Covid-patients are reported in individuals eating propolis versus 43% in those who do not eat propolis. The initially clinical Covid-19 disease diagnoses were subsequently confirmed by a positive Covid-19 serology. The observation of a lethal evolution was the same in propolis users and non-users (8% versus 9%).
The asymptomatic clinical forms (with positive seroconvertion) and the proportion of non-sick subjects (with absence of seroconversion to Covid-19) are greater in propolis users compared to others (respectively 38% versus 23% and 33% versus 21%).
The different results between users and non-users of propolis above are not statistically different (non-parametric Z tests comparing two proportions - er <1.96).
However, the proportion of very favorable clinical forms (sum of the proportions of asymptomatic and non-sick subjects) is significantly higher in propolis users (71% versus 44% - er = 2.04 - p <0.05).
Laboratory tests carried out in individuals sick with Covid-19 have all shown leukopenia often associated with big lymphopenia.
In individuals who used propolis after the onset of symptoms, and in whom a biological assessment was carried out at the onset of the disease, a very rapid rise in leukocytes was observed, in particular lymphocytes, with the absolute values doubling within a few days. This finding is not observed in those who did not use propolis.

3. Discussion

Several papers have studied the effect of propolis and / or its constituents on the SARS-Cov-2 virus. An in silico study has shown that several molecules of propolis including CAPE (present in brown poplar propolis) would be able to bind to a protein essential to the life cycle of this virus [1]. In order to enter the host cell, the SARS-Cov-2 virus needs to bind to an ACE-2 surface protein (angiotensin-converting enzyme) which is associated with a transmembrane protein (TMPRSS2).
In vitro studies have been shown that certain constituents of propolis (CAPE, chrysin, pinocembrin, kampferol) have a high binding affinity on these proteins, thus limiting their accessibility to the virus [2].
Once penetrated into the host cell, the virus activates a nuclear signaling pathway (PAK1) which results in immunosuppression of T and B lymphocytes supposed to fight the virus. A number of experimental observations, in vitro and in vivo, have been clearly shown the dependence on PAK1 of the coronavirus viral pathogenesis. Propolis has been shown to be an inhibitor of the PAK1 pathway [3].
Propolis PAK1 inhibitors appear to be active against the Covid-19 virus through complementary inhibitory effects with 2 processes. First, inactivation of PAK1 suppresses pulmonary inflammation and CCL2-dependent fibrosis induced by coronavirus (CCL2 is a chemokine-like

cytokine that is attractive to certain immune cells) [4]. This was recently shown using a phosphatase called PTEN. Second, PAK1 is responsible for blocking the host's immune system [5]. Thus, suppressing the PAK1 brake by a PAK1 inhibitor frees the immune system for the production of antibodies against the Covid-19 virus.
Among PAK1 inhibitors, phenethyl ester of caffeic acid (CAPE) found in propolis and caffeic acid have been the first natural ingredients capable of blocking the action of PAK1 [6]. The PAK1 inhibitor CAPE is involved in the anticancer action of different propolis, as well as in brown poplar propolis [7].
However, propolis does not seem able to reduce the serious lethal forms which affects approximately 8% (versus 9%) of dependent elderly people of this retrospective field study. This rate is very close to the case fatality rate of 8.7% reported by Public Health France on September 10, 2020, knowing that 90% of deaths concern individuals aged 65 and over and that death occurs at average age 84 years old. Can we say that the different mechanisms of action of propolis are at the origin of the very favorable clinical forms observed in propolis users in this retrospective field study (71% versus 44% - er = 2.04 - $p < 0.05$)? Does propolis mobilize the immunity of the individual infected with Covid-19 more effectively, by promoting a faster rise of white line cells? Further works are needed to answer these questions, to shed light on the results of this retrospective field study.
The PAK1 inhibitory power of propolis varies from product to product, depending on the chemical nature of the ingredients and their content. Likewise, the bioavailability and therefore the potency of propolis PAK1 inhibitors, which depends on their chemical structure, must be taken into account [8]. The use of a botanically characterized propolis and titrated in polyphenol is a minimum quality precaution to be observed.
Propolis is known to be a safe product, believed to only expose "minor" side effects such as contact sensitization. However, we must report that 4 users of propolis treated with Fluindione showed a decrease in the anticoagulant action of this molecule. This drop in anticoagulant action is characterized by a decrease in the INR (International Normalized Ratio) below the therapeutic efficacy value. This phenomenon disappeared when the propolis was stopped and it was not observed in non-users propolis, whether or not sick with Covid-19.

4. Bibliography

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