THE IMMUNOMODULATORY EFFECT OF PROPOLIS: A REVIEW

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Summary

Propolis has attracted the interest of the researchers' in the last decades because of several biological and pharmacological properties, such as immunomodulatory, antitumoral, antimicrobial, antiinflammatory, antioxidant, among others (3).

Propolis-containing products have been intensely marketed by the pharmaceutical industry and health-food stores (4). Propolis, sometimes called "nature's penicillin", is a complex mixture of mostly pollen and waxes that bees collect from plants and then use to sterilize, cement, and varnish the hives. Propolis also protects the colony from diseases because of its antiseptic efficacy and antimicrobial properties (19). It is rich in amino acids, trace minerals, flavonoids, and vitamin K. Although in preclinical studies propolis has been confirmed to be effective as antibacterial, antifungal, and anti-inflammatory, clinical studies are needed to confirm these roles and determine the therapeutic dosages and conditions for which it is best suited (8).

There seem to be promising uses for propolis as an alternative antibiotic and anti-inflammatory drug, especially due to lack of side effects encountered in other categories of medication.

This review aimed to discuss the immune stimulating effect of propolis.

Key words: propolis, immunomodulatory effect

The use of propolis goes back to ancient times, and it has been used as a medicine in local and popular medicine in many parts of the world, both internally and externally. Egyptians, Greeks and Romans reported the use of propolis for its general healing qualities and for the cure of some skin lesions. Propolis has always been reputed as an anti-inflammatory and ulcers healing agent (9). It is still one of the most frequently used remedies in the Balkan States (2), and it has only been in the last decades that scientists have investigated its constituents and biological properties. The color of the propolis varies from green, to dark redish-brown. Propolis has a characteristic smell and shows adhesive properties because it strongly interacts with oils and proteins of the skin. In general, the natural propolis is composed of 30% wax, 50% resin and vegetable balsam, 10% essential and aromatic oils, 5% pollen, and other substances. After its administration to mice or to humans propolis does not seem to have side effects (13, 14, 23).

At least 200 different constituents of propolis are defined as terpenes, various phenylpropane derivatives such as caffeic acid (CA) esters, flavonoids, amino acids, or a large number of aldehydes and ketones (1, 11).

An efficient, precise, and reliable method was developed for quantification of propolis extractive solution using HPLC with UV detection. The analytical procedure is reliable and offers advantages in terms of speed and cost of reagents.

Immunomodulatory action of propolis

Action on macrophages

Before the standardization of propolis, since researchers have used different concentrations of propolis, the greatest problem to carry out the immunological assays was to design the experimental protocols. Little was known about the immunomodulatory action of propolis until the 1990s, but in the last decade new and interesting results were published, providing an important contribution to this research field.

Different authors suggested that propolis modulates the non-specific immunity via macrophage activation. Propolis stimulated cytokines production, such as IL-1_ and TNF-_, by peritoneal macrophages of mice (7, 18), and it was also able to modulate both in vivo and in vitro production of C1q by macrophages as well as the complement receptor function either directly or via cytokines (7).

It was demonstrated that six isolated compounds of propolis, identified as caffeoylquinic acid derivatives, enhanced the motility and spreading of macrophages (24). Exposure of macrophages to a varied number of stimuli, such as microorganisms and their products, antibodies or complement components-opsonized antigens, phorbol miristate acetate (PMA), Con A, immune complexes, leukotrienes, chemiotactic peptide fMLP (n-formyl-methionylleucyl- phenylalanine) or cytokines may result in further metabolic changes, such as generation of oxygen intermediates. The production of such reactive species appears to be one of the mechanisms by which macrophages become microbicidal.

Propolis immunomodulatory action was thought to be limited mainly to macrophages, with no influence on lymphocyte proliferation (7). However, Ivanovska et al. (12) demonstrated that splenocytes from mice treated with cinnamic acid, a propolis constituent, possessed an enhanced ability to incorporate thymidine, in the presence of mitogens such LPS, phytohemagglutinin (PHA) or Con A, suggesting a proliferative tendency of these cell cultures in the absence of mitogens.

The immune- stimulating effect of prophylactic propolis treatment was studied in clinical studies. Propolis was given, and cytokine secretion capacity was studied during and after treatment. The cytokine secretion capacity (but not the cytokine plasma levels) increased significantly during the treatment period in a time-dependent manner. The authors concluded that propolis was able to elicit an enchanced immune reactivity without side effects (5). A report on immunomodulatory activities of aqueous extracts of propolis (7) showed that a water-soluble extract of propolis (WSDP) increased the protection towards Gram-negative infections, probably via macrophage activation.

Conclusions

Propolis exhibits broad-spectrum activities, including antibiotic (10), antiinflammatory (25), antioxidant (21), antiviral, and tumor cell arrest (15, 16, 17, 21). The literature review clearly indicates that antibiotic activities, immune modulatory properties as well as antiinflammatory, wound healing, and antitumor effects may be due to different components of the individual ethanolic or aqueous extracts of propolis. These data are promising for obtainment of new products with enhanced therapeutic effects and bioavailability.

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