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Review Article

Propolis: A Therapeutic Alternative for Oral Cavity

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Abstract

Propolis a natural product made by honey bees (*Apis mellifera*) from the shoots and exudates of different plants, has been used in traditional medicine since ancient times, due to its biological properties. The chemical composition of this product of the hive is highly complex and dependent on the vegetation surrounding the collection site. Propolis has a great variety of medicinal properties, among which we can mention its cicatrizant, anesthetic, anti-inflammatory, anti-fungal and anti-viral antibacterial, vasoprotective and anti-tumor capacity. Propolis is also an antioxidant. Countless uses can be distinguished for its application in various industries: pharmaceutical (both in human medicine and veterinary medicine), agriculture and in the food industry. The values of phenolic compounds (flavonoids), obtained through the analysis of propolis from different areas of the Province of Córdoba, show a good concentration of these active ingredients (up to 26% in the sample). These results are positive for the qualitative analyzes of flavonoids, but it is not an absolute result, but it is a result of great value about its chemical composition and possible relation with its biological activity. This review is based on providing an updated view on the use of propolis in the area of dentistry.

Keywords: Propolis; Dentistry; Antimicrobial; Flavonoid; Anti-Inflammatory

Introduction

Propolis is a resinous and complex product, with a variable physical appearance, which is collected and transformed by the honey bees, *Apis mellifera Linnaeus*, 1758, from the vegetation they visit. It may be ocher, red, brown, light brown or green, some are friable and firm, while others are gummy and elastic [1-3].

Due to the bee's participation, the composition of the propolis differs from the vegetable resins, so it can be considered as a product of mixed, vegetable and animal origin [4-6].

Recent research in the field of the chemistry and pharmacology of propolis has allowed for its broader and more effective use in improving human health because of its sui generis biological activity and its ability to be a "natural product capable of behaving as a living product "with possibilities of establishing multiple synergistic combinations, conditioned by its exceptional richness in natural active principles, which exceed 150 constituents [7-9].

The main phenol compounds identified are: flavonoids, aromatic acids and their esters, aromatic aldehyde, coumarins, phenolic triglycerides. In terms of pharmacological action, the main constituents of propolis are phenolic compounds. These are characterized by the presence of at least one hydroxyl group directly attached to an aromatic ring [10-12].

Studies on the uses of propolis and concluded that propolis is a natural product of great interest for medicine and dentistry, used in various investigations related to the treatment of multiple pathologies and thanks to the advancement of analytical techniques has allowed to know better Its composition and study the activity of its components, emphasized that it is a bioactive compound that has important antimicrobial, anti-inflammatory and anticariogenic effects; Suggesting that there is strong evidence confirming propolis as a source of increased oral health based on its biological principles [13,14].

With the passing of the years and the appearance of more and more frequent problems related to the use of pharmacological chemical compounds, patients are increasingly asking dental professionals to apply a natural treatment if possible to avoid problems related to intolerances all types [15,16].

Therefore, the fundamental objective of this review is to provide up-to-date information on the use of propolis in dentistry; As this compound has been and is currently used in a variety of entities such as mouth ulcers, facial septic wounds, gingivitis, periodontal disease and alveolitis, also helping the process of repair and healing of collagen fibers and fibroblasts; Reason why it constitutes a compound with great effectiveness in the elimination of the microbial flora buccal [17-19].

Biological and therapeutic properties

From the 1960s, the first scientific investigations were carried out, revealing the complex structure of propolis and revealing numerous pharmacological applications. Scientists from different disciplines have deepened their study, so today there is an answer to many questions about the mechanisms of action that explain their antimicrobial properties, healing, immune system stimulants and antioxidants [20-22].

Antimicrobial properties

The complex composition gives propolis antibacterial, antimycotic and antiviral capacity [23].

Antibacterial capacity

The indiscriminate use of antibiotics has generated bacterial

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resistance, so it is necessary to have preventive and therapeutic alternatives, such as propolis to which no resistance has been described [24].

The antibacterial properties of propolis have been attributed mainly to flavonoids such as pinocembrina, galangina, pinobanskina and phenylethyl ester of caffeic acid (CAPE), which is an active component of propolis that exerts a great variety of changes Systems.

The cinnamic and flavonic compounds of propolis, which alter the membranes and inhibit bacterial motility, probably contribute to this action and the synergism observed with some antibiotics. The use of flavonoids against bacterial or fungal infections aims to kill the cells of microorganisms or to hinder the diffusion effects of bacterial toxins [25].

A study conducted in the Department of Biochemistry at the University of Oxford, published in Microbiology Research, reports that cinnamic acid and some flavonoids deactivate the energy of the cytoplasmic membrane, inhibiting bacterial motility, making them more vulnerable to attack of the immune system and potentiating the antibiotics.

There are few studies related to the biochemical mechanism of antibacterial action of compounds present in propolis. Some authors report that the compounds present in several propolis induce a direct or indirect damage to the cytoplasmic membrane of Staphylococcus aureus, as is the case of flavonoid galangina. Also, some propolis is stronger than others against *S. aureus* cells that are developing in the late exponential phase [26].

Antiviral capacity

Propolis flavonoids induce the production of interferon's (INFs). These substances have several antiviral effects, including cell membrane strengthening, induction of nucleases that destroy the viral genome, and modification of the initiation factor phosphorylation pattern Eukaryotic (elFs), which influences the transduction of proteins and stops all biosynthesis of these, including that of viruses [27-29].

In France, Drs. Amoros and Sauvager of the Faculty of Medicine of Rennes confirmed the virulicidal action against herpes type 1 and 2, but also against poliovirus. They established that it reduces the synthesis of viral DNA and that those responsible are flavonoids, which act in synergism with an ester of caffeic acid and ferulic acid. Another type of viral pathology that responds favorably to propolis is Herpes Zoster, pathology with cutaneous expression, painful of poor response to conventional treatments. Treated early in the eruptive period, remission is shortened and post herpetic neuralgia is avoided [30-31].

A group of researchers from the Albert Einstein College of Medicine in New York published a paper in 1997 that determined the ability of propolis to suppress HIV-1 replication and its immunostimulatory effect [32,33].

Healing and anti-inflammatory capacity

Propolis gained important spaces in the treatment of wounds, because of its antibacterial capacity and because of its remarkable healing and anti-inflammatory capacity. The latter is comparable to that of anti-inflammatory synthesis such as diclofenac. Caffeic acid was reported as responsible for inhibiting dihydrofolate reductase, reducing the production of interleukins and prostaglandins. In 1996 a paper was published in the Department of Biochemistry of the University of Oxford, the authors attribute this action of propolis to a caffeic acid ester (CAPE), caffeic acid and quercetin. Acting at the macrophages level, it suppresses the production of prostaglandins and leukotrienes. Using "*in vivo*" and "*in vitro*" models, they found that propolis suppresses the lipoxygenase pathway of arachidonic acid [34-36].

In a murine model, they observed that propolis supplied in the diet at a concentration of 0.2%, markedly affected the inflammatory response by decreasing the amount of leukotrienes LTB4 and LTC4. They also state that the ethanolic extract of propolis, in the same animal species, inhibits the increase of prostaglandins E2 and nitric oxide in pleurisy induced by carrageenan [37].

Immunomodulatory capacity

Flavonoids that are part of propolis have the specific ability to activate T lymphocytes, cytotoxic and natural killer cells; Although there is no clear theory of the mechanism of action, the investigations allow to infer that this is due to the inhibition of the enzyme cyclooxygenase, whose function is to participate in the synthesis of prostaglandins responsible for suppressing the action of T lymphocytes [38,39].

Researchers argue that the flavonoids contained in propolis participate indirectly in the mechanism of cellular immunity, because they stimulate the T8 lymphocytes, they receive the message from the macrophages producing cytokines and interleukins and other cells that report on the presence of antigens in the body, T8 lymphocytes act as the second line of defense of the immune system, acting against invading cells, such as carcinogens, viruses and bacteria cells. In the same sense, they consider that the antitumor activity of propolis and some of its components is associated to its immunomodulatory action, mainly due to the increase of the innate antitumor immunity, activating the macrophages, which can produce soluble factors that interfere on the tumor cell or the functions of other immune cells [40,41].

Antioxidant capacity

In recent years, the consumption of antioxidants, especially those of a natural origin, has taken on importance for the prevention of diseases of great importance such as atherosclerosis, rheumatism and even cancer. Antioxidants, such as vitamin E (alpha tocopherol), prevent lipid oxidation (transformation of LDL cholesterol into HDL cholesterol), reducing the risk of cardiovascular disease, and also neutralize free radicals, which are responsible for cell aging [42].

Propolis has a potent antioxidant capacity, which allows it to acquire unsusceptible prospects of development. As the main bioactive components of propolis are phenolic compounds and flavonoids, which are common in plants, both protect from solar radiation to plant tissues [43].

The phenolic compounds are formed by an aromatic ring attached to at least one hydroxyl group. The simplest structure is that of benzoic acid, but with other substituents in the ring, phenolic acids such as caffeic, ferulic, cumaric and cinnamic acids, common in plants and propolis, are formed [44].

The flavonoids are formed by a basic structure consisting of 2 benzene rings at the ends of the molecule, joined by a ring of 3 carbon atoms to which groups such as hydroxyls, methoxy, sugars, etc. can be added. In this way different types of flavonoids. These compounds

have important antioxidant properties, since they minimize lipid peroxidation and the effect of free radicals, thus contributing to reduce the risk of cardiovascular diseases. Some examples of these are: apigenin, quercetin, kaempferol, pinocembrina, galangina, chrysin and hesperidin, which are the most common in plants and in propolis [45].

As antioxidants, phenols can protect cells against oxidative damage and thus limit the risk of various degenerative diseases associated with oxidative stress caused by free radicals. Oxidative stress is commonly defined as the imbalance between oxidative and reducing species at the cellular level in an organism [46].

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