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Review Article

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Apitherapy in Endodontics

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Abstract

Traditional & alternative medicine provide great prospect for disease prevention and treatment purposes and should be studied and verified pharmalogically to decrease our dependency on antibiotics. Globally, apitherapy (defined: the medicinal use of products made by honeybees) is used for their various medicinal properties. Propolis, a natural antibiotic is a resinous yellow brown to dark brown substance that honey bees (*Apis mellifera*) collect from tree buds, sap flows, shrubs or other botanical sources to seal unwanted open spaces in the hive, protecting it from outside contaminants. The main pharmacologically active constituents present in propolis are flavonoids, phenolics and other various aromatic compounds. Flavonoids are well known plant compounds that have antibacterial, antifungal, antiviral, antioxidant and analgesic proprieties. This review focuses on characteristics and application of propolis in endodontics.

Introduction

The emergence of **Antibiotic resistance** (**ABR**) to currently available antibiotics has reached to the level of endemic and urgently requires the search for new compounds and therapies. Traditional & alternative medicine provide great prospect for disease prevention and treatment purposes and should be studied and verified pharmalogically to decrease our dependency on antibiotics. Globally, apitherapy[1,2] (defined: the medicinal use of products made by honeybees) are used for their antibacterial, antifungal and antiviral properties. Infact, modern studies also show that bee products may help manage autoimmune diseases, cancer, Alzheimer's, HPV, Lyme Disease, multiple sclerosis, and arthritis.

The motivating reason for the use of complementary and alternative medicine (CAM) in endodontics is that these products are highly bioactive, they have various interactions that are synergistic in preventing infections, promoting healing and maintaining health in total.

One such medicament having wide use in dentistry is **Propolis** (bee glue/ royal jelly/ honey comb extract). The word propolis is derived from the Greek pro-, for or in defense, and polis-, the city, that is, defense of the city (or the hive). There is a long history of use of propolis, at least to 300 BC (Ghisalberti, 1979) and its use continues today in home remedies and personal products in countries like Egypt, Greece and China. Hippocrates, the founder of modern medicine, used it for healing sores and ulcers internally and externally. This non-toxic resinous substance was classified into 12 types according to physicochemical properties and related to geographic locations; however, the botanical origin of only three types was identified. A new type of propolis, named Brazilian red Propolis (BRP) because of its color, (A. Parolia et al., 2010). Current research involving Propolis in dentistry involves many fields, particularly endodontics due to its various properties, especially biocompatibility (Ghisalberti, 1979; Marcucci, 1995; Nieva Moreno MI et al., 1999; KR et al., 1996). This paper is an attempt to review various applications of this compound in endodontics.

Composition

The composition of propolis varies with its area of occurrence, botanical sources, method of harvest and climatic conditions. It is a sticky substance, but becomes hard and brittle at low temperature. It mostly yellow to dark brown colored with pleasant aroma and composed of resin and balsams (50% - 70%), essential oils and wax (30% - 50%), pollen (5% - 10%) and other constituents which are amino acids, minerals, vitamins A, B complex, E and the highly active bio-chemical substance known as bioflavonoid (Vitamin P), phenols and aromatic compounds (A. Parolia et al., 2010). The precise composition includes more than 300 components[5]. Flavonoids are known for their antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory properties. Flavonoids and caffeic acid present in propolis also play significant role in reducing the inflammatory response by inhibiting lipoxygenase pathway of arachidonic acid. Flavonoids and caffeic acid also aid the immune system by promoting phagocytic activities and stimulates cellular immunity (C. Scully, 2006).

Characteristics of propolis

Anti inflammatory action

Due to presence of flavonoids and caffeic acid phenyl ester (CAPE) present in propolis.[6.] Both of these compounds work through inhibition of the lipoxygenase pathway of arachidonic acid.[6,7] Propolis also speeds up the creation of granulation tissue and epithelialization as well as vascular and fibroblastic neoformation of the connective tissue. Therefore, topical application may promote faster tissue healing.

Antibacterial action

Propolis shows wide range of antibacterial properties against number of micro organisms, both gram positive and gram negative[8,9]. It shows more promising result against gram positives (such as *S. aureaus spp., Streptocossue spp., Actinimyces naeslundii*) than gram negatives (such *as E. coli, E fasecalis, P aeruginosa, Peptostreptococcus spp., S enteritidis*).[10,11.]

Factors that affect antibacterial efficacy are as follows:

1. *Its hygroscopic properties:* This effect is based on high osmotic properties so it can extract water from bacterial cells and cause them to die. Honey, like other saturated sugar syrups and sugar pastes, has an osmolarity sufficient to inhibit microbial growth.

2. *Its acidic pH:* Honey is characteristically quite acidic, its pH being between 3.2 and 4.5, which is low enough to be inhibitory to many animal pathogens. The optimum pH for growth of these species normally falls between 7.2 and 7.4.

3. *Hydrogen peroxide:* The major antibacterial activity in honey has been found to be due to hydrogen peroxide produced enzymatically in the honey.

Antimycotic action

The presence of flavonoid content in propolis render in its antimycotic properties and also prevents fungal cell division, breaks down fungal cell wall and cytoplasm. This action is comparable to the action of some antibiotics.[12.] It has been found to have antimicrobial action against several fungal species such as *Candida albicans, C. krusei, C..glabrata, C. tropicalis* and *Trichosporon spp*.[13]

Antiviral action

Propolis shows some action against viruses as well. There has been indirect evidence for a strong interaction between propolis extract and the surface of the vero cells, it may be as effective as acyclovir against the herpes simplex virus (HSV-1).[14.]

Antioxident properties

According to an Italian study, propolis extract and its active components showed a dose- dependent free radical scavenging effect, a significant inhibition of xanthine oxidase activity, and an anti-lipoperoxidative capacity.[15] Propolis can also prevent tissue damage from oxidative stress by decreasing the overproduction of superoxide anion and by restoring respiratory control ration in mitochondrial tissue.

Uses of propolis in Endodontics

Propolis has several documented therapeutic and medicinal effects. These documented benefits include anti-inflammatory, antibacterial, antiviral, antimycotic, antioxidant effects. These properties confer various therapeutic benefits to propolis, allowing its use in dentistry for a variety of reasons, ranging from pulp therapy to its use as intracanal medicament.

Anticaries action

The two pathways by which propolis extracts show cariostatic effect are - first by the reduction of acid production of *S. mutans* and secondly the inhibition of the proton translocating F-ATPase activities which is one of the mechanisms that *S. mutans* have developed to alleviate their influence of acidification.[16]

Pulp capping agent and dentinal bridge formation

There have been many attempts to find a substance that will predictably induce a hard tissue barrier after pulp exposure (Brita Willershausen et al 2011). Zohreh Ahangari, et al (2012) evaluated the effect of Propolis as a bioactive material on quality of dentin and presence of dental pulp stem cells. This study documented that propolis initiates stimulation of stem cells. In addition it causes no pulpal inflammation, infection or necrosis. Therefore, propolis can be used to induce the production of high quality tubular dentin.

Propolis was also compared to MTA and Dycal as a pulp capping agent in terms of hard tissue/ dentinal bridge formation.[17] The stimulation of various enzyme systems, cell metabolism, circulation and collagen formation could contribute to the hard tissue bridge formation by Propolis. These effects have been shown to be the result of the presence of arginine, vitamin C, provitamin A, B complex and trace minerals such as copper, iron, zinc as well as bioflavonoids.

Intracanal irrigant

Due to its antibacterial properties, particularly against anaerobes found in the root canal, propolis motivates to be tried as an endodontic irrigant. In an *in vitro* study, it was found that Brazilian propolis was as effective as 3% sodium hypochlorite against *E. faecalis* when used as a root canal irrigant in permanent teeth, but less effective than MTAD (mixture of doxycycline, citric acid and Tween-80).[17] Similar results were obtained in another *in vitro* study on permanent teeth using 30% Brazilian green propolis as an endodontic irrigant.[18] In this study, propolis was found to be more effective against *E. Faecalis*, but less effective against *C. albicans*, compared to chlorhexidine at the end of 48 hours and 10 days.[18]

Intracanal medicament

Oncag et al (2008) compared the antibacterial efficacy of three commonly used intracanal medicaments with propolis against *E. faecalis*.[19,20.] and Awawdeh et al (2009) evaluated the effectiveness of propolis and calcium hydroxide as a short-term intracanal medicament against *E. faecalis*. They concluded that propolis is very effective in rapidly eliminating *E. faecalis* and can be used as an alternative intracanal medicament.[20.]

Hazards of using propolis

The main chemicals in propolis are resins, which constitute 45 to 55% of propolis and consist of free aromatic acids (eg, benzoic, caffeic, cinnamic, coumaric, and ferulic acids); benzyl, methylbutenyl, phenylethyl, cinnamyl, and other esters of these acids; chalcones and dihydrochalcones; and terpenes.[3] Propolis also contains flavonoids, including quercetin, apegenin, galangin, kaempferol, luteolin, pinocembrin, pinostrobin, and pinobanksin. The phenolic ester caffeic acid phenethyl ester (CAPE) has been the subject of several clinical trials because of its potential for the treatment of a number of disorders.[4]

The very first detected chemical substance that is responsible in propolis allergy was LB-1.[20] LB-1 is consistently found in every chemical dissolution process from various bee propolis and poplar bud samples [2]. At the very beginning, LB-1 was initially identified to be entirely composed of 1, 1-dimethylallyl caffeic acid ester, but then as it has been shown by the latest study, LB-1 consist of other chemical substance like *3-Methyl-2-butenyl caffeate, methyl-2-butenyl caffeate and 3-methyl-3-butenyl caffeate*[20].

Among those chemical substance 3-Methyl-2-butenyl caffeate acts as the most powerful allergen factor[20]. It draws out a strong response found in subject experiment who acknowledge suffer to propolis allergy. The same result is also identified with *Phenylethyl caffeate.*

Apart from these two main allergens, there are few more compounds that are considered as moderate sensitizers:

- Benzyl isoferulate (Based on Hausen experiment, it is considered a noteworthy sensitizer).
- Coniferyl benzoate. This substance exists in fresh samples of balsam of Peru, while in propolis it has been detected only once so far.
- Benzyl salicylate and benzyl cinnamate.

However, people who suffer to propolis allergy still should be warned about potential reactions to cosmetics or products containing these substances. Flavonoids and other compounds such as waxes, fatty acids, essential oils, pollen, and other organics and minerals have no capability as allergen.

Conclusion

1. This paper reviews various clinical implications of propolis in context to endodontics.
2. Propolis is a non toxic natural medication which is generally biocompatible with oral tissues.
3. Propolis can be used in the various fields of dentistry as it has antibacterial, antiviral, antifungal, anti-inflammatory, analgesic, and many other applications.
4. The chief component that is responsible for its biological actions is flavonoids.
5. Though it has shown very promising results but clinician should be cautious while using this substance due to its allergic reactions shown in some patients.
6. Patients allergic to bee and bee products are more likely to experience allergic reaction, such as hypersensitivity, asthma, anaphylaxis, and occasionally allergic cheilitis and oral ulceration.

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