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Propolis and Its Implications in Dentistry: A Review

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ABSTRACT

Propolis is a resinous substance obtained from the beehives that has antioxidant, anti-bacterial, anti-viral, antifungal, and anti-inflammatory activity. Its diverse chemical content is responsible for many valuable properties. Multiple applications of propolis have been studied and described in detail for centuries. Propolis has been used for surgical wound healing, caries prevention, treatment of dentin hypersensitivity, treatment of aphthous ulcers and propolis as a storage medium for avulsed teeth, root canal irrigating solution, and mouthwash. This paper aims to indicate the uses of Propolis in various fields of dentistry.

Keywords: Dentistry, Propolis, Oral health

INTRODUCTION

The term propolis is derived from the Greek words ‘pro’ meaning for defense or in defense, and ‘polis’ meaning city; propolis thus stands for defense of the hive (city).[1] Propolis, which is also known as bee glue, is a natural nontoxic resinous sticky substance produced by honeybees by mixing the secretions of their pharyngeal glands with the digested product of resins collected from leaves, flowers of plants, trees, and certain barks, and is mainly used as a sealant and sterilizer in honeybee nests.[2,3] Propolis being a sticky substance, protects the hive from insects, rodents, robber bees, bacteria, fungi, larvae, maintains an ambient temperature, and also helps in repairing and covering the honeycombs.[4,5] The main propolis producing bees include the European honey bees (*Apis mellifera*) and Asian honey bees (*Apis cerana*, *Apis florea*, *Apis andreniformis*, and *Apis dorsata*). It also includes stingless bees, such as those of the genera Geniotrigona, Heterotrigona, Melipona, Tetragonula, and Trigona.[6-8]

Propolis is mainly composed of resin and balsams (50-70%); essential oils, aromatic oils, and wax (30-50%); pollen (5-10%); and other bioactive compounds such as amino acids, minerals, vitamins, phenolics, and flavonoids.[9-11]

Phenolics and flavonoids are responsible for the anti-oxidant properties exhibited by propolis. The extent of anti-oxidant activity of propolis is correlated with its total content of phenolics and flavonoids.[12]

Propolis has anti-inflammatory properties. Propolis-derived caffeic acid phenethyl ester (CAPE), quercetin, and naringenin suppress the production of prostaglandins and leukotrienes which are the main mediators of inflammation. CAPE is most effective in modulating the arachidonic acid cascade.[13] Terpenoids extracted from propolis reduce the expression of inflammatory mediators, such as inducible nitric oxide synthase (iNOS), interleukin (IL)-1b, and IL-10.[14] Propolis also suppresses the production of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB).[15,16] NF-kB plays an important role in many inflammation-associated human disorders including

metabolic syndrome-related diseases such as cardiovascular disease, diabetes, and cancers.[17-20]

Propolis has anti-angiogenic and anti-proliferative properties. It is able to inhibit cancer cell metastasis by producing CAPE, which reduces the production of matrix metalloproteinases.[21] CAPE has the ability to reduce the expression of various growth factors and transcription factors including NF-kB.[22] CAPE exhibits the antiangiogenic properties by reducing vascular endothelial growth factor (VEGF)[22] and downregulating the expression of multi-drug resistance 1 (mdr1)gene; thus inhibiting the development of resistance of cancer cells to various chemotherapeutic agents.[23]

Propolis exhibits antibacterial properties by its flavonoids and phenolics content; higher the content in the propolis variety, greater the antibacterial effect. It causes irreversible surface changes and reduces the surface negative charge resulting in pore formation in the membrane and extrusion of intra-cellular contents.[24] Caffeic acid, rutin, chrysin, kaempferol, galangin, and quercetin derived from propolis exhibit antiviral activities against herpesvirus, adenovirus, coronavirus (including Sars Cov- 2), rotavirus, influenza virus, and HIV.[25,26]

Use of Propolis in Dentistry

Due to its antimicrobial, anti-oxidant, anti-inflammatory, and anti-proliferative properties, propolis has immense potential in dentistry, oral health management, and medicine.[27]

Various genres of bacteria have been implicated in the development of caries. The most important are *Streptococcus mutans* and *Lactobacillus sp*. Other bacteria such as members of the mitis, anginosus, and salivarius groups of other *Streptococcus sp., Enterococcus faecalis, Actinomyces sp., Rothia dentocariosa, Propionibacterium sp., Prevotella sp., Veillonella sp., Bifidobacterium sp.,* and *Scardovia sp.* have also been shown to contribute to the development and progression of caries.[28-30] It has been found that propolis inhibits the growth of *Streptococcus sobrinus, S. mutans,* and *Streptococcus cricetus.*[31] Studies have shown that propolis-enriched drinking water resulted in a 50-60% reduction in the incidence of dental caries in S. sobrinus infected rats. In addition, two propolis constituents, apigenin and tt-farnesol, significantly reduced smooth-surface caries in S. sobrinus-infected rats.[32] It has been suggested that the protective effect of propolis is not only derived from phenolics and flavonoids; other fatty acids such as oleic, palmitic, linoleic, and stearic acid from propolis might also have beneficial properties.[33] Propolis extract-containing products have been effective in reducing and/or inhibiting the growth of S. mutans and other caries-causing bacteria in human clinical trials. A significant reduction in bacterial count has been observed among participants using propolis mouth rinse.[34] Propolis and its constituents reduce the numbers of caries causing bacteria by directly inhibiting growth and/or inhibiting glucosyltransferase activity. In addition, propolis inhibits the synthesis of water-insoluble glucan.[31] Propolis also significantly reduces bacterial acid production and inhibits the activity of F-ATPase, an important enzyme associated with the acid tolerance of S. mutans.[33]

Due to its antimicrobial and anti-inflammatory activities, propolis has been reported to reduce the incidence of plaque accumulation and gingivitis. Propolis-containing mouth rinse reduces supragingival plaque and insoluble polysaccharide by 44.7% and 61.7%, respectively, versus placebo where volunteers refrained from all oral hygiene and rinsed five times a day with 20% sucrose solution for 3 days.[33] Chlorhexidine (CHX) has been used as an active ingredient in mouthwash because of its antimicrobial properties and efficacy in reducing dental plaque. Santiago *et al.* compared the effect of mouthwash containing 2.6% (w/v) propolis and a commercially available

mouthwash containing 0.12% CHX on dental plaque accumulation. It was found that the propolis containing mouthwash was as effective as CHX mouthwash in reducing plaque accumulation over a trial period of 14 days.[35] In patients with type 2 diabetes and chronic periodontitis, propolis has been shown to reduce hemoglobin A1c (HbA1c), fasting plasma glucose, and serum NV-(carboxymethyl)lysine (CML).[36] Propolis also improves periodontal parameters, namely probing pocket depth (PPD) and clinical attachment level (CAL) (distance from the cement-toenamel junction to the base of the pocket). Additionally, topical application of propolis is beneficial in improving periodontal parameters, such as PPD, CAL, and reduce P. gingivalis in the gingival crevicular fluid (GCF) in patients with periodontitis.[37]

Disinfection of the tooth cavity prior to restoration determines the success of the restorative treatment. Propolis has a disinfection efficacy in primary teeth similar to that of 2% CHX and diode laser. Mohan U *et al.* investigated the efficacy of acidulated phosphate fluoride (APF) gel, propolis, laser diode, and 2% CHX as disinfecting agents in 68 children with cavitated dentinal occlusal caries. They found that propolis reduced the total viable counts on blood agar, S. mutans counts on Mutans-Sanguis (MS) agar, and lactobacilli counts on Rogosa agar by 98%, 99%, and 98%, respectively. The results were comparable to those of diode laser and 2% CHX.[38] Recently propolis has been incorporated into nanocomposites and applied as restorative agents.

A major cause of endodontic diseases is bacteria and their metabolic products, enzymes, and toxins, which consequently induce inflammatory responses. Propolis has bactericidal activity comparable to that of common intracanal medicaments such as calcium hydroxide, CHX, MTAD (mixture of tetracycline, citric acid, and detergent), EDTA (ethylenediaminetetraacetic acid), camphorated paramonochlorophenol, and formocresol against various anaerobic, endodontitic-causing bacteria such as *Prevotella nigrescens, F. nucleatum, Actinomyces israelii, Clostridium perfringens,* and *E. faecalis*. Studies have shown that propolis exhibits better reduction in colony counts of *E.fecalis* than any other intra-canal medicaments.[39,40]

Propolis and its phenolic and flavonoid constituents with their antimicrobial, anti-inflammatory, and immunomodulatory properties are potential dental pulp capping materials. Ahangari *et al.* have shown that propolis-containing pulp capping agents stimulate higher levels of stem cell production and produce better quality of dentin in guinea pigs than calcium hydroxide. These agents produce tubular dentin, whereas 14% of the calcium hydroxide caps produce porous dentin.[41] Propolis decreases the expression of Lipopolysaccharide(LPS)-induced inflammatory mediators in pulp cells and osteoclasts. The inflammatory mediators that are suppressed include IL-1a, IL-6, IL-12 (p70), IL-15, granulocyte colony-stimulating factor (G-CSF), tumor necrosis factor-alpha (TNF-a), macrophage inflammatory protein 1 alpha (MIP-1a), monocyte chemoattractant protein-1 (MCP-1), and interferon-inducible protein 10 (IP-10).[42] Parolia *et al.* compared Dycal, propolis, and mineral trioxide aggregate (MTA) as dental pulp capping materials in terms of inflammatory responses and dentine formation in patients aged 15-25 years and found that Propolis-and MTA-treated pulp exhibit less inflammation than that with Dycal. Propolis- and MTA treated pulp also show more dentine bridge formation than Dycal.[43] Propolis induces wound healing by promoting epithelialization of the surgical wounds. Propolis also has anti-inflammatory and analgesic effects.[44]

Oral candidiasis is an opportunistic infection of the oral cavity caused by yeast-like fungi, most commonly *Candida sp.* Propolis extract has fungicidal activity against *C. albicans, C. tropicalis, C.*

glabrata, and *C. parapsilosis* isolated from healthy subjects and patients with oral lesions.[45] The effect of propolis is similar to nystatin or miconazole in treating denture stomatitis.[46] The antifungal properties of propolis are due to its ability to disrupt the fungal cell wall and inhibit germ tube formation. Propolis prevents the adherence and colonization of fungi.[47] Propolis has the ability to prevent biofilm formation, eradicate mature biofilms, and inhibit filamentation of *Candida sp.* Propolis also induces cell apoptosis in *Candida sp*. by affecting the metacaspase pathway and disrupting the Rascyclic AMP (cAMP)-cAMP-dependent protein kinase (PKA) signaling pathway.[48]

The most prevalent virus affecting oral health is herpes simplex virus (HSV type I and II), type I being the most common. Propolis, owing to its constituents chrysin, galangin, kaempferol, and quercetin, have been reported to have antiviral properties against HSV in cell culture. The antiherpetic properties of propolis (and its phenolic constituents) are attributed to its ability to interfere with the virion envelope and consequently inhibit viral entry into cells.[49]

Propolis has antiangiogenic and antiproliferative properties. Propolis exhibits a time- and dose-dependent cytotoxic effect on human laryngeal epidermoid carcinoma.[50] Some components of Propolis such as chrysin, caffeic acid, p-coumaric acid, and ferulic acid, induce apoptosis of human tongue squamous carcinoma cells (CAL-27). The polyphenols in propolis decrease collagen biosynthesis, prolidase activity, and proline concentration in CAL- 27 cells.[51] Propolis has also been found to be effective in oral submucous fibrosis.

Adverse Effects

Propolis is a relatively safe product to be used in various aspects of dentistry. However, being a product obtained from bees, any allergic reaction from propolis or its constituents must be taken care of. Cases of contact dermatitis has been reported in literature.[52]

CONCLUSION

Propolis and its phenolic and flavonoid constituents have many therapeutic uses in dentistry, oral health, and medicine. Wide ranging therapeutic uses due to its antibacterial, antiviral, antifungal, anti-inflammatory, and anticancer properties have been demonstrated in various studies. However, there is a great need to standardize the content of phenolics and flavonoids in propolis to obtain the best therapeutic and medicinal benefits in dentistry and oral health.

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