

Propolis In Dentistry – A Review

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Abstract

Use of natural products with medicinal properties, derived from plants, animals or microorganisms has found significant popular acceptance in recent years. ‘Propolis’ is one such natural substance, a resin procured from honeybees collected from plants, buds and exudates has a spectrum of effects like antiviral, antioxidant, antitumor, antibacterial, antifungal, antitumor and immune enhancing properties. Considering oral health, propolis has been utilised in the management of dental caries, pulpitis, aphthous ulcers, plaque, periodontitis, halitosis, stomatitis, dentinal hypersensitivity, oral candidiasis, acute necrotizing ulcerative gingivitis (ANUG), pulp therapy, intra canal medicament and in oral cancer therapy. Pubmed, Google scholar and Medline databases were searched for articles related to propolis and dentistry, which is presented in this review.

Keywords: Propolis, Dentistry, Oral health

1. Introduction

Phytomedicine is increasingly gaining a key role in the dental arena with many plant-derived materials being researched upon. The use of products derived from natural sources such as plants, microorganisms or animals recorded in history dated back to centuries. Since our forefathers chewed on certain herbs for pain relief, natural products were the exclusive source to treat diseases and injuries.

‘Propolis’, one such natural product, is a resin obtained from bees (*Apis mellifera*) from materials collected from plants, exudates and buds ^{1,2}. The term propolis is derived from the Greek word ‘pro’ (in front of) and ‘polis’ (community), interpreting that this product is associated with hive defense^{3,4}. Propolis was customary to Egyptian high priests who had monopolized the proficiency of mummifying corpses ^{1,5}. The initial scientific work with propolis, was published in 1908⁶. The therapeutic use of products procured from honeybees is called Apitherapy ⁷. In the past 30 years, extensive scientific research had been performed to clarify the medicinal properties of this material^{8,9}.

Propolis is a composite mixture of more than 300 naturally occurring constituents identified to date mostly of resins, fatty acids, aromatic oils, pollen, bee wax, vitamins and minerals^{10,11,12}. Its chemical composition includes polysaccharides, phenols, terpenes, aldehydes, tannins, aromatic acids and many more compounds^{13,14}. Its composition varies with the species of bees, botanical source, geography, and climate, season. In temperate belt, the bud exudates of *Populus* species along with its hybrids are the primary source of Propolis. This is true for parts of Asia and Europe^{2,15,16}. The most common type of tropical propolis is the Brazilian green propolis^{17,18}.

The biologically active constituents of propolis are flavonoids, chrysin, caffeic acid, terpenoids, apigenin, pinocembrin, phenolic acids, pinobanksin, pinobanksin 3-acetate, pinobanksin 5-methyl ether^{19,20}.

Propolis is available in the raw form, tinctures, pills, semisolid preparations, mixtures, emulsions, concentrates, creams, ointments. In dentistry, it is used in toothpastes, mouth rinses, oral sprays and creams. The medicinal properties of this wonder material have rendered it of great scientific interest in recent years.

2. Potential uses of Propolis In Dentistry

Pubmed, Google scholar and Medline databases were searched for articles related to propolis and dentistry, which is presented in this review. The various applications of propolis include:

Caries Prevention: Ikeno *et. al.* (1991), demonstrated the in vitro anticariogenic potential of propolis in rats against *Streptococcus mutans*, *crictus* and *sobrinus*²¹. Steinberg *et. al.* (1996), assessed the antibacterial effect of propolis on oral bacteria and showed that total salivary bacteria and *Streptococcus mutans* counts were markedly reduced²². Similarly, Hayacibara M F *et. al.* (2005) and Duarte *et. al.* (2006), concluded that propolis inhibited the 'F'-ATPase activity and decreased acid production, demonstrating cariostatic property. Propolis reduced viability of the isolated fractions of mutans streptococci and inhibition of glucosyltransferases activity in rats^{23,24}. Koru *et. al.* (2007), found propolis to be effective against several bacteria implicated in caries²⁵. Duailibe SA *et. al.* (2007), showed that propolis mouthrinse exhibited antimicrobial activity against *Streptococcus mutans* in vivo and may be used as an adjunct in the prevention of dental caries²⁶. The antimicrobial effects of various propolis extracts in rats were studied by Arslan S. *et. al.* (2010). The ethanol and hexane extracts of propolis showed the highest antimicrobial activity²⁷. Kashi *et. al.* (2011), revealed that the ethanolic extract showed bacteriostatic and bactericidal activity against all the strains whereas the water extract showed bactericidal activity only against *S. mutans* in vitro²⁸. Liberio SA *et. al.* (2011), showed that the Propolis extract with the highest concentration of flavonoids, displayed the most powerful antimicrobial activity on oral pathogens and summarised that it can be made use of in the prevention of caries, candidiasis, and treatment of inflammation²⁹. Krumina G *et. al.* (2014), suggested that all ethanolic extracts demonstrated antibacterial activity against *S. mutans*³⁰. Franca *et. al.* (2014), carried out an in-vitro study with a sustained-release propolis impregnated chitosan varnish and chlorhexidine for biofilm formation prevention and found that, the cariogenic microorganisms of the biofilm showed more favourable results with propolis than chlorhexidine and the bioactive components of Propolis were discharged for more than seven days³¹. Another study showed definite antimicrobial action of propolis against *S. mutans* and *C. albicans*, the probable organisms involved in caries progression³². Tulsani SG *et. al.* (2015), documented about the anticariogenic action of Propolis gum in comparison to Xylitol gum³³.

Oral candidiasis: The antifungal efficacy of propolis was demonstrated by Ota *et. al.* (2001) on 80 strains of *Candida* yeasts³⁴. The inhibitory effect of 20% ethanol propolis extract (EPE) on the *C. albicans* multiplication collected from HIV positive persons was tested in vitro³⁵. D'Auria FD *et. al.* (2003), attributed the effects of propolis against *C. albicans* to be rapid, dose- dependent cytotoxic activity and an inhibitory effect on yeast-mycelial conversion³⁶. Patients with oral candidiasis treated with propolis had similar outcome as those treated with nystatin³⁷. Sinha DJ *et. al.* (2015), compared the effect of various herbal extracts and propolis on *Candida albicans* biofilm, on extracted human mandibular premolars and suggested that, sodium hypochlorite and propolis groups exhibited high antimicrobial efficacy against *C. albicans* and propolis was better than tea tree oil, turmeric and neem extracts³⁸.

Stomatitis and mouth ulcers: Denture stomatitis is a very common inflammatory lesion on the palatal mucosa of denture wearers. Studies indicate that administration of propolis significantly reduced the outbreaks of recurrent aphthous stomatitis^{39,40}. Denture stomatitis also responded well to propolis gel in a study and warranted to a complete clinical remission of stomatitis⁴¹. On the contrary, Da Silva *et. al.* (2008), concluded that a gel containing propolis, can have an adverse effect on the acrylic resin surface which becomes rough favouring microbial adhesion⁴². It was also found that Brazilian green propolis was beneficial in the management of *Candida*-associated denture stomatitis⁴³.

Plaque control: Murray MC *et. al.* (1997), analysed the effectiveness of a propolis mouthrinse in the plaque

inhibition and observed that chlorhexidine mouthrinse was superior in plaque inhibition⁴⁴. Giamalia *et. al.* (1999), found a steady increase in micro hardness of human enamel with increasing concentration of propolis from 0.4% - 2%⁴⁵. This was in accordance with other studies^{46,47}. Koo *et. al.* (2002), studied the efficacy of a propolis containing mouthrinse on a 3-day dental plaque accumulation and indicated that, the propolis mouthrinse was efficacious in inhibiting plaque formation⁴⁸. Similar finding was seen in a study by Dodwad V *et. al.* (2011)⁴⁹. Flavonoids in propolis may aid in the inhibition of calcium phosphate formation⁵⁰. Netto *et. al.* (2013), demonstrated that non-alcoholic propolis may have increased efficiency than 0.12% chlorhexidine when used as a mouthrinse because, after 28 days of use, it suppressed the levels of *Lactobacilli and Mutans streptococci* with better patient acceptability⁵¹. Hegde KS *et. al.* (2013), evaluated the antibacterial activity of a propolis extract in children and suggested it as an alternative antimicrobial agent to prevent plaque and caries⁵². Two other studies showed clinical effectiveness of a toothpaste and gel containing 3% ethanolic extract of propolis in patients with increased risk of gingivitis^{53,54}. Pedrazzi V *et. al.* (2015), studied the antiplaque activity of one of the plant sources of propolis origin⁵⁵. Ercan, *et. al.* (2015) found that the gingival and plaque indices of the propolis chewing gum group were higher than the propolis mouthwash group⁵⁶.

Dentinal hypersensitivity (DH): This condition is a sharp pain arising due to dentinal tubule stimulation. Mahmoud *et. al.* (1999), in their pioneer study found that Propolis was favourable in controlling dentinal hypersensitivity. Flavonoids in propolis, through chelation of metal ions, give rise to dentin desensitization⁵⁷. Geiger *et. al.* and Peres S. *et. al.*, stated that propolis inhibits the permeability of dentin by 85%^{58,59}. When compared to CPP-ACPF (Casein Phospho Protein- Amorphous Calcium Phosphate Fluoride) and Sodium Fluoride, Propolis performed better in terms of dentin desensitizing⁶⁰. Compared to hydroxyapatite, sodium fluoride and potassium nitrate Propolis reduced dentin hypersensitivity to the maximum extent as studied over a period of 7 days⁶¹.

Chronic Periodontitis: A study by Cairo de Maral (2006) where in the subjects with periodontitis and gingivitis were instructed to brush daily with propolis, and rinse with a propolis solution and apply in periodontal pockets once in 7 days for a period of five weeks demonstrated drop in gingivitis by 95%⁶². Propolis incorporated into a mucoadhesive hydrophilic gel can be useful in treatment of periodontitis⁶³. In an animal study, the systemic administration of propolis reduced the bone loss due to periodontitis⁶⁴. Propolis extract as a subgingival irrigant was more beneficial than scaling and root planing⁶⁵. Vinod KR *et. al.* (2015) observed excellent mucoadhesion due to addition of propolis, vitamin C and E. Propolis gel combination was stable for eight cycles with no agglomeration tendency, and causes augmentation of the contact time of the medicament with that of the mouth⁶⁶.

Storage media for avulsed teeth: Storage medium is an important factor that prevent damage to the periodontal ligament cells. Martin (2004) showed that propolis can be a substitute to Hanks balanced salt solution in order to maintain the viability of the PDL cells after avulsion⁶⁷. Propolis was recommended as a transport medium by Al-Shaher *et. al.*⁶⁸. Ozan *et. al.* (2007), showed that 10% propolis was an effective storage medium⁶⁹. Based on animal studies, it is proposed that, a combination of systemic antimicrobials and propolis could aid in the inhibition of inflammatory root resorption when used as a root surface treatment media^{70,71}. Several studies have shown that propolis and its combinations performed better than milk, egg white and saliva^{72,73,74}. Propolis also reduces the apoptosis of periodontium cells⁷⁵.

Pulp Therapy/ Dentinal Bridge Formation and Pulp Capping: Propolis has shown promising results in inducing a hard tissue barrier after pulp exposure. Bretz *et.al.* (1998), stated that direct capping with calcium hydroxide-based products and propolis, both materials offer an indistinguishable rate of healing of the pulpal inflammation, reducing the pathogenic microbial count and stimulating dentin bridge formation⁷⁶. Stimulation of various enzyme systems and collagen formation could contribute to hard tissue bridge establishment by Propolis⁷⁷. Flavonoids derived from propolis, when used as a pulp capping agent, aid in partial dentinal bridge formation at four weeks⁷⁸. Brazilian propolis paste combined with calcium hydroxide inhibited the growth of the microbes from in vitro primary root canal cultures. The ethanolic extract of propolis was able to produce larger inhibition zones compared to the non-ethanolic extract of propolis according to Rezende *et. al.* (2006). Propolis was comparable to Dycal and MTA as a pulp-capping agent in relation to hard tissue formation⁸⁰. Propolis causes stimulation of stem cells in the absence of pulpal inflammation, infection or necrosis⁸¹.

Obturator agent in primary teeth: Brazilian Propolis incorporated into calcium hydroxide showed larger growth inhibition zones against primary root canal microbe samples than Calcium hydroxide in vitro⁸². Propolis diffused through dentin is utilised as a vehicle for calcium hydroxide⁸³. Because of its effect on the periodontal cells, propolis can be used as a root canal disinfectant^{68,84}. Effectiveness of glycolic propolis as intracanal medicament against *E. faecalis*, *E. coli* and endotoxins in root canals was evaluated by Maekawa LE *et. al.* (2013)⁸⁵. Verma MK *et. al.* (2014), confirmed antimicrobial efficacy of 25% aqueous extract of propolis in the primary teeth root canals⁸⁶.

Irrigant and intra-canal medicament: Propolis was evaluated as an endodontic irrigant because of its antibacterial action. Al-Qathami (2003), indicated that the propolis and sodium hypochlorite have similar antimicrobial activity⁸⁷. Tandon S (2008), demonstrated that propolis is as effective as calcium hydroxide when used as a pulp capping agent⁸⁸. Several studies concluded that propolis is effective as an intracanal medicament in effective elimination of *E. faecalis*⁸⁹⁻⁹². Nara A *et. al.* (2010) found that, when used as an irrigant in permanent teeth, 3% sodium hypochlorite and Brazilian propolis showed equal efficacy against *E. faecalis*⁹³. Guajardo C *et. al.* (2011) demonstrated that calcium hydroxide was more effective than propolis up to 24 hours from application⁹⁴. Studies have demonstrated that propolis, when used in conjunction with passive ultrasonic irrigation is effective in the removal of *E. faecalis* biofilm from root canal wall^{95,96}. Ramani N *et. al.* (2012) suggested that the alcoholic extract of propolis is effective intracanal medicament⁹⁷. Pimenta HC *et. al.* (2015) showed that, 40% brown propolis paste and calcium hydroxide pastes were effective as an intracanal medicament, against *Enterococcus faecalis*⁹⁸. However, Jodhka S. *et. al.* (2015) found that propolis demonstrated antimicrobial activity only after 3 days and 2% chlorhexidine gel was a more effective intracanal medicament⁹⁹.

Oral wound healing: Local application of propolis hydroalcoholic solution had no effect on wound healing but accelerated epithelial repair after tooth extraction¹⁰⁰. Magro-Filho (1994) stated that hydroalcoholic mixture of Propolis helped in epithelial repair but had no effect on the wound healing¹⁰¹. The mechanism to hasten wound healing by propolis is through the activity of caffeic acid phenyl ester (CAPE) that enhances the production of submucosal collagen¹⁰². Propolis decreases inflammation and accelerates epithelialisation and formation of granulation tissue¹⁰³. Studies conducted on rats showed increased amounts of collagen following topical application of propolis on oral ulcers and increased quantity of osteoblasts and rapid remodeling within the palatine suture during bone forming process^{104,105}.

Oral cancer treatment: Animal studies suggest that propolis aid in the chemically induced lingual carcinogenesis in rats and several hydro soluble compounds of propolis, such as CAPE could be useful for the management of tumour growth in pilot studies^{106,107}. CAPE could be used as an agent to prevent oral cancer metastasis¹⁰⁸. CAPE is also an adjuvant for the management of oral squamous cell carcinoma¹⁰⁹.

3. Safety Issues and Drug Interactions

Phytomedicines although naturally derived, cannot always be regarded as safe. Complete knowledge of the biocompatibility should be present, prior to clinical usage. Allergens have been isolated from propolis. Adverse allergic reactions may manifest as peeling of lips, contact cheilitis, perioral eczema, contact stomatitis, oral pain, dyspnea and labial edema¹¹⁰. Presentation may be in the form of redness of skin, rashes, swelling, itching and fever¹¹¹. Allergies related to propolis containing toothpaste have increased from 0.5% to 1.4%¹¹². Routine patch testing should be done in patients before prescribing it. Propolis is said to have interactions with other drugs like metronidazole. Propolis may interact with antifungals, *H. pylori* agents, anticoagulants, antibiotics, anti-cancer agents, anti-inflammatories, immunosuppressants and antiretrovirals¹¹⁰.

4. Conclusion

Although most of the literature published on propolis is based on animal studies or *in-vitro* studies, extrapolating the result of these studies to clinical practice may not be necessarily replicated in human trials. While using this “api-herbal drug”, the clinician should be vigilant due to its hypersensitivity issues shown in a few cases. Evidence from randomized control trials and controlled clinical trials are lacking. Further studies need to be conducted to determine its effects on the oral cavity. In the subsequent years, propolis may find a definitive and promising contribution in dentistry..

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