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*Review*

# Propolis and its potential uses in oral health

**Abhishek Parolia[1]*, Manuel S. Thomas[1], M. Kundabala[1] and Mandakini Mohan[2]**

[1]Department of Conservative Dentistry and Endodontics, MCODS, Mangalore, India.
[2]Department of Prosthodontics, MCODS Manipal, India.

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**The health industry has always used natural products as an alternative, to the conventional allopathic formulations available for the treatment of various afflictions. 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 chemical classes present in propolis are flavonoids, phenolics and other various aromatic compounds. Flavonoids are well known plant compounds that have antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory proprieties. Propolis has been used in dentistry for various purposes and has a promising role in future medicine as well as in dentistry. This paper is an attempt to review various applications of this compound in dentistry.**

**Key words:** Propolis, oral health.

## INTRODUCTION

Propolis was used at the time of Egyptian and Greek civilizations which recognized its healing qualities. Hippocrates, the founder of modern medicine, used it for healing sores and ulcers internally and externally. The word propolis (Russian Penicillin) is derived from the Greek word "pro" before, polis "city" or defender of the city. 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 were identified (Wander, 1995). A new type of propolis, named Brazilian red Propolis (BRP) because of its color, it has attracted the attention of international business. Propolis has been used for treating different diseases and inflammatory conditions as both local and systemic applications. In nature, or when in room temperature, it is a sticky substance, but becomes hard and brittle at low temperature. It is 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 bioflavenoid (Vitamin P), phenols and aromatic compounds (Park et al., 2002; Almas et al., 2001).

*Corresponding author. E-mail: paroliaabhi@yahoo.com. Tel: 91-824-2428716, Extn 5660. Fax: 91- 824-2422653.

Flavonoids are well known plant compounds which have antibacterial, antifungal, antiviral, antioxidant and anti-inflammatory proprieties. Propolis has found to be very effective against gram positive bacteria (Seidel et al., 2008) especially against *Staphylococcus aureus (*Velazquez et al., 2007) and against gram negative bacteria against Salmonella (Orsi et al., 2005). The effect of propolis on growth and glucosyltransferase activity of *Streptococcus sorbinus, Streptococcus mutans and Streptococcus circuits* was observed *in vitro* and *in vivo* (Ikeno et al., 1991) and found that the insoluble *glycan synthesis* and glucosyltransferase activity were inhibited by multiple actions of Propolis. Koru et al., 2007 studied the antibacterial action against certain anaerobic oral pathogens and found to be very effective against *Peptostreptococcus anaerobius, Lactobacillus acidophilus, Actinomyces naeslundii, Prevotella oralis, Prevotella melaninogenica, Porphyromonas gingivalis, Fusobacterium nucleatum* and *Veillonella parvula.* They concluded that the antibacterial property of Propolis is due to the presence of Flavanoids and aromatic compounds such as cafeic acid. Kujumgiev et al. (1999) evaluated antibacterial against (*S. aureus* and *Escherichia coli*), antifungal against (*Candida albicans*) and antiviral against (*Avian influenza virus*) properties of propolis and found to be very effective. Anti-oxidant property of propolis which is the protection against gamma radiation could be attributed to its radical scavenging ability (Krol et al., 1990) which was better

than anti-oxidant property of vitamin C (Velazquez et al., 2007). Anti-inflammatory property of propolis is due to the presence of caffeic acid phenethyl ester (CAPE) in propolis (Borrelli et al., 2002). Propolis is dispensed in various forms, such as tooth paste, mouthwash, lozenges, wine, cake, powder, jelly, tablets, soap and others. The paper reviews various potential uses of propolis in oral health.

## POTENTIAL USES OF PROPOLIS IN ORAL HEALTH

### Wound healing

A study conducted by Magro-Filho and Carvalho, 1994 analyzed the effects of propolis mouth rinse on the repair of surgical wounds after sulcoplasty by the modified Kazanjian technique. Patients returned 7, 14, 30 and 45 days after surgery for cytological and clinical evaluation. It was concluded that:

(a). The mouth rinse containing propolis in aqueous alcohol solution aided repair of intra-buccal surgical wounds and exerted a small pain killing and anti-inflammatory effect.
(b). The vehicle employed had a minor irritant effect on infra-buccal surgical wounds.
(c). Exfoliative cytology showed epithelization of infra-buccal surgical wounds.

They also examined histologically the effects of propolis topical application to dental sockets and skin wounds. It was concluded that topical application of propolis hydro-alcoholic solution accelerated epithelial repair after tooth extraction but had no effect on socket wound healing (Magro Filho and Carvalho, 1990).

### Propolis: A promising new storage media following avulsion

Both length of extra-alveolar time and type of storage media are significant factors that can affect the long-term prognosis of replanted teeth. Numerous studies have examined various media in an attempt to determine the ideal material for storage of the avulsed tooth, Martin and Pileggi (2004) conducted a study and compared various storage media and it appeared that propolis may be a better alternative to HBSS, milk, or saline in terms of maintaining PDL cell viability after avulsion and storage.

Ozan et al. (2007) determined the ability of propolis to serve as a temporary storage medium for the maintenance of periodontal ligament (PDL) cell viability of avulsed teeth. PDL cells were obtained from healthy third molars and cultured in Dulbecco's Modified Eagles Medium (DMEM). Cultures were subjected to 10% propolis solution, 20% propolis solution, milk with lower fat content (milk), Hank's Balanced Salt Solution, tap water as the negative control, and DMEM as the positive control. Tissue culture plates were incubated with experimental media at 37°C for 1, 3, 6, 12 or 24 h. PDL cell viability was assessed by trypan blue exclusion. The results showed that 10% propolis was a more effective storage medium than other groups.

Gopikrishna et al. (2008) the potential of a new storage medium, coconut water, in comparison with propolis, Hank's balanced salt solution (HBSS) and milk in maintaining viable periodontal ligament (PDL) cells on simulated avulsed teeth. Seventy freshly extracted human teeth were divided into 4 experimental groups and 2 control groups. The positive and negative controls corresponded to 0 min and 8 h dry times, respectively. The experimental teeth were stored dry for 30 min and then immersed in 1 of the 4 media (coconut water, propolis, HBSS and milk). The teeth were then treated with dispase grade II and collagenase for 30 min. The number of viable PDL cells was counted with a hemocytometer and analyzed. Statistical analysis showed that coconut water kept significantly more PDL cells viable compared with propolis, HBSS or milk. Coconut water can be used as a superior transport medium for avulsed teeth.

Al-Shaher et al. (2004) examined the tolerance of fibroblasts of the periodontal ligament (PDL) and dental pulp to propolis and compared with that of calcium hydroxide in vitro. Cells from human dental pulp and PDL were obtained from healthy third molars and subjected to various concentrations of propolis (0 - 20 mg/ml) and calcium hydroxide (0 - 250 mg/ml). The cell viability after propolis treatment was analyzed by crystal violet staining of the cells followed by spectrophotometric analysis. Data revealed that exposure of PDL cells or pulp fibroblasts to 4 mg/ml or lower concentrations of propolis resulted in > 75% viability of cells. On the contrary, calcium hydroxide 0.4 mg/ml was cytotoxic and < 25% of the cells was found to be viable. In conclusion, propolis can be recommended as a suitable transport medium for avulsed teeth.

### As a pulp capping agent

Propolis has been shown to possess potent antimicrobial and anti-inflammatory properties. The main chemical classes present in propolis are flavonoids, phenolics and other various aromatic compounds. Flavonoids and caffeic acid present in propolis are known to play an important 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. Propolis also helps in hard tissue bridge formation; this has been attributed to the property of propolis, which has been shown to stimulate various enzyme systems, cell metabolism, circulation and

collagen formation. 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. All these factors of propolis help in good wound healing. In addition to wound healing ability, propolis is a good antimicrobial agent. It prevents bacterial cell division, breaks down bacterial cell wall and cytoplasm (Koo et al., 2000; Khayyal, el-Ghazaly et al., 1993). Sabir et al. (2005) evaluated the response of rat dental pulp to direct pulp capping with propolis.

Flavonoid and non-flavonoid materials were purified from an ethanol extract of propolis. The dental pulp was exposed and then capped with a zinc oxide-based filler as a control (group I), or with propolis flavonoids (group II) or non-flavonoids (group III). The animals were sacrificed at week 1, 2 or 4, biopsy samples were obtained and these were stained and viewed by light microscopy. The results showed that pulp inflammation occurred in groups I and III as early as week 1. No dentin bridge formation was seen in these groups. In contrast, there was no evident inflammatory response in group II at week 1. Mild and moderate pulp inflammation in this group occurred at 2 and 4 weeks after treatment, respectively. Partial dentinal bridge formation was seen in group II at week 4. Therefore, the present results suggest that direct pulp capping with propolis flavonoids in rats may delay dental pulp inflammation and stimulate reparative dentin.

**As an intracanal irrigant**

Al-Qathami and Al-Madi (2003) compared the antimicrobial efficacy of propolis, sodium hypochlorite and saline as an intracanal irrigants. Microbiological samples were taken from the teeth immediately after accessing the canal and after instrumentation and irrigation. The results of this study indicated that the propolis has antimicrobial activity equal to that of sodium hypochlorite.

**As a mouth rinse**

Ozan et al. (2007) performed a study to compare the effects of four different mouthrinse containing propolis solutions and mouth rinse containing 0.2% chlorhexidine (CHX) on oral microorganisms and human gingival fibroblasts. Mouth rinse containing propolis was prepared at four different concentrations as 10, 5, 2.5 and 1%. Besides, CHX was used as control group. The antibacterial effects of five solutions on oral microorganisms were tested and their cytotoxic effects on human gingival fibroblasts were evaluated by agar diffusion test. At this concentrations effectiveness of mouth rinse containing propolis samples on oral microorganisms were not found as effective as CHX. On the contrary, samples found less cytotoxic on human gingival fibroblasts than CHX.

Koo et al. (2002) evaluated the effect of a mouth rinse containing propolis on 3-day dental plaque accumulation. Six volunteers took part in a double-blind crossover study performed in two phases of 3 days. During each phase the volunteers refrained from all oral hygiene and rinsed with 20% sucrose solution 5 times a day to enhance dental plaque formation and with mouth rinse (placebo or experimental) twice a day. On the 4th day, the plaque index (PI) of the volunteers was scored and the supragingival dental plaque was analyzed for insoluble polysaccharide (IP). The plaque index for the experimental group was, significantly less than for the placebo group. The experimental mouth rinse reduced the insoluble polysaccharide concentration in dental plaque by 61.7% compared to placebo. An experimental mouth rinse containing propolis SNB-RS was thus efficient in reducing supragingival plaque formation and insoluble polysaccharide formation under conditions of high plaque accumulation.

**As a cariostatic agent**

Hayacibara et al. (2005) evaluated the influence of propolis on mutans streptococci viability, glucosyltransferases (GTFs) activity and caries development in rats. The data suggested that propolis is a potentially novel anti-caries agent.

**In dentinal hypersensitivity**

Mahmoud et al. conducted a pioneer study on the effect of propolis on dentinal hypersensitivity *in vivo* (Mahmoud et al., 1999). The clinical trial of propolis on female subjects for four weeks was conducted. Twenty-six female subjects with age range 16 - 40 years (mean 28 years) were included in the study. Propolis was applied twice daily on teeth with hypersensitivity. The hypersensitivity was assessed on a visual scale 0 - 10 and by slight, moderate and severe classification at baseline, after 1 and 4 weeks. Seventy percent of the subjects had severe hypersensitivity at the baseline. At first recall, 50% reported moderate hypersensitivity, 50% reported slight hypersensitivity at second recall and 30% had no hypersensitivity while only 19% had moderate hypersensitivity. It was concluded that propolis had a positive effect in the control of dentinal hypersensitivity. In another *in vitro* study using Scanning Electron Microscopic (SEM), it was found that propolis occluded the dentinal tubules in both 60 and 120 s application on human dentin (Almas et al., 2001).

**In treatment of periodontitis**

Toker et al. (2008) analyzed the morphometric and histopathologic changes associated with experimental

periodontitis in rats in response to the systemic administration of propolis. Changes in alveolar bone levels were clinically measured and tissues were histopathologically examined to assess the differences among the study groups. Propolis significantly reduced the periodontitis-related bone loss, the findings of this study provided morphologic and histologic evidence that propolis, when administered systemically, prevented alveolar bone loss in the rat model.

Murray et al. (1997) investigated the effectiveness of a propolis-containing mouth rinse in the inhibition of de novo plaque formation. Subjects used a propolis containing rinse, a negative control and a positive control in a double-blind, parallel, de novo plaque formation study design. The chlorhexidine mouth rinse was significantly better than the others in plaque inhibition. The propolis-containing rinse was marginally better than the negative control, but this difference was not significant.

Hidaka et al. (2008) studied the effects of honeybee products on the *in vitro* formation of calcium phosphate precipitates and inhibitory effect on the rate of amorphous calcium phosphate transformation to hydroxyapatite and on the induction time. Propolis reduced the rate of amorphous calcium phosphate transformation to hydroxyapatite by 12 - 35% and with a 2.5 - to 4.4-fold increase in the induction time. Propolis showed an inhibitory effect that was the same as or greater than 1-hydroxyethylidene- 1,1-bisphosphonate. These results suggested that propolis may have potential as anticalculus agents in toothpastes and mouthwashes.

**Effect on *Candida albicans***

Martins et al. (2002) assessed the susceptibility of *C. albicans strains*, collected from HIV-positive patients with oral candidiasis, to a commercial 20% ethanol propolis extract (EPE) and compare it to the inhibitory action of the standardized antifungal agents nystatin (NYS), clotrimazole (CL), econazole (EC) and fluconazole (FL). EPE inhibited all the *C. albicans* strained tested. No significant difference was observed between the results obtained with NYS and EPE, while significant differences were observed between EPE and other antifungals. The *C. albicans* strains tested showed resistance to the remaining antifungal agents. The propolis extract used in this study inhibited the *in vitro* growth of *C. albicans* collected from HIV-seropositive This fact suggested that commercial EPE could be an alternative medicine in the treatment of candidiasis from HIV-positive patients.

**In treatment of denture stomatitis**

Denture stomatitis presents as a chronic disease in denture-bearing patients, especially under maxillary prosthesis. Despite the existence of a great number of antifungal agents, treatment failure is observed frequently. Propolis, a natural bee product, possesses well-documented antifungal and anti-inflammatory activities. Santos et al. (2008) evaluated the clinical efficacy of a new Brazilian propolis gel formulation in patients diagnosed with denture stomatitis. Thirty complete-denture wearers with denture stomatitis were enrolled in this pilot study. At baseline, clinical evaluation was performed by a single clinician and instructions for denture hygiene were provided. Fifteen patients received Daktarin (Miconazole gel) and 15 received Brazilian propolis gel. All patients were recommended to apply the product four times a day during one week. Clinical evaluation was repeated by the same clinician after treatment. All patients treated with Brazilian propolis gel and Daktarin had complete clinical remission of palatal edema and erythema. They concluded this new Brazilian propolis gel formulation had efficacy comparable to Daktarin and could be an alternative topical choice for the treatment of denture stomatitis.

**As an intra-canal medicament**

Oncag et al. (2008) compared the antibacterial efficacy of three commonly used intracanal medicaments with propolis against *Enterococcus faecalis*. They concluded that propolis had good *in vitro* antibacterial activity against *E. faecalis* in the root canals, suggesting that it could be used as an alternative intracanal medicament. Awawdeh et al. (2009) evaluated the effectiveness of propolis and calcium hydroxide as a short-term intracanal medicament against *Enterococcus faecalis*. They concluded that propolis is very effective as intracanal medicament in rapidly eliminating *E. faecalis ex vivo.*

**Effect of propolis on recurrent aphthous stomatitis**

Recurrent aphthous stomatitis (RAS) is a common, painful, and ulcerative disorder of the oral cavity of unknown etiology. No cure exists and medications aim to reduce pain associated with ulcers through topical applications or reduce outbreak frequency with systemic medications, many having serious side effects.

Samet et al. (2007) evaluated the potential of a product to reduce the number of outbreaks of RAS ulcers. Propolis is a bee product used in some cultures as treatment for mouth ulcers. In this randomized, double-blind, placebo-controlled study, patients were assigned to take 500 mg of propolis or a placebo capsule daily. Subjects reported a baseline ulcer frequency and were contacted biweekly to record recurrences. Data were analyzed to determine if subjects had a decrease of 50% in outbreak frequency. The data indicated a statistically significant reduction of outbreaks in the propolis group. Patients in the propolis group also self-reported a significant improvement in their quality of life. This study

has shown propolis to be effective in decreasing the number of recurrences and improve the quality of life in patients who suffer from RAS.

**Bee propolis - how safe is it?**

In general, propolis is safe. It is a non toxic substance and for most people, will not caused irritation when used as supplements or applied to skin. However, like other honey bee products, there are people who are allergic to propolis. Allergic reaction due to this substance was first reported in beekeepers as an occupational effect but is now seen mainly in individuals who use propolis in cosmetics and supplement to treat various health conditions. It is believed that a substance called caffeic acids to be one of the causes of allergies to propolis.

**The symptoms of allergies**

If you are allergic to propolis, it may cause your skin to redden, develop rashes, swell, itch and may even lead your skin to crack. Apart from that, it may also irritate the skin area where it is applied on, cause eczema, lesions, psoriasis or mouth sores.

**Who can be allergic to propolis?**

Those already allergic to pollen: If you are already allergic to bee pollen or evergreens, you are advised not to use propolis. Pollens in propolis may come from any plants and not just plants in surrounding areas where you buy your product.

**Asthma patients**

If you have asthma, you should also avoid propolis because some chemicals or impurities in it may induce an attack. If you want to use it, ask your doctor's advise first.

**Allergic to bee stings**

Another group of people who may want to avoid propolis are those who are allergic to bee stings. Propolis could induce a side effect similar to a sting.

**Pregnant women**

There have not been many published clinical trials on the effect of propolis on pregnant women. Because the information in this area is limited, it has been advised to avoid using propolis during pregnancy and breastfeeding.

**Others at risk**

If you know that you're allergic to black poplar (also populas nigra), poplar buds, honey and balsam of Peru, avoid propolis as well. There are around 8 to 13 compounds that propolis and balsam of Peru have in common. Some of these compounds include benzyl benzoate, cinnamyl cinnamate and benzyl cinnamate. Several studies have suggested that patients who are sensitive to propolis also may react to balsam of Peru.

**A word of advice**

Even if you are not in the above categories, you should always take some precaution when using any form of medication. Take note that the best way to use propolis is to try it gradually. You should use small quantities of propolis for the first few days. After that slowly increase your propolis intake to the full outlined dosage if you could not detect any unwanted side effects. This way you would be able to test your comparability with the propolis product you are taking. It will also avoid annoying and painful allergic reaction to propolis. At the same time, if you decided to terminate the medical treatment prescribed by your doctor, it should also be done slowly and gradually.

**Will propolis interact with other drugs?**

At the moment there is no detrimental interaction between pure propolis and other man-made drugs. However, you must understand one thing. Propolis that is commercially used in cosmetics or as dietary supplement is normally extracted using ethanol. This high alcohol content in some propolis tinctures could lead to vomiting if you take it along with disulfiram (Antabuse) or metronidazole (Flagyl).

The second thing you must understand is the fact that the number of experiments involving propolis is still considered to be relatively small. Thus, not all interactions between propolis and other drugs are well known. So far the only well documented studies on propolis and its effect on other drugs is on its ability to improve the effect of antibiotics by 10 to 100 folds.

**CONCLUSION**

1. This paper reviews various clinical implications of propolis to improve the oral health.
2. Propolis can be used in the management of dental caries, endodontic as well as periodontal infections, vital

pulp therapy, in the treatment of oral lesions and repair of surgical wounds.
3. Though propolis has shown very promising results but clinician should be cautious while using this material due to its allergic reactions shown in some patients.

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