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A PARADIGM SHIFT FROM SYNTHETIC TO NATURAL DEFENDERS: PROPOLIS- A HEALING AGENT

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ABSTRACT

Over the last few decades, worldwide increase use of natural products in the for pharmacological purposes has been observed. Propolis is a natural resinous mixture produced by honeybees from substances collected from parts of plants, buds and exudates. Propolis has been extensively employed by man since ancient times, especially in folk medicine to treat several maladies. Propolis has a degree of anti microbial action against fungi such as Candida Albicans and some bacteria including a range of oral micro organisms and viruses and may be as effective as acyclovir against herpes simplex virus. It also has immuno modulatory activity with augmentation of non specific anti tumor resistance. In dentistry, Propolis has been used in dentifrices, as a storage medium for teeth that have avulsed, in periodontal therapy and in endodontic treatment. Propolis extract used as mouth rinse possesses anti microbial activity against *Streptococcus mutans* present in the oral cavity. Subgingival irrigation with Propolis extract as an adjunct to periodontal treatment may also be more effective than scaling and root planning alone. It has promising role in future medicine as well as dentistry. Thus, switching back to natural resources, Propolis seems to be a promising alternative for the control of oral diseases in terms of anti microbial response and lower associated risk. This paper is an attempt to

review various applications of this compound in dentistry.

KEYWORDS: Propolis; oral health; antimicrobial; antifungal; dental; gingivitis; periodontitis; mouthwashes

INTRODUCTION

Nowadays, there is a great trend to use natural materials as a cure for a variety of diseases. The health field has also always aimed to use natural products as an alternative to the conventional allopathic formulations. Propolis is one such natural substance, which has gone unnoticed inspite of its potential uses in curing a large array of diseases. The word propolis is derived from the Greek word "pro" which means before, and "polis" meaning city or defender of the city.^[1] 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.^[2] Incas employed propolis as an anti-pyretic agent. Greek and Roman physicians used it as mouth disinfectant and as an antiseptic and healing product in wound treatment, prescribed for topical therapy of cutaneous and mucosal wounds. These therapeutic applications were perpetuated in the middle age and among Arab physicians.^[3] In the end of 19th century, propolis was widely used due to its healing properties and in the Second Global War it was employed in several Soviet clinics for tuberculosis treatment, due to the observed decline of lung problems and appetite recovery.

appetite recovery. In the Balkan states it was one of the most frequently used remedies, applied to treat wounds and burns, sore throat and stomach ulcer.^[4] Another name of propolis is bee glue. Due to its waxy nature and mechanical properties, bees use propolis in the construction and repair of their hives,^[5] for sealing openings and cracks and smooth out the internal walls and as a protective barrier against external invaders likes snakes, lizards etc. or against weathering threats like wind andrain.^[3,6] Current applications of propolis include formulations for cold syndrome (upper respiratory tract infections, common cold, flu-like infections), as well as dermatological preparations useful in wound healing, treatment of burns, acne, herpes simplex and genitalis, neurodermatitis and in number of dental procedures.^[7] The aim of this article is to divert the attention and uplift the knowledge of general dentists from the conventional and newly emerging products in the market and utilizing the "back to nature" approach and highlighting uses of propolis in various branches of dentistry.

DISCUSSION

Propolis is a resinous material that honeybees (Apis mellifera L) collected from various plant species and mix with wax and other substances.^[8] Propolis is used as a sealant for unwanted open spaces in the hive. Propolis is composed of resin and balsams (50-60%), pollen (5-10%) and other constituents which are amino acids, minerals, Vitamins A, B complex and the highly active biochemical substance known as bioflavenoid (Vitamin P), phenols, aromatic compounds,^[9] cinnamic acid, terpenes and caffeic acid and several constituents which varies due to different geographical region and climate.^[8,9] It purpose several biological activities such as antimicrobial, antifungal, antiviral, immunostimulatory, antiinflammatory, anti-cancer anti-oxidant activity on the basis of their geographical region.^[10] The biological activity of propolis is associated mainly with flavonoids and derivatives of hydroxycinnamic acids.^[11] Flavonoids are wellknown plant compounds that have antimicrobial, antioxidant, antibacterial, antifungal, antiviral, and anti-infl amatory properties. Propolis is shown to inhibit synthesis of prostaglandins, activate the thymus gland, aid the immune system by promoting phagocytic activity, stimulate cellular immunity, and augment healing effects on

epithelial tissues thus resulting in its antiinflammatory action.^[12,13] Propolis is antibacterial because it can inhibit bacterial RNA-polymerase; it is immunomodulatory, antioxidative, and a healing agent because of the ability to sequester or inhibit free radical formation.^[13] Flavonoids (quercetin, galangin, and pinocembrin), caffeic acid, benzoic acid, and cinnamic acid may probably act on the microbial membrane or cell wall, causing functional and structural damages. Additionally, propolis contains elements, such as iron and zinc that are important for the synthesis of collagen.^[12] Aromatic compounds, such as caffeic acid, in propolis are known to be antimicrobial and antibacterial, antiinflammatory, immunomodulatory, and hepatoprotective.^[13]

USES OF PROPOLIS IN DENTISTRY Antibacterial Properties

Propolis has found to be very effective against gram positive bacteria (Seidel *et al*)^[14] especially against Staphylococcus aureus (Velazquez et al)^[15] and against gram negative bacteria against Salmonella (Orsi et al).^[16] 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*)^[5] and found that the insoluble glycan synthesis and glucosyltransferase activity were inhibited by multiple actions of Propolis. Koru et al., studied the antibacterial action against certain anaerobic oral pathogens and found to be very effective against Peptostreptococcus anaerobius, Lactobacillus acidophilus, Actinomyces naeslundii, Prevotella Prevotella oralis, 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.^[17] According to Amoros et al., and Bonhevi et al., the activity against microorganisms is more related to the synergistic effect of flavonoids or other phenolics than to the individual compounds. These findings are in agreement with those of Takaisikikuni and Schilcher, who observed that the antibacterial action against Streptococcus. Agalactiae was complex, involving different mechanisms including the formation of pseudomulticellular

Propolis- a healing agent

Streptococci, disorganization of the cytoplasm, the cytoplasmatic membrane, and the cell wall, partial bacteriolysis, and inhibition of protein synthesis. Propolis has mucoprotective properties, as described in oral and gastric mucosa. The presence of quercetin, myricetin, kaempferol, rutine, pinocembrin, coumaric acid, caffeic acid, and CAPE is found in Chilean propolis, which inhibits mutans streptococci growth.^[12] Propolis is relatively non-toxic, and studies have exhibited a no-effect level in mice at 1400 mg/kg weight/day and thus a safe dose in humans was proposed to be 1.4 mg/kg weight/day, or approximately 70 mg/day. Therefore, the administration of propolis at appropriate concentrations will be effective on oral microorganisms and non-cytotoxic to gingival fibroblasts.^[18]

Effect on Candida albicans

Propolis-based products have strong antifungal properties in relation to Candida albicans and other types of *Candida* species. *Candida* albicans is most sensitive to propolis. Propolis solutions can be also used in form of mouthwash or gel for local application in patients with oral candidiasis using removable dentures.^[19] The flavonoids in propolis, mainly pinocembrin with a high content of aromatic acids and amyrins, have been considered to be responsible for inhibitory effect on Candida.^[20] Martins et al., 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, clotrimazole, econazole and fluconazole. EPE inhibited all the C. albicans strained tested. This fact suggested that commercial EPE could be an alternative medicine in the treatment of from HIV-positive patients.^[21] candidiasis Streptococcus spp. and C. albicans are found to be susceptible to low concentrations of propolis, though Staphylococcus spp. and E. coli are found to be more resistant. The concentration at 10% of propolis solutions showed significant activity on Candida strains, and it is useful to prevent candidial infections.^[12]

As an Antiviral Agent

As an antiviral, it delays growth and progression of skin changes in an early stage of infection with *Herpes simplex* and does not cause cytotoxic effect. A study assessed Brazilian propolis against Herpes virus Type 1 infection in mice. Ethanol extracts of propolis significantly limited development of herpetic skin lesions. It significantly enhanced delayed type hypersensitivity to inactivated virus. Oral ethanol propolis extract administration also significantly increased production of interferon gamma.^[22] Kujumgiev et al., evaluated the antiviral against (Avian influenza virus) properties of propolis and found to be very effective.^[10]

As a Cariostatic Agent

Two groups of bacteria are responsible for initiating caries: Streptococcus mutans and Lactobacillus. If left untreated, the disease can lead to pain, tooth loss and infection. Propolis is associated with two mechanisms of action, i.e., anti-caries/anti-plaque properties: (1 It shows anti-microbial activity against cariogenic bacteria; and (2 it inhibites glucosyl transferase enzymes (GTFs) activity.^[17] Propolis limits the number of cariogenic microorganisms, slows down synthesis of insoluble glucans, and inhibits glucosyl transferase enzyme, which is essential for Streptococcus mutans to catalyze the formation of soluble and insoluble glycans and provide adherence. Cariostatic effect of propolis is through a high quantity of fatty acids, which slow down the production of acids by Streptococcus decrease the tolerance and of mutans, microorganisms to acid pH.^[5,23] Hayacibara et al., the influence of propolis evaluated on streptococci mutans viability, glucosyltransferases (GTFs) activity and caries development in rats. They suggested that propolis is a potentially novel anti-caries agent.^[24]

Role in Treatment of Periodontitis

Toker et al., analyzed the morphometric and histopathologic changes associated with experimental periodontitis in rats in response to the systemic administration of propolis. They concluded that systemically healthy administered propolis significantly reduced the periodontitis related bone loss.^[25] Hidaka et al., 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. Results suggested that propolis may have potential as anticalculus agents in toothpastes and mouthwashes.^[26]

As a Mouth Rinse

Ozan et al., performed a study to compare the effects of four different mouthrinse containing propolis solutions (conc. 10, 5, 2.5 and 1%.) and mouth rinse containing 0.2% chlorhexidine (CHX) on oral microorganisms and human gingival fibroblasts. 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.^[12] Dodwad V et al., showed that propolis is not better than chlorhexidine in reducing plaque formation, but it may be marginally better for reducing gingival inflammation.^[27] A study by Koo et al., to evaluate the effect of a mouthrinse containing propolis on 3 day plaque accumulation concluded that propolis containing mouthrinse was efficient in reducing supragingival plaque formation. Murray investigated the effectiveness of a propolis containing mouthrinse in the inhibition of plaque formation concluded that propolis containing Mouthrinse was marginally better then negative control.^[28] The antimicrobial properties of propolis against oral pathogens is attributed to the flavonone pinocembrin, the flavonol galangin, and the caffeic acid phenethyl ester (CAPE); the mechanism of action is probably based on the inhibition of bacterial RNA-polymerase.^[29] Wound Healing, Tissue Regeneration and Bone Remodeling

Magro-Filho and Carvalho in their study analyzed the effects of propolis mouth rinse on the repair of surgical wounds and concluded that the mouth rinse containing propolis in aqueous alcohol solution aided repair of intra-buccal surgical wounds and exerted a small pain killing and antiinflammatory effect. They also stated that the vehicle employed had a minor irritant effect on infra-buccal surgical wounds. Exfoliative cytology showed epithelization of infrabuccal surgical wounds.^[30] In another study Magro-Filho and Carvalho examined histologically the effects of propolis topical application to dental sockets and skin wounds. It was concluded that topical application of propolis hydroalcoholic solution accelerated epithelial repair after tooth extraction but had no effect on socket wound healing.^[31] Propolis accelerates the tissue regeneration process. Ethanol extract of propolis promotes the

healing processes in damaged cartilage and enhances ossification in the artificially induced bone defects. In malocclusions accompanied by a considerable narrowing of the maxilla, it is necessary to use a device to expand the palatine suture. During the treatment, bone remodeling takes place within the palatine suture. The research carried out by Altan et al., on rats showed an increased quantity of osteoblasts in preparations from rats, which received propolis during the treatment. In such cases, the bone remodeling within the palatine suture was quicker.^[32] The regenerative effect of propolis on the tooth pulp has been known for a long time. It not only prevents the inflammatory reaction, infection with microbes and pulp necrosis but also induces the formation of high quality tubular dentin through stimulation of stem cells.^[32]

In Treatment of Denture Stomatitis

Due to the increasing resistance to fluconazole and toxicity of some antifungal drugs, new alternatives in the treatment of denture stomatitis are a novel idea. Propylene glycol Brazilian green propolis has been shown to have an antifungal activity, which is similar to miconazole in the C. albicans colonies decrease and in the erythema reduction of patients with Candida-associated denture stomatitis. The study recommended propolis to be an alternative therapeutics for this condition.^[33] Santos et al., evaluated the clinical efficacy of a new Brazilian propolis gel formulation in patients diagnosed with denture stomatitis. 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.[34]

A Promising New Storage Media Following Avulsion

Martin and Pileggi conducted a study and compared various storage media and concluded that propolis may be a better alternative to HBSS, milk, or saline in terms of maintaining PDL cell viability after avulsion and storage.^[35] Ozan *et al.*, determined the ability of 10% propolis to serve as a temporary storage medium for the maintenance of periodontal ligament (PDL) cell viability of avulsed teeth.^[12] Al-Shaher *et al.*, examined the tolerance of fibroblasts of the periodontal

ligament (PDL) and dental pulp to propolis and compared with that of calcium hydroxide in vitro. They concluded that propolis can be recommended as a suitable transport medium for avulsed teeth.^[36]

In Dentinal Hypersensitivity

Mahmoud *et al.*, conducted a pioneer study on the effect of propolis on dentinal hypersensitivity in vivo and concluded that concluded that propolis had a positive effect in the control of dentinal hypersensitivity.^[37]

As an Intra-canal Medicament

Oncag et al., 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.^[38] Awawdeh et al., 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.^[39] Qatham et al., in their study stated that Sodium hypochlorite as an endodontic irrigant, possesses problems of toxicity, odor and discoloration of operatory items. An equally effective, but safe irrigant is desirable. The results of this study indicated that the propolis has antimicrobial activity equal to that of sodium hypochlorite.^[40] Since propolis has good diffusion abilities and adds to the antimicrobial action of calcium hydroxide, it can be used as a vehicle for calcium hydroxide.[32]

As a Pulp Capping Agent

Sabir *et al.*, evaluated the response of rat dental pulp to direct pulp capping with propolis. It has been suggested that the direct pulp capping with propolis flavonoids in rats may delay dental pulp inflammation and stimulate reparative dentin.^[41]

As an Intracanal Irrigant

Al-Qathami and Al-Madi compared the antimicrobial efficacy of propolis, sodium hypochlorite and saline as an intracanal irrigants. The results of this study indicated that the propolis has antimicrobial activity equal to that of sodium hypochlorite.^[40]

Effect of Propolis on Recurrent Aphthous Stomatitis

Samet et al., evaluated the potential of a product

to reduce the number of outbreaks of RAS ulcers. Propolis to be effective in decreasing the number of recurrences and improve the quality of life in patients who suffer from RAS.^[42] A study evaluated the effect of bee propolis on recurrent aphthous stomatitis (RAS), 500 mg of propolis capsule taken daily significantly reduced outbreaks of RAS ulcers. The quality of life of these patients significantly enhanced, and there was decrease in the number of recurrence of these ulcers.^[42,43] One of the complications which rarely can occur in patients using propolis containing products which can be in form of cosmetics, dietary supplements or dental products is an allergic reaction to propolis. Group of people those who are allergic to bee stings, those suffering from asthma, during pregnancy and breastfeeding, and those who are known allergic to black poplar (also populas nigra), poplar buds, honey and balsam of Peru, avoid propolis as well.^[2]

CONCLUSION

"Look back into the nature and then you will understand everything better." This quote by Albert Einstein clearly point towards the paradigm shift from costlier antibiotic therapies to the old tradition remedies with minimum side effects like in therapeutic uses of propolis. Propolis can be termed as a "natural antibiotic" as it shows inhibitory effect on a variety of pathogenic organisms. However, as propolis is a subject of recent dental research. There is limited evidence that propolis may actively protect against oral diseases, the extract can be used as an alternative measure to prevent periodontal and gingival problems, and because propolis is a gift from Mother Nature, it is non toxic and safe for most people.

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The author declares that there is no source of funding and there is no conflict of interest among all authors.

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