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**Dr. Hithaishe Raghunath**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

**Dr. Madhusudhan**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

**Dr. Archana Krishnamurthy**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

**Dr. Shilpashree KB**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

**Dr. M Vinod Kumar**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

**Corresponding Author:**  
**Dr. Hithaishe Raghunath**  
The Oxford Dental College,  
Bommanahalli, Bangalore,  
Karnataka, India

## Propolis: Insight

**Dr. Hithaishe Raghunath, Dr. Madhusudhan, Dr. Archana Krishnamurthy, Dr. Shilpashree KB and Dr. M Vinod Kumar**

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### Abstract

PROPOLIS, a wax-cum-resin substance, also known also as bee glue, a complex mixture made up of plant-derived and bee released compounds. Its multiple biomedical applications to treat a large array of systemic diseases have gained popularity. The purpose of this review is to present the possible use of propolis in treatment of various diseases of oral cavity based on their properties and explore the status and scope of propolis for its contemporary and potential future bio-dental applications.

**Keywords:** Propolis, Dentistry, Oral health

### 1. Introduction

The use of natural products such as natural silk, chitosan, herbal tea, miswak, neem, tulsi, amla, dhatura, nimbu etc, in the biomedical application to treat a large array of systemic diseases have gained popularity, many of which have become the basis for the development of new lead chemicals for pharmaceuticals in today's world [1].

A few proven beneficial plant and animal derived medicines widely being used in general and oral health care are: Quinine (Anti-malarial drug) – Cinchona tree bark, Aspirin (Analgesic, anti-inflammatory, body temperature regulator) – Meadowsweet plant root and Willow tree bark, Beeswax and honey for burns, 2 wounds and eye disorders, Clove as an essential oil for halitosis, bleeding gums, toothache in periodontitis, and as anesthetic. Clove gel can provide dentists with an alternative to benzocaine for topical anesthesia. Tulsi (anti-helminthic, analgesic, anti-pyretic, immune stimulatory, anti-ulcer, antimicrobial, anti-inflammatory) for periodontitis. Neem (inhibitory action on bacterial growth, adhesion) for gingival and other dental problems [3].

One such natural product is Propolis, a complex mixture made up of plant-derived and bee released compounds. Honey bees (*Apis mellifera*), harvest resins from various plant species and bring them back to the colony where they are then utilized as propolis [4].

Propolis, a wax-cum resin substance comes from Greek word “pro” (meaning outer wall) and “polis” (meaning city), which is made by bees for building and preservation of their hives.

This naturally occurring substance has a wide range of overlooked benefits such as anesthetic, antibacterial, antifungal, antiviral, antioxidant, anti-carcinogenic, anti-mutagenic, anti-thrombotic and immunomodulatory [3], being cost-effective and biocompatible with the human cell, with no toxicity, limited allergic reaction and ready availability that can be used widely in medicinal care [5].

### 2. Materials and Methods

#### Composition

Chemically propolis is composed of more than 180 different types of chemicals and season to season. Propolis is collected both in temperate zone and tropical zones and slightly different. As a result more than 300 different components have been identified in propolis. In general, propolis contains polyphenol (flavonoids, phenolic acids and esters), phenolic aldehydes and ketones, etc. [6]

**Properties**

As per various lines of evidences, propolis exhibits extensive

**Anti-bacterial** (more efficient against gram-positive bacteria than gram-negative bacteria) [7].

**Anti-fungal**

**Anti-viral** (The mechanism of propolis antiviral property in CD4+ lymphocytes appears to involve, in part, inhibition of viral entry),

**Anti-inflammatory** (Major component being CAPE which is lipophilic, can easily enter the cell to inhibit the LOX and COX enzymes, which indirectly inhibit arachidonic pathway. The inhibition of arachidonic acid prevents the release of prostaglandins and leukotrienes responsible for inflammation and pain. CAPE also enhances the production of anti-inflammatory cytokines IL4 and IL10. Decreases infiltration of monocytes and neutrophils as well.)

**Anti-cancer**, [8]

**Immunoregulator** properties (One of the biological effects of propolis is its immunomodulatory effect by either enhancing or suppressing the immune system. This contradictory effect is probably due to its complex chemical variety, the presence in different geographic regions, and the different forms of extraction) [9] and so on.

**Application of propolis in medical field:**

In the field of medicine, propolis has been prodigiously used to treat pain and hasten up the healing process. It has also found its way into the cancer research. The major component of propolis is Caffeic Acid-Phenethyl Ester (CAPE) which is a biologically active compound. CAPE has both anti-inflammatory and antioxidative properties thus reducing the pain and inflammation. CAPE also has an inhibitory effect and can be used as a chemical agent to prevent cancer metastasis [10, 11].

**Application of propolis in dentistry**

The use of propolis in dentistry has been studied and reported in various research works in all the departments pertaining to dentistry. Propolis is shown to be a great product in the improvement of oral hygiene by reducing the caries and periodontal disease causing bacterias. Researches are being carried out using propolis for the reduction of halitosis.

It is being used in the post-surgical wound healing by decreasing inflammation and speeds up creation of granulation tissue and epithelialization [12].

**Cariostatic effect:** it limits the number of microorganisms, slows down synthesis of insoluble glucans, and slows down activity of glucosyltransferase. Studies done by researchers unanimously show that extracts from bee glue limit the quantity of bacterial plaque which influences the reduction of tooth caries. Cariostatic effects of propolis by high quantity of fatty acids which slow down the production of acids by *Streptococcus mutans* and decreases the tolerance of microorganisms to acid pH.

Propolis can be also used in a form of a solution to decontaminate fibres of toothbrushes.

The antibacterial properties of propolis in relation to pathogens of periodontitis are conditioned by flavonoids, phenol acids, and their esters. As propolis mouth rinses and propolis-based toothpastes stop the growth of pathogens of gingivitis and periodontitis, they seem to be promising not

only as preventive but also as therapeutic agents [13].

The usage of propolis as a caries preventive measure can remarkably shift the preventive dentistry concepts. Propolis has already been tested as an adjuvant to vaccines and hence, may have a future role in caries vaccination or as adjuvant therapy to other anti-caries agents [e.g. fluorides, povidone-iodine, casein phosphopeptide – amorphous calcium phosphate (CPP-ACP)] [14].

Recent advances in the propolis propose that it can serve as a promising storage and transport medium for avulsed teeth. [15]

In the department of endodontics, propolis gained popularity as an effective intra-canal irrigant, [16] intra-canal medicament, pulp capping agent, [17, 18] as a vital pulp therapeutic agent, anti-resorptive agent for reimplanted teeth [19].

In the field of orthodontics, Propolis solution was shown to have a positive effect on bone formation during treatment with a device to expand the palatine suture.

Propolis may also have a role in reducing or delaying radiation-induced mucositis.

Other intriguing uses of propolis in dentistry are its use as a desensitizing agent, its commendable effect on the recurrent aphthous stomatitis, in the treatment of denture stomatitis, candida albicans [20].

Various lines of evidences are available with all the above mentioned properties of propolis while many researches are still being carried out to bring out the most of advantages of propolis that could be a path to newer inventions in the field of medicine as well as dentistry.

**3. Results and Discussion****Recants Trends and Developments In Propolis**

- **Bioassay-guided studies of active principles**

Studies based on bioassay-guided chemical analysis represent a very promising trend in propolis research. Using this approach, two new cytotoxic prenylflavones were isolated from Taiwanese propolis. Both compounds demonstrated cytotoxic properties on three cancer cell lines and also were potential radical scavengers – radicals of 1,1-diphenyl-2-picrylhydrazyl (DPPH) [21].

- **The beginning of modern research on propolis**

Polish investigators showed that without any doubt propolis:

1. stimulates regeneration of experimentally damaged tissue as well as tissue in pathological processes,
2. acts as antioxidant
3. acts radioprotectively
4. has strong immunostimulative properties
5. has extracts that have cytolytic activity on anticancer cells in animal studies
6. affects animals' life span by extending it
7. improves intellectual and life functions of the elderly
8. speeds up recovery in patients with prostatitis [22].

- **Nanoparticles and innovation products**

Nowadays, finding natural additives has increased the efforts both to obtain bioactive compounds from natural raw materials and develop stable and functional derivative products. The former mentioned properties attributed to propolis are valuable and find applications in several industries, such as pharmaceuticals, agrochemical, and food. The growing interest in propolis has also promoted technological development for the suitable application of propolis [23].

## Contra Indications

**Toxicity:** There have been many studies to estimate the toxicity of propolis because the method for propolis extraction remains unstandardized, variability in reported toxicity would be expected. And the results of studies have shown that there are very little to nil reported toxicities that have allowed its widespread use in cosmetics and skin creams.

**Contact allergy to propolis in beekeepers:** Beekeepers had suffered from allergy to propolis for 7.4 years on average. However, beekeepers were not confronted with the disease when they first began beekeeping. On average, allergy to propolis started after 9.5 years of beekeeping (range 0.1–35.0 years). Reactions to propolis occurred after various time intervals ranging between 5 min and 48 h. The various types of reactions reported are itching, burning skin, urticaria, local rash, mild systemic reactions and severe systemic reactions. This shows that allergy to propolis in beekeepers is not only a local problem but may cause systemic reactions as well. These may be less severe (urticaria and difficulty swallowing) or more severe (dyspnoea). The symptoms lasted for different time intervals ranging from 5 h to 20 days. Symptoms in beekeepers worsened over time in few cases, improved in some and remained the same in the remaining cases. In four cases symptoms were more severe or less severe in spring after beekeeper shared less contact with propolis.

A very recent one which focused on propolis allergy associated with the presence of other allergies which may also cause systemic reactions. In the cases studied, these reactions occurred during the administration of propolis containing solutions for the treatment of upper respiratory tract infections. These solutions are most likely to be ethanol, which could perhaps partially support the hypothesis presented by the beekeepers, who considered that the solvents used to clean the hands facilitated the development of contact allergy.

This hypothesis may explain how the antigen is transported into the deeper layers of the skin where it can lead to sensitisation. It is also in accordance with a study on the epidermal penetration of parabens depending on the type of solvent, and work which shows that propolis is absorbed after oral ingestion. This hypothesis should be addressed in future studies in order to avoid the development of allergy to propolis [24].

## 4. Conclusion

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.

The present review focuses on the potential health benefits of bee products such as honey, propolis, and royal jelly. These products are highly rich in active components such as flavonoids, phenolic acid, phenolic compounds, terpenes, and enzymes, which have biological functions in preventing some diseases and promoting good health. Honey, propolis, and royal jelly have distinct efficacies with significant nutritional properties and functional values. Thus, these bee products can be developed into potent apitherapeutic agents. However, some precautions need to be taken in case of allergens associated with bee products and in finding the right intake

dosage.

*In vitro* and animal studies seem to confirm the usefulness of using bee products (propolis, bee pollen, and royal jelly) as natural agents capable of counteracting the effects of oxidative stress underlying the pathogenesis of numerous diseases or disorders, such as neurodegenerative disorders, cancer, diabetes, and atherosclerosis, as well as negative effects of different harmful factors and drugs (e.g., cytostatic agents). However, studies on their role in humans are very limited, and the existing ones have aimed mostly at evaluating the effect of the supplementation of commercially available extracts of propolis or royal jelly in healthy people or type 2 diabetes.

There are various chemical compounds in propolis, most notably flavonoids. A review of the articles showed that propolis is an appropriate irrigant for the elimination of *Enterococcus faecalis* or *Candida albicans*, an intracanal medication in root canal therapy, also as a storage medium to maintain the vitality of the PDL cells. Propolis has the ability to inhibit osteoclastic activity or resorption, and induce high-quality tubular dentin in vital pulp therapy. The propolis has positive effect on animal hygiene by increasing the immunity and decreasing the stress via increase the globulin level in the blood, but the beneficial effect of propolis seems to be dose dependent.

The pharmacologically active molecules are flavonoids, phenolic acids, and their esters. These components have multiple effects on bacteria, fungi and viruses. In addition, propolis and its components have anti-inflammatory, immunomodulatory activities, and antitumor activity. Until this becomes available, physicians should weigh the benefits of propolis as an adjuvant therapy for the good of cancer patients.

Evidently, the approach based on typification according to the plant source gives good results in the field of propolis standardization. There is still a lot of work to be done by researchers to achieve a reliable standardization of propolis types other than poplar type. This is especially important with respect to the reliability of the results obtained in studies on propolis biological activities. Working with standardized material will allow scientists to connect a particular chemical propolis type to a specific type of biological activity and formulate recommendations for mainstream practitioners. This could help the general public to make more efficient use of the beneficial properties of propolis.

The priorities of future research lie on the influence of species and behaviour on propolis, together with feeding experiments to identify the plant part source, which will advance the understanding of the chemistry and quality of propolis, as well as honey bee biology. Characterization of propolis from various locations and plant sources is warranted to define acceptable quantitative standards for different types of propolis.

Furthermore, the biological activities of each type of propolis need to be correlated with their chemical composition, and eventually, standardized products should be used in clinical studies.

In conclusion, considering propolis components like resin, pollen, vitamins, flavonoids and phenols, propolis also has anti bacterial, anti inflammatory, anti microbial, anti cancer, anti viral and anti fungal properties. It can be used for various purposes and has a promising role in the field of medicine and dentistry.

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