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Review

Propolis – can it „bee" a breakthrough in dental care?

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ABSTRACT

Propolis, an intriguing natural material synthesized by bees, is characterized by its intricate resinous blend, which boasts a remarkably varied chemical composition. This unique blend contains various bioactive compounds that contribute to its numerous health benefits. The ability of propolis to combat inflammation, infections, and oxidative stress has made it a powerful candidate for enhancing overall health, with particular relevance to oral care practices. As the researchers continue to unravel the diverse properties of propolis, it is becoming an increasingly intriguing subject for clinical studies. In the present review, we aim to summarize and present the most recent data from clinical trials on the potential of propolis in the oral cavity diseases treatment and prevention. Propolis can be helpful in decreasing dental caries, effectively treating periodontitis, managing dentin hypersensitivity, treating gingivitis, and promoting overall oral hygiene. The results of our research suggest that propolis could serve as a valuable adjunct to dental therapies, potentially improving traditional methods and leading to enhanced outcomes for patients.

KEYWORDS: propolis, oral cavity diseases, antimicrobial activity, dentistry, flavonoids

1. Introduction

Propolis, also known as the bee glue, represents a natural complex resinous mixture characterized by an exceptionally diverse chemical composition, produced by honeybees (*Apis mellifera* L., Apidae). The etymology of the word "propolis" traces back to the Ancient Greek, where *pro* signifies "before", and *polis* means "city". This name is intrinsically linked to its primary biological role. Propolis functions predominantly as a hive-sealing material, safeguarding the colony environment against microbial invasion and pathogenic infections. Given the physical proximity of bees within colonies, propolis serves as a critical natural antibiotic. Furthermore, a thin coating of propolis forms an impermeable barrier, mitigating the water loss and maintaining consistent humidity levels within the hive [1].

Since ancient times, there has been an ongoing debate about the origins of propolis, revolving around the uncertainty of whether its source is purely botanical or a result of bee activity. The advancement in analytical techniques enabled the determination of the chemical composition of propolis and the identification of factors affecting its formation [2]. Propolis is created by bees using resins collected from plant buds, secretions, and other parts of plants. These materials are then combined with bee saliva enzymes and beeswax, resulting in the formation of this remarkably intriguing resinous substance. Due to the diverse habitats of bees and the variation of local flora, the composition of propolis is highly variable [1]. Despite the differences in plant species available to the bees across the continents, propolis demonstrates similar pharmacological properties, which has been a focus of numerous ongoing studies [3]. Particularly noteworthy are its antibacterial, antiviral, antifungal, and anti-inflammatory properties. Propolis has been mentioned as a therapeutic agent since ancient times, notably for treating infections, wounds, ulcers, muscle pain, and even rheumatism [1]. The progress of scientific inquiry has revealed novel domains, in which its therapeutic capabilities are remarkably beneficial. The neuroprotective, regenerative, cardioprotective, and anti-cancer attributes of propolis have garnered

considerable attention from researchers in the scientific field [3].

Recent data reveals that approximately 10% of the global population suffers from periodontal diseases, while every second adult contends with some form of oral health condition. This underscores the fact that oral diseases rank among the most widespread chronic inflammatory conditions worldwide [4]. Periodontal diseases result from inflammation caused by dysbiosis of the oral microbiome. Under the physiological conditions, oral bacteria proliferate into larger clusters, forming a thin, sticky layer on teeth known as dental plaque or biofilm. These clusters typically consist of both Gram-positive and Gram-negative microorganisms. When these bacteria overgrow or become imbalanced, they can lead to the formation of cavities or other periodontal conditions [5]. The traditional treatments of microbial infections of the oral cavity, such as periodontitis, gingivitis, pharyngitis, and the preventative products for caries, are inevitably associated with the possibility of serious side effects. This may include allergic reactions, nausea, or upset stomach [6]. Therefore, the attention towards natural methods of periodontal diseases management has significantly grown due to their reduced side effects. Consequently, there is an urgent need to develop new, natural, safe, and effective treatment methods [4]. The anti-inflammatory, immunomodulatory, antioxidant, antibacterial, and antifungal properties of propolis reveal its significant potential in promoting and maintaining oral health [5].

2. Chemical composition of propolis

As it has been already noted, the chemical composition of propolis is highly complex and closely linked to the types of plants used by the bees in its formation. It is also influenced by the environmental conditions and geographical origin [7]. The composition of raw propolis includes approximately 50% resins, 30% waxes, 10% essential oils, 5% pollen, and 5% various organic materials. Research has identified more than 300 chemical compounds in propolis. Its therapeutic effects are largely attributed to the presence of polyphenols: flavonoids, and phenolic acid esters, with polyphenols and terpenoids recognized as the most potent active ingredients [8].

Flavonoids, which represent one of the most important groups of biologically active compounds present in propolis, are organic chemical substances derived from polyphenols. Flavonoids fulfill many functions in plants, as they serve as plant pigments, antioxidants, natural insecticides and fungicides. Within the array of flavonoids identified in propolis, pinocembrin, galangin, chrysin, kaempferol, and quercetin are noted for their significant abundance (Figure 1) [2].

Particular attention has been directed towards artepillin C (3,5-diprenyl-p-coumaric acid) (Figure 2), a prenylated derivative of p-coumaric acid. This compound, which is primarily sourced from Brazilian green propolis, shows considerable antibacterial activity, particularly towards methicillin-resistant *Staphylococcus aureus* (MRSA) strains. Additionally, artepillin C is distinguished by its potent anti-inflammatory properties, achieved through the modulation of nuclear factor kappa B (NF-κB) and the inhibition of prostaglandin E2 and nitric oxide. These features suggest its potential utility in the treatment of diverse inflammatory diseases [9]. Numerous studies have proved that artepillin C holds much wider potential, as it exhibits antidiabetic, gastroprotective, immunomodulatory, neuroprotective and last but not least, the anticancer activity [10].

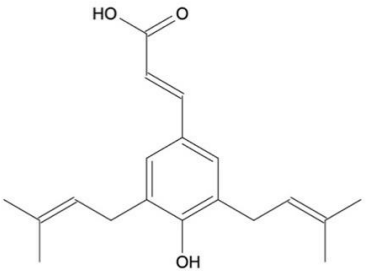

Fig 2. Chemical structure of artepillin C

Another significant group of compounds found in propolis belongs to the group of aromatic acids, namely ferulic, cinnamic, caffeic and benzoic acids (Figure 3) [11]. Cinnamic acid and its derivatives exhibit a broad spectrum of antibacterial activity, which mainly relies on the inhibition of ATPases, suppression of cell division and bacterial biofilm formation. This mechanism of action is particularly important in the treatment of antibiotic-resistant bacterial infections [12].

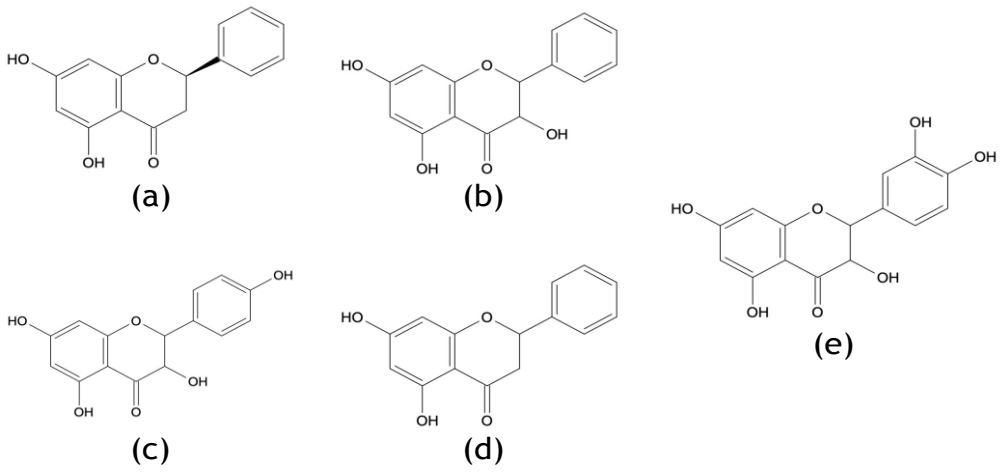

Fig 1. Structure of the flavonoids in propolis: (a) pinocembrin, (b) galangin, (c) kaempferol, (d) chrisin, and (e) quercetin.

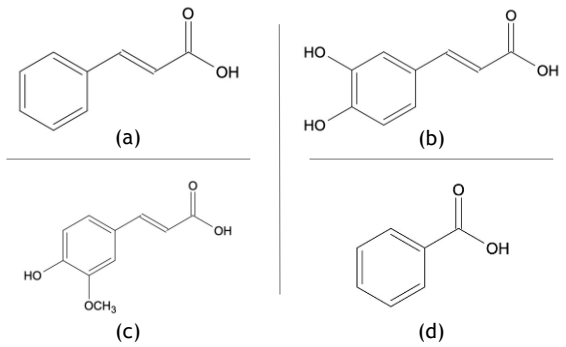

Fig 3. Structure of the aromatic acids in propolis: (a) cinnamic acid, (b) caffeic acid, (c) ferulic acid, and (d) benzoic acid

The chemical composition of propolis obtained in the temperate regions includes caffeic acid phenethyl ester (CAPE) (Figure 4), which exhibits significant antioxidant, anti-inflammatory, immunomodulatory and anti-cancer properties [13].

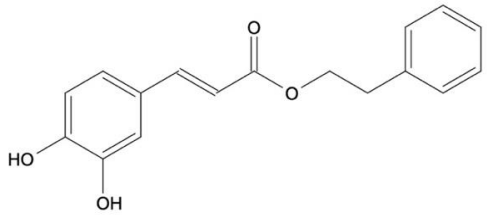

Fig 4. Chemical structure of caffeic acid phenethyl ester (CAPE)

Propolis, owing to its diverse array of chemical constituents, plays a significant role in healthcare. Polyphenols (flavonoids and aromatic acids), and terpenoids determine propolis' wide range of potential applications. These distinctive properties make propolis a compelling topic for scientific investigation and support its utilization in medicinal formulations, as well as in the pharmaceutical and cosmetic sectors.

3. Pharmacological properties of propolis

3.1. Antibacterial activity

One of the fundamental properties of propolis is its antibacterial action. It exhibits activity against both Gram-positive and Gram-negative bacteria. Among Gram-positive bacteria, *Staphylococci*, particularly *Staphylococcus aureus*, and *Streptococci* such as *Streptococcus pneumoniae* and *Streptococcus pyogenes,* show distinct sensitivity to propolis. Notable susceptible strains of Gram-negative bacteria include *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The antibacterial effects of propolis also extend to atypical bacteria, including *Mycobacterium tuberculosis* [14]. It is important to emphasize that the antibacterial activity of propolis is generally higher against Gram-positive bacteria than against Gram-negative ones. Flavonoids such as galangin, pinocembrin, and pinostrobin enhance the permeability of bacterial cell membranes and inhibit the transcription of their genetic code. This results in impaired nucleic acid synthesis, reduced adhesion, diminished biofilm formation, and a limitation of the bacteria's energy metabolism [4,14]. Additionally, propolis exhibits activity against *Streptococcus mutans* and facultative anaerobes present in the oral cavities. To harness this considerable potential, numerous companies have begun incorporating propolis into their products, such as toothpastes and mouth rinses, with the aim of preventing dental caries and gingival inflammation [15,16].

In a 2021 randomized, double-blind clinical trial, Neto et al. evaluated the antimicrobial activity of dental varnish containing Brazilian red propolis in preventing caries in pediatric patients. Seventy-five caries-free children aged between 36 and 71 months, identified as being at high risk for caries, were divided into three groups to receive different dental varnish treatments. The first group received a varnish containing 2.5% Brazilian red propolis, the second 1% chlorhexidine, and the third 5% fluoride. The varnishes were applied at three different time intervals – day 1, day 90 and day 180. To determine the antimicrobial activity, the saliva samples were collected, and the concentrations of *Streptococcus mutans* were measured. The 2.5% Brazilian red propolis dental varnish proved to be effective in inhibiting the proliferation of *Streptococcus mutans* colonies within the oral cavity when employed over a 90-day period, thereby serving as a valuable adjunctive approach in the prevention and management of dental caries [17].

González-Serrano et al. in a double-blind, randomized, clinical trial evaluated the effectiveness of a gel formulation containing propolis, nanovitamin C and nanovitamin E as an adjunctive therapy to mechanical debridement in the management of peri-implant mucositis. The 46 participants underwent professional prophylaxis and were randomized to use either the test gel or a control gel as toothpaste three times a day for a duration of one month. Both microbiological and clinical parameters were assessed, with the resolution of peri-implant mucositis defined by the absence of bleeding on probing. At the one-month follow-up, the reduction of *Tannerella forsythia* and *Porphyromonas gingivalis* were statistically more pronounced in the experimental group compared to the control group. Furthermore, 26.1% of the patients in the experimental group exhibited complete resolution of periodontal inflammation, in stark contrast to 0% in the control group [18].

In another study performed by Bapat and colleagues, the scientists compared the effectiveness of propolis mouthwash with chlorhexidine mouth rinse in reducing oral pathogens. This triple-blind, concurrent parallel randomized controlled trial enrolled 120 participants, who were divided into four groups, each receiving a different mouth rinse intervention: hot ethanolic propolis extract, cold ethanolic propolis extract, chlorhexidine, and distilled water. Participants were instructed to perform mouth-rinsing twice a day over a duration of three months. Saliva samples were collected at baseline, as well as at 5 minutes and 1 hour after rinsing, for microbiological analysis. The results demonstrated a significant decrease in the concentrations of *Streptococcus mutans*. Furthermore, the decrease in *Lactobacillus acidophilus* and *Streptococcus mutans* counts were noted in the hot ethanolic propolis group (5.5×10^2) and the chlorhexidine group (5.8×10^2), respectively. The results demonstrated that propolis mouth rinse exhibits an effectiveness that is on par with chlorhexidine concerning the reduction of plaque

formation, gum inflammation, and the depletion of bacteria that contribute to dental caries [19].

Dental caries develops as a result of the interaction between acid-producing bacteria and fermentable carbohydrates, leading to the demineralization of tooth enamel [20]. A variety of bacteria have been associated with the development of dental caries, with the most significant being *Streptococcus mutans* and *Lactobacilli* species [21]. Several authors have indicated that propolis is effective against *Streptococcus mutans*, thus exposing that it could be a viable treatment option for dental caries [15,22,23].

The commonly used chlorhexidine solutions, often recommended as effective oral rinses, may cause adverse effects such as changes in taste, tooth discoloration, sore mouth, and/or throat and tongue irritation [24]. Netto et al. conducted a randomized, double-blind, placebo-controlled clinical trial to examine the effects of propolis extract and chlorhexidine mouthwash on reducing the salivary levels of *Streptococcus mutans* and *Lactobacilli* species. Over the course of this 28-day study, propolis treatment consistently outperformed chlorhexidine in decreasing and controlling the levels of *Streptococcus mutans* and *Lactobacilli*. A lasting beneficial effect of propolis was still noted on day 45, when patients returned for a follow-up assessment [25].

To conclude, propolis is distinguished by its diverse antibacterial efficacy, which encompasses clinically important strains, including those pathogens that frequently display resistance to a variety of antibiotics. This quality indicates its potential as a complementary treatment in the fight against challenging bacterial infections.

3.2. Antioxidant properties

The antioxidant properties of propolis extracts can be attributed to the presence of polyphenolic compounds. These bioactive molecules effectively neutralize free radicals, positioning propolis as a promising source of potent natural antioxidants [26]. Free radicals contribute to the oxidation of cellular proteins, nucleic acids, and lipids, which accelerates cellular aging, mutagenesis, carcinogenesis, and the progression of neurodegenerative diseases such as Alzheimer's or Parkinson's. Moreover, oxidative stress caused by excessive free radical production heightens the risk of cardiovascular diseases by destabilizing cellular membranes and oxidizing low density lipoproteins. Notably, the polyphenols found in propolis demonstrate the ability to neutralize key enzymes, such as xanthine oxidase and lipoxygenase, which are responsible for generating the reactive oxygen forms, thereby reducing the generation of free radicals. [27].

Oxidative stress is characterized by an imbalance between pro-oxidants and antioxidants, with a predominance of pro-oxidants [28]. Soleimani et al. conducted a triple-blind randomized clinical trial to investigate the effects of propolis supplementation on oxidative stress and athletic performance of 54 military cadets. Participants who met the criteria were randomly assigned to receive either a single dose of 450 mg of propolis twice daily for four weeks or a corresponding placebo containing microcrystalline cellulose. The results of the trial indicated that while the impact of propolis on physical performance was minimal, it significantly influenced the total oxidant status, total antioxidant capacity and the oxidative stress index [29].

Furthermore, in a randomized, double-blind, placebo-controlled trial, the impact of propolis on the pro-oxidant-antioxidant balance was studied. In this research, 44 patients were randomly assigned to receive either propolis capsules at a daily dose of 250 mg or a placebo for a duration of three months. The authors concluded that propolis does not significantly affect the balance in individuals with chronic kidney disease. This conclusion is primarily due to the fact that the antioxidant effects of propolis are highly influenced by its dosage and the levels of polyphenols it contains. The discrepancies in findings across studies may be attributed to the various types of propolis sourced from different geographical regions and the diversity of plant species involved [30].

3.3. Anti-inflammatory properties

Inflammation is a process triggered by the immune system and serves as one of the body's primary defense mechanisms against bacterial and viral infections, as well as tissue damage. The body's immune response involves the secretion of inflammatory mediators, including cytokines, chemokines, prostaglandins, and reactive oxygen species. Propolis derives its anti-inflammatory properties from the flavonoids it contains. The flavonoids present in propolis, such as chrisin, pinocembrin, galangin, and pinobanksin, have been shown to inhibit the NF-κB and activate the nuclear factor erythroid 2-related factor 2 (NRF2) pathways [31]. Studies conducted on mice have demonstrated that pinocembrin significantly reduces the production of pro-inflammatory neuronal cytokines (TNF-α, IL-1 and IL-6), chemokines (intercellular adhesion molecule-1 and endothelial cell adhesion molecule-1), inducible nitric oxide synthase (iNOS) and aquaporin-4 [32].

Phenolic compounds, such as artepillin C also contribute to anti-inflammatory activity by modulating the NF-κB pathway, thereby inhibiting the production of pro-inflammatory prostaglandin E2 and nitric oxide [33]. Research findings indicate that aqueous extracts from green Brazilian propolis significantly lower the secretion of IL-6 and TNF-α, while promoting an increase in transforming growth factor beta (TGF-ß) and IL-10 levels. This alteration in cytokine profiles may help clarify the mechanisms involved in the reduction of inflammatory responses [34].

The anti-inflammatory effects of CAPE have recently garnered significant attention in the context of periodontal diseases. In a murine macrophage model, CAPE has been shown to suppress lipopolysaccharide-induced inflammatory responses by upregulating the heme oxygenase-1 (HO-1) expression while concurrently inhibiting the NF-κB and signal transducer and activator of transcription 1 (STAT1) signaling pathways [35]. A study conducted by Stähli et al., which employed a whole-genome microarray to identify the target genes of CAPE, revealed that CAPE regulates the p38 mitogen-activated protein kinase (MAPK)/NRF2 and the NF-κB signaling. These findings elucidate its antioxidative and anti-inflammatory capabilities [36]. Furthermore, CAPE suppresses both the activity and expression of cyclooxygenase-2 (COX-2) [37].

In a randomized, double-blind clinical trial, researchers intended to assess the impact of propolis on the clinical and physiological aspects of moderate persistent asthma, a condition characterized by an eosinophilic pattern of inflammation. Participants receiving propolis not only demonstrated better results on the asthma control test but also showed significant improvements in spirometry parameters compared to the placebo group. Furthermore, cytological assessment of sputum indicated that nearly half of the participants exhibited an eosinophilic inflammation pattern. The administration of propolis resulted in a significant reduction in eosinophilia [38].

In another clinical trial, Chermut et al. investigated the effects of propolis on inflammation marker levels in patients undergoing hemodialysis. Data were collected from 41 patients who received a daily dose of 400 mg of propolis dry extract and completed the follow-up. The study results indicated that interventions with propolis led to a significant decrease in serum levels of tumor TNF-α and also suggested a trend toward lowering levels of macrophage inflammatory protein-1β. In contrast, no significant changes were observed in the placebo group [39].

Propolis is a promising natural therapeutic agent for the treatment of inflammatory conditions. Its multifaceted mechanism of action, which includes the inhibition of pro-inflammatory enzymes, modulation of the immune system, and acceleration of healing processes, makes it a valuable complement in the therapy of various inflammatory disorders.

3.4. Propolis in wound regeneration

In 2021, Lisbona-González and her team conducted an intriguing study aimed at investigating the antibacterial effects of a mouth rinse containing propolis, as well as the impact of a propolis-infused toothpaste with propolis on the healing of extraction wounds in patients with periodontal disease. The mouth rinse experiment involved 40 patients, while the study of the propolis-containing toothpaste included 60 patients. Three days post-extraction, only 13.4% of the wounds in the group treated with the control toothpaste (without propolis) had completely healed. In contrast, among patients using the toothpaste containing propolis, 90% of the sockets had achieved complete healing. Additionally, a significant reduction in the counts of *Streptococcus mutans* and *Lactobacilli* was observed with the use of propolis. These findings suggest that oral hygiene products containing propolis may represent a promising alternative for enhancing the healing process of sockets after dental extractions. The knowledge gained from this research could serve as a foundation for the development of similar therapies aimed at enhancing wound healing processes [40].

Additionally, Hutami et al. conducted a scoping review in which the authors comprehensively screened eight articles that focused on the beneficial properties of propolis in the healing of wounds in the oral cavity. Among various journals, propolis has been shown to positively influence the healing process of oral wounds. Its advantageous properties have been highlighted in cases of abrasions located in the oral mucosa, labia, tooth sockets and gingiva [41]. Furthermore, new data from a double-blind clinical trial confirm the pain-relieving effects of an oral ointment containing propolis in patients following the harvesting of a free gingival graft. However, the authors concluded that additional research is necessary to evaluate its effectiveness for wound healing [42].

3.5. Propolis in cancer treatment

Propolis may exhibit anticancer activity through various molecular mechanisms, such as the induction of apoptosis, inhibition of cancer cell proliferation, and blockade of angiogenesis. The composition of propolis includes aromatic acids and their derivatives, notably CAPE, which acts as a natural inhibitor of NF-κB, thereby possessing anticancer properties [43,44]. Propolis and its compounds inhibit cell proliferation by suppressing cyclin complexes and cyclin-dependent kinases. They increase the levels of protein inhibitors such as p21, p16, and p27 in cancer cells, as well as induce cell cycle arrest by reducing the expression of ß-catenin [44]. Furthermore, compounds found in propolis inhibit numerous signaling pathways critical for the initiation and progression of cancer, including the phosphoinositide 3-kinase/protein kinase B/mammalian target of rapamycin (PI3k/AKT/mTOR), NF-κB, Janus kinases-signal transducer and activator of transcription proteins (JAK-STAT), toll-like receptor 4 (TLR4), vascular endothelial growth factor (VEGF), TGFß, as well as both intrinsic and extrinsic apoptosis pathways. Propolis may induce apoptosis, cause cell cycle arrest, and reduce the proliferation, viability, invasion, migration, and chemoresistance of cancer cells [45]. Moreover, there is limited data suggesting that propolis exhibits anticancer activity against tongue cancer cells in *in vitro* models [46].

Furthermore, propolis demonstrates significant efficacy in alleviating the side effects associated with chemotherapy and radiotherapy, as well as in enhancing the quality of life for patients [47]. A recently published randomized controlled trial has shown that propolis mouthwash may serve as a beneficial adjunct in high-dose chemotherapy treatment. The study revealed that both the incidence and duration of oral mucositis were significantly reduced in the propolis intervention group compared to the control group. Concurrently, the onset of oral mucositis occurred later in the intervention group, and patients reported lower levels of oral mucosal pain. However, further research that confirms the effectiveness of propolis with consistent or similar results will strengthen the evidence for its use [48].

3.6. Antifungal activity

In addition to its well-known antibacterial properties, propolis also exhibits significant antifungal activity. The polyphenolic compounds it contains, including flavonoids and phenolic acids, effectively inhibit the growth of various pathogenic fungi, particularly yeast species of the genus *Candida*. *Candida albicans* and other *Candida* species are opportunistic pathogens, primarily causing infections in individuals with compromised immune systems [49]. The antifungal mechanism of propolis mainly relies on damaging the integrity of the cell wall and cell membrane of *Candida albicans*, resulting in the loss of intracellular organelles and ultimately leading to fungal cell death. The polyphenols present in propolis play a crucial role in this process by forming complexes

with soluble proteins and disrupting chitin synthesis, a key component of the fungal cell wall. Consequently, this disruption compromises the integrity of the cell wall, inhibiting further growth and development of the fungi [50]. Propolis also demonstrates activity against other fungal pathogens, such as *Aspergillus flavus*. The compounds found in propolis effectively inhibit the growth of conidia of these fungi and limit the production of aflatoxin, thereby reducing the generation of toxic fungal metabolites. Furthermore, propolis has proven effective in eradicating Trichophyton species, which are responsible for dermatophyte infections, including tinea infections of the skin and nails [51].

The antifungal characteristics of propolis render it an important asset in combating fungal infections, especially in instances where traditional treatments demonstrate restricted efficacy. Its diverse mechanisms of action and natural composition position propolis as a viable alternative in the management of fungal infections, particularly in light of the growing resistance to antifungal agents.

3.7. Antiviral properties

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) triggers complex immune and inflammatory responses. Due to the immunomodulatory properties of propolis, it has been suggested that it may aid in the treatment of such viral infections. In a randomized, controlled, open-label, single-center trial, 124 hospitalized adult patients with COVID-19 received a standardized green propolis extract as a complementary treatment. Incorporating propolis into the standard care protocols provided clinical advantages for hospitalized COVID-19 patients, particularly evidenced by a reduction in the duration of their hospital stays. Therefore, the authors concluded that propolis may mitigate the effects of COVID-19 [52]. Ripari et al. explored the potential use of propolis in the treatment of COVID-19. The authors suggest that further research in this field should focus on assessing the effectiveness of propolis when used in conjunction with various antiviral medications, as well as evaluating the administration of propolis alongside vaccines, owing to its adjuvant properties, to enhance the immune response in individuals [53].

4. Propolis in dental care

As previously mentioned, propolis may be beneficial in reducing dental caries. However, its applications are significantly broader as reported in several clinical trials.

In a 2021 double-blind, randomized clinical trial, Kiani et al. focused on the potential use of propolis-containing mouthwash for the treatment of gingivitis. A total of 32 patients were enrolled in the study. The researchers assessed the papillary bleeding index, plaque index, and tooth discoloration both before the intervention and after the treatment. For follow-up assessments, the measurements were taken from the tooth in each quadrant that exhibited the most inflamed gingiva. The study revealed that the change in the plaque index was similar for both the propolis and placebo groups, indicating no significant difference. However, the reduction in the papillary bleeding index was notably higher in the propolis group. Additionally, the change in tooth color after the intervention was significant in the placebo group but not in the patients receiving propolis [54]. The role of propolis in the management of gingivitis has been investigated by Gunjal and Pateel. Their recent study, which was conducted at a single center and utilized a Latin-square cross-over design, was both double-masked and randomized. The researchers assessed the effects of a 0.2% propolis mouthwash in comparison to a chlorhexidine mouthwash and a placebo. Following a 21-days treatment period, 45 participants were analyzed for changes in their gingival and plaque indices. The results of the statistical analysis indicated that patients using the propolis mouthwash experienced a more significant reduction in both plaque and gingival scores than those in the chlorhexidine and placebo groups. Consequently, propolis mouthwash exhibited notable enhancements in gingival health and a reduction in plaque accumulation, suggesting it may serve as a viable herbal alternative to chlorhexidine mouthwash [55].

Dentin hypersensitivity is a frequently encountered dental issue that can present challenges in treatment for the dentists. It occurs when the dentinal tubules are exposed at both the oral surface and the pulp. In a randomized, double-blind, parallel-group clinical trial, Bantawa et al. compared several commonly used topical desensitizing agents namely Gluma®, VivaSens® and Propolis extract [56]. Gluma® is a widely utilized desensitizing agent that contains 5% glutaraldehyde and 35% hydroxyethyl methacrylate (HEMA). Upon application, the glutaraldehyde coagulates the serum albumins in dental fluid, what triggers the polymerization of HEMA, resulting in a formation of a plug in the dentinal tubules [57]. All three desensitizers significantly reduced the dentin hypersensitivity scores among 45 patients. However, the statistical analysis revealed no significant differences in the mean changes of dental hypersensitivity scores between the test groups [56]. The role of propolis in the management of dentin hypersensitivity was investigated by Shah and colleagues. In a 2023 single-blind, randomized controlled trial, the researchers compared the effectiveness of a 30% ethanolic extract of propolis with the Gluma® desensitizer. The results revealed that both the propolis extract and Gluma® effectively reduced dental hypersensitivity. However, it was noted that the effectiveness of propolis declined over a one-month treatment duration [58]. The desensitizers employed in these clinical trials are designed for use by dental professionals. Nevertheless, the management of dentin hypersensitivity also requires appropriate products for patients' daily home care. In this context, Takeuchi et al. evaluated the effectiveness of toothpastes containing two concentrations of propolis - 10% and 15%. The study found that the experimental groups exhibited a significantly greater reduction in dentin hypersensitivity compared to the placebo group. Furthermore, the results indicated similar efficacy in controlling dental hypersensitivity, with no statistically significant differences between the two concentrations of propolis [59].

The lack of appropriate oral hygiene, the use of tobacco products, and the inevitable aging of the population are factors that contribute to the development of a more serious oral disease - periodontitis. The disruption of microbial homeostasis leads to the extensive proliferation of gram-negative,

anaerobic bacteria called as the red-complex. The activity of *Tannerella forsythia*, *Treponema denticola*, and *Porphyromonas gingivalis*, which constitute the red complex, hampers the maintenance of periodontal defense functions, thereby increasing the likelihood of tissue damage [60]. A recently conducted single-blind, randomized controlled trial examined the role of propolis in the treatment of periodontitis. This study comprised 28 patients who were assigned to receive either a 0.2% chlorhexidine mouthwash or a 20% hydroalcoholic propolis for subgingival irrigation. The effectiveness of these interventions was determined by analyzing metalloproteinase 8 levels in saliva, as elevated levels of this enzyme are linked to the presence of periodontitis. Results demonstrated a significant enhancement in clinical outcomes for the group receiving propolis, while both groups exhibited a notable decrease in metalloproteinase 8 levels. Therefore, propolis may represent a beneficial adjunct in the management of periodontitis [61].

Furthermore, in a systematic review conducted in 2025, Aldosari et al. examined the role of propolis in the endodontic treatment of permanent teeth. The findings from various studies indicated that propolis could serve as a valuable therapeutic alternative, enhancing dentin formation, decreasing microbial infections, and alleviating post-operative pain. However, the efficacy of propolis was found to be similar to that of Biodentine®, calcium hydroxide, and triple antibiotic paste, with statistical analyses showing no significant differences among these treatments. Therefore, due to the limited evidence and variability in clinical outcomes, the use of propolis as a definitive treatment is not recommended [62].

5. Adverse effects of propolis

As per the World Health Organization (WHO), an adverse drug reaction refers to any unintended consequence of a pharmaceutical product that arises at doses commonly prescribed to patients, which is linked to the drug's pharmacological properties [63]. Both synthetic and natural medications can cause side effects, and propolis is no exception. The three main allergens of propolis are caffeic acid, CAPE and caffeic acid 1,1-dimethylallyl ester (CAAE) [64]. Allergic reactions predominantly present as contact dermatitis localized to the site of propolis application. However, hypersensitivity can also manifest as cheilitis, stomatitis, perioral eczema or in some cases, dyspnoea [65,66]. Propolis is commonly found in a variety of everyday items such as creams, shampoos, lip balms, and toothpastes. Due to its perception as a natural and safe component, consumers frequently utilize it in excessive amounts or without appropriate moderation. Nevertheless, it is crucial to approach its use with caution, as it may result in significant hypersensitivity reactions [67,68]. Belluco et al. documented a case involving a patient who consumed propolis drops orally on a daily basis for a decade. During the COVID-19 pandemic, the patient decided to increase the dosage, believing it would enhance their immune response. However, this increase led to the onset of contact allergic dermatitis. This case underscores the importance of recognizing propolis as a potential sensitizer, as it can elicit allergic reactions in certain individuals. Furthermore, it is essential to acknowledge the potential rise in propolis allergies within the general population, likely attributed to the increasing popularity of natural products [68].

6. Conclusions and future perspectives

The findings of the research demonstrate that propolis is emerging as a highly valuable therapeutic choice for the promotion of oral health and hygiene. Its efficacy against various pathogenic bacteria, particularly *Streptococcus mutans*, makes it especially relevant in the treatment and prevention of dental caries. That has been substantiated in numerous clinical studies. However, the beneficial effects of propolis extend beyond just its antimicrobial properties. The existing literature indicates that it may also play a significant role in the treatment of periodontal diseases and gingivitis, conditions that can lead to more serious dental health issues, if left untreated. Moreover, unlike the commonly prescribed antiseptic chlorhexidine, propolis demonstrates fewer side effects, which makes it a more favorable alternative for patients. The research strongly suggests that propolis could serve as a valuable adjunctive treatment in the dental practice, complementing the traditional methods to improve patient outcomes. Nevertheless, to maximize its efficacy in dental care, subsequent investigations should prioritize the standardization of propolis formulations. Such efforts could clarify its mechanisms of action, refine its application, and guarantee uniform quality across various products. This could lead to a notable improvement in the role of propolis in promoting oral health and preventing dental issues.

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