Pak. j. life soc. Sci. (2025), 23(2): 502-520 E-ISSN: 2221-7630;P-ISSN: 1727-4915

Pakistan Journal of Life and Social Sciences

www.pjlss.edu.pk

https://doi.org/10.57239/PJLSS-2025-23.2.00186

RESEARCH ARTICLE

Propolis in Dental Implant Treatment: A Scoping Review Running Title: Propolis in Dental Implant Treatment

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ARTICLE INFO

Received: Jul 16, 2025

Accepted: Sep 9, 2025

Keywords

Propolis,
Dental Implant, Bone,
Healing, Dental,
Extraction,

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ABSTRACT

Propolis has recently gained attention mostly due to laboratory and animal studies suggesting its antimicrobial, antioxidant, antitumor, and antimicrobial properties. Due to the advantages of propolis, it has been tried and is used in oral health and dental care products. Nevertheless, there is a lack of reliable evidence regarding the clinical efficacy of propolis in dental implant treatment. The aim of this scoping review was to provide more information on the characteristics of propolis in various clinical scenarios related to dental extraction, implant treatment and maintenance. This scoping review was conducted following specific criteria: Population: laboratory, animal, and human studies; Intervention: use of propolis; Comparison: bone healing and formation, other dental implant coating and agents that improve and maintain the health of peri-implant tissues; Outcomes: improvement in oral hygiene, improvement in tissue healing, improvement in socket healing, inhibition of microorganisms, inhibition of osteoclast, and promotion of bone growth. Only original relevant articles written in English were chosen from Web of Science, PubMed, MEDLINE, and Scopus databases using the search parameter "propolis AND (implant OR dental implant OR bone healing OR tooth extraction OR peri-implantitis)". A total of 21 original articles met the criteria and showed varying success levels achieved with propolis in dental implant treatment. Propolis improves healing following a tooth extraction, promotes bone healing and implant osseointegration and reduces biofilm related to peri-implantitis. Propolis may play a role in initiating bone healing after tooth extraction, promoting implant osseointegration, and maintaining peri-implant health.

INTRODUCTION

There is a growing interest in utilising natural products in the medical field due to their abundant supply, composition, nutrients, low expense, and minimal adverse effects (Martinotti and Ranzato, 2015). Propolis is a natural sticky product that honeybees collect from various plants rich in sap flows, resins, waxes, cellulose, pollen, essential oils, organic acids, vitamins, amino acids, and the exudates of the buds (Miguel and Antunes, 2011). Approximately 50% of the compounds found in propolis are a type of phenolic compound constituting the flavonoids, phenolic acids and their esters, coumarins, and stilbenes (Gatea et al., 2014; Park et al., 2002). The concentration and types of those compounds depend on multiple factors, such as the location and season of collection, climatic conditions of the area of collection, botanical origin, the genotypes of plants, extraction technique, and environmental conditions (Figueiredo et al., 2022; Sforcin, 2016; Stähli et al., 2021; Trusheva et al., 2007). Therefore, the colour and odour of propolis vary, ranging from brown to green, fragrant or odourless gummy material.

Propolis is introduced to the medical field due to various biological effects, including anti-inflammatory, antiviral, antitumor, and antimicrobial activities (Seal et al., 2016). The mechanisms of this activity still need to be fully understood. However, it is thought that the main role in its activity is played by flavonoids and phenolic compounds, which, along with the analgesic, antipyretic, and anti-inflammatory effects (Dulcetti et al., 2004; Paulino et al., 2008, 2006), have an impact on tissue

metabolism, detoxification of cells, cell membrane preservation cycles, and the cyclooxygenase model.

The literature reports many dental-related biological effects of propolis consumption and its extracts, such as reducing the risk of carcinogenesis, disease prevention of periodontal tissue, accelerating healing of ulcers, and preventing abscesses (Saeed et al., 2021). The beneficial effects of propolis suggest its potential to improve oral health and solve various dentistry-associated problems. Mainly as it exhibited antibacterial properties against cariogenic bacteria: *Streptococcus mutans* and *Lactobacillus* spp (Libério et al., 2009; Vanni et al., 2015). Moreover, it efficiently reduces plaque formation (Koo et al., 2002), hence reducing gingivitis and periodontitis (Cairo et al., 2006).

Many forms of propolis have been used in oral care products, such as chewing tablets, dental pastes, mouthwashes, or dental floss. Propolis-based dental products can be used clinically in many aspects, including cavity cleaning materials, desensitising agents, restorative resins, composites, or dental adhesives. Irrigants and canal sealers containing propolis can be used during endodontic treatment. Topical surgical and periodontal dressing formulas containing propolis have also been used (Ercan et al., 2015; Morawiec et al., 2015; Naghsh et al., 2024; Seal et al., 2016). In dental implantology, propolis showed potential applications in reducing inflammation, thereby increasing angiogenesis and promoting new bone formation on the contact surface between the dental implant and the surrounding hard and soft tissues (Abdulla et al., 2024a).

The antimicrobial activity of propolis, which is confirmed in many research studies, makes such material beneficial before, after, and during the maintenance of dental implant therapy. However, in the context of dental implant surgery, the evidence concerning the clinical effectiveness of propolis as a post-operative care is relatively scarce. This paper presents an attempt to review the clinical properties of propolis in clinical situations, starting from its use at tooth extraction to the role of propolis in implant treatment maintenance (Figure 1).

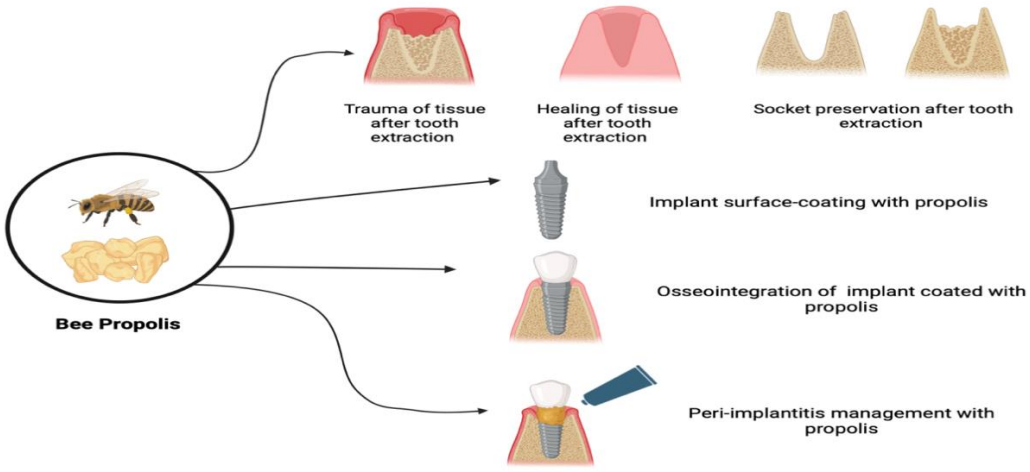

Figure 1. Parts Discussed in the Current Review

METHODOLOGY

This scoping review included studies involving humans, animals and laboratory investigations with an intervention based on the use of propolis in dental extraction and dental implant treatment. A comparison was made with bone healing, bone formation, other dental implant coating and agents that improve and maintain the health of peri-implant tissues. The studies reporting outcomes on improvement in oral hygiene, improvement in tissue healing, improvement in socket healing, inhibition of microorganisms, inhibition of osteoclast, and promotion of bone growth and osteoblasts were included.

Original articles written in English were sought and selected from Web of Science, PubMed, MEDLINE, and Scopus databases. The following search parameter was entered into the search engine: "propolis AND (implant OR dental implant OR bone healing OR tooth extraction OR peri-implantitis)". This search parameter was based on seven major keywords: propolis, implants, dental implants, bone healing, peri-implant, peri-implantitis and tooth extraction. Articles were selected based on originality, the use of propolis in dental implant treatment and/or alveolar bone healing

and/or peri-implant and/or after tooth extraction. Studies involving subjects with soft or hard tissue tumours or those undergoing chemotherapy were excluded.

Assessment of the quality of the studies was based on the study design, the methodologies, and the outcomes. Data were extracted using tables that identified the propolis origin, type of study, characteristics of participants, type of intervention, results and the outcomes of the study.

RESULTS

The parameters produced a total of 44 citations; 6 were duplicate studies, five studies were discarded because they were written in a different language other than English and 8 articles were discarded because they were review articles, and 3 were editorials. One article was excluded as it included individuals with cancer. The remaining 21 articles were examined as they fulfilled this review's inclusion/exclusion criteria (Figure 2).

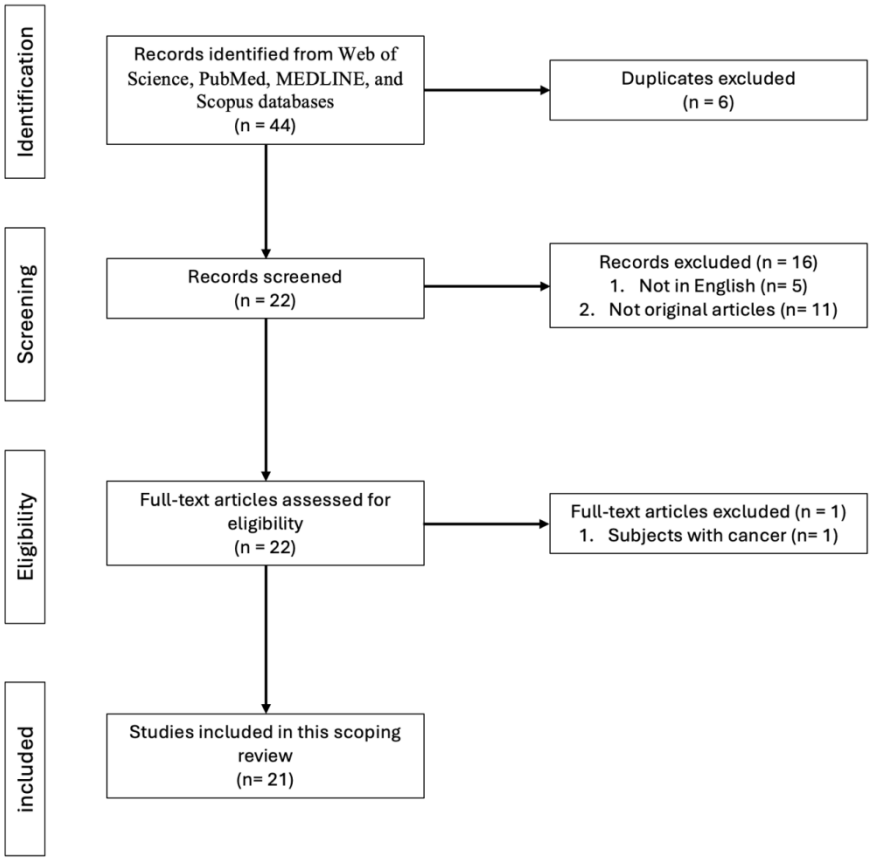

Figure 2. Flowchart for Identification, Screening, and Selection of Studies

Propolis and Tooth Extraction

Four studies evaluated propolis and tooth extraction, socket and tissue healing. The results of these studies revealed that propolis helped in the initial healing of the extraction site and preserved the extraction socket (Table 1).

Table 1. Studies Showing the Relation between Propolis on Tooth Extraction

No.	Author and year	Type and Origin of propolis	Type of study and no. of subjects	Type of intervention	Results	Outcomes
1	Magro Filho and de Carvalho 1990 (Magro Filho and de Carvalho, 1990)	Propolis, citrus sinensis, coffea arabica, saccharum officinarum, eucalyptus globulus.	Animal study n =45 rats	-Control group -Hydro-alcoholic solution -Hydro-alcoholic solution of propolis	On post-operative day 3, propolis group showed an acceleration of wound healing after tooth extraction. After 4th day, propolis group showed a delay in wound healing after tooth extraction compared with the control group. On post-operative day 21, propolis group showed more acceleration in wound healing after tooth extraction compared with the hydro-alcoholic group.	Hydro-alcoholic solution of propolis show no overall advantage on wound healing after tooth extraction.
2	Kresnoadi et al. 2020 (Kresnoadi et al., 2020b)	Raw propolis produced by *Apis melifera* bees, Lawang, East Java, Indonesia	Animal study n=56	Fill the socket with: -Groups I and II, (controls) polyethylene glycol. -Groups III and IV, bovine bone graft + polyethylene glycol -Groups V and VI, propolis extract + polyethylene glycol -Groups VII and VIII, propolis extract + bovine bone graft + polyethylene glycol.	On days 3 and 7, the highest number of osteocalcin expression was found in Groups VII and VIII (propolis groups) and the lowest number was found in the Groups I and II (controls). Groups VII and VIII, were found to present the highest number of heat shock protein (HSP70) expression, osteocalcin expression, and osteoblast cells as well as the lowest number of osteoclasts.	The combination of propolis and bovine bone graft to preserve tooth extraction sockets can reduce inflammation, increase HSP 70 and reduce osteoclast, and accelerate osseointegration, accelerating the growth in expression of osteocalcin, promoting osteoblast cells.
3	Kresnoadi et al. 2020 (Kresnoadi et al., 2020a)	Raw propolis, *Apis melifera* bees, Lawang, East Java, Indonesia	Animal study n= 56	Fill the socket with: -Groups I and II, (controls) polyethylene glycol.	Groups VII and VIII preserve socket by increasing the expression of FGF2, VEGF, and osteoblasts.	The combination of propolis and bovine bone graft for socket preservation maintained alveolar bone dimension which support the success of prosthetic treatment.

				-Groups III and IV, bovine bone graft + polyethylene glycol -Groups V and VI, propolis extract + polyethylene glycol -Groups VII and VIII, propolis extract + bovine bone graft + polyethylene glycol		
4	Lisbona-González et al. 2021 (Lisbona-González et al., 2021)	Propolis, Verbiotech I + D + i S.L, Granada, Spain.	Randomised control clinical trail n= 40	-chlorhexidine Mouthwash -Propolis mouthwash -Propolis + chlorhexidine mouthwash.	The propolis + chlorhexidine mouthwash reduced bacterial proliferation and prevented staining of the mouth/tongue when using chlorhexidine mouthwash.	Propolis helped in socket healing following tooth extraction and was more effective in controlling the inflammatory process.

Propolis and Implant Osseointegration

Five animal and in vitro studies were found that evaluated propolis and implant osseointegration, showing that propolis coating of dental implants improved osseointegration by inhibiting osteoclastogenesis, forming mature bone, therefore, can prevent and treat periodontal disease (Table 2).

Table 2 Studies Showing the Relation between Propolis Implant Osseointegration

No.	Author and year	Type and Origin ofpropolis	Type of studyand no. ofsubjects	Type of intervention	Results	Outcomes
1	Pileggi et al. 2009 (Pileggi et al., 2009)	Brazilian propolis, southern region of Brazil, Sao Paulo	Animal study n= not specified number of bone marrow cells from Swiss-Webster mice	Propolis extract	Propolis inhibited both osteoclast formation (numbers of tartrate-resistant acid phosphatase TRAP+-multinuclear cells) and maturation (production of actin rings) and did not prevent cell growth and survival.	Propolis inhibits osteoclastogenesis and osteoclast activation in tissue culture.
2	Somsanith et al. 2018 (Somsanith et al., 2018)	Raw propolis from poplars Auckland, New Zealand	Animal study n= 20 Sprague-Dawley rats	-Untreated CP-Ti -TiO_2 nanotubes (TNT) -TiO_2 nanotubes (TNT) loaded with a propolis (PL-TNT-Ti plates)	PL-TNT-Ti implant showed an increase in new bone formation, bone mineral density and osteoblast proliferation compared to TNT implants. PL-TNT-Ti implant decreased the expression of inflammatory cytokines such as IL-1β, and TNF-α, but increased the expression of collagen fibers	Propolis loaded TiO_2 nanotubes (PL-TNT-Ti) dental implant improved osseointegration.

					and osteogenic differentiation proteins, such as BMP-2 and BMP-7.	
3	Lim et al. 2020 (Lim et al., 2020)	Nutra-tech Australia (Silverwater), New South Wales, Australia.	In vitro study n= not specified number of human tissue (I mmortalized human gingival fibroblasts)	-Control group (1% Dimethylsulfoxide) -Group 1 (1.0 µg/ml mangosteen extract -Group 2 (0.5 µg/ml mangosteen extract -Group 3 (34 µg/ml propolis extract -Group 4 (17 µg/ml propolis extract -Group 5 (1.0 µg/ml mangosteen extract and 34 µg/ml propolis extract -Group 6 (1.0 µg/ml mangosteen extract and 17 µg/ml propolis extract -Group 7 (0.5 µg/ml mangosteen extract and 34 µg/ml propolis extract -Group 8 (0.5 µg/ml mangosteen extract and 17 µg/ml propolis extract.	The combination of 1 µg/ml mangosteen and 34 µg/ml propolis extracts were highly effective as anti-inflammatory and could be used to prevent and treat periodontal disease.	Mangosteen and propolis extract complex are natural products that could be used to prevent and treat periodontal disease as it showed an in vitro bone formation.
4	Abdulla et al. 2024 (Abdulla et al., 2024b)	Not mentioned	Animal study n= 72 implants placed in 24 dogs	Four types of implant surface modifications: -Group A: sandblasting + acid etching	Groups A and B showed bone growth and many osteoblasts with few osteocytes within lacunae in new bone trabeculae. Group C showed an increase in the number of osteoblasts lining thin bone trabeculae.	Propolis coating of implant resulted in growth, maturity and a remarkable remodelling of the bone.

				-Group B: sandblasting with $Al_2 O_3$ -Group C: Er,Cr:YSGG laser -Group D: propolis coating.	Group D showed a formation of bone. All groups showed a new matured bone with increased bone ingrowth after 90 days. After 180 days following delayed-loaded implant osseointegration, differences were observed between the groups with a remarkable remodelling of the bone, especially in the propolis coating group.	
5	Abdulla et al. 2024 (Abdulla et al., 2024a)	Iraqi propolis	Animal study n= 16 dogs using 48 implants	-Grade 4 titanium dental implant surface treatment with either: -Group A: Sandblasting with acid etching. -Group B: Sandblasting. -Group C: Er-Cr:YSGG laser. -Group D: Propolis coating.	Implant Stability Quotient (ISQ) was found to be dependent on surface treatment. Higher ISQ in sandblasting than the other treatments at 90 days.	Propolis coatings showed no improvement in ISQ levels.

Propolis and Implant Maintenance

Twelve studies evaluated propolis and tooth extraction. The results of these studies revealed that propolis could prevent post-operative complications after alveolar procedures. It could reduce microbial-causing periodontal diseases and lead to periodontal tissue regeneration. Moreover, propolis could be used as an adjunctive to scaling and root planning to improve gingival and periodontal health, which improves plaque accumulation and reduces gingival bleeding (Table 3).

Table 3 Studies Showing the Relation between Propolis on Implant Maintenance

No.	Author andyear	Type and Origin of propolis	Type of studyand no. ofsubjects	Type of intervention	Results	Outcomes
1	Coutinho 2012 (Coutinho, 2012)	Raw Propolis, Apis mellifera colonies	Clinical trail n=20	-Group A: Irrigation with propolis hydroalcoholic solution twice a week for 2 weeks	In group A: decrease in anaerobic bacteria, an increase in of Porphyromonas gingivalis	Propolis can be considered as an adjuvant to scaling and root planing.

				-Group B: Irrigation with a placebo of 14% ethanol solution twice a week for 2 weeks -Group C: Ultrasonic scaling and root planing.	and increase in bleeding on probing compared to group B and C.	
2	Morawiec et al. 2013 (Morawiec et al., 2013)	Brazilian green propolis	Clinical trail n= 16	-Toothpaste containing Brazilian propolis -Placebo (control) without active substance.	Propolis-containing toothpaste is effective in improving oral health and reduce gingivitis.	Propolis-containing toothpaste can be used as a natural alternative or additive to chemical mouthwashes in patients suffering from periodontal problems associated with implants.
3	Morawiec et al. 2015 (Morawiec et al., 2015)	Brazilian green propolis	Randomised clinical study n= 14	Two gel samples were compared: -Placebo gel (control) -Brazilian green propolis gel	The number of microorganism species (mainly affected Gram-positive rods and bacilli as well as Gram-negative rods) have increased following the use of placebo gel over the period of 5-6 weeks while Brazilian green propolis gel use Resulted in profound reduction in the amount of Neisseria spp. and Bifidobacterium spp. strains.	Propolis anti-inflammatory and antibacterial effects can prevent post-operative complications in dental patients after extensive, alveolar procedures.
4	Vanni et al. 2015 (Vanni et al., 2015)	Propodent, Bio Cumnatura, Ruti, Switzerland.	In vitro n= 54	Biofilms were exposed to: -Toothpaste without propolis -Toothpaste with propolis -Toothpaste with chlorhexidine -Mouthrinse with propolis	The strongest reduction in biofilm colony forming was shown after treatment with 0.12% chlorhexidine. All toothpastes showed a significant reduction in biofilm colony formation	All toothpastes showed some biofilm colony inhibition in supragingival biofilm model The propolis mouthwash had no effect on biofilm colony formation.

				-Mouthrinse with chlorhexidine -Saline solution (control).	compared to the saline control group. The propolis-containing mouthrinse showed no significant reduction in biofilm colony formation.	
5	Martorano-Fernandes et al. 2020 (Martorano-Fernandes et al., 2020)	Brazilian red propolis	In vitro n= 36 Commercially pure titanium discs	-Sterile saline solution (control) -Chlorhexidine -propolis.	The exposure to chlorhexidine and to Brazilian red propolis reduced the metabolism of biofilms. With regards the co-culture biofilms, chlorhexidine had the highest inhibitory effect.	Brazilian red propolis showed a potential antifungal activity against *Candida* biofilms, Brazilian red propolis can be an alternative treatment for peri-implantitis.
6	Son et al. 2021 (Son et al., 2021)	Propolis from Rapha Propolis Co., Jeonju, Korea	In vitro n= not mentioned.	-Poly(L-lactide) (PLA)/poly(ε-caprolactone) (PCL) polymer (PLA/PCl) pellets containing propolis-embedded zeolite nanocomposites -Propolis-embedded zeolite nanocomposites	PLA/PCL pellets containing propolis-embedded zeolite nanocomposites showed longer sustained release of antibacterial behaviour compared to propolis-embedded zeolite nanocomposites.	Dental implants fabricated from PLA/PCl polymer and propolis-embedded zeolite nanocomposites have antibacterial efficacy and negligible cytotoxicity against normal cells.
7	Stähli et al. 2021 (Stähli et al., 2021)	Red and green Brazilians propolis European propolis	In Vitro n= not mentioned	-Ethanol control -Brazilians ethanolic extracts propolis - Propolis of the European ethanolic extracts propolis.	All tested ethanolic extracts propolis were highly active against the tested oral strain (*Streptococcus mutans* cells, *Porphyromonas gingivalis,Candida albicans, Actinomyces naeslundii* and *Prevotella intermedia)* The European propolis seemed to act slightly less inhibitory	The European propolis exhibited the strongest effect on retarding biofilm formation, whereas the Brazilian propolis were highly active against biofilms.

					against *Actinomyces naeslundii* and *Prevotella intermedia*.	
8	Park et al. 2021 (Park et al., 2021)	Not mentioned	A Multi-Centered Randomized Controlled Clinical Trial n= 80	-Control group: Placebo capsule. -Test group: single capsule containing Mangosteen and propolis extracts.	There was a significant difference of modified gingival index between the test and control groups. In the test group, crevicular interleukin (IL)-6 was reduced, and the salivary matrix metalloproteinase increased.	Mangosteen and propolis extracts taken orally would reduce gingival inflammation in the patients with gingivitis and incipient periodontitis.
9	González-Serrano et al. 2021 (González-Serrano et al., 2021)	Propolis, South-east of South Korea.	Randomised clinical trail n= 46	-Test gel with Propolis -Ascorbic Acid -Tocopherol Acetate. (control)	Reductions in plaque index, BOP and probing depths in test gel with propolis compared with control group.	Propolis gel clinically improved peri-implant mucositis with antimicrobial effect after 1 month of use.
10	Srinivas et al. 2022 (Srinivas et al., 2022)	Raw Hubballi propolis	In vitro n= 3	Hubballi Propolis extracted with: -Water as solvent. -Alcohol as solvent.	Hubballi Propolis is effective against *Aggregatibacter actinomycetemcomitans*infection and may help in treating peri-implantitis. Propolis extracted with water as solvent showed better Minimum inhibitory concentration , higher Total phenolic contents and total flavonoid content than the propolis extracted using alcohol as solvent.	Hubballi Propolis showed antimicrobial effect against *Aggregatibacter actinomycetemcomitans* with minimum inhibitory concentration
11	Yazdanian et al. 2022 (Yazdanian et al., 2022)	9 Raw propolis from Iran	In vitro n= 63	The effect of different propolis on biofilm from: -Tabriz, East Azerbaijan	Propolis from Khalkhal showed the highest effect on the formation and degradation of biofilm while propolis from Fasa showed	Propolis extracts are effective against dental plaque biofilm.

				-Kurdistan, -Khalkhal (Ardabil Province), -Sarab (East Azerbaijan Province), -Neor Lake (Ardabil Province), -Fasa (Fars Province), -Qaleh Rudkhan (Gilan Province), -Fereydun Shahr (Isfahan Province), -Kermanshah.	the lowest effect on the degradation and formation of biofilm.	
12	Tang et al. 2024 (Tang et al., 2024)	Not mentioned	Animal and in vitro study n = 48 rats	-Total flavonoid extract of propolis (TFP) -TFP- propolis loaded liquid crystal hydrogel (TFP-LLC).	TFP-LLC could significantly inhibit alveolar bone resorption, increase bone mineral density and reduce trabecular bone space in rats with periodontitis.	TFP-LLC containing propolis could reduce periodontal inflammation and periodontal tissue regeneration.

DISCUSSION

Propolis and Tooth Extraction

Tooth extraction process is the removal of the tooth from its socket in the alveolar bone. The main concern for patients after dental extraction is the risk of post-operative problems, including pain, infection, bleeding, trismus, and dry socket. Haemostasis is often the first post-extraction problem addressed, and some studies have reported the use of various haemostatic agents after tooth extraction, such as the use of pressure with gauze, oxidised cellulose, microfibrillar collagen haemostat (Yerragudi et al., 2023), chitosan (Shen et al., 2006), honey (Pleeging et al., 2022), and propolis (Lisbona-González et al., 2021).

Different studies have reported the antimicrobial properties of propolis in the literature (Coluccia et al., 2022; Dulcetti et al., 2004; Paulino et al., 2008, 2006; Son et al., 2021; Srinivas et al., 2022; Stähli et al., 2021; Vanni et al., 2015). Tooth extraction changes the oral microflora and favours bacterial distribution, which results in post-operative inflammation (Marsh and Percival, 2006). Furthermore, the colonisation of microflora around the vulnerable extraction site results in inflammation of oral tissue and, consequently, an opportunistic infection (Chuang et al., 2008; Storoe et al., 2001).

Topical propolis-containing gel application following tooth extraction showed a profound reduction in oral microorganisms (Morawiec et al., 2015). The healing process following tooth extraction occurs in primary and secondary stages. More than 30 years ago, one animal study reported that the topical

application of 1 ml of alcoholic propolis extract in 9 ml distilled water solution increased epithelial repair following tooth extraction (Magro Filho and de Carvalho, 1990). A human study included 27 patients who had sulcoplasty and used propolis in an aqueous alcohol solution containing 40 g of propolis with

100 ml of alcohol diluted into double-distilled water as a mouthwash found that such patients used fewer analgesics and improved healing of the surgical wound (Magro-Filho and de Carvalho, 1994).

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The aim of post-operative care after tooth extraction is to support the healing process and minimise post-operative complications. Local antimicrobial agents such as propolis, which has an analgesic and anti-inflammatory effect, are of value in post-operative usage after tooth extraction (Lisbona-González et al., 2021).

Propolis, mainly in liquid form or as dressing (Ercan et al., 2015; Lisbona-González et al., 2021; Salari et al., 2023), can be applied to the bleeding area in various ways as a haemostatic agent, making it quite effective in oral mucosal lesions after tooth extraction. The local application of propolis affects post-operative inflammation, oedema, and haemorrhage in more aseptic conditions after tooth extraction. It is also helpful in preventing infections with its antioxidant and analgesic properties. The post-operative symptoms are also related to the patient's immune system. Therefore, these symptoms can be minimised effectively with pre-operative consumption of propolis systematically or with a local delivery agent before the extraction to reduce inflammation, pain, oedema, and haemorrhage post-operatively; however, further clinical research regarding the consumption of propolis before tooth extraction is necessary. Propolis was also beneficial during the extraction site healing, as one study reported that a mixture of propolis and bovine bone grafts placed at the extraction site showed a low number of osteoclasts, accelerated osseointegration and preserved the socket (Kresnoadi et al., 2020a, 2020b). Furthermore, administering 5% propolis gel in rats increased the number of osteoblasts in the alveolar bone (Wiwekowati et al., 2020). Propolis was used as socket preservation in combination with bovine bone graft in pegs after extraction. It was found that such treatment increased fibroblast growth factor, vascular endothelial growth factor, and osteoblasts after 3 to 7 days following tooth extraction (Kresnoadi et al., 2020a).

The main reasons for recommending propolis instead of other types of haemostatic agents are its ability to reduce complications like dry sockets, effectively support and shorten healing periods, be easily accessible for the patient, reduce the number of applications required, and be low-cost, which promotes the patient's post-operative quality of life.

Propolis and Implant Osseointegration

The success of the use of propolis during dental implant treatment depends highly on its anti-inflammatory, antiviral, and antimicrobial properties. Research has shown that propolis has a destructive effect on the bacterial cell membrane, destroying it and, as a result, leading to cell death (Yazdanian et al., 2022). Propolis can affect the permeability of the bacterial cellular membrane or reduce bacterial mobility (Przybyłek and Karpiński, 2019; Sforcin, 2016). On the other hand, propolis antioxidant properties have the ability to induce the activity of the human natural immune system therapy to fight microbial infections (Sforcin and Bankova, 2011).

In the first stage of dental implant placement, surgical injury to the soft and hard tissues of the oral cavity occurs, resulting in changes in oral microflora (Marsh and Percival, 2006). Such changes may lead to tissue inflammation and infections (Chuang et al., 2008). Propolis application results in a reduction of oral microorganisms (Morawiec et al., 2015). This is an advantageous feature since harmful bacteria present in the oral cavity could infect the implant during its placement. Therefore, antimicrobial agents containing propolis can be used during implant placement (Lisbona-González et al., 2021) to prevent post-implant placement infection. Nevertheless, the antimicrobial properties of propolis prophylactically promote the healing and conditions for effective osseointegration (Ercan

et al., 2015; Lisbona-González et al., 2021; Salari et al., 2023; Son et al., 2021; Vanni et al., 2015). All studies mentioned tested the efficacy of propolis in terms of reducing morbidity and improving tissue healing in the early healing phases after dental implant placement.

Studies on the protective effect of propolis are essential in the context of its potential application as a vehicle in implantology. Abundant bioactive compounds in natural products, including propolis, can stimulate osteoblast formation and/or bone matrix deposition (Kresnoadi et al., 2020a, 2020b). Hence, propolis can be incorporated as the surface coating of some dental implant fixtures (Abdulla et al., 2024a; Somsanith et al., 2018; Son et al., 2021). However, there is a gap in the clinical knowledge about propolis and its effects on the osseointegration of dental implants, especially in terms of allowing them to withstand immediate functioning. Further clinical studies are needed to evaluate the effect of propolis on dental implant surfaces, containing regenerative properties that benefit dental implant placement.

Propolis contain flavonoids, which are polyphenolic compounds. Flavonoids are not only present in propolis, but it is naturally found in fruits, vegetables, herbs, and essential oils (Ramesh et al., 2021). Incorporating flavonoids into bone grafts helps in healing bone defects (Yang et al., 2023). Hence, studies of propolis use with bone grafting and dental implants may help to achieve promising results in conditions where the loss of peri-implant bone occurs. Particularly, propolis reduced the formation of osteoclast cells in mice bone (Pileggi et al., 2009) and increased mineralisation and osteoblast cells (Lim et al., 2020).

Dental implants provide various treatment options, from simple tooth replacement to extensive full oral and maxillofacial reconstructions (Sartoretto et al., 2023). Since their production, dental implant manufacturing has focused on producing a biocompatible implant and supra-structure to replace the missed or damaged tissues. Today, the biocompatibility of available dental implants makes this treatment option successful in giving a patient the function and appearance of the mouth. The continuous growth of the implant market has made it possible to accelerate the development of new technologies to improve their long-term success. Proper healing and osseointegration of dental implants help them survive and succeed in the mouth (Louropoulou et al., 2015).

Implant osseointegration occurs as direct contact between the implant fixture and the jaw bone without connective tissue, thereby achieving stability and efficient transfer of stresses from the implant to the bone (Albrektsson and Jacobsson, 1987).

To enhance implant biocompatibility, different methods of mechanical instrumentation using instruments or air abrasion were used (Louropoulou et al., 2015). Others utilised surface modifications with implant coating to favour osseointegration (Inchingolo et al., 2023). Some have used naturally sourced materials for dental implant coatings to improve the implant-bone interface and osseointegration (Anees et al., 2024; Xu et al., 2020). Propolis can be incorporated into the scaffold or coat the dental implant (Abdulla et al., 2024a; Somsanith et al., 2018; Son et al., 2021). Flavonoids are significant components of propolis and are primarily responsible for their anti-inflammatory properties (Ramesh et al., 2021). It was also found that some flavonoids affect bone formation by stimulating osteoblastogenesis (Abdulla et al., 2024a). Bone formation due to flavonoid compounds is a complex process (Yamaguchi and Weitzmann, 2011; Zhao et al., 2019). The anti-inflammatory effect of propolis may inhibit the expression of pro-inflammatory mediators and stimulate osteoblasts to produce new bone around the dental implant (Kresnoadi et al., 2020b). The biomodification of the dental implant surface by incorporating propolis particles may contribute to treating bone infections without the clinical use of systemic antibiotics.

Many have tried to explain the potential effect of propolis on dental implant osseointegration by assessing propolis-coated implants on their osseointegration and bone-implant contact (Abdulla et al., 2024a). In an animal study, implants embedded with propolis were placed in rats' mandibles and showed better cell proliferation during osseointegration, forming new dense bone (Somsanith et al., 2018). A recent study evaluated different surface modifications of dental implants placed in dogs, including sandblasting, acid etching, laser treatment, and propolis-coated implants. They found that propolis-coated implants accelerate osseointegration and produce a sufficient bone matrix around the implants (Abdulla et al., 2024b). However, the effect of propolis on the rate of osseointegration and the long-term stability of implants has yet to be discovered.

Propolis and Implant Maintenance

Maintaining a healthy periodontium is necessary for the long-term success of dental implants (Louropoulou et al., 2015). Propolis has several major biological properties, such as anti-inflammatory and antimicrobial effects, which help maintain periodontal health (Cairo et al., 2006; Koo et al., 2002; Seal et al., 2016). Propolis showed a therapeutic effect when used in rats with periodontitis (Tang et al., 2024).

Peri-implantitis is one of the major issues related to the failure of implant treatment. It is defined as an inflammatory process that affects the soft and hard tissues around an osseointegrated implant in function, resulting in the loss of supporting bone. The main trigger of peri-implantitis is inflammation evoked by microbial infections (Quirynen et al., 2002). Biofilm is the etiologic factor in many infections, including those related to dental and maxillofacial tissues. Biofilm is a structured polymicrobial with a large number of aerobic and anaerobic bacteria tangled in a self-produced matrix of extracellular polymeric substances and adheres to an inert or living biological surface (Mombelli and Décaillet, 2011). The accumulation and colonisation of dental biofilms infect dental implants, leading to implant-associated infections. If not removed and treated, this can lead to an inflammatory reaction that causes the destruction of the supportive tissues, ultimately resulting in implant loss (Daubert and Weinstein, 2019).

Some benefits of incorporating propolis for peri-implantitis management have been widely discussed. Propolis may demonstrate efficacy in different aspects of peri-implant treatment, including anti-inflammatory, immunosuppressive, antioxidant, and antimicrobial effects and, as mentioned earlier, enhancing wound healing and osteogenesis.

In maintaining oral and implant health, propolis can inhibit both bacteria adhesion and plaque accumulation, which helps maintain good oral hygiene (Koo et al., 2002). Hence, it was found that propolis can help in reducing gingival and periodontal diseases. Patients with chronic gingivitis showed a significant reduction in plaque and gingival inflammation using propolis, similar to chlorohexidine mouthwash (Salari et al., 2023). In a study of 104 patients with gingivitis or periodontitis, an oral capsule containing 194 mg propolis for 8 weeks reduced gingival inflammation (Park et al., 2021). Propolis could also be used in the treatment of periodontal diseases and after scaling and root planning because it can counteract the bacteria that cause periodontal disease. It can also be used during the recall between appointments to maintain the optimal ecology of the gingival environment (Coutinho, 2012). Cario et al. found that propolis-containing gel has reduced gingivitis and chronic periodontitis (Cairo et al., 2006).

The use of propolis to treat and maintain peri-implant structures reduces inflammatory conditions and may support regeneration. Reduction of oral microflora is necessary for the long-term survival of dental implants. Aggregatibacter *actinomycetemcomitans,* one of the causative microorganisms of peri-implantitis (Cosyn et al., 2011) can be effectively removed by propolis as it prevents its adhesion and colonisation (Srinivas et al., 2022). Brazilian propolis extracts were found to be effective against species of *Candida* (Sawaya et al., 2002). Propolis exhibited antifungal properties against *Candida* biofilms around dental implants, potentially reducing peri-implantitis (Martorano-Fernandes et al., 2020).

In a study of sixteen patients with dental implants, propolis-containing toothpaste effectively improved oral health by reducing the occurrence of gingivitis (Morawiec et al., 2013). One randomised clinical trial to assess the efficacy of propolis-containing gel was used three times/day for 1 month on mucositis around the implant, which was loaded for at least 18 months. It was found that a significant reduction in gingival inflammation, propping depth, plaque and bleeding indexes was associated with using propolis-containing gel compared to not using it (González-Serrano et al., 2021).

It is essential to perform further controlled clinical studies concerning the effectiveness of propolis in the actual clinical scenarios of post-operative care of dental implant treatment.

Safety and Side Effects of Propolis

The safety of propolis use in humans is not yet a well-grounded matter. Many aspects should be evaluated scientifically, and reliable clinical data should be found to establish more rigorous scientific evidence on the safe use of propolis with standardisation of their composition to be used as a therapeutic agent. Although they are rare, the frequent side effect of propolis is allergic reactions (Callejo et al., 2001; Forkel et al., 2024; Parolia et al., 2010).

CONCLUSION

Alongside the growing interest in complementary medicine, there is a substantial increase in patients seeking treatments with appealing natural products. Propolis, a honeybee product with beneficial health properties, has been tested as a complementary herbal treatment in the post-operative phases of routine dental care with promising results.

Propolis has attracted the attention of the scientific and commercial communities to use it against pathogenic organisms related to oral diseases due to the increasing interest in developing natural treatment alternatives. Moreover, it decreases the resistance of microorganisms to antibiotics.

Propolis showed satisfactory results, not just because of its antimicrobial activity but also because of its healing properties. The use of propolis has a promising future since it fulfils the criteria of being biologically and implant-cellular compatible; hence, further thorough studies and clinical research are needed in dental implant treatments.

With all the advantageous properties of propolis in dentistry, few regulations evaluate the concentrations of propolis in dental products (Bankova, 2005; Sforcin, 2016). Hence, developing quality control measures via studies to establish the minimum inhibitory or bactericidal concentration is essential, as their effect depends highly on it (Hwu and Lin, 2014). Moreover, the therapeutic use of propolis lacks the standardisation of solvent type and percentage used with propolis (Cunha et al., 2004). To date, this is just the tip of the scientific evidence iceberg. More research is necessary to fill the existing knowledge gaps that will allow for a fair evaluation of propolis effects in the oral cavity and around dental implants. Therefore, well-designed clinical trials with standardised methods and long-term follow-up are recommended to assess the propolis use in clinical settings.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The author declares that she has no competing interests.

Funding

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

RA has conducted the search, written and approved the final manuscript.

Acknowledgements

The author would like to thank Prince Sattam bin Abdulaziz University for their help and support in conducting this research.

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