Mustansiria Dental Journal
DOI: 10.32828/mdj.v21i2.1209

E- ISSN: 2618-0944
P- ISSN: 1813-8500

Research Article | **Open Access** | **Volume: 21, Issue: 2, 2025**

Effect of Propolis Lozenges Extract on IL-10 and Oral Health Condition in (19_24) Years Old

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Received: 22 April 2025; Accepted: 16 September 2025; Published: 30 Dececmber 2025

Abstract

Aim of the study: Bees naturally create propolis from plant exudates mixed with pollen, wax, and enzymes. It has anti-inflammatory and antibacterial qualities well-known. Adhering firmly to the surfaces of teeth and other complicated structures in the mouth, plaque is a yellowish white or greyish material. The study aimed to assess how lozenges including propolis affected Interleukin-10 (IL-10) levels and plaque development.

Material and method: This study was a Prospective Interventional Controlled Clinical Trial**.** A total of eighty volunteers were divided into two groups 40 in the study group and 40 in the control group. Following a baseline saliva sample collection, study group volunteers received oral hygiene instruction plus propolis lozenge extract; the Plaque Index was then calculated. Over seven days, they were asked to use the lozenge twice daily, once in the morning and once in the evening. The control group, on the other hand, got just oral hygiene instructions (The importance of dental health and its effect on the overall body, the relevance of daily brushing and flossing, and the avoidance of cariogenic diet). During the second visit, saliva samples were collected again, and the Plaque Index (PI) was measured.

Results: The study group observed significant differences between the two visits regarding the mean Plaque Index (PI), whereas the control group did not show significant changes. Additionally, significant differences were found in the mean levels of interleukin-10 in the study group.

Keywords: Propolis, plaque, lozenges, Interleukin-10, Anti-bacterial, Anti-inflammatory

Introduction

Dental plaque is a yellowish white or greyish substance that adheres firmly to the surfaces of teeth and other complex oral structures. It is primarily biofilm composed of gram-positive, gram-negative bacteria (Masadeh et al., 2013), and its metabolites induce dental cavities and inflammation of the periodontal tissues (Pereira et al., 2011). It's possible that many people haven't done enough mechanical plaque removal, or if they have, it wasn't enough to prevent periodontal disease and plaque accumulation (Pereira et al., 2011; Tonetti et al., 2015).

Natural supplies have always been a goal in the health field as an alternative to synthetic ones (Al-Alawi & Ahmed, 2023). However, current dental research has focused on propolis, a natural and resinous ingredient that has been overlooked despite its potential to treat a wide range of illnesses. Pollen (5–10%), amino acids, resin and balsams (50–60%), minerals, vitamins A and B complex, the extremely potent biochemical material known as bioflavonoid (vitamin P), phenols, and aromatic components make up propolis (Park et al., 2002). It originally had an antiseptic means for preventing the beehive from microbial infections and decomposition

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DOI: 10.32828/mdj.v21i2.1209

by intruders. To ensure its protection, the hive's temperature must be sustained at 37°C and shielded from light and moisture. This situation is closely related to the human body, and propolis is significant in facilitating such conditions. Propolis is not utilized in its unprocessed state. It must be purified, and its aqueous or ethanolic extract should be obtained. Propolis possesses a distinctive aroma with various colorations, contingent upon the harvesting period and the botanical origin (Kasote et al., 2019).

Interleukin-10 (IL-10) is an anti-inflammatory cytokine synthesized by diverse cell types, such as macrophages, lymphocytes, and epithelial cells (Rallis et al.,2022). Saliva has long been proposed and used as a diagnostic medium since it is easily accessible, noninvasive, time-efficient, inexpensive, requires little training, and may be used for mass screening of large population samples (Salminen et al., 2014; Teles et al., 2009). An extra tool for daily dental care has been tested (chewing gum with an antiplaque ingredient), and the results indicated that it is a suitable vehicle for the release of an antiplaque chemical (Steinberg et al., 1992). Limited research has focused on the impact of Propolis lozenges on IL-10 and plaque accumulation. The study aimed to assess and compare the efficiency of propolis-containing lozenges against oral hygiene instructions alone in managing plaque accumulation, in addition measuring salivary levels of IL-10.

Materials and Methods

This study was approved by the Ethics Committee at the University of Mustansiriyah's, College of Dentistry (number: MUPRV0014). The study was conducted at the University of Mustansiriyah's Department of Peodontics, Orthodontics, and Preventive Dentistry College of Dentistry from November 2024 to April 2025. After being fully told about the purpose of the study, each volunteer was received their informed consent, indicating that they were willing to take part in the trial. Volunteers who consented to participate had to be male between the ages of 19 and 24 years, and appear to be in good overall health to be included. When there are no systemic disorders, the plaque index falls between 1.1 and 2.0. The exclusion criteria were people with systemic disorders. Those who now use mouthwash or other preventative measures. Those on antibiotics and anti-inflammatory medications during the study and the two weeks before. People have previously experienced hypersensitivity to any substances used in this study. Those who recently had extraction. People with a periodontal pocket depth of more than 4 mm, or attachment loss. People who smoke. Those who use removable dentures and orthodontic devices.

In this investigation, Europharma USA, a cGMP-compliant facility, produced 100 mg propolis lozenges containing the active ingredient, which is concentrated bee propolis (100mg of propolis).

Using the University of Michigan O probe marked by Williams, a clinical periodontal assessment includes the plaque index (Silness & Löe, 1964) to assess the levels of plaque buildup. The volunteer's plaque index was assessed by measuring dental plaque thickness on all teeth's surfaces (distal, mesial, palatal, and buccal) with a Williams periodontal probe. The measurements for every tooth were added together, and the averages were calculated. The plaque index

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was carried out using the reference values from Silness & Löe (1964).

Plaque index 0: No plaque

Plaque index 1: The gingival margin has a plaque that resembles a thin layer.

Plaque index 2: A visible plaque can be seen in the gingival edge and pocket.

Plaque index 3; Both the gingival pocket and the gingival edge are covered with a thick layer of plaque.

Study design

Eighty volunteers were divided into two groups for this crossover case-control clinical trial: forty in the study group and forty in the control group. During the first preparation session, saliva samples were collected, and each volunteer received motivation along with oral hygiene instructions (OHI) (The importance of oral health and its effect on the whole body, the significance of daily brushing and flossing, and the avoidance of cariogenic diet). Patients can significantly lower the incidence of plaque biofilm and gingivitis with frequent education and encouragement; the process is arduous, necessitating the patient's involvement, meticulous oversight with error rectification, and reinforcement at follow-up appointments until the patient attains requisite skill (Teles et al., 2008). The Plaque Index (PI) was then calculated. Volunteers in the study group were given a propolis lozenge extract to be taken twice a day for seven days, with one dose in the morning and another in the evening. They were instructed to chew the tablet for three to five minutes before swallowing it.

Next visit (Seven Days After the Initial Visit): On day eight, saliva samples were collected, and periodontal clinical measurements were taken. Throughout the seven days, the research team closely monitored each patient to ensure they were taking propolis as prescribed.

Salivary samples collection

As previously mentioned, unstimulated saliva samples were collected from the Volunteers before documenting their clinical data (Henson & Wong, 2010). Volunteers were instructed to refrain from dental activities on their teeth for one hour before the sample collection, between 9 AM and 12 PM. Volunteers washed their mouths with tap water ten minutes before gathering the sample to eliminate any last meal bits. After that, they were instructed to comfortably sit straight in front with their heads slightly down tilted. To get one milliliter of unstimulated saliva, the volunteers let their saliva accumulation on the floor of their mouths, then gently expectorated it into a graded sterile tube for five minutes.

Aliquots were made and kept at -20°C following 15 minutes of centrifugation of the samples at 3000 RPM until the levels of interleukins could be determined with an enzyme-linked immunosorbent assay (ELISA) kit (Belstrøm et al., 2017; Papagerakis et al., 2019).

Statistical Analysis

The data were analyzed using version 30 of the Statistical Package for Social Sciences (SPSS). Descriptive statistics were presented as means and standard deviations. The

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Shapiro-Wilk test determined whether the data followed a normal distribution. A paired t-test compares repeated measurements within the same group. The percentage change for each subject was calculated individually, and then the group mean of these percentage changes were compared. The equation utilized for calculating the mean percentage change was

$$\frac{\text{data at 2nd visit} - \text{data at 1st visit}}{\text{data at 1 st visit}} \times 100.$$

A p-value of equal or less than 0.05 was deemed statistically significant.

Results

Baseline 1st visits before Lozenges usage

Table 1 shows the results of the Shapiro-Wilk test, which assesses whether the data is normally distributed. The p-values for every group are not significant. The Plaque index of the groups did not differ significantly from one another since they were chosen based on predetermined criteria.

Table 1. The Shapiro-Wilk test

Interleukin &group	statistic	n	p-value	
IL-10(study group)	0.964	40	0.232	Non-significant
IL-10(control group)	0.970	40	0.359	Non-significant

(IL-10: interleukin 10, n: number of the sample)

Table 2. Descriptive statistics for PI, IL-10 at baseline, first visit.

Clinical periodontal and Immunological parameters	Groups			
	Study group		Control group	
	Mean ± SD	n	Mean ± SD	n
PI	1.51 ±0.18	40	1.52 ± 0.24	40
IL-10	867.17±83.91	40	991.89±95.59	40

(SD: standard deviation, PI: plaque index, IL-10: interleukin 10, n: number of the sample)

After Lozenge usage for one week (2nd visit)

Table 3 showed a decrease in the mean values of periodontal parameters during the second visit. Significant differences were observed between visits in the case group for the Plaque Index (PI) mean. In contrast, the control group did not show significant differences. Table 4 shows significant differences in the mean of Interleukin-10 in the case group.

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Table 3. Statistical comparison of plaque between the first and second visits in the two groups

Study Group	1st visit Mean ± SD	2nd visit Mean ± SD	paired t-test	P- value		Mean % Change
Study group	1.51 ± 0.18	0.8 ± 0.17	19.271	0.000	Highly significant	-46.24 %
Control group	1.52 ± 0.24	1.43 ± 0.27	2.966	0.005	significant	-4.29%

(SD: standard deviation, a minus sign (-) indicates a reduction in the mean value.)

Table 4. Statistical comparison of IL-10 between the first and second visits in the two groups

Groups	1st visit Mean ± SD	2nd visit Mean ± SD	paired t-test	P- value		Mean % Change
Study group	867.17±83.91	987.18±140.9	4.734	0.000	Highly significant	14.8%
Control group	991.89±95.59	964.31± 192.19	0.862	0.394	Non-significant	-2.08%

(SD: standard deviation, a minus sign (-) indicates a reduction in the mean value.)

Discussion

Baseline 1st visit:

The study groups were selected based on specific criteria, resulting in a comparable amount of plaque at the baseline visit. This indicates that there was minimal impact on the subsequent outcomes, as no significant differences were observed at the beginning. These findings are consistent with another study by Dehghani et al. (2019).

Second visit after 7 days' usage of the lozenges

Plaque Index:

A plaque index (PI) was used in this investigation to measure the amount of plaque development. According to the data adjusted for the evaluation of antiplaque activity, the mean PI was lower at the second visit than it was at the first for both groups, and there was a difference that is highly statistically significant in PI for the study group at the second visit compared to that at the first visit (baseline) between study groups. This finding implies that propolis effectively inhibits the formation of plaque. Similar studies (Tulsani et al., 2014; El-Allaky et al., 2020; Siqueira et al., 2021)

DOI: 10.32828/mdj.v21i2.1209

looking at the anti-plaque impact of propolis-containing lozenges in clinical trials indicate that propolis is safe and effective in preventing plaque accumulation.

A study by Savita et al. (2018) assessed the impact of propolis mouthwash on dental plaque accumulation and concluded that it was helpful. Inhibiting glucosyltransferase activity and the resulting polysaccharide synthesis may therefore reduce the pathogenicity of cariogenic biofilms, offering an alternate method of preventing biofilm-related diseases. Natural products continue to be the primary and mainly unexplored source of glucosyltransferases, and several of them have been identified (Ren et al., 2016). Propolis's antibacterial and antiplaque qualities are caused by a high concentration of phenolic compounds, such as flavonoids and caffeic acids. (Koru et al., 2007). Furthermore, Ercan et al., (2015) used mouthwash and chewing gum to examine the relative effects of propolis on plaque accumulation and gingival inflammation. As a result, they showed that propolis mouthwash and chewing gum both successfully reduced gingival inflammation and stopped plaque development. Studies by (Orsi et al., 2005: Velazquez et al., 2007) showed that propolis was highly effective in lowering the number of bacteria. Given that plaque is made of colonies of microorganisms, the drop in the plaque score could potentially be related (Bhat et al., 2015a). Plant-based antimicrobial agents offer great therapeutic promise since they can achieve the same goal with fewer side effects than antibiotics (Pathak et al., 2010). Propolis has about 300 ingredients, according to chemical testing; flavonoids and other phenolic chemicals make up most of them (Ansorge et al., 2003).

The flavanone, phenolic acid, and phenolic acid esters in propolis could be in charge of its antibacterial properties (Hazem et al., 2017b). Main compounds influencing the antibacterial qualities of propolis are pinocembrin, galangin, caffeic acid esters, and chrysin. Galangin (3,5,7-trihydroxyflavone) has been discovered among all the chemical agents present in propolis to be among the most powerful antibacterial agents (Bendtzen, 1994; Cobb, 2008; Hazem et al., 2017; Peycheva et al., 2019b).

Interleukin 10

At the second visit, the case group's mean of interleukin-10 was considerably higher than it was at baseline; when comparing the mean of interleukin-10 at the second visit to the baseline first visit, there was no statistically significant difference in the control group.

By modifying important inflammatory mediators, preventing the synthesis of proinflammatory cytokines, and boosting anti-inflammatory cytokines, propolis has been shown to have anti-inflammatory activity both in vitro and in vivo (Wang et al., 2009; Machado et al., 2012). As a result, propolis has a direct role as an anti-inflammatory agent.

T-helper 1 (Th1) immune response can trigger immunoglobulin production through the Th2 response, whereas IL-10 is an anti-inflammatory cytokine that can reroute the T-helper immune response (Hoene et al., 2015). Although IL-10 was previously believed to inhibit cytokine generation, new research indicates that it also has an immune-regulatory role. IL-10 is particularly well-known for its capacity to suppress the

DOI: 10.32828/mdj.v21i2.1209

expression of the majority of inducible chemokines, which occur during inflammatory processes, and prevent monocyte differentiation into antigen-presenting cells. By inhibiting cyclooxygenase-2-dependent prostaglandin E2 synthesis, IL-10 is known to prevent bone resorption. It also increases the production of anti-inflammatory mediators. Other stimulatory effects of L-10 include B-cell processes of proliferation and differentiation, which aid in the development of B cells into plasma cells. Additionally, IL-10 prevents osteoclast precursors from being recruited and from differentiating into mature multinucleated osteoclasts (Passoja et al., 2010).

According to Borrelli et al. (2002), propolis' main ingredient, caffeic acid phenethyl ester (CAPE), prevents rats from developing carrageenan pleurisy and adjuvant arthritis. This suggests that CAPE is responsible for propolis' anti-inflammatory properties.

The results of this study regarding the anti-inflammatory role of IL-10 supported the results from other investigations (Preethi et al., 2009; Boukhary et al., 2016; Gleiznys et al., 2019). It should be noted that this study had difficulty in doing longer follow up to the participants, further long-term studies therefore are recommended.

Conclusion

Propolis lozenges significantly reduced the plaque index and increased IL-10 levels. Therefore, it is recommended as an antiplaque and anti-inflammatory agent.

Supplementary Material

None.

Author Contributions

Summer Hilu Hammdallah: data curation, writing-original draft preparation. Mohammed Qays Mahmoud Fahmi: Conceptualization, methodology, writing-review and editing. Haider Al-Waeli: validation, formal analysis, investigation, supervision.

Funding

This research received no external funding.

Data Availability Statement

Data are available from the authors upon reasonable request.

Conflict of interest

The authors reported that they have no conflicts of interest.

Acknowledgments

The authors would like to thank Mustansiriyah University (www.uomustansiriyah.edu.iq), Baghdad, Iraq, for their support in the present work.

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