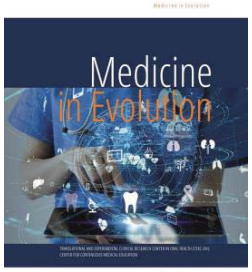
The applications of propolis in oro-dental health



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Abstract

Propolis is ranked among the few natural remedies that has still maintained its popularity over time due to its wide range of applications in both dentistry and medicine. Its extensive and wide variety of properties such as anti-inflammatory, antibacterial, antiviral, and antifungal have kept the attention and attention of many researchers. Most of the works on propolis are in vitro or animal studies. There is a clear need for human clinical studies to obtain the best benefits from this natural ingredient and to outline algorithms for its use in dentistry and other medical fields.

Propolis has demonstrated potential therapeutic effects on various oro-dental diseases due to its antimicrobial, anti-inflammatory, antioxidant, and immuno-modulatory properties. The present research aims to highlight the potential role of propolis in the treatment of dental caries, gingivitis and periodontal diseases, oral candidiasis, mouth ulcers, oral mucositis, or halitosis.

Keywords: gingivitis, propolis, oral micro-environment, antimicrobial, oral mucositis, halitosis

INTRODUCTION

The field of health has always emphasized the use of natural products for curing diseases rather than relying on conventional allopathic medicine. There are varieties of natural products used today in biomedical application in the treatment of a wide range of systemic diseases. These may include natural silk, [1,2] chitosan, [3,4] herbal tea [5] and miswak. [6] Propolis, a natural non-toxic resinous substance that exhibits antimicrobial, anticancer, antifungal, antiviral and anti-inflammatory properties, has gained attention in both cases. the dental and medical field. This waxy resinous substance comes from the Greek word "pro" (meaning outer wall) and "polis" (meaning city). This reflects the protective nature of the substance. [7,8] Propolis is one of the natural substances produced by bees for building and preserving their hives. It kills pathogens, protects the honeycomb from rain and, due to its adhesive nature, prevents foreign guests from entering the hive. [7]

This natural substance has a wide range of overlooked benefits. It is classified into twelve different types based on terrestrial location and physicochemical properties. However, only three different types of botanical origin have been identified. Propolis is considered the core and powerhouse of nutrients. [9] This resinous lipophilic material is sticky, soft, and flexible when exposed to wheat, but tough and brittle when cold. [8] Propolis is primarily composed of resins (55–60%). Waxes and fatty acids contribute about 30–45%, and aromatic oil and pollen about 10–5%. [10] Other substances may include minerals, vitamins, and flavonoids. The biological activity of propolis is mostly related to flavonoids and hydroxycinnamic acid. [11]

Research has shown that it is difficult to standardize the chemical constituents and flavonoid content of propolis because it is dependent on the environment, the place of collection, its origin, and the type of plant pollen and bee species that produced the propolis. [10,12] The commercial availability of propolis is in the form of pills, topical cream, mouthwash, and toothpaste. [8]

The purpose of this study is to explore the properties and chemistry of propolis in relation to its biomedical and dental applications, the status and scope of propolis as well as its potential bio-dental applications.

To achieve these objectives, experimental research related to food supplements based on propolis was carried out. Food supplements manufactured by FAVISAN were used in the scientific research.

Properties and chemical structure of propolis

The chemical variability of propolis is due to the different origin of plants, i.e., climatic, and geographical location, flora at the collection site and bee species. [12,13] For propolis production, bees use secretions from different plants as well as substances discharged from plant wounds, i.e., lipophilic materials from leaves, leaf buds, resins, gums, and matrices. [14,15] Therefore, there is striking chemical variability in the composition of propolis, especially from tropical regions. Kujumgiev et al. [16] compared the antibacterial, antiviral, antifungal and anti-inflammatory properties of propolis from different origins and concluded that they all showed significant properties, including important antiviral properties. Similarly, Popova et al. [17] reported the same findings when comparing the biological activity of propolis with geographical origin.

The chemical constituents of propolis include chrysin, galangin, pinocembrin, pinobaskin which is found in a temperate climate. These are flavonoids without ring B substituents. The major component of tempered propolis is caffeic acid phenethyl ester (CAPE). [14] Similarly, the chemical composition of propolis originating from tropical regions

includes prenylated phenylpropanoids (eg, artepillin C, while propolis found in Pacific and African regions contains geranyl flavanones as characteristic compounds. [14, 18]

Applications of propolis in dentistry

Mouthwashes are used as commercial antiseptics and used as a home remedy for better oral hygiene. These mouthwashes can be both cosmetic and therapeutic. Therapeutic mouthwashes reduce the number of bacteria, have anti-plaque effects, act as an astringent, and help reduce gingivitis and carious lesions. [19-21] One study evaluated the effect of propolis mouthwashes by comparing plaque scores and gingival index in the initial time and at a value of five. day interval. Chlorohexidine mouthwashes were more effective compared to propolis extract mouthwashes. [22] Furthermore, the effect of propolis mouthwash on gingival fibroblasts showed less cytotoxicity than chlorhexidine mouthwash. Ozan et al. and Arsalan et al. concluded that propolis mouthwashes were not as effective as chlorhexidine mouthwashes in preventing caries. gram-negative bacteria in the planktonic state and can be used as an alternative to chlorhexidine to avoid its side effects. Studies are needed to find the effects of propolis on biofilms. [19]

Research has shown that mouthwashes containing propolis in an aqueous alcohol solution heal intra-oral surgical wounds; therefore, it plays a role in epithelial repair after tooth extraction and exerts anti-inflammatory effect on orofacial pain. etiology of most oral diseases. Propolis-based toothpastes should be used as adjuncts to other substances in subjects at higher risk of periodontal problems. [23]

Dental hypersensitivity is defined as a sudden and brief pain arising from tactile, osmotic, thermal, or other stimuli from exposed dentin. [24] There are various theories for dental hypersensitivity. Among these theories, the hydrodynamic theory is considered the most acceptable and relevant. Propolis is proposed to reduce dentinal hypersensitivity by decreasing the hydraulic conductance of dentin. [25,26]

A recent study by Hussain et al. showed that propolis, when used in the treatment of post-bleaching dentin hypersensitivity, gave convincing results. [26] Similarly, another study by Hongal et al. showed contrasting results when Indian propolis was compared with RecaldentTM. RecaldentTM has shown significant results in reducing dentinal hypersensitivity. [27] Similarly, when 5% propolis extract was compared with potassium nitrate in reducing dentinal hypersensitivity, no difference was observed between the two groups. The use of propolis as a natural desensitizer is still a vague concept and requires further verification by research. [28]

An in vitro and in vivo study showed that propolis has a strong anti-inflammatory effect and can be used as a pulp coating agent. Flavonoids and caffeic acid are the main ingredients in propolis, responsible for the anti-inflammatory response by inhibiting lipoxygenase and the arachidonic pathway. [29,30] In addition, flavonoids and caffeic acid ensure the acceleration of the immune system by enhancing phagocytic activity. [8,29] There are numerous studies. over the years that have demonstrated the anti-inflammatory effects of propolis. [29,31,32,33] Bachiega et al showed that cinnamic acid and coumaric acid in propolis inhibit IL-6 and IL-10 but encourage the production of IL-8 by macrophages. [34] The anti-inflammatory effect of propolis depends on the potential dose and route of administration.

The efficiency of propolis use in oral health

In this study, we aimed to evaluate the effectiveness of the use of propolis-based products in oral health, as well as the verification of oral health habits, oral assessment and screening for gingivitis, periodontitis, and oral cancer.

The method used was the prospective observational study carried out between October 2022 and March 2023. The research was carried out in 3 medical offices. A total of 42

participants were selected, who after the oral assessment were divided into two equal groups of 21 patients each, the test group and the control group, with approximately the same oral health status, in order to avoid random error. The products given to the patients in the test group were the following: Favifresh – mouthwash with propolis, Favifresh – mouthwash with propolis and organic mint and Propolis mouth spray.

The socio-demographic characteristics of the groups are similar as can be seen in the table below.

Table 1. Socio-demographic characteristics of the groups

Variable	**Group no. I - test**		**Group no. II - control**	
Age	Medium age = 32,6 yrs ± 12,5 yrs Minimum = 19 yrs Maximum = 54 yrs		Medium age = 31,8 yrs ± 12,7 yrs Minimum = 19 yrs Maximum = 53 yrs	
Sex				
Men	11	52,38%	11	52,38%
Women	10	47,61%	10	47,61%
Residence				
Urban	18	85,71%	16	76,19%
Rural	3	14,38%	5	23,8%
Studies graduated				
Gimnasium	6	28,57%	7	33,33%
Highschool	9	42,85%	8	38,09%
College	6	28,57%	6	28,57%

The data obtained from completing the questionnaires and oral assessments were entered into a database in Microsoft Excel 365, where they were processed descriptively, and the comparison test used was the online chi square Chi Square Calculator 2x2. it was considered statistically significant at p< 0.05.

Comparative analysis of the effect on the presence of gingivitis

For the group I-test group the chi-square statistic is 9.7222. The p-value is 0.001821. Significant at p < 0.05. The chi-square statistic with Yates correction is 7.875. The *p*-value is 0.005012. Significant at *p* <.05.

Table 2. Comparative analysis of the effect on the presence of gingivitis for group I

	inițial	**final**	***Marginal Row Totals***
gingivitis +	17 (12) [2.08]	4 (9) [2.78]	21
gingivitis -	7 (12) [2.08]	14 (9) [2.78]	21
Marginal Column Totals	24	18	42 (Grand Total)

For group II-control the chi-square statistic is 1.0027. The *p*-value is 0.31667. Not significant at *p* < 0.05. The chi-square statistic with Yates correction is 0.4456. The *p*-value is 0.504421. Not significant at *p* < 0.05.

Table 3. Comparative analysis of the effect on the presence of gingivitis for group II

	inițial	**final**	***Marginal Row Totals***
gingivitis +	16 (14.5) [0.16]	13 (14.5) [0.16]	29
gingivitis -	5 (6.5) [0.35]	8 (6.5) [0.35]	13
Marginal Column Totals	21	21	42 (Grand Total)

From the above data we can conclude that food supplements with Propolis or oral hygiene products based on Propolis significantly influence the presence of gingivitis after 3 months of use.

Analysis of the cause of the difficulty in mastication symptom

For group I-test the chi-square statistic is 0.1414. The p-value is 0.706879. Not significant at $p < 0.05$. Chi-square statistic with Yates correction is 0. p-value is 1. Not significant at $p < 0.05$.

Table 4. Analysis of the cause of the difficulty in mastication symptom for group I

	initial	final	*Marginal Row Totals*
mastication pain +	5 (4.5) [0.06]	4 (4.5) [0.06]	9
mastication pain -	16 (16.5) [0.02]	17 (16.5) [0.02]	33
Marginal Column Totals	21	21	42 (Grand Total)

For group II-control the chi-square statistic is 0.1232. The p-value is 0.725625. Not significant at $p < 0.05$. Chi-square statistic with Yates correction is 0. p-value is 1. Not significant at $p < 0.05$.

Table 5. Analysis of the cause of the difficulty in mastication symptom for group II

	initial	final	*Marginal Row Totals*
mastication pain +	6 (5.5) [0.05]	5 (5.5) [0.05]	11
mastication pain -	15 (15.5) [0.02]	16 (15.5) [0.02]	31
Marginal Column Totals	21	21	42 (Grand Total)

From the above we can conclude that food supplements with Propolis or oral hygiene products based on Propolis do not influence the difficulty in mastication after 3 months of use.

The comparative analysis of the accusation of the **toothache symptom** compared to the end in the two groups revealed a chi-square statistic of 0.4667 on the I-test group. p-value of 0.494525. Not significant at p <0.05. The chi-square statistic with Yates correction is 0.1167. The p-value is 0.732678. Not significant at p <.05.

Table 6. Toothache symptom in group I

	initial	final	*Marginal Row Totals*
toothache +	7 (6) [0.17]	5 (6) [0.17]	12
toothache -	14 (15) [0.07]	16 (15) [0.07]	30
Marginal Column Totals	21	21	42 (Grand Total)

In the control group II, the chi-square statistic is 0.4286. The p-value is 0.512691. Not significant at $p < 0.05$. The chi-square statistic with Yates correction is 0.1071. The p-value is 0.743421. Not significant at $p < 0.05$.

Table 7. Toothache symptom in group II

	initial	final	*Marginal Row Totals*
toothache +	8 (7) [0.14]	6 (7) [0.14]	14
toothache -	13 (14) [0.07]	15 (14) [0.07]	28
Marginal Column Totals	21	21	42 (Grand Total)

Following the conducted study, we can say that food supplements with Propolis or oral hygiene products based on Propolis do not significantly influence tooth pain after using them during the research period.

Comparative analysis of gingival bleeding symptom accusation

Measurements performed on the group I-test lot showed that the chi-square statistic is 11.9576. The *p*-value is 0.000544. Significant at $p < 0.05$. The chi-square statistic with Yates correction is 9.8824. The *p*-value is 0.001669. Significant at $p<0.05$.

Table 8. Comparative analysis of gingival bleeding symptom accusation in group I

	initial	final	*Marginal Row Totals*
bleeding +	18 (12.5) [2.42]	7 (12.5) [2.42]	25
bleeding -	3 (8.5) [3.56]	14 (8.5) [3.56]	17
Marginal Column Totals	21	21	42 (Grand Total)

For the II-control group the chi-square statistic is 0.4667. The *p*-value is 0.494525. Not significant at $p <0.05$. The chi-square statistic with Yates correction is 0.1167. The *p*-value is 0.732678. Not significant at $p <0.05$.

Table 9. Comparative analysis of gingival bleeding symptom accusation in group II

	initial	final	*Marginal Row Totals*
bleeding +	16 (15) [0.07]	14 (15) [0.07]	30
bleeding -	5 (6) [0.17]	7 (6) [0.17]	12
Marginal Column Totals	21	21	42 (Grand Total)

From the above data we can say that food supplements with Propolis or oral hygiene products based on Propolis influence the presence of gingival bleeding after 3 months of use.

Analysis of the symptom of bad breath (halitosis)

For the I-test group the chi-square statistic is 6.0352. The *p*-value is 0.014023. Significant at $p < 0.05$. The chi-square statistic with Yates correction is 4.434. The *p*-value is 0.035229. Significant at $p < 0.05$.

Table 10. Analysis of the symptom of bad breath (halitosis) in group I

	initial	final	*Marginal Row Totals*
halitosis +	9 (5.5) [2.23]	2 (5.5) [2.23]	11
halitosis -	12 (15.5) [0.79]	19 (15.5) [0.79]	31
Marginal Column Totals	21	21	42 (Grand Total)

In the II-control group, the chi-square statistic is 0.525. The *p*-value is 0.468717. Not significant at $p < 0.05$. The chi-square statistic with Yates correction is 0.1312. The *p*-value is 0.71714. Not significant at $p < 0.05$.

Table 11. Analysis of the symptom of bad breath (halitosis) in group II

	initial	final	*Marginal Row Totals*
halitosis +	6 (5) [0.2]	4 (5) [0.2]	10
halitosis -	15 (16) [0.06]	17 (16) [0.06]	32
Marginal Column Totals	21	21	42 (Grand Total)

From the above data we can conclude that food supplements with Propolis or oral hygiene products based on Propolis influence the presence of bad breath after 3 months of use.

CONCLUSIONS

From the study undertaken by us, it could be observed that, using products based on propolis, the presence of gingival bleeding and bad breath decreased statistically significantly. On organic causes such as toothaches, they had a positive influence, greater than that of classic products, but not statistically significant.

Propolis is a natural biomaterial for oral health that needs human clinical studies to be able to get the best benefits from this natural ingredient. There is a great need for outlining algorithms for its use in dentistry as well as in other medical fields.

Propolis and its phenolic and flavonoid constituents have many therapeutic uses in dentistry, oral health, and medicine. Wide therapeutic uses due to its antibacterial, antiviral, antifungal, anti-inflammatory and anti-carcinogenic properties have been demonstrated in various in vitro, in vivo and ex vivo studies as well as in human clinical trials. However, there is a great need to standardize the content of phenolic acids and flavonoids in propolis to obtain the best therapies and drugs.

REFERENCES

1. Zafar M, Khurshid Z, Almas K. Oral tissue engineering progress and challenges. Tissue Engineering and Regenera-tive Medicine 2015; 12:387-97. doi: 10.1007/s13770-015-0030-6.
2. Zafar MS, Al-Samadani KH. Potential use of natural silk for bio-dental applications. Journal of Taibah University Medi-cal Sciences 2014; 9:171-7. doi: 10.1016/j.jtumed.2014.01.003.
3. Husain S, Al-Samadani KH, Najeeb S, Zafar MS, Khurshid Z, Zohaib S, Qasim SB. Chitosan biomaterials for current and potential dental applications. Materials 2017;10:602. doi: 10.3390/ma10060602.
4. Qasim SB, Najeeb S, Delaine-Smith R, Rawlinson A, Reh-man IU. Potential of electrospun chitosan fibers as a surface layer in functionally graded GTR membrane for periodontal regeneration. Dental Materials 2017;33:71-83. doi: 10.1016/j.dental.2016.10.003.
5. Khurshid Z, Zafar MS, Zohaib S, Najeeb S, Naseem M. Green tea (camellia sinensis): Chemistry and oral health. The Open Dentistry Journal 2016;10:166-73. doi: 10.2174/1874210601610010166.
6. Niazi F, Naseem M, Khurshid Z, Zafar MS, Almas K. Role of salvadorapersica chewing stick (miswak): A natural toothbrush for holistic oral health. European Journal of Dentistry 2016;10:301-8. doi: 10.4103/1305-7456.178297.

7. Wilson-Rich N. Genetic, individual, and group facilitation of disease resistance in honey bees (Apismellifera) and two species of paper wasps (Polistesdominulus and P. Fuscatus). Tufts University. 2011.
8. Deswal H, Singh Y, Grover HS, Bhardwaj A. Healing effect of propolis in medicine and dentistry: A review. Innovare Journal of Ayurvedic Sciences 2016;1-4.
9. Rathod S, Brahmankar R, Kolte A. Propolis-A natural re-medy. Indian J Dent Res Rev 2012;50:99-103.
10. Xiaobo H, Lifei Z, Baizhen L. Recent progress in the stu-dies on pharmacological activity of propolis. China Phar-maceuticals 2006;1:018.
11. Kamburoglu K, Ozen T. Analgesic effect of anatolian prop-olis in mice. Agri2011;23:47-50.
12. Toreti VC, Sato HH, Pastore GM, Park YK. Recent progress of propolis for its biological and chemical compo-sitions and its botanical origin. Evidence-Based Comple-mentary and Alternative Medicine 2013;2013:1-13. doi: 10.1155/2013/697390.
13. Salatino A, Fernandes-Silva C, Righi AA, Salatino MLF. Propolis research and the chemistry of plant products. Nat Prod Rep 2011;28:925-36. doi: 10.1039/C0NP00072H.
14. Huang S, Zhang C, Wang K, Li GQ, Hu F. Recent advances in the chemical composition of propolis. Molecules 2014;19:19610-32. doi: 10.3390/molecules191219610.
15. Bankova V. Recent trends and important developments in propolis research. Evidence-based complementary and al-ternative medicine 2005;2:29-32.
16. Kujumgiev A, Tsvetkova I, Serkedjieva Y, Bankova V, Christov R, Popov S. Antibacterial, antifungal and antiviral activity of propolis of different geographic origin. J Ethno-pharmacol1999;64:235-40. doi: 10.1016/S0378-8741(98)00131-7.
17. Popova M, Bankova V, Naydensky C, Tsvetkova I, Kujum-giev A. Comparative study of the biological activity of propolis from different geographic origin: A statistical ap-proach. Macedonian Pharmaceutical Bulletin 2004;50:9-14.
18. Sforcin JM, Fernandes A, Lopes C, Bankova V, Funari S. Seasonal effect on brazilian propolis antibacterial activity. J Ethnopharmacol2000;73:243-9.
19. Akca AE, Akca G, Topçu FT, Macit E, Pikdöken L, Özgen Ş. The comparative evaluation of the antimicrobial effect of propolis with chlorhexidine against oral pathogens: An in vitro study. BioMed research international 2016;2016:1-8. doi: 10.1155/2016/3627463.
20. Mhaske M, Samad BN, Jawade R, Bhansali A. Chemical agents in control of dental plaque in dentistry: An overview of current knowledge and future challenges. AdvApplSci Res 2012;3:268-72.
21. Prasad KR, John S, Deepika V, Dwijendra KS, Reddy BR, Chincholi S. Anti-plaque efficacy of herbal and 0.2% chlor-hexidine gluconate mouthwash: A comparative study. Jour-nal of international oral health: JIOH 2015;7:98.
22. Dodwad V, Kukreja BJ. Propolis mouthwash: A new begin-ning. Journal of Indian Society of Periodontology 2011;15:121.
23. Morawiec T, Dziedzic A, Niedzielska I, Mertas A, Tana-siewicz M, Skaba D, Kasperski J, Machorowska-PieniƒÖ≈⁰ek A, Kucharzewski M, Szaniawska K. The bio-logical activity of propolis-containing toothpaste on oral health environment in patients who underwent implant-supported prosthodontic rehabilitation. Evidence-based complementary and alternative medicine 2013;2013:1-12. doi: 10.1155/2013/704947.
24. Blaggana A, Vohra P, Nagpal A. Diagnosis and treatment of dentinal hypersensitivity. J Innov Dent 2011;1:1-4.
25. Lin P, Cheng Y, Chu C, Chien K, Lin C, Tu Y. In-office treatment for dentin hypersensitivity: A systematic review and network meta-analysis. J ClinPeriodontol2013;40:53-64. doi: 10.1111/jcpe.12011.
26. Hussain RA, Dannan A, Al-Ahmad M. Propolis treatment for dental sensitivity after tooth bleaching. Imperial Journal of Interdisciplinary Research 2017;2:1436-9.
27. Hongal S, Torwane NA, Goel P, Chandrashekar B. The ef-fect of 30% ethanolic extract of indian propolis on replica of human dentin compared against commercially available de-sensitizing agent: A methodological SEM study in vitro. Pharmacognosy research 2014;6:113-9. doi: 10.4103/0974-8490.129026.

28. Purra AR, Mushtaq M, Acharya SR, Saraswati V. A com-parative evaluation of propolis and 5.0% potassium nitrate as a dentine desensitizer: A clinical study. Journal of Indian Society of Periodontology 2014;18:466-71. doi: 10.4103/0972-124X.138695.
29. Sabir A. The healing actions of propolis on direct pulp cap-ping treatment: A review. Journal of Dentomaxillofacial Science 2016;1:186. doi: 10.15562/jdmfs.v1i1.145.
30. Ramos A, Miranda J. Propolis: A review of its anti-inflammatory and healing actions. Journal of Venomous An-imals and Toxins Including Tropical Diseases 2007; 13:697-710. doi: 10.1590/S1678-91992007000400002.
31. Ardo Sabir D ed. Analysis of Tumor Necrosis Factor-Alpha (TNF-a) Expression In Inflamed Rat Dental Pulp Tissue Following Propolis Application (An Immunohistochemistry Study). The 3rd ASEAN Plus and Tokushima Joint Interna-tional Conference, Program and Proceeding Book. 2014.
32. Ardo Sabir D. Using propolis as A therapeutic agent in den-tistry. Cakradonya Dental Journal 2012; 4:480-6.
33. Wi*f*ôckiewicz W, Miernik M, Wi*f*ôckiewicz M, Morawiec T. Does propolis help to maintain oral health? Evidence-Based Complementary and Alternative Medicine 2013; 2013:1-8. doi: 10.1155/2013/351062.
34. Zafar MS, Ahmed N. Therapeutic roles of fluoride released from restorative dental materials. Fluoride 2015;48:184-94. doi:http://www.fluorideresearch.org/483/files/FJ2015_v48_n3_p184-194_pq.pdf