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EFFECTIVENESS OF HONEY AND PROPOLIS IN THE TREATMENT OF PERIODONTAL DISEASE: A REVIEW

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ABSTRACT

Chronic multifactorial inflammation known as periodontitis is linked to dysbiotic plaque biofilms and is characterised by the progressive loss of the structures that support teeth. In order to prevent periodontal disease, natural therapies are currently gaining favour over synthetic ones. As a result, several oral health products, such as toothpaste, mouthwash, and dentifrices, have been developed that contain honeybee products like propolis, honey, Royal jelly. The purpose of this review is to explore the literature on the effectiveness of propolis and honey in the treatment of periodontal disease. In this study, we reviewed the literature on the efficacy of propolis and honey in the treatment of periodontitis. The data was collected from 6 databases, including PubMed, Web of Science, ScienceDirect, Scopus, clinicaltrials.gov, and Google Scholar. The MeSH terms used in the search were: honey and periodontal disease, propolis and periodontal disease, propolis and gingivitis treatment, honey and gingivitis treatment. A total of 8 Invitro and 11 Clinical studies were reviewed after applying inclusion and exclusion criteria. Based on results of these studies, Propolis and Honey demonstrated to have numerous applications in dentistry due to their antimicrobial, anti-inflammatory, anticancer, antioxidant properties. Based on this research it is concluded that using bee products such as Propolis and Honey to treat periodontitis are safer, economical, beneficial; nevertheless, additional clinical and experimental data is required to fully understand the bioactivities of bee products in treating periodontitis.

KEYWORDS: Propolis, Honey, Periodontitis, Gingivitis.

1.1 INTRODUCTION

Inflammation of the soft periodontal tissues is a sign of periodontal disease. The proliferation of a few species in tooth plaque, such as Bacteroides forsythus, Treponema denticola, and Porphyromonasgingivalis, is believed to be the cause of nearly all kinds of periodontal disease.[1,2]

In recent years, attention has grown towards use of natural therapies given the numerous advantages offered by natural products compared to synthetic drugs. Currently, more preference is given to natural therapies, due to the high safety margin, lower cost, and broad bioactivity compared to synthetic medicine. Apitherapy is an alternative therapy that uses products made by honeybees for medical purposes. These products include royal jelly, propolis, and honey.[2]

Propolis a naturally occurring nontoxic resinous compound produced by bees to defend their hives from outside intruders. Since ancient times especially in Europe and ancient Egypt propolis was utilized as homoeopathic remedy recognized for its anti-inflammatory effects. 10% pollen and other organic substances, 10% aromatic and essential oils, 30% waxes, and 50% vegetable resins contribute to its composition.[3,4,5,6] The primary components are phenolic esters, such as caffeic acid phenethyl ester and flavonoids and the composition is dependent on numerous factors including bee species, regional origin, and botanical origin. According to reports, propolis exhibits a range of bioactivities, including anti-inflammatory, anti-cancer, anti-microbial, and antioxidant properties.[2,7,8,9]

The expression of ARE-mediated antioxidant genes, such as -GCS and HO-1, causes propolis and its constituent pinocembrin to upregulate the enzymatic antioxidant pathway and stimulate Nrf-2 translocation to the nucleus. Other antioxidant markers TrxR1, GCLC, LOX-1, GCLM, and -GCS have their expression of protein and mRNA regulated by propolis as well.[10,12]

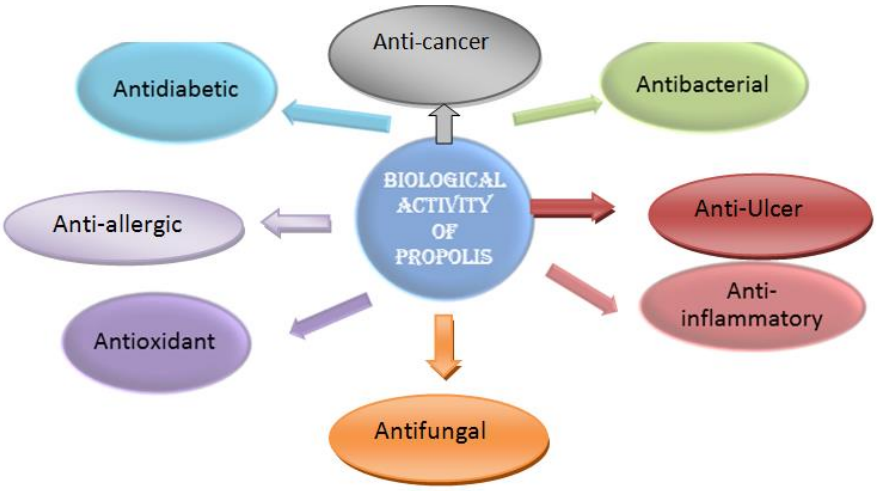

Figure 1: Biological activity of Propolis.

The honey bee converts nectar into honey, a delicious liquid. Because it contains many nutrients that are good for human health, honey is well-known on global scale. Ancient Egyptians, Greeks, Romans, and Chinese people all used it to treat wounds and digestive disorders such as gastric ulcers.[13]

Another name for honey is "supersaturated sugar solution." Natural honey has 82.4% of its mass in carbohydrates, 38.5% in fructose, 31% in glucose, 12.9% in other sugars, 17.1% in water, 0.5% in protein, organic acids, multiminerals, amino acids, vitamins, phenols, and a plethora of other minor constituents. Additionally, honey contains trace levels of other beneficial substances such phenolic acid, flavonoids, and tocopherol.[14] Phenolic acids, flavonoids, ascorbic acid, proteins, carotenoids and certain enzymes, such glucose oxidase and catalaseare among the components of honey that have positive health effects.[15]

In numerous oral conditions such as halitosis, stomatitis and periodontal disease honey is used as theraupeutic agent. Additionally, it has been used to prevent periodontitis, dental plaque, gingivitis, and mouth ulcers. Honey's antibacterial and anti-inflammatory qualities can promote development of granulation tissue, which in turn helps damaged cells heal. Honey inhibits periodontal disease by acting as antibacterial agent against anaerobic bacterias.[16,17] Stomatitis an inflammation of mucous membrane result in ulcers that are clearly visible and extremely painful. Honey is useful against stomatitis because it penetrates the tissues.[18,19] Bad breath is symptom of oral health disorder halitosis. Degrading microorganisms are primarily to blame forodour in the oral cavity. According to a recent

study, honey's significant antibacterial action from its methylglyoxal component helps reduce halitosis when consumed.[20,21]

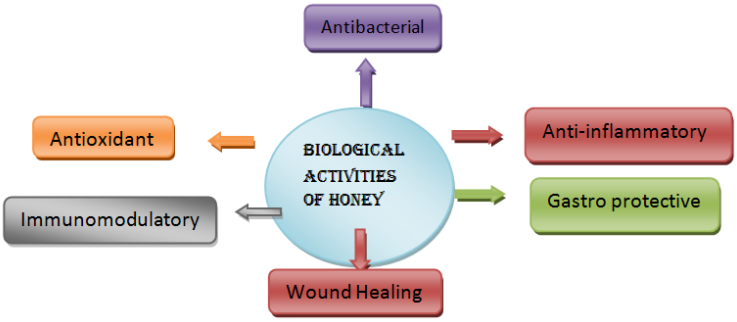

Figure 2: Biological activity of Honey.

The use of natural remedies with pharmacological activity in the treatment of various "oral bacterial diseases" and to promote improved oral health has increased, according to more clinical trials and experimental evidence published in recent years. The use of beeproducts in dentistry may be beneficial intreatment of "oral bacterial disease" such as periodontitis, dental caries, and gingivitis due to their anti-inflammatory, antibacterial, and antioxidant properties. This review's major goal is to provide insight on how honeybee products can be used to treat periodontal diseases.

1.2 MATERIALS AND METHODS

We evaluated several in vitro and clinical research on the use of bee products such as Honey and Propolis in the treatment of periodontal disease. The databases of PubMed, Web of Science, ScienceDirect, Scopus, clinicaltrials.gov, and Google Scholar were used to conduct an electronic literature search. Individual medical subject heading (MeSH) terms such as honey, propolis, periodontitis, gingivitis, and periodontal diseases were used in the search. The MeSH terms honey and periodontal disease, propolis and periodontal disease, propolis and gingivitis therapy, and honey and gingivitis treatment were used in combination.

1.2.1Inclusion criteria

(i) In vitro and clinical trials assessing the effectiveness of propolis and honey in the treatment of periodontal diseases.

(ii) Findings published in English.

(iii)Clinical studies that were randomly chosen and those that were not.

1.2.2 Exclusion criteria

(i) Studies for which the entire text was not readily available.

(ii) Clinical trials that do not adhere to ethical standards

(iii)Published studies in local languages except for English.

(iv)Studies that are non-relevant.

1.3 RESULTS

Data selection and Interpretation

1.3.1Antimicrobial Studies

The antibacterial activity of propolis against periodontal pathogenic bacteria in vitro was examined in six of the studies. Based on a 30% w/v concentration, an ethanolic extract of propolis (EEP) inhibits the growth of periodontal pathogenic bacteria such as Prevotella melaninogenica, Porphyromonasgingivalis, Porphyromonasasaccharolytica, and Prevotella intermedia. P. melaninogenica's zone of inhibition was 18.3 ± 0.64 mm, P. gingivalis was 18.9 ± 0.05 mm, P. asaccharolytica's was 22.8 ± 0.28 mm, and P. intermedia was 22.8 ± 0.18 mm.[22]

Another study used broth microdilution assays and agar dilution assays to test the antibacterial activity of EEP and EEP-derived compounds against P. gingivalis in vitro. The findings of both assays revealed MIC values of 64 g/mL (broth) and 128 g/mL (agar). Additionally inhibitory mechanism was being looked at. By increasing membrane permeability EEP reduced P. gingivalis activity and caused cell death within 30 minutes. Following bleb fusion, EEP on the bacterial surface promoted growth of abnormal membrane blebs. Additionally, the activity of molecules generated from EEP was investigated, results showed that ursolic acid prevented membrane rupture from causing bactericidal activity. Bacteriostatic activity of baccharin and artepillin C are demonstrated by membrane blebbing.[23]

The oral carcinogenic bacteria Streptococcus mitis, Lactobacillus acidophilus, Streptococcus mutansand Streptococcus sanguinis as well as periodontopathic bacteria Fusobacterium nucleatum, Eikenellacorrodens, and Actinomyces odontolyticus all showed inhibitory effects in vitro when treated with propolis at minimum inhibitory concentration of 12.5 g/mL. Propolis also prevents the growth of all oral carcinogens and periodontopathic bacteria, except for L. acidophilus, which has a MIC value of 6.3 g/mL.[24]

Propolis also had an inhibitory effect against the yeast and bacteria that cause tooth caries, Streptococcus mutans and Candida albicans. In addition, 50 mL of propolis produces a mean zone of inhibition for Candida albicans of 15.6 mm, as opposed to probiotics' 12 mm and chlorhexidine 14 mm. The average zone of inhibition for Streptococcus mutans was 9.4 mm probiotics, 14 mm for chlorhexidine, and 14.6 mm propolis. Propolis proved to be more effective at inhibiting Streptococcus mutans and Candida albicans than conventional chlorhexidine and probiotics.[25]

Propolis antibiofilm, cytotoxic, and antibacterial properties were evaluated in an in vitro biofilm of Streptococcus gordonii and Fusobacterium nucleatum. Lower-than-average thickness biofilms of F. nucleatum and S. gordonii were produced after treatment with methanolic fraction of propolis (chloroform partition) at doses of 1.563 mg/mL (7.37 1.620 m and 9.24 0.679 m) and 0.78 mg/mL (6.84 1.68 m and 8.02 1.6 m, respectively). A human gingival fibroblast cell line (HGF-1) was used in a cytotoxicity assay with 0.78 mg/mL propolis (chloroform partition) and the results showed 92.64% cell viability. In opposition to propolis combined with chlorhexidine, which had zones of inhibition of 14.33± 0.19 mm and 14.55±0.19 mm, the antimicrobial study ofmethanolic fraction of propolis demonstrated significant inhibition of F.nucleatum and S. gordonii bacteria.[26]

Propolis was tested in vitro for its antibacterial properties against multispecies biofilms containing periodontal pathogens. Beginning on Day 3 (twice daily for one minute), propolis was applied to the subgingival biofilm with 32 species of seven days old. The microbial makeup and metabolic activity of biofilms were assessed by DNA-DNA hybridization and results revealed1600 g/mL propolis did not significantly differ from that treated with chlorohexidine while also reducing metabolic activity by 45%. Based on findingspropolis and chlorhexidine were shown to be equally efficient in reducing the production of subgingival biofilm.[27]

The metabolic activity of multispecies biofilms was observed to be reduced by propolis at doses of 400, 800, and 1600 g/mL by 57, 56, and 56%, respectively, compared to a 65% reduction with amoxicillin therapy. Additionally, showned treatment with propolis had no impact on how many Actinomyces species were compatible with hosts.[28]

Propolis treatment inhibited the growth of bacteria that cause periodontal disease (Porphyromonasgingivalis), candida infection (Candida albicans), and dental caries

(Streptococcus mutans), with MIC values of 0.2, 6.25, and 0.2 mg/mL, respectively. It was also reported on how three separate P. gingivalis, C. albicans, and S. mutans biofilms responded to treatment with propolis. Bacterial counts from periodontal biofilms revealed that 100 mg/mL propolis therapy reduced biofilm 8.99 log10 colony forming units (CFU) after 4 hours to 3.21 log10 CFU. After 4 hours of treatment, 100 mg/mL propolis decreased bacterial count in carcinogenic control biofilm from 7.99 log10 CFU to 2.21 log10 CFU. After 4 hours of treatment, Candida biofilm comprising bacterial counts of 7.74 log10 CFU were decreased to 3.65 log10 CFU by 100 mg/mL propolis.[29]

Comparing the above-discussed in vitro investigations, it was found that propolis (12.5–400 g/ml) significantly inhibited growth of periodontal pathogenic bacteria. Additionally, it has been found that EEP is superior to raw propolis in treatment of periodontopathic bacteria.

1.3.2 Clinical studies

10 clinical studies investigating the use of proplis and honey in management of periodontal disease were discussed in the current study. The effectiveness of topical application of propolis into periodontal pockets larger than 5 mm in individuals with periodontitis was examined in a randomised double-blind controlled clinical experiment.

A total of 24 individuals with chronic periodontitis chosen and split into four groups, each with six patients. Each group received therapy with a distinct cream: Group I contains control group, Group II containspropolis group, Group III contains the curry leaf group, Group IV contains the minocycline group and Group V contains the placebo group. Three times, separated by one month, propolis ointment was applied.

After propolis treatment results showed P. gingivalis levels in GCF dramatically decreased. However, difference between propolis group (1.67±1.22 mm) and placebo group (0.33±0.82 mm) did not reachsignificance. The probing pocket depth score was also enhanced by propolis (1.83 1.17 mm) as compared to placebo (0.33±0.82 mm).[30]

In a double-blinded, random clinical experiment, the effectiveness of propolis-containing mouthwash in the treatment of gingivitis was assessed. Total of 32 patients with gingivitis chosen and separated into two groups: Group I received mouthwash containing propolis extract, whereas Group II received the same mouthwash without propolis extract (16 patients

in each group). Patients were instructed to gargle for one minute with the propolis mouthwash twice daily (30 drops diluted with 20 mL water).

The results revealed no difference between the propolis group's plaque index (PI) score of 85.19±51.6% and the placebo group's score of 83.93±36.1% ($p = 0.91$), which is a statistically insignificant difference. With a significant difference between the two groups of $p<0.001$, the results revealed a significant decrease in the papillary bleeding index (PBI) of the propolis group compared to the placebo group. The propolis group's ($p = 0.14$), but not the placebo group's, change in tooth colour over time was statistically significant.[31]

Propolis extract, nanovitamin E, and nanovitamin C in gel formulation were tested for their effectiveness as adjuvants to mechanical debridement in the treatment of peri-implant mucositis (PM) in double-blind, randomised clinical trial. 46 patients were included in this trial, all of them had at least one implant containing PM. They were split into two groups: Group I received treatment with a gel containing 2% propolis extract, while Group II served as the control group without propolis gel. Both the test group and the control group, each with 23 participants, were instructed to use gel as toothpaste three times a day for a month.

According to the finding's, completely resolved PM was present in 0 patients in the control group and 26.1% of patients in the test group following therapy ($p = 0.02$; $p = 0.01$). Comparing the test group to the control groups, a significant decrease in probing depths ($p=0.27$), plaque index score ($p=0.03$), and bleeding on probing ($p=0.04$) was observed. Tannerella forsythia ($p=0.02$) and Porphyromonasgingivalis ($p =0.05$) levels significantly dropped from baseline to the 1-month follow-up in the test group in comparison to the control group. The test gel exhibits antimicrobial activity after a month and clinically improved PM, according to the findings.[32]

In a double-blind randomised controlled field study, the effects of manuka honey and raw honey mouthwash on GI and PI were assessed. A total of 135 schoolchildren were chosen for the study and split into three groups, each with 45 participants: Group I used manuka honey, Group II used raw honey, and Group III used chlorhexidine mouthwash (control). Throughout a 21-day period, participants were told to use 10 mL of honey mouthwash twice daily. Participants were examined at three different times: baseline, one day after stopping mouthwash, and one week afterwards.

In both test groups (mouthwash containing manuka and raw honey) and control group (mouthwash containing chlorhexidine), clinical parameters PI and GI score displayed significant decreases. The raw honey mouthwash group GI score dropped from 1.465±0.17 at baseline to 0.927± 0.26 on day 22. The GI score in the group using manuka honey mouthwash decreased from beginning (1.457±0.18) to day 22 (0.976±0.15). Chlorhexidine mouthwash group's score dropped frombaseline (1.452± 0.19) to 22nd day (0.498±0.5). The raw honey mouthwash group's PI score dropped from baseline 1.525±0.2 to the 22nd day (0.723±0.11). Manuka honey mouthwash scored lower from the baseline 1.525±0.2 to the 22nd day 0.72±0.12, while chlorhexidine mouthwash scored lower from baseline 1.505±0.23 to 22nd day 0.495±0.13. According tofindings honey-based mouthwash exhibits comparable antimicrobial effects on PI and GI scores to chlorhexidine mouthwash.[33]

Propolis and mangosteen extract (PME) was tested inrandomised controlled clinical trial for its immunological and clinical effectiveness against gingivitis and early periodontitis. Eighty patients with incipient periodontitis or gingivitis were chosen and randomly divided into two groupswith 41 and 39 participants in Group Itest (capsule with PME) and Group IIcontrol (same capsule without PME), respectively. Patients in control group were instructed to take same capsule without PME daily for 8 weeks, whereas patients in test group were instructed to take capsules containing 194 mg of PME.

The results revealedsignificant difference in modified GI between test and control groups at 4 and 8 weeks. A rise in salivary matrix metalloproteinase-9 and a decrease in IL-6 were also observed in test group results after eight weeks. After 4 weeks test group exceeded placebo group in terms of patient-reported outcomes as measured by Oral Health Impact Profile (OHIP)-14 surveys.[34]

Another randomised clinical experiment examinedantibacterial properties of propolis (in mouthwash and paste formulations) in individuals with periodontal disease following tooth extraction. For propolis paste trial 60 individuals were chosen and for propolis mouthwash study 40 patients. The mouthwash users were separated into four groups as well Group I used placebo mouthwash; Group II mouthwash with 0.2% chlorhexidine; Group IIImouthwash with 2% propolis; and Group IVmouthwash with 0.2% chlorhexidine plus 2% propolis. There were 10 individuals in each group. The propolis mouthwash assay's findings indicated decreased bacterial growth. Patients who used a mouthwash with 0.2% chlorhexidine and 2% propolis in particular showed less than 105 CFU.

According to the propolis paste assay results, 90% of periodontal sockets had fully healed after three days of surgery, in contrast to 13.4% for control paste. On basis of these findings, propolis paste was determined to be substitute for periodontal socket healing following dental extraction.[35]

In a single-blind randomised controlled studythe anti-inflammatory effects of polyherbal mouthwash including Salvia officinalis, Plantago lanceolata leaf extract, 1.75% essential oil, and propolis extract were assessed. 40 patients with moderate to severe periodontitis were chosen and split into two groups: Group I received phytoherbal mouthwash and Group II received placebo mouthwash. Twenty people were divided among the groups. For period of three monthscontrol group was directed to rinse with a placebo mouthwash whiletest group was instructed to usephytoherbal mouthwash.

At baseline and three months later outcomes of probing depth (PD), clinical attachment level, full month plaque score (FMPS)and full month bleeding score (FMBS) were recorded. From baseline to three months, the P.D. (CG p = 0.011, TG p = 0.001), FMPS (CG p = 0.003, TG p = 0.001), CAL (CG p = 0.020, TG p 0.001), and FMBS (CG p = 0.002, TG p = 0.001) scores decreasedsignificantly in both control group and test group.[36]

The effectiveness of propolis and herbs (an antioxidant-based mixture) as an adjuvant therapy to nonstandard periodontal treatment was investigated in randomised controlled clinical experiment. 40 patients were chosen for study and randomly assigned to test group or control group. Clinical parameter values were noted at baseline, one month and three months. Between two groupsthere was no apparent clinical difference ($p > 0.05$). Additionally, it has been stated that test group's findings outperformed those of placebo group in terms of reducing oxidative stress.[37]

Polish propolis and plant oils (toothpaste) were tested in randomised placebo-controlled research. 50 patients in all were chosen and divided into two groups at random Group Ithe test group, which used toothpaste with active components like menthol, rosemary oil, Polish propolis, and tea tree oil and Group IIcontrol group, which used toothpaste without active ingredients as a placebo. Each group received a total of 25 patients. Over 35 days patients were instructed to brush their teeth three times a day for three minutes with propolis toothpaste or a placebo toothpaste.

The findings indicate that gingival bleeding index (GBI) was significantly reduced for molars (p = 0.0017), incisors (p = 0.007) and overall GBI (p = 0.002) following use of propolis toothpaste in Group I (toothpaste with propolis and plant oils) for gingival conditions. (p = 0.011) The oral hygiene index (OHI) showed improvement. The results of study suggest propolis and plant oil toothpaste are useful in avoiding and managing oral infectious illnesses that develop during orthodontic treatment of oral clefts.[38]

The impact of propolis mouthwash treatment on GI and PI was assessed in patients receiving orthodontic treatment in a triple-blind parallel-group clinical experiment. In this study, 40 patients in total were chosen and randomly assigned to two groups: Group I, which received test substance (propolis aqueous extract), and Group IIreceived control substance (chlorhexidine mouthwash). After cleaning their teeth twice, a day for three weeks straight, both test and control group were instructed to use mouthwash.

Results for the GI, PI, and periodontal index were assessed at baseline and three weeks later. In the test group, there was a statistically significant difference between the periodontal index (p = 0.005), PI (p 0.001), and GI (p = 0.006) values. Significant differences were also seen in the periodontal index (p = 0.003), GI (p = 0.001), and PI (p <0.001) in the chlorhexidine group. According to the findings, propolis mouthwash is just as efficient as chlorhexidine mouthwash.[39]

Eight of the 11 selected clinical trials have been recently talked about were randomised trials, including four single randomised trials, three double-blinded randomised trials, one triple-blinded clinical trial, and three non-randomized clinical trials. In one clinical research, the effect of raw honey was examined in addition to the effect of propolis, which was the object of a majority of clinical studies. In one of the four double-blind randomised clinical studies, there was no discernible change in clinical attachment level, CI, or probing pocket depth between propolis ointment group and control group. Allthe clinical studies showed propolis and honey-based products, including toothpaste, gel, ointment, capsuleand mouthwash, extensively exceeded control groups in treatment of periodontal disease.

1.4 DISCUSSION

Treatment based on natural products is regarded as alternative or complementary in certain oral conditions. Indeed, products from the hive such as honey and propolis, are used to treat mucositis and other disorders of the oral mucosa.

The aim of this review was to determine the effectiveness of propolis and honey in treatment of periodontal disease. According to the findings propolis acts better than standardized treatments for certain therapeutic goals such as reducing dental plaque and microbial activity and stabilizing gingival and periodontal indices.

The Antimicrobial effect of propolis against periodontal pathogens has been studied in vitro. Shabbir et al proved effectiveness of 30% w/v concentration of ethanolic extract of propolis (EEP) against periodontal pathogens Prevotella melaninogenica, Porphyromonasgingivalis, Porphyromonasasaccharolyticaand Prevotella intermedia. And it is seen that zone of inhibition for P. melaninogenica's was 18.3 ± 0.64 mm, P. gingivalis 18.9 ± 0.05 mm, P. asaccharolytica's22.8 ± 0.28 mm, and P. intermedia's 22.8 ± 0.18 mm.[22] Yoshimasu and colleagues proved effectiveness of isolated propolis products such as artepillin C, baccharin and ursolic acid as antimicrobial compounds against Porphyromonasgingivalis; artepillin C and baccharin are bacteriostatics and ursolic acid is a powerful destructor of bacterial membrane, probably because of its highly lipophilic nature.[23]

Tambur and colleagues showedinhibitory effect of propolis againstperiodontopathogenic bacteria and propolis prevent growth of all oral carcinogens and periodontopathic bacteria at MIC concentration of 12.5g/ml.[24]

Nakao and colleagues reported significant improvements in Clinical Attachment Loss (CAL) and Probing Pocket Depth (PPD) alongside a trend towards a reduction of Porphyromonasgingivalis in gingival crevicular fluid (GCF) in patients treated with propolis solutions.[40] The study by singhal et al showed the effectiveness of Manuka honey and Raw honey mouthwash on Gingival Index and Plaque Index. Group of 135 students split into 3 groups, and the mouthwash containing Honey and Manuka honey showed reduction in GI and PI from baseline to 22nd day.[33]

Giammarinaro and colleagues studied the efficacy of propolis as compared with chlorhexidine in a sample of 40 patients suffering from gingivitis, and found no significant differences between the control and the experimental group in probing pocket depth (PPD), bleeding on probing (BOP) and plaque index (PI); however, the patients treated with propolis achieved better results in terms of oxidative stress markers in the saliva, with considerable improvement in their periodontal health.[37]

In a study by Park et al. to determine the effectiveness of a complex extract of mangosteen and propolis in treating gingivitis. For eight weeks, patients were instructed to take 194 mg PME (propolis and mangosteen extract) capsule daily. Modified GI is reduced throughout the course of 4 and 8 weeks. Salivary matrix metalloproteinase-9 is also increased, while IL-6 levels are decreased.[34]

On subjects with moderate to severe periodontitis, Sparabombe and colleagues evaluated the efficacy of a polyherbal mouthwash containing Salvia officinalis, Plantago lanceolata leaf extract, 1.75% essential oil, and propolis extract. The results of probing depth (PD), clinical attachment level (CAL), full month plaque score (FMPS), and full month bleeding score (FMBS) were noted. The P.D, FMPS, CAL, and FMBS scores considerably decreased from baseline to three months.[36]

In the present literature we found that sample size and evaluation period are constrained. In each study, a different number of participants were chosen. Most studies used small sample sizes and there was variation in the length of time used to evaluate each clinical trial, which ranged from one week to a few months. Propolis and honey are examples of bee products that have demonstrated good outcomes in the treatment of periodontal disease; nevertheless, there are currently not much clinical research and experimental data available to support the benefit of bee products. Propolis's antibacterial and antioxidant properties, however, are well known, but there are just a few randomised clinical trials available. Therefore, in future, it will be crucial to conductmore randomised clinical trials to compare use of bee products with control group.

1.5 CONCLUSION

Various bee products, such as propolis, royal jelly, and honey, have been scientifically demonstrated to have numerous applications in dentistry due to their antimicrobial, anti-inflammatory, anticancer, immune-modulating, and antioxidant properties. Propolis is thought to be the most effective bee product for treating periodontal disease, with a dosage range of 12-400 g/mL, according to clinical and scientific data. In the future, these bee products may serve as an alternative to synthetic medications for the treatment of periodontal disease; however, there is currently scanty clinical data supporting the use of bee products, particularly honey and royal jelly. Additionally, various results from in vitro, in vivo, and clinical trials have confirmed that propolis-based products, including toothpaste, mouthwash, gels, ointments, and gels, may be used to treat periodontitis because they exhibit antioxidant

and antibacterial activity. Based on this research, it can be said that using bee products to treat periodontitis is safer, economical, beneficial; nevertheless, additional clinical and experimental data is required to fully understand the bioactivities of bee products in treating periodontitis.

1.6 REFERENCE

1. Eley, B.M. Antibacterial agents in the control of supragingival plaque–a review. Br. Dent. J., 1999; 186: 286–296.
2. Kim, E.H.; Kim, S.; Kim, H.J.; Jeong, H.O.; Lee, J.; Jang, J.; Joo, J.Y.; Shin, Y.; Kang, J.; Park, A.K.; et al. Prediction of Chronic Periodontitis Severity Using Machine Learning Models Based on Salivary Bacterial Copy Number. Front. Cell. Infect. Microbiol, 2020; 10: 698.
3. Gabrys J, Konecki J, Krol W, Scheller S, Shani J. Free amino acids in bee hive product (propolis) as identified and quantified by gas-liquid chromatography. Pharmacological research communications, 1986; 18(6): 513-8.
4. Sanghani NN, Bm S, S S. Health from the hive: propolis as an adjuvant in the treatment of chronic periodontitis - a clinicomicrobiologic study. Journal of clinical and diagnostic research: JCDR, 2014; 8: ZC41-44.
5. Wagh, V.D. Propolis: A Wonder Bees Product and Its Pharmacological Potentials. Adv. Pharmacol. Sci., 2013; 2013: 11.
6. Toreti, V.C.; Sato, H.H.; Pastore, G.M.; Park, Y.K. Recent progress of propolis for its biological and chemical compositions and its botanical origin. Evid.-Based Complement. Altern. Med., 2013; 2013: 697390.
7. Anjum, S.I.; Ullah, A.; Khan, K.A.; Attaullah, M.; Khan, H.; Ali, H.; Bashir, M.A.; Tahir, M.; Ansari, M.J.; Ghramh, H.A.; et al. Composition and functional properties of propolis (bee glue): A review. Saudi J. Biol. Sci., 2019; 26: 1695–1703.
8. Da Silva Barboza, A.; Aitken-Saavedra, J.P.; Ferreira, M.L.; Fábio Aranha, A.M.; Lund, R.G. Are propolis extracts potential pharmacological agents in human oral health? -A scoping review and technology prospecting. J. Ethnopharmacol, 2021; 271: 113-846.
9. Elnakady, Y.A.; Rushdi, A.I.; Franke, R.; Abutaha, N.; Ebaid, H.; Baabbad, M.; Omar, M.O.M.; Al Ghamdi, A.A. Characteristics, chemical compositions and biological activities of propolis from Al-Bahah, Saudi Arabia. Sci. Rep., 2017; 7: 414-53.
10. Chemical compositions and biological activities of propolis from Al-Bahah, Saudi Arabia. Sci. Rep., 2017; 7: 414-53.

11. El Adham, E.K.; Hassan, A.I.; Dawoud, M.M.A. Evaluating the role of propolis and bee venom on the oxidative stress induced by gamma rays in rats. Sci. Rep., 2022; 12: 2656.
12. Sawicki, T.; Starowicz, M.; Kł ˛ebukowska, L.; Hanus, P. The Profile of Polyphenolic Compounds, Contents of Total Phenolics and Flavonoids, and Antioxidant and Antimicrobial Properties of Bee Products. Molecules, 2022; 27: 1301.
13. P. V. Rao, K. T. Krishnan, N. Salleh, and S. H. Gan, "Biological and therapeutic effects of honey produced by honey bees and stingless bees: a comparative review," *Revista Brasileira de Farmacognosia*, 2016; 26(5): 657–664.
14. F. Ferreres, C. García-Viguera, F. Tomás-Lorente, and F. A. Tomás-Barberán, "Hesperetin: a marker of the floral origin of citrus honey," *Journal of the Science of Food and Agriculture*, 1993; 61(1): 121–123.
15. M. Moniruzzaman, M. Khalil, S. Sulaiman, and S. Gan, "Advances in the analytical methods for determining the antioxidant properties of honey: a review," *African Journal of Traditional, Complementary and Alternative Medicines*, 2012; 9(1): 36–42.
16. C. Anyanechi and B. Saheeb, "Honey and wound dehiscence: a study of surgical wounds in the mandibular bed," *Nigerian Journal of Clinical Practice*, 2015; 18(2): 251–255.
17. S. Eick, G. Schäfer, J. Kwiecinski, J. Atrott, T. Henle, and W. Pfister, "Honey–a potential agent against Porphyromonasgingivalis: an in vitro study," *BMC Oral Health*, 2014; 14(1): 24.
18. D. S. Halim, E. S. Mahanani, R. Saini, M. Omar, N. RubianteebtIbrahi, and M. K. Alam, "A comparison study on the effectiveness of local honey and salicylate gel for treatment of minor recurrent aphtous stomatitis," *International Medical Journal*, 2013; 20(6): 770–772.
19. J. J. Song, P. Twumasi-Ankrah, and R. Salcido, "Systematic review and meta-analysis on the use of honey to protect from the effects of radiation-induced oral mucositis," *Advances in Skin & Wound Care*, 2012; 25(1): 23–28.
20. N. Sterer and M. Rosenberg, *Breath Odors: Origin, Diagnosis, and Management*, Springer Science & Business Media, 2011.
21. H. Shiga, A. Jo, K. Terao, M. Nakano, T. Oshima, and N. Maeda, "Decrease of halitosis by intake of Manuka honey," *General Session of IADR Barcelona*, 2010; 14.
22. Shabbir, A.; Rashid, M.; Tipu, H.N. Propolis, A Hope for the Future in Treating Resistant Periodontal Pathogens. Cureus, 2016; 8: e682.

23. Yoshimasu, Y.; Ikeda, T.; Sakai, N.; Yagi, A.; Hirayama, S.; Morinaga, Y.; Furukawa, S.; Nakao, R. Rapid Bactericidal Action of Propolis against Porphyromonasgingivalis. J. Dent. Res., 2018; 97: 928–936.
24. Tambur, Z.; Miljkovic-Selimovic, B.; Opacic, D.; Vukovic, B.; Malesevic, A.; Ivancajic, L.; Aleksic, E. Inhibitory effects of propolis and essential oils on oral bacteria. J. Infect. Dev. Ctries, 2021; 15: 1027–1031.
25. Mary George, R.; Kasliwal, A.V. Effectiveness of Propolis, Probiotics and Chlorhexidine on Streptococcus Mutans and Candida Albicans: An In-Vitro Study. IOSR J. Dent. Med. Sci., 2017; 16: 15–18.
26. Gómez, P.A.; Jon, L.Y.; Torres, D.J.; Amaranto, R.E.; Díaz, I.E.; Medina, C.A. Antibacterial, antibiofilm, and cytotoxic activities and chemical compositions of Peruvian propolis in an In vitro oral biofilm. F1000Research, 2021; 10: 1093.
27. Miranda, S.L.F.; Damasceno, J.T.; Faveri, M.; Figueiredo, L.; da Silva, H.D.; de Alencar Alencar, S.M.; Rosalen, P.L.; Feres, M.; Bueno-Silva, B. Brazilian red propolis reduces orange-complex periodontopathogens growing in multispecies biofilms. Biofouling, 2019; 35: 308–319.
28. De Figueiredo, K.A.; Da Silva, H.D.P.; Miranda, S.L.F.; Gonçalves, F.J.D.S.; de Sousa, A.P.; de Figueiredo, L.C.; Feres, M.; BuenoSilva, B. Brazilian Red Propolis Is as Effective as Amoxicillin in Controlling Red-Complex of Multispecies Subgingival Mature Biofilm In vitro. Antibiotics, 2020; 9: 432.
29. Stähli, A.; Schröter, H.; Bullitta, S.; Serralutzu, F.; Dore, A.; Nietzsche, S.; Milia, E.; Sculean, A.; Eick, S. In vitro Activity of Propolis on Oral Microorganisms and Biofilms. Antibiotics, 2021; 10: 1045.
30. Nakao, R.; Senpuku, H.; Ohnishi, M.; Takai, H.; Ogata, Y. Effect of topical administration of propolis in chronic periodontitis. Odontology, 2020; 108: 704–714.
31. Kiani, S.; Birang, R.; Jamshidian, N. Effect of Propolis mouthwash on clinical periodontal parameters in patients with gingivitis: A double-blinded randomized clinical trial. Int. J. Dent. Hyg, 2021; 2021: 1–19.
32. González-Serrano, J.; López-Pintor, R.M.; Serrano, J.; Torres, J.; Hernández, G.; Sanz, M. Short-term efficacy of a gel containing propolis extract, nanovitamin C and nanovitamin E on peri-implant mucositis: A double-blind, randomized, clinical trial. J. Periodontal Res., 2021; 56: 897–906.
33. Singhal, R.; Siddibhavi, M.; Sankeshwari, R.; Patil, P.; Jalihal, S.; Ankola, A. Effectiveness of three mouthwashes—Manuka honey, Raw honey, and Chlorhexidine on

plaque and gingival scores of 12–15-year-old school children: A randomized controlled field trial. J. Indian Soc. Periodontol, 2018; 22: 34.

34. Park, J.Y.; Ko, K.A.; Lee, J.Y.; Oh, J.W.; Lim, H.C.; Lee, D.W.; Choi, S.H.; Cha, J.K. Clinical and Immunological Efficacy of Mangosteen and Propolis Extracted Complex in Patients with Gingivitis: A Multi-Centered Randomized Controlled Clinical Trial. Nutrients, 2021; 13: 2604.
35. Lisbona-González, M.J.; Muñoz-Soto, E.; Lisbona-González, C.; Vallecillo-Rivas, M.; Diaz-Castro, J.; Moreno-Fernandez, J. Effect of Propolis Paste and Mouthwash Formulation on Healing after Teeth Extraction in Periodontal Disease. Plants, 2021; 10: 1603.
36. Sparabombe, S.; Monterubbianesi, R.; Tosco, V.; Orilisi, G.; Hosein, A.; Ferrante, L.; Putignano, A.; Orsini, G. Efficacy of an All-Natural Polyherbal Mouthwash in Patients with Periodontitis: A Single-Blind Randomized Controlled Trial. Front. Physiol, 2019; 10: 632.
37. Giammarinaro, E.; Marconcini, S.; Genovesi, A.; Poli, G.; Lorenzi, C.; Covani, U. Propolis as an adjuvant to non-surgical periodontal treatment: A clinical study with salivary antioxidant capacity assessment. Minerva Stomatol, 2018; 67: 183–188.
38. Machorowska-Pieni ˛azek, A.; Morawiec, T.; Olek, M.; Mertas, A.; Aebisher, D.; Bartusik-Aebisher, D.; Cie´slar, G.; Kawczyk-Krupka, ˙ A. Advantages of using toothpaste containing propolis and plant oils for gingivitis prevention and oral cavity hygiene in cleft lip/palate patients. Biomed. Pharmacother, 2021; 142: 111992.
39. Dehghani, M.; Abtahi, M.; Hasanzadeh, N.; Farahzad, Z.; Noori, M.; Noori, M. Effect of Propolis mouthwash on plaque and gingival indices over fixed orthodontic patients. J. Clin. Exp. Dent, 2019; 11: e244.