The role of polyphenols in controlling periodontal inflammation: a systematic review

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Abstract

Introduction. Recent research has explored the therapeutic potential of polyphenols, natural compounds with antioxidant, antimicrobial, and anti-inflammatory properties, in modulating host responses to periodontal disease. This systematic review examines the impact of various polyphenols—including ellagic acid (pomegranate), catechins (green tea), curcumin, resveratrol, propolis, and quercetin—on periodontal health.
Materials and methods. A bibliographic search was conducted using Medline-PubMed with the following keywords: "(GSE) AND (periodontitis)"; "(quercetin) AND (periodontitis)"; "(catechin) and (periodontal)"; "(punica granatum) and (periodontitis)"; "curcumin and periodontitis"; "ellagic acid and periodontitis"; "epigallocath and periodontitis"; "phenols and periodontitis"; "polyphenols and periodontitis"; "propolis and periodontitis"; "resveratrol and periodontitis." No timeline restrictions were applied.
Articles regarding Bleeding Index (BI), Bleeding Point Index (BPI), Gingival Bleeding Index (GBI), Modified Gingival Index (MGI), Oral Hygiene Index (OHI), Simplified Oral Hygiene Index (OHI-S), Plaque Control Record (PCR), Plaque Index (PLI), Relative Attachment Loss (RAL), Sulcus Bleeding Index (SBI), Tooth Mobility (TM), Visible Plaque Index (VPI) were included.
Microbiological parameters such as colony-forming units (CFUs) and microbial counts of S. mutans, P. gingivalis, T. forsythia, and T. denticola were also included.
Results. A total of 405 articles were identified following the conducted searches as described above. After the removal of duplicates, 399 articles were further examined based on their title and abstracts. Of these, 207 were excluded after title review. A total of 192 abstracts were then screened, and 147 were excluded. As a result, 45 full-text studies were assessed for eligibility. A total of 30 studies remained and were included in the final analysis. Of these 30 studies, 8 focused on ellagic acid or pomegranate (where the molecule of interest is ellagic acid), 8 examined catechins, 5 investigated curcumin, 5 were related to propolis, 2 explored resveratrol, and 1 study each addressed GSE (grape seed extract) and quercetin combined with apigenin and gallic acid.
Conclusions. Polyphenols present a viable adjunct or alternative to conventional

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periodontal treatments, offering benefits in both local and systemic inflammation management. Their incorporation into dietary and oral hygiene regimens could enhance periodontal health and overall patient well-being. Future research should focus on refining formulations, determining optimal dosages, and evaluating their long-term clinical effectiveness in personalized periodontal treatment strategies.

Keywords: Polyphenols, Periodontitis, Gingivitis, Inflammation.

Introduction

Periodontitis (along with gingivitis) is a periodontal disease, affecting the periodontium, the supporting structure of the tooth, which includes the root cementum, alveolar bone, periodontal ligament (PDL) (a ligament that fills the space between the alveolus and the tooth roots), and the gingiva. These diseases are characterized by an inflammatory process associated with bacterial activity and mediated by the host immune response. Bacterial activity constitutes an aggression to which the immune-inflammatory response reacts, potentially leading to the destruction of both soft and hard tissues, resulting in the loss of connective tissue attachment and, consequently, bone loss. This series of events is termed periodontitis. If left untreated, periodontitis will cause the progressive loss of dental anchorage within the bone, eventually leading to tooth loss. (1)

Clinical indices defining the stage of periodontal disease, in both gingivitis and periodontitis, include clinical attachment loss (CAL), which represents the destruction of PDL fibers; probing depth (PD or PPD), where an increase indicates the formation of a periodontal pocket; bleeding on probing (BOP), an index of inflammation; plaque index (PI), which provides a precise indication of oral bacterial contamination; and gingival recession (GR), which indicates a loss of attachment but not necessarily the presence of inflammation. The radiographic index for periodontitis is alveolar bone loss.

The bacterial species associated with periodontitis include Porphyromonas, Filifactor, Treponema, Fusobacterium, Tannerella, Streptococcus, Actinomyces, and Veillonella. Gingivitis, caused by bacterial colonization forming biofilm (plaque), is a reversible form of periodontal disease. It initially manifests as gingival inflammation (early lesion) and, if persistent, may lead to ulceration of the pocket epithelium (stabilized lesion). In predisposed individuals, gingivitis may progress to an irreversible form of the disease (advanced lesion), periodontitis, characterized by the loss of periodontal ligament and apical migration of the junctional epithelium (2,3).

The gingival epithelium is the gingival epithelial attachment located in the apical region of the sulcus, a shallow subgingival space surrounding the tooth. When this sulcus deepens due to increased probing depth (PD), it forms a periodontal pocket, an invagination in the space usually occupied by the periodontal ligament, resulting in the loosening of tooth anchorage (4).

Risk factors such as genetics, diabetes, smoking, and poor oral hygiene have been linked to susceptibility, prevalence, and severity of the disease due to their role in modulating the host immune-inflammatory response, which varies among individuals. The 2017 classification of periodontitis introduced a staging and grading system, where diabetes and smoking are considered grade modifiers. (5)

Diet and smoking are modifiable factors, classified as environmental rather than genetic factors. For effective and long-term periodontal disease treatment, a thorough assessment of these factors through a personalized approach is increasingly necessary. This approach helps manage not only the bacterial biofilm-related etiological factor but also the inflammatory component influenced by diet and smoking. This, in turn, improves both long-term treatment outcomes and the quality of patient care at both local and systemic levels.

Regarding nutrition, even without adopting a personalized approach, general recommendations can be followed based on studies examining the role of dietary exposure in the etiology and therapeutic management of periodontitis. Van der Velden (6) suggested that daily nutrition should include sufficient antioxidants, vitamin D, and calcium for periodontitis prevention and treatment. In terms of antioxidant management, inadequate antioxidant levels can be addressed through increased consumption of vegetables, berries, and fruits or by supplementing with phytochemicals.

Graziani, F. (7) assessed the antioxidant effects of phenolic compounds (belonging to the polyphenol family) and vitamin C contained in kiwifruit through the consumption of two kiwifruits per day. The study concluded that, while no additional effects on periodontal treatment outcomes were observed, dietary intake of kiwifruit reduced gingival inflammation in the absence of periodontal instrumentation or behavioral changes by the patient.

In the context of the inflammatory aspect of periodontitis, it is essential to note that periodontal tissue is continuously exposed to factors that contribute to local mucosal immune training. The oral microbiota and physical and chemical stimuli generated by mastication and respiration maintain a healthy state through a balance between immune surveillance and microbiota tolerance, avoiding excessive inflammatory responses. Colonization by key pathogens disrupts the microbiota balance, increasing pathogenicity and leading to tissue homeostasis disruption. Under these conditions, the immune response becomes hyperactivated, resulting in immune cell infiltration, osteoclastic activity activation, and soft and hard tissue destruction (8).

This article will explore the role of polyphenols, natural compounds with antioxidant, antimicrobial, and anti-inflammatory properties, in modulating host responses and preventing or mitigating periodontal disease. Polyphenols have been studied in both systemic (oral supplementation) and topical (gels, subgingival irrigations, mouthwashes, and toothpaste) applications, highlighting their potential as therapeutic agents in periodontal care.

Materials and Methods

A bibliographic search was conducted using Medline-PubMed with the following keywords: "(GSE) AND (periodontitis)"; "(quercetin) AND (periodontitis)"; "(catechin) and (periodontal)"; "(punica granatum) and (periodontitis)"; "curcumin and periodontitis"; "ellagic acid and periodontitis"; "epigallocath and periodontitis"; "phenols and periodontitis"; "polyphenols and periodontitis"; "propolis and periodontitis"; "resveratrol and periodontitis." Filters applied included: clinical study, clinical trial, controlled clinical trial, randomized controlled trial, and human studies. No timeline restrictions were applied.

A search was also conducted on Cochrane using the keywords "polyphenols and periodontitis." Additionally, relevant articles cited in other studies were included.

This systematic review includes studies investigating the association between polyphenols and periodontal status in a clinical, human-based context. Only studies that assessed periodontal status were included, using standard clinical parameters such as plaque index (PI), bleeding on probing (BOP), clinical attachment loss (CAL), probing depth (PD or PPD), and similar indices, including:

Bleeding Index (BI), Bleeding Point Index (BPI), Gingival Bleeding Index (GBI), Modified Gingival Index (MGI), Oral Hygiene Index (OHI), Simplified Oral Hygiene Index (OHI-S), Plaque Control Record (PCR), Plaque Index (PLI), Relative Attachment Loss (RAL), Sulcus Bleeding Index (SBI), Tooth Mobility (TM), Visible Plaque Index (VPI).

Additional oxidative and inflammatory markers considered include total antioxidants (TAO), total antioxidant capacity (TAOC), macrophage inflammatory protein 1-alpha (MIP-1α), procalcitonin (PCT), C-reactive protein (CRP), chemokine ligand 28 (CCCL28), glutathione peroxidase (GPx), glutathione transferase activity (GST), malondialdehyde (MDA), interleukin 1-beta (IL-1β), interleukin 6 (IL-6), interleukin 8 (IL-8), interleukin 10 (IL-10), interleukin 12 p40 (IL-12 p40), tumor necrosis factor-alpha (TNF-α), interferon gamma (IFN-γ), matrix metalloproteinase 8 (MMP-8), and prostaglandin E2 (PGE2).

Microbiological parameters such as colony-forming units (CFUs) and microbial counts of S. mutans, P. gingivalis, T. forsythia, and T. denticola were also included. Studies including patients who had received periodontal treatment within six months before the study, those on antibiotics or anti-inflammatory agents in the last three months, immunocompromised individuals, pregnant or lactating women, and smokers or alcoholics were excluded. Additionally, duplicate studies, abstracts without full texts, or studies without relevant data tables were excluded.

Results

Following the conducted searches as described above, 405 articles were identified. The selection process of the research results is illustrated in Fig. 1. After the removal of duplicates, 399 articles were further examined based on their title and abstracts. Of these, 207 were excluded after title review. A total of 192 abstracts were then screened, and 147 were excluded based on exclusion criteria that were not entirely detectable from the title (e.g., studies focusing on plants whose studied compounds were not polyphenolic).

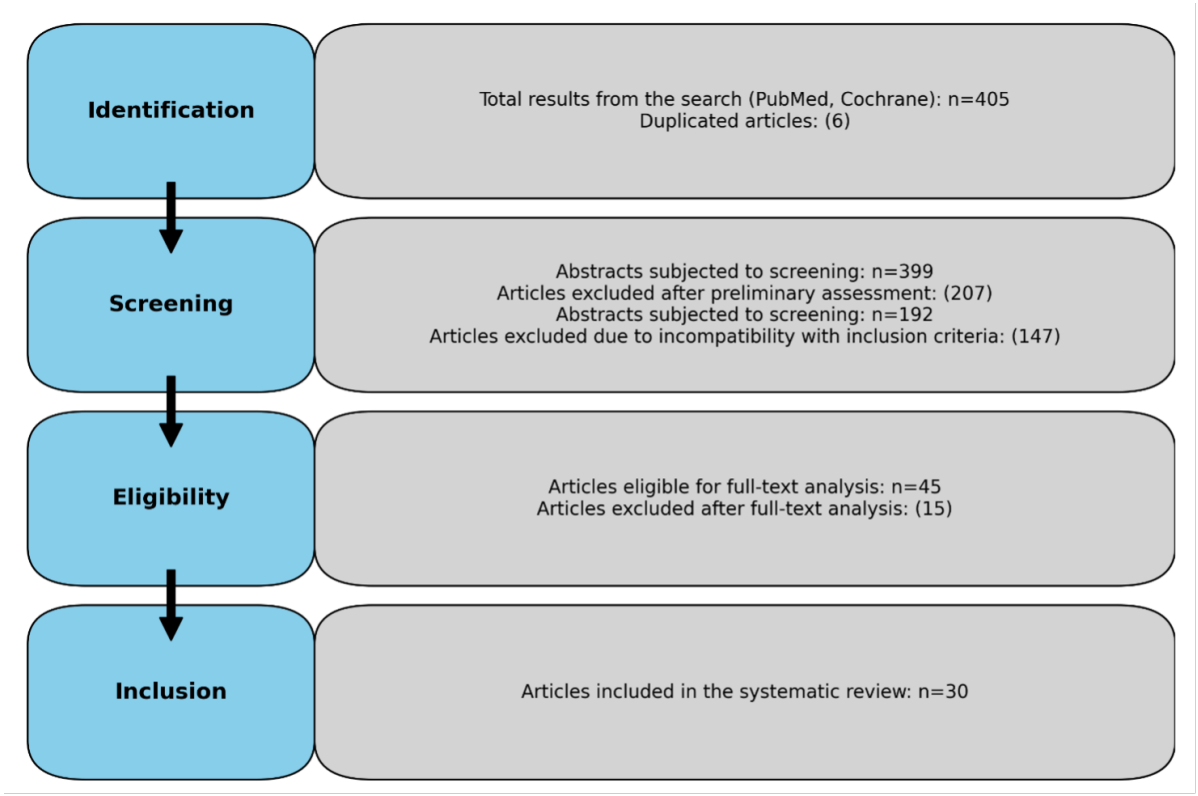

Figure 1 - PRISMA flow chart.

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Table 1. List of the included papers. Legend: API: Approximal Plaque Index; BI: Bleeding Index; BOP: Bleeding on Probing; BPI: Capillary Bleeding Index; BPR: Gram-negative anaerobic rods; CAL: Clinical Attachment Level; CRP: C-reactive protein; CCCL28: Chemokine Ligand 28; CFUs: Colony-Forming Units; CHX: Chlorhexidine; GBI: Gingival Bleeding Index; GI: Gingival Index; GPx: Glutathione Peroxidase; GST: Glutathione S-transferase Activity; MDA: Malondialdehyde; MDZ: Metronidazole; MGI: Modified Gingival Index; MIP-1α: Macrophage Inflammatory Protein 1 Alpha; NST: Non-Surgical Periodontal Therapy; NSPT: Non-Surgical Periodontal Therapy; OHI: Oral Hygiene Index; OHI-S: Simplified Oral Hygiene Index; ORD: Ornidazole; ORN: Ornidazole; PCR: Plaque Control Record; PCT: Procalcitonin; PD: Probing Depth; PI: Plaque Index; PLI: Plaque Index; PPD: Probing Pocket Depth; RAL: Relative Attachment Loss; RCT: Randomized Controlled Trial; RT: Root Planing; SBI: Sulcus Bleeding Index; SRP: Scaling and Root Planing (Non-Surgical Periodontal Therapy); TAO: Total Antioxidants; TAOC: Total Antioxidant Capacity; TM: Tooth Mobility; VPI: Visible Plaque Index; IL-1β (IL1β): Interleukin 1 Beta; IL-6: Interleukin 6; IL-8: Interleukin 8; IL-10: Interleukin 10; IL-12 (IL-12 p40): Interleukin 12; TNF-α: Tumor Necrosis Factor Alpha; IFN-γ: Interferon Gamma; MMP-8: Matrix Metalloproteinase 8; MMP-9: Matrix Metalloproteinase 9; PGE2: Prostaglandin E2.

Author (year)	Journal	Cohort	Indexes	Intervention	Study type	Results
Nikniaz, S., et al. (2023) (9)	Bmc oral health	40 (20+20) chronic periodontitis (II and IV°)	CAL, PD, PI, BI, IL-8 e IL-1β	Scaling e root planing + resveratrol 480mg vs placebo for 4 weeks	RCT, double blinded	Significant difference only for PI, with better results in the resveratrol group. A significant but similar reduction in BI, CAL, PD, and IL-1 in both groups.
Zhang, Q., et al. (2022) (10)	Medicine	160 (40+40+40+40) with periodontitis	CAL, BI, PPD, OHI, TNF-α, MIP-1α, fibrinogen, IL-2, CRP, INF-γ, IL-1β, IL-8, IL-10, IL-12p40	Resveratrol 500mg, 250mg, 125mg vs placebo for 8 week	RCT	Significant differences among all resveratrol and placebo groups for CAL, BI, OHI-S, and PPD. Reduction in systemic and local inflammatory markers, including TNF-α, MIP-1α, fibrinogen, IL-2, CRP, INF-γ, IL-1β, IL-8, IL-10, IL-12p40, and systemic endotoxin. Significant differences between resveratrol 500 mg and 250 mg compared to resveratrol 125 mg, but no significant difference between resveratrol 500 mg and resveratrol 250 mg.
Chava, V. K.; Vedula, B., D. (2013) (11)	J Periodontol	30 subjects (30 + 30 siti) with chronic periodontitis (PD 4-6mm)	GI, PD, CAL	97% green tea catechin gel, thermoreversible, applied in the periodontal pocket for 4 weeks vs. placebo gel.	Split mouth double blinded RCT	Statistically significant reduction in GI, PD, and CAL in both groups; better results in the test group with a significant difference between the two groups.
Wang, Y., et al. (2021) (12)	BMC Oral Health	18 Chronic periodontitis (PD≥4), II or III stadium, grade B	PD, CAL. Bacterial analysis of the red complex, P. gingivalis, T. forsythia, T. denticola	Aqueous solution of 5 mg/mL EGCG used as a coolant through a new-type ultrasonic scaler tip, in addition to SRP, vs. SRP alone. Evaluation at 3 and 6 months.	split-mouth RCT	CAL and PD were highly statistically significant in both groups at three months, but a statistically significant difference between the two groups was observed only at six months in favor of the EGCG group. A statistically significant difference was found only for the pathogen *T. forsythia* at six months.
Zeng, J., et al. (2022) (13)	Trials	15 moderate/ severe periodonditis	PPD, CAL, BI, GI and PI	Aqueous solution of (-)-epigallocatechin gallate (EGCG 5 mg/mL) used as an irrigant instead of water during scaling and root planing. Evaluation at 6 and 12 weeks.	split-mouth RCT	At the 6th and 12th weeks, PPD, CAL, PLI, and GI significantly decreased in both groups compared to baseline ($p < 0.001$). However, no statistical differences were observed between the groups at any time point. A significant improvement in BI was noted at 12 weeks ($p < 0.05$).

To be continued

Kerdar, T., et al. (2019) (14)	J Ethnopharmacol	50 (25+25) with chronic periodontitis	BOP, PI, PD, Streptococcus mutans	"Striata" mouthwash, standardized with gallic acid, quercetin, and apigenin, vs. "Iraha" mouthwash (Iranian Listerine) for 2 weeks + 2 weeks.	RCT	Significant differences in PI, BOP, and PD at the first follow-up ($p < 0.001$). No significant differences at the second follow-up. The number of S. mutans changed significantly in the long term ($p < 0.001$).
Nafade, S., et al. (2022) (15)	Journal of Herbmed Pharmacology	60 (30+30) with mild to moderate chronic periodontitis	GI, PI, PD, CAL, BOP, CFUs, GPx, TAO, MDA	NSPT + two cups of oolong tea per day (4 g of tea) for 3 months, swished in the mouth for one minute before swallowing. Evaluation at 1 and 3 months.	RCT	In both groups, at both 1 month and 3 months, GI, PI, BOP, GPx, and TAO significantly improved. Serum and crevicular MDA were reduced in both groups ($*p* < 0.05$).
Abdel-Fatah, R., et al. (2023) (16)	BMC Oral Health	54: 18 healthy + 36 with peridontitis stadium II, grade A (18+18)	PI, GI, PPD, CAL, procalcitonin (PCT)	ABT + instructions + application of 2% curcumin gel for 6 weeks in Group III. ABT + instructions only in Group II. Group I = Healthy group.	RCT	Group III showed greater improvement in PI, PD, and CAL compared to Group II ($*p* \leq 0.05$). A statistically significant decrease in PCT levels was observed in both Group II and Group III ($*p* \leq 0.05$).
Pérez-Pacheco, C. G., et al. (2021) (17)	Clin Oral Investig	16 with periodontitis stadium II, grade A (PPD ≥ 5)	PPD, CAL, BOP, IL-6 and TNF-α, bacterial count	Single local application of 0.05 mg/mL curcumin in nanoparticle gel vs. control.	Double blinded split mouth RCT	No statistically significant differences between the test group and the control group despite improvements in all indices.
Pulikkotil, S., J.; Nath, S. (2015) (18)	Australian dental journal	56 participants (19+19+18) with induced gingivitis (initially good periodontal health and no teeth with PD > 3 mm).	MGI, PI, BOP, PD; IL-1β, CCL28	Curcumin gel vs. CHX gel vs. CHX+MDZ gel in artificially induced gingivitis, applied twice daily for 10 minutes. Evaluation at 29 and 60 days (29 days for IL-1β, CCL28).	double blinded RCT	At 29 days, the curcumin and CHX+MDZ groups showed lower IL-1β and CCL28 levels compared to the CHX group, with a slight superiority of the curcumin group. A significant increase in MGI, PI, and BOP was observed at 29 days in all groups, with lower BOP scores in the curcumin group.
Hrishi, T. S., et al. (2016) (19)	International journal of dental hygiene	30 participants (15 + 15) with at least 6 sites having PD > 4 mm and CAL of 1-2 mm or 3-4 mm.	GI, PI, PPD, BOP, CAL; TAOC, GST	SRT + toothpaste containing 60–90% epigallocatechin-3-gallate (EGCG) vs. toothpaste containing triclosan, to be used with the modified Bass technique (2–5 minutes, twice daily). Abstention from interdental aids. Evaluation at 1 month.	RCT pilot study	Statistically significant improvements in PD, CAL, PI, BOP, and TAOC in both groups ($*p* < 0.001$). Better results in the test group for GI, BOP, CAL, and TAOC, with a significant difference between the groups. GST improved only in the test group, with a statistically significant difference.
Nóbrega, D., et al. (2015) (20)	Pesquisa Brasileira em Odontopediatria e Clínica Integrada	35 (19+16) with OHI-S ≥ 1,6	PI, BPI, *streptococcus* spp	Rinses with hydroalcoholic pomegranate extract mouthwash (6.25%) vs. 0.12% CHX mouthwash, twice daily for one minute. Evaluation at 7 and 14 days (streptococci assessed at 14 days).	double blinded RCT	Improvements in both groups, but statistically significant only for the CHX group.

To be continued

Salgado, A. D. Y., et al. (2006) (21)	Journal of Applied Oral Science	23 participants (4 teeth in the lower left quadrant per subject).	VPI, GBI	Initial phase with polishing and flossing + 30-day pause, followed by a one-minute application of 10% pomegranate gel vs. placebo gel with a dental shield for 21 days + polishing + another 30-day pause + another 21-day application. Brushing allowed only for non-test teeth, using the same toothpaste for both groups.	double blinded RCT	Ineffectiveness in preventing supragingival plaque formation and gingivitis development in both groups.
Mohammed, C., et al. (2017) (22)	Sulaimani Dental Journal	60 (15+15+15 with moderate gengivitis+15 healthy)	PLI, GI, BOP, IL-1β	Rinses for one minute with a single dose of 0.12% CHX mouthwash vs. a single dose of hydroalcoholic pomegranate extract mouthwash vs. two consecutive doses of pomegranate extract mouthwash vs. no mouthwash use (healthy group for salivary IL-1β control). Evaluation at 3 and 7 days post-rinse.	RCT	A significant reduction in PLI, BOP, and GI was observed in the double-rinse pomegranate mouthwash group after 3 and 7 days (*p* ≤ 0.05), but with no significant differences compared to the chlorhexidine group (*p* > 0.05). This group also showed a significant reduction in interleukin-1β, starting one day after rinsing and continuing for three days (*p* ≤ 0.05).
Waghmare, P. F., et al. (2011) (23)	The journal of contemporary dental practice	100 participants (50+50) with fair to poor gingival index scores and a plaque index score >1.	PI, GI, total microbial count	CHX mouthwash vs. mouthwash with 10 mg of curcumin, used after brushing for 14–21 days.	double blinded RCT	A statistically significant reduction in PI and GI was observed in both groups at 14 and 21 days, but with greater efficacy in the CHX group for PI. No differences were found for GI and microbial count.
Prakash, J., et al. (2017) (24)	Journal of clinical and diagnostic research	76 participants (18+19+19+20) with good periodontal health and no teeth with PD >3 mm, but with GI and PI ≥1.95.	IL-1β, IL-8 e CCL28 from GCF at 14 days. GI, PI, BOP, PD	Complete oral prophylaxis + 10% pomegranate extract gel vs. 1% CHX gel (*w/w*) vs. CHX + ORN gel (10 mg + 0.25% *w/w*) vs. placebo. Application (massage + dental shield) with abstention from routine oral hygiene procedures for 14, 30, and 60 days. Baseline starts on the seventh day after complete oral prophylaxis. ABT on the 14th day. Evaluation at 14 and 60 days.	RCT	The pomegranate gel group showed lower inflammation (reduced IL-1β, IL-8, and CCL28 levels) and lower GI and BOP compared to the other three groups at 14 days. It was equally effective against PI as the ornidazole gel.
Marya, C. M., et al. (2022) (25)	Journal of Indian Association of Public Health Dentistry	50 (25+25) with generalized chronic periodontitis	GI, PI	Rinses twice daily for 30 seconds with 0.05% pomegranate mouthwash vs. 0.2% CHX mouthwash for 7, 14, and 21 days.	triple blinded RCT	A statistically significant reduction in both groups at 21 days for both GI and PI. GI was slightly lower in the pomegranate mouthwash group, but there was no statistically significant difference between the two groups.

To be continued

Tyagi, P., et al. (2021) (26)	J Indian Soc Periodontal	30 (10+10+10) with chronic periodontitis (PD ≥4 at least in 3 sites)	PI, GI, PD, RAL	Scaling + root planing (SRP) + subgingival chips vs. pomegranate extract vs. pomegranate gel vs. placebo. Evaluation at 21 and 45 days.	RCT	A statistically significant reduction in GI was observed in all groups at 45 days and at 21 days for the chips and control groups, but no differences between groups. PI improved at 21 days in the chips group and at 45 days in the gel group, but with no significant differences. A statistically significant reduction in PD was observed in all groups at both 21 and 45 days, but without differences between groups. RAL reduction was observed in all groups at 21 days and was statistically significant both intra- and inter-group in the chips and gel groups at 45 days.
Batista, A.,L., et al. (2014) (27)	Complementary therapies in clinical practice	55 (18+19+18)	GBI	Instructions + SRP followed by 1-minute rinses with pomegranate mouthwash vs. chamomile mouthwash vs. CHX mouthwash for 15 days.	double blinded RCT	A statistically significant reduction was observed in all groups (*p* < 0.001), with the best results in the CHX group.
Andhare, M., G., et al. (2024) (28)	International journal of dental hygiene	60 (15+15+15+15) with induced generalized gengivitis	PI, GI, SBI	Scaling and root planing (SRP) followed by 1-minute rinses with green tea mouthwash (0.5% catechins) vs. CHX mouthwash (0.2%) vs. aloe vera mouthwash vs. control group (SRP only), evaluated at 14 and 21 days.	double blinded RCT	A statistically significant reduction in PI, GI, and SBI was observed in all groups at 14 and 21 days. The best results were seen with CHX mouthwash and green tea mouthwash (at day 21).
Rattanasuwan, K., et al. (2016) (29)	Odontology	42 (23+19) with PD 5/10 mm	GI, BOP, CAL, PPD	Intrasulcular application of green tea gel (80% catechins) on sites with PPD 5–10 mm vs. placebo, following ABT and SRP on days 1, 7, and 14. Evaluation at 1, 3, and 6 months from the second ABT and SRP.	RCT	A significant reduction (*p* < 0.001) in GI, CAL, and PPD was observed in the test group at the 1st and 3rd months, but without a statistically significant difference between the groups.
Hirasawa, M. et al. (2002) (30)	Journal of periodontal research	6 (3+3) with advanced periodontitis	MIC vs black stained BPR; PD	Strips with green tea (80% catechins) after scaling and root planing (SRP) in a 5 mm pocket vs. placebo gel in another 5 mm pocket vs. placebo gel in a group without SRP, for 8 weeks.	RCT pilot study	A statistically significant reduction in PD (*p* < 0.05) and BPR (*p* < 0.01) was observed only in sites treated with scaling and root planing (SRP) followed by gel application. A statistically significant difference was also found between this group and the placebo group that received SRP.
Anitha, V., et al. (2015) (31)	Indian journal of dental research	30 (30 + 30 sites) with chronic periodontitis (4-6 mm PPD)	CAL, PPD, CFU	SRP + 1% subgingival curcumin vs. SRP + subgingival CHX, both administered via resorbable collagen sponge, for 15 + 15 days.	blinded split-mouth RCT	A significant reduction in all parameters was observed, with greater improvement in the curcumin group (*p* < 0.05) at both 15 and 30 days. A statistically significant difference in CFU reduction between the two groups was noted at 30 days, with better results in the curcumin group (*p* = 0.001).

To be continued

Jung, J. S., et al. (2024) (32)	Nutrients	94(46+48) with incipient gengivitis and periodontitis	GI, BOP, PD, GR, CAL, PI. PGE2, IL-1ß, MMP-8, MMP-9	Daily intake of 388 mg of a mangosteen and propolis compound in a 2:68 ratio (mangosteen-propolis) vs. placebo for 4+4 weeks.	Double blinded RCT	A significant reduction in all measured GCF biomarkers was observed in the test group compared to the placebo group (*p* < 0.0001) at 8 weeks. Both groups showed a trend toward improvement, but intergroup differences were not statistically significant.
Nakao, R., et al. (2020) (33)	Odontology	24 (6+6+5+6) with chronic periodontits	PCR, TM, CAL + Microbial evaluation	Placebo ointment vs. ethanol-extracted propolis ointment (0.01 mg/mL) vs. water-extracted curry leaf ointment (1 mg/mL) vs. 2% minocycline hydrochloride ointment. Administered three times within one month.	Double blinded RCT	A statistically significant improvement in PPD and CAL (*p* < 0.05) and a reduction in *P. gingivalis* were observed in the propolis group.
Park, J. Y., et al. (2021) (34)	Nutrients	80 (41+39) with incipient gengivitis and periodontitis	PD, CAL, BOP, GR, MGI, PI, IL-6, IL-1β, MMP-8, MMP-9	Mangosteen and propolis compound (194 mg capsule) for 4+4 weeks vs. placebo.	Double blinded RCT	A statistically significant reduction in MGI was observed in both groups at 4 and 8 weeks, with a greater reduction in the test group. A non-statistically significant reduction in PD, CAL, PI, BOP, GR, IL-6, and MMP-8 was noted at 8 weeks in the test group. No significant differences between the groups.
Sahu, S. A., et al. (2023) (35)	Biomolecules	40 (20+20) with II or III statdium with at least PD 4-6 mm	GI, BOP, PPD, RAL	SRP + subgingival saline solution vs. SRP + subgingival nanoparticle solution. Evaluation at 1 and 3 months.	Double blinded RCT	A statistically significant reduction in GI, BOP, PPD, and RAL was observed at 3 months (for GI also at 1 month) in the test group and between the two groups. PI improved in the test group only at 3 months.
Kiani, S., et al. (2022) (36)	International journal of dental hygiene	32 (16+16) with gengivitis	BPI, PI	Rinses for one minute, twice daily, with propolis extract mouthwash vs. placebo mouthwash for one month.	Double blinded RCT	A higher number of plaque-free teeth was observed in the propolis group at 2 weeks. No significant differences in PI between the two groups at 2 and 4 weeks. A statistically significant reduction in BPI was observed in the propolis group (*p* < 0.001) and between groups at both 2 and 4 weeks.
Rayyan, M., et al. (2018) (37)	Journal of investigative and clinical dentistry	86 (38+48) sites from 5 subjects with at least PD >4	PD, GI, PI, BOP	SRP + four doses of mucoadhesive gel with 2% grape seed extract (GSE) vs. placebo gel, with repeated applications on the 3rd, 6th, and 9th days. Evaluation at 4 weeks and 6 months from the first application.	RCT	A significant reduction in all indices was observed between the two groups at 6 months of gel application (*p* < 0.05). A significant difference (*p* < 0.05) was found only in the reduction of GI and PI in the GSE group. No significant improvements in BOP were observed in either the control or GSE group. At 6 months, a more pronounced improvement in GI and PI was noted in the GSE group.
Eltay, E. G., et al. (2021) (38)	Complementary therapies in clinical practice	32 (15+17) with chronic periodontitis	PI, GI, IL-1β	NST + pulsating jet irrigation with 5% pomegranate peel extract solution vs. NST + irrigation with placebo. Irrigation repeated on the 7th and 15th days. Evaluation at 15 and 30 days (IL-1β assessed at 30 days).	Double blinded RCT	All indices showed a statistically significant difference compared to baseline in both groups.

As a result, 45 full-text studies were assessed for eligibility. A total of 30 studies remained and were included in the final analysis (9-38). Of these 30 studies, 8 focused on ellagic acid or pomegranate (where the molecule of interest is ellagic acid), 8 examined catechins, 5 investigated curcumin, 5 were related to propolis, 2 explored resveratrol, and 1 study each addressed GSE (grape seed extract) and quercetin combined with apigenin and gallic acid (Table 1).

Discussion

Regarding pomegranate and its main molecule, ellagic acid, as well as tannins, authors generally agree that pomegranate appears to be more effective in reducing gingival inflammation than in reducing plaque index. Gingival inflammation indices show greater improvements compared to plaque indices, with notable enhancements also observed at the level of interleukins (IL-beta and IL-8) and CCL28. In the study by Batista (27), a statistically significant improvement in GBI was observed in the pomegranate group, although the improvement was lower than in the CHX group. However, the intergroup difference favoring CHX was not statistically significant. Both 0.12% chlorhexidine, chamomile, and pomegranate proved effective, showing statistically significant and similar results ($p < 0.001$), suggesting that any of these three substances may be used to control gingival bleeding in periodontal disease. The conclusions indicate that, given the results on anti-inflammatory and antimicrobial activities (with improvements in PI but not statistically significant), it is sometimes possible to replace 0.12% chlorhexidine solution with tested herbal products or use them alternatively to control gingival bleeding in periodontal disease. As mentioned, there were improvements in PI, but they were less evident than those in gingival inflammatory indices.

In addition to Batista's study, Prakash, J. (24) also suggested that the anti-plaque efficacy of pomegranate gel, comparable to that of ornidazole gel, supports the replacement of synthetic agents with non-invasive natural extracts, such as pomegranate extracts. However, it was noted that the study was based on an experimental gingivitis model, which may not be entirely comparable to natural gingivitis, and a crossover design might be more suitable to avoid host-response biases.

In Eltay, (38), both the pomegranate irrigation group and the placebo irrigation group showed a progressive reduction in the mean periodontal indices (PI and GI). However, the study itself specified that such reduction might be attributed to behavioral modifications by subjects due to their participation in an experiment. Literature has reported studies indicating that even oral irrigation with water, compared to chlorhexidine, may modulate pro-inflammatory mediators such as IL-1β and PGE2 in patients with aggressive periodontitis, aligning with Eltay's findings. Notably, the study emphasized patient compliance: the introduction of plant extracts into oral and periodontal treatment might improve adherence to treatment.

In Marya, C. M. (25), it was reported that pomegranate extract mouthwash improves gingival status due to its significant hemostatic action, along with a moderate reduction in plaque scores.

Mohammed, C. (22) found unimpressive results on PLI despite some improvements. Similarly, no significant effects on VPI and PI were observed in studies by Salgado (21) and Nóbrega (20), the only studies reporting inefficacy in gingival inflammation indices. In the former study, a limitation may have been the lack of antimicrobial effects from saliva due to the application of the gel with a dental shield. The study also referenced in vitro research showing anti-Streptococcus effects and in vivo studies (without a control group) demonstrating significant reductions in gingivitis among patients using pomegranate extract toothpaste. In the latter study, while the pomegranate-based mouthwash was ineffective in controlling dental biofilm and gingival inflammation, it was effective in reducing oral streptococcus counts (though CHX showed a more significant reduction). The study also referenced in vitro research on the antimicrobial effects of pomegranate against various Streptococcus species as well as Aggregatibacter actinomycetemcomitans, Porphyromonas gingivalis, and Prevotella, likely due to its tannin content.

Notably, the authors highlighted that bacterial susceptibility to chemical agents can change when microbial action combines with the ability to penetrate live and well-organized microbial communities, such as dental biofilms. This property influences the in vivo action of an agent. However, two drawbacks were noted: this and other studies only considered the presence or absence of bleeding on probing without evaluating other inflammatory indices, such as edema, gingival contour changes, and, indirectly, tissue attachment loss. Additionally, the sample consisted of children aged 9 to 12, who may have lacked compliance at home (despite parental or guardian supervision), potentially influencing the mouthwash results.

Improvements in PD and RAL were discussed in the only two studies that included these indices. Tyagi, (26) analyzed differences between pomegranate gel and chip vs. placebo. Along with significant GI improvements and non-significant PI changes, relative attachment levels showed significance on day 21 between the chip and gel groups, and between the chip and control groups at 45 days. This led to the conclusion that pomegranate extracts in chip and gel forms may offer additional benefits in calculus removal and root planing for periodontal pocket treatment. In Prakash (24), PD was evaluated and remained largely unchanged across all intervals in all groups.

The potential of pomegranate, highlighted in studies emphasizing its anti-inflammatory and, to a lesser extent, anti-plaque properties, alongside studies where results were less pronounced, should be considered alongside study limitations (e.g., age). Further research is necessary to determine the translational effectiveness of pomegranate in professional and home oral hygiene practices. The goal is to assess its potential advantages over CHX, the chemical plaque control prototype, since all studies agree on its lack of adverse effects and, consequently, its potential long-term use as a natural substance.

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Regarding catechins, particularly epigallocatechin gallate (EGCG), the eight reviewed studies generally demonstrated significantly improved results, with frequent statistically significant intra-group and inter-group differences. The examined indices included standard clinical periodontal indices as well as red complex analysis, P. gingivalis, T. forsythia, T. denticola, and colony-forming units (CFUs). Additionally, oxidative stress markers such as GPx, TAO, MDA, TAOC, and GST were evaluated.

The study with the most promising results was conducted by Chava (11), where the application of 97% thermo-reversible green tea catechin gel in periodontal pockets for four weeks versus a placebo gel led to statistically significant reductions in GI, PD, and CAL in both groups, with superior outcomes in the test group. This confirms the potential of catechins in reducing pocket depth and inflammation. The observed effects may be attributed not only to pre-treatment scaling but also to EGCG's anti-inflammatory properties. This molecule inhibits enzymes such as lipoxygenases and cyclooxygenases, which are responsible for the production of prostaglandin E2, a potent inflammatory cytokine and bone resorption stimulator. Additionally, catechins inhibit the virulence factors of Prevotella intermedia and demonstrate the unique ability of green tea to be absorbed into epithelial cells within the subgingival pocket, preventing the growth of BPR, as reported by Hirasawa (30). The latter study highlighted statistically significant properties against BPR and in reducing PD.

In the study by Andhare (28), 0.5% catechin mouthwash was considered equivalent to 0.2% CHX, exhibiting both anti-plaque and anti-inflammatory properties attributed to its inhibition of collagenase (an enzyme responsible for gingival tissue degradation), P. gingivalis protease, and tyrosine phosphatase in Prevotella intermedia. Thus, green tea catechins may be considered a potent alternative to CHX for the prevention and treatment of gingival diseases. Less pronounced results were observed in the study by Rattanasuwan (29), which involved a single application of green tea gel to sites with PPD of 5-10 mm following scaling and root planing. While significant improvements were noted in all indices (GI, BOP, CAL), no statistically significant differences were detected between groups. Nonetheless, the study suggests that green tea gel may provide additional benefits in reducing gingival bleeding and inflammation when used as an adjunct to non-surgical periodontal therapy. The study also emphasizes the negative consequences of CHX on protein synthesis and tissue regeneration, highlighting the advantages of green tea gel due to its ease of application at the base of periodontal pockets and its fluid nature. This consistency allows it to solidify within the pocket and exert prolonged effects. However, since only a small number of deep-pocket sites were included in both the test and control groups, the potential benefits of green tea might have been masked by the effectiveness of scaling and root planing in shallower sites.

Positive findings were also reported in the study by Zeng (13), which suggested some benefits of EGCG in chronic periodontitis. However, further research is required due to study limitations, including a short observation period, low EGCG concentration, suboptimal delivery methods, and a limited number of clinical trials in this area. Similarly, Wang (12) explored the anti-inflammatory effects of EGCG on periodontal tissues, highlighting that a novel scaler used in the study facilitated deeper drug penetration into periodontal pockets, potentially promoting epithelial attachment formation. Statistically significant improvements in PD and CAL reinforce the need for multicentric studies with larger sample sizes.

An interesting perspective was provided by Nafade (15), who reported the antioxidant, anti-inflammatory, and antimicrobial effects of oolong tea (which also contains catechins), consumed as a mouth-rinsing beverage following an initial non-surgical periodontal therapy (NSPT) for three months. The study observed reductions in both local and systemic oxidative stress and inflammation, as evidenced by decreased GPx, TAO, and MDA levels. These findings are crucial for managing chronic periodontitis patients with systemic conditions, as local treatments can mitigate systemic oxidative stress and inflammatory burden. The authors emphasized that NSPT provides benefits in this regard, and dietary interventions rich in polyphenols may further enhance outcomes.

The use of green tea toothpaste was investigated by Hrishi (19), demonstrating statistically significant improvements superior to those achieved with a triclosan-containing toothpaste in GI, BOP, CAL, TAOC, and GST at four weeks, both intra- and inter-group. The study affirms the potential of green tea toothpaste as an adjunct to SRP during active and healing phases of periodontal therapy, enhancing clinical outcomes. While the study's pilot nature necessitates long-term validation, the authors conclude that green tea may be integrated into toothpaste formulations as an active ingredient for periodontal disease management.

The only identified study on grape seed extract (GSE) reported improvements in PD, GI, and PI, but not in BOP. PI and GI exhibited statistically significant differences favoring the GSE group over placebo. Further conclusions require larger sample sizes and higher GSE concentrations.

Regarding resveratrol, Nikniaz (9) reported that, considering the study's limitations, resveratrol supplementation in combination with non-surgical periodontal therapy significantly reduced PI over four weeks, yielding better results than periodontal treatment with placebo capsules. Overall, resveratrol appears beneficial in improving clinical parameters and inflammatory conditions in periodontitis patients, as CAL, BI, and IL-8 levels also improved, albeit similarly to the control group.

Zhang (10) explored resveratrol's significant antimicrobial properties against periodontal pathogens through various mechanisms. The study's objective was not only to analyze the pharmacokinetics of resveratrol in periodontitis patients but also to investigate its anti-inflammatory and anti-endotoxin effects, given previous reports of systemic resveratrol therapy reducing periodontitis progression and even improving periodontal health. The findings

indicated significant improvements in periodontitis symptoms, local inflammatory markers, and systemic endotoxins. However, the study had limitations: it lacked direct comparisons between resveratrol and other pharmacological agents for plaque and gingivitis reduction, did not analyze correlations between inflammation, endotoxins, and periodontitis severity, and did not conduct long-term follow-ups. The authors conclude: "Despite these limitations, to our knowledge, this is the first study evaluating the efficacy, tolerability, anti-inflammatory, and anti-endotoxin effects of resveratrol as a therapy for periodontitis patients. In conclusion, our study supports prescribing resveratrol to improve periodontal health. Further research is needed to investigate its therapeutic effects in a larger population of periodontitis patients."

Regarding curcumins, the observed positive effects are heterogeneous, encompassing antimicrobial, anti-inflammatory, and clinical attachment recovery properties, with particular emphasis on the latter two.

In the study by Anitha (31), intra-group comparisons demonstrated that both curcumin and chlorhexidine significantly improved clinical parameters at 15 and 30 days, with CFU reductions at 30 days. The reduction in PPD and CAL in the curcumin group was attributed to its anti-inflammatory and wound-healing capabilities, as the downregulation of inflammatory mediators led to decreased inflammatory edema and vascular congestion in connective tissues. Another proposed mechanism by which curcumin mitigates inflammatory changes involves its ability to inhibit epithelial cell migration, facilitating re-epithelialization. As reported, the study design aligns with previous research demonstrating that wounds treated with curcumin exhibited an upregulation of TGF-β1, which enhances wound healing and may contribute to improved attachment following its use in periodontal therapy. Additionally, studies indicate that curcumin functions similarly to nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, with the advantage of selectively inhibiting prostaglandin and thromboxane synthesis while preserving prostacyclin synthesis. Other investigations have compared the efficacy of curcumin as a mouthwash and as a local drug delivery system in periodontal therapy. While curcumin demonstrates benefits comparable to chlorhexidine, it is considered an excellent alternative due to its minimal side effects.

The study by Abdel-Fatah (16) demonstrated that curcumin gel serves as a promising local drug release agent with positive influences on all evaluated clinical indices without reported adverse effects. Repeated clinical applications of curcumin gel as an adjunct to standard SRP yielded substantial improvements across all assessed clinical parameters in the selected pockets, with greater improvements than SRP alone. Additionally, it significantly restored attachment loss and promoted periodontal tissue repair, even in deeper pockets. Although SRP remains the gold standard, curcumin's antioxidant, anti-inflammatory, antimicrobial, antiseptic, and immunostimulatory properties contribute to the restoration of normal gingival anatomy and tone. Therefore, curcumin presents itself as an optimistic local drug delivery agent that can complement SRP, mitigating the drawbacks of other chemical agents. Despite the statistically significant reductions in clinical parameters and salivary PCT levels post-treatment, no significant correlation was found between clinical indices and salivary PCT levels. The study's limitations include a short follow-up period and a small sample size. The authors suggest that future research should involve longer studies with larger sample populations and examine additional biomarkers more relevant to systemic inflammatory diseases, given that PCT is a systemic marker reflective of periodontal health.

In the study by Pérez-Pacheco (17), improvements in all inflammatory and clinical indices, albeit without statistical significance, were likely attributable to the single application of curcumin nanoparticle gel following SRP. It is therefore hypothesized that repeated applications and varying curcumin concentrations might enhance the observed cytokine expression trends. These considerations are further supported by curcumin's short half-life and its increased metabolic degradation rate. While not disputing SRP's well-established efficacy, evaluating curcumin's potential as an adjunct, particularly in non-responsive sites associated with altered host responses (e.g., smoking, diabetes) or severe dysbiosis, remains critical. The necessity for further research is reinforced by the positive results of two cited studies. In one, multiple irrigations with a 1% curcumin solution improved PPD, BOP, redness, and PI at 30 days compared to sites irrigated with saline, with significant differences in PPD and PI persisting at six months. In another study, a single local administration of 2% curcumin gel plus SRP significantly improved PPD, CAL, and GI at 30 and 45 days compared to SRP alone.

The study by Pulikkotil (18) found that both the curcumin and CHX-MTZ (chlorhexidine-metronidazole) groups exhibited similar reductions in clinical inflammation and cytokine levels, including IL-1β and CCL28. However, curcumin demonstrated a slight advantage over CHX-MTZ, primarily due to its anti-inflammatory effects, which are largely attributed to its anti-plaque action on oral biofilms. Notably, the curcumin group prevented any increase in CCL28 levels and exhibited the lowest BOP scores. These findings suggest that curcumin holds promise in treating inflammatory periodontal disease as an adjunct to mechanical plaque control. The topical application of chemotherapeutic agents plays an additional role in reducing disease severity, as mechanical plaque removal remains the gold standard. Thus, the primary expectation of this study was not to prevent experimental gingivitis or achieve complete resolution but rather to observe a reduction in the severity of gingival inflammation. The authors advocate for advanced formulations incorporating recent nanotechnology advancements to fully realize curcumin's antibacterial and anti-inflammatory potential. They further stress the need to explore both topical and systemic curcumin formulations as natural phytochemical alternatives to mitigate the side effects of CHX and MTZ.

The study by Waghmare (23) found that both the CHX and curcumin mouthwash groups exhibited statistically significant reductions in GI and total

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microbial count, suggesting that both mouthwashes were microbiologically effective. However, the CHX group demonstrated superior anti-plaque efficacy, potentially due to its greater substantivity. To support the use of curcumin mouthwash, long-term studies with varying concentrations and larger sample sizes are necessary to assess its efficacy as an anti-plaque and anti-inflammatory agent, as well as to investigate its substantivity and other properties. Additionally, beyond total microbial counts, microbiological culture methods should be employed to analyze the impact of curcumin on individual periodontal pathogens.

These findings suggest that curcumin, along with other natural compounds such as catechins, resveratrol, and propolis, exhibits significant antimicrobial, anti-inflammatory, and tissue-regenerative properties, making it a viable alternative to traditional chemical agents like CHX. However, further large-scale, long-term clinical studies are required to confirm its efficacy and determine optimal application methods in periodontal therapy.

Nakao et al. (33) strongly advocate for the identification of novel antimicrobial agents derived from natural products and their derivatives, given the increasing prevalence of antibiotic resistance, which is expected to render standard treatments ineffective in the near future. Recently, a wide range of chemical compounds, including flavonoids, terpenoids, and phenols such as artepillin C, have been isolated and identified from propolis. This phenolic molecule exhibits both antibacterial activity against Porphyromonas gingivalis and anti-inflammatory properties. Overall, the antibacterial and anti-inflammatory effects of propolis may explain why its local administration provides greater clinical benefits than other ingredients tested in clinical trials.

In their study, the authors observed that treatment with propolis significantly improved both probing pocket depth (PPD) and clinical attachment level (CAL), alongside a trend toward the reduction of P. gingivalis. The authors emphasize the necessity of further large-scale clinical studies to ensure the reproducibility of their preliminary findings. Nevertheless, they express confidence that a propolis-based therapy could emerge as an alternative treatment for chronic periodontitis, particularly during supportive periodontal therapy.

Jung (32) investigated the effects of a propolis-mangosteen complex. The study findings indicate that the significant reduction in all biomarkers within the gingival crevicular fluid suggests the compound's ability to mitigate gingival inflammation and periodontal tissue destruction by modulating key inflammatory mediators in gingival tissue, as confirmed by previous studies. The authors acknowledge the need for further research to determine whether biochemical changes in inflammatory mediators within the gingival microenvironment translate into significant short-term clinical improvements and to assess the long-term benefits in periodontal disease prevention and management. Additionally, they highlight the importance of effective prevention and early intervention strategies, particularly given the established association between periodontal disease and systemic conditions, which is underpinned by shared inflammatory mediators.

Sahu et al. (35) examined the subgingival administration of propolis nanoparticles in combination with scaling and root planing (SRP). The findings revealed significant improvements in periodontal parameters, including gingival index (GI), bleeding on probing (BOP), PPD, and relative attachment level (RAL), compared to control sites treated with saline and SRP alone. This study suggests that propolis nanoparticles hold promise as a natural and effective treatment for periodontal pockets. However, further research is required to fully elucidate their mechanisms of action and optimize their formulation and delivery for clinical application. The authors justified their exclusion of patients with stage IV periodontitis, asserting that this stage necessitates more complex approaches, such as surgical intervention. This decision aligns with previous studies that also excluded stage IV periodontitis patients.

Kiani (36) focused on bleeding index (BI) and plaque index (PI), the only two parameters assessed, which exhibited a greater improvement in the propolis-treated group. Based on current findings, propolis-based mouthwash appears to effectively reduce gingival inflammation and plaque accumulation. This outcome is particularly relevant, as a product that solely reduces plaque without significantly decreasing gingivitis would be considered incomplete. Furthermore, propolis exhibits antiseptic properties without significantly affecting tooth color, presenting a distinct advantage over chlorhexidine (CHX), which is known to cause noticeable dental discoloration. The authors reference a 2018 review (39) highlighting the antimicrobial properties of propolis. This review analyzed five clinical studies evaluating the use of propolis and chlorhexidine mouthwashes in preventing mucositis among chemotherapy patients, all of which demonstrated superior antimicrobial efficacy of propolis compared to chlorhexidine. Additionally, a 2019 randomized clinical trial (40) demonstrated that a propolis-based mouthwash could serve as a viable alternative for patients with fixed orthodontic appliances, effectively improving the gingival index, plaque index, and community periodontal index without the adverse effects associated with chlorhexidine.

Park (34) evaluated the effects of a propolis-mangosteen compound administered orally for four weeks. Given the significant reduction in the modified gingival index, this formulation may possess anti-inflammatory potential. The observed reduction in interleukin-6 (IL-6) levels in the gingival crevicular fluid correlates with clinical improvements documented in other studies referenced by the authors. These studies confirm that persistent secretion of pro-inflammatory cytokines—such as tumor necrosis factor-alpha (TNF-α), IL-1β, IL-6, and IL-12—combined with reduced levels of regulatory cytokines, including IL-10 and transforming growth factor-beta 1, is associated with sustained inflammation and periodontal attachment loss. These findings should be interpreted cautiously and remain open to further discussion in future research, as the study's outcomes position this compound as a potentially beneficial dietary supplement.

Finally, Kerdar (14) investigated the effects of quercetin, apigenin, and gallic acid extracted from Scrophularia striata and incorporated into a mouthwash. The effectiveness of this "Striata" mouthwash was then compared to Irsha mouthwash, an Iranian counterpart to Listerine. The authors observed a significant reduction in BOP, probing depth (PD), and PI in the S. striata mouthwash group, but only at the first follow-up. Consequently, they concluded that the mouthwash exerts short-term clinical effects. However, the study also confirmed its antibacterial effect against Streptococcus mutans, with significant changes in bacterial count observed over the long term. S. striata mouthwash is thus considered an effective treatment for chronic periodontitis and demonstrated greater antibacterial potency than the Iranian mouthwash Irsha.

Conclusions

Regarding the objective of the systematic review, we can confirm that polyphenols can improve periodontal health and, consequently, systemic indices, given the systemic involvement of periodontitis. However, further studies and refinements are needed to enhance current findings and translate the relatively safe nature of herbal extracts into a well-established practical application at both periodontal and systemic levels. This would optimize practices for dental hygienists (who, according to the latest updates, should develop personalized treatment plans based on systemic conditions) and for patients, who can contribute daily to preventing and treating their periodontal and general health conditions through oral hygiene and diet.

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