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Systematic Review

Potential of Propolis in Hard Candy and Related Oral Delivery Systems for Dental and Oral Health: A Systematic Review

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KEYWORDS

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ABSTRACT

Introduction: Dental and oral diseases remain major global health problems. Although propolis has antimicrobial, anti-inflammatory, and antioxidant properties, evidence regarding its use as a prolonged oral drug delivery system remains limited. No systematic review has specifically evaluated propolis hard candy as an oral delivery platform. This review aimed to synthesize evidence on propolis hard candy and related prolonged oral delivery systems for dental and oral health.

Review: This systematic review followed PRISMA 2020 guidelines. PubMed, Scopus, and Google Scholar were searched for studies published from January 2014 to March 2025. Eligible studies included randomized controlled trials, clinical studies, in vivo animal studies, and in vitro experiments evaluating propolis or related oral delivery systems. Two reviewers independently performed study selection, data extraction, and quality assessment using Cochrane RoB 2, the Newcastle–Ottawa Scale, and a modified checklist. Of 337 records, 10 studies met the eligibility criteria. In vitro studies demonstrated inhibition of Streptococcus mutans biofilm formation and Candida albicans growth, while solid oral delivery systems provided prolonged retention and sustained release. Clinical and in vivo studies indicated improved gingival health and anti-inflammatory effects, although evidence was limited by moderate risk of bias, small samples, and short follow-up.

Conclusion: Propolis hard candy shows promise as an adjunctive oral drug delivery platform, but direct clinical evidence remains insufficient. Well-designed, double-blind randomized controlled trials using standardized formulations are needed to establish its efficacy, safety, and clinical advantages.

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INTRODUCTION

Oral and dental health problems remain a global challenge with high prevalence, particularly in dental caries, periodontal disease, and oral candidiasis. These conditions are not caused by infection with a single microorganism, but involve the formation of a complex microbial biofilm in the oral cavity that is dynamic and protective against therapeutic agents. Within this biofilm, *Streptococcus mutans* plays a key role in cariogenesis, while *Candida albicans* contributes as an opportunistic pathogen in oral infections, even exhibiting synergistic interactions that can exacerbate disease progression.[1] The presence of this biofilm significantly increases the resistance of microorganisms to therapy, thereby reducing the effectiveness of conventional antimicrobial agents. [2]

Conventional therapies such as chlorhexidine and synthetic antifungals remain standard practice in clinical practice. However, long-term use is associated with various side effects, including disruption of the oral microbiota balance and the potential for antimicrobial resistance.[3,4] This situation encourages the need to explore safer and more sustainable alternative agents. In this regard, propolis as a natural product has attracted widespread attention because it contains flavonoids and phenolic compounds that have antibacterial, antifungal, antioxidant, and anti-inflammatory activities.[5,6] Furthermore, various studies have also demonstrated the potential of propolis in supporting oral health through complex biological mechanisms.[7-10]

However, most existing research still focuses on the biological activity of propolis *in vitro* and *in vivo*, without considering a crucial aspect of its application: the drug delivery system.[11,12] However, the success of therapy in the oral cavity is greatly influenced by the duration of contact of the active ingredient with the target tissue and its local bioavailability. Many conventional preparations, such as mouthwashes, have very short retention times, limiting their effectiveness despite their pharmacological potential.[13,14]

In this context, the development of alternative delivery systems is crucial. One emerging approach is the use of lozenges or hard candy-based preparations as a delivery medium for active ingredients in the oral cavity.[16,17,18] This system allows for sustained release of the active ingredient, increases retention time in the oral cavity, and provides higher local exposure with minimal systemic effects.[15,16,17] Furthermore, this dosage form also has a high level of compliance, especially in pediatric and elderly populations, and has demonstrated potential in reducing oral bacterial counts in clinical trials.[18] Propolis lozenges have been explored as oral delivery vehicles; their clinical adoption is often limited by lower palatability, astringent taste, and reduced long-term patient compliance. In contrast, hard candy formulations emerge as a superior and more accessible candidate by offering prolonged retention time in the oral cavity while significantly improving user acceptability. Therefore, this review primarily highlights the untapped potential of propolis hard candy as a frontline functional delivery system, using existing lozenge and mouthwash data merely as supporting context.[9,12,18]

However, the main challenge in developing propolis as an oral therapeutic agent currently lies no longer in proving its biological activity, but rather in optimizing its delivery system. To date, there is no consensus on the optimal dosage of propolis in hard candy formulations. The limited number of large-scale controlled clinical trials, the variation in propolis' chemical composition across

regions, and the limited data on local bioavailability are significant research gaps.[12,19]

Therefore, a comprehensive synthesis is needed that not only summarizes but also critically evaluates the available scientific evidence. This review aims to integrate the biological potential of propolis with innovative hard candy-based delivery systems, thereby providing a stronger scientific foundation to support its clinical translation in the field of dental and oral health.

REVIEW

This study was conducted as a systematic review following *the Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA 2020) guidelines. The review aimed to identify, critically appraise, and synthesize available evidence regarding the effectiveness of propolis and its potential application in hard candy formulations for dental and oral health.

A comprehensive literature search was performed in PubMed, Scopus, and Google Scholar for studies published between January 2014 and March 2025. The search was conducted using combinations of *Medical Subject Headings* (MeSH) terms and free-text keywords with Boolean operators.

The search strategy included the following terms: ("propolis" OR "bee propolis") AND ("hard candy" OR lozenge OR "oral delivery system" OR "oral formulation") AND ("oral health" OR dentistry OR "dental caries" OR gingivitis OR periodontitis OR "oral candidiasis" OR *Streptococcus mutans* OR *Candida albicans*). Reference lists of eligible articles were also manually screened to identify additional relevant studies.

Studies were included if they met the following criteria: 1) Published in English between 2014 and 2025, 2) Original primary research articles, 3) *Randomized Controlled Trials* (RCTs), clinical studies, *in vivo* animal studies, or *in vitro* experimental studies, 4) Evaluated propolis in relation to oral health or relevant oral drug delivery systems, 5) Reported antimicrobial, antifungal, anti-inflammatory, antioxidant activities, or release kinetics relevant to hard candy or lozenges.

Studies were excluded if they: 1) Were non-primary literature (narrative reviews, systematic reviews, editorials, letters, or book chapters; reviews were retained solely for background and discussion), 2) Were duplicate publications, 3) did not evaluate propolis or oral applications, 4) provided insufficient methodological information or incomplete outcomes.

All identified records were exported into a reference management program and duplicate records were removed. Two independent reviewers screened titles and abstracts according to the eligibility criteria. Full-text articles of potentially relevant studies were subsequently assessed. Any disagreement between reviewers was resolved through discussion until consensus was reached.

This systematic review addressed the following primary review question:

What is the available evidence regarding the effectiveness of propolis-containing hard candy or related oral delivery systems in improving dental and oral health outcomes? Because the available evidence comprised clinical, *in vivo*, and *in vitro* studies with different units of analysis, separate PICOS frameworks were applied according to study design.

Studies were considered eligible based on predefined population, intervention, comparison, outcome, and study design (PICOS) criteria. For clinical studies, eligible populations included individuals with dental and oral diseases or healthy participants evaluated for oral health outcomes. The intervention comprised propolis hard candy or other

propolis-containing oral delivery systems, while comparators included placebo, conventional oral care products, or no intervention. Eligible outcomes included reductions in oral microorganisms, improvements in gingival or periodontal conditions, reductions in inflammation, and other relevant clinical oral health outcomes. Randomized controlled trials and other clinical study designs were considered eligible. For in vivo studies, experimental animal models of dental and oral diseases were included. Interventions comprised propolis or propolis-containing oral formulations, with untreated controls, placebo, or conventional treatments as comparators. Outcomes included antimicrobial and anti-inflammatory effects, tissue healing, and histological or microbiological changes. For in vitro studies, eligible models included oral pathogenic microorganisms, biofilm models such as *Streptococcus mutans* and *Candida albicans*, and relevant oral cell models. Interventions included propolis extracts or propolis-containing formulations, compared with negative or positive controls or conventional antimicrobial agents. Outcomes included antimicrobial and antifungal activity, biofilm inhibition, minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC), antioxidant activity, and anti-inflammatory effects.

Data extraction was independently performed by two reviewers using a standardized data extraction form. The extracted variables included the first author, publication year, study design, study model or population, sample size, intervention characteristics, comparator, primary outcome measures, key findings, and methodological limitations. Any discrepancies between reviewers were resolved through discussion and, when necessary, consultation with a third reviewer.

The methodological quality and risk of bias of the included studies were independently assessed by two reviewers according to study design. Randomized controlled trials were evaluated using the Cochrane Risk of Bias 2 (RoB 2) tool across five domains: the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Observational and in vivo studies were assessed using the Newcastle–Ottawa Scale (NOS), adapted as appropriate for observational and animal studies, focusing on selection, comparability, and outcome assessment. In vitro studies were evaluated using a modified quality assessment checklist adapted from dental materials research, including criteria related to the presence of appropriate control groups, standardized extract concentrations, sample size justification, experimental replication, and outcome assessor blinding. Disagreements in methodological quality or risk-of-bias assessments were resolved through discussion and consensus, with a third reviewer consulted when consensus could not be reached.

Due to the heterogeneity of study designs, interventions, and outcome measures, a quantitative meta-analysis was not feasible. Therefore, findings were synthesized narratively by grouping studies into four major themes: 1) Oral delivery systems, 2) Antimicrobial activity against oral microorganisms, 3) Clinical and *in vivo* evidence, 4) Review evidence and future perspectives.

Evidence synthesis was based exclusively on primary studies because they provide original experimental or clinical data. Narrative reviews and systematic reviews were used only to contextualize the findings and discuss biological mechanisms, clinical implications, and future research directions. Consequently, the qualitative synthesis represents independent primary evidence while minimizing overlap among published studies

The electronic search retrieved 337 records. After removing duplicates (n = 17), 320 records were screened based on titles and abstracts, leading to the exclusion of 280 records. A total of 40 full-text articles were assessed for eligibility. Of these, 30 articles were excluded (20 review articles retained for background/discussion context only, 6 studies evaluating non-candy/unrelated delivery forms, and 4 studies with insufficient methodological data). Consequently, 10 primary studies met all eligibility criteria and were included in the qualitative synthesis (N = 10). The included primary studies comprised 3 clinical studies/RCTs, 2 *in vivo* animal studies, and 5 *in vitro* experimental studies. The study selection process is summarized in the PRISMA flow chart (Figure 1).

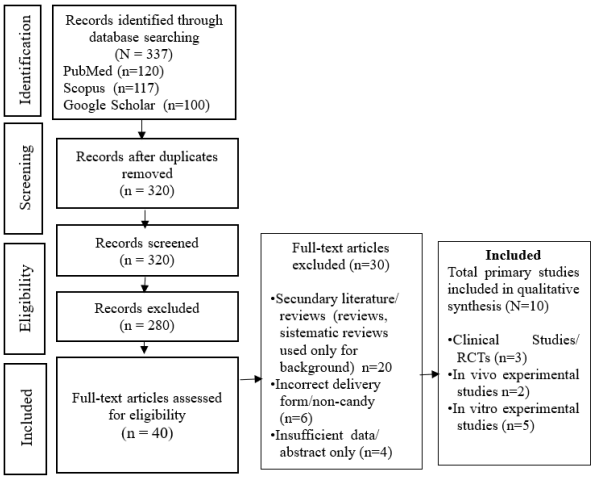

Figure 1. PRISMA 2020 Flow Diagram for Primary Study Selection.

The 10 primary studies evaluated propolis extracts or solid oral delivery systems (lozenges, hard candies, mouthwashes) regarding antimicrobial efficacy, anti-inflammatory responses, or release/retention kinetics. A comprehensive summary of these primary studies is presented in Table 1.

Table 1. Summary of primary studies included in the systematic review (N = 10)

No	Author	Study Design	Target/ Model	Intervention & Delivery Vehicle	Main Outcomes Evaluated	Key Findings	Reported Limitation
1	Ballouk et al[13]	Clinical RCT	Orthodontic patients	Propolis Mouthwash	Salivary bacterial count & oxidative stress	Significant bacterial reduction and reduced oxidative stress	Short intraoral retention time of liquid mouthwash
2	Erkmen Almaz et al[19]	Clinical RCT	Human participants	Herbal Candy/Solid vehicle	Salivary bacterial count	Significant reduction in oral bacteria via prolonged dissolution	Non-propolis specific formulation
3	El-Allaky et al[14]	Clinical Study RCT	Gingivitis patients	Propolis oral formulation	Gingival index & inflamation	Significant clinical improvement in gingival healing	Small sample size, short follow-up

4	Bueno-Silva et al[15]	*in vivo* animal	Oral tissue inflammation model	Propolis extract	Inflammatory markers	Reduces tissue inflammatory responses significantly	Animal model limits direct human translation
5	Shahoo et al[16]	*in vitro*	Oral infection pathogens	Propolis lozenges	Retention time & active release	Extended retention of active compounds in solid matrix	Simulated lab conditions
6	Zhang et al[17]	*in vitro*	Oral delivery model	Herbal lozenge Matrix	Release profile & stability	Sustained release profile over extended duration	Non-propolis formulation
7	Lou et al[18]	*in vitro*	Oral formulation model	Solid drug delivery vehicle	Matrix stability & release rate	Favorable stability and slow dissolution kinetics	Lacks dynamic physiological saliva flow
8	Freires et al[2]	*in vitro*	*S.mutans* biofilm	Red propolis extract	Biofilm adhesion & cell viability	High inhibition of biofilm formation and bacterial viability	Static *in vitro* model
9	Silva-Carvalho et al[10]	*in vitro*	Oral pathogens	Propolis extract	Intraoral retention profile	Prolonged active compound retention	Laboratory simulation only
10	Bonamigo et al[9]	*in vitro*	Oral micro-organisms	Propolis extract	Release profile kinetics	Sustained compound release over time	Static dissolution environment

*RCT = Randomized Controlled Trial

The methodological quality and risk of bias of the 10 included primary studies were evaluated using tool-specific criteria corresponding to each study design. Among the clinical studies (n = 3), RCTs evaluated using the Cochrane RoB 2 tool demonstrated an overall 'Low Risk' to 'Some Concerns' of bias. Randomization and outcome measurement domains were generally well-conducted; however, slight concerns arose regarding blinding of participants and personnel due to the distinct physical/sensory properties of propolis formulations.

For the included in vivo animal studies (n = 2), assessed using NOS adapted for animal research, both studies exhibited a 'Moderate Risk' of bias (NOS score = 6/9). Major limitations in this group included small animal sample sizes and insufficient reporting on the blinding of outcome assessors.

For the *in vitro* laboratory studies (n = 5), assessed via a modified dental material quality checklist, 3 studies were judged as having a 'Low Risk' of bias due to clear negative/positive controls, standardized propolis concentrations, and experimental replicates. The remaining 2 *in vitro* studies were rated as 'Moderate Risk' due to the absence of outcome assessor blinding and the use of static models that failed to fully replicate intraoral salivary clearance dynamics. A detailed summary of the risk of bias assessment across all primary studies is presented in Table 1.

Table 2. Risk of bias and methodological quality assessment of included primary studies (N = 10).

No.	Author	Study Design	Assessment Tool	Key Quality Domains Evaluated	Overall Risk of Bias
1	Ballouk et al.[13]	Clinical (RCT)	Cochrane RoB 2	Random sequence generation (Low risk); Deviations from intended interventions (Some concerns); Missing outcome data (Low risk); Outcome measurement (Low risk).	Some Concerns
2	Erkmen Almaz et al.[19]	Clinical (RCT)	Cochrane RoB 2	Random sequence generation (Low risk); Blinding of participants (Low risk); Missing outcome data (Low risk); Selective reporting (Low risk).	Low Risk
3	El-Allaky et al.[14]	Clinical Study	NOS	Selection of cohort (★★); Comparability (★); Assessment of outcome (★★).	Moderate Risk
4	Bueno-Silva et al.[15]	*In vivo* (animal)	NOS	Animal selection (★★); Control group setup (★); Blinding of outcome assessment (No star).	Moderate Risk
5	Shahoo et al.[16]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Standardized dosage (Yes); Replicates (Yes); Assessor blinding (No).	Moderate Risk
6	Zhang et al.[17]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Standardized dosage (Yes); Replicates (Yes); Assessor blinding (No).	Moderate Risk
7	Lou et al.[18]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Sample size justification (No); Replicates (Yes); Assessor blinding (No).	Low Risk
8	Freires et al.[2]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Standardized dosage (Yes); Replicates (Yes); Outcome reporting (Yes).	Low Risk
9	Silva-Carvalho et al.[15]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Standardized extract (Yes); Replicates (Yes); Static flow model (Limited).	Low Risk
10	Bonamigo et al.[9]	*In vitro*	Modified Quality Checklist	Clear control groups (Yes); Standardized extract (Yes); Replicates (Yes); Dynamic salivary simulation (No).	Low Risk

*RCT = Randomized Controlled Trial; RoB = Risk of bias; NOS = Newcastle-Ottawa Scale

Propolis is a natural substance with a complex composition containing flavonoids and phenolic compounds.[5] Its antibacterial activity against *Streptococcus mutans* has been demonstrated through various studies demonstrating biofilm inhibition and bacterial adhesion.[2,8] Furthermore, propolis also possesses antifungal activity against *Candida albicans* through cell membrane damage.[1,4,9] The antioxidant and anti-inflammatory effects of propolis contribute to the improvement of periodontal conditions.[20]

However, the effectiveness of propolis is greatly influenced by the delivery system, particularly in terms of retention time and stability of the active ingredient.[5,11,16,17] Conventional preparations such as mouthwashes are limited by their short contact time, thus encouraging the development of alternative systems such as hard candies or lozenges that allow for gradual release of the active ingredient.[6,15]

Several in vitro studies have shown that propolis can inhibit the growth of *S. mutans* biofilms and effectively reduce oral bacterial counts.[2,7,8] Limited clinical studies also report improvements in gingivitis and reduced inflammation in patients using propolis preparations. [13,14,15]

Furthermore, lozenge-based or hard candy-based delivery systems have been shown to increase retention of active ingredients in the oral cavity and enable more stable, gradual release compared to conventional mouthwashes.[15,16,17] This supports the potential of propolis as a therapeutic agent in oral health, although clinical evidence is still limited and further research is needed

for clinical validation and formulation standardization.[12,19]

Unlike previous narrative reviews, the present systematic review synthesized evidence derived exclusively from primary studies while using review articles only as supporting literature. This methodological approach strengthens the validity of the conclusions by reducing the risk of duplicate evidence and providing a more accurate representation of the available scientific evidence regarding the potential of propolis-containing hard candy as an oral drug delivery system.

Developing drug delivery systems in the oral cavity is an important strategy to increase the effectiveness of local therapy, particularly for dental and oral diseases such as caries, gingivitis, and oral candidiasis.[17,18] Various dosage forms, such as mouthwashes, lozenges, and herbal candies, have been extensively studied as delivery vehicles for bioactive compounds, including propolis.[12,16,17,19]

A study by Ibrahim et al.[13] showed that propolis-based mouthwashes can significantly reduce the number of oral bacteria. However, their effectiveness tends to be limited due to the short contact time with oral tissues. In contrast, solid dosage forms such as lozenges offer the advantage of increased retention time of active ingredients in the oral cavity.[13] Ghasemian et al. reported that propolis lozenges retain active ingredients longer than liquid preparations, while Khurshid et al. demonstrated a sustained release profile that has the potential to enhance therapeutic effects.[15,16]

In this context, propolis hard candy formulations can be viewed as a further development of the lozenge system. Hard candy has physical characteristics that allow for the slow release of active ingredients through dissolution in the oral cavity, thereby extending contact time with target tissues. This has the potential to increase the local bioavailability and antimicrobial effectiveness of propolis.[12,16,17,18]

However, most research still focuses on lozenges or non-propolis herbal candies and is dominated by in vitro studies. Therefore, while this delivery system concept is promising, scientific evidence specifically evaluating propolis hard candy is still limited and requires further validation, particularly through clinical studies.[10,17,18]

Propolis has been shown to have broad antimicrobial activity against major pathogens in the oral cavity, particularly *Streptococcus mutans*, which plays a role in biofilm formation and caries, and *Candida albicans*, the agent of oral candidiasis. A study by Freires et al. showed that propolis can significantly inhibit biofilm formation, a key factor in the pathogenesis of dental disease.[2]

Furthermore, studies by Silva-Carvalho et al. and Bonamigo et al. reported that propolis has an effective *Minimum Inhibitory Concentration* (MIC) value against various oral microorganisms. This activity is related to its flavonoid and phenolic compounds, which act through mechanisms such as microbial cell membrane damage and inhibition of key enzymes.[7,8]While these in vitro results support propolis's potential as an antimicrobial agent, the complexity of oral biofilms involving multispecies interactions, as described by Koo and Bowen, suggests that this effectiveness may not fully translate into clinical settings.[1]

In relation to hard candy formulations, this antimicrobial activity has the potential to be optimized by increasing the retention time of the active ingredient in the oral cavity. The gradual release of the hard candy allows for longer exposure to the target microorganisms, potentially increasing the effectiveness of biofilm inhibition compared to preparations with short contact times.[2,16,17,18]

In this context, the development of alternative oral drug delivery systems has become increasingly important to overcome the short retention time and limited local bioavailability associated with conventional mouthwashes. Lozenges and hard candy-based formulations have attracted increasing attention because they provide prolonged retention in the oral cavity, sustained release of bioactive compounds, and improved patient compliance compared with liquid formulations. Previous studies have demonstrated the potential of lozenges as oral drug delivery systems; however, evidence specifically addressing propolis incorporated into hard candy formulations remains scarce. Therefore, propolis hard candy represents a promising therapeutic strategy that warrants further investigation.[15,17,18,19]

Although numerous studies have investigated the antimicrobial and anti-inflammatory properties of propolis, and several studies have evaluated lozenges or other oral delivery systems, no comprehensive systematic review has specifically synthesized the available evidence regarding propolis hard candy as an oral drug delivery system for dental and oral health. This review was therefore conducted to critically evaluate the existing evidence and identify current knowledge gaps.[13,16,17,18]

In vivo and clinical studies have shown that propolis has promising therapeutic effects on oral health, particularly in reducing inflammation and improving gingival conditions. Hegazi et al.[14] reported significant improvements in gingivitis patients after propolis use, while Silva et al.[15] demonstrated a significant anti-inflammatory effect.[14,15]

However, most of these studies have not directly linked clinical effectiveness to a specific dosage form. Other limitations frequently encountered include small sample sizes, short study durations, and unstandardized study designs. This impacts the low level of generalizability of research results.[8,12,14,20]

In the context of propolis hard candy, this gap is crucial because, to date, there have been few clinical studies specifically evaluating the effectiveness of this dosage form.[8,12] However, the characteristics of hard candy, which allow for the slow release of active ingredients, have the potential to provide more optimal clinical benefits than other dosage forms.[16,17,18]

Therefore, controlled clinical studies with more robust designs are needed to evaluate the relationship between hard candy delivery systems and the therapeutic effectiveness of propolis in the oral cavity.[8,12,17]

Various review studies and systematic reviews consistently report that propolis has broad biological activities, including antibacterial, antifungal, anti-inflammatory, and antioxidant properties. This supports its potential as an adjuvant therapeutic agent in dentistry.[4,5,12]

However, a major challenge in developing propolis as a therapeutic product is the high variation in its chemical composition, which is influenced by geographic source and plant species. This variability impacts the consistency of effectiveness and complicates the process of standardizing dosages in formulations.[6]

In the development of propolis hard candy, standardization is crucial, including: 1) optimal concentration of active ingredients, 2) stability of bioactive compounds during heating, 3) release profile of active ingredients, and 4) safety for long-term use. Furthermore, most of the literature still highlights the lack of RCTs specifically evaluating propolis-based oral delivery systems, including

hard candy. This indicates a significant research gap.[19]

Thus, although propolis hard candy has great potential as an innovative delivery system for local therapy in the oral cavity, its development still requires a multidisciplinary approach encompassing pharmaceutical, microbiological, and clinical trial aspects.[5,8,12,17,18]

Overall, the literature indicates that propolis has potent biological activity against oral pathogens. However, its effectiveness is strongly influenced by the delivery system. Compared to mouthwashes and lozenges, hard candy formulations offer advantages in increased retention time and gradual release of the active ingredient.[10,13,15,16]

However, the existing evidence is still dominated by in vitro studies,[1,2] with limitations in clinical data and formulation standardization. Therefore, propolis hard candy can be positioned as a promising adjuvant therapy, but it requires further scientific validation through controlled and standardized clinical studies.[6,14,19]

Hard candy represents a promising oral drug delivery platform because its rigid matrix dissolves gradually in saliva, allowing prolonged residence time within the oral cavity and sustained release of incorporated bioactive compounds. This prolonged retention may enhance local exposure of propolis to dental biofilm and oral mucosal tissues, thereby potentially improving antimicrobial effectiveness while increasing patient compliance. Recent systematic evidence has demonstrated that propolis incorporated into controlled drug delivery systems exhibits prolonged release, favorable biocompatibility, and promising therapeutic potential for dental applications, although high-quality clinical evidence remains limited.[21]

Furthermore, recent advances in propolis delivery systems have emphasized that optimizing pharmaceutical formulations can improve the physicochemical stability, bioavailability, and therapeutic performance of propolis. Novel controlled-release delivery systems are therefore considered an important strategy for maximizing the clinical potential of propolis in oral healthcare.[22]

Nevertheless, the present evidence should be interpreted with caution. Most published studies have evaluated propolis incorporated into general drug delivery systems, mouthwashes, gels, membranes, or lozenges rather than propolis hard candy itself. Consequently, there is currently insufficient direct clinical evidence to conclude that propolis hard candy is superior to propolis lozenges. Instead, hard candy should be regarded as a potential pharmaceutical platform whose theoretical advantages warrant confirmation through well-designed randomized controlled clinical trials.[21,22]

Critical evaluation of the 10 primary studies revealed methodological variations that warrant careful interpretation of the synthesized findings. While in vitro experiments generally demonstrated low risk of bias regarding control setups and analytical replication, most relied on static laboratory models that fail to capture intraoral salivary flow, enzymatic degradation, and mechanical shear forces during hard candy dissolution. Furthermore, clinical evidence, though promising in demonstrating antimicrobial and anti-inflammatory efficacy was limited by small sample sizes, short follow-up periods, and potential blinding challenges inherent to bee propolis formulations due to their distinct aroma and taste. These methodological constraints underscore that while current evidence strongly supports the biological potential and plausible delivery benefits of

propolis hard candy, well-designed, double-blind randomized con efficacy and safety trolled trials with standardized propolis extracts are essential before definitive clinical

A principal hurdle in translating propolis hard candy into standardized clinical practice is the natural chemical variability of raw propolis across geographical regions and plant sources. Future pharmaceutical development must prioritize: 1) Standardizing bioactive marker concentrations (e.g., total flavonoids and phenolics), 2) Thermal stability verification during hard candy manufacturing, 3) Formulating carrier matrices with dynamic dissolution kinetics, 4) Conducting high-quality RCTs evaluating hard candy delivery formats directly in human populations.

CONCLUSION

Primary evidence demonstrates that propolis possesses potent antibacterial, antifungal, and anti-inflammatory activities against major oral pathogens such as *Streptococcus mutans* and *Candida albicans.* Incorporating propolis into a hard candy matrix offers theoretical and pharmaceutical advantages by extending intraoral contact time and enabling sustained release of bioactive compounds.

However, current evidence is predominantly derived from *in vitro* laboratory studies featuring static models, while available clinical and *in vivo* data carry moderate risk of bias due to small sample sizes and blinding challenges. Consequently, propolis hard candy should currently be positioned as a promising adjuvant oral health product rather than a substitute for conventional therapeutic agents. Well-designed, double-blind *Randomized Controlled Trials* with standardized propolis formulations and dynamic intraoral evaluation are required to establish its definitive clinical efficacy and safety.

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