



Systematic Review on Effectiveness of Magnolia Bark Extract (MBE) on *Streptococcus Mutans*

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Abstract

Background: *Streptococcus mutans* is one of the chief colonizers of the oral cavity and is regarded as the primary causative agent of Dental Caries. Many current studies focus on establishing the effectiveness of MBE against *Streptococcus mutans* and its other uses in dentistry. It is a naturally occurring, cost-effective adjunct with minimal adverse effects for improving oral health.

Aim: To determine the effectiveness of Magnolia Bark Extract (MBE) on *Streptococcus mutans*

Materials and Methods: A systematic review of clinical trials using Magnolia Bark Extract (MBE) as an effective agent against *Streptococcus mutans*. Electronic databases were searched, and 29 articles were obtained, among which four studies were included in this study.

Conclusion: Four studies were included in the systematic review: clinical trials. Among these, three studies showed that MBE, when used as a mouthwash or chewing gum, had a crucial role in reducing gingival bleeding and plaque pH and lowering salivary *Streptococcus mutans* concentration. In addition, one article provided robust but inconclusive evidence to support the efficiency of MBE. MBE as an antimicrobial and anti-inflammatory, is a good adjunct to preventing plaque biofilm formation, reducing gingival bleeding, and also minimizes salivary *Streptococcus mutans* concentration.

Keywords: Streptococcus Mutans, Dentistry, Magnolia Bark Extract, Traditional Chinese Medicine. Dental Caries

1. INTRODUCTION

Traditional Chinese Medicine (TCM) is a comprehensive branch of medicine that has been practised for over 3000 years. Based on restoring a dynamic balance between the Yin and Yang forces of the body, it has gained traction as an adjunct to western medicine in recent years. Different Magnolia-based preparations have been conventionally used in Chinese and Japanese medicine for treating conditions like anxiety, asthma, depression, menopausal symptoms, gastrointestinal disorders, Alzheimer's, headache, and more¹. *Magnolia Officinalis*, known under the pinyin name "HOU PO", is used as a dietary supplement because of its anti-inflammatory, antioxidant and antimicrobial activities, and these properties have been extensively researched in the last few years. (Greenberg M et al, 2007)

The bark of *Magnolia Officinalis* constitutes of Magnolol (94%) and Honokiol (6%), which contributes to its various pharmacological properties. (Poivre M, Duez P, 2017) Extensive research has revealed the antibacterial property of Magnolia Bark Extract against cariogenic and periodontopathic bacteria, thereby reducing the growth of harmful oral microbiomes. In addition, Magnolol and Honokiol have displayed extensive antimicrobial action against organisms like *Candida* species, *Staphylococcus aureus* and several periodontal bacteria like *Porphyromonas gingivalis* and *Prevotella spp.* (G.N Komorov et al, 2017). This indicates that MBE could be used as an ingredient in products meant to promote oral health, specially designed for people with special needs, who are unable to brush their teeth well or unable to brush their teeth by themselves. The efficacy of MBE preparations, including mouthwashes and chewing gums, have been evaluated against different oral commensals in recent years (F. Ghorbani et al, 2021).

As one of the chief colonizers of the oral cavity, *Streptococcus mutans* is regarded as one of the primary causative agents of dental caries (Banas JA, 2004). The ability to produce glucans, form a compact biofilm, resist acid activity and show natural competence bestows a certain advantage to *S. mutans* over other oral bacterial flora (Legenova K et al, 2015). Although *S. mutans* does not act alone in developing dental caries, various laboratories have demonstrated that *S. mutans* creates an extracellular polymer-rich and low pH environment, thereby fabricating a favourable niche for other oral commensals to thrive (Lemos JA et al, 2019). Thus, there is an imminent need to develop effective treatments against the colonization of *S. Mutans* for better oral hygiene.

Researchers have been working on determining the efficacy of Magnolia Bark Extract in preventing biofilm production and dental caries (Sakaue Y et al, 2019). Establishing the efficiency of this ancient Chinese herb on the most prevalent dental problems will prove to be an economical and revolutionary break in the field of natural medicine.

2. METHODOLOGY

2.1. MATERIALS AND METHOD

A systematic review of clinical trials using Magnolia Bark Extract (MBE) as an effective agent against *Streptococcus mutans*.

2.2. SEARCH STRATEGY

Original Studies and Clinical trials that are published on the efficacy of Magnolia bark extract (MBE) on *Streptococcus mutans* in electronic databases such as Cochrane Central Register of Controlled Trials (CENTRAL), Wiley, Scopus, Ovid Medicine, PubMed, Gray Literature, ScienceDirect were collected for review. Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) were used to select the studies. MeSH terms like Magnolia Bark Extract, Dentistry and *Streptococcus mutans* were used to conduct a systematic literature search for collecting pertinent data. A total of 74 articles appeared with these keywords. After the removal of duplicates, 29 articles were screened. Out of these, nine articles were research related. Finally, after applying the exclusion criteria, four papers were chosen for review. Figure 1 shows the flow diagram of some studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

2.3 ELIGIBILITY CRITERIA

Inclusion criteria:

1. Original articles
2. Studies analyzing the effect of Magnolia Bark Extract on *Streptococcus mutans* (MS)
3. In vivo studies
4. Studies published in English
5. Full-text articles

Exclusion criteria:

1. Review articles
2. Studies analyzing the effects of Magnolia Bark Extract on organisms other than *Streptococcus mutans* (MS)
3. Studies that are not of oral health significance.
4. In- vitro studies
5. Animal studies

2.4. SEARCH ENGINES

- Medline
- Scopus
- Wiley Online Library
- PubMed
- Cochrane Central Register of Controlled Trials (CENTRAL)
- ScienceDirect
- Cinahl
- Gray Literature
- Ovid Medicine

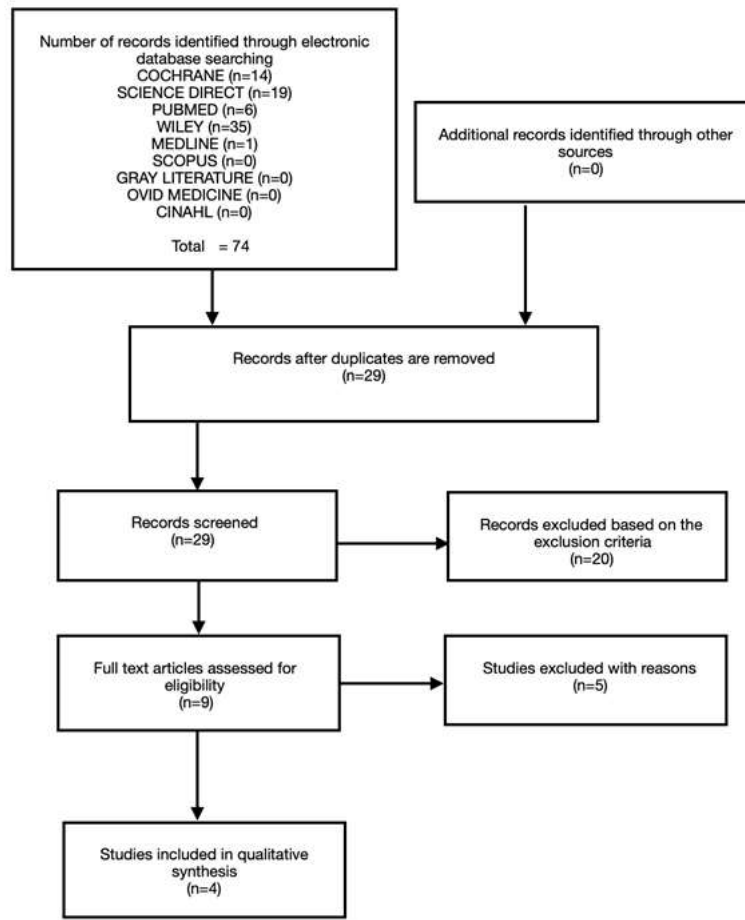


Figure 1: shows the Flow diagram depicting the number of studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDIES

Serial No.	Author	Year	Patient Selection	Duration	Preparation Used	Intervention
1	G.Campus, M.G. Cagetti, F. Cocco et al	2011	120 subjects with a high risk of caries and the presence of bleeding on probing >25%	30 days of gum use and evaluation after seven days of the end of gum use	Magnolia Bark Extract based gum; Xylitol based gum	Plaque pH and bleeding on probing were assessed. The number of salivary MS (CFU/ml) was counted.
2	G.N. Komorov, C. Hope, Q. Wang et al	2017	Twelve subjects between the age of 19-63 devoid of any pre-existing dental conditions	Four days	Magnolia Bark Extract-based chewing gum with 0.4% concentration	The number of Salivary MS (CFU/ml) was counted. In addition, plaque regrowth measurements were undertaken.

3	F. Ghorbani, R. Haghgoo, H. Aramjoo et al	2021	20 subjects between the age of 18-35 years with moderate to high risk of dental caries	Evaluation after 30 days of usage	Magnolia Extract based mouthwash (0.3%)	The plaque index was evaluated, and the number of Salivary MS (CFU/ml) was counted
4	M.G. Cagetti, F. Cocco, G. Carta et al	2020	271 subjects between the age of 30-45 years of age with a high risk of caries and bleeding on probing	Periodic evaluations are done over two years	Magnolia Bark Extract plus Xylitol based gum, Xylitol based gum	Gingival bleeding, Salivary MS (CFU/ml) and plaque pH were evaluated.

Table 1: shows the characteristics of the intervention in the included studies. In all the above studies, Magnolia Bark Extract (MBE) efficacy against *Streptococcus mutans* was evaluated, and the number of Salivary MS (CPU/ml) was counted. Efficacy trials were conducted in patients with moderate to high risk of dental caries and gingival bleeding. Trial durations and preparations used varied in each study.

TABLE 2: OUTCOME DATA AS REPORTED IN INCLUDED STUDIES

Serial No.	Author	Year	Outcome	Result
1	G. Campus et al	2011	Subjects from the magnolia and xylitol groups showed a significantly lower score at the end of the chewing period than at baseline ($p = 0.02$ and 0.04 , respectively).	Chewing gum containing MBE and xylitol has beneficial effects on oral health, reducing salivary MS, and bleeding and controlling plaque pH. These results prove the potential use of MBE chewing gum as a new functional food to improve hard and soft tissue health.
2	G. N. Komorov et al	2017	These differences were significant ($p < 0.15$) in all instances. An akin result was found when comparing the MBE (0.4%) vs MBE (0.4%) plus LAE in that the addition of the surfactant had a statistically significant ($p < 0.15$) effect in reducing plaque indices.	MBE (0.4%) + LAE (0.5%) delivered by chewing gum under the regimen described above had a significant inhibitory effect on plaque formation. Regular consumption of an MBE containing chewing gum could contribute towards good oral health.
3	F. Ghorbani et al	2021	The plaque index showed a significant difference between the Magnolia mouthwash group and the placebo one. ($P < 0.00$ and $P < 0.001$ in the first and second rounds of mouthwash administration. There was a significant difference ($P < 0.00$) in the colony count of saliva bacteria in the moderate and poor oral health groups.	The results revealed that Magnolia bark extract's minimum inhibitory concentration (MIC) on <i>S. mutans</i> was 0.3 mg/ml. The results showed that a mouthwash made from Magnolia could inhibit the growth of <i>S. mutans</i> in dental plaque.
4	M.G.Cagetti et al	2020	Subjects from the magnolia and xylitol groups showed significantly lower gingival bleeding scores and MS concentration at the end of the chewing period (t2) compared to baseline ($p = 0.01$ and < 0.01 , respectively).	The study provides robust but still non-conclusive evidence on the efficacy of Xylitol plus Magnolia chewing gum compared to Xylitol and Polyols gum to prevent caries and reduce levels of streptococcus mutans.

Table 2 shows the outcome and result of the effectiveness of Magnolia Bark Extract (MBE) against *Streptococcus mutans* in the studies mentioned above. The outcome and results were positive in the above studies showing MBE as a potent adjunct for reducing Salivary MS concentration, gingival bleeding, and controlling plaque pH, except for one where the results were non-conclusive and needed further research.

TABLE 3: BIAS ANALYSIS OF INCLUDED STUDIES

Serial No.	Author and Year	Random Sequence Generation	Allocation Concealment	Selective Reporting	Incomplete outcome data	Blinding of Assessment	Blinding of participants and Personals
1	G. Campus et al., 2011 ¹	++	-	++	++	++	++
2	G.N Komorov et al, 2017 ⁴	++	-	?	++	++	++
3	F. Ghorbani et al, 2021 ⁹	++	-	++	++	++	-
4	M.G. Cagetti et al., 2020 ¹⁰	++	-	++	-	++	++

Table 3 shows the bias analysis of all the included studies. It is categorized as high-risk bias “-”, low-risk bias “++” and unclear “?”. Categorization was done according to the Cochrane risk of bias tools for randomized controlled trials.

3. DISCUSSION

The "mutans streptococci" group was the most important bacteria forming dental caries and biofilm (Nicolas GG et al, 2011). Finding a cost-effective and compelling approach to preventing the most common oral cavity diseases is imperative for establishing sound dental health. Conventional drugs have numerous adverse reactions, but Magnolia Bark Extract occurs naturally, is abundantly available in Asia and has antimicrobial and anti-inflammatory properties. On this note, multiple studies have been conducted to establish the efficacy of MBE against *Streptococcus mutans*.

In 2011, G. Campus et al. conducted a randomized, double-blind interventional study on the effect of Magnolia bark extract (MBE) on different variables related to caries and gingivitis using sugar-free chewing gum. The study was conducted with 120 healthy adult volunteers with high risk for caries, who were enrolled and divided into three groups: magnolia, xylitol and control. The prerequisites for inclusion were a salivary concentration greater than or equal to 10 CFU/ml and the presence of bleeding on probing greater than 25%. Evaluations were conducted at baseline, after seven days, after 30 days of gum use and after seven days after the end of gum use. Plaque pH was assessed using the strip method followed by a sucrose challenge, the whole saliva was collected, and the number of salivary MS (CFU/ml) was counted. Bleeding on probing was recorded as a proxy for dental plaque. There was a significant reduction in plaque acidogenicity, salivary MS concentration and gingival bleeding after using MBE chewing gum compared to xylitol and control gums. In addition, a thirty-day use of MBE-containing chewing gum reduced *Streptococcus mutans* concentration.

In 2017, G. Komorov et al. conducted a double-blind, placebo-controlled, four-legged crossover study on 12 healthy subjects between the ages of 19 to 63 to assess the plaque-inhibiting properties of Magnolia Bark Extract (MBE) for four days. A chewing gum containing 95.42% magnolol, 1.94% honokiol and lauramide arginine ethyl ester (LAE) was administered to the subjects, who were asked to self-administer a serving of two pellets five times a day in the absence of other oral hygiene procedures. The gum preparations used were: placebo gum, MBE (0.4%), MBE plus LAE, and MBE (0.4% in the suck-then-chew method). In addition, saliva sampling and plaque imaging were undertaken at each experimental end. The intensity of red fluorescence (DR%) and the area of red fluorescence (mm) was assessed with the help of Quantitative Light-Induced fluorescence.

In contrast, the percentage area of the disclosed dental plaque was determined by image analysis. The study showed a significant inhibitory effect upon plaque formation during the formulation of MBE plus LAE chewing gum. However, MBE without the surfactant (LAE) did not have a plaque inhibitory effect. This suggests that the surfactant improved the bioavailability of MBE extract's efficacy on *Streptococcus mutans*.

In 2021, F. Ghorbani et al. conducted a crossover, placebo-controlled clinical study on 20 participants between the age of 18 and 35 on the efficacy of Magnolia grandiflora bark mouthwash on the prevalence of *Streptococcus mutans*. The study was conducted over four phases, with values taken at the beginning of the project (Phase 1) after the first prescription. (Phase 2), following the washout period (Phase 3) and after the second prescription (Phase 4). A member of the team took samples of saliva and dental plaque at each phase and evaluated for the prevalence of *Streptococcus mutans*. The data were analyzed using a T-Test (paired and independent) quantitatively. A significant difference was noted in the *Streptococcus mutans* frequency in dental plaque between when the participants used Magnolia mouthwash and when they washed out or placed in placebo. There was also a difference between the Magnolia and Placebo groups in the mean count of salivary bacterial colony counts after oral administration in the first and second phases. Hence, Magnolia bark mouthwash tends to significantly reduce the level of *Streptococcus mutans* in dental plaque and can be used as an adjunct in controlling dental plaque.

In 2020, M.G.Cagetti et al. conducted a randomized, controlled intervention trial to determine the caries preventive effect of Magnolia Bark Extract (MBE). The study was conducted with 271 subjects with high caries index between the ages of 30 to 45, who were enrolled and divided into three groups: Polyols, Xylitol and Xylitol plus Magnolia Bark extract. After two years, salivary mutans streptococcus (MS), gingival bleeding, plaque pH and carious lesions were re-evaluated. The subjects were instructed to chew 5 pellets for 5 minutes divided into three daily intakes. Plaque pH was evaluated using pH indicator strips, whole non-stimulated saliva was collected from the subjects, and ANOVA was utilized to analyze the data. Net caries increment was

significantly different among groups at the 2-year evaluation. *Streptococcus mutans* concentration and plaque pH were reduced considerably in the Xylitol plus Magnolia group and the Xylitol group. Lowered gingival bleeding was also noticed in Mag + Xyl group. Therefore, the study provided sound but inconclusive evidence, as the selected sample might not represent the entire adult population of that age range. The researchers reiterated that this clinical evidence paves the way for further research on the efficacy of MBE on *Streptococcus mutans* and caries prevention.

Various researchers also conducted multiple animal and in-vitro studies to prove the efficacy of Magnolia Bark Extract (MBE) as an adjunct for reducing salivary MS concentration, gingivitis and oral malodor. But as these articles do not come under the inclusion criteria and, henceforth not discussed in detail.

The above-discussed articles have reiterated that Magnolia Bark Extract can prove to be an effective adjunct in reducing *Streptococcus mutans* concentration in the oral cavity. However, there is scope for further research in developing a cost-effective natural remedy with minimal adverse effects.

4. CONCLUSION

Magnolia Bark Extract (MBE), a naturally occurring antibacterial and anti-inflammatory agent, has innumerable medicinal properties, including reducing menopausal symptoms, anxiety, Alzheimer's and Gastrointestinal problems. Its role in decreasing *Streptococcus mutans* in the oral cavity has been researched and proved by various in-vitro and in-vivo studies. MBE has minimal adverse effects, occurs naturally and is a cost-effective adjunct to prevent the most common conditions that attack the oral cavity - Dental caries, Dental Plaque and Oral Malodor.

CONFLICT OF INTEREST: No Conflict of Interest

SOURCE OF FUNDING: Self

ETHICAL CLEARANCE: This systematic review has not recruited any human or animal subjects. Hence ethical clearance was not obtained.

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