

Efficacy of traditional chinese medicine Magnolia bark (Magnolol and Honokiol extract) on dental caries and gingivitis: a systematic review

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Abstract:

Background: Magnolia bark is a traditional Chinese medicine that was originated thousands of years back. It received scientific attention as an anti-inflammatory effect used in Gingivitis and dental caries. **Aim:** To evaluate the efficacy of Magnolia bark extract on Gingivitis and dental caries. **Methods:** A literature review was performed using Pub Med, science direct, Medline, Cochrane, Scopus using keywords Magnolia bark, Gingivitis, dental caries and dental plaque. A total of 184 articles were from various sources; 6 articles were related to research topics. According to PRISMA guidelines, the review is reported. **Results and Conclusion:** Magnolia bark effectively against the bacteria that cause dental.

Keywords: Magnolia bark, Magnolia, Honokiol, Dental caries, Gingivitis

INTRODUCTION

Dental caries, also known as teeth decay or cavities, are the most prevailing public health disease worldwide. According to a survey that the global oral health data bank conducts, the incidence of dental caries varies from the ranges of 49% to 83%. [1] Dental caries is a common infectious disease resulting from a tooth-adherent type of specific bacteria, especially *Streptococcus Mutans*, that produce acid by metabolizing carbohydrates over time, which demineralizes the tooth structure and form a cavity over the surface of a tooth. Dental caries is more common in children, young age and old adults. dental caries is a multifarious disease that depends on various factors such as fermentable sugar, host factor, cariogenic microbial flora, and other associated environmental factors. [2]

Gingivitis is a commonly known form of gum disease (periodontal disease) that causes gingival tissues' redness, irritation, and swelling (inflammation). Gingivitis is caused by microbial plaque accumulating near the gingival sulcus. All the etiologic factors such as local and systemic either enhance plaque accumulation or plaque retention or enhance the possibility of a microbial attack in gingival tissue. [3] Other co-factor such as oral hygiene, socioeconomic status and ingress to dental care are prevalent in Gingivitis. Additional factors which impact Gingivitis are smoking habits, and fluoride used. [4] Microbial species, including the *Streptococcus group* and *Fusobacterium naviform*, are more prone to form Gingivitis. Bacteria responsible for Gingivitis include species of *Streptococcus*, *Actinomyces*, *Fusobacterium* and *Treponema*. [5]

Magnolia officinalis- is commonly called upon magnolia, or "magnolia bark."

Magnolia Bark is a type of plant extract obtained from the bark of Magnolia officinalis (Magnoliaceae), widely used in traditional Chinese medicine. Magnolia bark extract (MBE) has been widely used in medicine for 2000 years, and lately, MBE has received scientific attention as an anti-inflammatory, anti-platelet and even chemo-preventive agent [6]. The houpo magnolia tree is indigenous to China, where it has been used for thousands of years as a traditional supplement in Chinese medicine. Characteristically, the Magnolia bark of the magnolia tree has been bare away from its own branches and stems to make supplements. The bark of the magnolia plant is rich in two neolignanes that are responsible for its medicinal properties- *Magnolol* and *Honokiol*. Magnolol and honokiol seemingly inhibit gram-positive and negative bacteria involved in the decay process and are associated with gum disease. [7] On the study, Magnolia bark extract and its two components, magnolol and honokiol were assessed by a minimum inhibition concentration (MIC) test. The results indicated that the MBE and its two main constituents demonstrated a strong germ-kill effect against bacteria responsible for halitosis and *Streptococcus mutans*, bacteria involved in dental caries and gingivitis formation. [8] This study aims to evaluate the efficacy of magnolol and honokiol extract derived from Magnolia bark on dental caries and Gingivitis.

MATERIALS AND METHODS**STUDY DESIGN:**

A Systemic Review of clinical trials used traditional Chinese medicine MAGNOLIA BARK- derived magnolol and honokiol extract as an effective agent against Dental caries and Gingivitis.

SEARCH STRATEGY:

The following databases were used to find published articles on the effects of Magnolia Bark extract in Dental caries and Gingivitis. PubMed, Cochrane library, Elsevier science direct, Wiley online library, Ovid Medline, Prospero. Using Mesh representations, each database was searched to obtain the articles. The Mesh term used was Dental caries/Dental plaque/Gingivitis and Magnolia Bark.

ELIGIBILITY CRITERIA**Inclusion criteria:**

- The studies published in English
- Articles on the effectiveness of magnolia bark in dental caries and gingivitis
- Clinical trial studies
- Full-text articles
- Publications over the Year

Exclusion criteria:

- Articles published in other languages
- Abstracts available
- Animal studies
- Unrelated articles
- In-vitro studies

SEARCH ENGINES

- Pub Med
- Ovid Medline
- Cochrane library
- Elsevier science direct
- Wiley online library
- Grey literature

RESULT:

After the search using the appropriate mesh terms, 184 articles were found from the online databases. After duplicates removal, 86 articles were screened, and 12 full articles were available. Inclusion-Exclusion criteria were applied, and the final six related articles were selected for further assessment.

TABLE 1: CHARACTERISTICS OF THE INTERVENTIONS IN THE INCLUDED STUDIES

AUTHOR	YEAR	SAMPLE SIZE	AGE	DURATION	PREPARATION USED	INTERVENTION
Campus et al.[10]	2011	120 participants	18-30 Years	37 days	Magnolia chewing gum contained- xylitol 30%, MBE 0.17(magnolol 0.10% and honokiol 0.07%, respectively), sorbitol 26%, mannitol 11% and maltitol syrup 1%. Xylitol chewing gum contain- 30% Xylitol, 26% Sorbitol, 11% Mannitol and 1% Maltitol syrup. Control chewing gum was sugar-free and contained- 28% isomalt, 31% sorbitol, 9% mannitol and 1% maltitol syrup.	Magnolia group- 40 subjects Male- 19 Female- 21 Xylitol group- 40 subjects Male- 17 Female- 23 Control group- 40 subjects Male- 19 Female- 21

M-K Hellstrom et al.[13]	2014	102 participants	20-65 Years	6 months	Test dentifrice contain- 1.5% sodium lauryl sulphate (SLS), 0.243% sodium fluoride (1100 ppm F) and 0.3% Magnolia. Control dentifrice contain- 1.5% sodium lauryl sulphate (SLS), 0.243% sodium fluoride (1100 ppm F) and Placebo dentifrice.	Test group (Magnolia)- 51 subjects received dentifrice containing 0.3% Magnolia. Control group- 51 subjects received placebo dentifrice.
Seungjae Choi et al.[15]	2017	34 participants	Above 19 Years	4 weeks	Mouthrinse contained- sodium fluoride, and the ASM and OTM contained additional ingredients of bamboo salt, magnolia bark, and <i>Centella Asiatica</i> extracts. For the OTM, 50% essential oil was added to create an oil-water two-phase mouthrinse	1) control group 2) aqueous single-phase mouthrinse (ASM) group 3) oil-water two-phase mouthrinse (OTM) group.
Gleb N. Komarov et al.[17]	2017	12 participants	19-63 Years	8 weeks	Chewing gum containing- Placebo, MBE (0.4%) + LAE (lauramide arginine ethyl ester 0.5%) regarding plaque coverage (36.3% vs 34.0%)	The subjects were provided with SFG containing a placebo.
Maria Grazia Cagetti et al.[18]	2020	221 participants	30-45 Years	2 Years	Polyols chewing gum contain- 28% Isomalt, 31% Sorbitol, 9% Mannitol and 1% Maltitol syrup. Xylitol chewing gum contain- 30% Xylitol, 26% Sorbitol, 11% Mannitol and 1% Maltitol syrup. Magnolia chewing gum contain Xylitol group + 0.17% MBE of the gum weight.	Polyols group- 90 subjects received sugar-free gums containing several polyols except for Xylitol. Xylitol group- 89 subjects received gums containing the same polyols mixture plus a low amount of Xylitol. Xylitol plus MBE group- 92 subjects received the polyols mixture plus the low amount of Xylitol and magnolia.

Fateme Ghorbani et al.[21]	2021	20 participants	18-35 Years	4 weeks	Mouthwash 1 st contain- <i>Magnolia Grandiflora</i> 0.3% Mouthwash 2 nd contain- Placebo (p<0.005)	Intervention group- 10 subjects Placebo group- 10 subjects
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Table 1 shows the characteristics of the intervention in the included studies. In all the six studies, Magnolia bark extract (MBE) was compared with Xylitol or placebo in the form of chewing gum which contains several ingredients. However, the studies differed individually regarding the sample size, age of the population and the duration of the intervention.

TABLE 2: CHARACTERISTIC OF THE OUTCOME AND RESULTS

AUTHOR	YEAR	EFFECT MEASURE	RESULT
G. Campus et al.[10]	2011	Plaque pH measurement, salivary mutans Streptococci (MS) concentration, oral examination- bleeding on the probing score.	<i>Change in plaque pH</i> - Statistically significant fall in pH of the magnolia and xylitol groups when the t0 and t2 interim were compared (2.1 and 1.9 at t0 and 2.6 and 2.4 at t2) <i>Changes in MS concentration</i> - Subjects from the magnolia and xylitol groups showed a statistically significant lower bacterial concentration compared to baseline. <i>Changes in bleeding on probing</i> - Subjects from the magnolia and xylitol groups showed a significantly lower score at t2 compared to baseline.
M-K Hellstrom et al.[13]	2014	Gingival inflammation at six sites, Mean plaque and gingivitis scores.	It was found that unsupervised brushing for six months with a dentifrice containing 0.3% Magnolia extract reduced dental plaque and Gingivitis significantly more than with a corresponding control dentifrice. Furthermore, less gingival inflammation was observed at a site with a similar amount of plaque.
Seungjae Choi et al.[15]	2017	Plaque index and bleeding on probing.	A significant reduction in bleeding on probing 60.1% was observed in ASM experimental group. The Control group showed a higher increment of bleeding on probing 216.5% compared to the OTM group 34.6%. The ASM group without a concomitant decrease in the plaque index, bleeding on probing, which represents a state of gingival inflammation, and also reduce specific gingivitis-inducing bacteria including specific species of <i>Streptococcus</i> , <i>Fusobacterium</i> , <i>Actinomyces</i> , and <i>Treponema</i> and possibly <i>Bacteroides</i> , and <i>Eikenella</i> . Significantly, AMS showed a superior anti-gingivitis effect compared to OTM and control solutions.
Gleb N. Komarov et al.[17]	2017	Salivary streptococcus mutans concentration, dental plaque score.	The study results suggest that MBE(0.4%)+LAE(0.5%) delivered by chewing gum under the regimen had a significant inhibitory effect on plaque formation. On the other hand, MBE without surfactant (LAE) doesn't show any plaque-inhibiting effect, suggesting that the surfactant improved the bioavailability of the MBE components. Therefore, the regular consumption of an MBE containing chewing gum between tooth brushings could possibly contribute towards good oral health.
Maria Grazia Cagetti et al. [18]	2020	Plaque pH measurements, Streptococci mutans concentration in saliva.	The caries increment was lower in Xylitol plus Magnolia group as compared to Xylitol and Polyol group in any evaluation. Subjects treated with Magnolia chewing gum had a reduction of risk rate (RRR) of 39% with respect to those who were treated with the Polyols group. Subjects treated with Xylitol chewing gum had a RRR of 23%. Finally, subjects treated with Magnolia plus Xylitol chewing-gum had an RRR of 22%, concerning those treated with Xylitol only.
Fateme Ghorbani et al.[21]	2021	Plaque index, level of streptococcus mutans, Minimum inhibitory concentration.	A statistically valued reduction in the number of streptococcus mutans and plaque index scores was seen in Magnolia mouthwash consumers as compared to placebo mouthwash ones. (both the first and the second round)

Table 2 shows the outcome data of plaque & gingival scores with Streptococcus Mutans concentration. There was a positive decrease in plaque and gingival score in the Magnolia and Xylitol groups compared to the control group from the baseline till the end of the intervention period in the six studies with a significant p-value.

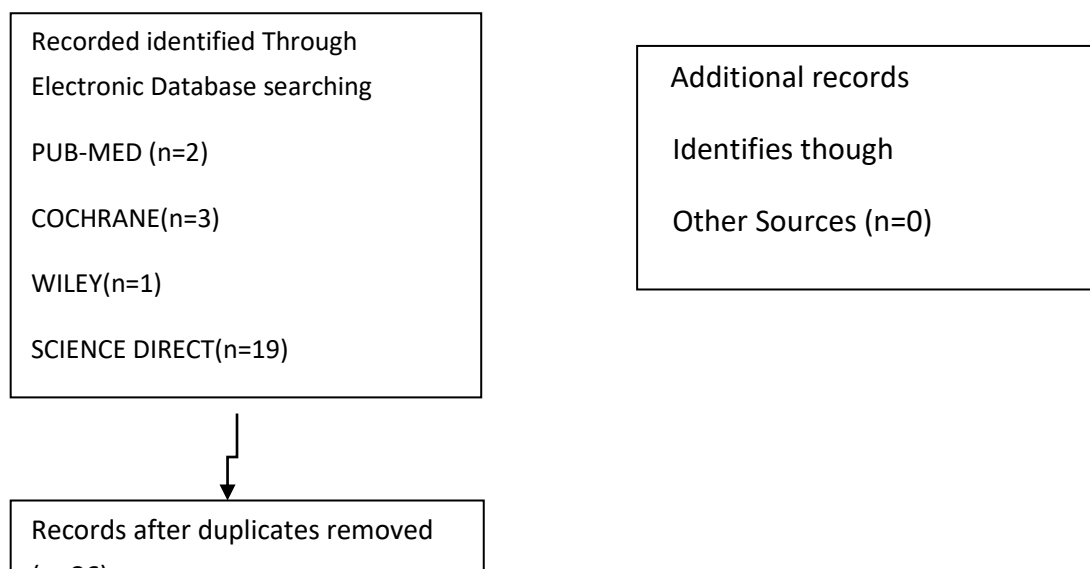
TABLE 3. OUTCOME DATA AS REPORTED IN INCLUDED STUDIES

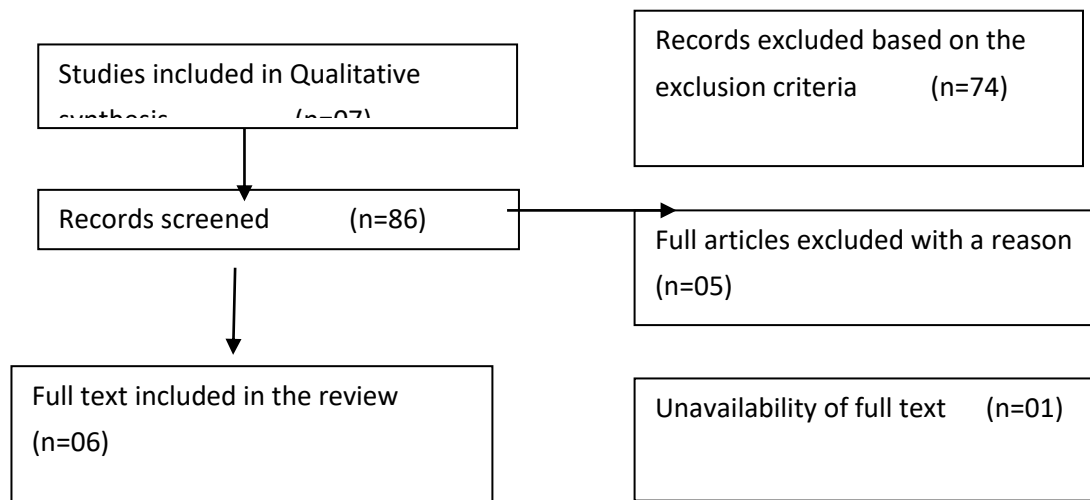
Author name, Year	Random sequence generation	Allocation concealment	Blinding of outcome	Incomplete outcome data	Blinding of participants and personnel	Selective reporting	Judgemental Bias
G.Campus et al.2011 [10]	+	-	+	+	+	+	+
Hellstrom et al.2014 [13]	+	-	+	+	+	+	+
Seungjae et al.2017 [15]	+	-	+	+	+	?	-
Gleb N. et al.2017 [17]	+	-	+	+	+	?	+
Maria. G et al.2020 [18]	+	-	+	-	+	+	?
Fateme. G et al.2021 [21]	+	-	+	+	-	+	?

+ = low risk bias, - = high risk bias, ? = unclear risk bias

Table 3 shows the bias assessment of the included studies. None of the studies shows a low risk of bias, and most of the domains had an unclear risk of bias.

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





DISCUSSION

Magnolia bark is traditionally used as Chinese and Japanese medicines. The bark of the magnolia plant began as an ancient treatment of oral health problems more than 2500-years of history [3]. Neolignans identified the two main active compounds of magnolia bark: magnolol and honokiol, which are commercially available in MBE preparation ranging from 40-90%. [9]

G.Campus et al [10] study the effect of chewing gum containing MBE and Xylitol on caries and Gingivitis in adult volunteers. The main substitutes used in chewing gum are polyols, such as Xylitol [11] The result of the randomized controlled trial shows a statistically significant lower bacterial concentration, maximum pH fall and lower score in bleeding on probing. The main result of this trial is that chewing gum containing MBE was more effective in reducing plaque salivary MS concentration as compared to Xylitol and sugar-free chewing gum. It has been shown that a relatively high daily dose of this polyol is needed to obtain these positive effects on caries prevention [12] MBE chewing gum also showed an effect on gingival tissue, measured through bleeding on probing; these indicated that MBE chewing gum improve hard and soft tissue health, thereby increasing oral health.

M-K Hellstrom et al [13] study the effect of dentifrice containing Magnolia extract on plaque and Gingivitis. It was found that unsupervised brushing with a dentifrice containing 0.3% Magnolia extract for six months reduced dental plaque and Gingivitis significantly more than control dentifrice. Also, less gingival inflammation was observed with similar amounts of plaque. The use of the Magnolia extract in dentifrice showed a statistically significant reduction in the mean gingival inflammation score; the number of bleeding gingival units was reduced by 60% compared with 30% with the control dentifrice. It indicates that the Magnolia extract has beneficial effects for patients with severe Gingivitis. The use of magnolia extract showed a statistically significant reduction in the mean GI score of similar magnitude as, for example, when CPC and chlorhexidine were incorporated in dentifrices. [14]

Seungiae Choi et al [15] study the regular effect of using mouth rinses containing antimicrobial and anti-inflammatory agents as magnolia bark extract as an adjunct to mechanical tooth brushing can reduce Gingivitis. An in vitro study showed that magnolol and honokiol had a significant antimicrobial effect against a range of periodontopathogens. [16]. The result of this study showed that bleeding on probing was effectively reduced in the ASM group (BOP represent the gingival inflammation). The study showed that chewing gum containing magnolia bark extract effectively reduced total oral bacteria compared to the control group. It showed a strong antibacterial effect against known pathogens of periodontal disease. ASM containing magnolia bark extract showed an anti-gingivitis effect compared to the control and OTM group; the plaque reduction effect was not statistically significant. Overall, for maintaining gingival health, the use of magnolia bark recommends as an oral hygiene care routine.

Komarov Gleb N. et al [17] study involving chewing sugar-free gum containing MBE for a period of twenty minutes causes an increase in salivary flow rate with increased salivary pH with an immediate increase in sodium concentration. The ecological plaque hypothesis proposes that such changes in saliva composition could potentially shift the plaque microbial composition. Other findings of the study show a reduction in the acidogenicity of plaque with a reduction in bleeding score.

Cagetti Maria Grazia et al [18] studied the long term effect of sugar-free chewing gums in a three-arm randomized clinical trial in which three types of chewing gums were included- a polyol chewing gum, a low-dosage Xylitol chewing gums, and chewing gums containing Xylitol plus Magnolia Bark Extract (MBE). During the first 5 min of chewing, the MBE was effective. The MBE release was tested at 6, 12 and 20 min of chewing, and it was found about 50-60% all time when used in the gum coating, while the release was negligible when the extract was used in the centre. [19] This trial was focused on the concentration of cariogenic bacteria in saliva, dental plaque and caries increment over a two-year period. MBE showed positive results in reducing oral bacteria including streptococci by 43% at 40 min. [20] At the end of the research, a statistically significant difference in caries lesions was compared to the baseline was observed. Subjects using the Xylitol plus Magnolia chewing gum showed the lowest caries increment compared to the Xylitol and the Polyol groups.

Ghorbani Fateme et al [21] study the effect of a mouthwash containing Magnolia against the *S. mutans* in dental plaque. The purpose of this study was to determine the minimum inhibitory concentration of magnolia bark against *S. mutans*, the role of Magnolia mouthwash in inhibition of *S. mutans* and the role of Magnolia mouthwash in the reduction of plaque index. This study shows that administrations of Magnolia mouthwash showed a significant reduction compared to the placebo mouthwash both in the first and the second rounds. The finding of the study showed that the mouthwash which contains Magnolia extract has the ability to inhibit the growth of bacteria in moderate and poor oral health status. The effect of magnolia has been reported not only on bacteria but also on other microorganisms, including fungi [22] Comparison of the effect of Magnolia mouthwash with the

placebo shows a significant difference in the growth inhibition of *S. mutans*. The result of the study showed that a mouthwash made from Magnolia is able to inhibit the growth of *S. mutans* in dental plaque, and it also revealed that the minimum inhibitory concentrations (MIC) of Magnolia bark extract on *S. mutans* was 0.3 mg/ml.

This Systematic review found conflicting results of using magnolia bark as an agent for mouthwash or chewing gum for improving oral health. Among the six included studies, four reported statistically significant effects with a reduction in the scores of the conditions measured from the baseline scores.[23] Two of these studies that used MBE+LAE and MBE+Xylitol reported a reduction in plaque index, MS concentration and dental plaque index from the scores that showed in the baseline.

CONCLUSION:

The antimicrobial activity of Magnolia bark extract can be effective against the wide species of bacteria involved in dental caries and Gingivitis. In addition, using Magnolia bark extract in chewing gum shows anti-inflammatory effects and contributes to good oral health. It can be used as a mouthwash in combination with Xylitol and LAE (Lauramide arginine ethyl ester 0.5%), which shows a significant effect in reduction of *Streptococcus mutans* concentration and dental plaque index and improved oral health.

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