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The effect of a dentifrice containing Magnolia extract on established plaque and gingivitis in man: a six-month clinical study

Abstract: *Aim:* The aim was to evaluate the clinical effect of a dentifrice containing 0.3% Magnolia extract on dental plaque and gingivitis. *Material and methods:* The trial was a 6-month double-blind, stratified, randomized and 2-armed parallel group study. Forty-six subjects in the test group brushed their teeth with a dentifrice containing 0.3% Magnolia extract and 48 subjects in the control group brushed with a placebo dentifrice. Plaque and gingivitis were assessed at baseline, 3 and 6 months. *Results:* There was a significantly larger gingivitis reduction in the Magnolia group than in the control group (0.26 ± 0.11 versus 0.11 ± 0.12) ($P < 0.001$). There was a greater increase in the total number of healthy gingival units Gingival Index (GI score 0) in the Magnolia group than in the control group (149% versus 31%) and a larger reduction in inflamed gingival units (GI score 2/3) (60% versus 30%). Furthermore, at sites with similar amounts of plaque, less clinical signs of gingival inflammation were observed in the Magnolia group than in the control group. *Conclusion:* Six months' unsupervised use of a dentifrice containing 0.3% Magnolia extract resulted in significantly greater gingivitis reduction than a corresponding control dentifrice.

Key words: 6-month clinical study; dentifrice; gingivitis; Magnolia; plaque

Introduction

The importance of mechanical plaque control in reducing dental plaque and the associated inflammatory reaction in the gingiva is well documented (1–3). Schätzle *et al.* (4, 5) analysed data included in studies describing 'the natural history of periodontal disease in man' presented by Löe *et al.* (6, 7). In these studies, a large group of subjects were examined at regular intervals during a 26-year period regarding a number of parameters characteristic of periodontal disease. Schätzle *et al.* (4) reported that (i) sites presenting gingivitis at all examinations had a higher risk of losing attachment than clinically healthy sites, and (ii) teeth with healthy gingiva had a much higher survival rate than teeth with clinical signs of gingivitis.

Van der Weijden *et al.* (8) reported in a systematic review on the effectiveness of self-performed plaque removal by the use of a manual toothbrush in adults with gingivitis that the quality of self-performed mechanical plaque removal was most often not sufficient to resolve gingivitis. In a study by Williams *et al.* (9) it was observed that 69% of the plaque remained after brushing with an electric toothbrush for 3 min.

Antiseptics incorporated in dentifrices and mouth rinses are used to improve the effectiveness of self-performed mechanical plaque removal. The effects of various antiseptics on plaque and gingivitis were presented in a review by Fine (10) who stated that when used as adjunctive to mechanical cleaning, the reduction in plaque after 6 months' daily rinsing with chlorhexidine was 48–61%, with essential oils 19–35% and with triclosan 0–30%. The corresponding gingivitis reduction was 27–67%, 15–37% and 20–75%, respectively.

Herbal-based toothpastes have been used in Europe for more than 20 years (11). Chamomile extract has been incorporated in oral care products due to its anti-inflammatory properties (12), while Echinacea may stimulate the immune response and activate leucocytes (13). Sage is described to decrease gingival bleeding, and myrrh has antiseptic properties (14). Clinical studies ranging from 6 weeks (13) up to 6 months (15) in which dentifrices containing herbal extracts have been tested against conventional dentifrices have shown improved efficacy of oral hygiene. However, an *in vitro* study (16) testing 14 different herbal dentifrices revealed great variations in antimicrobial inhibition.

An extract from the cortex of the Magnolia tree (*Magnolia officinalis*) has been used for several centuries in oriental medicine to treat a number of inflammatory disorders including asthma, gastrointestinal lesions, diarrhoea and allergic rhinitis (17, 18). The cortex of the Magnolia tree includes 3 different phenolic compounds: magnolol, isomagnolol and honokiol.

In vitro studies showed that Magnolia extract has an inhibitory effect on microorganisms associated with periodontitis, that is, *P. gingivalis*, *P. intermedia*, *A. actinomycetemcomitans*, *C. gingivalis* and *V. disper* (19–22). Moreover, Ito *et al.* (23) and Bang *et al.* (24) found that the Magnolia extract was effective against fungi. Chang *et al.* (19) stated that Magnolia extract was less effective as an antimicrobial agent than chlorhexidine, but had a low cytotoxic effect on human epithelial cells and suggested 'that magnolol and honokiol may have a potential therapeutic use as a safe oral antiseptic for the prevention of and treatment for periodontal disease'.

The antimicrobial effect of Magnolia bark extract incorporated in chewing gums has been tested in clinical studies (21, 25). Campus *et al.* (25) reported reduced salivary CFU/ml and less accumulation of plaque during a 30-day clinical trial and suggested that these antimicrobial effects might explain the observed reduction in bleeding on probing.

The clinical effect of Magnolia extract included in a dentifrice on plaque and gingivitis has so far not been examined.

The aim of this study was to test the clinical effect of a dentifrice containing 0.3% Magnolia extract on dental plaque and gingivitis.

Material and methods

Inclusion criteria

Subjects aged 20–75 years with gingivitis but without signs of destructive periodontal disease were eligible for the study. To be included, the subjects must (i) have a minimum of 24 teeth, (ii) be in good general health, (iii) show a mean gingivitis score of ≥1.0 according to the Gingival Index (GI) by Löe and Silness (26) and a mean plaque score ≥1.5 according to the Turesky modification of the Quigley and Hein Index (QHI) system (27, 28) and (iv) have no tooth sites with periodontal pockets >5 mm or clinical attachment loss of >2 mm.

Exclusion criteria

Patients were excluded if they (i) had major dental treatment anticipated during the course of the trial, (ii) had used antibiotics within the last 3 months prior to the study, (iii) were on regular anti-inflammatory medication or (iv) were smokers.

Study design

The trial was designed as a 6-month double-blind, stratified, randomized and 2-armed parallel study. Following a screening examination 102 subjects, 40 men and 62 women (mean age of 42 years, range 20–65 years) were recruited to the study among patients attending public dental clinics in the county of Västra Götaland, Sweden (Fig. 1). All subjects were given detailed oral and written information about participating in the study and gave their signed consent. The Regional Ethical Review Board at the University of Gothenburg, Sweden, approved the study (Dnr 353-03).

The subjects were stratified according to the screening gingivitis scores and randomly assigned to two different treatment groups using a randomized block technique including four subjects with similar levels of gingival inflammation in each block.

After a baseline registration, the 51 subjects who were assigned to the test group (Magnolia) were provided with a dentifrice containing 0.3% Magnolia, while the 51 subjects of

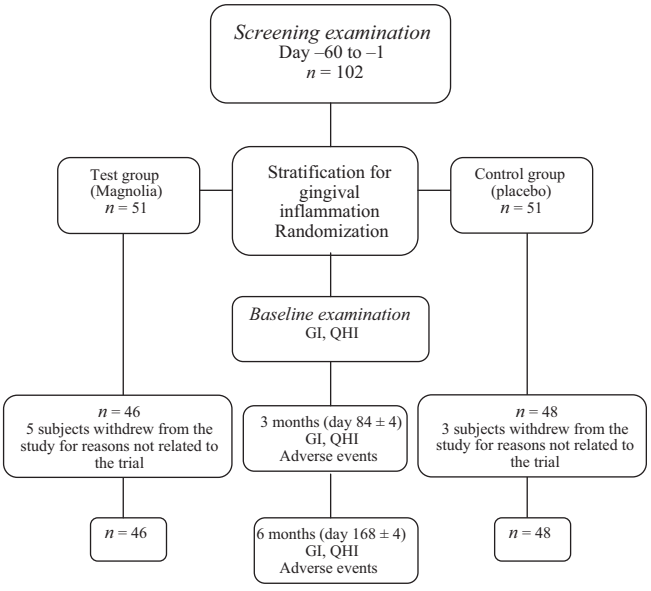

Fig. 1. Study outline. GI, Gingival Index; QHI, Quigley and Hein Index.

the control group received a placebo dentifrice. The dentifrices were supplied by a manufacturer (Colgate-Palmolive Company, Piscataway, NJ, USA) and were delivered in white, plain and coded tubes. Both test and control dentifrices contained standard ingredients including 1.5% sodium lauryl sulphate (SLS) and 0.243% sodium fluoride (1100 ppm F). The concentration of 0.3% Magnolia extract was chosen based on unpublished data from *in vitro* studies and several short-term clinical studies previously performed by the manufacturer. In addition, all subjects were provided with three toothbrushes (Colgate Navigator®; Colgate-Palmolive). The decision to replace the toothbrush every month was made to assure the same high quality of the brushes throughout the study. New supplies of dentifrice and toothbrushes were provided after 3 months. A dental assistant who did not take part in the clinical examinations administered the dentifrices and toothbrushes according to the randomization protocol. Thus, the examining dentist was kept unaware of which dentifrice the participants were assigned to. The subjects were instructed to apply 2 cm of the dentifrice on the brush at each time of brushing and to continue to exercise their regular self-performed plaque control measures twice a day, in the morning and in the evening during the entire 6-month period. No further instructions were given; however, the subjects were asked not to brush their teeth in the morning on the day of re-examination.

Clinical examinations

Gingival inflammation

The degree of gingival inflammation was scored at six sites (disto-, mid-, mesio-buccal and disto-, mid-, mesio-lingual) according to the criteria of the GI by Löe and Silness (26).

Dental plaque

Plaque was disclosed with a mini-sponge containing erythrosine (Diaplac®, Wallco AB, Enköping, Sweden). The sponge was gently pressed to the teeth, and the subjects were asked to rinse once with water. The stained tooth surface was scored at the disto-, mid-, mesio-buccal and disto-, mid-, mesio-lingual surfaces of each tooth according to the criteria of the Turesky modification of the QHI (29, 30).

Plaque and gingivitis were recorded at all teeth at the baseline and 3- and 6-month examinations. An experienced specialist in periodontology performed all clinical registrations (MKH). Intra-examiner reproducibility tests had been made prior to the present study, and the overall agreement of duplicate measurements of the GI was 84.5% and the corresponding kappa-value was 0.68. For duplicate measurements of QHI, the overall agreement was 73.5% with a kappa-value of 0.62.

Report of adverse effects

At the 3- and 6-month examinations, all participants were asked to disclose if they had experienced any discomfort in terms of taste impairment and/or smarting/burning sensation. In addition, the oral mucosa was examined for signs of epithelial desquamation and the teeth and the tongue with regard to discoloration.

Statistical analysis

Mean plaque and gingivitis scores at baseline, 3–6 months and the reductions in plaque and gingivitis scores from baseline to 3 and 6 months were calculated for each subject and then averaged for each treatment group. Only data for subjects who completed the 6 months were included in the analysis.

A one-factor ANOVA using the treatment as the factor was used to detect any significant differences between the test and the control group. Based on a standard deviation of 0.4 in previous studies (31), the power of the present study was 80% to detect a 20% difference in mean gingivitis reduction between the two groups.

Results

Ninety-four subjects completed the study. Eight subjects, five in the test and three in the control group, withdrew from the study for reasons not related to the trial (Table 1).

Mean gingivitis scores (GI)

The mean GI scores are presented in Table 2. At baseline, the mean GI score was 1.33 in the test and 1.30 in the control group ($P > 0.05$). At the 3-month examination, the mean GI score was reduced to 1.07 in the test and 1.15 in the control group. The mean GI reduction between baseline and the 3-month examination was statistically significant in both treatment groups ($P < 0.001$). However, the gingivitis reduction was significantly larger in the test than in the control group (0.27 versus 0.15; $P < 0.001$). At the 6-month examination, the mean GI score was 1.08 in the test and 1.19 in the control group ($P < 0.001$). The mean GI reduction between baseline and 6 months was statistically significant in both groups ($P < 0.001$) but significantly larger in the test than in the control group (0.26 versus 0.11; $P < 0.001$) (Table 2).

Mean plaque scores (QHI)

The mean QHI plaque scores are presented in Table 3. At baseline, the mean QHI score was 2.90 in the test group and

Table 1. **Baseline characteristics**

Characteristic	Test $n = 46$	Control $n = 48$
Male	17	18
Female	29	30
Mean age (± SD)	43 ± 13	42 ± 12
Age range	20–65	24–61
Mean plaque (QHI)	2.90 (0.39)	2.82 (0.32)
Mean gingivitis (GI)	1.34 (0.16)	1.30 (0.13)

GI, Gingival Index; QHI, Quigley and Hein Index.

Table 2. **Mean Gingival Index (SD)**

n = 94	Baseline	3 months	6 months	Diff BL–3 months	Diff 3–6 months	Diff BL–6 months
Magnolia	1.33 (0.16)	1.07 (0.18)	1.08 (0.13)	−0.27 (0.13)*	+0.01 (0.13)	−0.26 (0.11)*
Control	1.30 (0.12)	1.15 (0.15)	1.19 (0.12)	−0.15 (0.14)*	+0.04 (0.11)	−0.11 (0.12)*
P-value	n.s.	$P < 0.01$	$P < 0.001$	$P < 0.001$	n.s.	$P < 0.001$

BL, baseline; n.s., non-significant difference between treatment groups.
*$P < 0.001$ within treatment groups.

Table 3. **Mean Plaque Index, Quigley and Hein Index (SD)**

n = 94	Baseline	3 months	6 months	Diff BL–3 months	Diff 3–6 months	Diff BL–6 months
Magnolia	2.90 (0.39)	2.49 (0.46)	2.65 (0.40)	−0.41 (0.33)**	+0.16 (0.30)	−0.25 (0.28)**
Control	2.82 (0.32)	2.55 (0.40)	2.72 (0.33)	−0.27 (0.29)**	+0.17 (0.29)	−0.09 (0.28)*
P-value	n.s.	n.s.	n.s.	$P < 0.05$	n.s.	$P < 0.01$

BL, baseline; n.s., non-significant difference between treatment groups.
*$P < 0.05$; **$P < 0.001$ within treatment groups.

2.82 in the control group. At the 3-month examination, the mean QHI score was reduced to 2.49 in the test and 2.55 in the control group. The mean QHI reduction between baseline and the 3-month examination was statistically significant in both treatment groups ($P < 0.001$) but significantly larger in the test than in the control group ($P < 0.05$). At 6 months, the mean QHI plaque score was 2.65 in the test and 2.72 in the control group. The mean QHI reduction was statistically significant in both groups (test $P < 0.001$; control $P < 0.05$). However, the mean QHI reduction at 6 months was significantly larger in the test group than in the control group (0.25 versus 0.09; $P < 0.01$) (Table 3).

Number of sites with various GI scores

A total number of sites with GI scores 0 and 2, respectively, at baseline, 3 months and 6 months, are presented in Table 4. The number of gingival units showing overt signs of gingival inflammation (GI score 2) in the test group was reduced from 2581 at baseline to 1045 sites at 6 months (−60%) and from 2471 to 1734 sites (−30%) in the control group.

The number of healthy sites (GI score 0) increased from 207 to 516 sites (+149%) in the test group. The corresponding increase in the control group was from 213 to 278 sites (+31%).

The mean GI scores at sites with different QHI scores at baseline, 3 and 6 months, are presented in Fig. 2. Significantly lower gingivitis scores were observed in the test than in the control group at the 3- and 6-month re-examinations ($P < 0.05$) at tooth surfaces harbouring similar amounts of plaque as assessed by the QHI.

Table 4. **Total number of healthy Gingival Index (GI = 0), inflamed non-bleeding (GI = 1) and bleeding sites (GI = 2) in the Magnolia and control group at baseline and 6 months**

	Magnolia			Control		
	GI = 0	GI = 1	GI = 2	GI = 0	GI = 1	GI = 2
Baseline	207	4360	2581	213	4937	2471
6 months	516	5587	1045	278	5609	1734

Adverse events

The dentifrice containing the Magnolia extract was well tolerated by the majority of the participants. Three subjects in the test group experienced a strong taste during the initial phase of tooth brushing, which diminished by time. No staining of the teeth or tongue or epithelial desquamations were observed at any examination intervals.

Discussion

In the present trial, it was found that unsupervised brushing for 6 months with a dentifrice containing 0.3% Magnolia

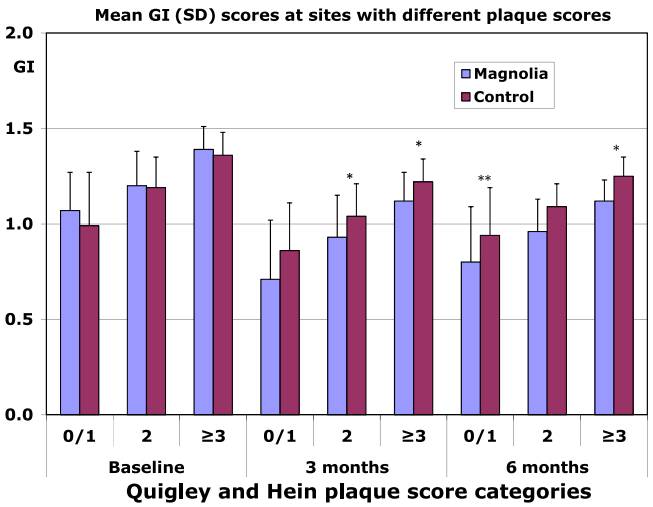

Fig. 2. Mean Gingival Index (GI) at sites with Quigley and Hein Index (QHI) score categories 0/1, 2 and ≥3 at baseline, 3 months and 6 months. *$P < 0.05$.

extract reduced dental plaque and gingivitis significantly more than with a corresponding control dentifrice. Furthermore, less gingival inflammation was observed at sites with similar amounts of plaque. The slight increase in plaque and gingivitis scores between the 3- and 6-month examinations, although not statistically significant, may in part be explained by the common observation in clinical studies with duration of 6 months or more that subjects tend to be less compliant over time (29).

Lindhe *et al.* (30) studied in a 6-month clinical trial the effect of a dentifrice containing a phenolic compound, triclosan, on plaque and gingivitis. After 6 months, the number of clinically healthy sites had increased with 146% and the number of bleeding sites was reduced with 57%. The findings in the present study of a 149% increase in the number of healthy gingival sites (207–516) and a 60% decrease in the number of bleeding sites (2581–1045) in the Magnolia group are in line with the results reported by Lindhe *et al.* (30).

The reduction in gingival inflammation observed in the present study also corroborates with results presented by Overholser *et al.* (32) and Charles *et al.* (33). Overholser *et al.* studied the effect of twice daily rinsing with essential oils (Listerine®; Johnson and Johnson, New Brunswick, NJ, USA) and chlorhexidine (Peridex®; 3M ESPE, St Paul, MN, USA) as an adjunct to regular mechanical oral hygiene measures. They found after 6 months a gingivitis reduction of 35.9% and 30.5% in the Listerine® and Peridex® groups, respectively, compared with a control group. In the study by Charles *et al.* (33), 108 subjects were instructed to rinse with either an essential oil, a chlorhexidine or a negative control mouth wash twice daily for 6 months as an adjunct to their regular oral hygiene measures. The mean GI was reduced from 1.31 to 1.04 in the essential oil group and from 1.35 to 0.99 in the chlorhexidine group. In the present study, a comparable gingivitis reduction was observed in the Magnolia group (1.33 to 1.08) and in the control group; the corresponding GI reduction was from 1.30 to 1.19. The negative control group in the study by Charles *et al.* (32) demonstrated a mean GI reduction from 1.27 to 1.21. The authors also reported a 69% reduction in the number of bleeding sites in the chlorhexidine group and in the essential oil group; the corresponding percentage reduction in the number of bleeding sites was 61% compared with 31% in the control group. In the present study, the percentage of bleeding sites in the Magnolia group was reduced with 60% and in the control group with 30%.

The mean plaque reduction in the Magnolia group was, however, smaller (9%) than the corresponding reduction reported by Charles *et al.* (33) in the essential oil group and the chlorhexidine group (29% and 35%, respectively). The mean plaque reduction in the control groups was similar: 4% in the present study and 6% in the study by Charles *et al.* (33).

The observation in the present study of a more pronounced reduction in gingival inflammation than of dental plaque in subjects who brushed with the Magnolia dentifrice may in part be explained by an anti-inflammatory effects *per se* as have been reported for phenolic compounds (34). There are indications based on the results from other studies that magnolol and honokiol have anti-inflammatory properties (17–20, 23, 24, 35–39). Lo *et al.* (36) found that the Magnolia extract had antioxidant properties, and Park *et al.* (18) observed in an *in vitro* study that magnolol reduced the release of IL-8 and TNF-α in THP-1 cells. Chen *et al.* (39) reported that magnolol suppressed IL-6-induced promoted activity of intracellular cell adhesion molecule (ICAM-1).

Lindhe *et al.* (30) reported that less clinical signs of inflammation were observed in the triclosan group than in the control group at tooth surfaces harbouring similar amounts of plaque. It was concluded that the regular use of a triclosan-containing dentifrice significantly reduced gingivitis beyond what could be explained by the reduction in dental plaque *per se*. Dewhirst *et al.* (34) observed that phenolic compounds inhibit the prostaglandin synthesis by affecting the cyclooxygenase pathway. Modéer *et al.* (40) who studied the anti-inflammatory mechanism induced by triclosan observed similar findings in an *in vitro* trial. They suggested that concomitant with the antibacterial properties of triclosan, the preventive effects on the inflammatory response in the gingiva are caused by inhibition of prostaglandin E synthase-1 expression in human gingival fibroblasts. Similar findings as well as additional anti-inflammatory mechanisms of triclosan were reported by Gaffar *et al.* (41) and Mustafa *et al.* (42–44).

The use of the Magnolia extract showed a statistically significant reduction in the mean GI score of similar magnitude as, for example, chlorhexidine and CPC when incorporated in dentifrices or mouth rinses (45–47). The fact that the final mean GI score remained >1, the observed reduction of about 20% in GI score, may be questioned from a clinical significance aspect. Only 7% of the gingival units were judged to be free of clinical signs of inflammation at the 6-month follow-up examination. However, the finding that the number of bleeding gingival units was reduced with 60% compared with only 30% with the control dentifrice indicates that the Magnolia extract could have beneficial effects for patients with severe gingivitis. Further studies are needed to substantiate this interpretation and to evaluate whether an increase in concentration of Magnolia extract may potentiate the beneficial effects.

Conclusion

Six months' unsupervised use of a dentifrice containing 0.3% Magnolia extract resulted in significantly larger reduction in gingivitis than a corresponding control dentifrice.

Clinical relevance

Magnolia extract incorporated in a dentifrice may due to its potential anti-inflammatory properties be beneficial to improve gingival health in subjects having difficulties to achieve optimal plaque control.

Conflict of interest and source of funding

The authors declare that they have no conflicts of interest. The study was funded by Colgate-Palmolive Company, but

the company had no influence on the final design and conduct of the present study.

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