

# Adjunctive Periodontal Treatment with *Centella asiatica* and *Punica granatum* Extracts. A Preliminary Study

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## Abstract

**Background:** *Centella asiatica* and *Punica granatum* are medicinal herbs that have been reported to promote tissue healing and modulate host responses. The purpose of this study was to investigate the effects of the combined extracts from *C. asiatica* and *P. granatum* pericarp on periodontal healing following scaling and root planing in adult periodontitis patients. **Methods:** An innovative herbal medicament was formulated in the form of biodegradable chips for subgingival application. Twenty patients with initial pocket depth 5–8mm were enrolled into the study. After baseline examination, scaling and root planing of non-target teeth, the target teeth received scaling and root planing followed by subgingival delivery of medicated chips in the test group and unmedicated chips in the placebo group. Probing pocket depth, attachment level, bleeding on probing, gingival index, and plaque index were recorded at baseline, 3 and 6 months. **Results:** The results showed significant improvements of pocket depth and attachment level in the test sites when compared with the placebo sites at 3 months and with the placebo and control sites at 6 months. All treatment sites exhibited a similar trend of decreasing plaque score. However, the test sites seemed to show slightly better percentage of bleeding on probing. **Conclusion:** The results indicate that local delivery with *C. asiatica* and *P. granatum* extracts plus scaling and root planing significantly reduced the clinical signs of chronic periodontitis.

**Key words:** Medicinal herbs/extracts, *Centella asiatica*/tissue healing, *Punica granatum*/tissue healing, non-surgical periodontal therapy/adjunctive treatment, biodegradable chips/subgingival application

## Introduction

With adjunctive treatment, various antibiotics and antimicrobial agents have been suggested to augment the efficacy of mechanical treatment (Genco, 1981). To overcome many disadvantages of systemic antibiotic therapy, antibacterial agents for local delivery into periodontal pockets have been extensively developed (Goodson *et al.*, 1985). While data from some studies show bacterial suppression by the use of both systemically and locally delivered antimicrobial therapy, there are reports which indicate that reemergence (von Troil-

Linden *et al.*, 1996; Flemmig *et al.*, 1998), low susceptibility (O' Connor *et al.*, 1990; Hagiwara *et al.*, 1998) and development of resistant subgingival microbial strains against different medication (Preus *et al.*, 1995; Van Winkel hof *et al.*, 2000) still do occur.

Another approach to cope with disease progression is to enhance resistance of the host and promote good healing of the periodontium. Supplementing traditional non-surgical care with pharmacotherapeutic agents that are aimed at modifying the destructive host response has also been shown to be of additional benefit in arresting disease progression and providing resolution of inflammation in the management and control of chronic periodontitis. Examples of such agents are non-steroidal anti-inflammatory drugs such as flurbiprofen and naproxen, which have been shown to reduce alveolar bone loss in chronic periodontitis

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through their inhibitory action on prostaglandin formation (Offenbacher, 1996). In addition, subantimicrobial dose doxycycline (SDD) has been demonstrated to be an effective inhibitor of matrix metalloproteinases (MMPs), especially collagenase (Golub *et al.*, 1990; Golub *et al.*, 1995) and has provided an adjunctive benefit to scaling and root planing (Caton *et al.*, 2000). Based on the scientific evidence, there are few documented studies of *Centella asiatica* and *Punica granatum* for use in dentistry as well as in the area of periodontics.

*Centella asiatica* Linn. is a small herb belonging to the family Apiaceae. It is commonly used in the Ayurvedic system of medicine for both internal and external applications to treat various diseases (Watt, 1883). The chemical structure of active compound from the plant was found to be a glycosidic terpene and was given the name asiaticoside (Lawrence, 1967). The three principal components, however, are asiatic acid, madecassic acid and asiaticoside (Maquart *et al.*, 1989). Suguna *et al.* (1996) reported that the alcoholic extract of *C. Asiatica* increased cellular proliferation and collagen synthesis at the wound site as marked by increase in protein and collagen content of granulation tissues. Quicker and better maturation together with cross-linking of collagen were also observed. The sensitising capacity of this herbal extract and its triterpenic components has been proved to be very weak. Although applied frequently to damaged skin, the risk of acquiring contact sensitivity to the extract and its constituents is low (Hausen, 1993).

*Punica granatum* Linn. (Pomegranate) is a plant in the family Punicaceae. The rind or pericarp of the fruit is known to contain considerable amount of hydrolysable tannins (Schmidt *et al.*, 1964), which have been demonstrated to inhibit prostaglandin synthetase (Kiuchi *et al.*, 1983). Chulasiri *et al.* (1995) showed that water soluble component from pomegranate rind possessed low acute toxicity, no mutagenic activity and caused no skin irritation.

The objective of this clinical study was to evaluate the effects of a newly formulated herbal medicament from combined extracts of *Centella asiatica* and *Punica granatum* pericarp as a subgingival adjunct to treat periodontal pockets in adult periodontitis patients, by monitoring changes of clinical parameters.

## Materials and methods

### Crude extracts

*Centella asiatica* L. dried whole plants were ground and refluxed three times for three hours, each with 95% ethanol. The combined alcoholic extracts were subsequently dried under vacuum. *Centella asiatica* dry extract has been analysed for the molecular structure of Asiatic acid and madecassic acid by NMR and Mass spectro-

photometry. The quality of Triterpene acid was assayed by titration (Pasich *et al.*, 1968). *Punica granatum* L. Dried fruit peels were ground and extracted using the same method as Centella.

### Preparation of medicated and unmedicated chips

Both the medicated and unmedicated chips were prepared into two types of thickness (300 and 400 micron). For medicated chips, hydrolysed collagen (Sigma-Aldrich Chemicals, USA) was dispersed in distilled water and the solution was brought to 85–90°C. The Centella extract was added and glycerine supplemented as a plasticising agent (Steinberg *et al.*, 1990). The mixture was stirred until homogeneous and then mixed with the extract of the Punica pericarp. (The extract contains tannic acid, which also serves as collagen cross-linking agent.) For unmedicated chips, the herbal extracts were not added to the mixture of hydrolysed collagen, distilled water and glycerine. Cross-linking of the collagen matrix was achieved by adding glutaraldehyde (Big *et al.*, 2001). The mixture was poured evenly onto stainless mold plates and allowed to cool down at room temperature and then dried in a refrigerator. The cross-linked sheets were removed from the plates and the thickness was measured to confirm even thickness. With an innovative chip-cutting machine, the sheets were uniformly cut into 4mm x 5mm rectangular chips with one rounded end, resembling a U shape. Each category of the chips was packaged in blister packs and submitted for sterilization by gamma irradiation. The characteristics and ingredients of the chips are summarised in Table 1.

### Case selection

Enrolment to select subjects was made at the Faculty of Dentistry, Mahidol University. Inclusion criteria included male or female patients aged between 35 to 65 years with good general health, presence of at least two teeth (except third molars) in three out of the four quadrants and the presence of 5–8mm periodontal pockets that bled upon probing on at least one site around each of the selected two teeth in each of the selected three quadrants. Exclusion criteria included patients who smoked or had a history of tobacco consumption, presence of underlying systemic diseases and patients who had received antibiotic treatment and/or periodontal treatment in the previous six months before participating in the project. An impression of the natural dentition of each subject was taken to obtain working models for fabrication of custom-made soft stents.

### Ethical aspect

This study was carried out according to the guidelines of the Committee on Human Rights Related to

**Table 1.** Summary of characteristics of chips in each category and amount of the ingredients contained

Features	Type of chips			
	300 $\mu$ med chip	400 $\mu$ med chip	300 $\mu$ unmed chip	400 $\mu$ unmed chip
Surface area (mm <sup>2</sup> )	12.25	12.25	12.25	12.25
Weight (mg)	5.3	7.1	4.9	6.5
Amount of Centella extract (mg)	1.4	1.9	-	-
Amount of Punica extract (mg)	0.2	0.3	-	-
Amount of hydrolysed collagen (mg)	2.8	3.8	4.3	5.8
Amount of glycerine (mg)	0.4	0.5	0.2	0.3
Amount of glutaraldehyde (mg)	-	-	0.05	0.07

Human Experimentation, Mahidol University. All patients were informed with the nature of the study (verbally and in writing) and were included in the trial only after having given their written consent.

### Clinical parameters

Probing pocket depth (PD) was measured to the nearest millimetre of the distance from the gingival margin to the bottom of the pocket by using a uniform periodontal probe (PCPUNC 15, Hu-Friedy, USA). Stent to gingival margin (SG) was measured with the same periodontal probe and represented the distance between the edge of the custom-made soft stent to the gingival margin of each target site. Attachment level (AL) was the summation of PD and SG at each corresponding site. Bleeding on probing (BOP) was indicated by bleeding detected following pocket probing (Ainamo, 1975). Gingival index (GI) was the determination of the gingival health condition (L e and Silness, 1963) and Plaque index (PI) was the determination of plaque covered tooth surface, using a method modified from the Greene and Vermillion debris index (Greene and Vermillion, 1960; 1964).

Measurement of PD, SG, BOP and GI was carried out at six sites around each tooth (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual). BOP, GI and PI were recorded at baseline, 1, 3 and 6 months. PD and SG were recorded and AL calculated at baseline, 3 and 6 months.

### Treatment procedures

All patients were thoroughly educated for oral hygiene maintenance and reinforced at periodic recall visits throughout the study. After baseline examination, the non-target teeth received scaling and root planing (SRP). Randomisation was then made among the patients for the quadrants to be designated as test, control or placebo groups:

- Test group (SRP+med) received SRP followed by one immediate subgingival application dose of 400 $\mu$  medicated chips and one booster dose of 300 $\mu$  medicated chips at each of the 1<sup>st</sup> and 2<sup>nd</sup> month visits.
- Placebo group (SRP+unmed) received SRP followed

by one subgingival application dose of 400 $\mu$  unmedicated chips and two booster doses of 300 $\mu$  unmedicated chips at the 1<sup>st</sup> and 2<sup>nd</sup> month visits.

- Control group (SRP alone) did not receive any chips.

One application dose consisted of two (medicated or unmedicated) chips per tooth, which were inserted into the deepest sites of the pockets. In order to fulfil the double blind split mouth design, the patients as well as the clinician who performed SRP and recorded the clinical data were unaware of the designation of the treatment modalities. All patients were instructed not to consume any food or drink for one hour after insertion of the chips and to refrain from using mouth rinse, oral irrigating devices and cleansing of the proximal areas at the target teeth for one week. The total follow-up period was six months. During this period, each patient was scheduled to come back every month for measurement of the clinical parameters, oral hygiene reinforcement and professional care.

### Statistical analysis

Data analysis was achieved by statistic software SPSS for Windows Release 10.0 package. Mean PD and AL together with changes from baseline at the 3rd and 6th month visits were calculated for all pockets and for initial pocket 7–8mm in each of the treatment groups. Percentage distributions of GI, BOP and PI at different examination visits were determined. Comparison between the three treatment groups and within each treatment group was performed by either one-way ANOVA or Kruskal-Wallis test where appropriate. A *p*-value of < 0.05 was considered statistically significant in all tests.

### Results

Of 24 patients, 4 (16.7%) dropped out due to non-treatment related reasons. One patient died from an accident, one became pregnant and the other two had difficulties to come for subsequent follow-up visits. Therefore, only the data from the remaining 20 subjects were used for statistical analysis. The mean age of the six male and 14 female subjects was 48.20 years (range 37–61 years). The total number of the selected

Table 2. Baseline recordings for mean probing pocket depth (PD) in different subgroups, % bleeding on probing (BOP) and % plaque index (PI)

Parameters	SRP+med		Treatment		SRP alone	
	SRP+med	n	SRP+unmed	n	SRP alone	n
PD $\pm$ SD (mm)						
1-4 mm	2.79 $\pm$ 0.90	102	2.79 $\pm$ 0.93	105	2.65 $\pm$ 0.95	104
5-6 mm	5.57 $\pm$ 0.50	98	5.46 $\pm$ 0.50	93	5.51 $\pm$ 0.50	88
7-8 mm	7.45 $\pm$ 0.50	40	7.50 $\pm$ 0.51	42	7.29 $\pm$ 0.46	48
All sites	4.70 $\pm$ 1.90	240	4.65 $\pm$ 1.93	240	4.63 $\pm$ 1.98	240
% BOP (GI = 2)	88.3		87.5		87.1	
% PI = 2 and 3	47.6		53.8		47.3	

n = number of pockets

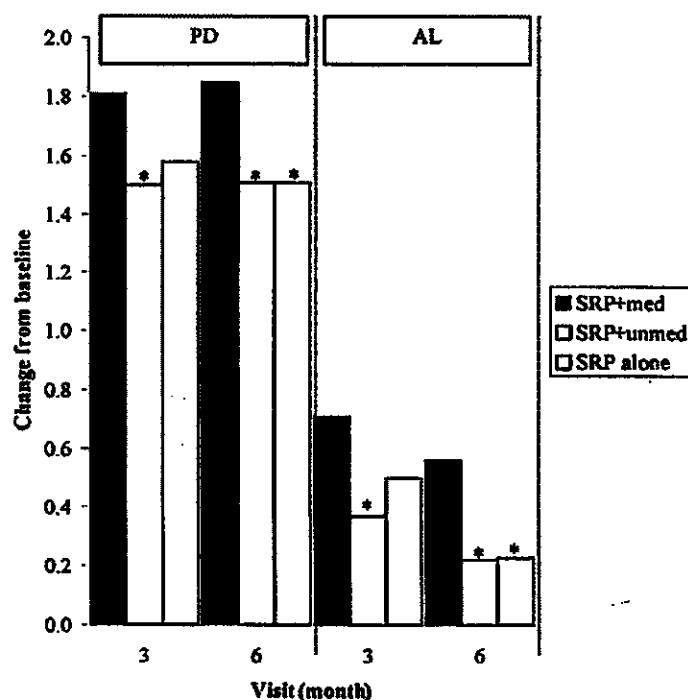


Figure 1. Probing pocket depth reduction and improvement of attachment level at 3 and 6 months for all pockets. \* Statistically significant compared to SRP+med ( $p \leq 0.05$ ).

target teeth was 120, 20 of which were incisors, 35 cuspids, 60 premolars and 5 molars. A summary of the clinical parameters at baseline is given in Table 2, showing no statistically significant differences among all the mean values. After baseline examination, the target teeth in each of the predetermined quadrants received the assigned treatment as previously described. Following chip insertion, there were only a few patients who reported about transient discomfort of the gingiva due to mechanical placement of the chips. None of the patients developed any adverse reactions or allergic conditions.

The number of treated sites was 240 in each treatment group. The mean changes in PD and AL are shown in Figure 1. At 3 months, the mean PD reduction in SRP+med showed significantly better improvement when compared to SRP+unmed ( $1.81\text{mm} \pm 1.49$  vs

$1.50\text{mm} \pm 1.42$ ,  $p = 0.05$ ). The improvement was significantly greater than both SRP+unmed and SRP alone at 6 months ( $1.85 \pm 1.45$  vs  $1.51 \pm 1.43$  and  $1.51 \pm 1.42$ ,  $p = 0.013$ ). As for improvement in AL, SRP+med showed significantly better improvement than that obtained in SRP+unmed at 3 months ( $0.71\text{mm} \pm 1.25$  vs  $0.37\text{mm} \pm 1.36$ ,  $p = 0.013$ ). The difference became statistically greater than both SRP+unmed and SRP alone at 6 months ( $0.56\text{mm} \pm 1.24$  vs  $0.22\text{mm} \pm 1.40$  and  $0.23\text{mm} \pm 1.30$  respectively,  $p = 0.006$ ).

Examination of the subset of pockets with PD = 7-8mm showed a similar but more pronounced decrease in the mean PD and AL with SRP+med providing significantly better results than SRP+unmed and SRP alone at both 3 and 6 months (Figure 2). At 3 months, the mean improvement in PD was  $3.68\text{mm} \pm 1.51$  for SRP+med versus  $2.74\text{mm} \pm 1.77$  for

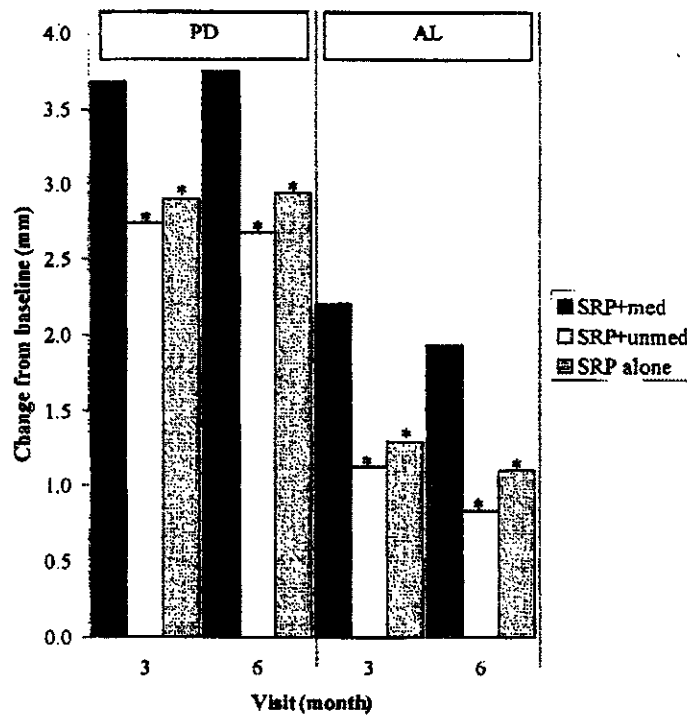


Figure 2. Probing pocket depth reduction and improvement of attachment level at 3 and 6 months for pockets 7–8mm.\* Statistically significant compared to SRP+med ( $p \leq 0.05$ ).

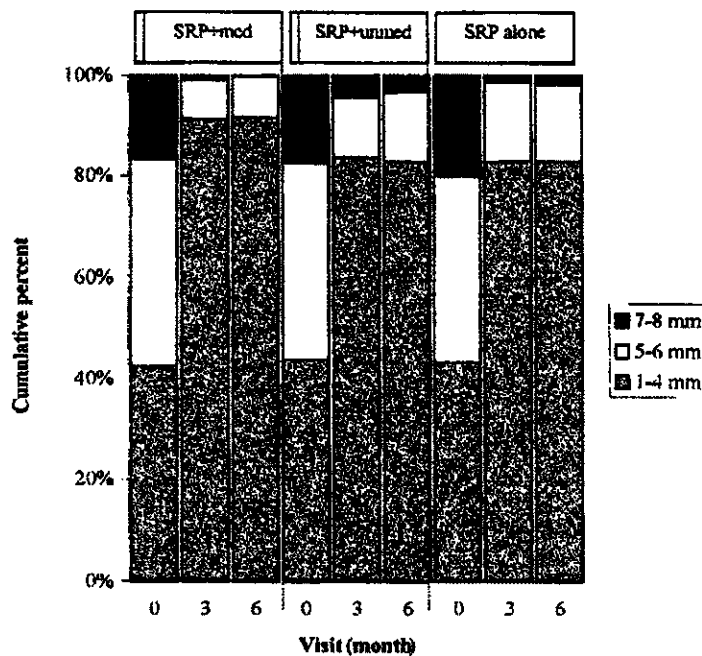


Figure 3. Distribution of probing pocket depth at baseline, 3 and 6 months.

SRP+unmed and  $2.90\text{mm} \pm 1.45$  for SRP alone ( $P = 0.018$ ) and at 6 months,  $3.75\text{mm} \pm 1.30$  for SRP+med versus  $2.67\text{mm} \pm 1.65$  for SRP+unmed and  $2.94\text{mm} \pm 1.12$  for SRP alone ( $p = 0.002$ ). Attachment gain was  $2.20\text{mm} \pm 1.18$  in SRP+med versus  $1.12\text{mm} \pm 1.76$  in SRP+unmed and  $1.29\text{mm} \pm 1.29$  in SRP alone at 3

months ( $P = 0.002$ ), and  $1.93\text{mm} \pm 1.16$  in SRP+med versus  $0.83\text{mm} \pm 1.79$  in SRP+unmed and  $1.10\text{mm} \pm 1.17$  in SRP alone at 6 months ( $p = 0.002$ ).

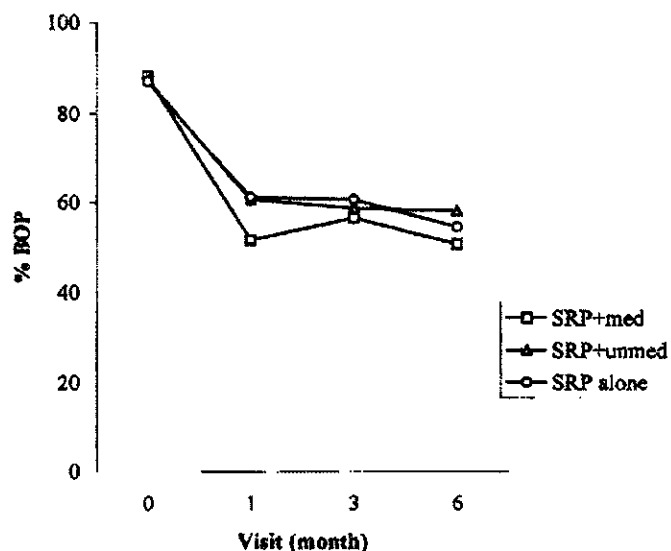
Distribution of probing pocket depth at the all examination visits is given in Figure 3. In all treatment groups, a dramatic shift from deeper pockets to shall-

**Table 3.** Percentage distribution of sites with PD improvement from baseline at 3 and 6 months for initial pockets 7–8mm

Time/Treatment	% of sites with PD improvement			
	0 mm	1–2 mm	3–4 mm	5–6 mm
<b>3 months</b>				
SRP+med	5.0	17.5	45.0	32.5
SRP+unmed	16.7	26.2	38.1	19.0
SRP alone	0	41.7	37.5	20.8
<b>6 months</b>				
SRP+med	0	17.5	52.5	30.0
SRP+unmed	9.5	40.5	35.7	14.3
SRP alone	0	39.6	56.3	4.2

**Table 4.** Percentage distribution of PI scores at baseline, 1st, 3rd and 6th month. Numbers of sites are provided in the parentheses

PI	Treatment group											
	Baseline	SRP+med			Baseline	SRP+unmed			Baseline	SRP alone		
		1	3	6		1	3	6		1	3	6
0	18.8% (15)	13.8% (11)	25.0% (20)	26.3% (21)	12.5% (10)	8.8% (7)	15.0% (12)	26.3% (21)	17.5% (14)	18.8% (15)	22.5% (18)	28.8% (23)
1	33.8% (27)	42.5% (34)	42.5% (34)	42.5% (34)	33.8% (27)	47.5% (38)	45.0% (36)	35.0% (28)	36.3% (29)	47.5% (38)	51.3% (41)	46.3% (37)
2	31.3% (25)	35.0% (28)	23.8% (19)	22.5% (18)	30.0% (24)	28.8% (23)	30.0% (24)	30.0% (24)	31.3% (25)	27.5% (22)	21.3% (17)	20.0% (16)
3	16.3% (13)	8.8% (7)	8.8% (7)	8.8% (7)	23.8% (19)	15.0% (12)	10.0% (8)	8.8% (7)	15.0% (12)	6.3% (5)	5.0% (4)	5.0% (4)

**Figure 4.** Percentage of BOP of target teeth in each treatment group at each examination visit.

lower ones was noted at 3 months. SRP+med, however, showed the highest proportion of 1–4mm pockets (91.3% vs 83.8% for SRP+unmed and 82.9% for SRP alone). The lowest proportion of 5–6mm pockets (7.9% vs 12.1% for SRP+unmed and 15.8% for SRP alone), and the lowest proportion of 7–8mm pockets (0.8% vs 4.2% for SRP+unmed and 1.3% for SRP alone). At 6 months, SRP+med presented with 0% 7–8mm pockets while 3.3% was observed in

SRP+unmed and 1.7% in SRP alone.

In Table 3, percentage distribution of PD improvement from baseline at 3 and 6 months for initial pockets 7–8mm is given. At the 3rd month visit, the highest percentage of sites with 3–4mm as well as 5–6mm PD improvement were observed in SRP+med group. At 6 months, the greatest percentage of sites with 5–6mm PD reduction was marked in SRP+med as compared to SRP+unmed and SRP alone.

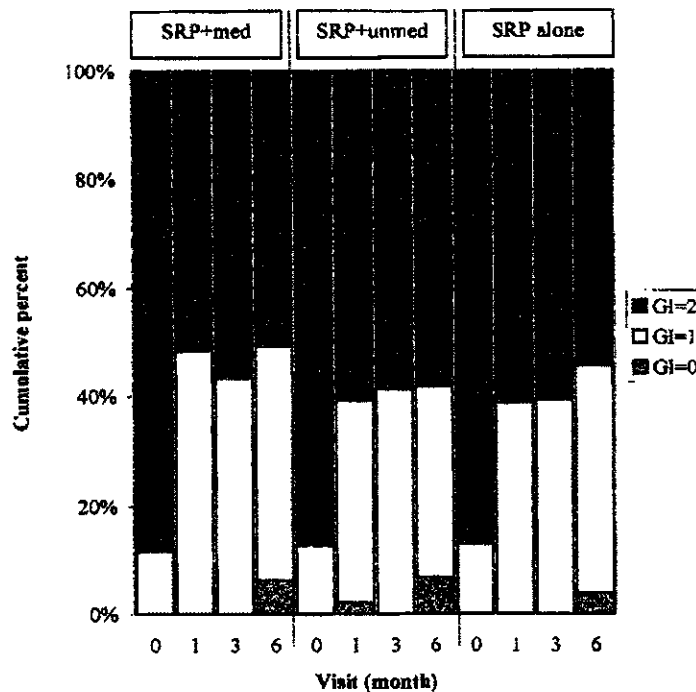


Figure 5. Distribution of GI scores of target teeth in each treatment group at each examination visit.

As for PI (Table 4), all groups generally showed decreasing proportion of PI score = 2 and 3, and increasing proportion of PI score = 0 and 1 from baseline towards 6 months. Figure 4 shows that all treatment groups exhibited a trend of decreasing bleeding sites. SRP+med, however, was marked with the lowest proportion of sites that still bled on probing compared to the other two groups at all the subsequent visits. In terms of GI (Figure 5), all groups were detected with decreasing proportion of GI score = 2 and increasing number of GI score = 1, at 1 month. While only a small proportion of sites with GI score = 0 was noticed in SRP+unmed (2.1%), SRP+med presented with the greatest percentage of GI score = 1 and the lowest percentage of GI score = 2. At 3 and 6 months, SRP+med continued to exhibit the lowest percentage of GI score = 2. All treatment groups, however, presented with some sites with GI score = 0 at the 6 month examination (6.3% in SRP+med, 6.7% in SRP+unmed and 3.8% in SRP alone).

## Discussion

The results of this study showed that treatment of periodontal pockets with a newly formulated herbal medicament from combined extracts of *Centella asiatica* and *Punica granatum* pericarp as a subgingival adjunct to SRP provided significantly greater improvement in PD compared to that obtained in the placebo group (SRP+unmed) and control group (SRP alone). This

adjunctive effect was apparent at 3 months compared to the placebo group and became even more pronounced at 6 months compared to both the placebo and control groups. Improvement in AL followed a trend similar to PD. In deeper pockets (7–8mm), the changes in PD and AL were statistically and clinically better in the test group (SRP+med).

In a study, investigation was carried out to evaluate the use of metronidazole and amoxicillin in the treatment of advanced periodontal disease. The attachment gain at 12 months was reported to be 1.8mm for initial pockets  $\geq 6$ mm in the SRP+antibiotics group and 1.3mm in the SRP alone group (Berglundh *et al.*, 1998). Our data seem to concur with these findings, although slight differences are noted. Attachment gain of 1.93mm for initial pockets 7–8mm at 6 months was observed in SRP+med and 1.10mm in SRP alone. Although there was a variation in the follow-up period of the two studies, it could be inferred that approximately the same amount of attachment gain may be obtained with the use of a different type of adjunctive agent other than the antibiotic family.

Another study was conducted to evaluate the efficacy of a degradable, subgingival delivery system containing chlorhexidine (CHX). Periodontal pockets with remaining PD of 5–8mm after SRP were entered into the experiment (Soslolac *et al.*, 1997). The mean improvements in PD and AL of the CHX treated group at 6 months were 1.16mm and 0.47mm respectively. The results from our study seem to be slightly better

with mean improvement of 1.85mm for PD and 0.56mm for AL in SRP+med, also at 6 months. However, comparison could only be made in the general view and within a certain limit. This is due to the different rationales in the use of the two adjunctive agents. In our study, the medicament was delivered following SRP at the time when enhancement of the healing was expected to take place from the beginning of the therapy. The purpose of the CHX delivery into the persisting pockets in the other study, on the other hand, was to eliminate or reduce the residual PD after the initial treatment had already been rendered.

In line with utilising adjunctive antibiotics aiming at modulating host response, subantimicrobial doxycycline (SDD) has been reported to provide additional benefits to standard periodontal therapy. In one study (Novak *et al.*, 2002), 20mg doxycycline hyclate tablets twice a day was administered for a period of 6 months, followed by a period of 3 months for drug washout, after completion of SRP in a group of severe, generalised periodontitis patients. At the end of the study at 9 months, the results for pockets with probing depth  $\geq$  7mm at baseline revealed significantly better PD improvement of 3.02mm in the adjunctive SDD group versus 1.42mm in the placebo group. Improvement in AL was reported to be 1.78mm in the SDD group versus 1.24mm in the placebo group, although the difference was noted to be neither clinically nor statistically significant between the two treatments. In comparison to this study, our data seem to show slightly better results both in terms of PD and AL improvements for initial pockets 7–8mm at 6 months (3.75mm for PD and 1.93mm for AL in the SRP+med group versus 2.67mm for PD and 0.83mm for AL in the SRP+unmed group respectively). Again, the outcomes could be compared only in general due to the differences between the two studies such as the route of ministration (systemic/local), follow-up period as well as other variations in the study design and settings.

When improvement of PD is taken into consideration, SRP+med showed quite impressive effects on PD reduction. This was manifested through the shift from deep pockets to shallow ones in greater proportions compared to SRP+unmed and SRP alone at both 3 and 6 months. At 6 months, no remaining sites with PD 7–8mm were observed in the SRP+med chip group. This enhancing effect on better PD reduction could be resulted from the astringent property of the tannin containing Punica extract in the medicated chips. The astringent action is usually accompanied by contraction of the tissue. As tissue shrinkage naturally occurs after SRP, therefore, it seems not too unreasonable to hypothesize that the additional PD reduction observed in the SRP+med chip group could be facilitated by the characteristic astringency mentioned above.

As for AL change, SRP+med showed greater improvement in AL compared to SRP+unmed and SRP alone. This augmenting effect may be postulated as a result of the stimulatory property of the Centella extract on collagen synthesis. As previously reported, the extract was found to increase collagen synthesis (Maquart *et al.*, 1990; Suguna *et al.*, 1996) and therefore may be accounted for contributing in the improved gain of attachment. However, further histologic studies may be required to assess true gain of attachment.

Although the results from this study seem to be quite promising, it was possible that the effects could not be so clearly observed in the presence of infection triggered by bacterial plaque. In this study, monthly full-mouth prophylaxis was reinforced in addition to meticulous oral hygiene instruction. The combined herbal medicament is primarily aimed at enhancing the healing of the periodontal tissues after a favourable environment is created. Theoretically, the Centella extract has the property of promoting collagen synthesis. Together with this, the tannin containing Punica extract may provide a synergistic effect. As tannins have affinity for proteins, they form bonds with collagen fibres. This property is stated to play an important role in collagen stabilisation (Leung and Foster, 1996).

As medicament vehicle controls have not always been present in clinical trials (Ainamo *et al.*, 1992) and evidence from other studies shows that positive results could be obtained from the activity of subgingivally placed vehicles themselves (Minabe *et al.*, 1989; Eckles *et al.*, 1990; Polson *et al.*, 1996), the SRP+unmed group was therefore included in this study. From the data derived, it was noted that no additional benefits were obtained in SRP+unmed as compared to SRP alone. Since this study was a split mouth design, the so called carry-over effect could have occurred. This could result in the reduction of the true difference among the treatment groups. However, this phenomenon, if real, did not seem to be so prominent, as the overall improvements in the pocket reduction and attachment level in the SRP+unmed and SRP alone groups were significantly inferior than those detected in the SRP+med group.

The initiation of periodontitis is multifactorial (Hallmon *et al.*, 1996). The scope of this study, however, did not concern investigation of influences from other factors such as patients' socioeconomic status, genetic factors, and varied individual host immune response. Exclusion of smoking subjects at the time of enrolment was made to avoid possible negative impact of tobacco consumption on the healing response. The results obtained from this clinical study are therefore sufficient to answer questions to a limited extent. Further investigations such as bacteriologic or histologic studies are required to gather more informa-

tion necessary to explain mechanisms or phenomena at different levels that may be responsible for the enhancing effects of *C. asiatica* in combination with *P. granatum* extracts on periodontal healing. Findings from this study also seem to be more related to single rooted teeth rather than multi-rooted teeth and the lack of adequate sample size may limit extrapolation of the results to larger populations.

### Acknowledgements

This research was supported by Mahidol University grant, 2000. The authors would also like to express their gratitude to Assoc. Prof. Suthi Athipanyakom and Assist. Prof. Sumol Yudhasaraprasithi, for their valuable advice in statistical analysis.

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