

Clinical Efficacy of Subgingivally Delivered Punica Granatum Chip and Gel in Management of Chronic Periodontitis Patients

Tyagi P,¹ Dodwad VM,² Vaish S,³ Chowdhery T,³ Gupta N,¹ Kukreja JB⁴

¹Department of Periodontology and Oral Implantology,
Shri Bankey Bihari Dental College,

²Department of Periodontology and Oral Implantology,
BVP Sangli,

³Department of Periodontology and Oral Implantology,
I.T.S Dental College,
Muradnagar, Ghaziabad,

⁴Department of Periodontology and Oral Implantology,
Teerthanker Mahaveer Dental College and Research Center, Moradabad, India.

Corresponding Author

Trishu Chowdhery

Department of Periodontology and Oral Implantology,

I.T.S Dental College and Hospital,

Muradnagar, Ghaziabad,

U.P, India.

E-mail: trishu.chowdhery@gmail.com

Citation

Tyagi P, Dodwad VM, Vaish S, Chowdhery T, Gupta N, Kukreja JB. Clinical Efficacy of Subgingivally Delivered Punica Granatum Chip and Gel in Management of Chronic Periodontitis Patients. *Kathmandu Univ Med J.* 2020;71(3):279-83.

ABSTRACT

Background

Periodontitis has a multifactorial etiology, and the pathogenic bacteria that reside in the subgingival area are the primary etiologic agent.

Objective

The study aimed to evaluate the clinical efficacy and benefits of herbal chip and gel made from extracts of Punica granatum as a subgingival adjunct to scaling and root planing (SRP).

Method

A randomized control clinical trial was conducted on 30 systemically healthy patient's sites having chronic periodontitis, and they were randomly allocated to into three treatment groups followed by Scaling and Root Planing in all patients. Group 1 - Ten patients received Scaling and Root Planing and Punica granatum chip at selected sites. Group 2 - Ten patients received Scaling and Root Planing and punica granatum gel at selected sites. Group 3 - Ten patients with Scaling and Root Planing alone. Clinical parameters were recorded at baseline, 21 days and at 45 days which included plaque index (PI), gingival index (GI), probing pocket depth (PPD) and relative attachment level (RAL).

Result

Plaque Index and Gingival index showed better reduction in group I compared to group II and group III at 21st day 45th day follow up. Analysing Pocket Probing Depth the intergroup comparison revealed similar results with maximum reduction being seen in group I from baseline to 21 and baseline to 45 days ($p < 0.001$). On analysing Relative Attachment Loss revealed reduction in all three groups with maximum reduction in group I from baseline to 45 days and reduction in group III was not statistically significant ($p < 0.090$).

Conclusion

The study concluded that Punica granatum chip as an adjunct to Scaling and Root Planing was more effective than Punica granatum gel and scaling and root planing alone.

KEY WORDS

Hydrolysable tannins, Periodontal regeneration, Punica granatum, Relative attachment level, Subgingival drug delivery

INTRODUCTION

Periodontitis has a multifactorial etiology, and the pathogenic subgingival microflora being the primary etiologic agent.^{1,2} Clinical trials indicate that meticulous scaling and root planing, in conjunction with a patient's proper plaque control, can arrest periodontitis.^{3,4} Locally delivered agents controls the re growth of bacteria following SRP. The administration of local drug delivery is associated with less systemic side effects, less drug resistance and enhanced penetration of the drug in the diseased site resulting in the elimination of harmful pathogens.^{5,6} Subgingival chlorhexidine, tetracycline fibers, subgingival minocycline, subgingival doxycycline, and subgingival metronidazole are commonly used.⁷ Currently, the use of herbal products in dentistry is increasing probably due to their easy availability, low cost and lesser side effects.⁸

Punica granatum belonging to family Punicaceae, commonly known as pomegranate.⁹ Pomegranate juice contains anthocyanins, glucose, ascorbic acid, ellagic acid, catechin, epigallocatechin, quercetin, rutin, iron and amino acids. They possess anti-atherosclerotic, antihypertensive, antiaging and potent antioxidative properties. The pericarp contains punicalagins, flavones, flavonones, and others containing anti-inflammatory, antimutagenic and antifungal activity.⁹ Its excellent anti-inflammatory effects along with the ability to scavenge free radicals, decrease macrophage oxidative stress and lipid peroxidation beneficial in treatment of periodontitis. Its anti-gingivitis effect can be attributed to flavonoids that influences direct antioxidant properties and indirect effects by enhancing the free radical scavenging activity of hepatic enzymes that includes catalase, super oxide dismutase and peroxidase.⁹

Thus, the aim of present study was to evaluate the effects and benefits of herbal chip and gel made from extracts of *Punica granatum* as a subgingival adjunct to scaling and root planning.

METHODS

This in vivo study was conducted in the Department of Periodontics, Institute for Technical Studies Centre for Dental Studies and Research Muradnagar, U.P, India after getting ethical clearance from the Institutional Ethical Committee *Punica granatum* chip and gel were prepared at, Sree Dattha Institute of Pharmacy, Sheriguda, Telangana, India. This study was conducted on 30 systemically healthy subjects, between 35-50 years of age, who visited the department with definite clinical evidence of periodontitis with at least three sites of periodontal pockets of ≥ 4 mm. They were informed about the study and their inclusion was purely voluntary and written informed consent was taken from the patient. Patients on anti-inflammatory drugs, systemic antibiotics in last three months, undergone periodontal therapy, smokers, pregnant women or lactating mothers, medically compromised patients, and mentally

challenged, and physically challenged cases were excluded from the study.

The patients were randomly allocated into three groups viz.

Group I – Ten patients received scaling and root planing followed by placement of *Punica granatum* chip at selected sites.

Group II – Ten patients received scaling and root planing followed by placement of *Punica granatum* gel at selected sites.

Group III – Ten patients received scaling and root planing alone.

Local Drug Delivery was followed by placement of periodontal dressing for group I and II, which was removed after a period of 14 days.

Patients were advised to follow normal oral hygiene instructions without any additional professional care for six months in all the three groups.

The following clinical parameters were recorded at the baseline, 21 days and 45 days in the three groups: Gingival Index (Fig. 1) and Plaque Index (Fig. 2).^{10,11} Pocket Probing depth (Fig. 3) and relative attachment level were recorded to nearest millimeter from reference point to the base of pocket was measured with UNC 15 probe using customized occlusal acrylic stents (Fig. 4).



Figure 1. Gingival Index



Figure 2. Plaque Index



Figure 3. Probing Depth



Figure 4. Relative Attachment Level

Preparation of *Punica granatum* chip

To prepare *Punica granatum* chip hydrolyzed collagen was dispersed in distilled water and solution was heated upto 85-90°C followed by mixing of extract of *Punica pericarp*. (The extract contains tannic acid, which also serves as collagen cross linking agent). The mixture was stirred continuously and poured evenly on to stainless mold plates and cooled down at room temperature and then dried in a refrigerator. The sheets were uniformly cut into 4 mm x 5 mm rectangular chip with one rounded end, using a chip cutting machine to resemble a U shape and sterilized by γ radiation.⁶ (Fig. 5)



Figure 5. Placement of Punica granatum Chip



Figure 6. Placement of Punica granatum Gel

Preparation of Punica granatum gel

Fresh pomegranates were used for the preparation of punica granatum gel. First the barks and juice were separated followed by drying of barks at room temperature for 5 days and then they were ground to powder form. An infusion was prepared with powdered material at a ratio of 100 g powder to 1000 ml distilled water, cooled at room temperature and filtered. Thereafter, 50 g of carboxymethylcellulose was added to the infusion (1000 ml) and the mixture was kept boiling until complete dissolution to obtain the 10% gel concentration. The pomegranate extract concentration used in this work was based on the findings of previous in vitro studies given by Somu et al. that tested the gel at different concentrations and found that the 10% concentration yielded the most favorable results.¹² A glycerin/ ethanol mixture (50 ml: 50 ml) was added and vigorously stirred for 15 minutes until gel formation took place. A very small amount of menthol (flavouring) and a conservative agent was then added. (Fig. 6)

All the data were collected and analyzed. Statistical data analysis was performed using SPSS 15.0 program package (SPSS Inc, Chicago, IL). All the clinical parameters were evaluated at baseline, 21 days and 45 days using ANOVA test and Bonferroni test. For all tests, a $p < 0.05$ was considered as statistically significant.

RESULTS

The presented study evaluated and compared the clinical efficacy of local drug delivery of punica granatum chip and gel as an adjunct to SRP and SRP alone in treating patients with chronic periodontitis. The study included 30 sites from 30 patients between age group of 35 to 50 years of age having probing depth of ≥ 4 mm; and clinically diagnosed with chronic periodontitis.

The evaluation was done by comparing plaque index (PI), gingival index (GI), pocket probing depth (PPD) and relative attachment level (RAL) in three groups at baseline, 21 days and 45 days on completion of procedure. Comparison of clinical finding in all three groups at various time interval has been shown in Table 1. Statistically significant difference in PI and GI were found at baseline, 21 days and 45 days in all the three groups. PPD and RAL was found to improve significantly in Group I and Group II but no significant difference was found in Group III.

Table 1. Comparison of clinical parameters in three groups at baseline, 21 days and 45 days.

Group	Clinical Parameters	Mean \pm SD			p-value
		Baseline	21 days	45 days	
Group I: (CHIP)	PI	2.00 \pm 0.47	1.10 \pm 0.48	0.90 \pm 0.70	<0.001*
	GI	1.80 \pm 0.42	0.90 \pm 0.32	0.50 \pm 0.48	<0.001*
	PPD	5.40 \pm 0.52	4.00 \pm 0.79	3.40 \pm 0.70	<0.001*
	RAL	10.70 \pm 0.82	8.70 \pm 1.08	7.80 \pm 0.95	<0.001*
Group II: (GEL)	PI	1.90 \pm 0.48	1.30 \pm 0.48	1.10 \pm 0.32	<0.001*
	GI	1.80 \pm 0.52	1.10 \pm 0.32	0.70 \pm 0.52	<0.001*
	PPD	5.30 \pm 0.00	4.30 \pm 0.32	3.80 \pm 0.48	<0.001*
	RAL	10.50 \pm 0.47	9.20 \pm 0.57	8.40 \pm 0.82	<0.045*
Group III: (CONTROL)	PI	2.00 \pm 0.47	1.60 \pm 0.52	1.40 \pm 0.42	<0.040*
	GI	1.90 \pm 0.32	1.30 \pm 0.32	1.00 \pm 0.32	0.060
	PPD	5.20 \pm 0.42	4.80 \pm 0.52	4.40 \pm 0.74	0.090
	RAL	10.40 \pm 0.97	9.80 \pm 1.26	9.40 \pm 1.10	

Table 2 evaluates the comparison of change in clinical parameters in all three groups at various time intervals. A reduction in PI, GI, PPD and RAL was seen in all three groups from baseline to 45 days and this difference was found to be statistically significant.

Table 2. Comparison of change in clinical parameters in three groups at baseline, 21 days and 45 days

Clinical parameters		Group I (Chip)	Group II (Gel)	Group III (Control)	p-value
		GI	Baseline - 21 days	0.90 \pm 0.32	
	Baseline - 45 days	1.30 \pm 0.48	1.10 \pm 0.57	0.90 \pm 0.32	0.018*
PI	Baseline - 21 days	0.90 \pm 0.57	0.60 \pm 0.70	0.40 \pm 0.52	0.019*
	Baseline - 45 days	1.10 \pm 0.32	0.80 \pm 0.63	0.60 \pm 0.70	0.036*
PPD	Baseline - 21 days	1.40 \pm 0.52	1.00 \pm 0.00	0.40 \pm 0.52	<0.001*
	Baseline - 45 days	2.00 \pm 0.67	1.50 \pm 0.53	0.80 \pm 0.42	<0.001*
RAL	Baseline - 21 days	1.90 \pm 0.32	1.30 \pm 0.48	0.60 \pm 0.52	<0.001*
	Baseline - 45 days	2.80 \pm 0.42	2.10 \pm 0.88	1.00 \pm 0.47	<0.001*

A greater reduction in gingival inflammation 0.90 \pm 0.32 and 1.30 \pm 0.48 was seen in group I from baseline to 21 days and baseline to 45 days respectively compared to those of group II and group III showing reduction in inflammation from 0.70 \pm 0.48 and 1.10 \pm 0.57 for group II and 0.60 \pm 0.52 and 0.90 \pm 0.32 for group III respectively.

Plaque accumulation was also seen to be reduced in group I 0.90 \pm 0.57 and 1.10 \pm 0.32 at baseline to 21 days and

baseline to 45 days compared to that of group II 0.60 ± 0.70 and 0.80 ± 0.63 ; and group III 0.40 ± 0.52 and 0.60 ± 0.70 respectively.

Comparison of probing pocket depth revealed similar results with maximum reduction being seen in Group I from baseline to 21 days and baseline to 45 days showing reduction of 1.40 ± 0.52 mm and 2.00 ± 0.67 mm whereas group II and group III were assessed to show 1.00 ± 0.00 mm and 1.50 ± 0.53 mm; and 0.40 ± 0.52 mm and 0.80 ± 0.42 mm respectively.

Relative attachment level gain in Group I, Group II and Group III was further evaluated and observed a gain of 1.90 ± 0.32 mm and 2.80 ± 0.42 mm; 1.30 ± 0.48 mm and 2.10 ± 0.88 mm; 0.60 ± 0.52 mm and 1.00 ± 0.47 mm from baseline to 21 days and baseline to 45 days respectively.

Use of punica granatum chip and gel as an adjunct to SRP were found to be statistically better in reduction of pocket probing depth and also in improvement of relative clinical attachment level from baseline to 45 days which was statistically significant.

DISCUSSION

The current study reveals effect of punica granatum chip and gel on clinical parameters as an adjunct to scaling and root planing and scaling and root planing alone in management of chronic periodontitis patients. Studies have revealed that due to the presence of phytochemicals such as phenolic compounds, tannins and flavonoids pomegranate may have value as natural antioxidant with its high polyphenol content.¹³ Various investigations done on both Gram positive and Gram negative non oral bacteria using ethanolic, water, methanolic and acetone extract of pomegranate have shown strong antimicrobial activity.¹⁴ A hydroalcoholic extract of pomegranate fruit was investigated for antibacterial effect on dental plaque microorganisms and was found to be effective against *Staphylococcus*, *Streptococcus*, *Klebsiella*, and *Proteus* species, as well as *Escherichia coli*. Most likely ellagitannin and punicalagin are fractions responsible for pomegranate's antibacterial activity.¹⁵

Significant reduction in PI was seen in Group I, II and III, however statistically significant result was seen from baseline to 45 days in group I and Group II. Bhadbhade et al. also had similar results in study conducted on pomegranate mouthrinse and found statistically significant difference ($p < 0.05$) between the chlorhexidine and placebo rinse and the pomegranate and placebo rinse, but no statistically significant difference was found between the chlorhexidine and pomegranate rinse with respect to the PI.¹⁶ The plaque inhibitory effects of pomegranate can be attributed to the ability to remove dental plaque bacteria from teeth.¹⁶

GI was also seen to be significantly reduced which was in accordance with the study conducted by DiSilvestro et al. who evaluated anti gingivitis effect of pomegranate

extract and concluded that pomegranate extract could produce an antigingivitis effect because pomegranate flavonoids possess direct antioxidant properties, such as a radical scavenging ability and indirect antioxidant effects such as induction of endogenous antioxidant enzymes.¹⁷ Oxidative stress is thought to be harmful to the gingiva and an enhancer of gingivitis development. Pomegranate flavonoids can exert anti-inflammatory effects such as a restriction of low stimuli activation of inflammatory processes.¹⁸

Pomegranate gel and chip showed clinically significant reduction in PPD and gain in RAL in Group I and Group II compared to SRP alone which was similar to study conducted by Sastravaha et al. who found significant improvement in pocket depth and attachment level in local delivery done using *Centella asiatica* and *Punica granatum* extracts following scaling and root planing compared to placebo.¹⁹ *Punica granatum* extract provides a synergistic action in collagen stabilization by its constituent tannin that have affinity for proteins, thus, forming bonds with collagen fibers. They observed significant improvement in the periodontal parameters and a decrease in the IL-1 β and IL-6 compared to baseline in follow up studies.²⁰

Both Group I and Group II showed better results compared to SRP alone, punica granatum in chip form seemed to be more efficient in improving the periodontal condition as it contains sufficient quantity of the drug to provide adequate therapeutic level and can be used as a beneficial adjunctive treatment modality to enhance periodontal health.

More clinical trials with similar designs using different concentrations of pomegranate along with microbiological and biochemical analysis are necessary to verify its action upon plaque microflora in vivo and severity of gingivitis and periodontitis.

CONCLUSION

The present study was designed to evaluate and compare the effect of Punica granatum chip and gel on clinical parameters placed after scaling and root planing and scaling and root planing alone in management of chronic periodontitis patients. From the results it was concluded that the Punica granatum chip therapy enhances the benefits of scaling and root planing in the treatment of periodontal pockets. This controlled drug delivery consists of sufficient quantity of the drug to provide adequate therapeutic level as a beneficial adjunctive treatment modality to enhance periodontal health. Local drug delivery with the use of Punica granatum chip is a simple and non-invasive technique. It reduces the recurrence of periodontal pathogens in periodontal pockets. As evident from this study, it can be assumed that Punica granatum chip along with scaling and root planing is more effective than Punica granatum gel and scaling and root planing alone.

The present study was a short term clinical trial which showed that Punica granatum chip was significantly better in restoring periodontal health as compared to Punica granatum gel and scaling and root planing alone. Future research will be needed to identify the real benefits of pomegranate as a therapeutic and preventive agent for periodontitis, in addition to its common use in popular medicine.

REFERENCES

- Behal R, Mali AM, Gilda SS, Paradkar AR. Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. *J Indian Soc Periodontol*. 2011;15(1):35-8.
- Vennila K, Elanchezhian S, Ilavarasu S. Efficacy of 10% whole Azadirachta indica (neem) chip as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. *Indian J Dent Res*. 2016;27(1):15-21.
- Chava VK and Vedula BD. Thermo-Reversible Green Tea Catechin Gel for Local Application in Chronic Periodontitis: A 4-Week Clinical Trial. *J Periodontol*. 2013;84(9):1290-6.
- Kinane DF and Radvar M. A Six-Month Comparison of Three Periodontal Local Antimicrobial Therapies in Persistent Periodontal Pockets. *J Periodontol*. 1999;70(1):1-7.
- Nandini N, Dodwad V, Arora K. Comparative evaluation of 1% Curcumin solution and 0.2% Chlorhexidine irrigation as an adjunct to scaling and root planing in management of chronic periodontitis: A clinico microbiological study. *J Pharma Biomed Sci*. 2012;14(14):1-6.
- Goodson JM, Offenbacher S, Farr DH and Hogan PE. Periodontal Disease Treatment by Local Drug Delivery. *J Periodontol*. 1985; 56(5):265-72.
- Anitha V, Rajesh P, Shanmugam M, Priya BM, Prabhu S, Shivakumar V. Comparative evaluation of natural curcumin and synthetic chlorhexidine in the management of chronic periodontitis as a local drug delivery: A clinical and microbiological study. *Indian J Dent Res*. 2015;26(1):53-6.
- Pistorius A, Willershausen B, Steinmeier EM, Kreisler M. Efficacy of Subgingival Irrigation Using Herbal Extracts on Gingival Inflammation. *J Periodontol*. 2003; 74(5): 616-22.
- Prasad D, Kunnaiah R. Punica granatum: A review on its potential role in treating periodontal disease. *J Indian Soc Periodontol*. 2014;18(4):428-32.
- Loe H, Silness J. periodontal disease in pregnancy. *Acta Odontol Scand*. 1963; 21:533-51.
- Turesky S, Gilmore ND, Glickman I. Reduced plaque formation by the chloromethyl analogue of vitamin C. *J Periodontol*. 1970; 41(1):41-3.
- Somu CA, Ravindra S, Ajith S, Ahamed MG. Efficacy of a herbal extract gel in the treatment of gingivitis: A clinical study. *J Ayurveda Integr Med*. 2012;3(2):85-0.
- Rajan S, Mahalakshmi S, Deepa VM, Sathya K, Shajitha S, Thirunalasundari T. Antioxidant potentials of Punica granatum fruit rind extracts. *Int J Pharm Pharm Sci*. 2011; 3(3):82-8.
- Sadeghian A, Ghorbani A, Mohamadi-Nejad A, Hassan Rakhshandeh. A. Antimicrobial activity of aqueous and methanolic extracts of pomegranate fruit skin. *Avicenna J Phytomed*. 2011; 1(2): 67-73.
- Menezes SM, Cordeiro LN, Viana GS. Punica granatum (pomegranate) extract is active against dental plaque. *J Herb Pharmacother*. 2006; 6(2):79-92.
- Bhadbhade S, Acharya A, Rodrigues S, Thakur S. The antiplaque efficacy of pomegranate mouthwash. *Quintessence Int*. 2011; 42(1):29-36.
- DiSilvestro RA, DiSilvestro DJ, DiSilvestro DJ. Pomegranate extract mouth rinsing effects on saliva measures relevant to gingivitis risk. *Phytother Res*. 2009;23(8):1123-7.
- Sastravaha G, P Yotnuengnit, P Booncong and P Sangtherapitkul. Adjunctive periodontal treatment with centella asiatica and punica granatum extracts. A preliminary study. *J Int Acad Periodontol*. 2003; 7(1):106-15.
- Sastravaha G, Gassmann G, Sangtherapitkul P, Grimm WD. Adjunctive periodontal treatment with Centella asiatica and Punica granatum extracts in supportive periodontal therapy. *J Int Acad Periodontol*. 2005;7(3):70-9.
- Salgado ADY, Maia JL, Pereira SL, Lemos TL, Mota OM. Antiplaque and Antigingivitis effects of a gel containing punica granatum linn extracts. A double blind clinical study in humans. *J Appl Oral Sci*. 2006; 14(3):162-6.

ACKNOWLEDGEMENT

We thank Dr. SA Sreenivas, Principal, Sree Dattha Institute of Pharmacy, Sheriguda, Telangana, India for helping us in preparation of punica granatum chip and gel form used in the study and Dr. Sukhvinder Singh Oberoi (MDS, Public Health Dentistry) for helping us with the statistics.