

## Original Research Article

# Efficacy of Pluronic F-127 gel containing green tea catechin extract on chronic periodontitis – A clinical study

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### Abstract

**Purpose:** To evaluate the efficacy of pluronic F-127 gel containing green tea catechin extract as a local drug delivery system in the treatment of chronic periodontitis.

**Methods:** A total of 20 chronic periodontitis patients participated as per the set inclusion and exclusion criteria. Complete scaling and root planing (SRP) was done for all subjects and pluronic F-127 gel containing green tea catechin was applied on one site. The contralateral site received SRP alone. The plaque index (PI), gingival index (GI), and probing pocket depth (PPD) were recorded at baseline and on the 28th day.

**Results:** At the 28th-day follow-up, green tea catechin tooth sites showed significantly lower mean scores (GI = 0.55,  $p = 0.30$  and PPD = 3.35 mm) than the corresponding SRP tooth sites (GI = 1.25, PI = 1.15, and PPD = 4.40 mm) ( $p < 0.05$ ).

**Conclusion:** When compared to scaling and root planing alone, the local drug delivery gel containing green tea catechin as an adjuvant was more effective in reducing the clinical parameters of periodontitis.

**Keywords:** Adjuvant therapy, *Camellia sinensis*, Local drug delivery, Periodontal pocket

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## INTRODUCTION

Chronic periodontitis is one of the most common oral health conditions. Among the various etiological agents, gram negative anaerobic micro-organisms such as *Treponema denticola*, *Porphyromonas gingivalis*, and *Tannerella forsythia* have significant role in the etiology of periodontal diseases [1].

The management of chronic periodontitis such as scaling and root planing and surgical therapies are aimed at eliminating the sub-gingival microflora responsible for local bacterial infection [2]. Complete bacterial elimination from periodontal pockets is often difficult due to the indigenous nature of the sub-gingival microflora, therefore the chances of repopulation after periodontal therapy is high [3]. Administration of systemic antibiotics specifically aimed at the

periodontal pathogens, as an adjunct to mechanical therapy, has been recommended [4]. However, drug concentrations in the gingival crevicular fluid through systemic anti-microbial therapy do not attain the minimum inhibitory concentration (MIC) against the pathogenic microorganisms for a sustained period [5]. Several local drug delivery (LDD) systems containing anti-microbial agents have been introduced as adjunct to mechanical therapies for overcoming this limitation.

The various forms of LDD systems developed for periodontal therapy include gels, films, strips, and chips containing chlorhexidine, metronidazole, and/or doxycycline [6]. In recent years, several herbal extracts have been tested for their therapeutic effects, such as anti-oxidant, anti-inflammatory, anti-arthritis, anti-bacterial, anti-angiogenic, and anti-viral properties, owing to the adverse effects of synthetic drugs [7]. Green tea is one of the herbal products that has gained popularity for its health-promoting effects [8].

Green tea catechins have been found to inhibit the growth of periodontal pathogens such as *P. gingivalis* [9]. Thermoreversible gels are the recently developed LDD system that degrade slowly in the biologic environment to form safer by-products that provide long-term retention of the anti-microbial agent at the desired site [10]. Pluronic F-127 (PF-127), one of polyethylene-polyoxypropylene block copolymers, possesses the properties of low toxicity, reverse thermal gelation, and high drug loading rendering it suitable for use as an LDD system [11].

The objective of this study was to evaluate the efficacy of PF-127 gel containing green tea catechin extract in the treatment of chronic periodontitis.

## METHODS

### Study subjects

All patients visiting the outpatient clinic of the Department of Periodontics at the KSR Institute of Dental Sciences and Research, India were evaluated to determine their eligibility for the study. The selection of subjects for the study was based on inclusion and exclusion criteria. Patients aged between 20 and 40 years and with a probing pocket depth of 4-6 mm in the molars were included. Patients were excluded if they revealed one or more of the following conditions: smoking or tobacco-chewing habit, pregnancy, indication for definitive surgical therapy, and/or history of allergies. Patients with history of

systemic diseases or of scaling and polishing of teeth within 6 months of commencement of the study were excluded. Patients on existing or past 3 months antibiotic therapy were also excluded. The purpose and outcomes of the research were explained to the patients, and a written informed consent was obtained from the subjects willing to participate in the research. Ethical approval was obtained from the Institutional Review Board, KSR Institute of Dental Sciences & Research, India (no. 008/KSRIDSR/EC/2011). The research was conducted in compliance with the Helsinki Declaration of 1975 and its subsequent amendments [12].

### Pluronic F-127 gel preparation

The green tea catechin extracts and the drug carrier polymer PF-127 were obtained from NESSO - Natural & Essential Oils Pvt. Ltd. The extract consisted of 90% catechins (polyphenols), of which 45 % consisted of epigallo catechin gallate (EGCg). The gel was prepared by adding 25 mg green tea extract to 5 g PF-127 polymer using the cold process. A carefully weighed amount of PF-127, sufficient to yield a concentration of 20 %, was slowly added to cold water (5 °C) with constant stirring. The dispersion was refrigerated until a clear solution was obtained (after approximately 5 hours). The solution would convert to gel form at room temperature after removal from the refrigerator.

### Study design

This research adopted a split-mouth randomized controlled study design (Figure 1). The two interventions included in the study were: scaling and root planing (SRP) alone and SRP followed by the placement of PF-127 gel, containing green tea catechin, in the periodontal pocket. The right and left quadrants were coded and only one molar satisfying the inclusion criteria of probing pocket depth of 4 - 6 mm was selected and recorded by the principal investigator. All subjects underwent phase I therapy including SRP at the first visit, and baseline scores for gingival index (GI), plaque index (PI), and probing pocket depth (PPD) were recorded (Figure 2 a). Only one investigator performed the clinical evaluations throughout the study. PF-127 gel containing green tea catechin was placed into the periodontal pocket of the molar randomly in either quadrant by the operating investigator. The molar receiving the PF-127 gel was coded for the test group, and the contralateral molar receiving SRP alone was coded for the control group (Figure 2 b).

After placing the PF-127 gel containing green tea catechin into the periodontal pocket, a periodontal dressing (Coe-Pak™, GC America Inc., IL, USA) was placed to protect the surgical site. The periodontal dressing was placed on the contralateral side only to ensure that the clinical examination during the follow-up visit was free of possible bias (Figure 2 c). All subjects were recalled after 14 days for re-application of the PF-127 gel. Only the operating investigator performed the re-application procedure in all the patients to obtain outcome investigator blinding. Follow-up evaluations were performed on the 28<sup>th</sup> day, and scores for clinical indices were recorded.

### Statistical analysis

The collected data were entered in a computer application (Microsoft Excel 2010) and subjected to statistical analysis using SPSS software version 16 (IBM Inc, Chicago, IL, USA). The data were analyzed using paired Student's and

independent sample t-tests. The level of significance was set at  $p < 0.05$ .

## RESULTS

At baseline, the SRP and green tea catechin tooth sites showed no statistically significant differences in their mean GI, PI, and PPD scores ( $p > 0.05$ ). At the 28<sup>th</sup>-day follow-up, the green tea catechin tooth sites showed significantly lower mean GI, PI, and PPD scores than the corresponding SRP tooth sites ( $p < 0.05$ , Table 1). Table 2 shows the mean GI, PI, and PPD scores of the SRP and green tea catechin tooth sites at baseline and at the 28<sup>th</sup>-day follow up. Both SRP and green tea catechin group showed statistically significant reduction in their mean GI, PI, and PPD scores from baseline to the 28<sup>th</sup>-day followup ( $p < 0.05$ , Table 2). The mean differences in GI, PI, and PPD scores were greater among the green tea catechin tooth sites than that among the SRP sites (Table 2).

**Table 1:** Gingival index, plaque index, and probing pocket depth scores at baseline and at the 28<sup>th</sup>-day follow up (N = 20)

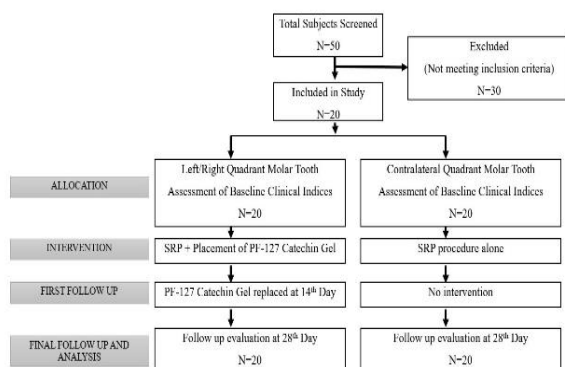
Parameter	Group	Mean±SD	t	df	P-value	
Gingival index	Baseline	SRP	2.30±0.571	0.282	38	0.780
		Green tea catechin	2.25±0.550			
	After 28 days	SRP	1.25±0.550	3.829	38	0.000*
		Green tea catechin	0.55±0.605			
Plaque index	Baseline	SRP	2.05±0.224	0.000	38	1.000
		Green tea catechin	2.05±0.224			
	After 28 days	SRP	1.15±0.366	6.378	38	0.000*
		Green tea catechin	0.30±0.470			
Probing pocket depth	Baseline	SRP	5.25±0.55	0.902	38	0.373
		Green tea catechin	5.05±0.83			
	After 28 days	SRP	4.40±0.82	4.653	38	0.000*
		green tea catechin	3.35±0.59			

\*Statistically significant difference; SRP: scaling and root planing; SD: standard deviation

**Table 2:** Gingival index, plaque index, and probing pocket depth scores within groups at baseline and at the 28<sup>th</sup>-day follow up (n = 28).

Parameter	Assessment	Mean±SD	Mean difference	t	df	P-value	
Gingival index	SRP	Baseline	2.30±0.571		9.200	19	0.000*
		after 28 days	1.25±0.550	1.05			
	Green tea catechin	Baseline	2.25±0.550		10.376	19	0.000*
		after 28 days	0.55±0.605	1.70			
Plaque index	SRP	Baseline	2.05±0.224		13.077	19	0.000*
		after 28 days	1.15±0.366	0.9			
	Green tea catechin	Baseline	2.05±0.224		14.226	19	0.000*
		after 28 days	0.30±0.470	1.75			
Probing pocket depth	SRP	Baseline	5.25±0.550		5.667	19	0.000*
		After 28 Days	4.40±0.821	0.85			
	Green tea catechin	Baseline	5.05±0.826		13.309	19	0.000*
		after 28 days	3.35±0.587	1.7			

\*Statistically significant; SRP: scaling and root planing; SD: standard deviation



**Figure 1:** Flow chart of study design



(a)



(b)



(c)

**Figure 2:** Location of thermoreversible gel containing catechins. (a) Pre-operative probing pocket depth; (b) Insertion of PF-127 gel with Green tea extract; (c) Periodontal pack in place

## DISCUSSION

Consumption of the beverage tea originated in China around 2700 BC [13]. Based on the

manufacturing process, tea can be broadly classified into three main types: fermented black and red tea, semi-fermented oolong tea, and non-fermented green tea. The most widely produced and consumed variety is the black tea, followed by the green and oolong tea. Green tea is manufactured from the shrub *Camelia sinensis*, which is known for its health-promoting effects. The major constituents of green tea are polyphenols, which comprise flavanols, flavonoids, and phenolic acids. Flavanols are also known as catechins. Catechin, gallocatechin, epicatechin, epigallocatechin, epicatechin gallate (ECG), and epigallocatechin gallate (EGCg) are the primary catechins in green tea. EGCg is among the most studied polyphenol component of green tea. Catechins possess anti-oxidant, anti-carcinogenic, and anti-inflammatory properties [14,15]. Recently, the anti-microbial property of catechins has become a subject of extensive research [16].

Development of chronic periodontitis in adults is influenced by a combination of periodontal pathogens, host, and environmental factors. Tissue damage is aggravated by excessive release of proteolytic enzymes and reactive oxygen species [17]. There is a steady release in reactive oxygen species such as superoxide ( $O_2^-$ ), hydroxyl (OH), and nitric oxide (NO) in the healthy periodontium. The tissue-damaging effects of free radicals could be the result of mutations in DNA, which eventually could lead to cell death. Free radicals trigger interleukin (IL)-1-induced osteoclastic bone resorption [14]. Antioxidants in green tea can neutralize the harmful effects of free radicals and promote the health of the periodontium.

Mechanical periodontal therapy such as SRP remains the conventional first line therapy for the elimination of local etiological factors. However, complete elimination of bacterial plaque is difficult by the use of mechanical periodontal therapy alone. Adjuvant systemic antibiotic therapy to mechanical periodontal therapy requires high antibiotic dosages for a prolonged period to attain the necessary MIC in the periodontal pockets.

Advances in the management of periodontal diseases to overcome the limitations of systemic route of drug delivery have led to the development of several LDD systems. Use of high-viscosity hydrophilic gels is one of the approaches for controlled drug delivery at desired site. Thermoreversible gels are newer pharmaceutical formulations that have the capacity to make, break, and/or modify the bonds responsible for holding the molecular network.

They are liquid when refrigerated (4 – 5 °C), but gel upon warming to room temperature [18]. PF-127 has been used as a carrier for various routes of drug administration including ocular application [19]. This is the first study to use green tea catechin extract coupled with PF-127 gel in the management of chronic periodontitis.

In this study, both test and control group tooth sites, i.e., SRP with green tea catechin and SRP alone, respectively, showed significant reduction in clinical parameters of periodontitis. However, the reduction in mean scores was greater with green tea catechin adjuvant group for all the clinical parameters. Mechanical therapies are simply based on the elimination of local etiological factors. Hence, improvement in the clinical indices is expected. The plaque-inhibitory effects of green tea catechins could be the result of the anti-bacterial properties of catechin fractions. ECG is found to be effective in mitigating bacterial virulence by neutralizing toxic metabolites. Penetration of catechin gallates by displacing lipoteichoic acid of the bacterial lipid bilayer has shown to modulate the sensitivity of methicillin-resistant staphylococcus aureus to  $\beta$ -lactam antibiotics [13].

Green tea extracts in mouthwashes are effective in reducing plaque scores [20]. The reduction in GI scores observed in this study is in agreement with the results of similar studies that used strips impregnated with green tea extracts [21,22]. EGCg inhibits interleukin (IL)-1, -6, and -8 and enzymes such as lipooxygenase, cyclooxygenase, and matrix metalloproteinase-1, which are responsible for the production of several other inflammatory mediators [23]. The anti-collagenase property of catechins prevents bone resorption and thereby aids in the reduction in pocket depths [24]. Green tea catechins are known inhibitors of cysteine proteinases (Arg-gingipain and Lys-gingipain) of *P. gingivalis* and protein tyrosine phosphatase of *Prevotella intermedia*, which are considered potent virulence factors in the development of periodontitis, and thus reduce the potential periodontal breakdown [25,26].

This study attempted to test the efficacy of green tea extracts in the treatment of chronic periodontitis using PF-127 gel as an LDD vehicle. The limitations of this study include a small sample size and the incorporation of individual tooth sites in analyzing the interventions. Further studies with larger sample sizes involving full-mouth interventions need to be conducted to validate the use of green tea extracts for the treatment of chronic periodontitis.

## CONCLUSION

When compared to scaling and root planing alone, the local drug delivery gel containing green tea catechin as an adjuvant is more effective in reducing the clinical parameters of periodontitis. Thus, green tea catechins is a potentially effective local drug delivery agent in adjunct to conventional periodontal therapy in moderate to deep periodontal pockets.

## DECLARATIONS

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### Conflict of interest

No conflict of interest is associated with this work.

### Contribution of authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors.

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