

# Evaluation of Curcumin 10 mg (Curenex<sup>®</sup>) as Local Drug Delivery Adjunct in the Treatment of Chronic Periodontitis: A Clinical Trial

<sup>1</sup>Priyanka Shivanand, <sup>2</sup>Kangowkar V Vandana, <sup>3</sup>Kharidhi L Vandana, <sup>4</sup>Shobha Prakash

## ABSTRACT

**Introduction:** Plaque control combined with scaling and root planing (SRP) is an effective therapeutic modality for arresting periodontitis. Due to limitation of mechanical therapy such as SRP, local application of drugs has been initiated. Turmeric is not just a remedy, it is the “cure.”

**Materials and methods:** A total of 14 patients diagnosed with chronic periodontitis were included in a split mouth study. Using the split study protocol, upper arch received SRP alone (control group) and lower arch received SRP + intrapocket application of curcumin (CU) 10 mg (Curenex<sup>®</sup>; experimental group) in selected sites. Plaque index (PI), gingival bleeding index (GBI), gingival index (GI), probing pocket depth (PPD), and clinical attachment level (CAL) were assessed at baseline and 21st, 30th, and 90th day.

**Results:** Intragroup analysis and intergroup analysis showed significant reduction ( $p < 0.000$ ) in clinical analysis from baseline to 90th day with comparatively better outcomes in the SRP + CU group. No adverse effects were reported.

**Conclusion:** Curcumin has a number of medicinal properties; it is beneficial in many ways and acts as a capable adjunct to SRP in the treatment of periodontal disease.

**Keywords:** Curcumin, Local drug delivery, Periodontitis, Scaling and root planing.

**How to cite this article:** Shivanand P, Vandana KV, Vandana KL, Prakash S. Evaluation of Curcumin 10 mg (Curenex<sup>®</sup>) as Local Drug Delivery Adjunct in the Treatment of Chronic Periodontitis: A Clinical Trial. CODS J Dent 2016;8(2):59-63.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Periodontitis is an infectious inflammatory disease of the supporting tissues of teeth<sup>1</sup> involving multiple interactions of biofilm with host immune-inflammatory response

and eventual alterations in bone and connective tissue homeostasis.<sup>2</sup> This disproportion between bacterial virulence and host defense ability<sup>1</sup> determines the initiation of periodontal disease.<sup>3</sup>

The foremost pathogens including *Porphyromonas gingivalis*, *Prevotella intermedia*, and *Aggregatibacter actinomycetemcomitans* from more than 300 species comprise the dental biofilm.<sup>3</sup> The focal intent of periodontal therapy is to rehabilitate the inflamed tissue and suppress the diseased pockets and the load of pathogenic bacteria.<sup>4</sup> Scaling and root planing is customarily practiced in the treatment of periodontal diseases and epitomized as the “gold standard” of mechanical therapy.<sup>5</sup>

Neither all the patients, nor all the sites reciprocate uniformly and appropriately to conventional mechanical therapy.<sup>6</sup> Accordingly, administering systemic and local antibiotics and antiseptics has been successfully used to treat moderate-to-severe periodontal disease. To avoid the drawback of the systemic approach, local delivery systems have been introduced that<sup>7</sup> can attain 100-fold higher concentrations of drug delivery<sup>8</sup> of the antibiotic or antiseptic agents.<sup>7</sup>

Alternative therapies for treating periodontal disease embrace the use of diverse of herbs that can help to suppress infection and inflammation associated with periodontal diseases.<sup>9</sup>

Medicinal plants are a long-established treatment used for innumerable human diseases since ages in many parts of the world. Following the hunt for alternatives led to the extraction of natural phytochemicals from plants, which have been used as traditional medicines, in order to study alternative sources.<sup>10</sup>

Turmeric is a dietary spice, coloring agent in foods and textiles, and used in treatment for a diversity of ailments. The most active element of turmeric is CU, which composes 2 to 5% of the spice and has been effective in acute as well as chronic conditions of inflammation.

It has properties, such as being an antioxidant, antimicrobial, anti-inflammatory, antiseptic, immunostimulant, hepatoprotective, and antimutagenic agent, thus making it useful in dentistry.

Curcumin is a natural anti-inflammatory agent with varied biologic and medicinal attributes. Its therapeutic

<sup>1</sup>Postgraduate Student, <sup>2</sup>Professor, <sup>3</sup>Senior Professor, <sup>4</sup>Head and Senior Professor

<sup>1-4</sup>Department of Periodontics, College of Dental Sciences Davangere, Karnataka, India

**Corresponding Author:** Priyanka Shivanand, Postgraduate Student, Department of Periodontics, College of Dental Sciences Davangere, Karnataka, India, Phone: +919901851519, e-mail: cooldent7@gmail.com

tic implementation has been observed in a variety of conditions, with few studies analyzing the efficacy of CU as a local drug delivery agent in the treatment of periodontitis.<sup>11</sup>

Nagasri et al<sup>12</sup> evaluated the efficacy of the adjunctive use of CU with SRP in the treatment of chronic periodontitis, which resulted in the reduction of PI, GI, PPD, CAL, and microbiologic parameters. This leads one to conclude that the local application of CU in conjunction with SRP enhances periodontal parameters with a favorable influence in patients with chronic periodontitis.

The frequent use and misuse of the currently used therapeutic agents have led to the evolution of resistant strains of common pathogens as well as increased incidence of adverse effects associated with their usage. Hence, the search for alternative products continues. The natural phytochemicals isolated from plants, which have been used as traditional medicines, are considered as a good alternative source.<sup>13</sup>

Here, an attempt was made to clinically evaluate Curenext<sup>®</sup> that contains CU 10 mg as a local drug delivery agent in the treatment of a chronic periodontitis patient.

## MATERIALS AND METHODS

A total of 14 systemically healthy chronic periodontitis patients selected from the outpatient Department of Periodontics, College of Dental Sciences, Davangere, Karnataka, India, were included in this double-blinded, split-mouth clinical trial to evaluate the effect of CU 10 mg (Curenext<sup>®</sup>). The study protocol was approved by the Institutional Ethical Board with Ref. No. CODS/IRB/19/2013-2014 affiliated to the Rajiv Gandhi University of Health Sciences, Jayanagar, Bengaluru, India.

The 14 patients selected had mild-to-moderate periodontal pockets (5–7 mm) clinically with radiographic evidence of bone loss.<sup>14</sup> The exclusion criteria were patients who were with ongoing antibiotic treatment or any systemic disease, as well as patients who were pregnant, lactating, smokers, alcoholic, or who had undergone any surgical or nonsurgical therapy within the 6 months prior to the start of the study. All patients gave their informed consent.

### Study Design

The clinical parameters recorded were: PI,<sup>15</sup> GI,<sup>15</sup> GBI,<sup>16</sup> PPD,<sup>17</sup> and CAL.<sup>17</sup> The PPD and CAL were measured for the selected teeth using University of North Carolina 15 probe. The treatment modalities were divided according to the split-mouth protocol.<sup>18</sup> The upper arch was the control group where SRP was performed and the lower arch was experimental group, which received SRP + CU. The clinical parameters were recorded at baseline, and



Fig. 1: Local delivery of Curenext<sup>®</sup> gel using disposable syringe

on the 21st, 30th, and 90th day. The main investigator recorded the clinical parameters throughout the study, who was masked on the treatment type.

Curenext oral gel 10 gm (Ayurvedic proprietary medicine) containing *Curcuma longa* extract (Abbott Health care Pvt. Ltd., Chembur, Mumbai India, Mfg. Lic. No.: NK/AYU/006-A/10) was taken in a disposable syringe and dispensed subgingivally to the base of the pocket at the test site (Fig. 1).

Patients were instructed to perform regular oral hygiene habits, and report on the 7th day for removal of COE-PAK placed at the experimental site and on the subsequent 21st, 30th, and 90th day periods for evaluation.

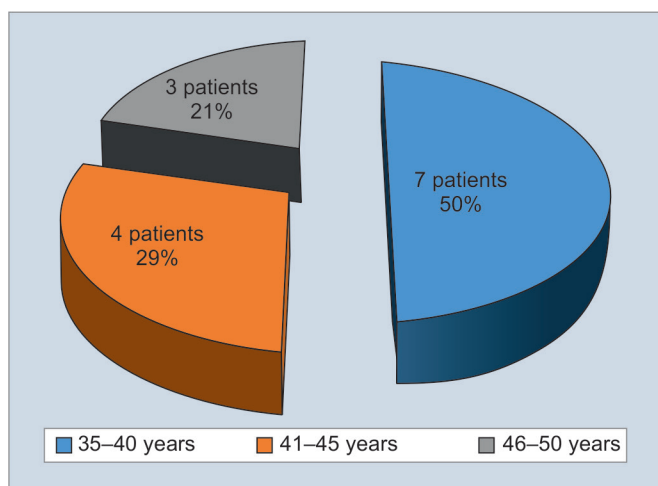
### Statistical Analysis

Statistical analysis was done with Statistical Package for the Social Sciences (version 20) USA. Statistical tests employed repeated measures of analysis of variance test used for intragroup comparisons at different time intervals followed by unpaired t-test for intergroup comparisons.

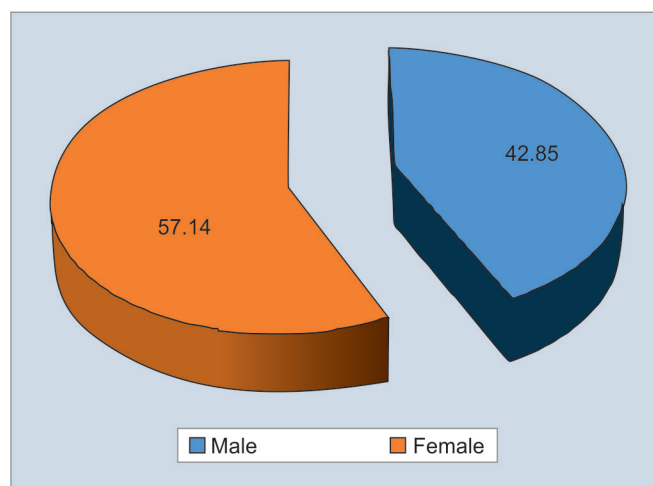
## RESULTS

The study included six males and eight females in the age group of 35 to 50 years (Graphs 1 and 2). The clinical parameters at baseline between the experimental and control groups were statistically nonsignificant (Table 1). On intragroup comparison and intergroup comparison of SRP group and SRP + CU group, clinical parameters showed statistically high significance from baseline to 90th day (Tables 2 to 6).

At the end of 90 days in both the SRP group and SRP + CU group, the PI, GI, GBI, PPD, and CAL showed statistically significant reduction within the groups. The GBI reduction was highly statistical significant ( $p < 0.000$ ) in the SRP + CU group than the SRP group.



Graph 1: Age distribution among patients



Graph 2: Demographic data

Table 1: Baseline results—clinical parameters

Groups	PI	GI	GBI	PD	CAL
SRP	2.31 ± 0.55	2.37 ± 0.51	89.47 ± 28.88	6.36 ± 1.35	5.96 ± 1.56
SRP + CU	2.43 ± 0.50	2.54 ± 0.41	95.08 ± 12.85	6.65 ± 1.08	5.50 ± 1.18
p-value*	0.55 NS	0.33 NS	0.38 NS	0.53 NS	0.38 NS

\*p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; NS: Not significant

Table 2: Intragroup and intergroup comparison: PI

Group PI	Baseline	21 days	30 days	90 days	Mean reduction	p-value
SRP	2.31 ± 0.55	1.09 ± 0.11	1.04 ± 0.06	1.06 ± 0.08	1.24 ± 0.54	0 (HS)
SRP + CU	2.43 ± 0.50	1.10 ± 0.10	1.04 ± 0.04	1.12 ± 0.28	1.31 ± 0.60	0 (HS)
p-value	0.55 (NS)	0.10	0.009	0.045 (S)		

p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; HS: Highly significant; NS: Not significant; S: Significant

Table 3: Intragroup and intergroup comparison: GI

Group GI	Baseline	21 days	30 days	90 days	Mean reduction	p-value
SRP	2.37 ± 0.51	1.20 ± 0.28	0.97 ± 0.35	0.47 ± 0.38	1.89 ± 0.72	0 (HS)
SRP + CU	2.54 ± 0.41	1.34 ± 0.44	0.88 ± 0.43	0.27 ± 0.37	2.26 ± 0.59	0 (HS)
p-value	0.33 (NS)	0.2	0.006	0.05 (S)		

p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; HS: Highly significant; NS: Not significant; S: Significant

Table 4: Intragroup and intergroup comparison: GBI

Group GBI	Baseline	21 days	30 days	90 days	Mean reduction	p-value
SRP	89.47 ± 28.88	36.65 ± 13.62	15.75 ± 5.86	6.54 ± 5.17	89.32 ± 14.39	0 (HS)
SRP + CU	95.08 ± 12.85	28.39 ± 14.47	10.77 ± 7.28	4.24 ± 4.64	90.84 ± 12.94	0 (HS)
p-value	0.38 (NS)	0.19	0.005 (S)	0.001 (HS)		

p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; HS: Highly significant; NS: Not significant; S: Significant

Table 5: Intragroup and intergroup comparison: PPD

Group PD	Baseline	21 days	30 days	90 days	Mean reduction	p-value
SRP	6.36 ± 1.35	5.55 ± 0.87	4.69 ± 0.89	3.81 ± 0.76	2.55 ± 1.42	0 (HS)
SRP + CU	6.65 ± 1.08	5.57 ± 0.86	4.88 ± 0.80	3.62 ± 0.57	3.03 ± 1.03	0 (HS)
p-value	0.53 (NS)	0.34	0.010	0.05 (S)		

p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; HS: Highly significant; NS: Not significant; S: Significant

Table 6: Intragroup and intergroup comparison: CAL

Group CAL	Baseline	21 days	30 days	90 days	Mean reduction	p-value
SRP	5.96 ± 1.56	5.62 ± 1.01	5.06 ± 0.78	5.04 ± 0.70	0.91 ± 1.72	0 (HS)
SRP + CU	5.50 ± 1.18	5.68 ± 1.50	5.27 ± 0.94	5.36 ± 0.58	0.14 ± 0.86	0 (HS)
p-value	0.38 (NS)	0.25	0.007	0.045 (S)		

p-value ≤0.05 is significant; p-value ≤0.001 is highly significant; HS: Highly significant; NS: Not significant; S: Significant

## DISCUSSION

With microbial challenges, factors, such as genetics, environment, and host factors also play a role in the pathogenesis of periodontitis. The most common form encountered is chronic periodontitis, characterized by a slow, gradual loss of periodontal attachment.<sup>19</sup>

For periodontopathic bacteria to initiate periodontitis, it is essential that they are able to colonize in the subgingival pockets and produce virulence factors that directly damage host tissue. Thus, a major goal of non-surgical periodontal therapy is to suppress, to the extent possible, the subgingival pathogenic microbial flora and, thereby, significantly reduce or eliminate the associated inflammatory lesion.

The traditional treatment modality of SRP remains the “gold standard” for the nonsurgical management of periodontitis.

Currently, the use of herbal products in dentistry is ever increasing. This can be attributed to their easy availability, low cost, and fewer side effects.<sup>20</sup> One such herbal product is turmeric (*C. longa*). Commercial available preparations of “CU” contain approximately 77% CU, 17% demethoxycurcumin, and 3% bisdemethoxycurcumin.

The current study evaluated the clinical parameters at baseline, 21st, 30th, and 90th day which is similar to a study conducted by Paolantonio et al<sup>21</sup> on clinical, microbiologic, and biochemical effects of subgingival administration of a xanthan-based chlorhexidine gel in the treatment of periodontitis, where clinical microbiological and biochemical parameters were measured at 0, 60, and 180 days. The study showed the reduction of the condition, which was due to the reduction of the supragingival plaque following SRP and oral hygiene practices instructed.

In the present study, SRP + CU obtained significant reduction in PI, GI, GBI, and PD reduction followed by SRP in accordance to that reported by Anuradha et al<sup>22</sup> and Gottumukkala et al.<sup>23</sup>

Curcumin has wound healing and anti-inflammatory properties by which it reduces the inflammatory mediators generated via arachidonic acid pathway and, thereby, reduces inflammatory edema and vascular engorgement of connective tissue. Curcumin as such has anti-inflammatory, antioxidant, antimicrobial, hepatoprotective, immunostimulant, antiseptic, and antimutagenic properties, which may also help in the improvement in clinical and microbiologic parameters following its use as an adjunct in periodontal therapy.<sup>13</sup>

Intragroup comparisons of the mean PPD and CAL scores showed significant improvement in both the groups, although intergroup comparison showed slight, but not statistically significant reduction ( $p < 0.045$ ) from

baseline to 90 days. This is in accordance with a study by Nagasri et al,<sup>12</sup> where in a randomized split-mouth, single-blinded study, they evaluated the efficacy of the adjunctive use of CU with SRP in the treatment of chronic periodontitis. The researchers stated that the mechanisms of the anti-inflammatory action of CU, which modulates the inflammatory response, are by inhibiting the production of proinflammatory cytokines, repressing the activation of activator protein 1 and nuclear factor kappa B, inhibiting the biosynthesis of inflammatory prostaglandins, and enhancing neutrophil function during the inflammatory response. Slight, but not statistically significant reduction ( $p = 0.473$ ) in mean CAL levels were due to increased levels of transforming growth factor- $\beta$ 1 in healing tissue, earlier re-epithelialization, improved neovascularization, reduced inflammatory cell infiltration, increased collagen and fibroblastic cell numbers, and enhanced wound repair in sites treated with CU.

Anitha et al<sup>20</sup> noticed CU results in the effective improvement of clinical and microbiologic parameters following its use as an adjunct in periodontal therapy. Curcumin is stated to possess a similar mode of action as the nonsteroidal anti-inflammatory drugs, such as aspirin, with an advantage in that it selectively inhibits the synthesis of prostaglandins and thromboxane, while not affecting the synthesis of prostacyclin. Hence, CU, being an Ayurvedic herb, is an excellent alternative to chlorhexidine due to minimal side effects.

No adverse reactions were reported by the patient or observed by the clinician during the current study period similar to other studies.<sup>22</sup>

Overall, CU 10 mg (Curenex<sup>®</sup>) brought about clinical significant reduction and acts as a potential herbal adjunctive agent for supportive periodontal therapy.

## CONCLUSION

The present randomized controlled trial confirms the plaque inhibition (antiplaque), anti-inflammatory, and antibacterial effects of CU 10 mg (Curenex<sup>®</sup>). Hence, CU 10 mg (Curenex<sup>®</sup>) could be recommended during non-surgical therapy and maintenance phase of periodontal treatment. Considering the beneficial effects, this could serve a useful adjunct in periodontal treatment in systemic situations wherein SRP is contraindicated. Further studies with frequent intervals of application would be required to observe if there would be any greater effects with the increase in frequency.

## ACKNOWLEDGMENT

Authors would like to thank Dr Kishore G Bhat, Professor and Head of Department, Dr Vinayak Joshi, Professor, and Ms Preeti, Lecturer, Department of Microbiology,

Molecular Biology and Immunology, Maratha Mandal's NGH Institute of Dental Sciences and Research Centre, Belgaum, Karnataka for the microbiological and biochemical evaluations of the study.

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