

## Antimicrobial And Antibiofilm Activity of 5% Curcumin Gel Against Periodontal Pathogens

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### Abstract

**Background:** Periodontitis is a chronic inflammatory condition affecting the tissues supporting tooth that leads to connective attachment loss and alveolar bone. Although, traditional scaling and root planing (SRP) reduces microbial deposits efficiently, often fails to completely eliminate microorganisms residing in deep periodontal pockets and complex root anatomies, leading to possible reinfection. Adjunctive therapeutic agents have been explored to enhance the effectiveness of SRP. Curcumin, a natural component of *Curcuma longa*, widely acknowledged for anti-inflammatory, anti-oxidant and anti-bacterial properties acts as a beneficial adjunct by local drug delivery.

**Aim:** To assess the antimicrobial and antibiofilm activity efficacy of a 5% curcumin local drug- delivery gel as an adjunct to Scaling and Root planning in subjects with periodontitis.

**Materials and Methods:** This double-blind, randomized, split-mouth study included 15 subjects (mean age 31.73± 8.34 years). Contralateral sites were assigned to SRP alone (Control) or SRP with 5% curcumin gel (Experimental). Plaque Index (PI), Gingival Index (GI), Probing Pocket Depth (PPD), and Clinical Attachment Level (CAL) were recorded at baseline, 4, and 8 weeks. Subgingival plaque was analyzed via PCR for *P. gingivalis*, *T. denticola*, and *A. actinomycetemcomitans*.

**Results:** During the 8-week period follow-up both groups showed significant intragroup reductions in Plaque and Gingival indices (**p < 0.001**), with no significant intergroup difference. Probing pocket depth also decreased markedly from baseline in both groups (**p < 0.001**), indicating comparable improvements. The curcumin group demonstrated a more substantial gain in clinical attachment (**p = 0.001**) compared with the minimal change in controls (**p = 0.050**). PCR analysis showed significant intragroup reductions in *T. denticola* and *P. gingivalis*, while *A. actinomycetemcomitans* decreased sharply only in the curcumin group (**p < 0.001** vs. control **p = 0.054**).

**Conclusion:** Adjunctive use of 5% curcumin gel with SRP significantly improved clinical and microbiological parameters compared to SRP alone, establishing curcumin as a safe, natural, and effective therapeutic option in managing chronic periodontitis

**Keywords:** Curcumin; Periodontal pathogens; Antimicrobial efficacy; PCR; Local drug delivery; Scaling and Root planning

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## Introduction

Periodontitis is a chronic inflammatory condition of tooth-supporting apparatus leading to gradual destruction of periodontal ligament and bone resorption in alveolar compartment eventually leading to tooth loss. Although it is multifactorial in origin, with the subgingival microbial colonization appears to play a pivotal role of which *Porphyromonas gingivalis* (*P. gingivalis*), *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*) and *Treponema denticola* (*T. denticola*) are the key pathogens [1]. However, scaling and root planing (SRP) as the golden nonsurgical standard may not be effective enough in anatomically complex areas like furcation involvements, root concavities, and deep pockets of periodontal pockets, which can result in re-colonization of pathogens [2, 3].

To circumvent these therapeutic constraints, adjunctive antimicrobial regimens—delivered either systemically or via localized application—have been incorporated into periodontal management. Systemic antibiotics, essential for infection control, can cause several side effects when administered over extended periods or at high doses. These side effects include the development of antimicrobial resistance development, disruption of the commensal microbiota, and potential systemic adverse reactions. [4, 5] Invention of local drug delivery (LDD), controlled-release approach capable of delivering high drug concentrations directly into the periodontal pocket while minimizing systemic exposure, aids as an ideal modality for continuous, localised treatment for a disease confined primarily to the gingival sulcus. [6,7] However, despite their potential, synthetic antimicrobials' adverse effects such as cytotoxicity, microbial resistance, and hypersensitivity reactions restrict their usage in therapy. The paradigm has changed in favor of phytotherapeutics as safer and more biocompatible substitutes. Among these is curcumin, a naturally occurring polyphenolic chemical that comes from the Zingiberaceae plant *Curcuma longa*. It is well-known for having a wide range of anti-inflammatory, antioxidant, antibacterial, and reparative qualities. [8,9] Curcumin promotes regenerative tissue processes, inhibits inflammatory cascades, and prevents microbial colonization in addition to its local therapeutic impact. [10-12] The usage of LDD systems such as chlorhexidine, tetracycline, and minocycline has proved to be effective clinically; however, their pharmacological drawbacks have prompted the search of safer and biocompatible alternatives. While curcumin's systemic pharmacological profile is well-known, there is only limited number of clinical trials that explore its localized use as a 5% gel adjunctive to SRP in chronic periodontitis. Therefore, this study was intended to determine and compare the effectiveness of curcumin local drug delivery gel at 5% concentration and SRP in chronic periodontitis treatment, and to evaluate the antimicrobial activity of this gel against *P. gingivalis*, *A. actinomycetemcomitans*, and *T. denticola*. This paper attempts to fill in the gap of translation between phytotherapy and periodontal therapeutics, thereby positioning curcumin as a naturally available, potent, and safe combination therapy in the treatment

of periodontal disease.

## Methodology

This double-blind, parallel-group, clinico-microbiological study was ethically approved by the Institutional Review Board and conducted at the Department of Periodontology, Dayananda Sagar College of Dental Sciences, Bengaluru. After signing the informed consent, a total of 15 subjects (eight males and seven females), between 20 to 60 years, with chronic periodontitis (as per AAP 1999 classification) exhibiting probing pocket depth (PPD)  $\geq 4$  mm at two or more non-adjacent sites of maxillary teeth, with clinical attachment level (CAL) of  $\geq 3$ mm were enrolled. The exclusion criteria included the presence of systemic illness, known hypersensitivity to curcumin, pregnancy or lactation, smoking, antibiotic use within the past three months, and receipt of periodontal therapy within the previous six months. The 5% curcumin in-situ gel was the experimental material, which was prepared by acetone extraction of *Curcuma longa* rhizomes and then dissolved in a poloxamer-based polymeric system to get a thermoresponsive formulation (Sami Labs Limited, Bengaluru). To eliminate inter-individual differences and salivary cross-contamination a split-mouth design was used. The contralateral sites with similar tooth type (premolars or molars) and pocket depth were randomly assigned by a coin toss to the experimental group (scaling and root planing [SRP] + 5% curcumin gel) and control group (SRP alone). Clinical parameters Plaque Index (Silness & Loe, 1965), Gingival Index (Loe & Silness, 1967), PPD, and CAL by using customized acrylic stents to ensure the standardization of the measurements at baseline, four and eight weeks. After isolation and supragingival cleaning, subgingival plaque samples were collected using sterile No. 40 paper points inserted into the deepest sites for 40 seconds and immediately transferred to Tris-EDTA buffer. Scaling and root planing were performed with piezoelectric ultrasonic scalers and Gracey curettes, after which 5% curcumin gel was delivered to the experimental sites using a syringe; upon exposure to intraoral temperature, the sol-gel transition enabled optimal site adaptation and retention. To prevent the ingress of fluids, the sites were sealed with Coe-Pak. Control sites received only SRP. Subjects were instructed to continue routine oral hygiene and refrain from the use of any adjunctive chemical plaque control. The same protocol was followed for clinical and microbiological evaluations at 4 and 8 weeks. Plaque samples were labeled (E1A-E1C for the test; C1A-C1C for the control at baseline, 4, and 8 weeks) and processed for DNA extraction, polymerase chain reaction (PCR), and electrophoretic profiling at HiTech Microbiological Laboratory, Belgaum. DNA was extracted by using a modified Proteinase-K method. The samples were centrifuged, washed with Tris-EDTA buffer, lysed sequentially with buffer I and II, digested with Proteinase-K at 37 °C, and heat-inactivated in a boiling water bath before being stored at -20 °C. Amplification of the target by PCR was done in a Veriti™ 96-well thermal cycler (Applied Biosystems),

by Thermo Scientific Maxima HotStart PCR Master Mix (2X) containing Taq polymerase, dNTPs, MgCl<sub>2</sub>, and organism-specific primers for Porphyromonas gingivalis, Treponema denticola, and A. actinomycetemcomitans. Each 25 µL reaction contained 12.5 µL of the master mix, 0.3 µL of each primer, 1 µL of the DNA template, and nuclease-free water. The cycling protocol comprised 40 cycles of denaturation (95 °C), annealing (60 °C), and extension (72 °C). PCR products—316 bp for T. denticola, 404 bp for P. gingivalis, and 443 bp for A. actinomycetemcomitans—were detected by agarose gel electrophoresis carried out using Tris-acetate-EDTA buffer and ethidium bromide staining under a UV transilluminator. Statistical analysis: This was performed with the help of SPSS v10.5 (IBM Corp., Armonk, NY). Descriptive data were shown as mean ± standard deviation. Changes within the groups were tested by the Chi-square test, differences between the groups by the Mann–Whitney U test and changes over time by the Wilcoxon signed-rank test. A p-value of less than 0.001 was considered as statistically significant.

## Results

In this split-mouth study, 15 patients (8 males, 7 females; mean age 31.73± 8.34 years) were evaluated. Clinical parameters and subgingival plaque samples were collected at baseline, 4 weeks, and 8 weeks from both experimental sites (SRP + 5% curcumin gel) and control sites (SRP alone). A total of 90 plaque samples underwent microbiological assessment.

### Plaque Index (PI)

Intergroup comparison revealed no statistically significant difference in mean PI scores between experimental and control sites at any interval ( $p > 0.05$ ). Intragroup analysis demonstrated a progressive reduction in plaque scores across the study period in both groups. The control group exhibited a significant decline from baseline (1.63) to 4 weeks (1.25) and 8 weeks (0.98) ( $p < 0.001$ ), whereas the experimental group showed a similar downward trend with significance at  $p = 0.01$  (Table 1). Pairwise comparison revealed that only the difference from baseline to 8 weeks was highly significant in both groups ( $p < 0.001$ ).

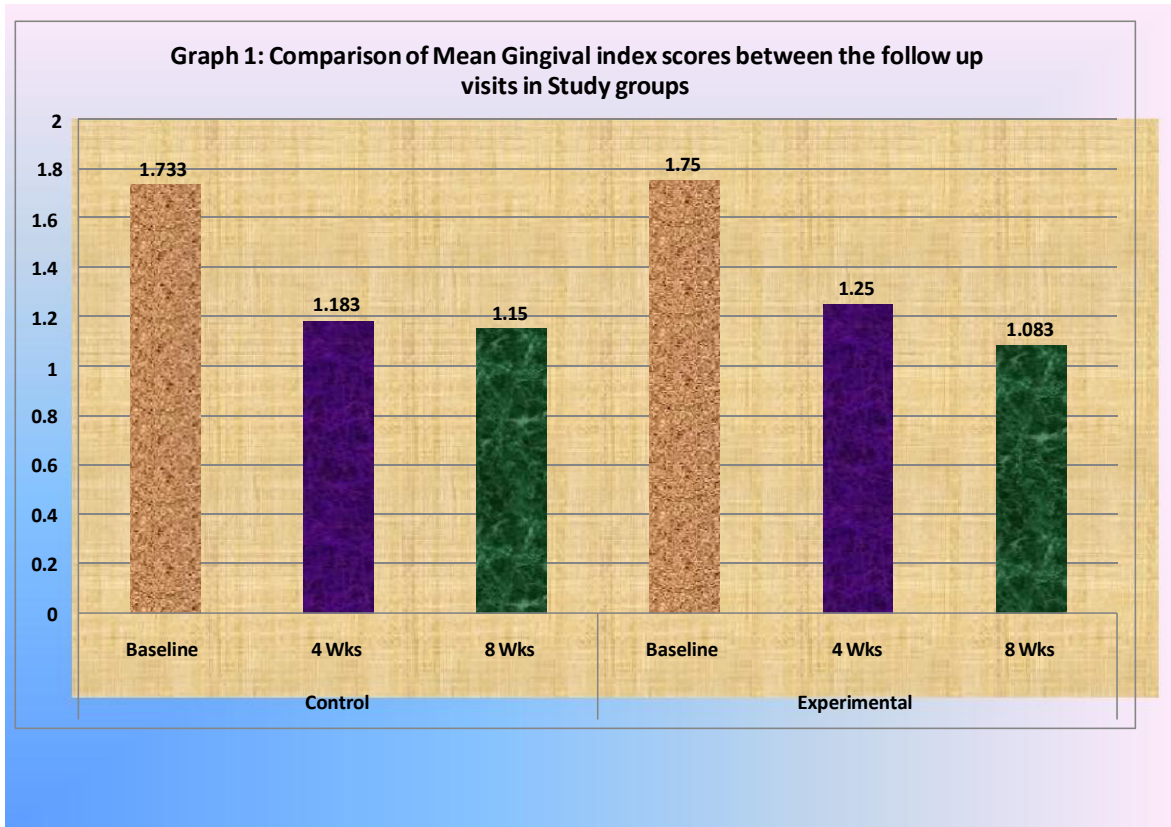
**Table 1 : Intragroup Comparison of Plaque index scores between each follow-up visit**

Group	Visit	N	Mean	SD	Median	Min.	Max.	Chi-square	P “value”
Control	Baseline	15	1.63	0.508	1.50	1.00	3.00	16.994	<0.001
	4 Wks	15	1.25	0.366	1.00	1.00	2.25		
	8 Wks	15	0.98	0.291	1.00	.00	1.25		
Experimental	Baseline	15	1.63	0.471	1.50	1.00	2.75	14.674	0.01
	4 Wks	15	1.20	0.316	1.00	1.00	2.00		
	8 Wks	15	1.02	0.359	1.00	.25	1.50		

### Gingival Index (GI)

No significant intergroup difference was observed in mean GI scores at any interval ( $p > 0.05$ ). However, intragroup comparison revealed a statistically significant reduction in gingival inflammation in both groups from baseline to 4 weeks and 8 weeks ( $p < 0.001$ ) ( Graph 1). Pairwise analysis confirmed that the improvement from baseline to 8 weeks was highly significant in both experimental ( $p < 0.001$ ) and control ( $p = 0.001$ ) sites.

**Graph 1: Comparison of Mean Gingival index scores between the follow up visits in Study group**



**Probing Pocket Depth (PPD)**

Mean PPD decreased progressively in both groups throughout the study. The difference between groups was not statistically significant at baseline ( $p = 0.238$ ), 4 weeks ( $p = 0.692$ ), or 8 weeks ( $p = 0.463$ ). Within-group comparison revealed a highly significant reduction in mean PPD from baseline to 8 weeks in both experimental ( $p < 0.001$ ) and control sites ( $p = 0.001$ ). Pairwise comparisons indicated that changes from baseline to 8 weeks were most significant ( $p < 0.001$ ), whereas intermediate intervals did not reach statistical significance.

**Clinical Attachment Level (CAL)**

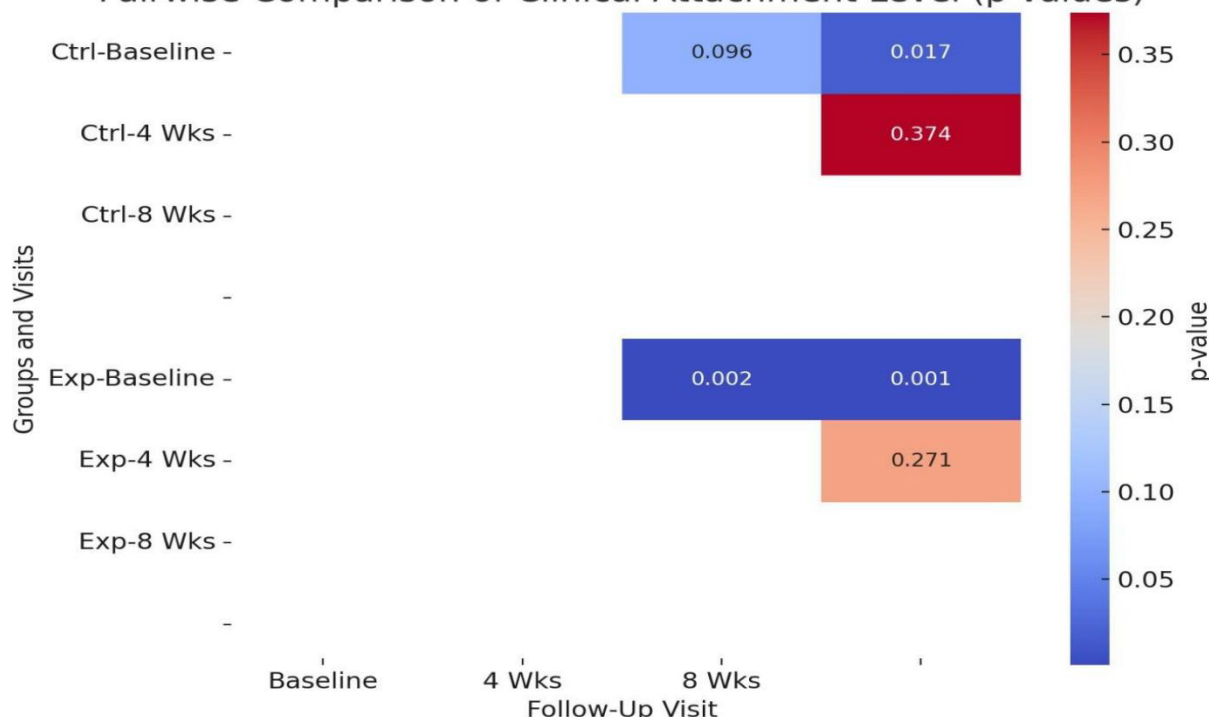
Intergroup comparison showed no statistically significant difference in mean CAL values between groups at any interval (baseline:  $p = 0.342$ ; 4 weeks:  $p = 0.373$ ; 8 weeks:  $p = 0.338$ ). Intragroup evaluation demonstrated a significant gain in CAL in the

experimental group from baseline to 8 weeks ( $p = 0.001$ ), whereas the control group exhibited only marginal improvement ( $p = 0.050$ ). Pairwise analysis confirmed a highly significant attachment gain in the experimental group from baseline to 8 weeks ( $p < 0.001$ ) (Graph-2).

Graph-2 heat map showing pairwise p-values for both control and experimental groups across all follow-up visits.

- The **top half** represents the control group comparisons, and the **bottom half** represents the experimental group.
- **Darker blue cells** indicate statistically significant improvements ( $p < 0.05$ ), especially notable in the experimental group between baseline and later

Pairwise Comparison of Clinical Attachment Level (p-values)



**Microbiological Findings**

PCR-based detection revealed a progressive decline in the prevalence of *T.denticola*, *P. gingivalis*, and *A .actinomycetemcomitans* in both groups across the study period.

**Treponema denticola:** Reduction in prevalence between groups was not statistically significant at baseline (p = 0.439), 4 weeks (p = 1.000), or 8 weeks (p = 0.143). However, within both groups, the decline from baseline to 8 weeks was highly significant (p < 0.001)

**Porphyromonas gingivalis:** No significant intergroup difference was found at baseline (p = 0.409), 4 weeks (p = 0.361), or 8 weeks (p = 1.000). Intragroup analysis showed a significant reduction from baseline to 8 weeks in the control group (p < 0.001) and moderate significance in the experimental group (p = 0.002).

**Aggregatibacter actinomycetemcomitans:** Intergroup difference was non-significant at baseline (p = 0.136) and 4 weeks (p = 1.000). At 8 weeks, prevalence was minimal and not statistically comparable. Intragroup comparison revealed a highly significant reduction in the experimental sites (p < 0.001), while the control sites showed no significant change (p= 0.054)

**Table 2: PCR-Based Detection and Statistical Comparison of Periodontal Pathogens Across Study Period**

Microorganism	Comparison Type	Baseline (p-value)	4 Weeks (p-value)	8 Weeks (p-value)	Intragroup Comparison (Baseline → 8 Weeks)	Interpretation
<b>Treponema denticola</b>	Intergroup	0.439	1.000	0.143	p < 0.001 (Both groups)	Significant reduction within both groups; intergroup difference non-significant.
<b>Porphyromonas gingivalis</b>	Intergroup	0.409	0.361	1.000	Control:p < 0.001 Experimental: p = 0.002	Significant decline in both groups, more pronounced in control group; no intergroup significance.
<b>Aggregatibacter actinomycetemcomitans</b>	Intergroup	0.136	1.000	Not comparable	Control:p = 0.054 Experimental: p < 0.001	Highly significant reduction in experimental sites only; minimal difference at 8 weeks.

## Discussion

This split-mouth investigation evaluated 5% curcumin gel as a local drug delivery adjunct to SRP in patients with chronic periodontitis. Fifteen participants completed the 8-week study, with clinical parameters and subgingival plaque samples analyzed at baseline, 4 weeks, and 8 weeks. While both the control (SRP alone) and experimental (SRP + curcumin) groups demonstrated significant **intragroup** improvements, the **intergroup** differences were not statistically significant. In the present study, both groups showed a gradual decrease of plaque index and gingival index scores from baseline to 8 weeks, which reflects improved oral hygiene and gingival health. The same outcomes were obtained in the experiments where SRP was efficiently supplemented by local drug delivery systems such as chlorhexidine gels and antibiotics.<sup>[1-3,5,7]</sup> The anti-inflammatory and antimicrobial effectiveness of curcumin in this experiment is also supported by earlier studies on *Curcuma longa*.<sup>[8-12]</sup> In particular, Kim<sup>[13]</sup> showed that curcumin could decrease inflammatory substances by interfering with interleukin-6 (IL-6) and prostaglandin production in macrophages activated by lipopolysaccharide (LPS) from *Prevotella intermedia*. On the other hand, Habiboallah et al.<sup>[14]</sup> observed that the improved gingival healing in the test sites could have been influenced by the biomodulating effect of insulin-like factors as explained by Dixit et al.<sup>[19]</sup> which are known to stimulate fibroblast proliferation and collagen production. Both groups exhibited a gradual decrease in PPD and gain in CAL, which are signs of periodontal healing. Nevertheless, the curcumin group evidenced somewhat better changes, thus, confirming the additional effect of curcumin when combined with SRP. This is consistent with the evidence from Yaghini et al.<sup>[21]</sup> who tested herbal gel formulations as complements to SRP and showed significantly better results in moderate chronic periodontitis. In a similar vein, Gottumukkala et al.<sup>[22]</sup> found that subgingival irrigation with 1% curcumin solution brought about clinical parameters and microbial reduction that were better than those achieved by SRP alone. On the molecular level, curcumin's regulation of matrix metalloproteinases (MMPs) is the main reason for connective tissue stability and the prevention of collagen degradation. Sajithal<sup>[23]</sup> and Sidhu et al.<sup>[24]</sup> reported that curcumin influenced the arachidonic acid metabolism and had the ability to speed up wound repair. Besides, Swarnakar et al.<sup>[25]</sup> explained that curcumin modulated MMP-9 and MMP-2, thus, supporting its role in regeneration during soft tissue healing. Moreover, Gopinath et al.<sup>[26]</sup> proved that collagen films loaded with curcumin drastically supported fibroblast proliferation, angiogenesis, and collagen deposition—processes that are anatomically consistent with clinical attachment gain in the present study. Periodontal PCR-based analyses demonstrated that the levels of periodontopathogens *T. denticola*, *P. gingivalis*, and *A. actinomycetemcomitans* decreased substantially from the baseline to the 8 weeks. Both groups showed statistically significant intragroup reductions ( $p < 0.001$ ) whereas intergroup differences remained non-significant. These outcomes are in agreement with the results of Nayyar et al.

herbal topical formulations enhanced periodontal tissue repair in their animal test models. Moreover, the present data agree with Nayyar et al.<sup>[15]</sup> who had a comparative study of 1% curcumin solution and 0.2% chlorhexidine irrigation and recorded that curcumin was as effective in reducing microbial load and gingival health improvement. Correspondingly, Guimarães et al.<sup>[16]</sup> found that curcumin given systemically in their in vivo study had strong anti-inflammatory effects through cytokine modulation and NF- $\kappa$ B inhibition. Similarly, Suhag et al.<sup>[17]</sup> and Waghmare et al.<sup>[18]</sup> stated that the use of subgingival curcumin and a turmeric mouthwash, respectively, led to the reduction of plaque and gingival inflammation, thus, their results are in line with those of the present study. Dixit et al.<sup>[19]</sup> demonstrated that insulin potentiates the growth-promoting response of curcumin in human primary gingival fibroblasts, which is in line with the present study's therapeutic premise. Armitage<sup>[20]</sup> has identified a detailed staging and grading system for periodontal diseases and conditions that provide a clinical basis to understand the current findings. The beneficial effects of curcumin can also be attributed to its bioactive compounds—antioxidant activity, inhibition of free radicals, and regulation of inflammatory mediators.<sup>[10,11,13,16]</sup> <sup>[15]</sup> who found significant microbial suppression after the application of subgingival curcumin. Curcumin antimicrobial effectiveness is derived from the fact that it changes bacterial cell membranes and inhibits lipopolysaccharide (LPS)-induced cytokine expression.<sup>[13,16,28]</sup> The lack of significantly different intergroup results in this research could be due to a short-term evaluation and possible microbial crossover in a split-mouth design. Anyway, the continuous decrease of the pathogenic microorganisms points to the use of curcumin as a very attractive source of antimicrobials to be used as a supportive agent for periodontal therapy. Clinical Relevance and Correlation with Literature The beneficial effects of curcumin in terms of inflammation inhibition, antioxidation, and wound healing that were the focus of the experimental work, are in harmony with the findings of a previous investigation conducted by Habiboallah et al.<sup>[14]</sup> Curcumin's properties such as biocompatibility, cheapness, and lack of staining or irritation of the mucosa make it a very attractive and viable substitute to the likes of chlorhexidine.<sup>[17,18]</sup> The shortcomings of this research include a limited number of participants ( $n = 15$ ), a short post-treatment duration (8 weeks), and a split-mouth design which can cross microbial species between two sides. So, it will take more RCTs with bigger samples, longer follow-up periods, and histopathology to prove curcumin's regenerative capacity. Even though this study has limitations, the adjunct use of 5% curcumin gel with SRP resulted to significant intragroup improvements in plaque index, gingival index, probing depth, and clinical attachment level, and also, a marked reduction of periodontopathogens was evident. These are the effects of curcumin to be anti-inflammatory, antimicrobial, and wound-healing, which are supported by the research of Kim<sup>[13]</sup> Guimarães et al.<sup>[16]</sup> Nayyar et al.<sup>[15]</sup> Reem Al-Kattan and Vijay M. Kumbar et al.<sup>(27,28)</sup> Consequently, the use of curcumin gel as a safe, effective,

and economical adjunct in the non-surgical management of chronic periodontitis can be encouraged.

### Conclusion

Considering the inherent constraints of this split-mouth investigation, it was observed that both therapeutic modalities facilitated substantial amelioration of clinical parameters and a concomitant reduction in the microbial burden over the designated eight-week observational period. Although both SRP in isolation and SRP supplemented with a 5% curcumin gel yielded statistically significant intragroup improvements, the experimental protocol demonstrated a superior capacity for the suppression of pathogenic species and the promotion of enhanced periodontal tissue regeneration. Consequently, these findings suggest that 5% curcumin gel represents a safe, economically viable, and efficacious adjunctive local drug delivery agent. It may be inferred that the integration of such pharmacological adjuncts into conventional non-surgical periodontal regimens possesses the potential to optimize healing outcomes and facilitate the long-term maintenance of periodontal stability in patients afflicted with chronic periodontitis.

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