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Edited by Ashwini Dhopte

E-mail: ashwinidhopte@gmail.com

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Subgingival 2% melatonin versus 2% curcumin as adjuncts to scaling and root planing in chronic periodontitis

Utkarsh Singh, Shruti Gupta*, Deepshikha Singh, Rohit Ranjan, Shikha Verma & Ishatm Dwivedi

Department of Periodontology, Rama Dental College Hospital & Research Centre, Kanpur, Uttar Pradesh, India; *Corresponding author

Affiliation URL:

<https://www.ramadentalcollege.com/>

Author contact:

Utkarsh Singh - E-mail: drutkarshsinghsurgeon@gmail.com

Shruti Gupta - E-mail: shrutz26@gmail.com

Deepshikha Singh - E-mail: singhdeepshikha04@gmail.com

Rohit Ranjan - E-mail: drohitperio2611@gmail.com

Shikha Verma - E-mail: vermashikha544@gmail.com

Ishatm Dwivedi - E-mail: dr.mds.id@gmail.com

Abstract:

Chronic periodontitis is a biofilm-induced inflammatory disease in which deep periodontal pockets and intrabony defects may limit the effectiveness of scaling and root planing alone. Therefore, it is of interest to compare the subgingivally delivered 2% melatonin gel and 2% curcumin gel as adjuncts to scaling and root planing in 22 systemically healthy patients contributing 66 periodontal sites, with placebo gel serving as the control. Plaque index, gingival index, probing pocket depth and clinical attachment level were recorded at baseline, 1, 3 and 6 months, while standardized intraoral periapical radiographs were used to assess intrabony defect depth at baseline and 6 months. All groups improved significantly, but melatonin produced the greatest 6-month reductions in plaque index (2.27 ± 0.22 to 1.04 ± 0.22), gingival index (2.32 ± 0.25 to 1.05 ± 0.21), probing pocket depth (6.11 ± 0.57 to 4.92 ± 0.60 mm) and radiographic defect depth (5.95 ± 0.87 to 4.53 ± 0.84 mm), while curcumin also outperformed placebo for inflammatory and radiographic outcomes. Thus, data shows that both natural gels improved non-surgical periodontal outcomes, with 2% melatonin showing the most consistent clinical and radiographic advantage.

Keywords: Chronic periodontitis, curcumin, melatonin, local drug delivery, scaling and root planning (SRP), intrabony defects

Background:

Periodontitis is a chronic inflammatory disease characterized by progressive periodontal attachment and alveolar bone loss and current management uses a stage-and-grade framework to describe disease severity, complexity and progression risk [1, 2]. Severe periodontitis remains a major global health burden and can lead to tooth mobility, tooth loss, impaired mastication and reduced quality of life [3]. Disease progression reflects reciprocal interactions between a dysbiotic subgingival biofilm and a susceptible host inflammatory response [4, 5]. Pro-inflammatory mediators, osteoclastogenic signaling and oxidative stress contribute to connective-tissue destruction and alveolar bone resorption [5, 6]. Subgingival instrumentation through scaling and root planing remains the foundation of non-surgical periodontal therapy, although access to deep pockets, root concavities, furcations and intrabony defects can limit complete debridement [7, 8]. Local drug-delivery systems can place therapeutic agents directly into periodontal pockets at high site-specific concentrations while reducing systemic exposure [9, 10]. Curcumin, a polyphenolic compound derived from *Curcuma longa*, has anti-inflammatory, antioxidant, antimicrobial and wound-healing properties relevant to periodontal therapy. Clinical evidence indicates that locally delivered curcumin used with scaling and root planing can improve plaque, gingival inflammation, probing depth and attachment outcomes [11, 12]. Melatonin is an endogenous indoleamine with antioxidant, anti-inflammatory, immunomodulatory and bone-regulatory actions that may support osteoblast activity and limit osteoclast-mediated resorption [13, 14]. Systematic evidence suggests that melatonin used as an adjunct to non-surgical periodontal therapy may improve probing depth, clinical attachment and gingival outcomes [15]. Direct comparative evidence between locally delivered curcumin and melatonin remains limited despite the potential value of both agents as non-antibiotic adjuncts for periodontal defects [11, 15]. Recent clinical evidence likewise supports locally delivered curcumin as an adjunct to scaling and

root planing, with improvements reported in periodontal indices and inflammatory outcomes [16-18]. Therefore, it is of interest to compare the clinical and radiographic efficacy of subgingivally delivered 2% melatonin gel and 2% curcumin gel as adjuncts to scaling and root planing in patients with chronic periodontitis.

Materials and Methods:**Study design and setting:**

This was a single-center, split-mouth; site-level randomized controlled clinical study conducted in the Department of Periodontology, Rama Dental College Hospital and Research Centre, Kanpur, Uttar Pradesh, India. The study period was 12 months. Ethical approval was obtained from the institutional ethics committee and all participants provided written informed consent before enrollment.

Sample size:

Sample size was calculated for a split-mouth design using a paired comparison approach, with 80% power, 5% level of significance, an expected clinically meaningful difference of approximately 0.8 mm and an estimated standard deviation of paired differences of 1.2 mm. The minimum required sample was 18 paired sites. To compensate for possible attrition and missed follow-up visits, the sample was increased to 22 patients. Each patient contributed three sites, resulting in 66 total study sites.

Participants:

Systemically healthy patients aged 25-60 years with chronic periodontitis were screened from the outpatient department. Inclusion criteria were periodontal sites with probing pocket depth of at least 5 mm, clinical attachment level of at least 4 mm and radiographic evidence of vertical bone loss or intrabony defect depth of at least 3 mm. Each participant was required to have at least three eligible sites in three different quadrants.

Exclusion criteria:

Patients were excluded if they had received periodontal therapy in the previous 6 months, antibiotics, anti-inflammatory drugs, or antioxidants during the previous 3 months; if they were pregnant or lactating; if they were unwilling to provide consent; if they worked night shifts or used drugs known to alter melatonin levels; or if the selected tooth had furcation involvement. Patients with aggressive periodontitis, diabetes, immunocompromised status, tobacco use in any form, or alcoholism were also excluded.

Randomization and groups:

A total of 22 participants, comprising 12 males and 10 females, were included. The mean age was 42.27 ± 7.25 years, with an age range of 31-55 years. In each participant, three eligible sites were selected and randomly allocated by lottery method to one of three interventions. Group I received scaling and root planing with placebo gel. Group II received scaling and root planing with 2% melatonin gel. Group III received scaling and root planing with 2% curcumin gel. Each group contained 22 sites.

Clinical procedure:

At baseline, all selected sites were examined and full-mouth scaling and root planing was performed using ultrasonic scalers and Gracey curettes. The assigned gel was delivered subgingivally into the selected periodontal pocket using a syringe and needle. A periodontal dressing was placed where required and post-operative oral hygiene instructions were provided. Participants were recalled for follow-up evaluation at 1 month, 3 months and 6 months.

Clinical measurements:

Plaque index and gingival index were recorded using standard scoring criteria. Probing pocket depth and clinical attachment level were measured using a UNC-15 periodontal probe. A customized acrylic stent with a guiding notch was fabricated for each participant to standardize probe position and angulation across visits. Clinical parameters were recorded at baseline, 1 month, 3 months and 6 months.

Radiographic assessment:

Standardized digital intraoral periapical radiographs were taken at baseline and 6 months using the long-cone paralleling technique and positioning devices to maintain reproducibility. Intrabony defect depth was measured using digital image analysis. Defect depth was calculated from linear measurements between the cemento-enamel junction, alveolar crest and base of the defect. Radiographic assessment focused on change in residual intrabony defect depth between baseline and 6 months.

Statistical analysis:

Data were summarized as mean $\pm$ standard deviation. Within-group changes over time in clinical parameters were assessed using repeated measures analysis of variance. Baseline and follow-up intergroup comparisons were performed using one-way analysis of

variance. Paired t-test was used for baseline-to-6-month radiographic comparisons within groups. Tukey post-hoc test was applied for multiple intergroup comparisons. A p-value less than 0.05 were considered statistically significant.

Results:

Twenty-two patients completed the study, providing 66 sites for analysis. There were 12 males and 10 females. The mean age was 42.27 ± 7.25 years. Baseline clinical and radiographic parameters were comparable among the three groups, indicating balanced allocation of disease severity before treatment. There was no significant intergroup difference at baseline for plaque index, gingival index, probing pocket depth, clinical attachment level, or radiographic intrabony defect depth (**Table 1**). All groups demonstrated progressive clinical improvement from baseline to 6 months (**Table 2**). In the placebo group, plaque index reduced from 2.32 ± 0.21 to 1.51 ± 0.26 , gingival index from 2.40 ± 0.25 to 1.55 ± 0.25 , probing pocket depth from 6.35 ± 0.58 mm to 5.42 ± 0.63 mm and clinical attachment level from 6.92 ± 0.65 mm to 5.92 ± 0.63 mm. Repeated measures analysis showed significant improvement for all clinical parameters ($p < 0.001$). The melatonin group showed the greatest clinical improvement. Plaque index reduced from 2.27 ± 0.22 to 1.04 ± 0.22 , gingival index from 2.32 ± 0.25 to 1.05 ± 0.21 , probing pocket depth from 6.11 ± 0.57 mm to 4.92 ± 0.60 mm and clinical attachment level from 6.83 ± 0.64 mm to 5.74 ± 0.61 mm. The curcumin group also showed substantial improvement, with plaque index decreasing from 2.32 ± 0.21 to 1.32 ± 0.24 , gingival index from 2.26 ± 0.24 to 1.21 ± 0.23 , probing pocket depth from 6.13 ± 0.56 mm to 5.06 ± 0.59 mm and clinical attachment level from 6.92 ± 0.63 mm to 5.91 ± 0.60 mm. Intragroup changes in both active treatment groups were statistically highly significant ($p < 0.001$). At 6 months, intergroup differences were statistically significant for plaque index, gingival index, probing pocket depth and clinical attachment level ($p < 0.001$). Tukey post hoc analysis showed that melatonin was significantly superior to placebo for all clinical parameters and superior to curcumin for plaque index, gingival index and probing pocket depth. The clinical attachment level difference between melatonin and curcumin was not statistically significant, suggesting broadly comparable attachment gain between the two active gels. Radiographic assessment showed significant reduction in intrabony defect depth in all groups (**Table 3**). The placebo group improved from 5.96 ± 0.87 mm at baseline to 5.13 ± 0.95 mm at 6 months, with a mean reduction of 0.83 ± 0.22 mm. The melatonin group improved from 5.95 ± 0.87 mm to 4.53 ± 0.84 mm, with a mean reduction of 1.42 ± 0.31 mm. The curcumin group improved from 5.97 ± 0.98 mm to 4.71 ± 0.88 mm, with a mean reduction of 1.26 ± 0.29 mm. Paired t-test showed significant radiographic improvement in all groups ($p < 0.001$). Post-hoc comparison demonstrated significantly greater radiographic improvement for melatonin and curcumin compared with placebo, while the difference between melatonin and curcumin was not statistically significant.

Table 1: Baseline comparability of clinical and radiographic parameters among groups

Parameter	Group I: SRP + Placebo	Group II: SRP + 2% Melatonin	Group III: SRP + 2% Curcumin	F-value	p-value
Plaque Index	2.32 ± 0.21	2.27 ± 0.22	2.32 ± 0.21	0.42	0.658
Gingival Index	2.40 ± 0.25	2.32 ± 0.25	2.26 ± 0.24	1.12	0.333
Probing Pocket Depth (mm)	6.35 ± 0.58	6.11 ± 0.57	6.13 ± 0.56	1.34	0.269
Clinical Attachment Level (mm)	6.92 ± 0.65	6.83 ± 0.64	6.92 ± 0.63	0.76	0.471
Intrabony defect depth (mm)	5.96 ± 0.87	5.95 ± 0.87	5.97 ± 0.98	0.003	0.997

Values are presented as mean ± standard deviation. SRP: scaling and root planing.

Table 2: Baseline-to-6-month clinical changes in the three treatment groups

Group	Parameter	Baseline	6 Months	Mean Change	F-value	p-value
Group I: SRP + Placebo	PI	2.32 ± 0.21	1.51 ± 0.26	0.81	74.26	<0.001
Group I: SRP + Placebo	GI	2.40 ± 0.25	1.55 ± 0.25	0.85	81.52	<0.001
Group I: SRP + Placebo	PPD (mm)	6.35 ± 0.58	5.42 ± 0.63	0.93	49.84	<0.001
Group I: SRP + Placebo	CAL (mm)	6.92 ± 0.65	5.92 ± 0.63	1.00	45.17	<0.001
Group II: SRP + 2% Melatonin	PI	2.27 ± 0.22	1.04 ± 0.22	1.23	132.44	<0.001
Group II: SRP + 2% Melatonin	GI	2.32 ± 0.25	1.05 ± 0.21	1.27	145.82	<0.001
Group II: SRP + 2% Melatonin	PPD (mm)	6.11 ± 0.57	4.92 ± 0.60	1.19	92.64	<0.001
Group II: SRP + 2% Melatonin	CAL (mm)	6.83 ± 0.64	5.74 ± 0.61	1.09	85.31	<0.001
Group III: SRP + 2% Curcumin	PI	2.32 ± 0.21	1.32 ± 0.24	1.00	108.73	<0.001
Group III: SRP + 2% Curcumin	GI	2.26 ± 0.24	1.21 ± 0.23	1.05	118.27	<0.001
Group III: SRP + 2% Curcumin	PPD (mm)	6.13 ± 0.56	5.06 ± 0.59	1.07	78.45	<0.001
Group III: SRP + 2% Curcumin	CAL (mm)	6.92 ± 0.63	5.91 ± 0.60	1.01	70.96	<0.001

A repeated measure ANOVA was used for within-group changes. PI: plaque index; GI: gingival index; PPD: probing pocket depth; CAL: clinical attachment level.

Table 3: Radiographic intrabony defect depth changes from baseline to 6 months

Group	Baseline (mm)	6 Months (mm)	Mean reduction/gain (mm)	t-value	p-value	Post hoc interpretation
Group I: SRP + Placebo	5.96 ± 0.87	5.13 ± 0.95	0.83 ± 0.22	17.53	<0.001	Reference
Group II: SRP + 2% Melatonin	5.95 ± 0.87	4.53 ± 0.84	1.42 ± 0.31	21.48	<0.001	Superior to Group I (p=0.031)
Group III: SRP + 2% Curcumin	5.97 ± 0.98	4.71 ± 0.88	1.26 ± 0.29	19.86	<0.001	Superior to Group I (p=0.041)
Group II vs Group III	-	-	Difference: 0.16	-	0.412	Not significant

Paired t-test was used for intragroup comparison; Tukey post hoc test was used for intergroup comparison.

Discussion:

The present study evaluated two biologically active non-antibiotic local drug delivery agents as adjuncts to scaling and root planing in chronic periodontitis. The findings showed that all three groups improved over 6 months, confirming that mechanical periodontal therapy remains effective when combined with oral hygiene reinforcement and follow-up care. However, both adjunctive gels produced better outcomes than placebo and melatonin showed the strongest overall clinical and radiographic response. Baseline comparability is important in a split-mouth study because it reduces the possibility that post-treatment differences are due to unequal initial disease severity. In this study, all clinical and radiographic parameters were similar before treatment. This strengthens the interpretation that the greater 6-month improvements observed in the active gel groups were related to the adjunctive biological effects of curcumin and melatonin rather than baseline imbalance. The improvement in the placebo group reflects the known benefits of scaling and root planing. Mechanical debridement reduces the microbial burden, disrupts the subgingival biofilm and creates a root surface more favorable for soft-tissue healing [7, 8]. The reduction in probing depth and improvement in clinical attachment level in this group are therefore expected. Nevertheless, residual pocket depth remained higher in the placebo group than in the active adjunctive groups, reinforcing the clinical reality that mechanical therapy alone may not be sufficient for deeper or anatomically complex defects. Curcumin produced significant improvement in plaque index, gingival index, probing pocket depth, clinical attachment level and radiographic defect depth. This benefit can be explained by its combined anti-inflammatory and antimicrobial activity. By suppressing inflammatory pathways and limiting oxidative injury, curcumin may reduce gingival inflammation and probing penetration. Its antimicrobial effect may also contribute to improved plaque-related outcomes and lower bacterial challenge. Clinical improvements observed here are consistent with previous periodontal studies where curcumin gel enhanced the response to non-surgical periodontal therapy [11, 12]. Melatonin demonstrated the most favorable clinical profile in this study. The reduction in plaque and gingival indices was greater with melatonin than with

curcumin and placebo. Although plaque index is influenced by patient-level oral hygiene, reduced inflammation and improved tissue tone may have contributed to easier plaque control and less gingival bleeding. Melatonin's antioxidant capacity, immune-regulatory action and ability to down regulate inflammatory mediators provide a strong biological explanation for its superior effect on gingival inflammation and pocket depth [13-15]. The radiographic results are particularly relevant because periodontal treatment of intrabony defects should ideally improve not only soft-tissue parameters but also the underlying osseous defect. Both active gels produced greater radiographic defect reduction than placebo, with melatonin showing the largest mean gain. This observation is biologically plausible because melatonin has been associated with bone-protective effects, including support of osteoblast function and inhibition of excessive resorption [14]. Curcumin also showed meaningful radiographic improvement, probably through reduced inflammation, decreased osteoclastogenic signaling and enhanced wound healing. The difference between melatonin and curcumin was clinically visible for inflammatory outcomes and probing pocket depth, but the difference in clinical attachment level was not significant. This suggests that both active agents may support attachment stabilization, while melatonin may provide additional benefits in reducing inflammation and soft-tissue pocket depth. It is also possible that a longer follow-up period would be required to detect clearer separation in attachment-level outcomes, because clinical attachment gain is influenced by soft-tissue adaptation, probing reproducibility, defect morphology and patient plaque control. The post hoc radiographic comparison showed both active agents to be superior to placebo, but melatonin and curcumin were not significantly different from each other. This finding should be interpreted cautiously. The numerical advantage of melatonin may be clinically meaningful, but a larger sample with three-dimensional imaging would be needed to confirm true superiority for bone-related outcomes. Intraoral periapical radiography is practical, economical and widely available, but it is two-dimensional and cannot fully distinguish true periodontal regeneration from bone fill, changes in mineral density, or radiographic projection differences. The study also supports the broader idea of host-modulation in

periodontal therapy. Periodontitis is not only a bacterial infection; it is a host-mediated inflammatory disease in which tissue destruction reflects the intensity and persistence of the immune response [4-6]. Therefore, agents that reduce oxidative stress, regulate inflammation and support bone metabolism are rational adjuncts to mechanical biofilm control. This concept is also useful from an antibiotic-stewardship perspective because repeated use of antibiotics or antiseptics may be limited by resistance, staining, altered flora, hypersensitivity, or patient acceptability [9-11]. Several limitations must be considered. The sample size was modest and all patients were systemically healthy non-smokers, which limits generalizability to high-risk groups such as smokers, diabetics and medically compromised patients. The study did not include microbiological or biochemical markers, so mechanistic interpretation are based on known biological actions rather than direct biomarker confirmation. The follow-up period was limited to 6 months; longer follow-up is necessary to assess stability of clinical and radiographic gains. Future studies should include larger multicenter samples, standardized defect morphology assessment, three-dimensional radiographic evaluation and biochemical markers of oxidative stress, inflammation and bone turnover. Despite these limitations, the findings are clinically relevant. The split-mouth design reduced inter-individual variability, standardized stents improved reproducibility of probing measurements and radiographic assessment added a structural outcome to the clinical evaluation. The results suggest that both 2% curcumin and 2% melatonin gels may be useful adjuncts in chronic periodontitis with intrabony defects, with melatonin showing the most consistent advantage across inflammatory, pocket depth and radiographic parameters. The curcumin response observed here is consistent with local-delivery studies reporting improved probing depth, attachment, gingival inflammation or related biomarkers when curcumin was added to scaling and root planing [16-18].

Conclusion:

Subgingival delivery of 2% curcumin gel and 2% melatonin gel as adjuncts to scaling and root planing significantly improved clinical

and radiographic outcomes in chronic periodontitis compared with placebo. Melatonin showed the greatest overall improvement, particularly for gingival inflammation, probing pocket depth reduction and radiographic intrabony defect reduction. These findings support the clinical value of non-antibiotic biologically active local drug delivery agents, while larger long-term trials are required before routine protocol-level recommendations can be made.

References:

- [1] Sanz M *et al.* *J Clin Periodontol.* 2020 **47**:4. [PMID: 32383274]
- [2] Marini L *et al.* *J Clin Periodontol.* 2021 **48**:205. [PMID: 33260273]
- [3] Wu L *et al.* *J Periodontol.* 2022 **93**:1445. [PMID: 35305266]
- [4] Scannapieco FA & Dongari-Bagtzoglou A. *J Periodontol.* 2021 **92**:1071. [PMID: 33902163]
- [5] Hajishengallis G *et al.* *Periodontol 2000.* 2020 **84**:14. [PMID: 32844416]
- [6] Szczepanik FSC *et al.* *Periodontol 2000.* 2020 **84**:45. [PMID: 32844417]
- [7] Tomasi C *et al.* *Periodontol 2000.* 2023. [PMID: 37162295]
- [8] West N *et al.* *J Dent.* 2021 **107**:103562. [PMID: 33573801]
- [9] Amato M *et al.* *Pharmaceutics.* 2023 **15**:1312. [PMID: 37111796]
- [10] Elnagdy S *et al.* *Molecules.* 2021 **26**:5661. [PMID: 34577132]
- [11] de Sousa ET *et al.* *Clin Oral Investig.* 2021 **25**:4599. [PMID: 33527193]
- [12] Siddharth M *et al.* *J Contemp Dent Pract.* 2020 **21**:494. [PMID: 32690830]
- [13] Wang C *et al.* *Int J Mol Sci.* 2022 **23**:14541. [PMID: 36498871]
- [14] Lu X *et al.* *Int J Mol Med.* 2021 **47**:82. [PMID: 33760138]
- [15] Liu RY *et al.* *Inflammopharmacology.* 2022 **30**:695. [PMID: 35290552]
- [16] Gupta S *et al.* *J Pharm Bioallied Sci.* 2025 **17**:S1683. [PMID: 40655860]
- [17] Siddharth M *et al.* *J Contemp Dent Pract.* 2020 **21**:494. [PMID: 32690830]
- [18] Abdel-Fatah R *et al.* *BMC Oral Health.* 2023 **23**:883. [PMID: 37981665]

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