



Evaluation of the Effectiveness of Two Local Drug Delivery Agents in the Management of Chronic Periodontitis – A Comparative Study

Eeva Sunny ^{a^o}, M. P. Shyamala Devi ^{b[#]}, Anusha Anish ^{c[†]},
Sanjeev Ravindran ^{b[‡]}, Hari S. Pillai ^{c[¥]} and P. T. Annamalai ^{c[†]}

^a Thazhath Dental Clinic, Chalakudy, Thrissur, India.

^b Department of Periodontics and Implantology, PSMCDSR, Akkikavu, Thrissur, India.

^c PSM College of Dental Science & Research, Akkikavu, Thrissur, India.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/93797>

Original Research Article

Received 11 September 2022

Accepted 14 November 2022

Published 01 December 2022

ABSTRACT

Background: The prime aim of periodontal therapy is the arrest of bacteria/host induced inflammation and to maintain healthy periodontium. Pathogenic organisms which are not mechanically accessible can be eliminated by antibacterial agents. Several local antimicrobial drug delivery agents have been developed with a view to maintain adequate levels of crevicular fluid at the target site and preventing systemic uptake.

Aim: Tetracycline fibers (Periodontal plus AB) and curcumin gel (Curenex) are two such drugs used as adjuncts to scaling and root planing in the treatment of chronic periodontitis. Comparative evaluation of the effectiveness of these two agents will be helpful in the selection of a particular type of treatment modality.

Methodology: Eighty sites from 30 patients were selected for the study and were divided into two groups of 40 sites for tetracycline fibers and 40 sites for curcumin gel application as adjuncts to

^o Consultant;

[#] Professor;

[†] Professor of Pathology & Deputy Research Director;

[‡] Professor & Head;

[¥] Principal;

[†] Research Director;

*Corresponding author: Email: dranushaanish@gmail.com;

scaling and root planing in the treatment of chronic periodontitis. Clinical parameters such as gingival index, plaque index, oral hygiene index, probing pocket depth and gain in clinical attachment level were assessed in all the patients after 30 days and 90 days in both groups.

Results and Discussion: Study revealed that both tetracycline fibers and curcumin gel are effective agents as adjuncts to scaling and root planing in the treatment of chronic periodontitis.

Conclusion: Though both tetracycline fibers and curcumin gel were found to be effective for the treatment of chronic periodontitis, tetracycline was found to be slightly more effective. This may be due to the property of substantivity exhibited by tetracycline.

Keywords: Periodontitis; local drug delivery; tetracycline fibers; curcumin gel.

1. INTRODUCTION

“Chronic periodontitis is a multifactorial disease resulting from the formation of periodontal pocket and progressive loss of attachment. Periodontal pocket formation represents the pathologic sequelae of microbial and inflammation mediated degradation of collagenous connective tissue and alveolar bone. Periodontal disorders include a spectrum of infections affecting the oral cavity, in which the chief etiology is dental plaque that causes inflammation in the tissues supporting the dentition” [1]. Mechanical debridement may fail to eliminate the putative pathogens from the pockets completely because of the inaccessibility of the location of the organisms within the gingival tissue. Systemic administration of drugs leads to absorption into the blood stream and distribution throughout the body. According to Chaturvedi et al [2] local drug delivery mode is considered more beneficial in the control of localized periodontal disease as adjunct to non-surgical periodontal therapy. Local drug delivery mode is considered more beneficial in the control of localized periodontal disease as adjunct to non-surgical periodontal therapy. Commonly used antimicrobial local drug delivery agents include Chlorhexidine- containing chip (Periochip), Doxycycline gel (Atridox), Minicycline microspheres (Arestin), ethylene or vinyl acetate copolymer fiber containing tetracycline and bioresorbable tetracycline fiber (Periodontal Plus AB). Curcumin Longa has been used as a therapeutic agent in ayurvedic medicine for years. A comparative study on the clinical effectiveness of a synthetic drug tetracycline fiber (which may have side effects) and an ayurvedic drug curcumin gel (supposed to have no side effects) is considered worthwhile.

2. REVIEW OF LITERATURE

Several authors have found that effective treatment of periodontitis is the mechanical debridement to remove biofilm and calculus from

the affected root surfaces followed by adjunct therapy by local delivery of drugs [3–7]. The advantages of local drug delivery are:

1. Achieving high concentration of the drug at localized site (100 times as compared to systemic therapy)
2. Suitable for agents which cannot be given systemically (such as chlorhexidine)
3. No systemic side effects
4. Low chances of super-infection or drug resistance
5. Reduction in total drug usage, drug accumulation and frequency

The adjunctive use of local delivery of drugs may enhance the results in isolated periodontal pocket sites that do not respond to conventional therapy [8]. Purucker et al. [9] compared “the clinical response of local versus systemic treatment as adjuncts to scaling and root planing and observed that local delivery of tetracycline fiber and the systemic administration of amoxicillin/clavulinate given for 3 months after scaling and root planing produced similar clinical outcomes over the 9-month observation period”. Newman et al. [10] in their evaluation study to “compare the efficacy of scaling and root planing (SRP) alone versus SRP plus adjunct therapy with tetracycline fiber observed that SRP plus adjunct therapy was more effective in the treatment of periodontitis”. Kinane et al. [11] compared the effectiveness of three periodontal local antimicrobial therapies: scaling and root planing alone, in conjunction with 25% tetracycline, 2% minacycline gel or 20% metronidazole gel and observed that application of three locally applied antimicrobial systems offered benefits and also that tetracycline gave the best effect.

Curcumin (diferuloylmethane), the main bioactive component of turmeric, is reported to have anti-inflammatory [12-14], antioxidant [15–18], antiallergic, anticarcinogenic, antimutagenic,

anticoagulant, antidiabetic, antibacterial, antiprotozoal, antifungal, antiviral, antiulcer, hypotensive and hypocholesterolemic activities [19,20]. Kudva et al. [21] in a comparative study on “the adjunctive efficacy of turmeric, curcumin and traditional nonsurgical methods for treating periodontal pockets found that plaque index and gingival index showed significant improvement in curcumin treated group”. Several authors have recommended the local delivery of curcumin as an adjunct therapy in the treatment of chronic periodontitis [22-24].

3. MATERIALS AND METHODS

Thirty patients in the age group 30 – 55 years attending the Department of Periodontics, PSM College of Dental Science & Research with chronic periodontitis having periodontal pocket depths of 5 – 8 mm after scaling and root planing were selected for the study.

3.1 Selection Criteria

3.1.1 Inclusion criteria

Patients in the age group 30 – 55 yrs with chronic periodontitis having periodontal pocket depths of 5 – 8 mm after scaling and root planing and who were willing to take part in the study were included.

3.1.2 Exclusion criteria

Patients with medically compromised conditions, on antibiotics within 6 months prior to the study, who have undergone periodontal therapy in past 6 months, who were pregnant/lactating mothers and those reported to have any form of allergy to tetracycline or curcumin were excluded.

Sample size calculation:

$$n = 2 \left[\frac{(Z_1 + Z_2) \times sd}{d} \right]^2$$

$$n = 2 \left[\frac{(2.8) \times 0.81}{0.5} \right]^2$$

$$= 41.15$$

≈ 40 in each group

Z₁ = constant at 95% confidence interval Z₂ = constant at 80% power
sd = standard deviation from parent article d = clinically significant difference

A total of 80 sites (40 sites for each group) were included for evaluating the effectiveness of curcumin gel and tetracycline fibers. The sites were grouped as follows:

Group A: Application of curcumin gel – 40 sites
Group B: Application of tetracycline fibers – 40 sites

Tetracycline fibers were soaked and placed into the pocket with the help of a tweezer and periodontal probe was used to insert into periodontal pocket with gentle pressure. Curcumin gel was applied directly from a disposable syringe into the pocket without traumatizing or damaging the periodontal tissue. After insertion of the drug locally, the region was secured with Coe-pak™ [25].

The clinical parameters: Plaque index, Oral hygiene index, Gingival index, Probing pocket depth, and Clinical attachment level were assessed using the techniques employed by Newman et al. [26]. Clinical parameters were assessed before starting the therapy and recorded as baseline values. All patients were refrained from chewing hard and sticky food, flossing on the treated side and not to disturb the area with tongue, finger or tooth pick. For the removal of coe-pak the participants were recalled after 1 week. Clinical parameters were reassessed at 30 days and 90 days and recorded.

3.2 Statistical Analysis

Data obtained were analysed using IBM SPSS-23 software. Statistical comparisons were performed using students “t” test.

4. RESULTS

4.1 Gingival Index

Mean gingival index showed significant decrease (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days. The results obtained are represented in Table 1.

4.2 Oral hygiene Index

Mean oral hygiene index values showed significant improvement (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are depicted in Table 2.

Table 1. Gingival index values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	2.03 ±0.16	1.02 ±0.15*	1.02 ±0.15 ^{ns}
Tetracycline	40	2.15 ±0.18	1.04 ±0.14*	1.04 ±0.14 ^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value
*Significant P <0.001., ns: Not significant

Table 2. Oral hygiene index values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	1.08 ±0.27	0.08 ±0.01*	0.08 ±0.01 ^{ns}
Tetracycline	40	1.05 ±0.22	0.05 ±0.01*	0.05 ±0.01 ^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value.*Significant P <0.001., ns: Not significant

4.3 Plaque Index

Mean plaque index showed significant decrease (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated group. The results are given in Table 3.

4.4 Probing Pocket Length

Mean probing pocket length showed significant improvement (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant

difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are depicted in Table 4.

4.5 Clinical Attachment Level

Mean clinical attachment level showed significant improvement (p<0.001) on treatment with curcumin and tetracycline observed at 30 days when compared to baseline level. No significant difference was seen at 90 days when compared to 30 days in either curcumin or tetracycline treated groups. The results are given in Table 5.

Table 3. Plaque index values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	1.98 ±0.36	0.98 ±0.15*	0.98 ±0.15 ^{ns}
Tetracycline	40	2.05 ±0.32	1.05 ±0.22*	1.05 ±0.22 ^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value. * Significant P <0.001., ns: Not significant

Table 4. Probing pocket depth values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	5.10±0.30	4.28±0.51*	4.28±0.51 ^{ns}
Tetracycline	40	5.05 ±0.22	3.78±0.53*	3.73±0.55 ^{ns}

Values are expressed as mean ± SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value
*Significant P <0.001., ns: Not significant

Table 5. Clinical attachment level values in curcumin gel and tetracycline fibers treated patients with chronic periodontitis

Group	No. of sites	Baseline	30 days	90 days
Curcumin	40	2.03 \pm 0.16	1.02 \pm 0.15*	1.02 \pm 0.15 ^{ns}
Tetracycline	40	2.15 \pm 0.18	1.04 \pm 0.14*	1.04 \pm 0.14 ^{ns}

Values are expressed as mean \pm SD. The values obtained at 30 days were compared with those obtained at baseline level. The values obtained at 90 days were compared with those obtained at 30 days. Independent 't' test was performed to calculate p value

*Significant $P < 0.001$, ns: Not significant

5. DISCUSSION

Periodontitis is a biofilm associated disease and are difficult to treat with antibiotics unless biofilm is disrupted mechanically. Chronic periodontitis develops as a result of host-bacterial interaction in which the pathogens produce harmful byproducts that initiate host immune inflammatory responses leading to the breakdown of extracellular matrices and bone resorption, creating bone defects eventually leading to tooth loss" [27]. "It is characterized by the presence of gingival inflammation, periodontal pocket formation, clinical attachment loss and development of osseous deformities around the affected teeth. Scaling and root planing (SRP) in conjunction with antibacterial agents were administered either systemically or locally" [28]. However, systemic administration has been found to be associated with side effects and local delivery of drugs was found more beneficial [28,29]. "SRP with adjunctive chlorhexidine chips showed better clinical outcomes than SRP alone for the management of periodontal pockets in patients with chronic periodontitis" [30-32].

In this study, effort has been made to compare the effectiveness of two commercially available local delivery agents – curcumin gel (curenex - an ayurvedic drug) and tetracycline fibers in treating chronic periodontitis. Kataria et al. [33] applied "tetracycline fibers as an adjunct to scaling and root planing and found it to be very effective in reducing gingival and periodontal inflammation". "A Tetracycline-Serratiopeptidase-a combination gel of tetracycline and serratiopeptidase was investigated" by Maheshwari et al. [34] and observed that the formulation had shown statistically significant results along with mechanical debridement. Sachdeva and Agarwal [35] made "tetracycline in the form of a modified collagen matrix and used along with scaling and root planing. They concluded that there was significant probing pocket depth reduction and gain in clinical

attachment for the SRP plus tetracycline group compared to SRP alone".

Newman [36] reported that "adjunctive curcumin showed better improvement in the reduction of gingival inflammation and bleeding. The mechanism of periodontal disease involves the production of several inflammatory mediators. Periodontal pathogens activate NF- κ B, Janus kinase (JAK) signal transducer activator of transcription (STAT), mitogen-activated protein kinases (MAPK), and other signaling pathways and produce inflammatory cytokines such as IL-6, TNF- α and IL-1 β to promote inflammation" [37]. "Curcumin, the active ingredient in turmeric, has various anti-inflammatory properties and may delay the disease process of periodontal disease in its initial stages. It has been shown to suppress the NF- κ B pathway in human gingival fibroblasts in early stages and thus may inhibit *P. gingivalis* LPS-induced COX-2 synthesis" [38] and "the production of TNF- α , IL-8 and IL-6 by inhibiting NF- κ B activation in mast cells" [39]. "Additionally, curcumin could exert an anti-inflammatory effect by directly inhibiting the JAK/STAT signaling pathway and phosphorylation of p38 MAPK, thereby reducing the expression of iNOS, COX-2, monocyte chemoattractant protein-1 (MCP-1), and intercellular adhesion molecule-1(ICAM-1) to reduce the inflammatory response" [40,41]. In the present study statistically significant improvements were observed in all the clinical parameters (oral hygiene index, gingival index, plaque index, probing pocket depth and clinical attachment level) measured at 30 days compared to the values at baseline level, the response being slightly better in the case of tetracycline treated group. No difference was observed when the values at 90 days were compared with those at 30 days. The findings were in agreement with earlier studies [23,27,28].

In this study microbial evaluation was not carried out. Long term studies with a large sample size are required to further assess the clinical efficacy of both local delivery drugs.

6. CONCLUSION

Though scaling and root planing (SRP) alone is efficient in managing chronic periodontitis, superior results can be obtained by employing topically delivered tetracycline fibers and curcumin gel. It may be concluded that tetracycline fibers (Periodontal Plus AB) and curcumin gel (Curenex) can be used as adjuncts to scaling and root planing in the treatment of chronic periodontitis. Application of both agents showed significant beneficial effects, but tetracycline showed slightly better effect. The more beneficial effect of tetracycline may be due to the property of substantivity exhibited by this drug. Curcumin being an ayurvedic drug with little or no side effects can be an excellent alternative to tetracycline in the treatment of chronic periodontitis.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

Ethical clearance was obtained for the study from the Institutional ethics committee (No.17/Ethics/PSMCD SR/2018 dt. 04/12/2018).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

- Jalaluddin Mohammed, Shruthi Shivakumar, Sandeep S Arora, Deesha Kumari, Mahesh Jayachandran, Rethi Gopakumar, Thilla S Vonothkumar. Clinical assessment of the effectiveness of three different controlled release drugs in the management of chronic periodontitis: An *in vitro* study. World J of Dentistry. 2022;11(3): 234-38.
- Chaturvedi TP, Srivastava R, Srivastava AK, et al. Evaluation of metronidazole nanofibers in patients with chronic periodontitis: a clinical study. Int J Pharm Investig 2012;2(4):213–217.
- Drisco C. Non-surgical periodontal therapy. Periodontology. 2001;25(1):77 – 78.
- Drisco C. Periodontal debridement still the treatment of choice. J Evidence based Dent Practice.2014;14: 33-41.
- Pihlstrom B. Commentary: Treatment of periodontitis: Key Principles. J Periodontology. 2014;85(5):655-656.
- Sanz I, Alonso B, Carasol M, Herrera D, Sanz M. Nonsurgical treatment of periodontitis. J Evidence Based Dent Practice.2012;12(3): 76-86.
- Raju Anarthe, Preeti Kale, Amit Mani, Shriram Kendre. Local drug delivery in periodontitis. An innovative treatment modality. Int J Pharmaceutical Sciences & Research. 2021;12(9):4616-25.
- Verma E, Belludi SA, Banthian R. Local drug delivery with chlorhexidine chip and tetracycline fibers as an adjunct to mechanical therapy in isolated periodontal pockets – A case report. Int J Clin Dentistry.2011;4(4):383-90.
- Purucker P, Mertes H, Goodson H, Bernimoulin JP. Local versus systemic adjunctive antibiotic therapy in 28 patients with generalized aggressive periodontitis. J Periodontology. 2001;72(9):1241-45.
- Newman MG, Kornmann KS & Doherty FM. A six-month multicentre evaluation of adjunctive tetracycline fiber therapy used in conjunction with scaling and root planing in maintenance patients: Clinical results. J Periodontology. 1994;65(7): 685-91.
- Kinane DF, Radvar M. A six month comparison of three periodontal local antimicrobial therapies in persistent periodontal pockets. J Periodontology. 199;70(1): 1-7.
- Sajithlal GB, Chithra P, Chandrakasan G. Effect of curcumin on the advanced glycation and cross linking of collagen in diabetic rats. Biochemical Pharmacology.1998;56(12):1607-14.
- Chainani-Wu N. Safety and anti-inflammatory activity of curcumin: a component of turmeric (*Curcuma Longa*). J Alternative & Complementary Medicine. 2003;9(1):161-68.
- Motterlini R, Foresti R, Bassi R, Green CJ. Curcumin, an antioxidant and anti-inflammatory agent, induces heme oxygenase-1 and protects endothelial cells against oxidative stress. Free Radical Biology & Medicine. 2000;28(8):1303-12.
- Bhatia M, Urolagin SS, Pentyala KB, Urolagin SB, Menaka KB, Bhoi S. Novel therapeutic approach for the treatment of

- periodontitis by curcumin. *J Clinical & Diagnostic Res.*2014;8(12): ZC65-ZC69.
16. Ramsevak RS, DeWitth DL, Nair MG. Cytotoxicity, antioxidant and anti-inflammatory activities of curcumin I-III from *Curcuma Longa*. *Phytomedicine.* 2000;7(4):303-08.
 17. Osawa T, Sugiyama Y, Inayoshi M, Kawakishi S. Antioxidant activity of etrahydrocurcuminoids. *Bioscience, Biotechnology & Biochemistry.* 1995;59(9):1609-12.
 18. Elavarasu S, Suthanthiran T, Thangavelu A, Alex S, Palanisamt A, Kumar T S. Evaluation of super oxide dismutase levels in local drug delivery system containing 0.2% curcumin strip as an adjunct to scaling and root planing in chronic periodontitis: A clinical and biochemical study. *J Pharmacy Bioallied Sciences.* 2016;8(Suppl 1): S46.
 19. Siddiqui AM, Cui X, Wu R, Dong W, Zhou M, Hu M, Simms HH, Wang P. The anti-inflammatory effect of curcumin in an experimental model of sepsis mediated by upregulation of peroxisome proliferator-activated receptor- γ . *Critical Care Medicine.*2006;34(7):1874-82.
 20. De R, Kundu P, Swarnakar S, Ramamurthy T, Chowdhury A, Nair GB, Mukhopadhyaya AK. Antimicrobial activity of curcumin against *Helicobacter pylori* isolates from India and during infections in mice. *Antimicrobial Agents and Chemotherapy.*2009;53(4):1592-97.
 21. Kudva P, Tabassum ST, Gupta S. Comparative evaluation of the efficacy of turmeric and curcumin as a local drug delivery system – A Clinico-microbiological study. *General Dentistry.* 2012;60(5): e283-87.
 22. Anitha V, Rajesh P, Shanmugham M, Priya R M, 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. *Ind J Dental Res.* 2015;26(1): 57-60.
 23. Siddharth M, Singh P, Gupta R, Sinha A, Shree S, Sharma K. A comparative evaluation of subgingivally delivered 2% curcumin and 0.2 % chlorhexidine gel adjunctive to scaling and root planing in chronic periodontitis. *J Contemp Dental Practice.*2020;21(5):494-99.
 24. Raghava KV, Sistla KP, Narayan SJ, Yadalam U, Bose A, Mitra K. Efficacy of curcumin as an adjunct to scaling and root planing in chronic periodontitis patients. – A randomized controlled clinical trial. *J Contemp Dent Practice.* 2019;20(7): 842-46.
 25. Newman M, Takei H, Caraza F. *Caraza's Clinical Periodontology*, Philadelphia, WB Sanders Co., 2002.
 26. Gupta R, Pandit N, Aggarwal S, Verma A. Comparative evaluation of subgingivally delivered 10% doxycycline hyclate and xanthan-based chlorhexidine gel in the treatment of chronic periodontitis. *J Contemp Dent Practice.* 2008;9(7):25-32.
 27. Kirkwood KL, Cirelli JA, Rogers JE, Giannobile WV. Novel host response therapeutic approaches to treat periodontal disease. *Periodontology.* 2000;43:294–98.
 28. Reynolds MA, Kao RT, Nares S, Camargo PM, Caton JG, Clem DS et al. Periodontal regeneration –intra-bony defects: Practical applications from the AAP regeneration workshop. *Clinical Advances in Periodontics.*2015;5(1):21-29.
 29. Mao L, Diao X. Effect of chlorhexidine chip as an adjunct therapy in non-surgical management of periodontal pockets: A meta-analysis. *BMC Oral Health* 2020;20(1): 262.
 30. Zao H, Hu J, Zhao L. Adjunctive subgingival application of chlorhexidine in nonsurgical periodontal treatment for chronic periodontitis. : A Systematic Review and Meta-analysis. *BMC Oral Health* 2020;20(1),34.
 31. NK Sharma and A Prasad: Evaluation of efficacy of tetracycline as a local drug delivery system in the treatment of chronic periodontitis as an adjunct to scaling and root planing – a clinical and microbiological study. *International Journal of Con Medi Res* 2017; 4(5): 998-03.
 32. Rupali K, Vandana KL, Shobha P. Effect of local drug delivery in chronic periodontitis patient: A meta-analysis. *J Ind Soc Periodontol.* 2011;15(4): 304-09.
 33. Kataria S, Chandrashekar KT, Mishra R, Tripathi V and Galav A: Effect of tetracycline HCL (Periodontal plus AB) on Aggregati bacter actinomycetemcomitans levels in chronic periodontitis. *Arch Oral Dent Res* 2015; 2(1): 1-8.
 34. M Maheshwari, G Miglani, A Mali, A Paradkar, S Yamamura and S Kadam: Development of tetra cyclineserratio

- peptidase-containing periodontal gel: formulation and preliminary clinical study. AAPS Pharm Sci Tech 2006; 7(3): 76.
35. Sachdeva S, Agarwal V. Evaluation of commercially available biodegradable tetracycline fibre therapy in chronic periodontitis. J Indian Soc Periodontol. 2011;15(2): 130–34
 36. Newman, Carranza`s *Clinical Periodontology E-Dition*. Philadelphia: WB Saunders, 2015.
 37. Li Y, Jiao J, Qi Y, Yu W, Yang S, Zhang J et al. Curcumin: A Review of Experimental Studies and Mechanisms Related to Periodontitis Treatment. J. Periodontal Res. 2021;56(5):837–47.
 38. Hu P, Huang P, Chen MW. Curcumin Attenuates Cyclooxygenase-2 Expression via Inhibition of the NF-Kb Pathway in Lipopolysaccharide-Stimulated Human Gingival Fibroblasts. Cell Biol Int. 2013; 37(5):443–48.
 39. Kong R, Kang OH, Seo YS, Zhou T, Kim SA, Shin DW, et al. MAPKs and NF-κB P-athway I-nhibitory E-ffect of B-isdemethoxycurcumin on P-horbol-12-myristate-13-acetate and A23187-induced I-nflammation in H-uman M-ast C-ells. Mol. Med. Rep. 2018; 17(1):630–35.
 40. Guimarães MR, Leite FR, Spolidorio LC, Kirkwood KL, Rossa C, Jr. Curcumin Abrogates LPS-Induced Pro-inflammatory Cytokines in RAW 264.7 Macrophages. Evidence for Novel Mechanisms Involving SOCS-1, -3 and P38 MAPK. Arch. Oral Biol. 2013;58(10):1309–17.
 41. Boyle DL, Soma K, Hodge J, Kavanaugh A, Mandel D, Mease P, et al. The JAK Inhibitor Tofacitinib Suppresses Synovial JAK1-STAT Signalling in Rheumatoid Arthritis. Ann. Rheum. Dis. 2015;74 (6): 1311–16.

© 2022 Sunny et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:

The peer review history for this paper can be accessed here:

<https://www.sdiarticle5.com/review-history/93797>