

# Comparative Assessment of the Effect of Three Various Local Drug Delivery Medicaments in the Management of Chronic Periodontitis

Soniya Hatila<sup>1</sup>, Banibrata Lahiri<sup>2</sup>, Gowrish Sunnanguli<sup>3</sup>, Mahesh Jayachandran<sup>4</sup>, Rethi Gopakumar<sup>5</sup>, Konsam Bidya Devi<sup>6</sup>, Mona Awad Kamil<sup>7</sup>

## ABSTRACT

**Aim:** The aim of this study was to evaluate the efficacy of three different local drug delivery medications in the treatment of chronic periodontitis.

**Materials and methods:** Sixty participants, aged 30–55 years, were involved in the current research. Participants who fulfilled the inclusion criteria entered the study and were allocated at random to one of the three groups, each comprising 20 patients as: group A: Scaling and root planing (SRP) with local application of doxycycline gel, group B: SRP with local application of tetracycline fibers, and group C: SRP with local application of chlorhexidine gel. The plaque index (PI), the gingival index (GI), and periodontal pocket depth (PPD) were documented at baseline visit (prior to local drug delivery), and these indices were again documented 30 and 90 days post-local drug delivery.

**Results:** At baseline, GI score for doxycycline gel use decreased from  $1.38 \pm 0.05$  to  $0.94 \pm 0.02$ ,  $1.36 \pm 0.11$  to  $0.76 \pm 0.19$  for tetracycline fibers use, as well as from  $1.38 \pm 0.10$  to  $0.84 \pm 0.21$  for chlorhexidine gel use post 90 days. The PI value at baseline for doxycycline gel use lessened from  $1.26 \pm 0.01$  to  $1.02 \pm 0.06$ ,  $1.30 \pm 0.14$  to  $0.82 \pm 0.16$  for tetracycline fibers use, as well as  $1.30 \pm 0.22$  to  $0.98 \pm 0.11$  for chlorhexidine gel use post 90 days. At baseline, PPD values for doxycycline gel use decreased from  $5.88 \pm 0.24$  to  $3.72 \pm 0.11$ , tetracycline fibers use lessened from  $5.90 \pm 0.09$  to  $3.02 \pm 0.06$ , as well as for chlorhexidine gel group from  $5.82 \pm 0.18$  to  $3.44 \pm 0.16$  post 90 days.

**Conclusion:** Within the limitations of the current research, it may be inferred that tetracycline fibers exhibited somewhat superior enhancement to chlorhexidine as well as doxycycline gel.

**Clinical significance:** Local administration of antibacterial agents in continued or regulated delivery arrangement is employed to augment the actions of nonsurgical periodontal management, and it may be likely to attain gingival well-being by eliminating the requirement for invasive methods with the aid of local drug delivery arrangements. Chosen elimination or prohibition of microbial pathogens with locally administered antibacterial agents coupled with SRP is an efficient move toward treatment of chronic periodontitis.

**Keywords:** Chronic periodontitis, Local drug delivery, Nonsurgical periodontal therapy, Scaling and root planing.

*The Journal of Contemporary Dental Practice* (2023): 10.5005/jp-journals-10024-3455

## INTRODUCTION

A frequent condition that affects the mouth is an inflammatory process of the supporting tissues around the teeth, referred to as "Periodontitis", which is chiefly a result of building up of a complex, multimicrobial dental biofilm. This process is prompted by gram-negative dental microbial plaque deposits that initiate a host reaction, leading to a progressing, permanent bone and soft-tissue annihilation (periodontal pocket development, gingival recession, or either), dental mobility in addition to loss of teeth.<sup>1</sup>

Conventional periodontal management focuses on mechanical debriding of the radicular surfaces to preserve a healthy sulcus or create an environment appropriate for novel attachment. The incapability of mechanical management to create an advantageous radicular surface in every situation, together with the character and intricacy of the subgingival plaque, has hastened the hunt for adjunctive therapy plans to enhance the probability of triumphantly handling periodontal pathosis.<sup>2</sup>

Utility of the various antibacterial substances acquired eminence as a chemical means to avoid preliminary bacterial recolonization owing to a superior probability of consequent clinically significant enhancement. Such chemical substances acquire entry to the periodontal pocket following local/systemic route of administration. As systemic administration of antibiotics

<sup>1</sup>Department of Periodontology, Government College of Dentistry, Indore, Madhya Pradesh, India

<sup>2</sup>Department of Oral and Maxillofacial Surgery, Kalinga Institute of Dental Sciences, KIIT (Deemed to be University), Bhubaneswar, Odisha, India

<sup>3</sup>Department of Conservative Dentistry and Endodontics, AB Shetty Memorial Institute of Dental Sciences (ABSMIDS), NITTE (Deemed to be University), Mangaluru, Karnataka, India

<sup>4</sup>Department of Periodontics, Noorul Islam College of Dental Sciences, Trivandrum, Kerala, India

<sup>5</sup>Department of Conservative Dentistry and Endodontics, Noorul Islam College of Dental Sciences, Trivandrum, Kerala, India

<sup>6</sup>Department of Periodontology, Dental College, JNIMS, Porompat, Imphal, Manipur, India

<sup>7</sup>Department of Preventive Dental Science, College of Dentistry, Jazan University, Saudi Arabia

**Corresponding Author:** Gowrish Sunnanguli, Department of Conservative Dentistry and Endodontics, AB Shetty Memorial Institute of Dental Sciences (ABSMIDS), NITTE (Deemed to be University), Mangaluru, Karnataka, India, Phone: +91 9449959686, e-mail: gsbhat78@gmail.com

**How to cite this article:** Hatila S, Lahiri B, Sunnanguli G, et al. Comparative Assessment of the Effect of Three Various Local Drug

is associated with numerous side effects, contemporary research is now focused on the role of topical/local antimicrobial agents in the treatment of periodontitis.<sup>3</sup>

Local treatment with antimicrobial agents in various forms like mouthwashes dentifrices/gels might prove efficacious in eliminating supragingival biofilms. The drawbacks of rinsing, irrigation, plus comparable techniques of drug delivery encompass quick clearance that leads to inadequate exposure to drug with subsequent deficient clinical outcomes.<sup>4</sup> Subgingival antibacterial liberation mechanism is broadly utilized as it employs dissimilar antimicrobial substances while using varied delivery methods that influence the amount and preserve the amount of existing drugs over a particular tenure. Numerous clinical research investigations have assessed the advantages of dissimilar locally administered antimicrobial agents as a solitary therapy or in addition to traditional scaling and root planing in the management of chronic periodontitis.<sup>5</sup> The subgingival use of antimicrobial delivery system is a complex technique that incorporates a number of antimicrobial agents and delivery mechanisms that have an impact on the concentration and long-term preservation of local medications. Therefore, the current research was performed to evaluate the outcome of three different local drug-release medications in the treatment of chronic periodontitis.

## MATERIALS AND METHODS

The present study was conducted in the Department of Periodontology, Government College of Dentistry, Indore. Sixty patients, aged 30–55 years (36 males and 24 females), were involved in the current research, and consent was obtained from all participants. Participants with a minimum of four periodontal pockets having a depth on probing amid 5–7 mm, lack of periodontal treatment 6 months prior to preliminary assessment, and lack of exposure to antibiotics in the prior 6 months constituted the inclusion criteria. The exclusion criteria included participants with systemic illnesses, smokers, pregnant or lactating women, area with overhanging restorations, individuals with recognized or assumed allergy, and periodontal pocket depth <5 mm after primary prophylaxis.

### Primary Therapy

The study participants underwent phase-I management comprising SRP by a single clinician, subsequent to which oral cleanliness preservation suggestions were given. After 7 days of phase-I therapy, the patients were recalled and assessed again to validate the selected criteria.

After SRP, participants who fulfilled the inclusion criteria entered the study and were allocated at random to one of the three groups, each comprising 20 patients as the following:

#### Group A: SRP with Local Application of Doxycycline Gel

Following subgingival SRP of the region, it was subjected to drying and isolation with the aid of cotton rolls. Doxycycline gel (*Atridox*®) was introduced subgingivally within the chosen periodontal pocket with a syringe that expelled the gel to the bottom of the periodontal pocket while slowly moving back the syringe needle from the bottom of the pocket.

#### Group B: SRP with Local Application of Tetracycline Fibers

Tetracycline fibers (Periodontal Plus AB™) agent holds 25 mg of uncontaminated fibrillar collagen comprising about 2 mg of uniformly impregnated tetracycline hydrochloride in every vial.

Delivery Medicaments in the Management of Chronic Periodontitis. *J Contemp Dent Pract* 2023;24(3):162–167.

Source of support: Nil

Conflict of interest: None

#### Group C: SRP with Local Application of Chlorhexidine Gel

Scaling and root planing were performed at baseline till a smooth, tidy, and solid surface was procured as anticipated by the clinician. A syringe was employed for application of chlorhexidine gel (CHLO-SITE) straightforwardly within the periodontal pocket.

## Clinical Evaluation of the Efficacy of Three Local Drug Delivery Medicaments

Initially, periodontal evaluation of the complete oral cavity was done and patients gratifying the inclusion criteria underwent SRP. Summon-up visit was regarded as the baseline post 7 days. The plaque index (PI), the gingival index (GI), and periodontal pocket depth (PPD) were documented at the baseline visits (prior to local medication delivery), and these indices were again documented 30 and 90 days post local medication delivery.

### Statistical Analysis

Statistical Package for Social Sciences (SPSS) version 21 (SPSS Inc., Chicago, IL, USA) was employed to evaluate the data. For statistical investigation, the ANOVA test was utilized to ascertain the importance of the intergroup disparities. A  $p$ -value < 0.05 was regarded as statistically significant.

## RESULTS

Table 1 and Figure 1 depict the mean GI values at baseline, after 30 days and 90 days. About  $1.38 \pm 0.05$  was the GI value at baseline for doxycycline gel use,  $1.36 \pm 0.11$  for tetracycline fibers, as well as  $1.38 \pm 0.10$  for chlorhexidine gel. Post 90 days, the greatest value decrease was noted with tetracycline fibers at  $0.76 \pm 0.19$  in pursuit by chlorhexidine gel use at  $0.84 \pm 0.21$  as well as doxycycline gel use at  $0.94 \pm 0.02$ . At dissimilar time gaps, every group exhibited statistically important disparity with  $p < 0.001$ .

Table 2 and Figure 2 show the mean PI values at baseline, after 30 days and 90 days. At baseline, PI value was  $1.26 \pm 0.01$  for doxycycline gel use,  $1.30 \pm 0.14$  for tetracycline fibers, as well as  $1.30 \pm 0.22$  for chlorhexidine gel use. Post 90 days, the highest value decrease was noted with tetracycline fibers use at  $0.82 \pm 0.16$ , in pursuit by chlorhexidine gel use at  $0.98 \pm 0.11$  as well as doxycycline gel use at  $1.02 \pm 0.06$ . At dissimilar time gaps, just the tetracycline fibers cohort exhibited statistically noteworthy disparity at  $p < 0.001$ .

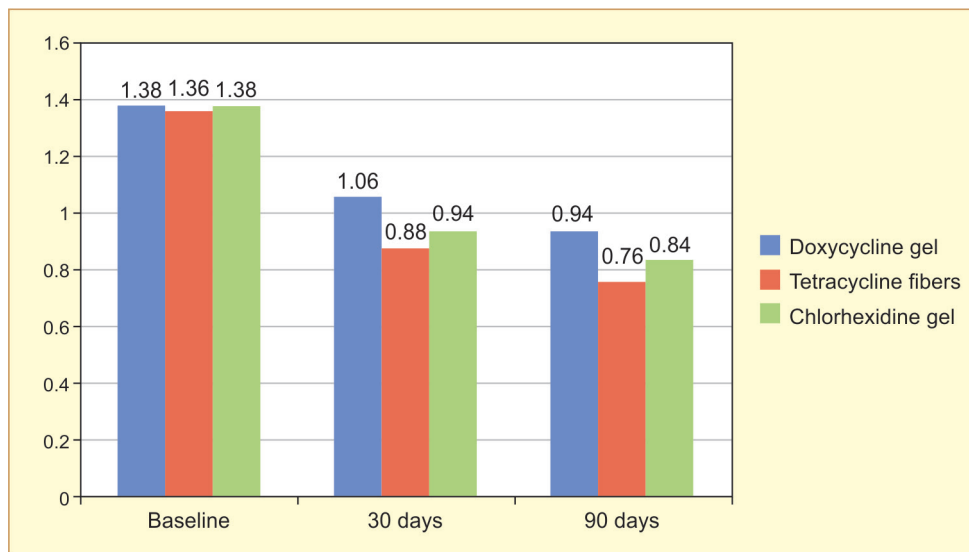
Table 3 and Figure 3 depict the mean periodontal pocket depth values at baseline, after 30 days and 90 days. At baseline, the periodontal pocket depth value was  $5.88 \pm 0.24$  for doxycycline gel use,  $5.90 \pm 0.09$  for tetracycline fibers use, as well as  $5.82 \pm 0.18$  for chlorhexidine gel use. Post 90 days, the utmost value decrease was noted with tetracycline fibers use at  $3.02 \pm 0.06$ , in pursuit by chlorhexidine gel use at  $3.44 \pm 0.16$  as well as doxycycline gel use at  $3.72 \pm 0.11$ . At dissimilar time gaps, every cohort exhibited statistically important dissimilarity with  $p < 0.001$ .

The inference of the present study indicates that tetracycline fibers showed slightly better improvement than chlorhexidine gel and doxycycline gel.

**Table 1:** Evaluation of mean gingival index scores at baseline, 30 days and 90 days

Index	Experimental groups	Study duration	Mean ± SD	F value	p-value
Gingival index	Group A: Doxycycline gel	Baseline	1.38 ± 0.05	6.026	0.001*
		30 days	1.06 ± 0.14		
		90 days	0.94 ± 0.02		
	Group B: Tetracycline fibers	Baseline	1.36 ± 0.11	6.136	0.001*
		30 days	0.88 ± 0.06		
		90 days	0.76 ± 0.19		
	Group C: Chlorhexidine gel	Baseline	1.38 ± 0.10	5.582	0.001*
		30 days	0.94 ± 0.01		
		90 days	0.84 ± 0.21		

\*Statistically significant



**Fig. 1:** Mean gingival index scores at different intervals

**Table 2:** Evaluation of mean plaque index scores at baseline, 30 days and 90 days

Index	Experimental groups	Study duration	Mean ± SD	F value	p-value
Plaque index	Group A: Doxycycline gel	Baseline	1.26 ± 0.01	5.137	0.194
		30 days	1.14 ± 1.19		
		90 days	1.02 ± 0.06		
	Group B: Tetracycline fibers	Baseline	1.30 ± 0.14	7.960	0.001*
		30 days	0.90 ± 0.08		
		90 days	0.82 ± 0.16		
	Group C: Chlorhexidine gel	Baseline	1.30 ± 0.22	5.031	0.176
		30 days	1.12 ± 0.02		
		90 days	0.98 ± 0.11		

\*Statistically significant

## DISCUSSION

The final aim of all periodontal management strategies is to retain most of the dentition by decreasing, ceasing, and causing reversal of periodontal damage. Although the consequence of mechanical

debriding generally gratifies decrease in periodontal pathosis, challenges in accessing the base of the periodontal pocket can cause treatment to fail. Owing to this, additional management is unavoidable.<sup>6</sup> Local administration of the medication can achieve a hundred-times greater concentration of antibacterials

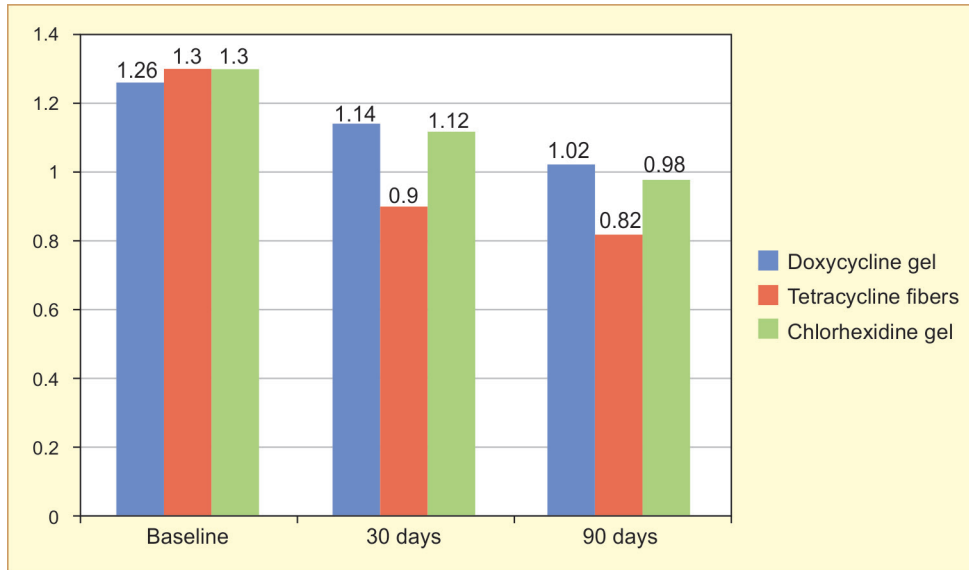


Fig. 2: Mean plaque index scores at different intervals

Table 3: Assessment of mean periodontal pocket depth scores at baseline, 30 days and 90 days

Index	Experimental groups	Study duration	Mean ± SD	F value	p-value
Periodontal pocket depth	Group A: Doxycycline gel	Baseline	5.88 ± 0.24	8.368	0.001*
		30 days	4.24 ± 0.01		
		90 days	3.72 ± 0.11		
	Group B: Tetracycline fibers	Baseline	5.90 ± 0.09	10.024	0.001*
		30 days	3.98 ± 0.12		
		90 days	3.02 ± 0.06		
	Group C: Chlorhexidine gel	Baseline	5.82 ± 0.18	9.388	0.001*
		30 days	4.08 ± 0.31		
		90 days	3.44 ± 0.16		

\*Statistically significant

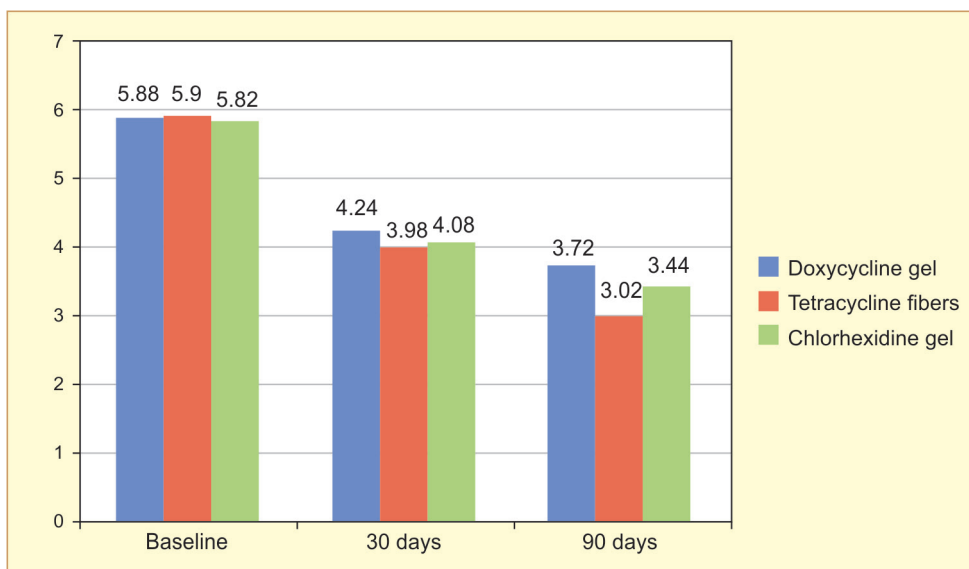


Fig. 3: Mean periodontal pocket depth scores at different intervals

in subgingival areas versus systemic administration schemes. It is also probable that chemical antibacterial substances when subjected to a local application within the periodontal pockets might additionally repress periodontal microorganisms, therefore enhancing the actions of traditional mechanical periodontal management.<sup>7</sup>

In the current research, the highest value decrease in the GI, PI, and depth of the periodontal pocket was noted with tetracycline fiber use, in pursuit by chlorhexidine gel use as well as doxycycline gel use. Decrease in GI value was statistically noteworthy with tetracycline use. These findings are in harmony with the research performed by Soares et al.<sup>8</sup> and Unsal et al.<sup>9</sup> who infer that decrease in bleeding is owed to reversal of gingival inflammatory process post SRP and the recognized antibacterial action of tetracycline.

As per Jeong et al.,<sup>10</sup> decrease in supragingival biofilm value in tetracycline fiber cohort may be pointed out to the chemical regulation of subgingival biofilm by tetracycline fibers that may also exert a preventive action on supragingival biofilms.

As per Friesen et al.<sup>6</sup> and Perinetti et al.,<sup>11</sup> the enhanced gingival well-being might cause a documented decrease of PPD, probably by lessening the marginal gingival edema as well as (or) by reducing the periodontal tissue pocket probing depth due to greater collagen concentration. These inferences are not in accordance with those by Drisko et al.<sup>12</sup> who noted no disparities.

Tetracycline is superior to various other antimicrobials as they have the ability to stick onto cementum and soft tissues together. Additionally, tetracycline is the only antibiotic that reaches high levels in the GCF as compared with levels in the serum. Tetracycline also leads to prohibition of the effects of collagenase, collagen degradation, and bone resorption. Tetracyclines have recognized effectiveness across Gram-positive/Gram-negative anaerobic pathogens associated with chronic adult periodontitis. They exert antimicrobial consequences by limiting protein creation.<sup>13</sup>

All participants exhibited a noteworthy improvement in plaque plus gingival index post therapy, and the outcomes were preserved throughout the trial duration. Participant inclusion was based on intent to treat and scaling and root planing were done at baseline for all teeth. Every patient was rendered an all-encompassing oral hygiene advice that was retold at all visits. These results are in harmony with Heasman et al.<sup>14</sup> and Jeffcoat et al.<sup>15</sup>

In the current research, doxycycline gel use delineated noteworthy decrease in gingival and periodontal pocket values. Likewise, Al Hulami et al.<sup>16</sup> noted that locally administered doxycycline was efficient in treating periodontitis as an additional therapy to SRP. Javali and Vandana<sup>17</sup> showed that 10% doxycycline gel was equally efficient as SRP in decreasing the clinical symptoms of periodontitis. As per Tonetti et al.,<sup>18</sup> locally delivered and gradually releasing doxycycline gel may offer advantages for a smaller duration in regulating the inflammatory process as well as deep pockets post SRP in individuals with periodontitis.

In the current research, chlorhexidine gel use too delineated a noteworthy decrease in gingival plus periodontal pocket depth values. Likewise, Mizrak et al.<sup>19</sup> infer that it has been recognized that chlorhexidine has a valuable action when employed as a supplementary periodontal therapy. Chlorhexidine prevents bacterial proteases generated by mighty periodontal microorganisms as well as alters the microorganisms in the periodontal pocket. As per Anitha et al.,<sup>20</sup> it exerts actions by decreasing the pellicle creation, modifying the attachment of bacteria to the dentition, as well as modifying the bacterial cell

wall. The steps that cause antimicrobial actions of chlorhexidine may enhance the cell membrane diffusion capacity, after which the macromolecules existing in the cell cytoplasm may form a mass.

The limitations of this research are that the locally administered antimicrobial substances were evaluated for advantages over a shorter span in periodontal treatment. Research extending over longer periods of time with extended follow-up may be beneficial in delineating the real elucidation of these consequences. Microbiological evaluation, biochemical assessment, and the probable adverse actions of subgingival introduction like allergy, gingival redness, pain, as well as uneasiness were not appraised.

## CONCLUSION

Within the limitations of the current research, it may be inferred that local administration of tetracycline fibers, chlorhexidine gel, and doxycycline gel is a secure and effective technique coupled with SRP in the treatment of periodontal pathosis. Tetracycline fibers exhibited somewhat superior enhancement than chlorhexidine as well as doxycycline gel.

## REFERENCES

1. Pradeep AR, Sagar SV, Daisy H. Clinical and microbiologic effects of subgingivally delivered 0.5% azithromycin in the treatment of chronic periodontitis. *J. Periodontol* 2008;79(11):2125–2135. DOI: 10.1902/jop.2008.070589.
2. Socransky SS, Haffajee AD. Periodontal microbial ecology. *Periodontol* 2000 2005;38:135–187. DOI: 10.1111/j.1600-0757.2005.00107.x.
3. Srivastava R, Verma PK, Tandon P, et al. Chlorhexidine chip and tetracycline fibers as adjunct to scaling and root planing – A clinical study. *Braz J Oral Sci* 2009;8(4):201–205. DOI: 10.20396/bjos.v8i4.8642081
4. Kalsi R, Vandana KL, Prakash S. Effect of local drug delivery in chronic periodontitis patients: A meta-analysis. *J Indian Soc Periodontol* 2011;15(4):304–309. DOI: 10.4103/0972-124X.92559.
5. Nandini N, Dodwad V, Arora K. Comparative evaluation of 1% curcumin solution and 0.2% chlorhexidine irrigation as an adjunct to scaling and root planing in management of chronic periodontitis: A clinico-microbiological study. *J Pharma Biomed Sci* 2012;14:1–6. [https://www.jpjbs.info/index.php?option=com\\_docman&task=doc\\_details&gid=361&Itemid=41](https://www.jpjbs.info/index.php?option=com_docman&task=doc_details&gid=361&Itemid=41).
6. Friesen LR, Williams KB, Krause LS, et al. Controlled local delivery of tetracycline with polymer strips in the treatment of periodontitis. *J Periodontol* 2002;73(1):13–19. DOI: 10.1902/jop.2002.73.1.13.
7. Pathak T, Gupta B, Tiwari V, et al. A comparative study to evaluate the effectiveness of subgingivally delivered antimicrobial bio-absorbable controlled release 0.5% azithromycin gel and 2 mg tetracycline hydrochloride fibres as an adjunct to scaling and root planing in the treatment of chronic periodontitis. *Int J Prev Clin Dent Res* 2018;5(2):46–52. [http://www.ijpcdr.com/pdf/2018/April-June/10\\_DR\\_SAURAV\\_SHARMA\\_final%20manuscript\\_OA.pdf](http://www.ijpcdr.com/pdf/2018/April-June/10_DR_SAURAV_SHARMA_final%20manuscript_OA.pdf).
8. Soares PB, de Menezes HH, Naves MM, et al. Effect of absorbent tetracycline-loaded membrane used in the reduction of periodontal pockets: An *in vivo* study. *Braz Dent J* 2009;20(5):414–418. DOI: 10.1590/s0103-64402009000500010
9. Unsal E, Akkaya M, Walsh TF. Influence of a single application of subgingival chlorhexidine gel or tetracycline paste on the clinical parameters of adult periodontitis patients. *J Clin Periodontol* 1994;21(5):351–355. DOI: 10.1111/j.1600-051x.1994.tb00725.x.
10. Jeong SN, Han SB, Lee SW, et al. Effects of tetracycline-containing gel and a mixture of tetracycline and citric acid-containing gel on non-surgical periodontal therapy. *J Periodontol* 1994;65(9):840–847. DOI: 10.1902/jop.1994.65.9.840.

11. Perinetti G, Paolantonio M, Cordella C, et al. Clinical and microbiological effects of subgingival administration of two active gels on persistent pockets of chronic periodontitis patients. *J Clin Periodontol* 2004;31(4):273–281. DOI: 10.1111/j.1600-051x.2004.00481.x.
12. Drisko CL, Cobb CM, Killoy WJ, et al. Evaluation of periodontal treatments using controlled-release tetracycline fibers: Clinical response. *J Periodontol* 1995;66(8):692–699. DOI: 10.1902/jop.1995.66.8.692.
13. Nitesh Kumar Sharma, Anushree 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. *Int J Contemp Med Res* 2017;4(5):998–1003. [https://www.ijcmr.com/uploads/7/7/4/6/77464738/ijcmr\\_1429\\_june\\_16.pdf](https://www.ijcmr.com/uploads/7/7/4/6/77464738/ijcmr_1429_june_16.pdf).
14. Heasman PA, Heasman L, Stacey F, et al. Local delivery of chlorhexidine gluconate (PerioChip TM) in periodontal maintenance patients. *J Clin Periodontol* 2001;28(1):90–95. DOI: 10.1034/j.1600-051x.2001.280114.x.
15. Jeffcoat MK, Bray KS, Ciancio SG, et al. adjunctive use of subgingival controlled release chlorhexidine chip reduces probing depth and improves attachment level compared with scaling and root planing alone. *J Periodontol* 1998;69(9):989–997. DOI: 10.1902/jop.1998.69.9.989.
16. Al Hulami H, Babay N, Awartani F, et al. The effect of locally delivered doxycycline as an adjunctive therapy to scaling and root planing in smokers. *Saudi Dent J* 2011;23(3):143–148. DOI: 10.1016/j.sdentj.2011.04.001
17. Javali MA, Vandana KL. A comparative evaluation of atrigel delivery system (10% doxycycline hyclate) Atridox with scaling and root planing and combination therapy in treatment of periodontitis: A clinical study. *J Indian Soc Periodontol* 2012;16(1):43–48. DOI: 10.4103/0972-124X.94603.
18. Tonetti MS, Lang NP, Cortellini P, et al. Effects of a single local doxycycline administration adjunctive to mechanical debridement in patients with persistent/recurrent periodontitis but acceptable oral hygiene during supportive periodontal therapy. *J Clin Periodontol* 2012;39(5):475–482. DOI: 10.1111/j.1600-051X.2012.01864.x.
19. Mizrak T, Güncü GN, Caglayan F, et al. Effect of a controlled-release chlorhexidine chip on clinical and microbiological parameters and prostaglandin E2 levels in gingival crevicular fluid. *J Periodontol* 2006;77(3):437–443. DOI: 10.1902/jop.2006.050105.
20. Anitha V, Rajesh P, Shanmugam M, et al. Comparative evaluation of natural curcumin and synthetic chlorhexidine in the management of chronic periodontitis as a local drug delivery: A clinical and microbiological study. *Indian J Dent Res* 2015;26(1):53–56. DOI: 10.4103/0970-9290.156806.