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Evaluation of nanofiber scaffolds laden *Ashvakatri* in the management of chronic periodontitis-a randomized, controlled split pocket study

Pragati Dubey [a], Neelam Mittal [a,*], Brahmeshwar Mishra [b], Anju Gautam [a], Naveen Kumar [a], M. Rashika [a]

[a] Faculty of Dental Sciences, Institute of Medical Sciences, Banaras Hindu University, Varanasi, 221005, India
[b] Department of Pharmaceutical and Technology, IIT- BHU, Varanasi, 221005, India

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ABSTRACT

Background: The main objective of periodontal treatment is to stop the progression of periodontal disease. Controlled-release drugs yield promising outcomes when conventional treatment is proven to be insufficient in establishing periodontal health in chronic periodontitis. A low-dose controlled-release delivery method for the treatment of periodontal infection was attempted to be developed in this study. With effective electrospinning, a novel sustained-release medication system including polycaprolactone (PCL) nanofibers containing *Ashvakatri* (A2) and Tetracycline (TET) was accessed clinically for periodontitis.

Method & materials: The electrospinning technique prepared nanofibers with A2 and TET in PCL and gelatin. The A2-loaded nanofiber followed the Higuchi model release and had a sustained impact of 9 days (220 h). 75 periodontal sites from 31 patients with chronic periodontitis (≥5 mm probing depth) followed by 3 groups: Group I received Scaling and root planning (SRP) and blank polymer mat whereas Group II treated with SRP and PCL-GE-A2 nanofiber scaffold/mat, and Group III received SRP + PCL-GE-TET (tetracycline) nanofiber scaffolds. Clinical evaluations of GI, PI, PPD, and CAL were performed on each patient group.

Conclusion: Compared to the placebo and standard group, the test group was remarkably associated with improved GI, PI, PPD, and CAL at the end of the study. Therefore, drug-loaded nanofiber was found to be efficacious in treating periodontal diseases and may be appropriate as an alternative treatment.

Clinical significance: The fabricated PCL-GE-A2 nanofiber mat was more cost-efficient, minimized the dosage amount, and dosage frequency, and showed no adverse effects or discomforts with increased patient compliance.

1. Background

India is a very diverse country in terms of eating habits and lifestyles. India is a country where eating pan, chewing tobacco, beetle nut, and supari are in various forms, and smoking is very common in their culture and dietary items. A healthy population is necessary for a country to become developed, and this includes having good oral health.[1]

Periodontitis is a serious health disease that reduces the quality of life by causing tooth loss, disability, masticatory dysfunction, low nutritional status, and impaired speech. Periodontitis is also independently related to systemic chronic inflammatory disorders such as atherogenic cardiovascular disease, type 2 diabetes, rheumatoid arthritis, chronic renal disease, obesity, and chronic obstructive pulmonary disease.[2]

Conventional periodontal treatment involves systemic antibiotic delivery and mechanical cleaning, which is not promising. Scaling and root planning, as well as surgical intervention, are examples of potential therapeutic strategies.[3] Systemic antibiotics and mouthwashes containing chlorohexidine are also recommended. Deep pockets are frequently difficult to debride with scaling and root planing, and recovery following surgical intervention is time-consuming. Adjuvant systemic antibiotic use places a burden on the patient since it may result in side effects, and it also leaves the periodontal pockets with an inadequate concentration of the active ingredient. Furthermore, the use of adjuvant antibiotics may have a role in the development of resistant bacterial strains or undesirable side effects such as gastrointestinal discomfort, and hypersensitivity.[2]

Over the past ten to fifteen years, there has been a lot of focus on the

* Corresponding author.
E-mail addresses: pragait@bhu.ac.in (P. Dubey), dr.neelammittal@gmail.com (N. Mittal), bmishra.phe@itbhu.ac.in (B. Mishra), dranjugautam@gmail.com (A. Gautam), pgnaveenkumar@gmail.com (N. Kumar), rashika.muralisekar@gmail.com (M. Rashika).

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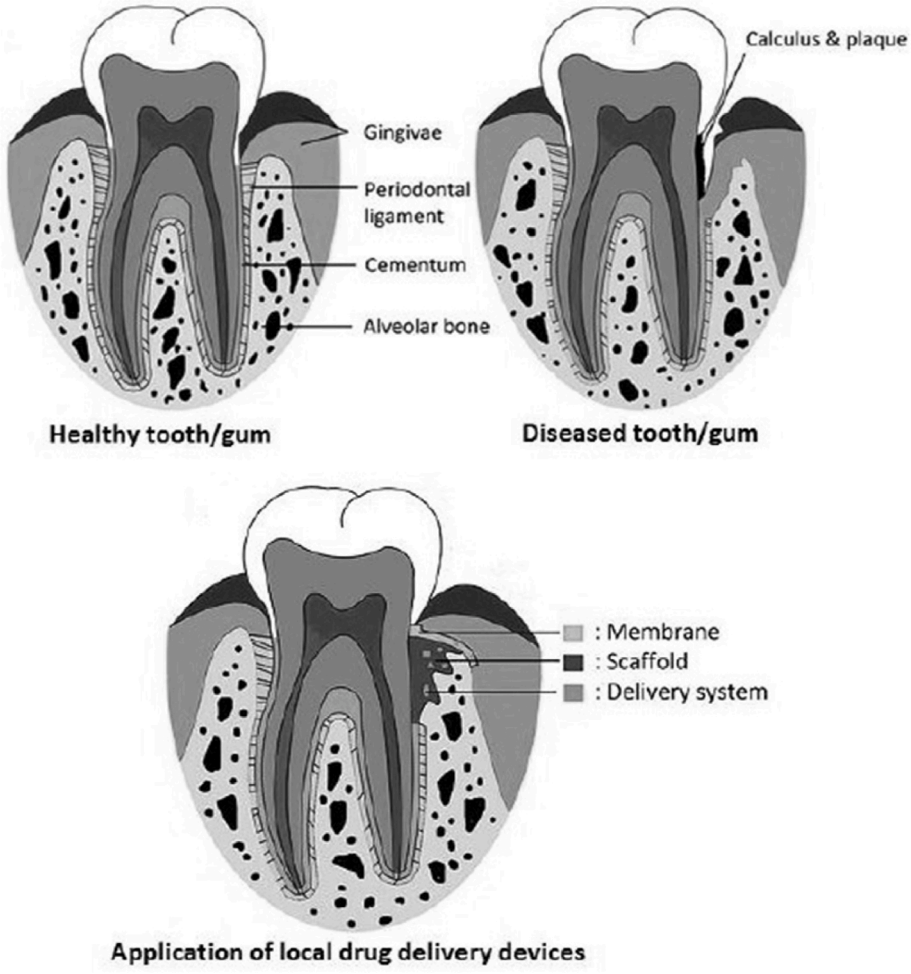


Fig. 1. Diagrammatic structure of Periodontitis condition and insertion of Nanofiber scaffolds.

local intra-pocket drug delivery system.[4] Several articles addressed local drug delivery systems for antibacterial medications. It has been shown that local medication delivery devices, either used alone or in conjugation with other dental treatments, can provide more effective treatment than systemic antimicrobial drug administration.[5] Thus, a possible method of treating periodontitis is to use local delivery systems that include antibiotics.

Also, it is imperative to develop optimal carrier systems for topical application using herbal formulation to enable a safer, more extensive, inexpensive, and more promising use of active ingredients, especially in the perspective of anticipated features of formulations.[6] The goal of the current study was to assess how well *Ashvakatri* nanofiber works as an adjuvant to SRP in the treatment of chronic periodontitis. effectiveness of some herbal formulations against periodontal disease *Ashvakatri* was evaluated for this investigation. Also, there is no any published research regarding Ashvaktari nanofiber.

2. Materials & method

2.1. Procurement of herbs & identification

The live plants of *Ashvakatri* were collected from the western ghats of Kerala, India in July 2023. The plant parts were identified and authenticated by Dr Jasmeet Singh, Department of Dravyaguna, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, India. The voucher specimen with reference number DG/22–23/563 has been deposited in the same department.

The rhizome was cut, shade-dried, and powdered by an electrical mixer grinder, followed by stored in an airtight container until further studies.

2.2. Extraction of the drug

The powder (2 kg) of *Ashvakatri* dried rhizome was extracted with 3 L of ethanol: water (6:4) by using a maceration process for 72 h.[6] After this, the mixture was filtered and evaporated using a water bath to afford a brownish sticky mass (256.78 gm) and then freeze-dried using a lyophilizer. Until usage, the dried HAE was kept at −4 °C.[6,7] The extraction yield was calculated as

$$Yield\,\% = Extracted/Total \times 100.$$

2.3. Electrospun method

The polymeric solution was prepared in two separate beakers using 10 % PCL and 5 % gelatin in 10 ml trifluoroethanol. Afterward, 10 % *Ashvakatri* was completely dissolved in one beaker of this polymeric solution and simultaneously, 10 % TET was dissolved in another beaker of polymeric solution. These resultant solutions were then separately transferred to a 10 ml syringe pump with a 21-G needle attached to it. The drug-loaded polymeric solution was then electrospun at a voltage of 1.5 kV/cm, a temperature of 22 °C, a relative humidity of 60 %, and a flow rate of 0.2–0.6 ml/h.

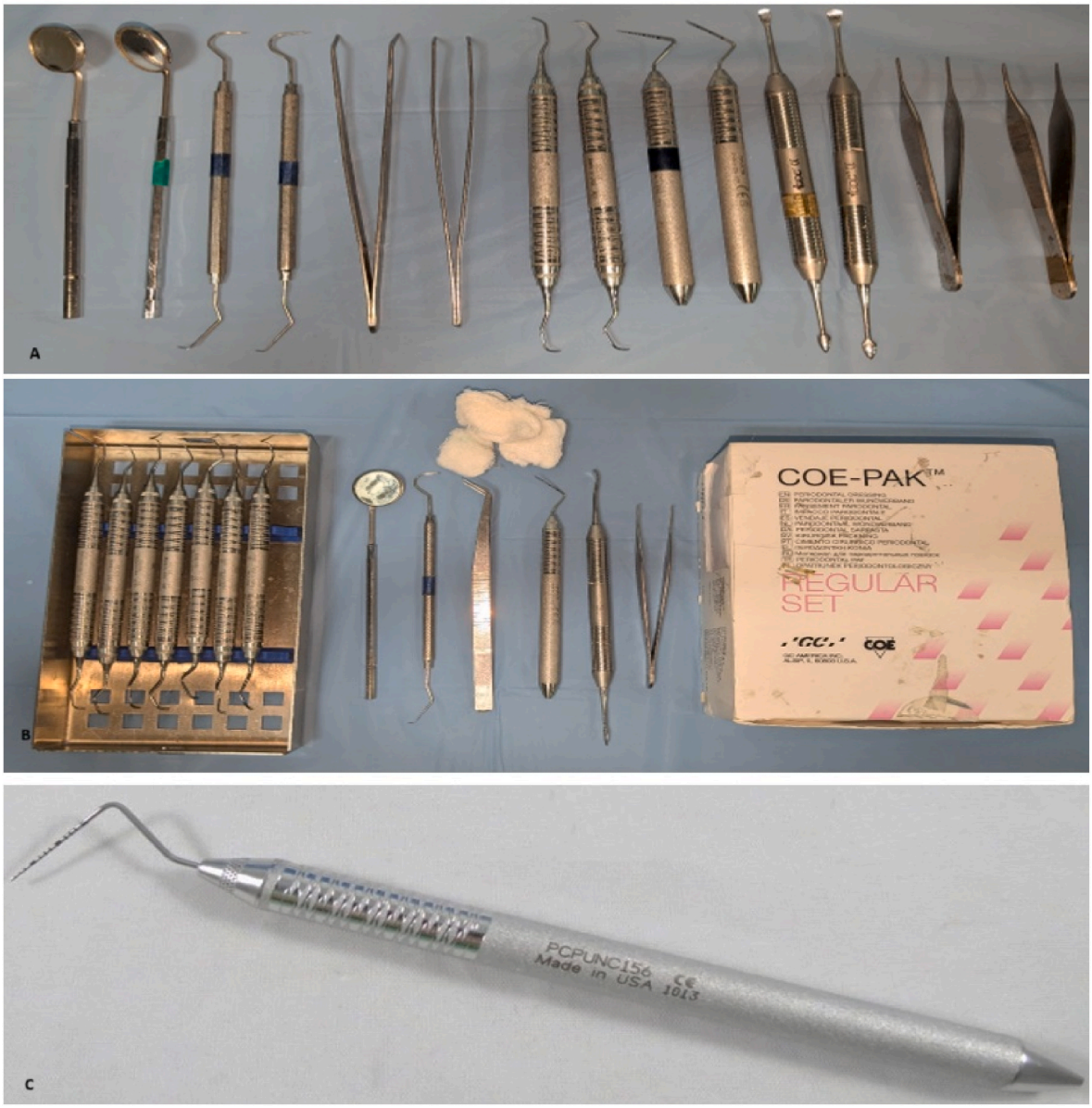


Fig. 2. (A) Armamentarium used in the clinical study, (B) Prepared armamentarium for study with periodontal dressing, (C): UNC-15 probe for pocket depth measurement.

2.4. Characterization of composite nanofiber

The uniformity of thickness of each composite nanofiber (surface area 1 cm^2) was evaluated using high-resolution scanning electron microscopy (HR-SEM). Also, the uniformity of weight of both selected nanofibers was determined using an electronic balance (surface area 1 cm^2). Furthermore, the drug-loaded nanofiber was then cut and kept in 100 ml artificial saliva for 12 h and the amount of drug present was measured spectrophotometrically.

2.5. Clinical study

The present study was conducted in the Department of Periodontics in the outpatient department of the Faculty of Dental Sciences, Institute of Medical Sciences, Banaras Hindu University. First, this study was approved by the Ethical Committee of the Institute of Medical Sciences, Banaras Hindu University with reference number Dean/2024/EC/6970. The Clinical Trial Registry- India (CTRI) was also done with the reference registration number CTRI/2024/04/065742. Before the study began, each participant was provided with written informed consent after being given proper instructions about the objective of our investigation.

2.5.1. Recruitment of subjects

Randomly, 75 periodontal sites in 31 subjects with chronic periodontitis of either gender were recruited for this investigation. The inclusion and exclusion criteria were examined before the recruitment of the patient from OPD room no. 6, Department of Periodontics, Sir Sunderlal Hospital & Trauma Centre, Faculty of Dental Sciences, Institute of Medical Sciences, Banaras Hindu University. The criteria were based on.

2.5.1.1. Inclusion criteria.

➢ Age 18–55 years

➢ Good health with no illness.

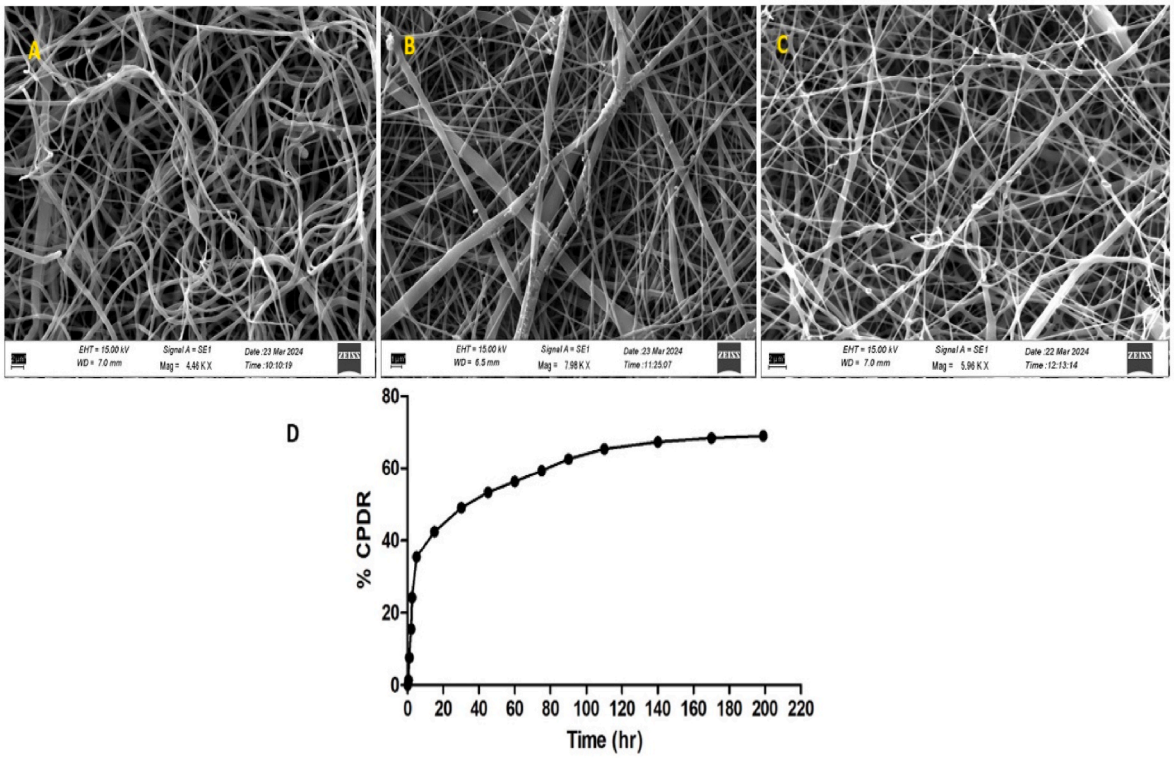


Fig. 3. (A, B, C) SEM images of blank, A2-loaded nanofiber, and TET-loaded nanofibers; (D) graphical representation of cumulative percentage drug release of composite A2 loaded nanofiber up to 220 h.

Table 1
Statistical changes in PI value in overall duration.

Variables	Mean ± SD			Intergroup* p-value
	Group I	Group II	Group III	
Pre PI	1.170 ± 0.172	1.140 ± 0.126	1.230 ± 0.142	0.321
Post PI @ 2W	1.092 ± 0.158	1.062 ± 0.149	1.186 ± 0.194	0.304
Post PI @1M	0.960 ± 0.118	0.990 ± 0.152	0.920 ± 0.236	0.296
Post PI @2M	1.140 ± 0.126	1.100 ± 0.125	1.080 ± 0.156	0.235
Intragroup**p value	**0.000**	**0.001**	**0.000**	–

Test applied: *Kruskal Wallis test, **Friedman test.

Table 3
Statistical changes in GI value in overall duration.

Variables	Mean ± SD			Intergroup* p value
	Group I	Group II	Group III	
Pre GI	1.360 ± 0.126	1.410 ± 0.202	1.320 ± 0.210	0.378
Post GI @2W	1.296 ± 0.142	1.138 ± 0.166	1.274 ± 0.172	0.346
Post GI @1M	1.040 ± 0.138	1.070 ± 0.184	1.010 ± 0.134	0.315
Post GI @2M	1.120 ± 0.127	1.230 ± 0.175	1.160 ± 0.159	0.072
Intragroup**p value	**0.000**	**0.000**	**0.000**	–

Test applied: *Kruskal Wallis test, **Friedman test.

Table 2
Pairwise comparison of plaque index in group I.

Variable	P value	
GROUP I		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	1.00
Post GI @1M	Post GI @2M	**0.00**
GROUP II		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	1.00
Post GI @1M	Post GI @2M	0.10
GROUP III		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	0.07
Post GI @1M	Post GI @2M	0.04

Table 4
Pairwise comparison of the gingival index in group I, II & III.

Variable	P value	
GROUP I		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.00**
Post GI @1M	Post GI @2M	0.413
GROUP II		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.02**
Post GI @1M	Post GI @2M	**0.01**
GROUP III		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.05**
Post GI @1M	Post GI @2M	**0.01**

Table 5
Statistical changes in PPD value in overall duration.

Variables	Mean ± SD			Intergroup p-value*
	Group I	Group II	Group III	
Pre PPD	4.96 ± 0.676	5.24 ± 0.723	5.12 ± 0.600	0.321
Post PPD @1M	4.76 ± 0.723	4.04 ± 0.676	4.12 ± 0.600	**0.001**
Post PPD @2M	4.72 ± 0.843	3.28 ± 0.458	3.24 ± 0.436	**0.000**
Intragroup p** value	**0.018**	**0.000**	**0.000**	–

Test applied: *Kruskal Wallis test, **Friedman test.

Table 6
Pairwise comparison of the PPD index in group I, II & III.

Variable	P value	
GROUP I		
Pre PPD	Post PPD @1M	0.96
Pre PPD	Post PPD @2M	0.77
Post PPD @1M	Post PPD @2M	1.00
GROUP II		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.00**
Post GI @1M	Post GI @2M	**0.02**
GROUP III		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.00**
Post GI @1M	Post GI @2M	**0.00**

Table 7
Statistical changes in CAL value in overall durations.

Variables	Mean ± SD			Intergroup* p-value
	Group I	Group II	Group III	
Pre CAL	5.08 ± 0.759	5.16 ± 0.746	5.12 ± 0.600	0.919
Post CAL @1	5.04 ± 0.735	4.20 ± 0.707	4.36 ± 0.700	**0.001**
Post CAL @2	4.96 ± 0.735	3.68 ± 0.748	3.88 ± 0.833	**0.000**
Intragroup**p value	**0.174**	**0.000**	**0.000**	–

Test applied: *Kruskal Wallis test, **Friedman test.

Table 8
Pairwise comparison of CAL index in group I, II & III.

Variable	P value	
GROUP I		
Pre PPD	Post PPD @1M	0.85
Pre PPD	Post PPD @2M	0.74
Post PPD @1M	Post PPD @2M	1.06
GROUP II		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.00**
Post GI @1M	Post GI @2M	**0.02**
GROUP III		
Pre GI	Post GI @1M	**0.00**
Pre GI	Post GI @2M	**0.00**
Post GI @1M	Post GI @2M	**0.02**

Table 9
Pairwise comparison of PPD values among all the three groups.

Group		P** value
Group I	Group II	**0.003**
Group I	Group III	**0.010**
Group II	Group III	1.00

**Friedman test.

Table 10
Pairwise comparison of CAL among all the three groups.

Group		P** value
Group I	Group II	**0.001**
Group I	Group III	**0.014**
Group II	Group III	1.00

**Friedman test.

➢ Male or female both.

➢ Subjects having chronic periodontitis with ≤5 mm pocket depth.

➢ Having bleeding on probe (BOP) from pocket base.

➢ No periodontal treatment from 6 months.

➢ No systemic antibiotics from the last 1 month before the investigation.

2.5.1.2. Exclusion parameters.

➢ Pregnant or lactating women.

➢ Unreliable follow-up patients.

➢ Poor oral hygiene and maintenance

➢ Smoking habits.

➢ Pan or tobacco chewing habits.

2.5.2. Study group

By using the randomized sampling technique, the recruitment of subjects was done with three non-adjacent sites on each patient divided as.

1) Group I (placebo group): Scaling and root planning (SRP) + Blank polymer mat
2) Group II (test group): SRP + PCL-GE-A2 nanofiber scaffold/mat
3) Group III (standard group): SRP + PCL-GE-TET (tetracycline) nanofiber scaffolds

2.6. Treatment procedures

Before being administered, all the fabricated NFs were kept in a UV-Sterilizer under suitable conditions. Fig. 1 suggests the administration of composite nanofiber in diseased sites. The 31 subjects with 75 periodontal sites were initially recruited for the presence of bleeding on the

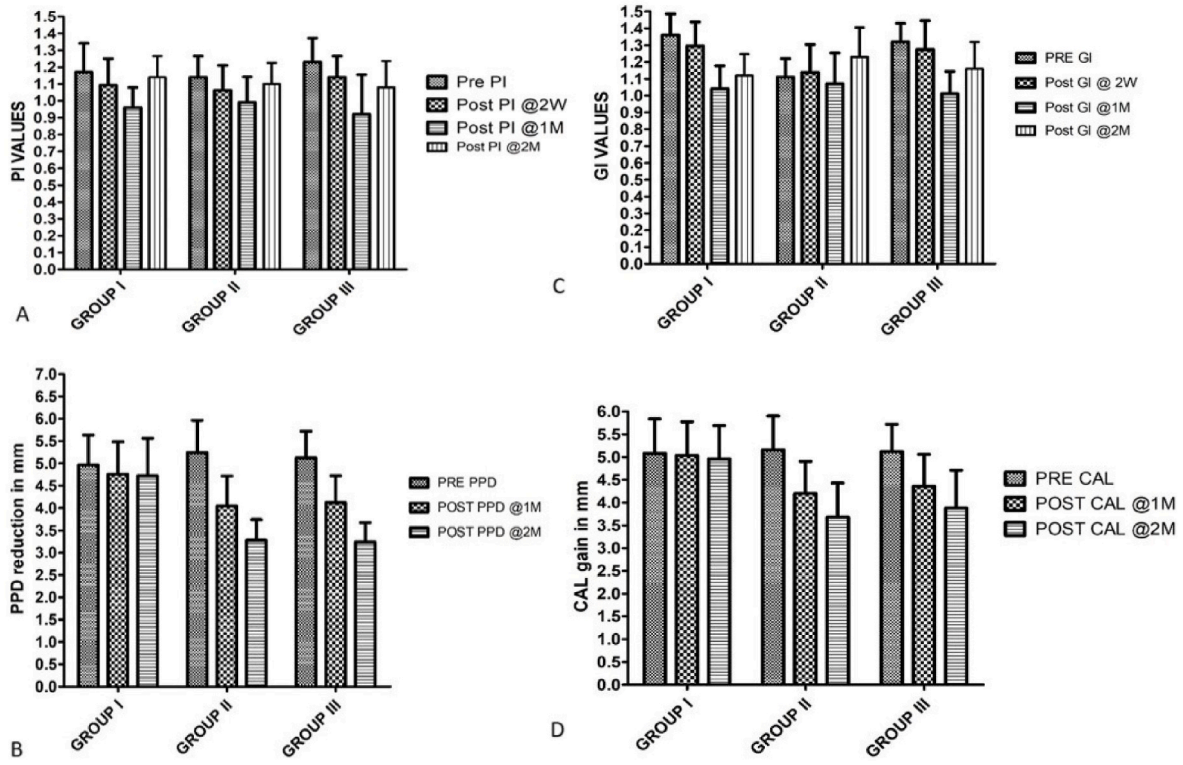


Fig. 4. Post-operative results of PI, GI, PPD, and CAL respectively.

probe from the pocket base and PD $\geq$ 5 mm. Subsequently, the supragingival scaling and root planing (SRP) were done using an ultrasonic scaler (Woodpecker UDS-P) for all the subjects enrolled in this investigation after the baseline was recorded followed by giving instructions to each individual to maintain oral hygiene until the study was done. Afterward, in 25 periodontal sites, blank (PCL-GE) nanofiber scaffolds were inserted using periosteal PPbuser (HU-FRIEDY) followed by periodontal dressing (Coe-Pak) was applied at the entrance of the periodontal pocket and marking them as a placebo group or group I.

Similarly, the recruiters with other 25 periodontal sites, were inserted with PCL-GE-A2 NF mat using periosteal PPbuser (HU-FRIEDY) followed by periodontal dressing (Coe-Pak) as shown in Fig. 2 at the periodontal pocket's entry and were recorded as a test group or group II, and likewise, subjects with other 25 periodontal sites received with PCL-GE-TET NF mat were recorded as a standard group or group III after periodontal dressing was applied. Additionally, until the periodontal dressing was removed, the subjects were instructed to avoid the use of a brush or other interdental cleaning tools.

All three marked group subjects were requested to visit again for follow-up at certain intervals, such as from baseline to the 15th day (2 weeks), 30th day (1 month), and 60th day (2 months) for Coe-Pak removal, and the results were recorded accordingly. In the interim, a telephonic survey on post-operative reassurance was conducted with all the participants on the 7th day (1 week) followed by the 15th day (2 weeks).

2.7. Statistical evaluation

Clinical data of patients from the OPD of BHU's hospital were collected in numbers and percentages and additionally, demonstrated using SPSS software (version 20.0) in the form of tables and graphs.[7]

For each clinical parameter such as GI, PI, PPD, CAL, and GR the mean and standard deviation were calculated. For intergroup comparison, parametric one-way ANOVA tests were utilized for baseline data. Additionally, for follow-up durations, the one-way ANOVA with the Kruskal Wallis H test was used.[8] Similarly, for intra-group comparison, two-way ANOVA with Friedman paired "t" test was used where the distribution was normal. The level of significance for analysis was conducted at $p \leq 0.05$.[9]

3. Results

3.1. Fabrication of nanofibers and characterization

The fabrication of nanofiber with Ashvakatri, Tetracycline, and the Blank polymer was done by using the electrospinning method. Morphological characteristics were evaluated using HR-SEM resulting in thickness of diameter ranges from 110 to 150 nm, smooth texture, continuous mat, beads-free, good mechanical strength, and higher yielded nanofibers as shown in Fig. 3. Additionally, in-vitro drug release followed the Higuchi kinetic model release of drug in a sustained manner for up to 220 h.

3.2. Clinical trials

All the surgical parameters, followed by clinical safety, were taken care of by a professional registered practitioner. The clinical study was carried out in 75 periodontal sites in 31 subjects having chronic periodontitis with $\geq$ 5 mm pocket depth. All subjects were revisited for follow-up at certain intervals for comparison from baseline value to 1 month and 2 months. There was no discomfort, pain, swelling, or redness recorded or felt by any subjects during follow-up.

3.2.1. Plaque index (PI)

Table 1 suggested the statistical changes in PI values from baseline values to the 15th, 30th' and 60th days within the groups. The intergroup comparisons between all three groups showed the PI value at baseline was 1.170 $\pm$ 0.172, 1.140 $\pm$ 0.126, and 1.230 $\pm$ 0.142, respectively. At the end of the study, the statistical PI value was found to be 1.140 $\pm$ 0.126, 1.100 $\pm$ 0.125, and 1.080 $\pm$ 0.156 for group I

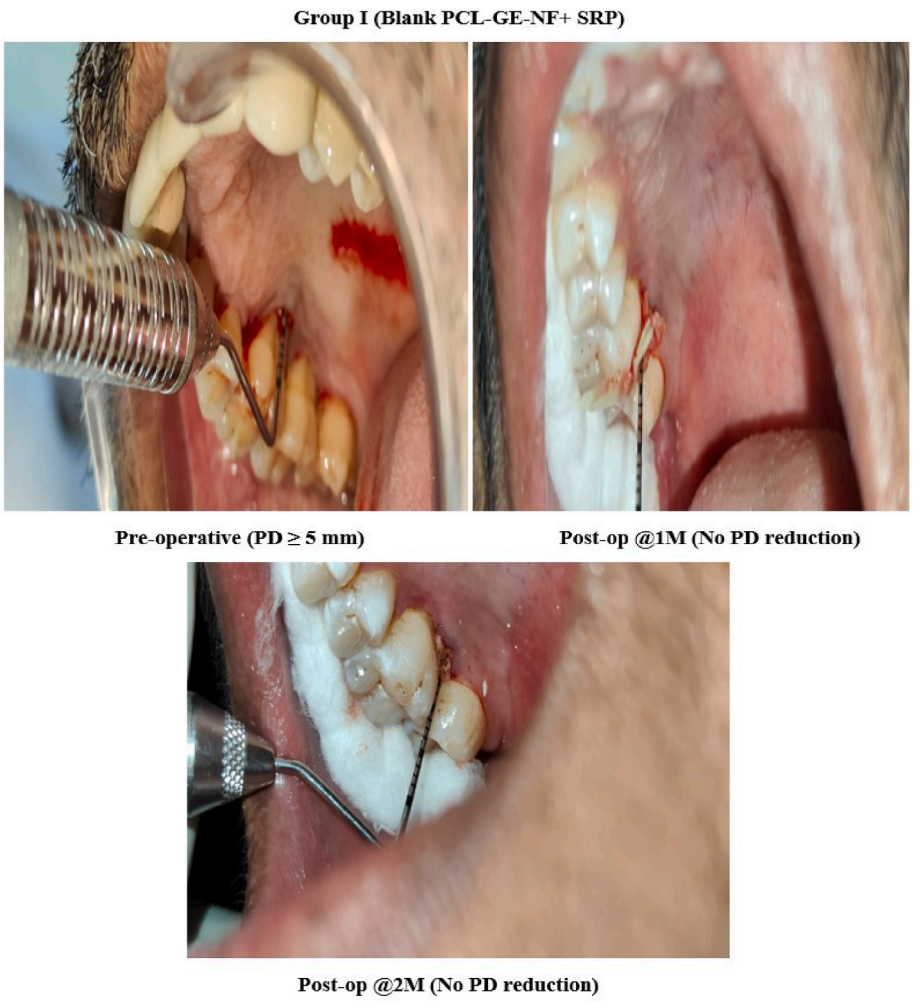


Fig. 5. Operative analysis involved in Group I subjects at different periodontal sites.

(placebo/PCL-GE NF), group II (PCL-GE-A2 NF), and group III (PCL-GE-TET NF), respectively. Henceforth, the result revealed that there was no significant difference, and the p-value was found to be ≥ 0.05.

Similarly, for intra-group comparison, the Friedman test was applied and showed the statistical difference with $p \leq 0.05$ in data from baseline to the 15th, 30th, and 60th day. Also, the two-way ANOVA test for pairwise intragroup comparison suggested no significant difference from the pre-operative baseline value compared to the 30th day and 60th day, and the p-value was found to be ≥ 0.05 for groups I, II, and III respectively as shown in Table 2.

3.2.2. Gingival index (GI)

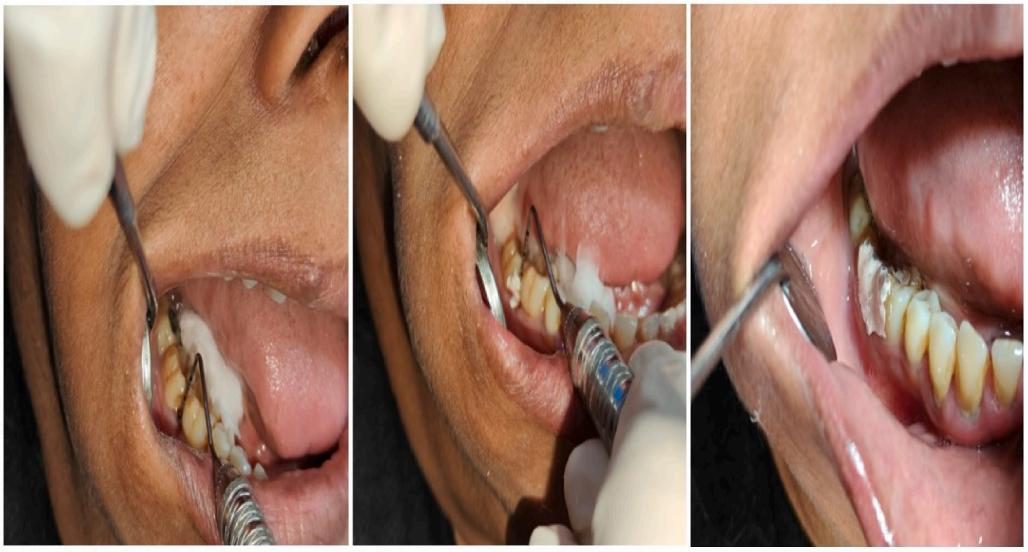
Table 3 suggested the statistical changes in PI values from baseline values to the 15th, 30th, and 60th days within the groups. The inter-group comparisons between all three groups showed the GI value at baseline was 1.360 ± 0.172, 1.140 ± 0.202, and 1.320 ± 0.210 respectively. At the end 60th day, the statistical GI value was changed to 1.120 ± 0.127, 1.230 ± 0.175, and 1.160 ± 0.159 for group I (placebo/PCL-GE NF), group II (PCL-GE-A2 NF), and group III (PCL-GE-TET NF) respectively. Henceforth, the result revealed that there was no significant difference obtained, and the p-value was found to be ≥ 0.05.

Similarly, for intra-group comparison, the Friedman test was applied and showed the statistical difference with $p \leq 0.05$ in data from baseline to the 15th, 30th, and 60th day. Also, the two-way ANOVA test for pairwise intragroup comparison of GI values suggested no significant difference in group I from the pre-operative baseline value comparison to the 30th day and 60th day, and the p-value was found to be ≥ 0.05 for group I. However, the GI values for groups II, and III were statically significant ($p \leq 0.05$) from baseline to the 30th and 60th day respectively as shown in Table 4.

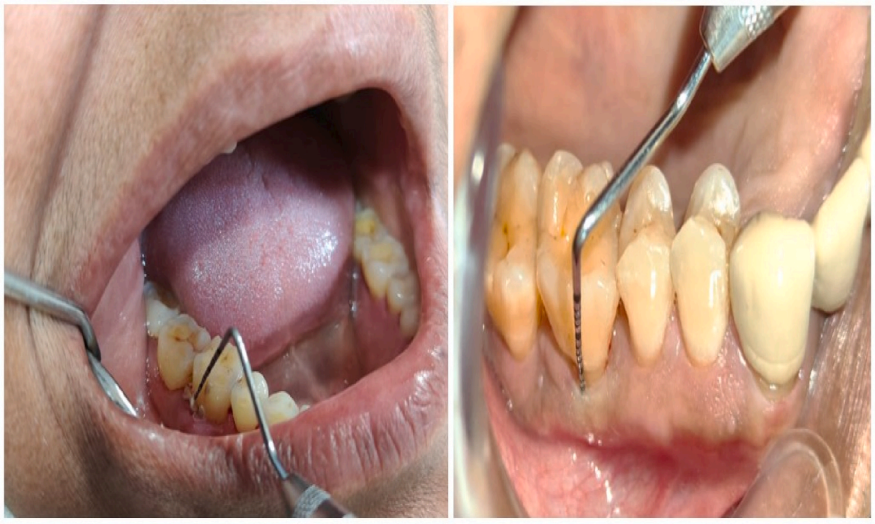
3.2.3. Probing pocket depth (PPD)

The statistical changes of PPD from baseline to the 30th and 60th day within the group are indicated in Table 5. The inter-group comparisons between all three groups for group I (placebo/PCL-GE NF), group II (PCL-GE-A2 NF), and group III (PCL-GE-TET NF) showed the PPD value at baseline was 4.96 ± 0.676, 5.24 ± 0.723, and 5.24 ± 0.0600 respectively. The 30th-day statistical difference was found to be 4.76 ± 0.723, 4.04 ± 0.676, and 4.12 ± 0.600 respectively. Additionally, at the end 60th day, the statistical PPD value was changed to 4.72 ± 0.843, 3.28 ± 0.458, and 3.24 ± 0.436 respectively. Henceforth, the result revealed that there was a significant difference obtained between pre-operative and post-operative PPD values and the p-value was found to be ≤ 0.05.

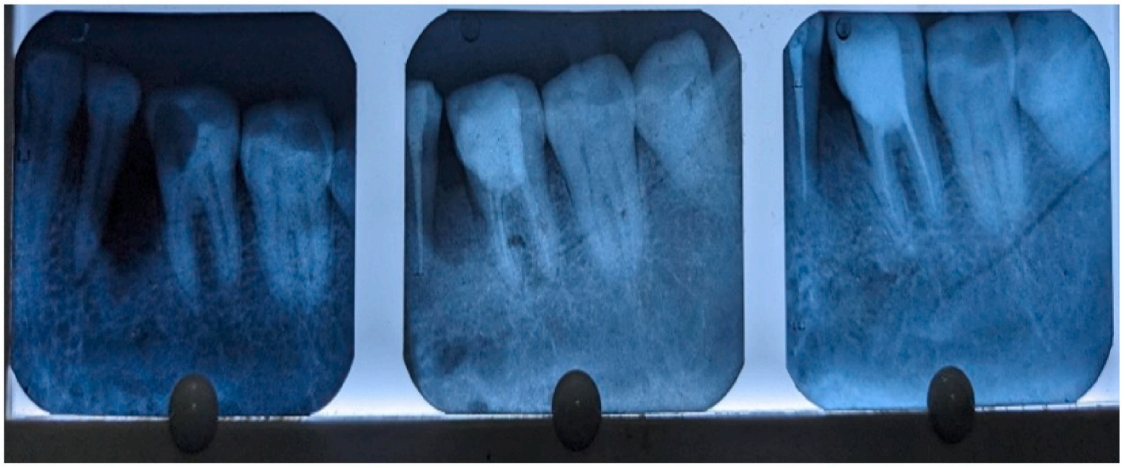
Consequently, for intra-group comparison, the Friedman test was applied and showed the statistical difference with $p \leq 0.05$ in data from baseline to the 30th and 60th day. Also, the two-way ANOVA test for pairwise intragroup comparison of PPD values suggested no significant difference in group I from the pre-operative baseline value comparison to the 30th day and 60th day, and the p-value was found to be ≥ 0.05 for group I. Nevertheless, the PPD values for groups II, and III values were statically significant ($p \leq 0.05$) from baseline to the 30th and 60th day respectively as shown in Table 6.



Pre-op PCL-GE-A2 NF placement Periodontal dressing (Coe-Pak)



Post-op @1M Post-op @2M



Pre-op (Group II) Post-op@1M (Group II) Post-op@2M (Group II)

Fig. 6. (A) Detailed operative procedure and result involved in Group II, (B) IOPA result for PPD in Group II patients.

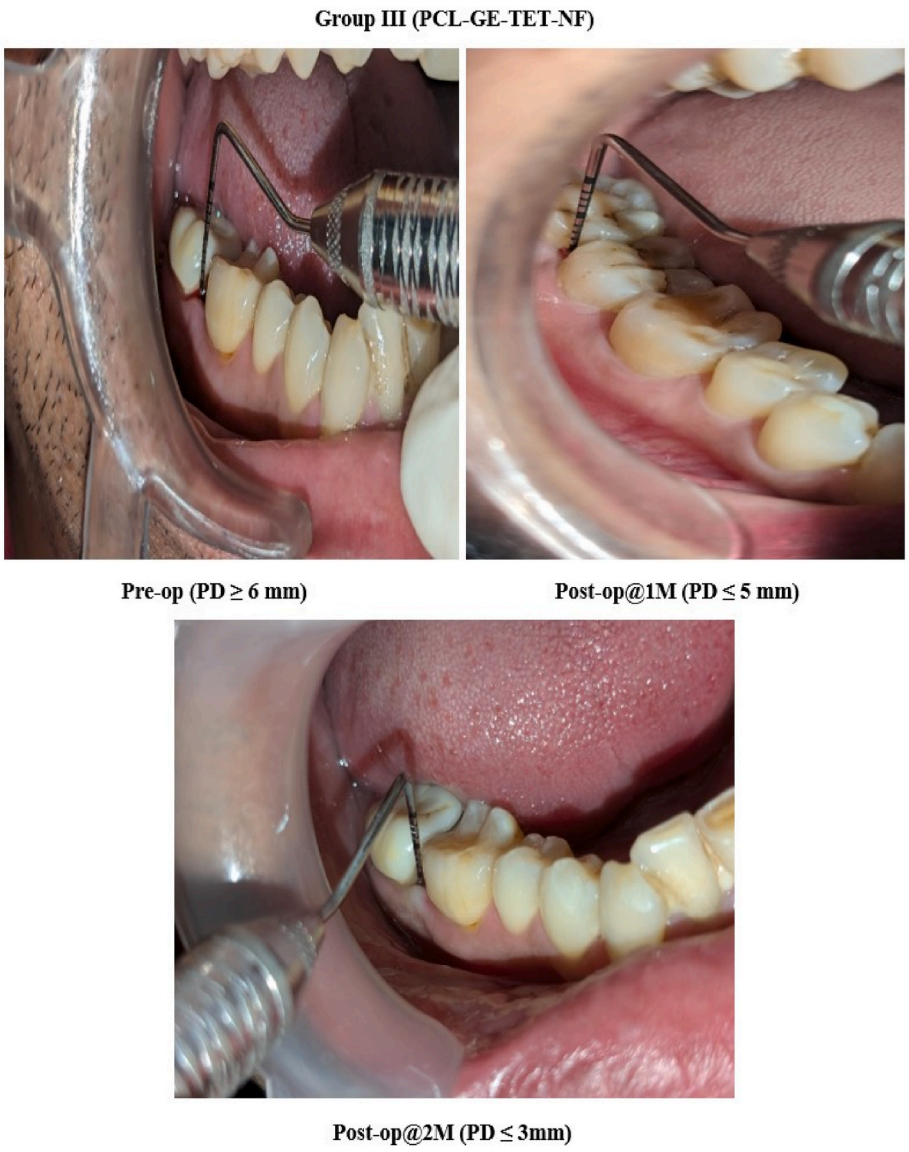


Fig. 7. Detailed operative procedure and result involved in Group III.

3.2.4. Clinical attachment level (CAL)

The Kruskal-Wallis test used for inter-group comparisons between all three groups for group I (placebo/PCL-GE NF), group II (PCL-GE-A2 NF), and group III (PCL-GE-TET NF) showed the CAL value at baseline was 5.08 ± 0.759, 5.16 ± 0.746, and 5.12 ± 0.600 respectively. The 30th-day statistical difference was found to be 5.04 ± 0.735, 4.20 ± 0.707, and 4.12 ± 0.700 respectively. Additionally, at the end 60th day, the statistical CAL value was changed to 4.96 ± 0.735, 3.68 ± 0.748, and 3.88 ± 0.833 respectively. The CAL statistical values difference from baseline to the 30th and 60th day within the group are demonstrated in Table 7. Henceforth, the result revealed that there was a significant difference obtained between pre-operative and post-operative CAL values, and the p-value was found to be ≤ 0.05.

Likewise, for intra-group comparison, the Friedman test was applied and showed the statistical difference with $p \leq 0.05$ in data from baseline to the 30th' and 60th day. Also, the two-way ANOVA test for pairwise intragroup comparison of CAL values suggested no significant difference in group I from the pre-operative baseline value comparison to the 30th day and 60th day, and the p-value was found to be ≥ 0.05 for group I. Nonetheless, the PPD values for groups II, and III values show statically significant ($p \leq 0.05$) from baseline to the 30th and 60th day respectively as shown in Table 8.

3.2.5. Group-wise comparison of clinical parameters among all groups

According to the group-wise comparison, group I sites do not exhibit any statistical significance in PI, GI, PPD, and CAL. Additionally, group II and group III suggested a significant difference in p-value as compared to group I.

Tables 9 and 10 suggested the intragroup pairwise comparison of PPD, and CAL values among all three groups, and the result revealed a significant difference ($p \leq 0.05$) between groups I II, and III. The statistically significant difference in p-values between groups I, II, and III was ≤ 0.05. However, the changes in pairwise intra-group comparison between groups II and III do not suggest a statistically significant activity difference at all time intervals, and the p-value was found to be ≥ 0.05. Henceforth, the pairwise comparison of PPD, CAL, and GR values was ≤ 0.05 as shown in Fig. 4. This may indicate that group II has statistically significant activity compared to groups I and III at all time intervals.

4. Discussion

Dental plaque is the main cause of periodontal disease, which is simply a collection of oral infections that cause an inflammatory lesion in the tissue that supports them.[5,10] The major goal of both nonsurgical and surgical treatment plans is to eliminate the cause and its

consequences. Mechanical SRP is the main non-surgical treatment strategy. Antimicrobials are frequently used as in supplement to SRP because of the infectious nature of illness.[1,11] Since local drug delivery of herbal formulations results in a large concentration of antibiotics at the desired site of action with a lower dose and a corresponding decrease in adverse effects compared to systemic administration, becoming more and more common.[12,13]

Medicinal plants have been discovered to be helpful in the management and treatment of numerous medical conditions over time. Researchers have been more interested in using naturally occurring biologically active chemicals that have medical utility in the past few years.[14] And for our research, we have selected a rare plant named *Ashvakatri, which* possesses antibacterial, anti-inflammatory, anti-oxidant, cytotoxicity, and antibacterial potential against Periodontal pathogens.[15]

A local drug delivery method avoids the first pass of hepatic processing and offers direct access to the systemic circulation through the jugular vein, resulting in high bioavailability. Additional benefits include minimal enzymatic activity, painless administration, and outstanding accessibility.[16,17] Additionally, nanofiber composites of gelatin and PCL polymers are biocompatible, biodegradable, non-toxic, and also exhibit sustained release up to 75 days, which may improve patient compliance.[18,19] And the solvent trifluoroethanol can dissolve various polymers, and it has potential impacts on improving nanofibers' characteristics.[20,21]

The electrospun method was used to fabricate blank, *Ashvakatri*-loaded, and TET-loaded nanofibers with a concentration of 10 % w/v by using a mixed biodegradable polymer of polycaprolactone (10 % w/v) and gelatin (5 % w/v) in a solvent of trifluoroethanol under the conditions as previously mentioned. The nanofiber mats were produced with a size of 15 × 8 cm. The obtained electrospun nanofibers on aluminum foil were dried overnight due to the complete elimination of solvents. Finally, all fabricated electrospun nanofiber was stored at 4 °C in the dark under defined environmental conditions (temperature: 22 °C and relative humidity: 60 %). The collected fibers were always visually examined and then subjected to procedures for characterization via HR-SEM, resulting in continuous, bead-free, and uniformly loaded nanofibers. Furthermore, the PCL-GE-A2 hybrid nanofiber scaffolds followed the Higuchi model since the correlation coefficient was higher than in the other models, suggesting Fickian diffusion regulated drug release.

The composite herbal drug-loaded nanofiber and other nanofibers (blank and TET) were subjected to perform a clinical evaluation of patients suffering from periodontitis to establish the therapeutic potential of composite scaffolds. Results obtained from recruited patients demonstrated the therapeutic efficacy of NF scaffolds by significantly reducing clinical markers of periodontitis ($p \leq 0.05$), including PI, GI, PPD, and CAL, as shown in Figs. 5–7, respectively.

Therefore, based on the results of our investigation, it is possible to conclude that the developed PCL-GE-A2 hybrid NF scaffold, has a promising performance for treating periodontal infections by extending the duration of periodontal residence, which improves therapeutic efficacy.[4,22] Furthermore, it facilitates intimate contact between the dosage and periodontal pocket, which may lead to a high concentration of drugs in the local area.[6,23] As a result, the created NFs drug delivery system has shown to be an innovative method for treating periodontal diseases more effectively since it minimizes the dosage amount, minimizes the dosage frequency, and shows no adverse effects, no discomforts, avoids surgical treatments and increases patient compliance with maximize therapeutic efficacy.

Conclusively, the composite nanofiber containing herbal formulation by the electrospinning method can be used as local drug delivery and shows potent activity against periodontal diseases.

Informed consent statement

All patients gave informed consent before the treatment, including permission to publish photographs and images here.

Ethics declarations

All methods followed relevant guidelines and regulations, and Banaras Hindu University approved all the experimental protocols.

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Author contributions

P.D., N.M., and B.M. did the concept and design of the experiment. P. D. wrote the manuscript. N.M., A.G., and N.K. reviewed the whole manuscript. A.G. and R.M. provided resources and supervised the project. N.M., N.K., and B.M. also validated the manuscript. All authors are approved for the submission.

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Abbreviations:

A2	Ashvakatri
CAL	Clinical attachment loss
GI	Gingival index
HAE	Hydroalcoholic extract
PCL	Poly-caprolactone
PI	Plaque index
PPD	Periodontal pocket depth
SRP	Scaling & root planing
TET	Tetracycline

Data availability

The corresponding author can make the data used to verify the article's results accessible upon reasonable request.

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