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RESEARCH PAPER

Ethyl Cellulose and Polyethylene Glycol-Based Sustained-Release Sparfloxacin Chip: An Alternative Therapy for Advanced Periodontitis

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ABSTRACT

This study reports the development of a sustained-release system of sparfloxacin for use in the treatment of periodontal disease. A sustained-release sparfloxacin device was formulated, based on ethyl cellulose (EC) 10 cps, polyethylene glycol (PEG) 4000, and diethyl phthalate (DEPh). It will hereafter be called the sparfloxacin chip (SRS chip). The chip has dimensions of 10 mm length, 2 mm width, and 0.5 mm thickness. The in vitro drug release pattern and clinical evaluation of the formulations were studied. Reports of the short-term clinical study show that the use of the SRS chip may cause complete eradication of the pathogenic bacteria in the periodontal pockets of patients who have chronic generalized periodontitis. In this clinical study, the baseline and follow-up measurements of various clinical indices, such as oral hygiene index(es), plaque index, sulcular depth component of periodontal disease index, gingival crevicular fluid flow measurement, and dark field microscopic examinations of oral pathogens in

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plaque samples were studied. Significant improvements were observed in many parameters of the treatment group compared with the placebo group.

Key Words: *Dental chip; Periodontitis; Sparfloxacin; SRP chip; Sustained-release device*

INTRODUCTION

Periodontitis, which is a common cause of tooth loss in adult populations, is an inflammatory response to the over-growth of anaerobic organisms such as bacteroides and aerobic organisms such as spirochaetes, etc.[1] in the subgingival plaque. Treatment aimed at controlling periodontal disease should contain one or more antimicrobial components directed to the reduction and elimination of periodontopathic organisms.[2]

Conventional periodontal therapy has relied almost exclusively upon mechanical debridement of the tooth surface as the antimicrobial component. The diagnosis and treatment evaluation of chronic periodontitis relies primarily on the use of gingival indices and radiographs. Most often, periodontitis can be arrested and probing pocket depth can be reduced by a conventional regime of meticulous oral hygienic measures, thorough scaling, root planing[3] and, in certain circumstances, surgery including curettage or flap. The systemic administration of antibiotics is often resorted to as a useful method of controlling the subgingival microflora. It has been found that the discontinuation of systemic antibiotic therapy results in the recolonization[4] of pathogens, and hence long-term antimicrobial therapy is required for the complete eradication of microbial flora. It is a potential disadvantage of systemic antimicrobial therapy.

A sustained-release device like the sparfloxacin chip is advantageous over conventional therapy because it is introduced directly into the periodontal pocket. This direct route of administration establishes and maintains an effective concentration of the active agent at the site of infection without the risk of incurring many of the side-effects like nausea, vomiting, abdominal pain, diarrhea, headache, insomnia, convulsion, tremor, hallucination, etc.[5,6] that can accompany systemic administration of sparfloxacin.

Sparfloxacin is a new synthetic, orally administered member of the quinoline class of broad spectrum antibacterial agent which is particularly active against anaerobes. It is chemically designated as 5-amino-1-cyclopropyl-7(*cis* 3,5-dimethyl-1-piperazinyl)-6,8-difluoro-1,4-dihydro-4-oxo-3-quinoline carboxylic acid. Sparfloxacin is active against anaerobic isolates such as bacteroides, *Prevotella melaninogenicus*, *Bacteroides fragilis*, *Fusobacterium necrophorum*, *Actinobacillus actinomycetem comitans*, etc. and aerobic isolates such as spirochaetes, *Pseudomonas aeruginosa*, *Escherichia coli*, *Enterobacter*, *Streptococcus sanguis*, *Streptococcus salivarius*, etc.[5,6] These isolates are often found in periodontitis patients. Therefore sparfloxacin has been chosen as a drug candidate for the present study. The literature survey revealed that the possibility of using sparfloxacin as a chip has not been attempted so far.

Nowadays, novel drug delivery systems are becoming very popular commercially. For example: (i) chlorhexidine chip (Perio chip™),[7–9] (ii) doxycycline hyclate gel (Atridox®),[10–12] (iii) minocycline Hcl microspheres (Arestine®),[13] (iv) tetracycline film strips,[14–16] (v) metronidazole acrylic strips,[17] (vi) benzyl pencilline, tetracycline composite wafer,[18] etc.

The aim of the present study is to develop sparfloxacin as a targeted sustained-released device that can be placed directly into periodontal pockets of chronic periodontitis patients in order to reduce periodontal pathogens.

EXPERIMENT

Size of the SRS Chip

In chronic periodontitis the pocket depth of inflamed gingiva[19] ranges from 5 to 8 mm and the width is around 2 mm. The chip of sparfloxacin was made with 10 mm length, 2 mm width, and 0.5 mm thickness, so that it could easily be introduced into the periodontal pockets.

Dosage Amount Calculation

After oral administration of a single dose of 200 mg of sparfloxacin in the form of a tablet, maximum plasma concentration[5,6] of 0.4 to 0.7 μg/mL

was achieved in 3.5 to 6.0 hr. The minimum inhibitory concentration[20] of sparfloxacin to the pathogens which cause periodontitis, such as bacteroides, *P. melaninogenicus*, *B. fragilis*, *F. necrophorum*, *A. actinomycetem comitans* and spirochaetes, *P. aeruginosa*, *E. coli*, *Enterobacter*, *S. sanguis*, *S. salivarius*, etc., ranges from 0.25 to 0.5 μg/mL. These factors were considered for fixing the dose of drug in each SRS chip. In the present study a 100 times reduced oral dose of sparfloxacin, i.e., 2 mg targeted into the periodontal pocket in the form of a chip of size $10 \times 2 \times 0.5\,mm^3$, was expected to release the drug well above the minimum inhibitory concentration required for oral pathogens.

Method of Casting Drug Film and Making SRS Chips

Accurately weighed quantities of polymers, ethyl cellulose (EC) and polyethylene glycol (PEG) 4000[21–23] with or without plasticizer, namely diethyl phthalate (DEPh)[23] (Table 1), were transferred into a 100-mL glass beaker and dissolved in 10 mL of a 1:1 mixture of analytical grade isopropyl alcohol and methylene chloride using a magnetic stirrer. The mixing was continued until a clear solution of polymers in solvent was obtained. To this accurately weighed quantity of drug was transferred and mixing was continued for 2 hr to achieve uniform mixing of drug in polymer solution. The whole quantity of polymer mixture with drug was then poured into a stainless steel ring of diameter 5.7 cm and thickness 0.5 mm, which was already placed over a glass plate to control the thickness of the film. The solvent was allowed to evaporate slowly by covering the glass plate with a glass funnel, and set aside for 12 hr in a dark place. The film was removed carefully from the stainless steel ring and stored in an air-tight and light-resistant container, since the drug is more sensitive to light and moisture. The film was cut into chips of $10 \times 2 \times 0.5\,mm^3$ size.

Preparation of Placebo Chip

The placebo chip was prepared in a similar manner without incorporating sparfloxacin.

In Vitro Drug Release Pattern

In order to simulate the condition prevailing in an inflamed gingival cavity, the in vitro drug release pattern of a chip was carried out at pH 7.8, since the pH of gingival crevicular fluid[24] is between 7.5 and 8.0, and the flow of fluid at an individual site is 150–200 μL/hr, i.e., around 5 mL/day. Keeping the above physiological condition in mind, a suitable in vitro model[25] was designed.

Table 1

Different Ratios of Polymers EC 10 cps and PEG 4000, and Amount of DEPh Containing 0.2553 g of Sparfloxacin Used for Casting 1.255 g of Drug Film

EC:PEG Ratio	% Diethyl Phthalate with Respect to Polymer Amount	EC:PEG Ratio	% Diethyl Phthalate with Respect to Polymer Amount
9:1	—	9:4	10
9:2	—	9:4	15
9:3	—	9:4	20
9:4	—	9:5	10
9:5	—	9:5	15
9:6	—	9:5	20
9:7	—	9:6	10
9:8	—	9:6	15
9:9	—	9:6	20
9:1	10	9:7	10
9:1	15	9:7	15
9:1	20	9:7	20
9:2	10	9:8	10
9:2	15	9:8	15
9:2	20	9:8	20
9:3	10	9:9	10
9:3	15	9:9	15
9:3	20	9:9	20

Method

The chips of sparfloxacin were placed in 10 mL vials. To these, 5 mL of phosphate buffer of pH 7.8 was transferred and tightly closed. The temperature of the dissolution medium was maintained at 37°C by placing the vial in an incubator. Every 24 hr the dissolution medium was taken out and replaced with fresh medium. The amount of drug released into the medium was determined by measuring the absorbance at 289.5 nm using a Shimadzu 1601UV PC spectrophotometer after suitable dilution. The in vitro study was done with five replicates for 21 days. The formulation which had shown

the best release profile was chosen for the clinical evaluation.

Clinical Study

Ten patients (six males and four females) with chronic generalized periodontitis were selected in the Department of Periodontics, Faculty of Dentistry, Rajah Muthiah Dental College and Hospital, Annamalai University, Tamil Nadu, India. Patients participating in this study were informed of the benefits and risks involved in the study and their consent was obtained. The subjects chosen had at least 20 teeth and had displayed advanced breakdown of periodontal support at several interproximal sites in each quadrant.

Placebo Group Study

The clinical parameters[26] such as simplified oral hygiene index (debris index and calculus index), plaque index, gingival sulcus measurement component of the periodontal disease index, gingival crevicular fluid flow measurement, and sulcus bleeding index were recorded after supragingival scaling in both the experimental and control groups.[27] A sample of plaque was taken for darkfield microscopic examination of microorganisms, and studied for baseline examination.

Placebo chips of size $10 \times 2 \times 0.5\,mm^3$ were inserted into the periodontal pockets of the placebo group with the help of a tweezer. The chips were maintained in situ with a small amount of periodontal dressing. In all patients tooth number 26 was kept as control. The microbiological examination of the placebo group was done for days 0, 1, 7, 14, and 21.

Treatment Group Study

Plaque samples were collected for darkfield microscopic examination using a periodontal curette. The patients were subjected to the baseline examination followed by routine, supragingival scaling. The microbiological examination of the sparfloxacin group was done for days 0, 1, 7, 14, and 21. Plaque samples were collected for darkfield microscopic examination using a periodontal curette from tooth number 16, 36, 46 for the test group and tooth number 26 for the control group. Though the other teeth were treated with sparfloxacin, to get uniform results regarding the effect of sparfloxacin, all the first molars, namely 16 (right upper first molar), 36 (left lower first molar), and 46 (right lower first molar), were taken as test sites and tooth number 26 (left upper first molar) was taken as the site for the placebo group. The patients were subjected to baseline examinations followed by routine supragingival scaling. In all patients tooth number 14, 15, 16, 17, 34, 35, 36, 37, 44, 45, 46, and 47 were chosen for the treatment. The total number of sites included 120 teeth for the test group. The SRS chips were inserted into the periodontal pockets of the treatment group with the help of a tweezer. The chips were maintained in situ with a small amount of periodontal dressing.

The sparfloxacin chip is a matrix-type drug delivery system and remained as a matrix even after 21 days of treatment, without altering its structure. At the end of the 21 days of treatment, the chip was removed from the periodontal pocket.

Statistical Analysis of Clinical Study

Analysis of variance (ANOVA) was used to interpret the data using the software package IRRISTAT. The data were analyzed in order to determine whether statistically significant relationships existed between disease state category and the counts of spirochaetes, cocci, other motiles, and other organisms between the various clinical parameters and the percentage of spirochaetes.

One-way ANOVA was performed. Each ANOVA generated an *F*-value which was converted by a programmed *F*-table to the level of significance (p). After obtaining the *F*-value and the level of significance, the Duncan procedure (DMRT, Duncan Multiple Range Test), a post-hoc multiple range test, was carried out to compare all possible pairs of means. As per the DMRT, if two or more mean values possess the same letter, such as ''a'' or ''b'' or ''c'' or ''d,'' then the means in the pair do not differ significantly. For example: if two treatment means have the letters ''b'' and ''b'' they do not differ significantly, but if one mean has letter ''b'' and another mean has letter ''c'' they differ significantly (as per the IRRISTAT package).

Darkfield Microscopy

The most important aspect of the present study was to find the relationship between the microbial

count and the application of the treatment.[28] For the darkfield microscopic examination, a drop of plaque suspension was placed on a glass slide covered with a cover slip and examined by darkfield microscope (Kyowa microscope, Tokyo, Japan). Approximately 200 microorganisms were counted from a randomly chosen field based on morphology and motility of microorganisms. Microorganisms were grouped[29] as spirochaetes, cocci, motile rods, and others including non-motile rods, filaments using the technique described by Listgarten and Hellden[30] and Addy and Alam.[31] The average number of a particular microorganism in each group of persons after the insertion of the sustained-release device with sparfloxacin (SRS chip) was found on different days. For the placebo study the same set of observations was taken in a similar way. The mean microbial count of the placebo study and the drug-treated study was calculated.

RESULTS

The sustained-release sparfloxacin chips were formulated by impregnating sparfloxacin in different ratios of polymers, EC 10 cps and PEG 4000, with or without incorporating DEPh. The formulation containing EC and PEG 4000 9:1 with 10% DEPh was selected as the best formulation on the basis of drug release pattern and film characteristics.

The in vitro release of sparfloxacin from the SRS chip was done as per the method described earlier.[16,25,32] The results are given in Table 2.

In Vitro Drug Release Pattern

The percentage cumulative release of sparfloxacin into phosphate buffer pH 7.8 from the SRS chip was determined each day from the replicates of five specimens for a period of 21 days. The results are summarized in Table 2.

The results of the drug release pattern showed the greatest release of sparfloxacin on the first day, i.e., 293.67 µg. The release of drug reduced considerably on the second day onwards, up to the 21st day, i.e., 11.46 µg. The drug release on each day from the SRS chip was found to be well above the minimum inhibitory concentration required by the oral pathogens (Fig. 1).

Table 2

In Vitro Release of Sparfloxacin from Dental Chip Made of EC 10 cps and PEG 4000 with 10% DEPh in Phosphate Buffer pH 7.8[a]

Day	Average Drug Release (µg)[b]	Cumulative Drug Release (µg)	Cumulative % Release of Drug
1	293.67	293.67	14.68
2	130.53	424.20	21.21
3	71.86	496.06	24.80
4	52.10	548.16	27.40
5	28.70	576.86	28.84
6	27.07	603.93	30.20
7	24.45	628.38	31.42
8	22.56	650.94	32.55
9	20.66	671.60	33.58
10	19.87	691.47	34.57
11	19.27	710.74	35.54
12	18.33	729.07	36.45
13	17.83	746.90	37.35
14	15.60	762.50	38.13
15	13.38	775.88	38.80
16	12.64	788.52	39.43
17	12.39	801.00	40.05
18	12.15	813.60	40.65
19	12.02	825.08	41.25
20	11.83	836.91	41.85
21	11.46	848.37	42.42

[a]The drug content of each insert is 2.001 mg.
[b]Average of five replicates.

Results of Clinical Study

The results of the clinical study are given in Table 3. The mean oral hygiene index(es) of the treatment group were compared with the placebo group on different days, and a significant difference was observed between days 1 and 7, days 7 and 14, and days 14 and 21 after treatment (Fig. 2).

The plaque index of the treatment group was compared with the placebo group, and a significant difference was observed between days 1 and 7 and days 7 and 14, but no appreciable difference was found to exist between days 14 and 21 (Fig. 3).

The sulcular depth component of the periodontal disease index in the treatment group was compared with the placebo group, and a significant improvement in therapy was observed between days 1 and 7, days 7 and 14, and days 14 and 21 after treatment (Fig. 4).

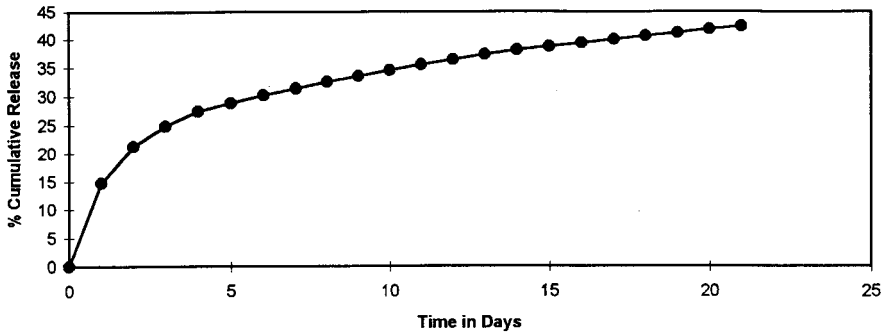

Figure 1. In vitro release of sparfloxacin from sustained-release sparfloxacin chip formulated with ethyl cellulose : polyethylene glycol 4000 with 10% diethyl phthalate in phosphate buffer pH 7.8.

Table 3

Results of Various Indices on Different Days in Placebo Group (Tooth Number 26) and Sparfloxacin-Treated Group (Tooth Number 15, 16, 34, 35, 36, 37, 44, 45, 46)

			Mean Values of Treatment and Placebo Group on Different Days[a]				
Clinical Measurements		*F* Ratio	Day 0	Day 1	Day 7	Day 14	Day 21
Oral hygiene index(es)	PG	—[b]	5.0	5.0a	5.0a	5.0a	5.0a
	TG	48.68[c]	5.0	3.0a	3.0a	3.0a	3.0a
Plaque index	PG	—[b]	2.8	2.8a	2.8a	2.8a	2.8a
	TG	179.32[c]	2.5	1.9a	1.16b	0.88c	0.80d
Periodontal disease index	PG	—[b]	3.0	3.0a	3.0a	3.0a	3.0a
	TG	52.90[c]	3.0a	2.9a	1.65b	1.0c	0.70d
Sulcus bleeding index	PG	—[b]	2.8	2.8a	2.8a	2.8a	2.8a
	TG	25.25[c]	3.0	2.9a	1.06b	0.60c	0.60c
Gingival crevicular fluid	PG	—[b]	3.0	2.8a	2.8a	2.8a	2.8a
volume measurement index	TG	146.74[c]	2.8	2.6a	2.12b	1.15c	0.68d

[a]Means followed by a common letter are not significant at 5% level by DMRT.
[b]The *F* ratio for the placebo group is not calculated because we are concerned only with the variation of indices under consideration on different days of the treated group and not compared with the placebo group.
[c]Highly significant at 1% level.
PG, placebo group; TG, treatment group.

The sulcus bleeding index of the treatment group was compared with that of the placebo group, and a significant difference was observed between days 1 and 7, but no appreciable difference was found to exist between days 7 and 21 (Fig. 5).

The gingival crevicular fluid flow measurement component of the treatment study was compared with that of the placebo study, and a significant difference in flow was observed between days 1 and 7, days 7 and 14, and days 14 and 21 after treatment (Fig. 6).

Results of Darkfield Microscopic Examination of Plaque Sample from the Patients

The results of the darkfield microscopic examination of the plaque sample collected from both the placebo group and the drug-treated group are given in Table 4.

The mean value of total spirochaetes (SP) count in the placebo group study (SP^X) was 42, and the mean value of total spirochaete count

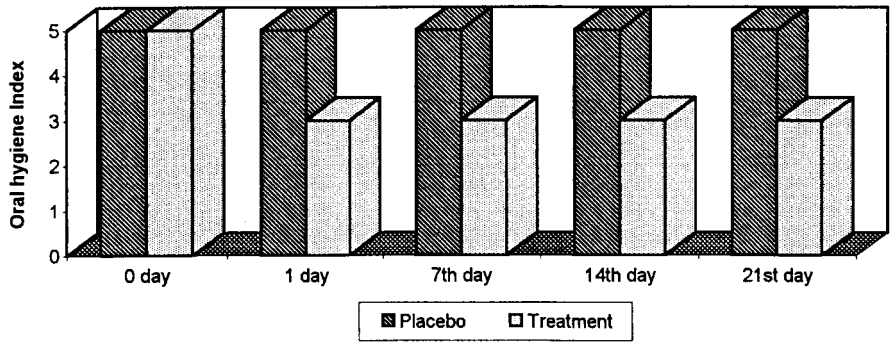

Figure 2. Oral hygiene index of placebo and sparfloxacin-treated group on different days.

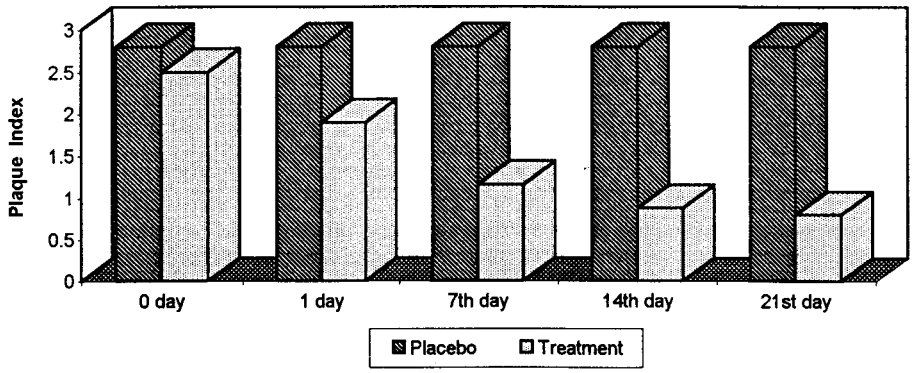

Figure 3. Plaque index of placebo and sparfloxacin-treated group on different days.

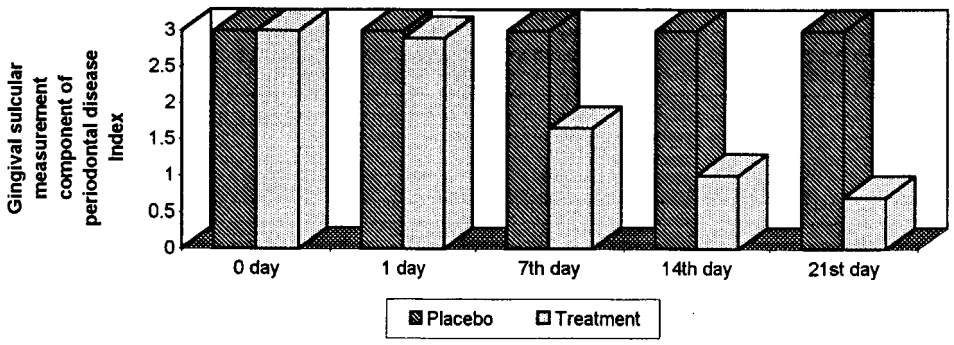

Figure 4. Gingival sulcular measurement component of periodontal diseases index of placebo and sparfloxacin-treated group on different days.

in the drug-treated group study (SP^Y) was 40.2 on the day of commencement of the study (day 0). The mean total spirochaete count in the drug-treated group was reduced to 25.2 on day 1, and there was no significant change in the mean value of the placebo group study. The spirochaete count reduced considerably in the successive days of observation, and there was no spirochaete

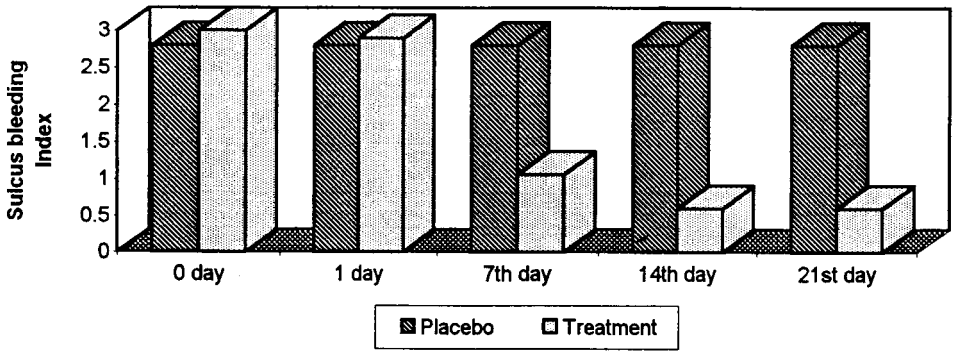

Figure 5. Sulcus bleeding index of placebo and sparfloxacin-treated group on different days.

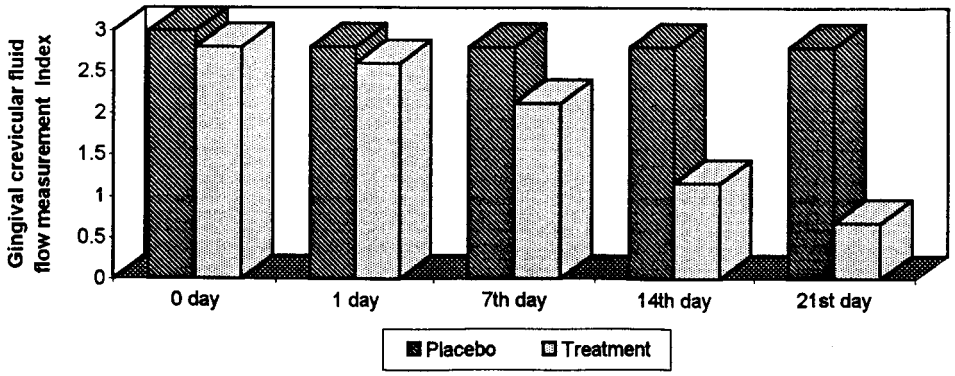

Figure 6. Gingival crevicular fluid flow measurement of placebo and sparfloxacin-treated group on different days.

Table 4

The Results of Darkfield Microscopic Examination of Plaque Samples from Placebo and Sparfloxacin-Treated Group

		Mean Values of Microbes in Placebo and Treatment Group on Different Days				
Microorganisms		Day 0	Day 1	Day 7	Day 14	Day 21
Spirochaetes	SP^X	42.0	41.4	43.6	44.8	46.2
	SP^Y	40.2	25.2	0.0	0.0	0.0
Other motiles	OM^X	60.2	59.8	60.6	61.8	62.4
	OM^Y	61.2	36.8	0.0	0.0	0.0
Cocci	CO^X	36.6	35.8	38.0	38.8	38.8
	CO^Y	36.2	26.2	0.0	0.0	0.0
Others	OT^X	65.4	66.6	66.6	66.4	67.2
	OT^Y	64.2	41.2	0.0	0.0	0.0

X, placebo group; Y, treatment group.

present on the plaque sample from day 7 onwards (Fig. 7).

The mean value of the total other motile organisms (OM) in the placebo group study (OM^X) was 60.2, and the mean value of the total other motile organisms in the drug-treated group study (OM^Y) was 61.2 on the day of commencement of the study (day 0). The mean total of the other

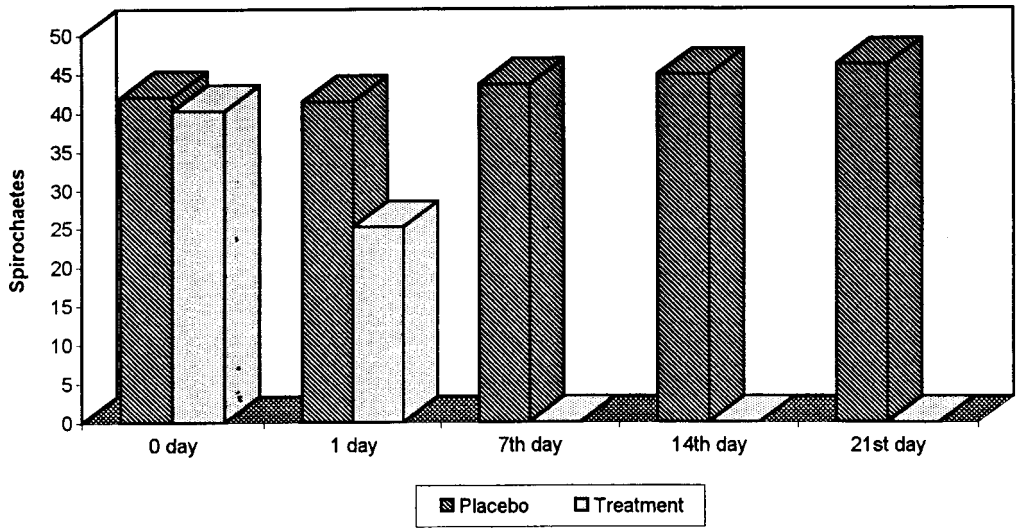

Figure 7. Mean values of spirochaetes in placebo and sparfloxacin-treated group on different days.

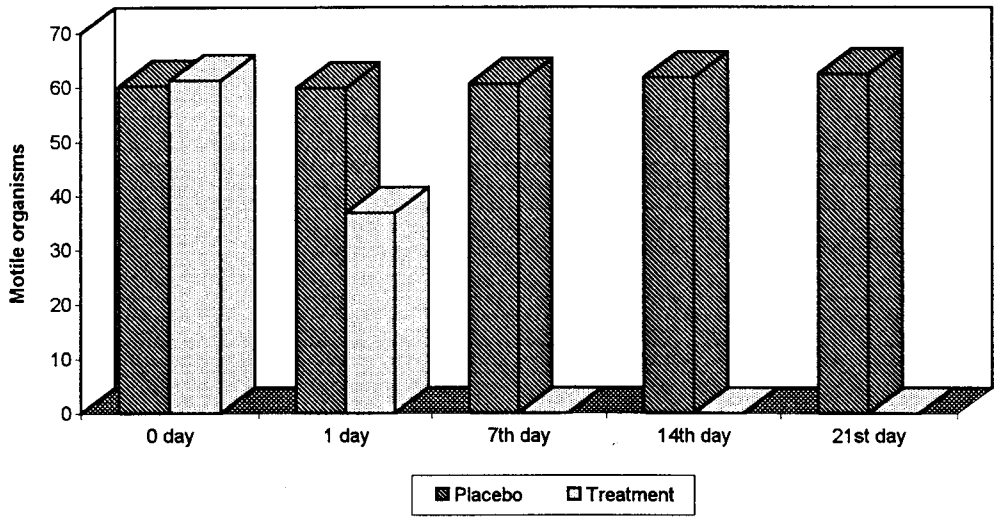

Figure 8. Mean values of other motile microorganisms in placebo and sparfloxacin-treated group on different days.

motile organisms in the drug-treated group was reduced to 36.8 on day 1, and there was no significant change in the mean value in the placebo group study. The other motile microbial count reduced considerably on the successive days of observation, and there was no such organism found in the plaque sample from day 7 onwards (Fig. 8).

The mean value of the total cocci (CO) count in the placebo group study (CO^X) was 36.6, and the mean value of the total cocci count in the drug-treated group (CO^Y) was 36.2 on the day of commencement of the study (day 0). The mean total cocci count in the drug-treated group study was reduced to 26.2 on day 1, and there was no significant reduction in the mean value in the placebo study group. The cocci count reduced considerably in the successive days, and there was no cocci found in the plaque sample from day 7 onwards (Fig. 9).

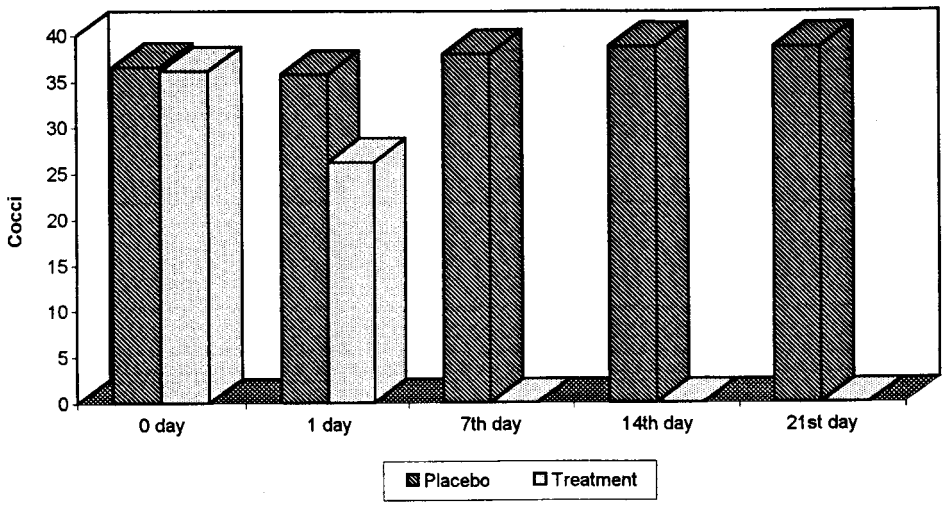

Figure 9. Mean values of cocci in placebo and sparfloxacin-treated group on different days.

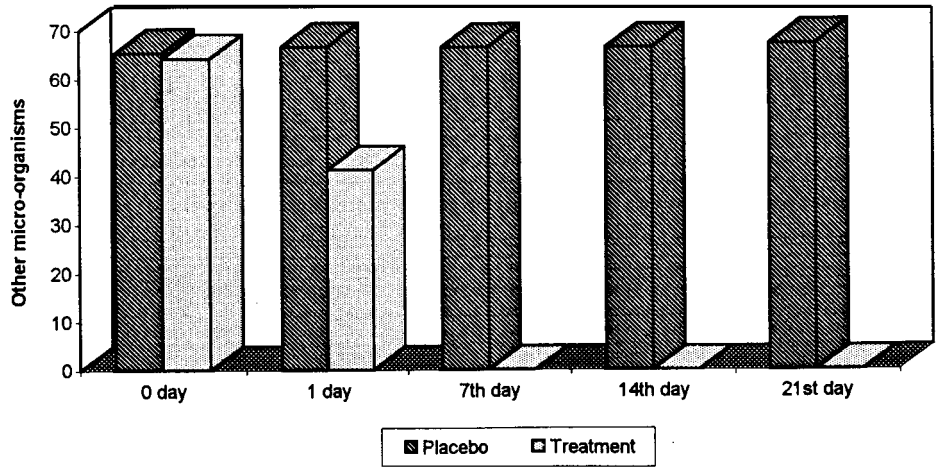

Figure 10. Mean values of other microorganisms (non-motile rods and filamentous) in placebo and sparfloxacin-treated group on different days.

The mean value of the count of other microorganisms (OT) in the placebo group (OT^X) was 65.4, and the mean value of other microorganisms in the drug-treated group (OT^Y) was 64.2 on the day of commencement of the study (day 0). The mean count of the other microbes in the drug-treated group study was reduced to 41.2 on day 1, and there was no significant change in the mean value of the placebo group study. The count of the other microbes reduced considerably in the successive days, and there was no microorganism in the plaque sample from day 7 onwards (Fig. 10).

DISCUSSION

The most often cited initial attempt to utilize controlled local drug delivery and its potential benefits for the management of periodontitis is the work of Goodson and coworkers.[33–35] The advantages of this system include: (a) better patient compliance, (b) enhanced or improved pharmacokinetic response, (c) improved drug access to the site of disease, (d) lower total drug dosage, (e) alternative to systemic antibiotics, (f) elimination of non-oral side-effects due to extremely low or

undetectable serum drug level, (g) reduced risk for developing drug-resistant microbial populations.

Many researchers, like Mura et al.,[22] Friedman and Golomb,[36] Soskolne et al.,[37] have demonstrated the ability of ethyl cellulose to sustain the release of drugs.

The literature shows that methylene chloride, isopropyl alcohol, and diethyl phthalate can be used as the safest additives for the pharmaceutical formulations.[23] Based on these data, a sustained-release sparfloxacin chip containing a polymer combination of EC and PEG 4000 in 9:1 ratio with 15% of plasticizer DEPh with respect to the total polymer weight was formulated. For the formulation of SRS chip the solvents isopropyl alcohol and methylene chloride in 1:1 ratio were used, and 2 mg of sparfloxacin was incorporated into each chip for the present study.

The release pattern of the drug from an SRS chip inserted into a periodontal pocket might provide about 848.37 μg of sparfloxacin over a period of 21 days. The minimum inhibitory concentration of sparfloxacin is about 0.5 μg/mL.[20] Thus, the above-mentioned device could release and maintain an effective bactericidal dose throughout the period of 21 days.

The biphasic release pattern in the SRS chip is favorable to subgingival plaque control because the rapid increase of sparfloxacin concentration in the early stage is expected to kill most of the bacteria and the following constant release is sufficient to inhibit the possible growth of residual bacteria. This concept was based on the study done by Higashi and Morisaki.[38]

The results of the antimicrobial activity tests proved that the embedding of sparfloxacin in a polymeric matrix consisting of ethyl cellulose sustains and does not inhibit the biological activity of the drug. The release of the drug was for many days at levels in excess of the minimum inhibitory concentration for many oral bacteria. A microbiological susceptibility test for sparfloxacin was carried out according to the guidance given in Bailey and Scott.[39]

A split mouth therapy design described by Newman[40] was used to compensate for the biological variability of individual patients. Supragingival plaque was removed to avoid contamination of the sample taken for microscopic examination and for easy insertion of a chip into the periodontal pocket.

Retention of intracrevicular controlled drug delivery devices may present a clinical problem. Preliminary studies using mechanical locking (acrylic stents), periodontal dressings, and various dental cements or bonding agents were unsuccessful in retaining film strips for a longer period.[41] In the present study zinc oxide-eugenol periodontal dressing was used.[42]

Since the patient followed the same oral hygiene throughout the period of study, there was no change in oral hygiene index(es) between the test and placebo groups. The benefits to bleeding and crevicular fluid flow presumably arose from a considerable reduction in the microbial load in the pockets, with a shift to less pathogenic flora produced by the introduction of the SRS chip. The resulting reduced inflammation, together with some epithelial reattachment, would explain the decreases in pocket depth, i.e., sulcular depth component of periodontal disease index, and sulcular bleeding index.[42]

According to Greenstein,[43] complete elimination of subgingival deposits using closed procedures is difficult. When pocketing exceeded 5 mm, clinicians often failed to debride roots of plaque and calculus, apparently due to decreased accessibility and visibility.[43]

Although one might conclude that scaling and root planing by themselves produce the maximum change possible in clinical attachment level and therefore no adjunct could be superior, it is not a very convincing argument in deep pockets ($\geq$7 mm).[13] It is reasonable to conclude that sparfloxacin delivered subgingivally in a non-biodegradable sustained-release device as an adjunct to scaling and root planing may provide significant benefits in reducing probing depths beyond the benefit observed with scaling and root planing alone. The effect of the SRS chip on plaque microbes would explain the reduction in plaque index in the treatment group.

In the present investigation, darkfield microscopy was carried out to analyze qualitative shifts as described by Listgarten and Hellden.[30] According to them darkfield microscopy is a dynamic method involving the counting of a few groups of organisms based on motility and morphology.[30] According to Listgarten and Hellden[30] and Winkelhoff et al.,[44] qualitative evaluation of the subgingival microflora by differential darkfield microscopy had revealed higher proportions of spirochaetes and motile

rods in periodontal pockets in adult periodontits than at healthy sites, and higher proportions of cocci at healthy sites than at diseased sites. The technique was only a measure of difference in bacterial numbers in a plaque sample obtained from a pocket on a curette tip before and after the placement of the SRS chip. The counts did not indicate the total bacterial counts of the pockets.

In the present investigation a sustained-release sparfloxacin chip in the periodontal pocket produced dramatic and significant shifts in subgingival flora as measured by darkfield microscopy. In particular, motile organisms were reduced. In most of the pockets treated with sparfloxacin, it was difficult to identify any bacteria in the pocket samples immediately after periodontal therapy (after 7 days), similar to the results obtained by Soskolne et al.[37] in 1983.

Overall, the result has demonstrated that sparfloxacin has shown a reduction in pathogenic microorganisms and clinical improvement in all the parameters. Further, long-term evaluation was not possible since patients were not available for future ''re-call visits.''

CONCLUSION

This study was concerned with the development of sustained-release chips of sparfloxacin for periodontitis. The clinical study shows that SRS chips provide immediate effect upon pocketing, bleeding on probing, and crevicular fluids flow and completely eradicate the pathogens present in the periodontal pocket. Darkfield microscopy demonstrated the significant reduction in spirochaetes, other motile organisms, cocci, and other oral pathogens immediately after sparfloxacin therapy in the form of SRS chips.

It is concluded that SRS chips of sparfloxacin may be a useful method, adjunct to routine mechanical methods of root debridement and also avoiding large oral doses of drug administration and related side-effects. The only disadvantage of sustained-release sparfloxacin chips is that they are not a biodegradable matrix. However, the present study will act as a nucleus for the development of a biodegradable sparfloxacin chip.

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