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Research Article

Design and Evaluation of Biodegradable Periodontal films containing Ciprofloxacin and Ornidazole

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Abstract: Local controlled drug delivery system of Ciprofloxacin and Ornidazole for the treatment of periodontitis is highly advantageous. For the present investigation, polycaprolactone strips containing Ciprofloxacin and Ornidazole in different ratios were prepared by solution casting method using acetone. All strips were cross-linked by exposing to the vapours of 2% v/v glutaraldehyde in water. FT-IR and UV spectroscopic methods revealed that there was no interaction between drugs and polymer. The patches were evaluated for their thickness uniformity, folding endurance, weight uniformity, content uniformity, percentage moisture loss, tensile strength, percentage elongation, *in vitro* antibacterial activity, and surface pH. Data of *in vitro* release from films were fit to different equations and kinetic models to explain release profiles. Kinetic models used were zero and first-order equations, Hixon-Crowell, Higuchi and Korsmeyer's-Peppas models. Short-term stability study revealed that drug content decreased in various patches was negligible. Cross-linked formulations were considered as the best formulations.
Keywords: Ciprofloxacin; Ornidazole; polycaprolactone; local drug delivery; cross-linking; *in vitro* release

INTRODUCTION

Periodontitis is an inflammatory response to the overgrowth of anaerobic organisms such as spirochetes and bacteroides and in some cases, micro-aerophilic organisms in the subgingival plaque. Periodontal disease may result in the destruction of the bone and soft tissues supporting the tooth, which causes tooth loss. The clinical signs include changes in the morphology of gingival tissues, gingival bleeding as well as periodontal pocket formation. This pocket provides an ideal environment for the growth and proliferation of anaerobic pathogenic bacteria [1,2]. The oral cavity is colonized by more than 400 species of aerobic and anaerobic bacteria. Anaerobic bacteria outnumber their aerobic counterparts by a ratio of 10:1 to 100:1. These organisms inhabit the teeth, the gingival crevice, the mucous membranes, the dorsum of the tongue and saliva [3]. Conventional local application (as mouth rinse, gels, tooth paste) control only supragingival microbial plaques or mucosal infection, but not effective against periodontal disease involving pocket formation and also requires high initial concentration and multiple applications in order to provide sustained effectiveness [4,5]. Local application of antibiotics has been achieved either by subgingival irrigation or by incorporating the drug into different devices for insertion into periodontal pockets. In contrast to irrigation, the devices may secure antimicrobial effect for a prolonged period of time at the site. So a delivery system is developed by immobilizing antimicrobial agents with a carrier substance to provide controlled local release. Controlled local delivery of antibiotics has shown to reduce periodontopathogenic microorganisms with minimal side effects. Controlled release local delivery devices, which may secure an antimicrobial effect for a prolonged period of time at the disease site, than that can be achieved by systemic or local topical application and also bypass systemic complication. These devices employ the control release technologies to assure therapeutic concentrations of the antimicrobials in the subgingival area for atleast three or more number of days following a single application. Hence a better, safer and effective low dose drug delivery device is highly desirable [6]. Many antibacterial agents have been tested for intra-pocket delivery, including tetracycline [7,8], doxycycline [4], chlorhexidine [9], metronidazole [10], ofloxacin, minocycline, and Ornidazole for their contribution to therapeutic response in periodontal disease [11].

The main objective of the study is to prepare biodegradable polymeric polycaprolactone strips containing Ciprofloxacin and Ornidazole for the local delivery into the periodontal pockets. The objectives of the present work are as follows;

Preformulation factors such as melting point, assay, loss on drying, partition co-efficient, etc. were studied. Evaluation of the prepared films for their

physicochemical characteristics such as, film thickness, weight uniformity, content uniformity, surface pH, viscosity, folding endurance, tensile strength, percentage elongation, percentage moisture loss including *in-vitro* drug release were carried out. Establishment of suitable analytical method for the simultaneous estimation of Ciprofloxacin and Ornidazole and compatibility between drugs and polymer to rule out the possibility of chemical interaction under experimental conditions using IR spectra and UV were done. Release pattern of drugs from the strips before and after cross-linking by conducting dissolution studies, antibacterial activity of the prepared formulations and short term stability studies on the most satisfactory film as per ICH guidelines were done.

MATERIALS AND METHODS

Ciprofloxacin and Ornidazole were obtained from Dr. Reddy's Laboratories, Hyderabad and Lincoln Pharmaceuticals Ltd, Ahmedabad. Other essential chemicals were obtained from Sigma Aldrich, st.Louis, USA; E-Merck (India) Ltd., Mumbai; S.D. Fine Chem Ltd., Mumbai. *UV*- Visible spectrophotometer [(*UV*-1601 PC) Shimadzu Corporation, Kyoto, Japan]; FT / IR spe ctrometer 4100 [(4000/6000 Series) Jasco Corporation, Japan], Brookfield viscometer [(LV DV-E) Brookfield Engineering Labs. Inc, USA], Digital thickness tester [Mitutoyo Corporation, Japa n]; Cyclone mixer [Remi Equipments, Bangalore]; pH-meter [Control Dynamics, Bangalore] etc. were used for carrying out the study.

Preformulation studies

The following prefomulation studies were performed for drugs and polymer;

Interference of Polymers

UV method: Solution of polymer was prepared as per the concentration given in the table 10 using acetone. The solution was scanned in *UV* region i.e., 200-400 nm, using corresponding blank solution. The Figure 09 represents the *UV* scan of polymeric solution.

Fourier Transform Infrared Spectroscopy: The pure drugs (Ciprofloxacin and Ornidazole) and polymer were subjected to FT-IR studies alone and in combination.

Melting Point Determination: Melting point was determined by capillary tube method taking small amount of drug in a capillary tube whose one end was closed by melting. The mean of three readings was recorded.

Loss on Drying : The loss on drying of Ciprofloxacin and Ornidazole were determined by taking 1.0 g of drug and dried in an oven at 100-105 ^{o}C for two hours.

Assay: The purity of dried Ciprofloxacin and Ornidazole were carried out as per British Pharmacopoeia.

Partition Co-efficient: Distribution co-efficient of Ciprofloxacin and Ornidazole were determined in the mixture of *n*-butanol-phosphate buffer solution, pH 6.6 by using shake flask method [12].

Formulation Development

Preparation of Drug Loaded Polycaprolactone Films: Polycaprolactone (10% w/v) was soaked in acetone for 24 hours to get a clear solution. To the above solution different plasticizers were add. This dispersion was filtered through a muslin cloth to remove undissolved portion of the polymer . Required amount of the drugs were added and mixed for 15 minutes to dissolve the drugs in polycaprolactone solution. The viscous dispersion was kept aside for 30 minutes for complete expulsion of air bubbles. The films were casted by pouring the drug-polymer dispersion into the centre of levelled glass moulds of 5 x 3 cm^2 and allowed to dry at room temperature (30 ^{o}C) for 48 hours. After drying, films were cut into strips of 7 × 2 mm^2, wrapped in aluminium foil and stored in desiccator for further use [13].the formulation are prepared as per the formula below in Table 1. The selected film with dibutyl phatalate was prepared with the varying proportion of the drugs as given in Table 2.

Preparation of cross-linked polycaprolactone films: The films were prepared as described above and subjected to cross-linking by exposing to glutaraldehyde vapours in a chromatography chamber.

Table 1: Formulation Table

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11
Ciprofloxacin	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg
Ornidazole	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg	15mg
Poly-Caprolactone	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg	200 mg
Glycerine	10%	20%	30%	---	---	---	---	---	---	---	---
Propylene Glycol	---	---	---	10%	20%	30%	---	---	---	---	---
PEG 400	---	---	---	---	---	---	10%	20%	30%	---	---
Dibutyl Pthalate	---	---	---	---	---	---	---	---	---	10%	20%
Acetone	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml	10ml
Observation	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Brittle film	Flexible film

Table 2: Polycaprolactone strips containing drugs – parameters for preparation

	Strip code	% of drug	
		Ciprofloxacin	Ornidazole
Uncross-linked films	F11(A)	7.5%	7.5%
	F11(C)	10%	5%
	F11(E)	5%	10%
Cross-linked films	F11(B)	7.5%	7.5%
	F11(D)	10%	5%
	F11(F)	5%	10%

Evaluation of Polymer Strips

Thickness Uniformity : The thickness of films was measured using Digimatic Micrometer. The thickness of each film was determined at six different places and the average was calculated.

Weight Uniformity of Films : Patches (size of 7 x 2 mm^2) were cut from different areas of film. The weight of each patch was taken and the weight variation of six patches was calculated.

Surface pH: Periodontal films were left to swell for 1 hr on the surface of the agar plate, prepared by dissolving 2% w/v agar in warmed phosphate buffer solution, pH 6.6 under stirring and then poured the solution into the petridish till gelling/solidify at room temperature. The surface pH was measured by means of pH paper placed on the surface of the swollen film. The mean of three readings were recorded [14].

Viscosity: Aqueous solutions containing polymer were prepared in the same concentration as that of films. Brookefield viscometer (LVDV-E model) attached to the helipath spindle number 18 was used. The viscosity was measured at 6 rpm at room temperature. The recorded values were the mean of three determinations [14].

Folding Endurance: The folding endurance of the films was determined by repeatedly folding one film at the same place till it broke or folded upto 300 times, which is considered satisfactory to reveal good film properties [15]. The number of times of film could be folded at the same place without breaking gave the value of the folding endurance. This test was done on all the films for five times.

Percentage Moisture Loss: Percentage moisture loss was determined by keeping the films (7 x 2 mm^2) in a desiccator containing anhydrous calcium chloride. After 3 days, the films were taken out, re-weighed and the percentage moisture loss was calculated using the following formula [16],

Percentage Moisture Loss = ((Initial weight – Final weight)/ Initial weight) x 100

Drug Content Uniformity of Films: Patches (7 x 2 mm^2) were taken from different areas of film and placed into 10 ml volumetric flask. 10 ml of acetone was added. The contents were stirred in cyclone mixer to dissolve the patch. The absorbance of the solution was measured using acetone as blank at 277 nm and 318 nm.

Tensile Strength and Percentage Elongation : Tensile strength and percentage elongation of the films was determined with Universal strength testing machine. The sensitivity of the machine is 1 gram. The test film of specific size (4 × 1 cm^2) was fixed between these cell grips and force was gradually applied till the film breaks. The percentage elongation of films was calculated by applying the equation ; Percentage elongation = (Increase in length/ Original length) x 100 [13].

***In Vitro* Drug Release:** *In vitro* drug release was performed by placing films of known weight and dimension (7 × 2 mm^2) into small vials containing 2 ml of phosphate buffer solution, pH 6.6. The vials were sealed and kept at 37 ^oC for 24 hours. One ml of buffer was withdrawn and immediately replaced with a fresh 1 ml phosphate buffer solution, pH 6.6 after 24 hours [17]. The concentrations of drugs in the buffer were measured at 274.8 nm and 318 nm. The procedure was continued for 6 days and 16 days for uncrosslinked and crosslinked films respectively.

RESULTS AND DISCUSSIONS:

Preformulation Studies

Drug – excipient compatibility studies: described in the methodology section the FT-IR studies were carried out for pure drugs, and along with polymer. IR spectra of Ciprofloxacin, Ornidazole and polycaprolactone combinations are shown in Figures 1 to 4 [19].

Figure 01: IR spectrum of Ciprofloxacin pure

Figure 02: IR spectrum of Ciprofloxacin and polycaprolactone mixture.

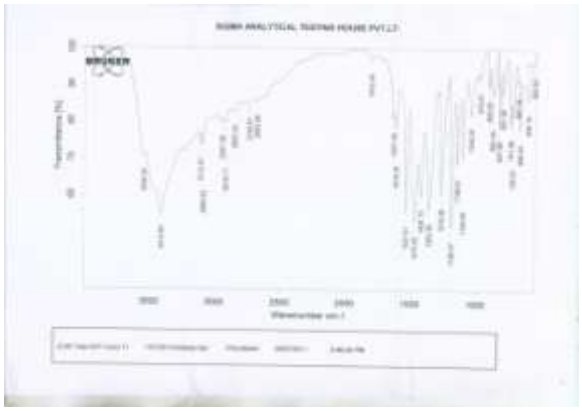

Figure 03: IR spectrum of Ornidazole pure mixture

Figure 04: IR spectrum of Ornidazole and polycaprolactone

The study showed there are no observable interactions between drugs and the excipients. Therefore the combination can be used for further formulation and development.

Melting point: Melting point was determined by capillary tube method. It was found to be 256.33 ± 0.5774 ^{o}C and 89.37 ± 0.5774 ^{o}C for Ciprofloxacin and Ornidazole respectively. This value is same as that of the literature citation.

Loss on drying: The loss on drying of drugs was determined as described in B.P. It was found to be 0.84% and 0.20% for Ciprofloxacin and Ornidazole respectively.

Assay: The assay of both drugs was determined by potentiometric method. The % purity of Ciprofloxacin and Ornidazole was found to be 99.48% and 99.62% respectively.

Partition co-efficient: The partition co-efficient of Ciprofloxacin and Ornidazole was found to be 1.8380 ± 0.2183 and 0.7812 ± 0.5233 respectively in *n*-butanol-phosphate buffer solution (pH 6.6).

Evaluation

Thickness uniformity of films: The results obtained are given in table 3.

Weight uniformity of films: Standard deviation of all the patches ranged between 0.2317 and 0.3777. Resultsgiven in table 4.

Viscosity: All films had shown high viscosity. It helps for sustained drug release, results are given in table 5.

Surface pH: The pH of all films was approximately 6.7 to 7.0. Thus the pH is similar to the pH of the oral cavity. Hence chances of irritation is very less.

Folding endurance: Films did not show any cracks even after folding for more than 300 times. Thus the flims had a good tensile strength.

Percentage moisture loss: The data are given in the Table 6.

Drug content uniformity of films: The results were expressed in AM ± SD and reported in Table 7. The results indicated that the drug was uniformly dispersed.

Table 3: Thickness determinations of films

Film Code	Average thickness* (mm) AM ± SD
F11(A)	0.1325 ± 0.0019
F11(B)	0.1392 ± 0.0040
F11(C)	0.1382 ± 0.0039
F11(D)	0.1500 ± 0.0035
F11(E)	0.1373 ± 0.0031
F11(F)	0.1488 ± 0.0069

*Each reading is an average of six determinations

Table 04: Weight uniformity of films

Film Code	Average weight* (mg) AM ± SD
F11(A)	2.4167 ± 0.2317
F11(B)	2.6833 ± 0.2858
F11(C)	2.5000 ± 0.2608
F11(D)	2.6333 ± 0.3204
F11(E)	2.5167 ± 0.2858
F11(F)	2.7666 ± 0.3777

*Each reading was an average of six determinations.

Table 05: Viscosity of polymer determined by Brookfield viscometer

Film Code	Polymer and drugs (mg)		Solvent, (10ml)	Plasticizer (20%)	Viscosity* (cps) AM ± SD
F11(A)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 15mg 15mg	Acetone + Dibutylpthalate		353.67 ± 10.0664
F11(B)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 15 mg 15 mg			353.67 ± 10.0664
F11(C)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 20 mg 10 mg			356.00 ± 7.0000
F11(D)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 20 mg 10 mg			356.00 ± 7.0000
F11(E)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 10 mg 20 mg			353.00 ± 15.5242
F11(F)	Polycaprolactone Ciprofloxacin Ornidazole	200 mg 10 mg 20 mg			353.00 ± 15.5242

*Each reading is an average of three determinations.

Table 06: Percentage moisture loss of films

Film Code	Moisture loss (%)* AM ± SD
F11(A)	9.0931 ± 2.1678
F11(B)	4.8668 ± 1.7641
F11(C)	8.9451 ± 2.6599
F11(D)	4.6062 ± 1.7890
F11(E)	9.2138 ± 2.1137
F11(F)	5.6807 ± 1.9642

*Each reading is an average of three determinations.

Table 07: Content uniformity of films

Film code	Amount of drug present * (mg) AM ± SD		% Drug present AM ± SD	
	Ciprofloxacin	Ornidazole	Ciprofloxacin	Ornidazole
F11(A)	126.9144 ± 1.2481	124.7625 ± 2.0105	84.6096 ± 0.8915	83.1750 ± 1.4360
F11(B)	129.8193 ± 1.3396	133.2160 ± 4.0478	86.5462 ± 0.9568	88.8107 ± 2.8913
F11(C)	163.9800 ± 2.9208	88.2440 ± 4.3492	81.9900 ± 1.5647	88.2440 ± 4.6600
F11(D)	166.2622 ± 2.6508	80.7589 ± 2.8345	83.1311 ± 1.4200	80.7589 ± 3.0371
F11(E)	89.1309± 3.5321	174.5694 ± 10.2689	89.1309 ± 3.7846	87.2847 ± 5.5011
F11(F)	81.3252 ± 2.7298	163.0860 ± 2.6267	81.3252 ± 2.9249	81.5430 ± 1.4071

Tensile strength and percentage elongation of polycaprolactone films: The data for tensile strength are given in the Table 8.The tensile strengths of drug loaded films are in the order of F11(F) > F11(B) > F11(D) > F11(E) > F11(A) > F11(C). Elongation was higher for uncrosslinked than for crosslinked films, as shown in table 9. The order of percentage elongation of the film is F11(C) > F11(E) > F11(A) > F11(D) > F11(B) > F11(F).

Table 08: Tensile strength of films

Film code	Tensile strength* (kg) AM ± SD
F11(A)	2.9467 ± 0.1021
F11(B)	4.3467 ± 0.1850
F11(C)	2.8100 ± 0.1400
F11(D)	4.1133 ± 0.0603
F11(E)	3.1700 ± 0.2000
F11(F)	4.3533 ± 0.0603

Table 09: Percentage elongation of films

Film code	Percentage elongation* (%) AM ± SD
F11(A)	67.0025 ± 2.6963
F11(B)	24.8900 ± 5.3055
F11(C)	68.2775 ± 1.7350
F11(D)	33.7583 ± 1.5893
F11(E)	67.7767 ± 3.0042
F11(F)	22.9758 ± 1.8080

***In Vitro* Release Studies**

The release data of Ciprofloxacin and Ornidazole studied are given in tables 10 and 11 with the graphical representation as in Figure 5 and 6. The crosslinked formulation B, D, F showed a sustained drug release for a period of days in comparison to the uncrosslinked ones namely 11(A),11(C),11(F) which dumped the total drug within 6 days. Thus crosslinking proved to be beneficial for prolonging the drug action.. The relative drug release followed the following pattern. The drg release per day for the indivijual drugs were found above the MIC level .

Kinetics study:

Initial all the formulations were compared with the zero order or first order release pattern to define whether the process is concentration dependent or independent process. The study of the indivijual drugs R^2 (regression) values as shown in table 12 and 13 clearly shows that all the formulation had a higher R^2 (regression) values for the zero order release than the first order. Or it can be concluded that the drug relese is independent of the concentration process.

Table 10: Drug release study for the ciprofloxacin

Time (Days)	F11(A)	F11(B)	F11(C)	F11(D)	F11(E)	F11(F)
0	0.00	0.00	0.00	0.00	0.00	0.00
1	34.75	28.21	35.82	34.20	28.76	28.06
2	50.50	34.16	55.19	44.42	47.76	36.02
3	64.40	41.87	70.16	47.36	64.37	40.36
4	80.90	44.36	87.05	50.69	80.12	46.24
5	95.23	48.44	96.48	56.56	93.54	50.34
6	97.21	53.90	98.64	59.82	97.00	54.70
7		59.18		64.43		60.36
8		63.93		68.03		63.31
9		71.30		73.42		70.47
10		75.28		76.93		73.15
11		77.53		79.33		80.33
12		82.60		82.43		88.21
13		85.31		87.06		91.56
14		87.53		91.35		94.05
15		93.41		94.30		97.34
16		97.12		97.32		98.55

Figure 5: Drug release study for the ciprofloxacin

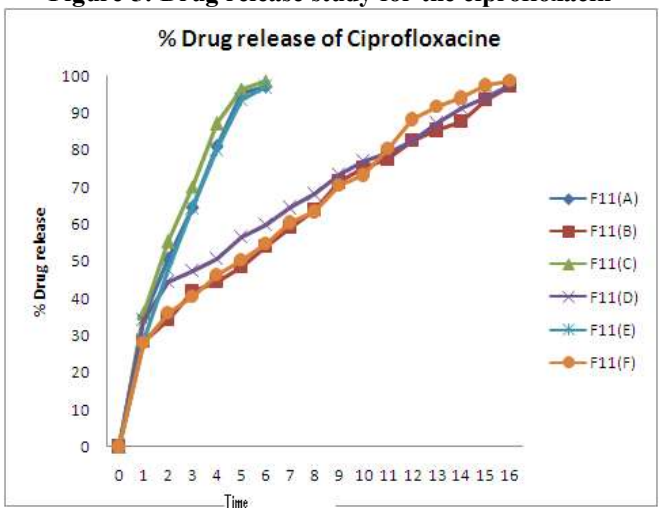

Table 11: Drug release study for the Ornidazole

Time (Days)	F11(A)	F11(B)	F11(C)	F11(D)	F11(E)	F11(F)
0	0.00	0.00	0.00	0.00	0.00	0.00
1	34.76	29.30	26.71	28.32	37.54	34.12
2	50.75	34.54	46.82	36.32	60.43	40.32
3	66.17	42.35	66.97	39.42	75.87	43.87
4	80.40	45.21	84.63	46.75	84.76	52.42
5	95.27	49.64	95.50	53.34	95.73	57.32
6	97.32	53.60	97.38	61.62	97.86	62.73
7		59.37		65.54		65.46
8		62.97		69.15		69.37
9		68.67		72.63		73.36
10		71.26		77.22		75.86
11		76.00		78.46		82.28
12		81.54		81.96		88.60
13		84.26		89.56		91.54
14		89.45		93.47		94.70
15		94.58		95.99		98.34
16		98.72		97.81		98.83

Figure 06: Drug release study for the Ornidazole

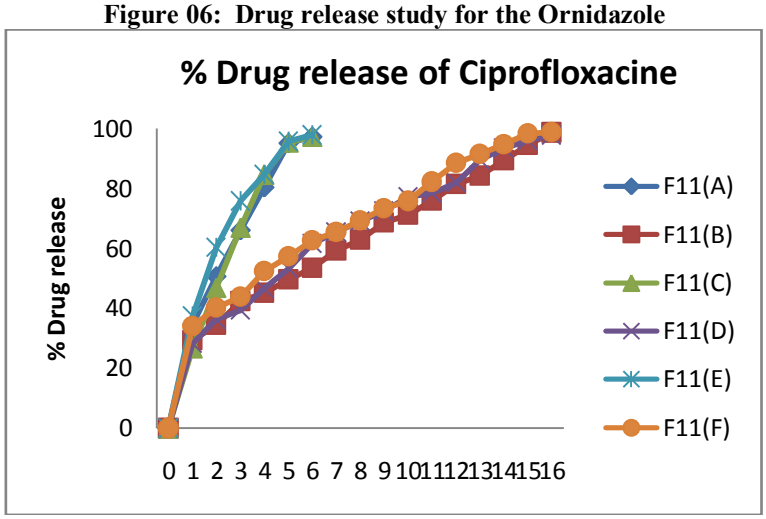

Table 12: Comparison of orders of *in vitro* release of Ciprofloxacin from films F11 (A) - F11 (F)

Film code	*In vitro* release in phosphate buffer pH 6.6 Regression equations	
	Zero order	First order
F11(A)	y = -15.821x + 87.036 R² = 0.946	y = -0.2625x + 2.1396 R² = 0.9312
F11(B)	y = -5.0635x + 79.088 R² = 0.9444	y = -0.0753x + 2.0565 R² = 0.8947
F11(C)	y = -16.039x + 84.726 R² = 0.9242	y = -0.3093x + 2.1736 R² = 0.9424
F11(D)	y = -4.7005x + 72.448 R² = 0.8991	y = -0.0767x + 2.0165 R² = 0.8996
F11(E)	y = -16.176x + 89.734 R² = 0.9598	y = -0.2526x + 2.1447 R² = 0.9415
F11(F)	y = -5.349x + 79.672 R² = 0.9518	y = -0.097x + 2.1431 R² = 0.8712

Table 13: Comparison of orders of *in vitro* release of Ornidazole from films F11 (A) - F11 (F)

Film Code	*In vitro* release in phosphate buffer pH 6.6 Regression equations	
	Zero order	First order
F11(A)	y = -15.808x + 86.758 R² = 0.9442	y = -0.2639x + 2.1382 R² = 0.9311
F11(B)	y = -5.0362x + 79.027 R² = 0.9473	y = -0.0826x + 2.1018 R² = 0.8041
F11(C)	y = -16.698x + 90.377 R² = 0.9527	y = -0.2753x + 2.1641 R² = 0.9486
F11(D)	y = -5.1575x + 77.286 R² = 0.9312	y = -0.0864x + 2.0797 R² = 0.8982
F11(E)	y = -15.51x + 81.933 R² = 0.8944	y = -0.2769x + 2.1049 R² = 0.9635
F11(F)	y = -5.048x + 74.024 R² = 0.9176	y = -0.101x + 2.1202 R² = 0.8583

Further to determine the nature of the release pattern of the drug from the films the drug release data were fitted to the various release kinetics models like Higuchi's model, Korsmeyer- Peppas model and Hixon-Crowell

cube root law models. The data that are obtained fom the study is enlisted in the table 14 and 15. R^2 values are higher for Higuchi's model compared to Hixon – Crowell for all the films. Hence Ciprofloxacin and Ornidazole release from all the films followed diffusion rate controlled mechanism.. The release pattern mainly indicated as the non fician type.

Table 14: Regression equations of *in vitro* release of Ciprofloxacin from films F11(A) to F11 (F)

Film code	*In vitro* release of Ciprofloxacin in phosphate buffer pH 6.6		
	Hixon-Crowell model	**Higuchi's model**	**Korsmeyer's-peppas model**
F11(A)	y = -0.5495x + 4.7045 R² = 0.9789	y = 8.478x - 3.8001 R² = 0.9869	y = 0.6048x + 0.6985 R² = 0.9917
F11(B)	y = -0.1679x + 4.5214 R² = 0.9675	y = 4.8216x - 0.3483 R² = 0.9913	y = 0.4695x + 0.7539 R² = 0.9628
F11(C)	y = -0.5989x + 4.6913 R² = 0.9916	y = 8.7083x - 2.6374 R² = 0.9903	y = 0.5907x + 0.7468 R² = 0.9903
F11(D)	y = -0.1652x + 4.3841 R² = 0.962	y = 4.5774x + 6.5171 R² = 0.9869	y = 0.3813x + 0.9826 R² = 0.9667
F11(E)	y = -0.5426x + 4.7463 R² = 0.9881	y = 8.5714x - 6.1418 R² = 0.979	y = 0.7077x + 0.4888 R² = 0.9931
F11(F)	y = -0.1969x + 4.6273 R² = 0.9579	y = 5.0594x - 1.6933 R² = 0.9857	y = 0.4847x + 0.7305 R² = 0.968

Table 15: Regression equations of *in vitro* release of Ornidazole from films F11(A) to F11 (F)

Film code	*In vitro* release of Ornidazole in phosphate buffer pH 6.6		
	Hixon-Crowell model	**Higuchi's model**	**Korsmeyer's-peppas model**
F11(A)	y = -0.5508x + 4.6995 R² = 0.9805	y = 8.4871x - 3.629 R² = 0.9887	y = 0.6034x + 0.7031 R² = 0.9936
F11(B)	y = -0.1748x + 4.5634 R² = 0.9318	y = 4.7787x + 0.0449 R² = 0.9873	y = 0.4572x + 0.7809 R² = 0.9651
F11(C)	y = -0.5761x + 4.7728 R² = 0.9866	y = 8.8345x - 7.2116 R² = 0.9688	y = 0.7573x + 0.3973 R² = 0.9853
F11(D)	y = -0.1826x + 4.5214 R² = 0.9699	y = 4.955x + 0.4979 R² = 0.995	y = 0.4735x + 0.763 R² = 0.974
F11(E)	y = -0.5599x + 4.5792 R² = 0.9934	y = 8.5712x - 0.3346 R² = 0.9922	y = 0.5428x + 0.8482 R² = 0.9808
F11(F)	y = -0.196x + 4.5121 R² = 0.9562	y = 4.875x + 3.9669 R² = 0.9909	y = 0.4169x + 0.9092 R² = 0.9726

CONCLUSION

Suitable analytical methods based on *UV-Visible* spectrophotometry were developed for Ciprofloxacin and Ornidazole. Periodontal films of antibacterial drugs Ciprofloxacin and Ornidazole were formulated by solvent casting technique. The drugs were incorporated in polycaprolactone polymer strips in three different concentrations. All strips were further cross-linked with glutaraldehyde 2% and which was aimed to extent and control the drug release for more number of days. The FT-IR spectra revealed that, there was no interaction between polymer and drugs. Polymer used was compatible with the drugs. Evaluation parameters like thickness, tensile strength, percentage elongation, percentage moisture loss, folding endurance, indicates that films were mechanically stable. Percentage weight variation and content uniformity were found to be uniform in all the films. *In vitro* release studies of Ciprofloxacin and Ornidazole were carried out in phosphate buffer solution, pH 6.6. Crosslinked films were giving 16 days and uncrosslinked films were giving 6 days of drug release. An average amount of

drug released per day was found to be above the minimum inhibitory concentration of Ciprofloxacin (MIC ≤ 1 μg/ml) and Ornidazole (MIC ≤ 1 μg/ml). Throughout the *in vitro* release studies, the films remained intact without any disintegration. All the six formulations of Ciprofloxacin and Ornidazole prepared followed zero order release kinetics. Hixon - Crowell cube root law was applied to test the release mechanism. R^2 values are higher for Higuchi's model compared to Hixon – Crowell for all the films. Hence Ciprofloxacin and Ornidazole release from all the films followed diffusion rate controlled mechanism. The release mechanism from all the films follows non-Fickian diffusion (anomalous behavior). All the films were found to be stable over the storage period and conditions tested. Overall study suggests that among the films prepared crosslinked films were found to show the best results. Thus the specific objectives listed in this work were achieved namely design and evaluation of periodontal films containing Ciprofloxacin and Ornidazole for periodontitis, certainly these finding can be applied for controlled delivery of drugs

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