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Formulation and Evaluation of Different Polymer based Periodontal Film of Ofloxacin

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Abstract

In present investigation periodontal films of ofloxacin was formulated using different polymers. Simple casting method was used to prepared films of chitosan, carbopol 934, polyvinyl pyrrolidine K30 and hydroxy propyl methyl cellulose K4M. In different formulations glycerine was used as plasticizer. Prepared films were evaluated for thickness uniformity, weight uniformity, tensile strength, folding endurance, moisture loss, content uniformity and drug release. Results obtained from different studies were found within acceptable limits. Film containing chitosan showed maximum tensile strength over other batches. Films prepared using Carbopol 934 showed maximum drug release (98.35) over a long period of time. The findings of the results easily predict the fact that chitosan, carbopol 934, polyvinyl pyrrolidone K30 and hydroxy propyl methyl cellulose K4M can be used to prepare film for the treatment of peridontal disease.

Key words: periodontal film, ofloxacin, periodontitis.

INTRODUCTION

Periodontal diseases are recognized as the major public health problem throughout the world. Daily oral hygiene plays a vital role in maintaining healthy teeth and gums. Periodontal disease can do occur in all age groups, ethnicities, races, genders and socioeconomic levels. Periodontal (gum) diseases, including gingivitis and periodontitis, are serious infections that, left untreated, can lead to tooth loss. The word *periodontal* literally means "around the tooth." Periodontal disease is a chronic bacterial infection that affects the gums and bone supporting the teeth. Periodontal disease can affect one tooth or many teeth. It begins when the bacteria in plaque (the sticky, colorless film that constantly forms on your teeth) causes the gums to become inflamed. Periodontal diseases range from simple gum inflammation to serious disease those results in major damage to the soft tissue and bone that support the teeth. In the worst cases, teeth are lost [1]. Periodontitis is a set of inflammatory diseases affecting the periodontium that is, the tissues that surround and support the teeth. Periodontitis involves progressive loss of the alveolar bone around the teeth, and if left untreated, can lead to the loosening and subsequent loss of teeth. Periodontitis is caused by microorganisms that adhere to and grow on the tooth's surfaces,

along with an overly aggressive immune response against these microorganisms [2]. A diagnosis of periodontitis is established by inspecting the soft gum tissues around the teeth with a probe and x-ray films by visual analysis, to determine the amount of bone loss around the teeth. Specialists in the treatment of periodontitis are periodontists; their field is known as "periodontology" or "periodontics". The main cause of periodontal disease is bacteria plaque, a sticky, colourless film that constantly forms on teeth.However, factors like smoking/ tobacco use, genetics, pregnancy and puberty, stress, medication, clenching or grinding teeth, diabetes and poor nutrition also lead to periodontal diseases. Periodontal pathogens grow only where atmosphere and nutrient composition are strictly conductive to their requirements and the disease once established, causes major changes in the periodontal microenvironment. The gingival crevicular fluid (GCF) flow occurs at extremely low levels in healthy gingival sulci but increases enormously to 3.5 ml/day or more. The most commonly grown anaerobic pathogenic bacteria are Actinobacillus actinomycetencomitans, Bacteroides gingivalis; Bacteroides melaninogenicus sub species intermedius, Porphyromonas gingivalis and Prevotella intermedia. Clinical signs such as bluish red thickened marginal gingiva, bluish red vertical zone from the gingival margin to the oral mucosa, gingival bleeding and localized pain are suggestive of the presence of periodontal pockets [3, 4, 5]. Ofloxacin is a synthetic chemotherapeutic antibiotic of the fluoroquinolones drug class considered to be a second-generation fluoroquinolones. Ofloxacin is a broad-spectrum antibiotic that is active against both Gram-positive and Gram-negative bacteria. It functions by inhibiting gyarase, a type II, topoisomeras and topoisomerase IV, which is an enzyme necessary to separate replicated DNA, thereby inhibiting cell division.). Ofloxacin is a racemic mixture, which consists of 50% levofloxacin (the biologically active component) and 50% of its “mirror image” or enantiomer dextrofloxacin. When levofloxacin disks were not available in early clinical trials, a 5-pg Floxin (ofloxacin –floxacin) disk was substituted. It functions by inhibiting DNA gyrase, a type II topoisomerase, and topoisomerase IV which is an enzyme necessary to separate replicated DNA, thereby inhibiting cell division. The fluoroquinolones interfere with DNA replication by inhibiting an enzyme complex called DNA gyrase. Ethyl cellulose is a derivative of cellulose in which some of the hydroxyl groups on the repeating glucose units are converted into ethyl ether groups. Ethyl cellulose is a polymer used to prepare sustained-release medications of various types. Chitosan is obtained by deactylation of Chitin, is a natural, non-toxic, biocompatible and biodegradable polysaccharide suitable for applications in pharmaceutical technology. Chemically it is poly-b-(1, 4)-2-amno-2-deoxy-D-glucopyranose. It is soluble in dilute acid solutions such as dilute lactic acid and dilute acetic acid. It is insoluble at pH >6.5 and in water and most organic solvents. It is used as film forming agent, gel forming agent, with its immunostimulatory activities, anticoagulant properties, antibacterial and antifungal action and for its action as a promoter to be used in periodontitis. Carbopol-934 polymer is a cross-linked polyacrylate polymer. It offers excellent stability at high viscosity and produces thick formulations for opaque gels, emulsions, creams and suspensions. PVP K-30 of industry grade can be used as film forming agent, viscosity enhancement agent, lubricator and adhesive. Hydroxy propyl methyl cellulose (HPMC) is a semisynthetic ether derivative of cellulose. has been the dominant hydrophilic vehicle used in controlled release dosage forms because of its non-toxic nature, ease of compression, and accommodation to high levels of drug loading.

Peridontal films were prepared with an aimed to extend and control the drug release for more number of days. The greatest advantages associated with the use of intra-pocket delivery systems over systemic delivery system are that the administration is less time consuming than mechanical debridement and a lesser amount of drug is sufficient to achieve effective concentration at the site of action.

MATERIALS AND METHODS

Materials: A gift sample of ofloxacin was obtained from Unicure Pharmaceutical Pvt. Ltd. Roorkee. Chitosan was obtained from Sigma Aldrich, co 3050 Spruce Street, St. Louis USA. Ethyl Cellulose, Hydroxy Propyl Methyl Cellulose (HPMC K4M), Carbopol-934, and Poly Vinyl Pyrrolidone (PVP K-30) were obtained from Central Drug House (P) Ltd. New Delhi. All other chemicals used were of analytical grade.

Preparation of film containing ofloxacin: Periodontal films were prepared by solvent casting technique. Glass moulds were used for casting of films. Formulations were designed as shown in table1, in which ethyl cellulose was taken as the main non-biodegradable polymer in combination with different co-polymers for each cast films. Films were prepared by dissolving Ethyl cellulose alone and with co-polymers (Chitosan, Carbopol®934, PVP K-30, and HPMC K4M) in chloroform and dichloromethane (1:1) solution, using glycerine and PEG-400 as plasticizers. Ofloxacin was added in to the polymeric solution and mixed homogenously using magnetic stirrer in a closed beaker .After complete mixing 10 ml of the solution was poured into clean labelled glass moulds of 15 cm^2. The solvent was allowed to evaporate slowly by inverting a glass funnel with a cotton plug closed into the stem of the funnel at room temperature for 24 hours. After complete evaporation of solvent, cast films obtained, which were then cut into pieces of (7mm × 2 mm), wrapped in an aluminium foil and stored in a desiccators at room temperature in a dark place for further evaluation studies [5, 6, 7].

Table1: Composition of different formulation containing ofloxacin

Ingredients	F1	F2	F3	F4	F5
Ethyl cellulose (mg)	890	800	800	800	800
Chitosan (mg)	-	90	-	-	-
Carbopol-934 (mg)	-	-	90	-	-
PVP-K30 (mg)	-	-	-	90	-
HPMC K4M (mg)	-	-	-	-	90
Glycerine (ml)	0.3	0.3	0.3	0.3	0.3
PEG 400 (ml)	0.05	0.05	0.05	0.05	0.05
Ofloxacin (mg)	10	10	10	10	10

(-) No ingredient added; PVP = Poly Vinyl Pyrrolidone; HPMC= Hydroxy Propyl Methyl Cellulose; PEG=Poly Ethylene Glycol; F1 to F5=Films codes

Characterization of the films: Fourier transforms infrared (FTIR) spectroscopy of the drug alone, polymer alone, and polymer along with the drug. Physicochemical properties such as size, thickness, content uniformity, weight variation, folding endurance, tensile strength, and percentage moisture loss of the prepared films were determined [5, 7, 8].

Thickness measurement: The thickness of the polymer films (1 × 1 cm) was determined by using a film thickness tester (Digimatic micrometer mitutoyo, Japan). The thickness of each strip at six different places was determined and a standard deviation was calculated [5, 7, 8].

Weight determination: Twenty films of the same size (7 mm× 2 mm) were weighed on an electronic balance and the average weight was calculated. The results were recorded as one set. Six sets of such films were weighed and the standard deviation was calculated [5, 7, 8].

Estimation of Drug content: The drug-loaded films of known weight (7 mm× 2 mm) were dissolved in 10 ml of aqueous acetic acid, suitably diluted and the amount of drug present was estimated by UV/VIS spectrophotometer (Shimadzu) at 288 nm [3, 7, 8].

Tensile Strength Measurement: Film strips in special dimensions and free from air imperfections were held between two clamps positioned at a distance of 3 cm. During measurement, the strips were pulled by the top clamp at a rate of 100 mm/min, and the force and elongation were measured in triplicate when the film broke. This property was evaluated using the Instron universal tensile strength measurement instrument (Model 2046, Instron Ltd., Japan), with a 2-kilogram load cell. Two mechanical properties, namely tensile strength and percent elongation were computed for the evaluation of the film. Tensile strength is the maximum stress applied to a point at which the film specimen breaks, and can be computed from the applied load at rupture and cross-sectional area of fractured film. As described from the following equation-

Tensile strength = Force at break (N) / Initial cross sectional area of the sample (mm^2)

% Elongation = (Increase in length / original length) x 100

Estimation of moisture loss: The 20 films of different concentrations of size (7 × 2 mm) are weighed accurately and then they are kept in desiccators for 3 consecutive days and then reweighed.[11] And by using the formula % moisture loss was calculated by formula [8, 9] :
Moisture loss = (initial wt – final wt/initial wt) ×100.

Folding endurance studies: This study was determined by repeatedly folding a small strip of film, 2 × 2 cm in size, at the same place, till it broke.

***Invitro* drug release studies:** The pH of gingival fluid lies between 6.5 – 6.8, phosphate buffer pH 6.6 was used as simulated gingival fluid. Also, since the film should be immobile in the periodontal pocket, a static dissolution model was adopted for the dissolution studies. Sets of five films of known weight and dimension were placed separately in small sealed test tubes containing 1.0 ml of phosphate buffer (pH 6.6) and kept at 37 ± 0.5 °C for 24 h. The buffer was then drained off and replaced with a fresh 1.0 ml of buffer. The concentration of drug(s) was determined by UV/Visible spectrophotometer (Shimadzu) at 288 nm the procedure was continued for 10 consecutive days for the films of different polymers respectively.

Stability studies: The stability of the entire drug loaded polymer films were studied at different temperatures using the reported procedure. The films of size (7mm × 2 mm) were weighed in three sets (12 strips in each set). The films were wrapped individually in aluminum foil and also in butter paper and placed in petri dishes. These containers were stored at room temperature (27 ± 2°C), oven temperature **(**40 ± 2°C) and in a refrigerator (5–8 ± 2°C) for a period of three months. All the polymeric films were observed for any physical changes, such as color, appearance, flexibility, or texture, and the drug content was estimated at an interval of one week. Furthermore, the amount of drug in the films was estimated spectrophotometrically. The drug solutions were further scanned to observe any possible spectral changes. The drug content data obtained showed that the content did not differ from the initial drug content by more than 5% [10, 11, 12].

RESULTS AND DISCUSSIONS

FT-IR spectrum of Ofloxacin alone, and in combination with polymers were studied. FT-IR spectrum of ofloxacin and the drug polymer mixture have characteristic bands at 1723cm^{-1} (carbonyl group), 1884cm^{-1} (carbonyl group of quinolone moiety), 2935cm^{-1} (aromatic C-H stretching), and 3275.5cm^{-1} (-OH group of carboxyl moiety) indicating that ofloxacin is not involved in any chemical reaction with the polymer used.

Table 2: Physiochemical characteristics of periodontal films containing Ofloxacin

Films	Thickness uniformity (mm)	Weight uniformity (mg)	Tensile strength (kg)	Folding endurance	Moisture loss (%)	Contents uniformity (%)
F1	0.21 (0.01)	2.22 (0.01)	1.25 (0.02)	50.87 (0.23)	10.23 (0.13)	93.35 (0.21)
F2	0.31 (0.05)	2.12 (0.05)	1.89 (0.05)	113.56 (0.27)	10.13 (0.17)	92.17 (0.36)
F3	0.20 (0.01)	2.12 (0.02)	1.26 (0.05)	108.75 (0.26)	10.32 (0.12)	90.66 (0.18)
F4	0.14 (0.01)	2.11 (0.01)	1.28 (0.03)	103.39 (0.25)	10.51 (0.14)	95.89 (0.19)
F5	0.22 (0.02)	2.22 (0.02)	1.29 (0.03)	107.42 (0.29)	10.28 (0.16)	96.10 (0.22)

In the present study, periodontal films of Ofloxacin were formulated using the polymer matrix of ethyl cellulose and the effect of chitosan, carbapol-934, PVP-K30, HPMC K4M as rate controlling polymers. The prepared films were the translucent and smooth surface with good tensile strength. The procedure developed to prepare the film was reproducible.

The physiochemical evaluation data presented in table2 showed that the thickness of the films ranged from 0.14 to 0.31 mm. The films of all the batches were found to be of uniform weight, ranging from 2.11 to 2.22mg. The tensile strength of all drug loaded films was studied (table 2). The tensile strength of the films ranged from 1.25 to 1.89kg/sq cm. The effective cross linking was observed on addition of chitosan as a co-polymer, which also shows higher tensile strength when compared all other formulation the tensile strength of films were in the order of F2>F5>F4>F3>F1. Folding endurance of the films was > 100 times indicate that the formulation have good film properties but the film containing ethyl cellulose it was found to be 50.87. Content uniformity studies of all the films shows that the drug was uniformly dispersed, and recovery was possible the tune of 90.66 to 96.10for the formulation F1 to F5 (table 3).

Table 3: *Invitro* release profile of Ofloxacin from different films

Time (Days)	% Drug Release				
	F1	F2	F3	F4	F5
0	0.00	0.00	0.00	0.00	0.00
1	41.11	44.73	53.78	49.37	47.12
2	46.33	52.43	56.98	55.26	50.62
3	52.89	63.21	65.46	61.47	56.36
4	58.56	67.31	69.42	65.89	62.36
5	63.01	69.12	74.11	67.67	65.53
6	67.71	72.19	78.88	70.38	68.89
7	69.01	76.92	83.18	74.19	70.45
8	72.05	79.16	88.9	77.33	73.19
9	76.67	88.67	94.19	84.82	79
10	87.64	96.38	98.95	95.8	93.74

Invitro release studies of Ofloxacin was carried out in pH 6.6 phosphate buffer for 10 days which shows that there was an abrupt release observed in first three days and there after the release of drug was found to be controlled (table 3). In-vitro release studies shows the drug release was more sustain in case of film F3 followed by F2>F4>F5>F1 (figure1). The *invitro* release studies showed an initial burst release of the drug by more than 40% and the release was sustained up to 10 days. The order of the drug release was found to be zero order. Furthermore, studies are in progress to evaluate the clinical efficacy, patient acceptability, and compatibility of the designed cast periodontal films for the effective treatment of periodontitis.

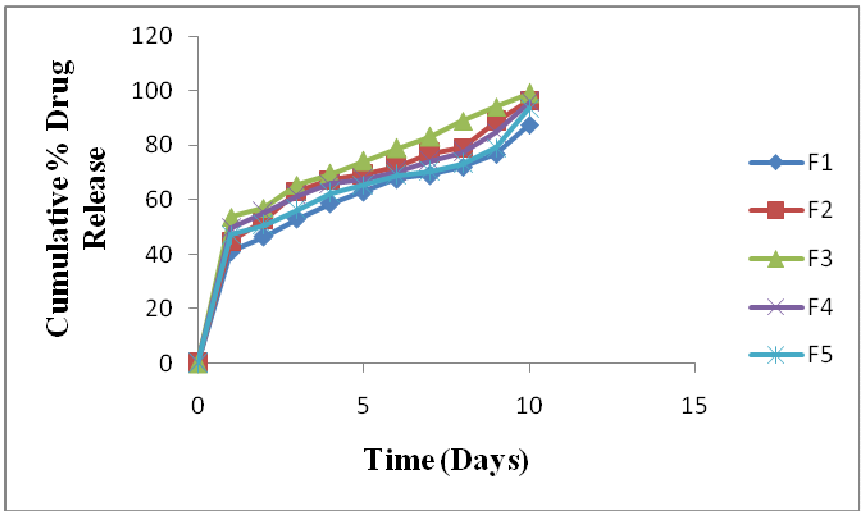

Figure1: *Invitro* drug release profile of ofloxacin from film F1 to F5

The stability studies carried out for a period of 10 weeks showed that there were no significant physical changes. The drug content did not deviate by more than 4% from the initial drug content.

CONCLUSIONS

It can be concluded from the results that ofoxacin based films can be easily prepared for the treatment of periodontitis using different polymers. Carbopol 934 is able to formulate periodontal films for sustained release of drug and provide maximum release within 10 days.

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REFERENCES

[1] A. Steinberg, M. Friedman, Sustained release drug delivery for local treatment of dental diseases, Drug delivery devices: Fundamentals and applications. Editor: Tyles P. Marcel Dekker Inc., New York, **1998**, 32, 492-515.
[2] J.M. Goodson, D. Holborow, R.L. Dunn, P. Hogan, S. J. Dunham, *Periodontol* **1983**, 54, 11, 575-579.
[3] S. Rahman, A. Ahuja, J. Ali, R.K. Khar, *Indian J. Pharm. Sci*, **2003**, 65, 2, 106-112.
[4] M. Verho, V. Malerczyk, E. agrosa, A. Korn, *Curr Med Res Opin*, **1986**, 10, 166-171.
[5] E. Khor, L.Y. Lim, *Biomaterials*, **2003**, 24, 6, 2339-2349.
[6] C. Viney, H. Dureja, *Indian Drugs* **2002**, 39, 4, 191-194.
[7] K. Muthusamy, T.K. Ravi, G. Govindharajan, S. Gopalkrishnan, *Indian J Pharm Edu* **2004**, 38, 3, 138-140.
[8] K.S. Aithal, N. Udupa, B.R. Varma, R. Kurian, *Indian J Dent Res*, **1995**, 6, 82-85.
[9] A. Prakki, R. Cilli, A.U. Da Costa, S.E. Gonçalves, R.F. Mondelli, J.C. Pereira, *J Prosthodont*, **2007**, 16, 172-178.
[10] Y. Venkateshwari, R.B. Jayachandra, D.K. Sampath, N. Mittal, J.K. Pandit, *Indian Drugs*, **1995**, 32, 205-209.
[11] R.C. Mashru, V.B. Sutariya, M.G. Sankalia, P.P. Parikh, *Drug Dev Ind Pharm*, **2005**, 1, 25-34.
[12] A.K. Seth, G.P. Agarwal, T.R. Saini, *Indian Drugs*, **1985,** 23, 45-47.