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Research Article

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Formulation and Evaluation of Biodegradable Films of Levofloxacin for the Management of Periodontitis

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Abstract The present study succeeded in the formulation and evaluation of biodegradable films of levofloxacin for the management of periodontitis. Processing factors such as chitosan and plasticizer concentration have significantly affected the physical characteristics of film and were found within acceptable range. Chitosan concentration has negatively affected drug release and positively affected T90 due to altered matrix density. On the contrary, plasticizer concentration has positively affected the rate of drug release and negatively affected T90 of drug attributed to increased membrane permeability. This study succeeded in the fabrication of levofloxacin biodegradable, mucoadhesive chitosan film which is cheap, less resource-requiring film devices having greater market potential to administer medicament locally into the periodontal pockets for the management of periodontitis.

Keywords Formulation, Evaluation, Biodegradable Films, Levofloxacin, Periodontitis

1. Introduction

Periodontitis is a globally widespread bacterial infectious disease which is characterized by the damage of the periodontal tissues followed by the loss in periodontal ligament and alveolar bone.(1) Periodontal disease is considered as the major cause of tooth loss and other oral problems, and it is also associated with other diseases such as diabetes mellitus, atherosclerotic vascular disease, infective endocarditis, and chronic nephritis.(2)

Levofloxacin, is an antibiotic used to treat a number of bacterial infections like acute bacterial sinusitis, pneumonia, H. pylori (in combination with other medications), urinary tract infections, chronic prostatitis, and some types of gastroenteritis. Along with other antibiotics it may be used to treat tuberculosis, meningitis, or pelvic inflammatory disease.

2. Materials and Methods

Table 1: Formulation Levofloxacin Biodegradable Chitosan Films

Formulation	Chitosan (g)	Propylene glycol (g)	Glutaraldehyde (g)	Levofloxacin (g)
F-1	0.6	0.12	0.02	0.1
F-2	0.6	0.16	0.02	0.1
F-3	0.6	0.20	0.02	0.1
F-4	0.6	0.24	0.02	0.1
F-5	0.7	0.12	0.02	0.1
F-6	0.7	0.16	0.02	0.1
F-7	0.7	0.20	0.02	0.1

F-8	0.7	0.24	0.02	0.1
F-9	0.8	0.12	0.02	0.1
F-10	0.8	0.16	0.02	0.1
F-11	0.8	0.20	0.02	0.1
F-12	0.8	0.24	0.02	0.1

Calibration Curve for Levofloxacin

Preparation of standard solutions

Preparation of standard solutions

The levofloxacin reference standard solution (200.0 μg mL^{-1}) was prepared by accurately weighing 20.0 mg of levofloxacin reference in a 100.0 mL volumetric flask. The volume was completed with methanol. This flask was sonicated for 25 min. The above solution was diluted in a 100 mL volumetric flask with methnol to obtain a final solution containing 10.0 μg mL^{-1} of levofloxacin. [123]

Determination of maximum absorption λ_{max}

From the standard solution (200.0 μg mL) approximately 3.0 mL was taken and scanned from 200 to 400 nm with HP 8453 UV-Visible spectrophotometer. The methanol was used as blank. Levofloxacin presented maximum absorption at 298 nm. [123]

Calibration curve of Levofloxacin

The calibration curve was constructed by analyzing 6 different concentrations of standard solution, prepared on the same day. The range of solutions varied from 3.0 to 8.0 μg mL^{-1}. [123]

Table 2: Formulation Levofloxacin Biodegradable Chitosan Films

Formulation	Chitosan (g)	Propylene glycol (g)	Glutaraldehyde (g)	Levofloxacin (g)
F-1	0.6	0.12	0.02	0.1
F-2	0.6	0.16	0.02	0.1
F-3	0.6	0.20	0.02	0.1
F-4	0.6	0.24	0.02	0.1
F-5	0.7	0.12	0.02	0.1
F-6	0.7	0.16	0.02	0.1
F-7	0.7	0.20	0.02	0.1
F-8	0.7	0.24	0.02	0.1
F-9	0.8	0.12	0.02	0.1
F-10	0.8	0.16	0.02	0.1
F-11	0.8	0.20	0.02	0.1
F-12	0.8	0.24	0.02	0.1

Fabrication of levofloxacinbiodegradable chitosan films

Periodontal films were prepared by solvent casting method [124]. The films were prepared as per formula given in Table 2.

Accurately weighed quantity of Chitosan was dissolved in 40 ml of 0.5% acetic acid solution and stirred for 24 h for complete solubilization. The weighed amount of Levofloxacin was incorporated in the polymer solution and stirred for 6 h.

A measured quantity of propylene glycol (as a plasticizer) was added. After deaerating under vacuum for 6 h, the solution was poured on levelled glass mould having size of 5 × 4 × 1.2 cm and placed in an oven maintained at 50°C (Tempo Industrial Corporation, Mumbai). The system was left undisturbed for 24 h to allow complete evaporation.

The formed films were completely removed from the glass mould and punched out in desired size, wrapped in aluminium foil and stored in desiccators until further use.

For crosslinking, the films were dipped into the solution of crosslinking agent glutaraldehyde for 24 h and then removed and dried. Placebo films without drug containing only CS and plasticizer were prepared as control.

3. Results and Discussion

Table 3: Characterization of Levofloxacin

S. No	Test	Specification	Results
1	Description	White or yellow light crystalline powder	A white crystalline powder
2	Loss on drying	≤3 W/W	2.17% W/W
3	Solubility	Freely soluble in glacial acetic acid, chloroform; sparingly soluble in water	Complies
4	Melting point	225 °C - 227 °C	224 °C - 226 °C

Table 4: IR Spectral Interpretation of Levofloxacin

S.No	Functional group	Observed peak
1	>C=O of lactum ring	1723 cm^{-1}
2	>C=O of quinolone moiety	1884 cm^{-1}
3	Aromatic C-H stretching	2935 cm^{-1}
4	O-H group of carboxyl moiety	3275.5 cm^{-1}

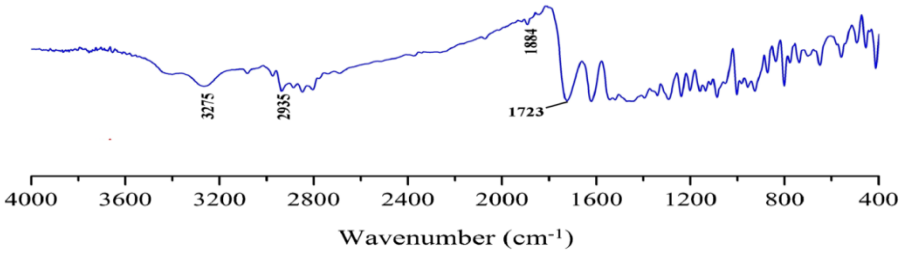

Figure 1: FTIR of Levofloxacin

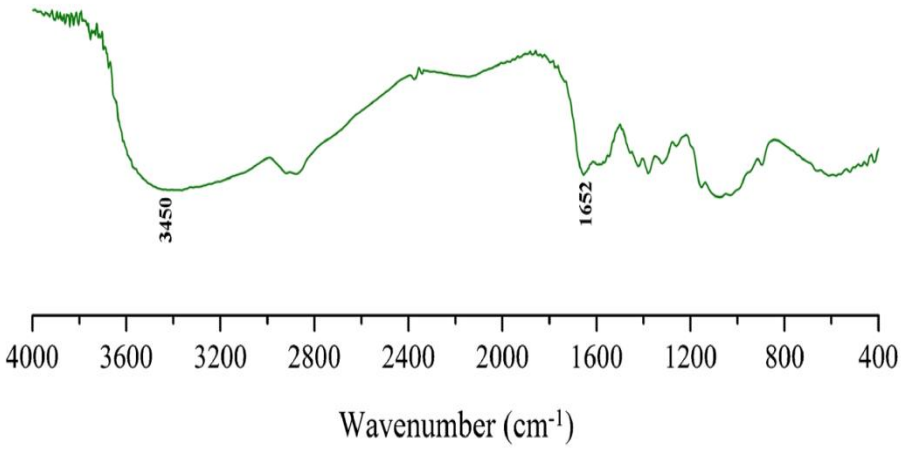

Figure 2: FTIR of Chitosan

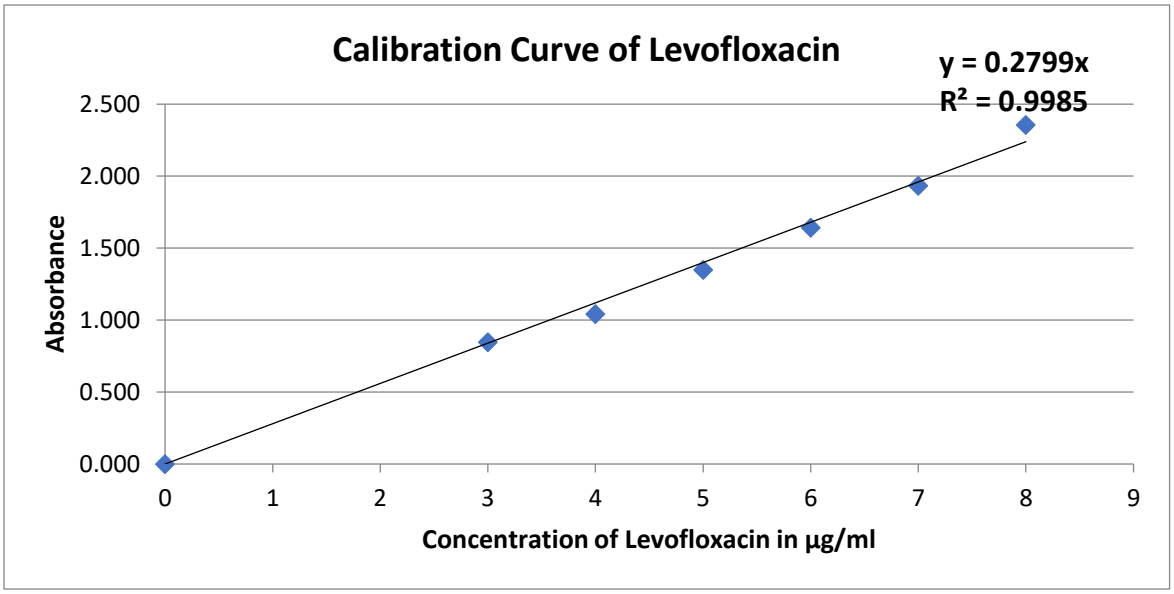

Figure 3: Standard Curve of Levofloxacin

The calibration curve showed linearity over a concentration range from 3.0 to 8.0 µg mL^{-1}.

Evaluation of Levofloxacin Biodegradable Films

Thickness and Weight Variation

The thickness and weight variation of films are directly associated with the uniformity and accuracy of dosing. The average thickness of all prepared periodontal films F-1 to F-12 ranged from 0.29 ± 0.05 mm to 0.35 ± 0.06 mm (Table 5).Weight variation values varied between 5.96 ± 0.07 mg and 6.31 ± 0.08mg (n = 3).

Table 5: Thickness and Weight Variation Levofloxacin Biodegradable Chitosan Films

Formulation	Thickness[a] (mm ± SD)	Weight variation[a] (mg ± SD)
F-1	0.29 ± 0.05	6.26 ± 0.05
F-2	0.32 ± 0.08	6.14 ± 0.06
F-3	0.35 ± 0.06	6.31 ± 0.08
F-4	0.32 ± 0.06	5.96 ± 0.07
F-5	0.30 ± 0.07	6.40 ± 0.08
F-6	0.32 ± 0.08	6.20 ± 0.06
F-7	0.32 ± 0.05	6.28 ± 0.02
F-8	0.31 ± 0.05	6.26 ± 0.04
F-9	0.32 ± 0.03	6.20 ± 0.01
F-10	0.33 ± 0.04	6.27 ± 0.02
F-11	0.34 ± 0.02	6.13 ± 0.04
F-12	0.32 ± 0.02	6.23 ± 0.06

SD (standard deviation)

[a] Result is presented as mean ± SD, n = 3

Table 6: Uniformity of Drug Content of Levofloxacin Biodegradable Chitosan Films

Formulation	Total drug content[a] (%)
F-1	95.70 ± 2.67
F-2	96.24 ± 2.27
F-3	95.16 ± 2.43
F-4	94.19 ± 2.96
F-5	94.50 ± 2.12
F-6	95.20 ± 3.07
F-7	93.70 ± 2.32
F-8	94.00 ± 2.14
F-9	97.40 ± 2.46
F-10	96.50 ± 2.49
F-11	98.72 ± 2.19
F-12	95.80 ± 2.27

SD (standard deviation)

[a] Result is presented as mean ± SD, n = 3

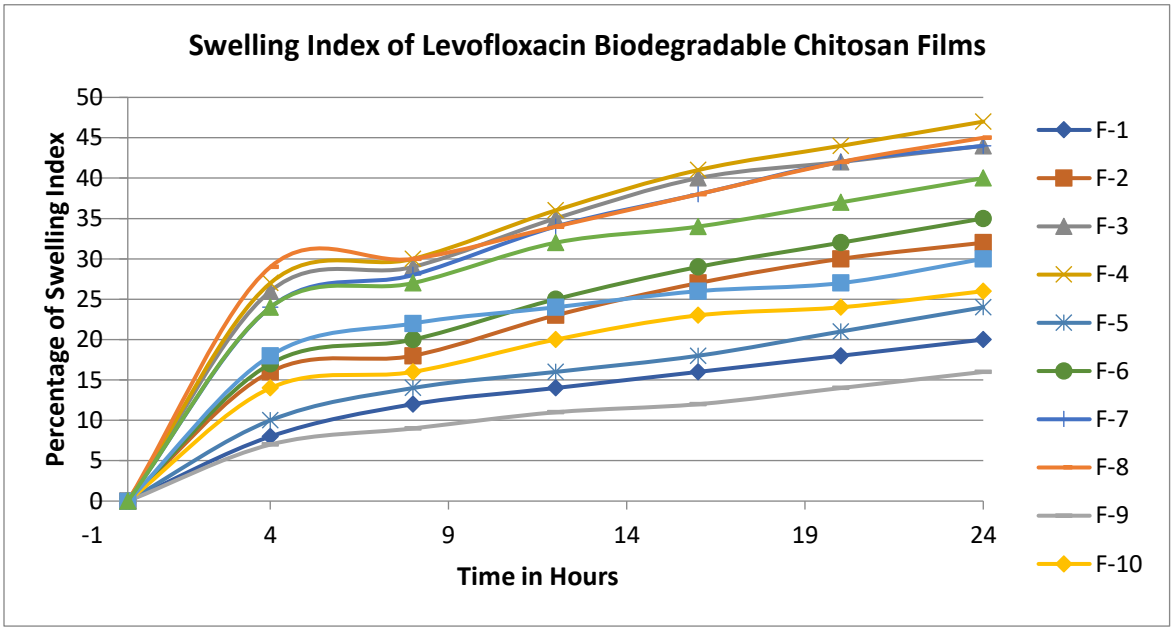

Figure 4: Swelling Index of Levofloxacin Biodegradable Chitosan Films

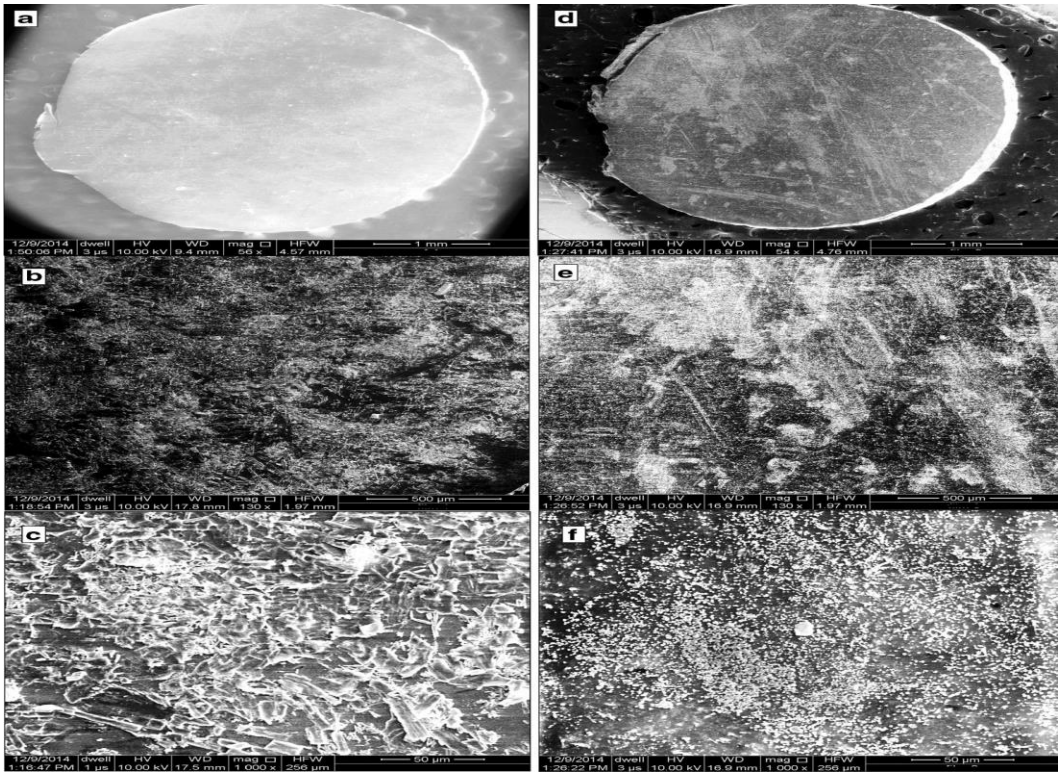

Figure 5: Scanning electron microscopic images showing surface morphology of a–c placebo films and d–f drug-loaded films at different resolutions

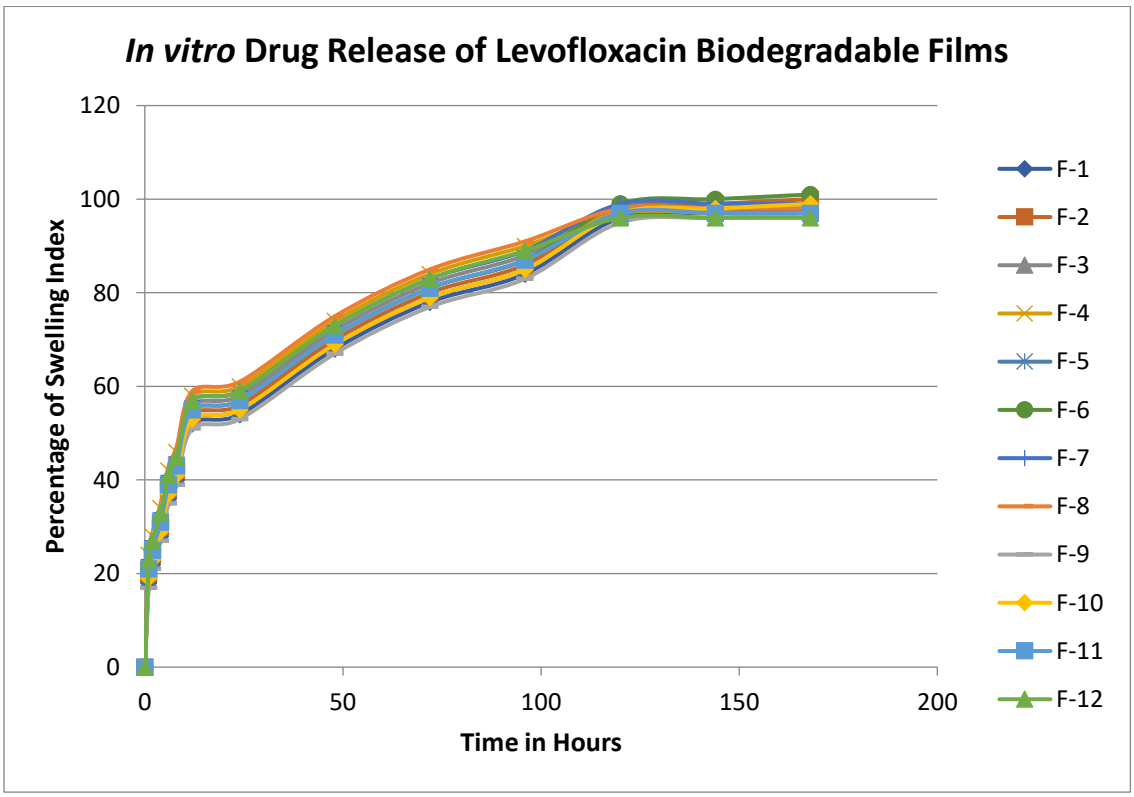

Figure 6: In Vitro Drug Release Studies In vitro Drug Release of Levofloxacin Biodegradable Chitosan Films

Table 7: Kinetic Modelling for Optimized Batch F-11

Batch code	r^2 value			Korsemeyer-Peppas model	
	Zero order	First order	Higuchi model	r^2 value	n value
F-11	0.70	0.83	0.88	0.97	0.624

***In Vitro* Antibacterial Activity of Periodontal Films**

The antibacterial activity of the films was estimated by measuring zone of inhibition against *S. aureus* (ATCC25323) and *E. coli* (ATCC25922). Zone of inhibition was calculated for optimized polymeric film (batch F-11) containing Levofloxacin, placebo film at every day until 5 days (Fig.17).

Levofloxacin films exhibited good zone of inhibition against *S. aureus* with value of 40.1 ± 0.52 mm whereas lesser activity for *E. coli* having zone of inhibition of 36.53 ± 1.55 mm on the first day of the assay and then it slowly decreased to 8.5 ± 0.40 mm and 7.24 ± 0.48 mm after 5 days of incubation (Fig. 17).

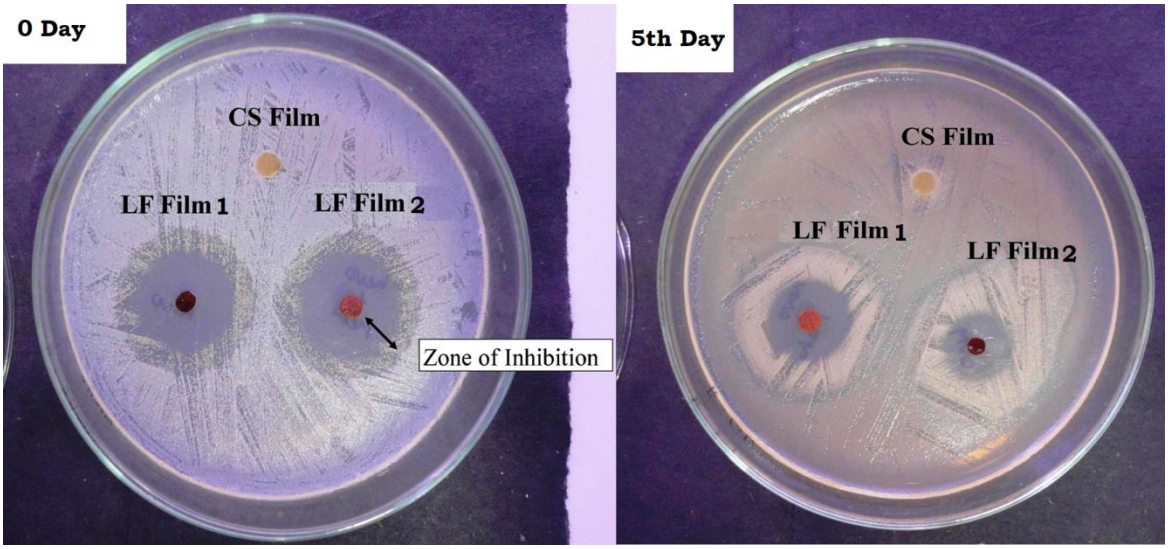

Figure 7: Anti-Bacterial Activity of Levofloxacin Film

4. Conclusion

The present study succeeded in the fabrication of biodegradable, mucoadhesive film of chitosan by solvent casting. Processing factors such as chitosan and plasticizer concentration have significantly affected the physical characteristics of film and were found within acceptable range.

Chitosan concentration has negatively affected drug release and positively affected T_{90} due to altered matrix density. On the contrary, plasticizer concentration has positively affected the rate of drug release and negatively affected T_{90} of drug attributed to increased membrane permeability.

This study succeeded in the fabrication of levofloxacin biodegradable, mucoadhesive chitosan film which is cheap, less resource-requiring film devices having greater market potential to administer medicament locally into the periodontal pockets for the management of periodontitis.

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