Preparation and Evaluation of Ornidazole Levofoxacin Periodontal Drug Delivery Systems

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Abstract

Periodontitis is a plaque-induced chronic inflammatory condition that affects the periodontal ligaments and alveolar bones and may lead to the loss of tooth-supporting structures. It is an irreversible disease and of high prevalence and mortality, that is why it is of great importance to develop new and effective formulations to control and treat it.

Several types of anaerobic and Gram-negative bacteria such as Porphyromonas gingivalis, Prevotella intermedia and Filifactor alocis can cause this disease to develop. For that reason, most of the treatment approaches involved the use of antimicrobial agents whether administered systemically by oral and parenteral routes or locally using films, fibers or gels.

In this study, levofoxacin (a broad-spectrum antimicrobial agent) and ornidazole (an antimicrobial agent that acts against Gram negative anaerobic pathogens) were incorporated (0.5% w/w of each) with different concentrations of poloxamer 407 (a thermo reversible, biocompatible and biodegradable polymer) alone and in combination with sodium alginate or hydroxypropyl methylcellulose (HPMC). Seven different in situ gel formulations (S1(20P), S2(22P), S3(24P), S4(26P), S5(28P), S6(16P-2H) and S7(16P-1S)) were prepared after performing compatibility studies using Infra-Red (IR), Ultra Violet (UV), Differential Scanning Calorimetry (DSC) and High Performance Liquid Chromatography (HPLC). Neither drug-drug nor drug-polymer interactions were observed during the study.

The evaluation of the prepared drug delivery systems revealed that the gelation temperature of all seven formulations ranged between 12-37°C while the gel melting temperature was between 7-30°C, and that all prepared systems except S5(28P) were syringeable through a 22 gauge needle at both 5 and 10°C. On the other hand, rheological studies revealed that all the prepared periodontal gels except S4(26P) and S5(28P) present a non-newtonian pseudoplastic behavior at all three temperatures (5, 15 and 37°C) and that viscosities of the formulations at temperature (37°C) were around 0.1 Pa.s and a shear stress of more than 70 Pa in all formulations except S4(26P) and S3(28P). The bioadhesive forces of the prepared in situ gels were between ~955 and ~1995 Dyna/cm². In vitro cumulative release study showed that all formulations (except S5(28P)) were able to release more than 2% of the levofoxacin and ornidazole (~10ug/ml) within half an hour and a sustained drug release pattern was observed up to 144 hours from most of the formulations. In addition, the presence of HPMC and Sodium alginate in S6(16P-2H) and S7(16P-1S) respectively did alter the release pattern of the drugs to a certain extent, while ex-vivo cumulative drug permeation showed that the active ingredients in the gels were permeable through biological membrane. The microbiological study showed that all seven systems exhibited a zone of inhibition against Escherichia coli, Staphylococcus aureus, Klebsiella pneumoniae and Bacillus subtilis bacteria. All formulations were chemically and physically stable up to 60 days at 25±2°C temperature (60% RH) and 5±3°C except for S5(28P).

The formulations S2(22P) and S6(16P-2H) were found to be comparatively better than the other formulations in the over all qualities, while S5(28P) failed to reach more than one criteria.