ABSTRACT

DEVELOPMENT AND EVALUATION OF _IN SITU_ GELLING SYSTEM FOR THE TREATMENT OF PERIODONTITIS

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Background: Local drug delivery systems have been investigated in the release of antimicrobials since decades to treat periodontal pockets in periodontal diseases. _In situ_ gelling formulations allow easy application to the target area. Gelation is induced by physiological stimuli at the site of application where the formula attains semisolid properties and exerts sustained drug release. **Aim:** In the present research work, an attempt has made to formulate _in situ_ gel of for the effective management of periodontitis with local delivery into the periodontal pockets for a controlled release.

**Materials and Methods:** _In situ_ gelling formulations containing 1% tinidazole prepared for local application into the periodontal pockets using various concentrations of carbopol 934, gellan gum, and poloxamer 407. The formulated periodontal _in situ_ gel was evaluated for clarity, _in vitro_ gelling capacity, gelation time in GCF fluid, pH, viscosity, gelation temperature, % drug content, syringeability, effect of sterilization, _In vitro_ drug release, and sterility testing. $3^2$ full factorial design was applied for optimization. Selected dependent variables are concentration of gellan gum ($X_1$) and concentration of poloxamer 407 ($X_2$). Selected independent variables are viscosity ($Y_1$), drug release up to 1 hr ($Y_2$), and drug release up to 24 hr. ($Y_3$). All the prepared
formulations were evaluated for clarity, *in vitro* gelling capacity, gelation time, pH, viscosity, gelation temperature, % drug content, syringeability, and *in vitro* drug release. By compatibility study drug was found to be compatible with formulation excipients. Optimized batch was evaluated for effect of sterilization, sterility testing, kinetic release study, mucoadhesive strength, *in vitro* antimicrobial activity, clinical study, and stability study was carried out for 6 months. **Results and discussion:** From preliminary trials, gellan gum as an ion activated gelling agent and poloxamer 407 as a temperature activated gelling agent were used in combination to prepared ion sensitive and temperature sensitive periodontal *in situ* gel. Based on maximum desirability and cost effectiveness formulation containing 1.32% w/v of gellan gum and 10% w/v of poloxamer 407 was consider as an optimized batch. In this study, the release profile depends on the concentration of gellan gum and poloxamer 407. The selected formulation showed sustained release for the period of 24 hr thus showing increased residence and contact time. Sterility testing was carried out on an optimized formulation and was found to be sterile. The kinetics release study of optimized formulation indicated non-Fickian behavior. Mucoadhesive force of optimized formulation was found to be 0.3136 N which indicated good adhesion. The *in vitro* antibacterial activity studies for gel revealed that the drug released exceeded the MIC against *Staphylococcus aureus* MTCC 11949 and *E.coli* MTCC 10312 than the pure drug solution. Clinical evaluation of *in situ* gel containing showed significant improvement in chronic periodontitis patients, manifested by decrease in pocket depth, gingival index, bleeding index, and plaque index. Stability studies of optimized formulation indicated that the formulation was stable up to 6 months. **Conclusion:** The developed tinidazole *in situ* gel system is a novel approach for the treatment of chronic periodontitis since it reduces the dose and side effects by passes the usual surgical procedures and improves patient compliance.