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Factorial design of injectable chlorhexidine *in situ* gelling system for the treatment of periodontitis

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Periodontitis is one of the most widespread bacterial infectious oral diseases that affects a significant percentage of the population worldwide. Different bacterial strains are responsible for the chronic inflammation and subgingival plaque that could be effectively treated with prolonged exposure to therapeutic levels of antibiotics and antiseptics in the periodontal pockets.

Chlorhexidine (CHX) loaded *in situ* gelling system were prepared in a two-compartment system for long-lasting antiseptic effect in the periodontal cavities where one compartment was loaded with sodium alginate solution while other was filled with CHX and calcium chloride solution. At the time of administration, the mixing of two solutions resulted in gelation. For optimization, two 3^3 full factorial designs were applied where initially the effects of concentration of gelling agent, crosslinker, and pH of the system on the dependent variables were investigated. Afterwards, the effect of gelling agent, drug content, and pH of the system were correlated with the gel strength and water loss through another factorial design. Optimized formulations were tested for mucoadhesion, *in vitro* drug release, and microbiological investigation.

Based on the results of the two factorial designs, mucoadhesiveness, antimicrobial investigation, and drug release pattern, a 4 % alginate composition can be considered optimal. Overall, the optimized *in situ* periodontal gel was found to be effective with prolonged retention time and antimicrobial effects.

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