Ibuprofen Nanoemulsion *In Situ* Gel for Mucosal Adhesion in Periodontitis

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Abstract

Periodontitis is an inflammatory response to subgingival pathogenic bacteria which results in progressive destruction of the gingiva, periodontal ligament, and the supporting alveolar bone. The aim of Ibuprofen, a non-steroidal anti-inflammatory drug, is commonly used in the systemic and local treatment of periodontitis. This work was to develop ibuprofen nanogels for local periodontal pockets application. Oil phase, surfactant, and cosurfactant, used in the preparation of ibuprofen nanoemulsion, were chosen based on the solubility studies. The optimized nanoemulsion system was used for the preparation of ibuprofen nanogels. Different concentrations of Pluronic® F127 and ibuprofen nanoemulsions formulations of 1: 1 ratio were initially developed and tested for their flow behavior and sol-gel transition temperatures ($T_{sol \rightarrow gel}$) using the tube inversion method Based on these studies, constant concentration of P127 solution (11.1% *w/v*) and different concentrations of ibuprofen nanoemulsion were used to prepare ibuprofen nanogels Ibuprofen nanogels were characterized in terms of their flow behavior, $T_{sol \rightarrow gel}$ and rheological properties at 25°C and 37°C using a controlled stress rheometer. The release of ibuprofen from nanogels was studied

in vitro using Franz diffusion cells. Stability studies were performed to investigate the rheological properties and $T_{sol \rightarrow gel}$ of nanogels as a function of time. Transition behavior studies demonstrated that nanogels are thermo sensitive systems, being liquid at room temperature and converted to gel when their temperatures are elevated to reach the periodontium temperature of 34-37°C. Ibuprofen nanogels exhibited viscoelastic properties with elastic property dominated viscous property (G'> G''). Results showed that $T_{sol \rightarrow gel}$, viscosity, and viscoelastic properties of ibuprofen nanogels were dependent on the concentration of nanoemulsion, where $T_{sol \rightarrow gel}$ decreased with increasing nanoemulsion concentration, whereas, viscosity and viscoelastic properties increased with increasing nanoemulsion concentration. Stability studies demonstrated that $T_{sol \rightarrow gel}$ increased whereas viscosity and viscoelastic properties decreased after one month. Owing to the rigid structure of nanogels, the release of ibuprofen from nanogels showed a controlled-release pattern.