Nanocomposite Gels for Controlled Topical Delivery of Simvastatin

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Abstract

In this study, the lipophilic drug is solubilized using PF127-Chol micelles and then the solubilized drug was incorporated in to chitosan/HPMC gel in order to use as a wound dressing.

Introduction: Simvastatin (Sim) is a HMG-COA reductase inhibitor, and is used conventionally for cholesterol reduction but recent studies demonstrated the potential of this agent for diverse pathologic conditions such as wound healing due to its antioxidant, anti-inflammatory, and antibacterial properties. However, the systemic bioavailability of Sim is very low (approximately 5%). Moreover, the systemic administration of Sim can cause several adverse effects such as myopathy and liver problems. Therefore, topical application of Sim can increase the accessibility of drug in wound area at lower systemic level and decrease the possible incidence of side effects.

Methods and Results: Polymeric micelles containing Sim were prepared by the thin film hydration method and optimized using irregular full factorial design. The mean diameter, PDI, and zeta potential of the prepared drug loaded micelles were determined by dynamic laser scattering method using Malvern nanosizer. The gels were prepared using chitosan or/and HPMC at 3% (W/W). Bioadhesion was determined using a tensile strength machine. The *in vitro* release of Sim from different gel formulations was studied using dialysis method. Statistical analysis showed that solvent type had the most impact on the amount of drug loading and zeta potential. The optimized formulation suggested by desirability of 93.5% was prepared using 1 mg of Sim, 10 mg of copolymer, dichloromethane as the organic solvent, hydration time of 45 min, and hydration temperature of 25 ^{o}C. The release of the drug from nanomicelles was found to be biphasic and showed a rapid release in the first stage followed by a sustained release for 96 hrs. The gel-contained nanomicelles exhibited pseudo-plastic flow and more sustained drug release profile compared to nanomicelles.

Conclusions: The results indicate the obtained composite gel has great potential for topical applications at the site of wounds.

Key words: Wound, Simvastatin, Pluronic, Nanomicelles

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