

Chitosan-Nanoparticles Loaded with Insulin in Buccal Films: Preparation and Characterization

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Extended Abstract

The main objective of this work is to prepare Chitosan nanoparticles loaded with insulin (IN-CS-NPs) and to disperse them in films that will be applied buccally. Buccal route has many advantages including: bypass the liver metabolism, rapid drug absorption, high drug stability, self-administration of the dosage form and low price [1, 2]. In this work, the NPs were prepared using ionic gelation method and TPP as a crosslinker [3,4]. The physicochemical properties in terms of size, polydispersity index, entrapment efficacy and loading capacity using zeta sizer and HPLC were measured. The morphology of the nanoparticles was investigated using SEM. Buccal films were prepared and characterized, and the best film was used to disperse the IN-CS-NPs. The films physicochemical and mechanical properties such as thickness, weight, folding endurance and mucoadhesiveness were investigated before loading the NPs in the films. After choosing the components that is to be used in the films and their concentrations, a film loaded with the NPs was prepared and its physicochemical and mechanical properties were measured. Further, the stability of insulin and its release from the NPs, as well as, the loaded films were investigated. The nanoparticles size, polydispersity, zeta potential, entrapment efficacy and loading capacity were 325.07 ± 1.32 nm, 0.38 ± 0.03 , and 8.41 ± 0.80 mV, 73.27% and 18.03%, respectively. The NPs showed a bead-like structure under SEM. The insulin was stable after loading in the NPs and its 3D structure was preserved when it was compared to reference insulin. The insulin release from the NPs was controlled over 6 hrs. The weight of the plain films ranged between 24.7 ± 1.7 mg and 2.1 ± 0 mg, and their thickness ranged between 0.32 ± 0.04 mm and 0.08 ± 0.01 mm depending on the materials used and their concentrations. Hydroxy propyl methyl cellulose (HPMC) and glycerine were found to be essential to prepare strong and flexible films. In contrast, Eudragit RL 100 was found to give the films a milky colour and did not enhance films physical properties. Therefore, Eudragit RL 100 was excluded from the final formula. IN-CS-NPs were dispersed in films that composed of 30% HPMC, 10% sodium carboxy methyl cellulose, 10% carboxypolymers 934 and 50% glycerine. The weight and thickness of the film loaded with the IN-CS-NPs were 23.0 ± 3.0 mg and 0.32 ± 0.04 mm. The folding endurance of the loaded film was more than 200, which indicates high flexibility. The mucoadhesiveness of the loaded films was 2.3 ± 0.2 N, which was acceptable in comparison to the other unloaded films. The drug was stable in the films and the drug release was slower when the NPs were suspended in the film. For example, the cumulative drug release from the NPs was $60 \mu\text{g/ml}$ after 6 hrs, while it reached $40 \mu\text{g/ml}$ from the NPs loaded in the films. At the end, the films loaded with IN-CS-NPs were studied in vivo and compared to the subcutaneously commercially available insulin in the market. The films prepared in this work were found to decrease glucose level significantly in diabetic rats.

References

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