PROTEIN NANOPARTICLES FOR ORAL INSULIN DELIVERY

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Abstract - Diabetes mellitus (DM) is a chronic disease that affects over 537 million people worldwide, requiring effective long-term management to prevent serious complications. While insulin is a cornerstone in DM treatment, its oral administration has been limited by rapid degradation in the gastrointestinal (GI) tract, necessitating alternative delivery methods, such as subcutaneous route. This study presents the development of protein-based nanoparticles designed to encapsulate insulin, protecting it from GI degradation and enhancing its oral bioavailability. The nanoparticles were produced using the antisolvent precipitation method, and exhibited favorable characteristics, including an average diameter of 215 ± 11 nm, a polydispersity index of 0.069 ± 0.027, and a positive zeta potential of +41.0 ± 3.6 mV, with an encapsulation efficiency of 35 ± 6%. Microscopy revealed spherical nanoparticles with uniform distribution.

Comprehensive drug-matrix interaction analyses—X-ray diffraction, infrared spectroscopy, thermogravimetry, and differential scanning calorimetry—confirmed that the encapsulation process preserved the chemical integrity of insulin. Stability assessments showed that the nanoparticles remained stable for 90 days under refrigeration and for 15 days at room temperature. Importantly, the nanoparticles demonstrated protection against pH variations and enzymatic degradation in simulated GI fluids. In vitro release studies indicated that 87% of insulin was released over 48 hours, following Korsmeyer-Peppas kinetics, with diffusion as the primary release mechanism.

In vitro mucoadhesion tests showed strong adhesion to the mucus layer, with an increase in nanoparticle diameter and a shift from positive to negative surface charge upon interaction with mucin, suggesting enhanced residence time in the GI tract. Pharmacokinetic studies in rats revealed that orally administered insulin-loaded nanoparticles achieved a pharmacokinetic profile comparable to subcutaneously administered insulin, with similar peak plasma concentrations (Cmax) ($p>0.05$).

Efficacy tests in streptozotocin-induced diabetic rats showed that insulin-loaded nanoparticles administered orally significantly reduced blood glucose levels and stabilized biochemical markers and oxidative stress parameters. These effects were comparable to those achieved with subcutaneous insulin administration ($p>0.05$), highlighting the potential of this nanoparticle system to provide effective glycemic control.

In conclusion, this protein-based nanostructured system offers a promising platform for oral insulin delivery, providing protection against GI degradation, enhanced bioavailability, and sustained efficacy. This innovative approach could transform insulin therapy, improving patient compliance and quality of life in the management of diabetes mellitus.

Keywords - Diabetes; Nanoparticles; Insulin.

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