Enhancing oral insulin delivery via ionic liquids, protein nanogels and lipid nanoparticles: formulation, cytotoxicity, nanostructure, stability, and permeability analysis

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Oral delivery of therapeutic peptides like insulin offers superior patient compliance, convenience, and cost-effectiveness. However, significant biological barriers within the gastrointestinal (GI) tract—such as extreme pH, enzymatic degradation, and limited permeability—severely reduce bioavailability, hindering the success of commercial oral insulin formulations and FDA-approved clinical trials. Recently, ionic liquid-based nanomedicines and lipid-based nanoparticles have emerged as promising candidates for oral drug delivery due to their high biocompatibility and bioadhesivity[1,2].

This study explores innovative approaches to address these challenges by utilizing ionic liquid-based nanomedicines, lipid-based nanoparticles, and protein nanogels. High-throughput methods, including Chemspeed synthesis and small-angle X-ray scattering, were employed to prepare and characterize the structural stability of insulin, ionic liquid nanostructures, protein nanogels, and lipid liquid crystalline mesophases. Dynamic light scattering and zeta potential analyses were performed on protein nanogels, lipid nanoparticles, and micelles, while cytotoxicity and cellular uptake were evaluated in Caco-2 cells via confocal microscopy.

The results indicate that ionic liquids, specifically choline decanoate and choline geranate, influence micelle formation, pH, cytotoxicity, and permeability, achieving effects comparable to commercial permeation enhancers in Caco-2 cells. These ionic liquids and salts enhance transcellular permeability, while monoolein-based lipid nanoparticles maintain stability under acidic conditions, though higher cytotoxicity is observed. Caco-2 monolayer assays further reveal increased permeability for lipid nanoparticles.

This study underscores the synergistic potential of ionic liquids, protein nanogels, and lipid nanoparticles in advancing oral peptide therapeutics, paving the way for future clinical translation.

REFERENCES

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