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Insulin nanoparticulatedelivery systemcomposed of quaternized aromatic derivatives of chitosan

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Background and Aims: In this study, in-vitro characterization of insulin nanoparticles composed of three aromatic derivatives of chitosan: Methylated N-(4,N,N-dimethyl amino benzyl) chitosan, Methylated N-(4-pyridinyl) chitosan and Methylated N- (benzyl) chitosan have been investigated.
Methods: The derivatives were synthesized by Schiff base reaction. Nanoparticles were prepared by Poly-Electrolyte Complexation (PEC) and their size, zeta potential and entrapment efficiency were determined. D-Optimal response surface methodology was used for optimization of nanoparticles. The independent factors were considered as pH of polymer solution, concentration ratio of polymer to insulin as quantitative factors and also polymer type as categorical factors. Dependent variables include size, zeta potential, PdI and Entrapment Efficiency (EE %). Morphology of optimized nanoparticles was studied by Atomic Force Microscopy (AFM) and Transmission Electron Microscopy (TEM). Invitro insulin release from nanoparticles were studied in Simulated Intestinal Fluid (SIF) and Phosphate Buffer Saline (PBS) media. Cytotoxic effects of nanoparticles were investigated on Caco-2 cells by MTT.
Results: The size of particles were found to be 346, 318 and 289 nm; zeta potentials were 28.5, 27.7 and 22.2 mV and calculated EE% were 70.3%, 84.5% and 69.2% for (amino-benzyl), (pyridinyl) and (benzyl) chitosan nanoparticles, respectively. The in-vitro release profile has shown low burst release of insulin from aromatic nanoparticles. Higher burst release was reported in PBS compare to SIF. Cytotoxicity studies on Caco-2 cell culture have shown no significant cell cytotoxicity for prepared nanoparticles.
Conclusions: This nanoparticulate system seems to be a promising delivery system for oral insulin delivery.

Keywords: Methylated N-(4,N,N-dimethyl amino benzyl) chitosan; Methylated N-(4-pyridinyl) chitosan; Methylated N- (benzyl) chitosan; Insulin; Nanoparticle; Oral drug delivery