"Formulation and Evaluation of Pectin-Chitosan Composite Particles of an Anticancer Drug for Colon Targeting."

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Abstract

Pectin solution gelled with chitosan and calcium ion produced composite particles with a double layer structure, which may contribute to the undesirable premature and localized release of the drug. The aim of present study was to formulate pectin-chitosan composite particles of 5-fluorouracil and selection of most satisfactory formulation by *in vitro* evaluation. These multiparticulate systems showing simultaneously specific biodegradability and pH dependent drug release were prepared based on chitosan, pectin, and calcium ions. Fourier transform infrared spectroscopic (FTIR) studies and Differential scanning calorimeter (DSC) studies were performed to study drug and excipients compatibility. The pectin-chitosan composite particles were prepared by complex coacervation from chitosan and pectin dispersions. Box Behnken Design was used to optimize three critical formulation parameters; concentration of chitosan, pectin and calcium chloride. The pectin-chitosan composite particles were characterized for particle size, % yield, swelling ratio and percent drug entrapment. Scanning electron microscopy was performed to study morphological behavior. *In vitro* drug dissolution was performed using dissolution apparatus (USP type I). Cytotoxicity study was performed on HCT-15 colon carcinoma cell line using MTT assay. Stability study was performed at room temperature and accelerated condition. FTIR and DSC study

confirmed that the drug and excipients was found to be compatible. Particle size, %yield, swelling ratio and percent drug entrapment of optimized batch containing chitosan 0.1%w/w, pectin 10%w/w and calcium chloride 11%w/w were found to be 2.00±0,007mm, 87.57±0.05%, 357±2.45% and 96.77±0.90% respectively. SEM images of pectin-chitosan composite particles confirmed spherical shape and complexation. *In vitro* drug dissolution study confirmed that negligible drug was released from the chitosan-pectin composite particles in pH 1.2 HCl. Pectin degrading enzyme increased the protein release from 31.15±0.005 to 92.84±0.007% within 12 h in phosphate buffer saline pH 7.4 . Cell line toxicity study had confirmed the better anticancer activity of pectin-chitosan composite particles against human colorectal adenocarcinoma cell line HCT-15. Hence, the developed 5-fluorouracil containing pectin-chitosan composite particles were effectively target the colon and shows better anticancer activity in colon cancer. These characteristics of the chitosan-pectin composite particles would be promising tool for targeting anticancer drugs to the colon.