عنوان مقاله:

(Effect of quaternization alkylated chitosan chloride on colonal absorption enhancement (ex-vivo and in-vivo studies

محل انتشار:

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خلاصه مقاله:

The intestinal absorption of peptides and proteins has a very low bioavailability due to extensive hydrolysis by the proteolytic enzymes and poor membrane permeability of gastro intestinal tract (GIT). Colonic drug delivery for either local or systemic effects has been the subject of much research over the last decade. Recent researches have determined that polymeric compounds are useful carriers for high molecular weight drugs. Biodegradable polymers such as chitosan have been used extensievly in medical fields. Chitosan with mucoadhesive properties and ability to interact with cell membrane is able to open the paracellular permeation of hydrophilic macromolecules. Chitosan exhibits poor solubility at pH values above 6.0 that prevent enhancing effects at sites of absorption of drugs. In the present work , triethyl chitosan (TEC) and N-diethyl methyl chitosan (DEMC) were prepared based on a modified twostep process via a 22 factorial design to optimize the preparative conditions. TEC and DEMC polymers with different degree of quaternization for pharmacological and pharmaceutical experiments were achieved. The reaction was optimized using different amounts of reactants. pH-metric titration and infrared methods predetermined the degree of deacetylation of the starting chitosan. TEC and DEMC were characterized using FTIR and 1H-NMR spectroscopies. Based on NMR calculation, high degree of quaternization was achieved through the optimized one and two-step procedures. The antimicrobial activities of chitosan and DEMC against Escherchia coli were compared by calculation of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC). Our data indicates that although the antimicrobial activity of DEMC is higher than that of chitosan in acetic acid medium, the both compounds are pH dependent and an increase in concentration of acetic acid results in a significant decrease in both MIC and MBC. Ex-vivo studies have shown a significant increase in absorption of brilliant blue (as modeling drug) in the presence of TEC or DEMC in comparison with chitosan. TEC and DEMC with positive charges are able to interact with tight junctions of colon epithelia cells and hence increase permeability of brilliant blue across the tight junctions. In-vivo investigations have exhibited the absorption enhancer effects of DEMC on the colon absorption of insulin in normal and diabetic rats. The insulin absorption from the rat’s colon was evaluated by its hypoglycemia ... effect. A significant decrease in blood lucose was observed, when mixture of insulin and DEMC wa

کلمات کلیدی:

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