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Effect of a Non-methoxylated N-trimethyl Chitosan Chloride Derivative over Capreomycin Sulfate Permeability in CaCo-2 cell Monolayers

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***SUMMARY*. The effect of N-trimethylchitosan chloride on the intestinal permeability of capreomycin sulfate, a polypeptide antibiotic, using an *in vitro* model, was evaluated. To improve the mucoadhesivity and permeation enhancer properties of N-trimethylchitosan chloride, it was used a synthetic pathway that selectively alkylated the amino groups and not the hydroxyl groups in carbons 3 and 6, which decreases the potency of the polymer, leading to use higher quantities and limit its potential as a functional excipient. This non-methoxylated derivative of the studied polymer reduced in a reversible way the transepithelial electrical resistance of CaCo-2 monolayers at concentrations not higher than 0.003 % w/v, indicating that the absence of steric hindrance from methoxyl groups improves the effect of N-trimethylchitosan chloride, but at expense of a narrow range of action and higher cytotoxicity. The results of *in vitro* permeation studies conducted in bicameral Transwell® systems suggested that the permeability of capreomycin sulfate is low, although it was not established if the transport is exclusively paracellular or membrane transporters are involved. By using increasing concentrations of the polymer in the range of 0.001 - 0.003% w/v, it was observed a slight increase in the transport of capreomycin. Therefore, it was concluded that further studies should use N-trimethylchitosan chloride with a lower degree of quaternization or controlled methoxylation, in order to increase the mass to use and obtain a product that is able to remain retained in the intestinal lumen and which in turn interacts with the epithelium.**

KEY WORDS: Absorption enhancern CaCo-2, Capreomycin sulfate, N-trimethyl chitosan.

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