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Synthesis and investigation of a mucoadhesive chitosan derivative for intranasal drug delivery

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Chitosan is in the focus of scientific interest due to its remarkable properties such as biodegradability and mucoadhesiveness among others. Its amino group content is mainly responsible for the mucoadhesivity as a result of the positive charge after protonation. Covalent modification of amino groups of chitosan with L-cysteine can result in further mucoadhesiveness improvement because the total number of amino groups will not change after the reaction and the thiol groups of L-cysteine might result in stronger interaction with nasal mucosa. In this work, our aim was to synthesize chitosan-cysteine conjugate containing moderately high amount of L-cysteine. Further aim was to determine the thiol content of the derivative, as well as to evaluate its mucoadhesiveness under nasal conditions (pH=5.6, 32°C) compared to the starting chitosan by measuring the loss and storage moduli, and the work of adhesion. The characterization of crystallographical and thermoanalytical properties also belonged to our goals. The reaction mixture contained 0.50 g of chitosan 0.70 g of L-cysteine, 1.2 g 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide and 0.32 g of N-hydroxysuccinimide in 50 ml of pH=4.7 2-(N-morpholino)ethanesulfonic acid solution. After 5 h of reaction the polymer was dialyzed multiple times and the product was freeze-dried. The chitosan-cysteine polymer contained moderately high amount of thiol groups. The product showed amorphous nature, moreover DSC and TG thermograms indicated different entity from the starting polymer. The adhesion work of the derivative was significantly higher ($p < 0.001$) in comparison to starting chitosan. The chitosan derivative seems to be highly mucoadhesive in nasal conditions, however additional measurements are required to confirm the feasibility of this material in nasal formulations.

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