

Modification of chitosan with methacrylic and crotonic anhydrides as new mucoadhesive excipients for nose-to-brain delivery

Shiva Vanukuru, Hisham Al-Obaidi, Vitaliy Khutoryanskiy

School of Pharmacy, University of Reading, Reading RG6 6UR, U.K.

Background: Nasal drug delivery is attracting increased interest due to it being a promising avenue for drug delivery to the brain. Globally, there is an increasing incidence of people developing neurodegenerative diseases. Most common conditions such as Alzheimer's and Parkinson's do have treatments available which focus on symptomatic relief rather than a cure. However, patients on these treatments have an increased risk of developing side effects. The conventional oral medicine formulations cannot cross the BBB effectively leading to increased risk of systematic side effects. For nasal drug delivery, mucoadhesive polymers are important as they will increase the retention time within the nasal mucosa. Chitosan is a cationic polysaccharide exhibiting excellent mucoadhesive properties. Modifications of chitosan with methacrylic and crotonic anhydrides results in introduction of unsaturated groups, which are capable of forming covalent bonds with thiols, present in mucins.

Methods: Chitosan was modified by a single step reaction with methacrylic and crotonic anhydrides. ¹H NMR spectroscopy was used to characterise the structure of these derivatives. Turbidity measurements were conducted to evaluate the effect of pH on the solubility of chitosan and its derivatives in water. Tensile test with sheep nasal mucosa was used to study the mucoadhesive properties of the new derivatives in comparison with unmodified chitosan.

Results: The degree of chitosan substitution with anhydrides was calculated based on the ¹H NMR spectra of the resulting products. Chitosan derivatives were found to have better pH-solubility profile compared to unmodified chitosan. Methacrylated derivatives precipitate at a higher pH compared to unmodified chitosan; in comparison, crotonated derivatives have constant solubility throughout. The mucoadhesion and retention studies showed that modified derivatives have better adhesion and retention time in the mucosa compared to unmodified chitosan.

Conclusions: Methacrylated and crotonated chitosan exhibit greater mucoadhesive properties compared to parent chitosan. This study demonstrates the future potential for these derivatives to be used for nose-to-brain drug delivery.