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| **Synthesis and characterisation of novel chitosan derivatives to improve retention for nasal drug delivery**  |
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| **Background:** Nasal drug delivery is attracting increased interest as it is a promising avenue for drug delivery to the brain. For nasal drug delivery to be effective over conventional formulations, mucoadhesive polymers such as chitosan needs to play a key role in the formulation to increase the retention time within the nasal mucosa. Chitosan is a cationic biopolymer with wide ranging pharmaceutical applications. Previously, methacrylic anhydride has been used to modify chitosan via N-alkylation reaction to produce methacrylated derivatives that improve its solubility and mucoadhesive properties. However, its toxicology and safety profile were not considered. |
| **Methods:** Chitosan was modified by a single step reaction with 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. Spray drying technique was used to produce microparticles, which were used to study mucoadhesion and planaria toxicity. DLS were used to measure charge and particle size. Furthermore, tensile tests with sheep nasal mucosa were conducted to study the mucoadhesive properties of the new derivatives in comparison with unmodified chitosan. Fluorescence flow through studies were conducted to understand the mucoadhesion properties.  |
| **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. DLS data showed that the charge of the modified polymer is lower than 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 nasal drug delivery to improve retention time. |