

Joint Event

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## 2,2'Dithiodinicotinyl ligands: Key to more reactive thiomers

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The goal of this study was to establish a new type of preactivated thiomers showing comparatively higher reactivity with mucus and improved mucoadhesive properties. The dimeric form of 2-mercaptocotinic acid (MNA-MNA) was directly attached to the polymeric backbone of chitosan (CHI) to achieve a higher reactivity. Amide bond formation mediated by 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (EDAC) was used as a coupling reagent. The remaining free amino groups were reacted with succinic anhydride (Succ) to gain a homogeneously anionically charged polymer (CHI-Succ-MNA-MNA). Within our study, various coupling rates of up to 170  $\mu\text{mol}$  MNA-MNA per gram polymer were obtained. The coupling of the dimeric ligand resulted in a preactivated thioimer with a more reactive disulfide substructure due to the additional nitrogen atom in conjugation over the aromatic moieties. Furthermore, the obtained polymer is completely preactivated and therefore protected against unwanted oxidation reactions. Our kinetic studies of disulfide exchange reactions showed a 3.8-fold higher reactivity of CHI-Succ-MNA-MNA compared to a state-of-the-art preactivated thioimer. Rheological measurements showed that CHI-Succ-MNA-MNA with a coupling rate of 170  $\mu\text{mol}$  (CHI-Succ-MNA-MNA 170) lead to a 5.7-fold higher mucus viscosity than the non-thiolated control polymer (CHI-Succ). This indicates a rheological synergism due to mucoadhesive properties. These results were confirmed by an additional mucoadhesion experiment, which showed a significantly prolonged retention time of CHI-Succ-MNA-MNA on the small intestinal mucosa compared to CHI-Succ ( $P < 0.02$ ). According to the presented results, the double preactivation seems to be a promising strategy to obtain entirely preactivated polymers with improved mucoadhesive properties.

### Biography

Claudia Menzel is a PhD student from the Institute of Pharmacy at University of Innsbruck. Her work focuses on the improvement of drug bioavailability and the development of drug delivery systems for the non-invasive administration of poorly absorbed drugs. She has published three papers and one review article in reputed journals.

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