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Pre-activated thiomer for nasal delivery of Apomorphine: Synthesis and *in vitro* evaluation

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Apomorphine is a non-selective dopamine agonist which is used for the treatment of Parkinson's disease. Apomorphine, however, shows low oral bioavailability of less than 2% due to hepatic first-pass metabolism. Thus, the aim of this study was to investigate an improvement of apomorphine absorption through nasal mucosa by co-administration with a pre-activated thiomer. Poly(Acrylic Acid) (PAA) molecular mass of 250 kDa was used as polymer backbone. PAA was first thiolated by coupling with L-cysteine (Cys) followed by pre-activation via immobilization of 2-Mercapto-Nicotinic Acid (2MNA) in order to protect sulfhydryl groups towards oxidation. *In vitro* permeation across freshly excised porcine nasal mucosa was investigated. The influence of degree of pre-activation on drug absorption was thereby addressed. In total, 2816.7±185.0 µmol of thiol groups were immobilized per gram of polymer. Due to the omission of DMSO and pH variations, different degrees of pre-activation were achieved. In the presence of thiomer, 67.3% and 82.6% pre-activated thiomers, the cumulative amount of apomorphine permeating the mucosa was 1.2, 2.7 and 3.4 fold higher than the control (buffer only). Because of this pronounced effect, highly pre-activated thiolated PAA could be considered as promising excipient for nasal apomorphine delivery.

Biography

Kesinee Netsomboon is a PhD student of Department of Pharmaceutical Technology, Institute of Pharmacy, University of Innsbruck, Austria since 2012. She graduated Bachelor of Pharmacy from Chiang Mai University, Thailand in 2008 and Master of Science in Pharmacy from Chulalongkorn University, Thailand in 2012. She was awarded the scholarship from the Chula-Chiba University Pharmaceutical Student Exchange Program during her Master's degree study to carry on a part of her research at Chiba University, Japan in 2009.

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