# Mucoadhesion - A Prerequisite or a Constraint in Nasal Drug Delivery?

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The nasal cavity offers an attractive route for systemic drug delivery. Administration is easy with a rapid onset, first-pass metabolism can be avoided and there is a potential possibility to circumvent the blood-brain barrier. One major problem with nasal administration, however, is to circumvent the effect of mucocilliary clearance and prolong duration of an applied formulation at the site of action. The most common way to accomplished this is by adding various polymers to the formulation to induce interactions with the mucosa. However, this also lowers the water activity of the formulation and imposes a water gradient over the mucosa, which potentially induces a mucosal response affecting the barrier structure and properties.

The aim of this project was to determine if a nasal formulation with low water activity, that favours mucoadhesion, would also induce a mucosal response detrimental to drug absorption. We approached this problem by performing drug permeability studies ex vivo in flow-through diffusion cells with porcine nasal mucosa at 32°C. Donor formulations comprised Xylometazoline HCl dissolved in PBS pH 7.4 and PEG 1500 were used to adjust the water activity in these formulations from 1 to 0.8 (=65% PEG)[1]. Drug solubility was determined to match the thermodynamic activity of the drugs in the alternative formulations.

Our results show that a water gradient can be used to regulate drug flux over nasal mucosa, similar to what has previously been shown with oral mucosa and skin[1, 2]. We have also shown that drug permeability over nasal mucosa is much higher than over oral mucosa and skin (nasal > oral > skin)[1,2]. If mucoadhesion is achieved through water sorption by the applied formulation this mechanism will counteract drug uptake. The present data shows the importance of understanding water sorption and how it affects drug transport in nasal drug delivery systems.

References:

[1] Björklund S, Engblom J, Thuresson K and Sparr E, J Control Release 143:2 (2010) 191-200

[2] Wahlgren M, Pedersen L and Engblom J, manuscript