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A Model for Studying Nasal Drug Delivery: RPMI 2650 Human Nasal Epithelial Cell Line

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Studies on nasal epithelial models are important to develop vehicles for systemic nasal drug delivery, and also for targeting drugs to brain via the nasal route. RPMI 2650 human nasal septum carcinoma cell line was used in our experiments as an *in vitro* cell culture model for toxicity and permeability assays.

For toxicity tests cells were cultured in 96-well plates, and MTT dye conversion and lactate dehydrogenase release were determined after treatments. For permeability tests RPMI 2650 cells were cultured on collagen-coated Millipore CM inserts (hydrophilic PTFE membranes, pore size: 0.4 µm, surface 4.2 cm^2) in 6-well plates. Fluorescein was selected as a marker of paracellular permeability, and TEER and P_{app} were measured.

RPMI 2650 cells passaged at high cell density grew as confluent multilayers on inserts. To induce barrier properties several treatments and culture conditions were tested. The effects of serum, hydrocortisone, cAMP and air-liquid interface on RPMI 2650 cell layers were examined. Hydrocortisone and cAMP increased the tightness of the nasal epithelial barrier, and induced the expression and junctional localization of claudin-1, claudin-4, ZO-1, and β-cathenin visualized by immunohistochemistry and confocal microscopy. The changes in cell and junctional morphology were confirmed by electron microscopy. The resistance of the monolayers reached 240 ± 13 Ωcm^2, and P_{app} of 2.7 ± 0.2 10^{-6} for fluorescein indicating a barrier typical for nasal epithelium. The model was used to test the non-toxic nasal doses of absorption enhancers Tween 80, Cremophor RH40, Transcutol P, and water soluble sucrose esters and to determine their effects on paracellular permeability. Tween 80 and Cremophor RH40 decreased TEER by 50 % and significantly increased P_{app} values of RPMI 2650 layers.

We have successfully established a human *in vitro* nasal epithelial model that can be used to study the effects of absorption enhancers and their mode of action.

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