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Improved nasal absorption of drugs using poly-L-arginine: effects of concentration and molecular weight of poly-L-arginine on the nasal absorption of fluorescein isothiocyanate-dextran in rats

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The effects of the concentration and molecular weight of poly-L-arginine (poly-L-Arg) on the in vivo nasal absorption of fluorescein isothiocyanate-labeled dextran (MW, 4 kDa, FD-4) in rats were studied. When poly-L-Arg with a rangeof different molecular weights (MW, 8.9, 45.5 and 92.0 kDa) was applied intranasally at various concentrations, the bioavailability ($F_{0\text{-}9\ h}$) of FD-4 increased with the increasing concentration of poly-L-Arg. The enhanced absorption was dependent on the molar concentration, in that the poly-L-Arg with a higher molecular weight increased $F_{0\text{-}9\ h}$ at a lower molar concentration. In addition, for each applied concentration, the poly-L-Arg exhibited a molar-weight-dependent as far as the enhancement of FD-4 absorption was concerned. On the other hand, the maximum absorption rate (MAR) of FD-4, calculated by means of a deconvolution methods, tended to reach a maximum plateau level at a lower applied concentration for the poly-L-Arg with the highest molecular weight, but this plateau level was almost the same for poly-L-Arg with molecular weights of 45.5 and 92.0 kDa. Moreover, the simulated absorption profiles of FD-4 indicate that the degree of enhancement (the level of MAR and the subsequent reduction in the absorption rate) was dependent on the molecular weight of poly-L-Arg, while the effect of poly-L-Arg was maintained for a longer period, depending on the applied concentration, although the MAR was relatively similar. These results indicate that the molecular weight of

poly-L-Arg appears to affect both the enhancing efficacy (absorption rate) and the time-frame of this enhancing effect, whereas the concentrations of each poly-L-Arg system applied onlu have an effect on the time-frame. These effects may also be associated with tha charge density of a poly-L-Arg molecule.