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Analysis of Transient and Reversible Effects of Poly-L-Arginine on the in vivo Nasal Absorption of FITC-dextran in rats

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We have investigated whether poly-L-arginine, with a mean molecular weights of 8.9 and 45.5 kDa (poly-L-Arg (10) and Poly-L-Arg (50)), can induce transient and reversible effects involving enhancement of the nasal absorption of fluorescein isothiocyanate-labeled dextran (MW 4.4 kDa, FD-4) and determined the main pathway for the increased transport of FD-4 in rats in vivo. Pre-administration and repeated administration studies were conducted involving the selection of different time intervals between intranasal administration of poly-L-Arg and administration of FD-4, with and without poly-L-Arg, to characterize these transient and reversible effects. The degradation of poly-L-Args in a diluted nasal drip was determined from the fluorescence of degraded poly-L-Arg-fluorescamine products. In the pre-administration study, poly-L-Arg exhibited a transient effect on the increased nasal FD-4 absorption depending on its molecular weight, associated with the degradation rate of poly-L-Arg in mucus. In the repeated administration study, additional poly-L-Arg produced similarly enhanced FD-4 absorption. Confocal laser scanning microscopy showed that fluorescence of FD-4 after co-administration of poly-L-Arg (50) was confined mainly to the paracellular spaces. In conclusion, poly-L-Arg exhibited molecular weight-dependent transient and reversible effects on the enhancement of nasal FD-4 absorption paracellularly in rats in vivo. The enzymatic degradation of poly-L-Arg is one of the key determinants of the transient effect on in vivo enhanced absorption of FD-4.