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Effect of poly-L-arginine on the nasal absorption of FITC-dextran of different molecular weights and recombinant human granulocyte colony-stimulating factor (rhG-CSF) in rats

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The effect of poly-L-arginine (poly-L-Arg) on the in vivo nasal absorption of FITC-dextrans with a mean molecular weight ranging from 4.3 to 167 kDa and recombinant human granulocyte colony-stimulating factor (rhG-CSF) in rats were studied. When FITC-dextrans were co-administered intranasally with 1.0 w/v% poly-L-Args of differentmolecular weight (MW, ca. 45.5 and 92 kDa, poly-L-Arg (50) and poly-L-Arg (100)), the bioavailability (F_∞) increased markedly compared with that after administration of FITC-dextran alone. However, the F_∞ decreased exponentially with the increasing molecular weight of FITC-dextrans. There was no significant difference between the enhanced nasal absorption of FITC-dextrans achived by the co-administration of poly-L-Arg (50) and poly-L-Arg (100). Moreover, the relationship between the F_∞ and the molecular weight of FITC dextrans indicated that the molecular weight of protein drugs, which exhibited efficient absorption with poly-L-Arg, was about 20 kDa, when the lower limit of bioavailability for developing a potent transdermal delivery system was assumed to be about 10%. Indeed, the nasal absorption of rhG-CSF, which has a molecular weight of 18.8 kDa, was also increased after co-administration of 1.0 w/v% poly-L-Arg (50) and the F_∞ was about 11%. It seems likely that poly-L-Arg

can be used to provide adequate nasal absorption of various protein drugs which have a molecular weight of about 20 kDa, thereby allowing the successful development of a variety of transnasal drug delivery systems.