THE ABSORPTION OF β-, DM-β- AND HP-β-CYCLODEXTRINS FROM THE RABBIT LUNG

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Recently cyclodextrin (CD) derivatives have been shown to sustain the release rate of drugs following oral administration (Uekama et al. 1987; Hirayama et al. 1988). A previous study reported on the formation of a complex between salbutamol and β-CD (Cabral-Marques et al., 1989). In order to examine the feasibility of using such complexes for sustaining pulmonary drug action or for controlling systemic drug levels following pulmonary administration, it is necessary to first determine the absorption of CDs from the lung.

This work reports on the pharmacokinetics of 10 mg kg^{-1} doses of β-, dimethyl(DM)-β- and hydroxypropyl(HP)-β-CDs following administration to NZW male rabbits (n = 5; 2.7 - 4.2 kg) by means of the marginal ear vein (i.v.) and intratracheal instillation (i.t.) at the bifurcation of the trachea.

Blood samples were withdrawn from the ear vein at designated time intervals, spun with 10 µl of heparinised saline (100 IU/ml) and the plasma assayed for β-CD by HPLC (Frijlink et al. 1987) and for the DM-β- and HP-β-CDs by scintillation counting as both were ^{14}C radiolabelled in the side chain.

Table 1. Pharmacokinetic parameters for CDs (Mean ± SEM)

	C_{max} (i.t.) (µg/mL)	t_{max} (i.t.) (min)	$t_{1/2z}$ (i.t.) (min)	$t_{1/2z}$ (i.v.) (min)
β-	23.46 ± 1.92	30.0 ± 4.47	44.20 ± 3.90	41.54 ± 6.85
DM-β	26.78 ± 5.66	22.4 ± 1.94	44.28 ± 6.81	52.86 ± 8.15
HP-β	14.44 ± 2.42	113.0 ± 10.6	62.96 ± 4.78	44.24 ± 3.57

A lag phase was observed for the i.t. absorption of HP-β-CD which resulted in an extended t_{max}. In the absence of such a lag period for both β- and DM-β-CD, peak plasma levels were achieved at significantly earlier times (Table 1). Maximum plasma levels (C_{max}) for all three CDs were not statistically different ($0.05<p<0.1$). The terminal half-life ($t_{1/2z}$) for HP-β-CD was longer after i.t. than after i.v. bolus injection but was not statistically different when either β- or DM-β-CD was given by the two routes of administration.

Although the CDs are apparently well absorbed in the rabbit lung, the unusual behaviour of HP-β-CD requires further examination in order to elucidate the nature of the lag phase. Future studies will also examine the influence of the CD-salbutamol complex on the pharmacokinetics of salbutamol following i.t. administration.

Cabral-Marques, H.M. et al. (1989) J. Pharm. Pharmacol. 41: 62P
Frijlink, H.W. et al. (1987) J. Chrom. 415: 325 - 333
Hirayama et al. (1988) J. Pharm. Sci. 77: 233 - 236
Uekama et al. (1987) Ibid. 76: 660 - 661