薬物担体としての多糖類：フルオレセイン標識デキストランのマウスにおける体内動態

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Polysaccharides as Drug Carriers: Biodisposition of Fluorescein-Labeled Dextrans in Mice

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ABSTRACT The biodisposition of fluorescein-labeled dextrans (FDs) with different molecular weights (MW = 4–500 kDa) was systematically examined in mice. After intravenous injection of FDs at a dose of 120 mg/kg, the levels of FDs in the blood circulation and in the various organs were measured fluorometrically. FDs with a molecular weight lower than 20 kDa showed poor hepatic distribution (2.1–3.7 % of dose/g tissue) due to their rapid elimination from the blood circulation. FDs with higher molecular weights were appreciably distributed in the liver (18.9–24.0 % of dose/g tissue) and accumulated there over a long period, whereas the FD levels in the other organs were almost negligible a few days after injection. The hepatic mean residence time of FDs ranged from 22.5 to 28.1 d. Partial depolymerization of FDs which accumulated in the liver was observed within 10 d after administration. The hepatic uptake clearance of FDs was decreased with an increase in molecular weight. A marked molecular weight dependency was also seen in the urinary and fecal excretions of FDs. An appreciable dose-dependency was demonstrated in the hepatic uptake of FDs (MW = 40 kDa), as well. The amount of hepatic uptake as a function of dose showed saturation kinetics and was analyzed by a Michaelis-Menten type equation. The apparent values of Km (dose) and Vmax (hepatic level) estimated were 116 ± 5 mg/kg and 1.10 ± 0.05 mg/g tissue, respectively.

抄録 分子量の異なるフルオレセイン標識デキストラン（FD）のマウスにおける体

内動態を評価した．分子量20kDa未満のFDは血中から速やかに消失し，肝への分布は低かった．より高い分子量をもつFDは顕著に肝へ分布し，長期にわたって蓄積した．肝平均滞留時間は22.5～28.1 日であった．肝に蓄積したFDの一部は低分子化を受けた．肝取込みクリアランスは分子量の増加に伴って減少した．尿中並びに糞便中排泄にも顕著な分子量依存性が認められた．肝取込みには顕著な投与量依存性が観察された．みかけのKm（投与量）とVmax（肝臓のレベル）の値は，それぞれ116 ± 5 mg/kg 並びに1.10 ± 0.05 mg/g tissue と算出された．