SPECIFIC INTRAVENOUS DELIVERY OF DRUGS TO THE LUNGS USING ION-EXCHANGE MICROSPHERES

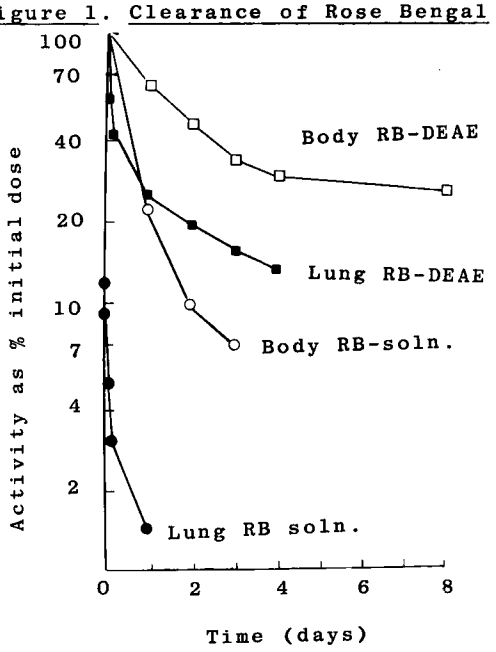
Lisbeth Illum and S.S. Davis, Royal Danish School of Pharmacy, Copenhagen, Denmark, and University of Nottingham, United Kingdom.

The fate of colloidal systems (eg liposomes) in the body following intravenous administration is determined by the chemical and physical characteristics of the colloid (Singer et al 1967). Large particles (greater than 5 μm) will be trapped in the lungs by mechanical filtration while small particles will be cleared by the reticuloendothelial system (Davis and Taube 1978). Large degradable gelatin microspheres containing mitomycin C have been used for the specific delivery of the anticancer agent to the lung (Yoshioka et al 1981).

DEAE-cellulose microspheres (40-160 μm diameter) (DEAE-Sephacel, Pharmacia) have been tested as model drug carrier systems for the selective delivery of drugs to the lungs. DEAE-cellulose is a basic ion-exchange material (binding capacity 0.7 Meq/g) which can bind acidic drugs (eg methotrexate) strongly. Radiolabelled rose bengal (^{131}I-rose bengal), an anionic dye, was used as a model drug. The binding capacity in normal saline at 25°C was determined as 380 mg/g. The labelled cellulose microspheres (∿ 10^8 particles, ∿ 100 μCi) were administered intravenously to New Zealand White rabbits (n=3). The clearance of the microsphere-bound rose bengal from the blood and organ deposition were followed and compared to that of free rose bengal solution using the techniques of gamma scintigraphy, blood level measurements and histology of the lung tissue. Processed computer images displayed in the form of scintiscans for the lung region of the rabbit showed a distinctive shape and position. The DEAE-cellulose microspheres were trapped in the lungs within one minute following administration.

The bound rose bengal was slowly leached from the microspheres in the lungs in a sustained release fashion with a half time for clearance of the order of 4 hours (Figure 1). A low blood level activity for the microsphere system supported the observation of rapid lung uptake. Histological examination of lung tissue 11 days after administration demonstrated the presence of intact undegraded DEAE-cellulose microspheres deeply deposited in the capillary beds. These preliminary results suggest that DEAE-cellulose microspheres may have utility as a model sustained release drug targeting system where the process of drug leaching from an ion-exchange matrix can be differentiated from release via biodegradability.

Figure 1. Clearance of Rose Bengal



Davis, M.A. and Taube, R.A. (1978) J. Nucl. Med. 19 1209.
Singer, J.M. et al (1967) In The Reticuloendothelial System (Eds. DiLuzio, N.R. and Paoletti, R.) p18, Plenum Press, New York.
Yoshioka, T. et al (1981) Intern. J. Pharmaceut. 8 131

0022-3573/82/120089 P-01$02.50/0