THE EFFECT OF MOLECULAR MASS OF POLYVINYLPYRROLIDONE ON ITS ACCUMULATION IN INFLAMMATORY TISSUE IN THE RAT

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As a non-biodegradable inert polymer, polyvinylpyrrolidone (PVP) has previously been used as a plasma expander, and as such its blood clearance and body distribution after intravenous (i.v.) administration have been widely studied, (Ravin et al 1952). Specific uptake by the reticuloendothelial system (RES) has led to it being used as an indicator of reticuloendothelial activity,(Regoeczi 1976). The in vivo fate of the polymer is molecular weight dependent, (Hulme et al 1968), with increased RES uptake of higher molecular weight PVP while polymers of 40kDa and below are able to pass the glomerular membrane to be excreted in the urine.

Inflammatory tissue is characterised by an increase in blood vessel permeability and an infiltration of phagocytic cells such as macrophages. Due to the similarity of inflammatory tissue to the RES, PVP may be expected to accumulate in such tissue.

A range of molecular weights of PVP (10, 40 and 360kDa) were radiolabelled with iodine-125 (Regoeczi 1976) and injected i.v. into normal and adjuvant-induced arthritic rats. Subsequent blood clearance and tissue uptake profiles of the polymer have been investigated. Chromium-51 labelled erythrocytes have been used as a blood pool marker to correct for the blood volume of the tissues investigated. Following i.v. administration of each polymer (1-8 mg per rat), blood samples were collected until approximately 80% of the injected activity had been cleared. Rats were then killed and tissues removed for gamma counting.

Plasma half lives of PVP were found to increase with increasing molecular weight;10, 40 and 360kDa molecular weights had half lives of 11, 34 and 960 minutes respectively.

Tissue uptake was also found to be molecular weight dependent, the highest molecular weight PVP accumulated to a greater extent than the two lower molecular weight polymers in the spleen, liver, lungs and paws in both normal and arthritic rats (ANOVA, $P<0.01$). The 360kDa PVP was located mainly in the RES while there was little uptake of the 10 and 40kDa PVP preparations, probably because of their rapid elimination by the kidneys. In all cases uptake by arthritic paws exceeded that of normal paws, (even when expressed as percentage uptake per gram of tissue), (ANOVA, $P<0.01$), and uptake of 360kDa PVP exceeded that of 40kDa and 10kDa in both normal and inflamed tissue, (ANOVA, $P<0.01$).

The enhanced uptake of PVP by arthritic compared with normal paws (percentage of the total dose administered) is shown in Table 1 (total for all paws).

Table 1. Uptake of intravenous PVP by paws (%).

PVP kDa	NORMAL	ARTHRITIC	RATIO
10	0.53	1.09	2
40	0.28	2.16	8
360	0.91	12.38	14

These results indicate the potential use of polymeric carriers such as PVP for targeting anti-inflammatory drugs to inflamed tissues.

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Regoeczi, E. (1976) Br.J.Exp.Path.57:431-442