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The Permeability of the Plasma-Lymph Barrier of the Small Intestine of Various Species to Macromolecules

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Summary

The filtration coefficients of polyvinylpyrrolidone (PVP) of molecular weight 10,000–110,000 were measured at the plasma-lymph barrier of the upper small intestine of rabbits, rats and cats. For this purpose the animals were given intravenous injections or infusions of PVP in such a way as to produce a constant blood level; PVP concentrations were measured in lymph obtained by cannulating the mesenteric duct and also in the plasma. In these species low molecular weight PVP had a filtration coefficient of 0.85–0.64, while high molecular weight PVP (MW 110,000) either had a very low filtration coefficient – 0.22 – or was not detectable in the intestinal lymph. The three species, representing herbivores, omnivores and carnivores, showed no differences in the penetration behavior of PVP, i.e., in the permeability of the plasma-lymph barrier to macromolecules.

Conclusions

The plasma-lymph barrier of the small intestine, in the direction blood → lymph, is only slightly more permeable to macromolecules than the plasma-lymph barrier of the hind limb (skeletal muscle). The dietary habits of the species investigated – a herbivore, an omnivore and a carnivore – had no influence on the results obtained.

Introduction

A peculiarity of the intestinal lymph is the fact that in it and with it are transported various corpuscular elements such as fat droplets and cells which have penetrated the intestinal mucosa by "persorption" (3, 15). In view of this peculiarity it seemed desirable to analyse the permeability of the plasma-lymph barrier to macromolecules. The aim of the experiments was to study the penetration behavior of PVP of various molecular weights in species with different dietary habits – herbivores, omnivores and carnivores.

Materials and Methods

The animals were male rabbits weighing 2.7–3.1 kg (grey-silver hybrids, supplied by Messrs Buchner, Kienberg and fed on Altromin®-K), cats of both sexes weighing 2.5–3.0 kg (supplied by Messrs. Hauk, Rosenau and fed on Whiskas® (canned meat)) and male rats weighing 280–320 g (supplied by Messrs. Mus rattus, Brunnthal b. München and fed on ssniff®) The rabbits and cats were fasted for 20 hours and the rats for 16 hours before the experiments. The animals were anaesthetized with pentobarbital, for rabbits 40 mg/2 ml/kg i.v., for cats 30 mg/1.5 ml/kg i.p. and for rats 40 mg/2 ml/kg i.p. If necessary a further dose of the anaesthetic was injected by the same route. The batches of PVP (Table 1) were injected or infused into the auricular vein of the rabbits, the femoral vein of the cats and the jugular vein of the rats. Blood samples were taken from the carotid artery in all three species, and to facilitate respiration the trachea was cannulated. After opening the abdominal cavity by a flank incision (on the left for rabbits and cats, and on the right for rats) the lymphatic vessel situated cranial to the mesenteric artery (the ductus mesentericu

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Dedicated to Dr. med. Rolf Madaus on his 60th birthday.

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Tab. 1

Species	Weight	PVP MW	Pretreatment mg/ml/kg	Time Inj. ← → Inf. min	Infusion mg/ml/min/kg
Rabbit	ca 3 kg	11500	500/5	10	4/0.2
		38000	500/5	60	1/0.1
		62000	500/5	60	1/0.1
		94000	500/5	60	1/0.1
		110000	200/5	10	1/0.2
		650000	500/10	–	no infusion
Rat	ca 300 g	10000	600/2 after 60 min 300/1	15	1.5/0.02
		38000	400/2	10	1/0.1
		110000	200/4	60	1/0.02
Cat	ca 3 kg	38000	500/5	30	1/0.1

PVP MW 10000: Roth, Karlsruhe
PVP MW 11500–650000: BASF, Ludwigshafen
Solvent: Saline, buffered pH 7.2

was cannulated by the technique described by *Bollman* (2), *Lambert* (8) and *Warshaw* (16). The lymph was collected over 30 min periods in weighed heparinized test tubes and measured gravimetrically. Blood was taken in the middle of each lymph collection period. Plasma and lymph PVP concentrations were measured by the method of *Levy* and *Fergus* (9). The filtration coefficient was determined from the ratio

$$\frac{\text{PVP concentration in lymph}}{\text{PVP concentration in plasma}}.$$

Results

Fig. 1 and Table 2 show the filtration coefficients of PVP of molecular weight 10,000 to 110,000 in the three species. In rats the filtration coefficient for PVP of MW 10,000 was 0.85, and in rabbits the coefficient for PVP of MW 11,500 was 0.64. In rabbits the plasma-lymph barrier of the small intestine is so "tight" that PVP 110,000 is not detectable in the lymph, while for rats the filtration coefficient of this PVP is as high as 0.22. The filtration coefficients for PVP of MW 38,000 are closely coincident, a fact which shows that there are virtually no differences in this respect between the three species, and in particular that the dietary habits of herbivores, omnivores and carnivores have no bearing on the measurements.

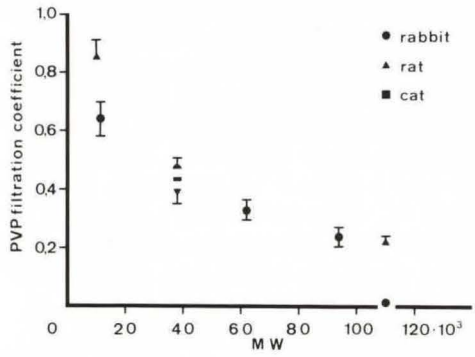

Fig. 1 Dependence of the intestinal plasma-lymph barrier-PVP filtration coefficient on the molecular weight

Discussion

Most of the previous work on the permeability of the plasma-lymph barrier of the small intestine has been based on measurements of the filtration coefficients of total protein, of protein fractions such as albumin, globulin, gammaglobulin, or of dextran of various mole-

Tab. 2 Dependence of the intestinal plasma-lymph barrier PVP filtration coefficient on the molecular weight

PVP MW	10000	11500	38000	62000	94000	110000
rabbit		0.64 ± 0.06	0.47 ± 0.04	0.33 ± 0.03	0.24 ± 0.03	no PVP
rat	0.85 ± 0.06		0.40 ± 0.05			0.22 ± 0.02
cat			0.44 ± 0.05			

cular weights. In dogs, the filtration coefficient of the plasma-lymph barrier of the small intestine for total protein is 0.6, while the coefficients for albumin and globulin are of the same order (1). According to *Granger* et al. (6) the filtration coefficient in the isolated intestine of the cat at a venous pressure of 0 mmHg is between 0.7 and 0.3; depending on molecular radius it initially shows a steep decrease, but with molecular radii > 80 Å it remains practically constant. In the same preparation, *Granger* et al. (7) found that the filtration coefficient for total protein was between 0.48 and 0.63. *Mayerson* et al. (10) used labeled dextrans of various molecular weights in their experiments with dogs. The most permeable of all proved to be the plasma-lymph barrier of the liver, while that of the neck was much less permeable. The permeability of the plasma-lymph barrier of the small intestine was between these two values, but closer to that of the liver. *Renkin* (11), who also worked in dogs with dextrans of various molecular weights, found that the lowest value was 0.2, while the liver had the highest value of 0.9. The value for the small intestine was 0.45 – exactly in the middle.

When we compare these results with our own findings obtained with PVP of various molecular weights in the liver, kidney and hind limb (4, 5, 12, 13, 14), it becomes clear that the permeability of the plasma-lymph barrier of the intestine to PVP is by no means as low as that of the rabbit's hind leg, though it is considerably closer to the values for the hind leg than to those for the liver or kidney. There is hence a certain discrepancy between our own findings obtained with PVP and the fact that the filtration coefficient for total protein is undoubtedly greater than that for PVP of comparable molecular weights or molecular radii. This discrepancy may be attributable to the fact that the capillary filtration of proteins is not the only source from which protein can enter the lymph (1). In addition it must be remembered that for proteins it is appropriate to think in terms of molecular radius, because in the geometrical sense their molecules are rotation ellipsoids, while PVP forms cross-linked thread-like molecules having a bean-shaped or kidney-shaped geometrical configuration. The penetration behavior of both kinds of macromolecules is undoubtedly influenced by their shape. From the teleological viewpoint it seems reasonable that the plasma-lymph barrier of the small intestine should possess limited permeability to macromolecules, because massive escape of proteins from the plasma into the intestinal lymph would certainly not offer any advantage. However, it must be remembered that the permeability of the plasma-lymph barrier of the small intestine is not dependent on the dietary habits of the experimental animals investigated. This statement applies to the penetration of macromolecules from the plasma into the lymph; the present experiments throw no light on the structure and penetration behavior along the pathway from the interstitial space into the intestinal lymphatics in relation to the dietary habits of the experimental animals.

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