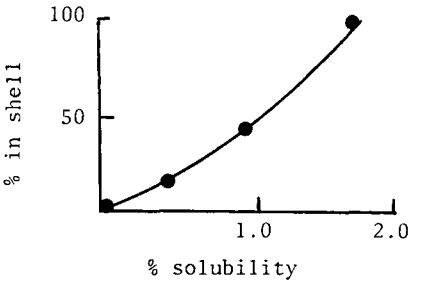
DRUG MIGRATION IN SOFT GELATIN CAPSULES

N.A. Armstrong, K.C. James and W.K.L. Pugh*, Welsh School of Pharmacy, U.W.I.S.T., Cardiff.

It has been reported that when a solution of p-hydroxybenzoic acid (PHBA) is packed in soft gelatin capsules, as much as 90% of the solute can migrate into the shells (Armstrong, James & Pugh 1980). A possible reason for this high result is that p-hydroxybenzoic acid has a solubility profile which favours the gelatin mix. Three other solutes, acetomenaphthone, ephedrine and phenobarbitone were examined to test this hypothesis, the 4 compounds representing a 250-fold range of aqueous solubilities. Solutions in isopropyl myristate were encapsulated, and the shells assayed after storage at room temperature for 3 days in a sealed container. All capsules were prepared identically. The results are plotted in the figure, which shows that the amount transferred is related to the aqueous solubility of the encapsulated drug, and is negligible when the solubility is of the order of 0.1% or less.



Migration should also be influenced by the partition coefficient between the encapsulated solution and the capsule shell. Water was used as model for the shell, and partition coefficients of phenobarbitone and p-hydroxybenzoic acid against octanol/isopropyl myristate blends measured. Shell contents using these blends, were determined as before, and the results are compared with oil/water partition coefficients in the table. Shell uptake decreases with increasing partition coefficient.

Soft gelatin capsules are used mainly as a dosage form for lipophilic drugs, which have low aqueous solubilities. The indications are therefore that significant migration to the capsule shell is not normally encountered, and that when it is a potential complication, it may be reduced by changing the solvent, though this might affect drug release in the gastrointestinal tract. Alternatively, a solvent could be chosen to introduce an element of migration, thereby giving a high initial concentration in the gut when the capsule is taken.

% Octanol in blend	100	75	50	25	0
Partition coefficient	24.2	21.7	17.7	12.1	2.3
% Phenobarbitone in shell	0	0	3	6	12
Partition coefficient	25.4	23.9	19.6	9.8	0.6
% PHBA in shell	6	9	12	30	92

Armstrong, N.A., James, K.C., Pugh, W.K.L. (1980) J. Pharm. Pharmacol. 32 (Suppl.) 25P

We thank R.P. Scherer Ltd. for the support and facilities provided.

*Present address: Biosciences Research Centre, Beechams Pharmaceuticals, Yew Tree Bottom Road, Epsom, Surrey.

0022-3573/82/120005P-01$02.50/0