THE USE OF POLYAMIDE MEMBRANES AS AN IN VITRO MODEL FOR DRUG ABSORPTION

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We have previously reported the permeability properties of polyamide (nylon) 6 membranes to benzocaine, where it appears that only the unionized species permeates the membrane (Uyokpeyi & others, 1975). Further studies have indicated a correlation between the permeability and sorption properties for polyamides 6, 11 and 12 and their phase transition temperatures (Ho & others, 1977). We have used these characterised membranes to investigate their permeability to a structurally-related group of steroids (Table) and a structurally-unrelated group of neutral, acidic and basic drugs (salicylic acid, imipramine hydrochloride, ampicillin trihydrate, hexylresorcinol, spironolactone, cephaloridine) which are reported to show marked differences in their biological availability. The aim of these studies was to determine whether polyamide membranes can reflect rank orders of *in vivo* availability and hence be of value in early screening studies on new drug candidates.

Permeability studies were performed using a simple all-glass permeation cell at 60°. The donor compartment concentration was essentially constant throughout, and sink conditions were operational in the receptor compartment. Studies using steroids utilised solutions in distilled water in the donor compartment and pH 7.4 buffer in the receptor compartment. The remaining studies utilised pH 6.0 and pH 7.4 phosphate buffers, each adjusted to an ionic strength of 0.154M with sodium chloride, in the donor and receptor compartments respectively. Permeability (P) and diffusion (D) coefficients were calculated from the steady-state flux and the lag-time respectively according to Barrer (1939).

Correlation of this *in vitro* data with *in vivo* data was achieved using carefully-assessed data from the literature [e.g. extent of buccal absorption (B_A) of steroids (Beckett & Pickup, 1975)]. The Table gives an example of the results of the *in vitro* and *in vivo* data for one group of drugs through one type of membrane; the correlation is approximately the same for other polyamide membranes. It is evident from the Table that, with the exception of β-oestradiol, decreased absorption is reflected by decreased permeation. However, the relative contributions of partition into and diffusion through the membrane depend upon the structure of the drug. For drugs of similar structure (e.g. the steroids) the permeation rate was controlled by the partition (sorption) coefficient (K) since D was essentially constant. However for the structurally-unrelated drugs it appears that both partition and diffusion play important roles since neither alone correlate satisfactorily with *in vivo* data yet, when combined as the permeability coefficient, a significant correlation can be achieved. Although this study is of a preliminary nature it does suggest that polyamide membranes have potential as models for drug absorption.

Table. *In vitro* and *in vivo* data for correlation of permeation through a non-oriented polyamide 6 membrane (21.77 μm thick) at 60°.

Drug	P(x 10^{-11} m^2 s^{-1})	D(x 10^{-13} m^2 s^{-1})	K(=P/D)	B_A(%)
Testosterone Acetate	2.29 ± 0.16	0.86 ± 0.24	266	87
Progesterone	1.53 ± 0.09	1.38 ± 0.07	111	53
Testosterone	1.25 ± 0.08	1.13 ± 0.33	110	45
Deoxycorticosterone	0.94 ± 0.10	1.50 ± 0.19	62	39
β-oestradiol	3.77 ± 0.64	0.84 ± 0.23	451	31

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