Tablets administered to dogs under different feeding conditions were recovered from the faeces after transit through the alimentary canal. Drug content of recovered tablets was analysed and the results are summarized in the table.

Feeding conditions	No. of dogs	Approx. transit time (h)	Propranolol (%, recovered ± s.d.)
1. No food ± 24 h of dose	4	44 ± 9	2 ± 1
2. No food 16 h before dose	7	28 ± 9	28 ± 11
3. Dosed 1 h after ~100 g food (light feed)	5	28 ± 3	35 ± 9
4. Dosed 1 h after ~800 g food (full feed)	4	25 ± 3	53 ± 12

The results indicate a dependence of the amount of drug retained in the matrix on the feeding conditions before its administration. Condition 1 demonstrates almost complete release of drug from the matrix; thereafter, as the amount of food present at the time of dosing is increased, there is a corresponding increase in the amount of drug which is *not* released *in vivo*. This is probably due to the tablet becoming embedded in the food mass, which affects the penetration of water into the pores of the matrix, and thus inhibits dissolution and hence release of drug.

This effect could introduce a large degree of variability into blood levels achieved with such a tablet, and is apparently a restriction on the use of this type of sustained-release formulation.

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The renal clearance of practolol in man

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Practolol is a potent β-blocking drug which is not protein bound and which is not metabolized to any extent (Scales & Cosgrove, 1970; Bodem & Chidsey, 1972). This communication reports on the renal clearance of practolol in man, comparing the renal clearance of practolol to glomerular filtration rate (GFR) measured by inulin clearance and examining the effect of frusemide on GFR and practolol clearance.

The results are presented in Table 1. Practolol clearance was, on average, less than GFR, but not significantly so (Group 1). Administration of frusemide caused a fall in GFR and in practolol clearance measured over the following 3 h in normal volunteers (Group 2) and practolol clearance in patients (Group 3) also fell on administration of frusemide (Group 4). Aspirin did not produce a significant fall in practolol clearance in normal volunteers.

It is concluded that practolol is eliminated largely by filtration at a rate approximately equal to GFR, and that factors which alter GFR will cause a parallel change in body clearance of practolol.

Table 1. *Renal clearance of practolol and inulin (GFR) in man; results are mean ± s.e.m. of (N) observations.* The groups are defined in the text. a; less than group 1, $P<0.05$; b; less than group 1, $P<0.02$, greater than practolol clearance at same time, $P<0.05$; c: less than group 3, $P<0.05$.

Group	1	2	3	4
Practolol clearance	105·4 ± 9·4 (20)	81·9a ± 7·2 (29)	103·6 ± 14·4 (8)	83·0c ± 14·4 (8)
GFR	123·9 ± 9·6 (20)	102·5b ± 5·8 (29)	—	

This work was supported by the Scottish Home and Health Department. Assistance was also received from ICI Pharmaceuticals. The work was made possible by the skilled technical assistance of Miss Rona McMillan.

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Elimination biokinetics of some topically-applied steroids

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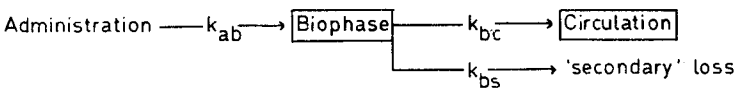
Time variation of a visible, pharmacological response may be expressed mathematically by kinetic theory and a pre-determined relationship between drug level in the receptor compartment (biophase) and observed effect. The vasoconstrictor effects of topical corticosteroids have not yet been described biokinetically.

Ten μl of ethanolic steroid solutions were applied randomly to the forearms of 10 volunteers with Betnovate cream (5 mg) as a control. Application sites were occluded for 6 h with Melinex film, washed with soap and warm water, dried gently and scored in constant lighting conditions using a 0–4 scale with half-point ratings (Barry & Woodford, 1974). Sites were read hourly from 6–13 h and 2 hly from 16–32 h, by separate trials on the same panel.

As peaks occurred in the vascostriction profiles, the biophase and central, systemic compartments were considered kinetically separate. Neglecting any effect of steroid reservoir on transfer rates, the simplest kinetic model postulated had a minimum of two compartments, although curve convexity suggested other compartments were directly communicating with the biophase.



Apparent vasoconstriction half-lives ($t_{\frac{1}{2}}' = 0{\cdot}693/K_{VC}$) were obtained from the descending, linear portion of log % total possible score' against 'time' curves. Although related,

Steroid	% concn	$K_{VC}(h^{-1})$	$t_{\frac{1}{2}}'$ (h)
Betamethasone 17-valerate	0·1 cream)	0·039	18
,,	0·1	0·042	16
,,	0·01	0·036	19
Triamcinolone acetonide	1·0	0·042	17
,,	0·1	0·041	17
,,	0·01	0·037	19
Desonide	0·1	0·037	19
,,	0·01	0·032	22

($K_{VC} = f(k_{bc} + k_{bs})$), vasoconstrictor and biophase drug level half-lives are not necessarily identical.

The 6 h occlusion period was regarded as 'lag' time, corresponding to primary saturation of steroid into membranes before adequate, biophase drug levels produced visible responses. Linearity in the post-absorptive region of the semi-log plots indicated that steroid clearance from the biophase through both systemic absorption and 'secondary' loss (e.g. enzymic bio-transformation) was under the control of apparent first order processes such as passive diffusion.

Conclusions were dependent on several main assumptions. (a) vasoconstriction grading was linear and was always directly related to biophase drug level; (b) all responses were