DEMONSTRATIONS

A buffer system at the oral mucosa—determination of intrinsic pH and buffer capacity

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Drug absorption is generally interpreted in terms of the pH-partition theory (Brodie, 1964) as diffusion of the unionized, non-protein bound species across a lipid membrane. Suzuki, Higuchi & Ho (1970) postulated an 'aqueous diffusion layer' adhering to the membrane surface. Their view is supported by findings of the buccal absorption test.

Strict application of the classical pH-partition theory allows one to calculate, for ionic drugs, a 'true rate constant of absorption' (k) to characterize the transfer of the unionized species across the membrane (Khalil & Martin, 1967). This rate constant is expected to be independent of the test pH, i.e. constant when calculated at different test pHs from the respective absorption values.

For a number of drugs in the buccal absorption test, the pH appears to exert an influence on the true rate constants. Instead of (horizontal) parallels to the abscissa, plots of log k versus pH yield straight lines with positive or negative slopes. The direction of slope depends upon whether a drug is an acid or a base.

To maintain the principle of constancy nonetheless, a buffering system at the membrane surface has to be postulated. Through local buffer action any experimental bulk pH (pH) would be changed into a corresponding effective pH (pH_{eff}) at the site of absorption. The effective pH would only equal the bulk pH when the bulk pH was identical with the intrinsic pH of the buffer system ($pH_{intr.}$).

The intrinsic pH can be determined from the fact that the buffering surface system exerts a diametrically opposite effect on acids and basis. For the absorption of *unionized* molecules across a lipid phase it should not play a role whether they are acids or bases; the unionized species of both an acid and a base are expected to be absorbed with the same true rate constant, if the partition properties into the membrane are the same. Thus it may be assumed for an acid and a base with identical partition coefficients, that at the intersection of their respective log k:pH plots, i.e. at that point on the pH-scale at which they are absorbed with the same true rate constant, the buffering system exerts no influence. This pH represents its intrinsic pH.

With the corresponding true rate constant the effective pH can be calculated for every experimental bulk pH. The gradient $\Delta pH/\Delta pH_{eff}$ is a measure of the buffer capacity of the system.

Propranolol and p-n-hexylphenylacetic acid were used as model drugs with identical partition coefficients. Their published pH-absorption data (Beckett & Moffat, 1969; Schürmann & Turner, 1977) lead to the following parameter values for the human oral mucosa: $pH_{intr} = 6.7$, $\Delta pH/\Delta pH_{eff} = 2.9$.

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