

(J) of the drug through the stratum corneum can be stated in terms of the diffusion coefficients from Eqs. 1 and 2, as follows:

$$J = (A_p D_p + A_L P D_L) C_w / L \quad [3]$$

where A_p and A_L are the area fractions of the polar and lipophilic pathways, respectively; P is the partition coefficient of the nonpolar phase; C_w is the drug's water solubility (in mg/ml); and L is the thickness of the stratum corneum (in cm). Berner and Cooper suggest that $A_p = 0.1$ and $A_L = 0.9$. The octanol/water partition coefficient is used for P , and a value of 0.0015 cm is suggested for the thickness of the stratum corneum. Using these values for the parameters, J will have the units $\text{mg}/\text{cm}^2 \cdot \text{hr}$.

Berner and Cooper have also proposed a three-parallel-pathway model (4), which combines not only the polar and lipophilic pathways, but also an oil-water multilaminate pathway (2). Use of the same values for I , D_L , D_p , and A_p as for the two-parallel-path model, and decreasing the value for A_L from 0.9 to 0.5, the equations to calculate the upper (J_{\max}^U) and lower (J_{\max}^L) bounds of the maximum flux through the stratum corneum are given in Eqs. 4 and 5. The values for J_{\max}^U and J_{\max}^L have been averaged in this evaluation to provide a single value for the three-parallel-path model.

$$J_{\max}^U = \frac{2(C_w)e^{-0.016(M)}}{15} \left\{ \frac{[85(P) + 190][38 + 153(P)]}{(228 + 238(P))} \right\} \quad [4]$$

$$J_{\max}^L = \frac{(C_w)e^{-0.016(M)}}{15} \left[85(P) + 38 + \frac{5 \times 10^{-3}(P)}{380 + 170(P)} \right] \quad [5]$$

In the heterogeneous structural model (model 3) described by Michaels and associates (5), the barrier function is treated as a dispersion of hydrophilic protein in a continuous lipid matrix through which the drug migrates by dissolution and Fickian diffusion. Given this reasonable assumption about the structure of the stratum corneum, the simplified flux equation is where P is the lipid/protein partition coefficient, which in the original paper, is set equal to the mineral oil/water partition coefficient. The octanol/water partition coefficient has also been successfully used.

$$J = 0.27(P)(C_w) \left[\frac{1160 + 3.4 \times 10^{-3}(P)}{160 + 2(P)} \right] \quad [6]$$