Table 7.4 Predicted Transdermal Flux Values for a Series of Benzodiazepines Calculated Using Experimentally Determined Partition Coefficients and Melting Points

Drug	MW	PC	Melting point (°C)	Calc. CW[a]	Calc. flux[b]
Diazepam	285	309	130	0.089	3.8
Oxazepam	287	97	205	0.044	1.0
Lorazepam	321	73	167	0.15	2.9
Temazepam	301	62	120	0.49	8.9
Desmethyldiazepam	271	54	216	0.054	0.98
Triazolam	343	48	234	0.050	0.74
Midazolam	326	43	115	0.82	11
Bromazepam	316	30	237	0.066	0.75
Chlordiazepoxide	300	28	236	0.068	0.75
Alprazolam	309	18	228	0.12	0.96
Clobazam	301	9	181	0.65	3.1

[a]Using equation for rigid polycyclic aromatic hydrocarbons in Table 3.
[b]Average of the four models ($\mu g/cm^2 \cdot hr$).
Source: PC from Ref. 24; MP from Ref. 11.

sulted in increased permeability and that major changes in molecular weight were required to produce significant differences in diffusivity (27). Although these generalities were very useful, more detailed insight into the relationship between a drug's physical properties and percutaneous permeation can be obtained by use of contour plots of the predicted flux that are plotted as a function of the partition coefficient versus water solubility at a fixed molecular weight.

Contour plots for molecular weights of 50, 100, 300, and 500 are given in Figures 1 and 2. For molecular weights of 500 to 1000, the contours were indistinguishable on this scale from the plot for molecular weight 500. As seen, for each molecular weight, the predicted flux values smoothly increase as both water solubility and partition coefficient increase. Although drugs, such as the prostaglandins and some antibiotics, have both relatively high water solubilities and partition coefficients, generally speaking, the upper