

Table 13.3 (Continued)

Derivative, R = /vehicle	Solubility ^a	$J_i^{s,v}$, ^b mg/cm ² h × 10 ³ (± SD)		log $P_i^{s,v}$, cm/h
2, R = CH ₃ /H ₂ O	0.44	1.58	(0.88)	- 2.44
3, R = C ₂ H ₅ /H ₂ O	0.25	1.97	(0.16)	- 2.11
4, R = C ₃ H ₇ /H ₂ O	0.030	0.81	(0.081)	- 1.57
5, R = C ₄ H ₉ /H ₂ O	0.0071	0.50	(0.12)	- 1.15

^aThe solubilities are given in mg equivalents of 6-MP per ml of solution.

^bSteady-state fluxes, number of cells per run = 3.

^cSource: Fluxes of 6-MP from the vehicles from Ref. 21.

bilities of the bis-derivatives in various solvents are given in Table 3 along with their respective $J_i^{s,v}$ and $P_i^{s,v}$ from the same vehicles, and the comparable data for the mono-series are given in Table 4. Plots of the calculated δ_i of the prodrugs versus their corresponding log experimental $P_i^{s,v}$ for the delivery of 6-MP by both series of prodrugs from water, isopropyl myristate (IPM), and propylene glycol (PG) are given in Figure 6.

It is clear from Figure 6 that there is a fairly good correlation between log experimental $P_i^{s,v}$ and δ_i for each series for the delivery of 6-MP from each solvent. However, the form of the relationship depends on the vehicle. For the delivery of 6-MP from IPM, as the prodrug becomes more lipophilic and more like the vehicle (i.e., the value of δ_i decreases), the log experimental $P_i^{s,v}$ decreases. Whereas for the delivery of 6-MP by the prodrugs from water, as the prodrug becomes more lipophilic and less like the vehicle, the log experimental $P_i^{s,v}$ increases. Conversely, there is not much change in the log experimental $P_i^{s,v}$ values for the delivery of 6-MP by the prodrugs from propylene glycol. This last result may be because the δ_i are not that different from that of δ_v .

The other article that has been published in this area describes the effect of the structure of *N*-Mannich base prodrugs of 5-FU and theophylline on their ability to deliver their respective parent drugs