is useful only if water is the vehicle being considered. In addition, many, if not most, of the vehicle components for which it would be useful to calculate theoretical partition coefficients are either miscible with, or at least partially soluble in, both octanol and water. These include, for example, solvents such as propanol, dimethyl sulfoxide, dimethylformamide, propylene glycol and formamide. Other solvents, such as isopropyl myristate and oleic acid, are soluble in octanol or other solvents that serve as models for biological membranes. Thus, it is virtually impossible to experimentally measure partition coefficients for model chemicals in a two-phase system that would give fragment constants that could be used to calculate theoretical partition coefficients for a drug distributing between the solvents (vehicles) of interest and skin.

For the drugs that were investigated by Sloan and co-workers (5-fluorouracil, 6-mercaptopurine, theophylline, and salicylic acid), the theoretical partition coefficients, $K_i^{s,v}$, were calculated assuming that the solubility parameter of the skin, $\delta_s$, was about 10 $(cal/cm^3)^{1/2}$ (18). The solubility parameters of the vehicles, $\delta_v$, were literature values (28) except for isopropyl myristate (19) and are listed in Table 1, whereas the solubility parameters of the drugs, $\delta_i$, and the molar volumes of the drugs, $V_i$, were calculated according to Fedors (29). These theoretical partition coefficients are given in Table 1. The experimental permeability coefficients, $P_i^{s,v}$, for the delivery of these four relatively polar molecules from vehicles exhibiting a broad spectrum of polarity, from water to oleic acid, through hairless mouse skin are also given in Table 1 along with the corresponding fluxes, $J_i^{s,v}$, and solubilities, $C_i^v$.

The values for log theoretical $K_i^{s,v}$ and log experimental $P_i^{s,v}$ for each drug are plotted against $\delta_v$ in Figures 2 through 5. In each case, the plot of the log experimental $P_i^{s,v}$ versus $\delta_v$ approximates a parabola that is similar to that of the plot of log theoretical $K_i^{s,v}$ versus $\delta_v$, except for the data obtained when octanol and isopropyl myristate (IPM) were used as vehicles. However, both of those vehicles caused a much higher flux of the standard solute–vehicle in the second application part of the experiment than did the other vehicles; therefore, it has been assumed that the inordinately high flux of drug, hence, $P_i^{s,v}$, caused by those vehicles is due to damage to the skin. If the data for these obvious outliers are disregarded, a plot of log theoretical $P_i^{s,v}$ versus $\delta_v$ can be constructed from log theoretical $P_i^{s,v}$ values, each of which can be obtained from the sum of the corresponding log theoretical $K_i^{s,v}$ and the average of the differences between the log theoretical $K_i^{s,v}$ and log