membrane (h_s) (Eq. 12). If D_i^s is independent of the vehicle used and h_s does not change much within the limits of biological variability, then D_i^s/h_s is a constant and Eq. 12 reduces to Eq. 13 (19). It has already been shown that $K_i^{s,v}$ can be calculated from Eq. 6 or 7. Thus, to determine whether or not variations in the rates of delivery of a drug from a series of vehicles can be explained by regular solution theory, it is merely necessary to plot the log calculated (theoretical) $K_i^{s,v}$ against the solubility parameters of the vehicles (δ_v), and determine if the plot of log experimental $P_i^{s,v}$ versus δ_v approximates the shape of the log theoretical $K_i^{s,v}$ versus δ_v curve and is separated from it by a constant amount (D_i^s/h_s).

$$P_i^{s,v} = K_i^{s,v}(D_i^s/h_s) \quad [12]$$

$$P_i^{s,v} = K_i^{s,v} \cdot \text{constant} \quad [13]$$

There are two reasons why it is useful to be able to calculate these theoretical partition coefficients based on regular solution theory to understand the dermal delivery process. First, from the foregoing discussion, it is obvious that if it is possible to predict $K_i^{s,v}$, it is possible to predict permeability coefficients and, hence, flux. The ability to predict the effect of changes in vehicles on the solubility of a drug in a formulation and, hence, its flux is essential for the rational design of topical formulations. Second, it is virtually impossible to obtain an accurate and appropriate experimental partition coefficient for a solute distributing between a vehicle and skin. The concentration of a drug in a vehicle is easily determined, but the concentration in the skin is difficult to quantitate because of the different degrees of changes in hydration and of changes in other physicochemical properties of the skin that would result if samples of skin were allowed to equilibrate with different vehicles for extended periods (27). Thus, a method for determining theoretical $K_i^{s,v}$ would be advantageous because there are serious difficulties in obtaining experimental $K_i^{s,v}$.

Conversely, it is possible to calculate theoretical partition coefficients using other methods. The most popular method uses fragment constants for the various functional groups in a drug to calculate the drug's distribution between water and a water-immiscible solvent that serves as a model for the biological membrane (29,30). Usually, the water-immiscible solvent is octanol, but many other water-immiscible solvents have also been used. The fragment constants for a two-phase partitioning system are derived from experimentally determined partition coefficients for model chemicals in the same two-phase system. However, by using the available data, this approach