skin. Most drugs are crystalline, and the mere rubbing of small crystals on the surface of skin will result in very poor transfer to the skin. Delivery from volatile solvents, such as ethanol and acetone, will transfer small portions of drugs into the outer layers of the skin, and the flux will quickly drop off. In fact, any transport study conducted with such solvents, will more than likely measure the dissolution rate of the drug, rather than the transport properties of skin.

B. Thermodynamic Factors

The driving force for transport is the chemical potential gradient, and within a single phase, this reduces to the concentration gradient. To create this gradient within the skin, one normally dissolves the drug in a solvent or vehicle and establishes a certain concentration of drug in the outer surface of the skin. Different vehicles can provide different concentrations of drug at this interface and, thus, the driving force and, hence, the flux will be a function of the vehicle. In general, one does not know the concentration of drug in the outer surface of the skin, but there is a simple thermodynamic relationship to compare the concentration of drug in the skin for different vehicles.

The *chemical potential* or *activity* is the continuous variable across interfaces (1) and, thus, one has the following equation at the skin–vehicle boundary:

$$a_V = a_S \qquad [1]$$

where a_V is the activity of the drug in the vehicle, and a_S is the activity of the drug in the skin (assumed to be a lipid medium for most situations). Thus, to produce equivalent activity in the skin with different vehicles, one only has to ensure equal activities in the vehicles. The activities are usually written as

$$a = \gamma C \qquad [2]$$

where γ is the activity coefficient and C is the concentration. Thus, for equivalent activity for vehicle 1 and 2, one has

$$\gamma_1 C_1 = \gamma_2 C_2$$

To estimate the concentration in vehicle 1 to give equal activity to vehicle 2, one has