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The Use of Solubility Parameters of Drug and Vehicle to Describe Skin Transport

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I. INTRODUCTION

The use of solubility parameters of drugs and vehicles to describe the transport of drugs through skin is based on the efforts of Hildebrand (1) and others (2–4) to account, in a rational way, for solvent–solvent and solute–solvent interactions in the process of dissolution. The results of those efforts to develop a theoretical basis for solubility is represented in simplified form by Eq. 1 where X_i^v is the mole fraction solubility of drug (i) in the solvent or vehicle (v), ΔH_f is the heat of fusion of the drug at its melting point, T_m is the melting point of the drug, T is the temperature at which the solubility is being measured and γ_i^v is the activity coefficient of the drug in the vehicle, which can be calculated from Eq. 2. In Eq. 2, δ_i and δ_v are the solubility parameters of the drug and vehicle, respectively, ϕ_v is the fraction of the solution volume occupied by the vehicle, and V_i is the molar volume of the drug. The calculated mole fraction solubility of the drug, then, is composed of two components; one is a contribution from its ideal solubility, the other is a contribution from its activity coefficient to take into account deviations of the actual solubility from the ideal solubility. The evolution of this approach to predicting solubility strictly from theoretical considerations of the physicochemical properties of solute and solvent (drug and vehicle) has recently been reviewed by Martin and Mauger (5).

$$-\log X_i^v = (\Delta H_f/2.3\ RT)[(T_m - T)/T_m] + \log \gamma_i^v \qquad [1]$$