Prediction of Solubilities of Pharmaceutical Compounds in Solvent + Co-solvent Systems Using a One-Parameter Activity Coefficient Model

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The solubility of drugs is extremely important to the medical field. Therefore, the solubilities in water of pharmaceutical compounds are essential properties for the pharmaceutical industry. Poorly water-soluble drugs have increased in number due to the drugs' increased molecular weight and complicated chemical structures, even though the pharmacological activities of the drugs have been enhanced. From a practical point of view the consideration of enhancing the solubility by the addition of a co-solvent is essential. In the application of drugs with high medical activity, co-solvents such as ethanol, propylene glycol, and poly ethylene glycol, are commonly used in pharmaceutical formulations in order to increase the solubility of hydrophobic drugs. Therefore, the solubilities in water of pharmaceutical compounds, and the enhancement of the solubilities by the addition of a co-solvent are important parameters in pharmaceutical processes.[1)] The development of a predictive model of solubilities for ternary systems on the basis of the constituent binary systems is useful for selecting the co-solvent. This paper deals with the prediction of solubilities of pharmaceutical compounds in solvent + co-solvent systems using a one-parameter Wilson activity coefficient model.[2)] The pharmaceutical compounds include salicylic acid, acetaminophen, benzocaine, acetanilide and phenacetin. The solvents treated are water, ethanol, ethyl acetate, methanol, 1,4-dioxane and acetone. Firstly the solubilities have been predicted using the data for binary systems only. A modification of the method is proposed in order to achieve better results, although it requires ternary solubility data.

[1] H. Matsuda, K. Kaburagi, S. Matsumoto, K. Kurihara, K. Tochigi and K. Tomono: J. Chem. Eng. Data, in press
[2] B.E. Poling, J.M. Prausnitz and J.P. O'Connell: The Properties of Gases and Liquids, 5th ed, p. 8.18, McGraw-Hill (2001)