Solubility in Solvent- Antisolvent Mixtures. A Calorimetric Study of Solid-Liquid Phase Diagrams in Ternary Systems

M.H. Hamedi
Mechanical Engineering Department, K.N. Toosi University of Technology, Tehran, Iran

J-P.E. Grolier [C, S]
Laboratory of Thermodynamics of Solutions and Polymers, Blaise Pascal University, Aubière, France
J-Pierre.Grolier@univ-bpclermont.fr

The ultimate step in crystallization engineering production line is the crystallization of a solid solute in an appropriate solvent in order to obtain an end product in the form of pure small crystals. Water-alcohol binary mixtures employed as solvent–antisolvent mixtures are certainly the most suitable liquid solvents in terms of cost and recycling feasibility. Titration calorimetry has been used to construct the solid-liquid equilibrium line in ternary systems containing a crystallized solute and an aqueous alcohol mixed solvent, by measuring the heat of dissolution of the solid solute during successive additions of the liquid solvent–antisolvent mixture. The cumulated heat plotted versus the mole ratio, nsolvent / nsolute number of moles of solvent over number of moles of solute, gives two practically straight lines. The intersection of the two lines yields the solubility and the enthalpy of dissolution of the solute. Phase diagrams have been established over the whole concentration range for different components of interest in pharmaceutical industry, such as for example urea, phenyl urea, caffeine, nicotinamide, nicotinic acid, salicylic acid in water methanol, ethanol, or n-propanol at 303, 313 and 318 K.

From this study general conclusions can be drawn: i) influence of the chemical structure of the solute on its solubility, ii) distinct influence of temperature on the solubilization, iii) isothermal titration calorimetry can be recommended as a convenient technique to obtain non only a qualitative description of solid-liquid phase diagrams in ternary systems, but also precise concentrations of the components along the solid-liquid line. The fitting equations developed to represent this line can be used for engineering calculations.

[1] M.H. Hamedi, B. Laurent, J-P.E. Grolier, Construction of solid-liquid phase diagrams, Titration Calorimetry, *Thermochimica Acta*, in press (2006).
[2] F. Dan, M.H. Hamedi, J-P.E. Grolier, New developments and applications in titration calorimetry and reaction calorimetry, *J. Therm. Anal. Cal.*, in press (2006).