Calorimetric Studies on Diclofenac Sodium, Diclofenac, and Sodium Bicarbonate Mixtures

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In a previous work [1], the sodium salt of 2-[(2,6-dichlorophenyl)amino]benzeneacetic acid (diclofenac sodium, DCLNa) was chosen as model drug to comparatively study the solubility in supercritical carbon dioxide (SC-CO_2) of the tetrahydrate and the anhydrous form. The differential scanning calorimetry (DSC) trace of untreated DCLNa showed an endothermic peak in the 313-333 K range (assigned to water removal by thermogravimetry), followed, above 533 K, by complex exo-endo phenomena, mainly due to decomposition. The DSC patterns of the solid phases recovered after SC-CO_2 treatment evidenced a series of thermal events between 373 and 443 K. This peculiar behavior was attributed to possible reaction taking place among DCLNa, SC-CO_2, crystal water (in the case of DCLNa $4H_2O$) or surfacial moisture (when the anhydrous form was involved), leading to the formation of diclofenac (DCLH) and $NaHCO_3$. For this reason, inside the extractor vessel, mixtures of DCLNa (unreacted), DCLH and $NaHCO_3$, in different proportions depending on the varying operative conditions, were present. To achieve a thorough comprehension of the thermal phenomena shown by this multicomponent system, DSC analyses of the single components and of the possible binary mixtures were carried out.

The exo/endothermic events and the relevant parameters shown by the DSC traces of the DCLNa/DCLH mixtures were used to draw the phase diagram of the binary mixture. A satisfactory agreement between the theoretical liquidus curves (calculated using a simplified form of the Schroder-Van Laar equation [2]) and the experimental points was found. The phase diagram of the DCLNa/DCLH binary system showed the presence of a eutectic at 426 K. Thermal events at higher temperatures proved to be of much more difficult interpretation due to massive decomposition phenomena [3].

[1] R. Bettini, G. Bertolini, E. Frigo, A. Rossi, I. Casini, I. Pasquali and F. Giordano, *J. Thermal Anal. Cal.* **77**, 625 (2004).
[2] J.T. Carstensen, *Advanced Pharmaceutical Solids: Melting point depressions and purity assessment by the Van Laar equation,* p. 171, Marcel Dekker Ed., New York 2001.
[3] F. Giordano, A. Rossi, I. Pasquali, R. Bettini, A. Gazzaniga, V. Mileo, S. Catinella, *J. Thermal Anal. Cal.* **73**, 509 (2003).