Preparation and characterization of niacinamide-ethylparaben interaction compound

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Aim

To investigate the solid-state characteristics of the niacinamide (NA)-ethylparaben (EP) interaction compound obtained by re-crystallization from the melt or solutions.

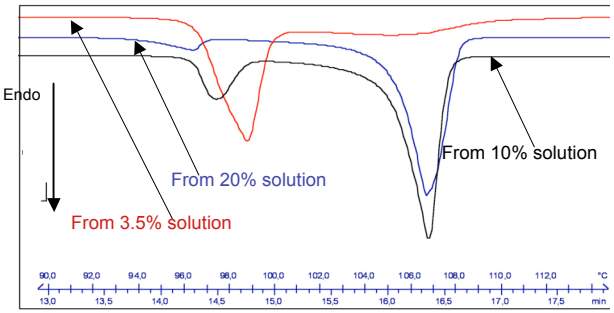
Methods

The solid phases obtained by fusion, recrystallization from ethanol or precipitation from aqueous solutions of EP/NA mixtures were analyzed by means of differential scanning calorimetry (DSC), hot stage microscopy, powder X-ray diffraction (PXRD) and CHN elemental analysis. Re-crystallization was carried out by slowly evaporating an EP:NA ethanol solution. Phase solubility experiments, according to Higuchi and Connors, were performed by equilibrating an excess of EP with NA aqueous solutions (from 0 to 20% w/v) at 25 °C. The EP concentration of the solutions was determined by HPLC and the relevant phase solubility diagram was drawn; the recovered precipitates were submitted to solid-state analysis. Finally, the liquidus curves calculated with the Schroeder-Van Laar equation (1) were compared with the experimental temperature values.

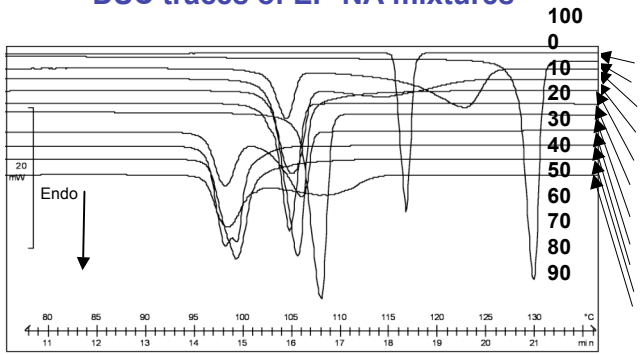
RESULTS

EP solubility in water was slightly depressed by NA; only in the 20% w/v NA solution a two-fold increase of EP solubility was observed (see poster # T2122).

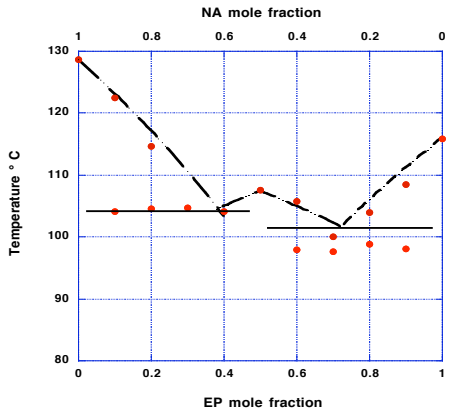
DSC traces of recovered precipitates



DSC traces of EP-NA mixtures



Binary diagrams from experimental points and theoretical liquidus curves calculated from the simplified form of the Schroeder-Van Laar equation



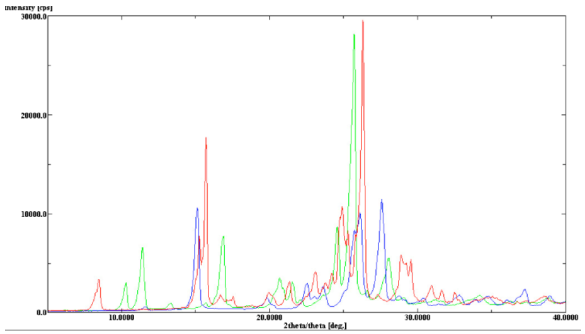
$$\ln x = \frac{\Delta H_f^A}{R}\left(\frac{1}{T_f^A} - \frac{1}{T_f}\right)$$

x is the mole fraction of the more abundant component of a mixture whose melting terminates at T_f; ΔH^A_f and T^A_f are the enthalpy of fusion and melting point of the pure component, respectively, and R is the gas constant

Elemental Analysis (%)

	Theoretical for 1:1 mole composition	Actual
C	62.5	62.7
H	5.6	5.6
N	9.7	9.5

PXRD on EP, NA and 1:1 recrystallised Interaction Compound



Conclusions

- EP and NA form a co-crystal having a 1:1 mole:mole composition.
- This compound has lower water solubility with respect to each component.
- It crystallizes from ethanol and precipitate in aqueous solutions at ambient temperature.

Reference [1] J.T. Carstensen, Advanced Pharmaceutical Solids, Marcel Dekker, New York 2001, p. 171