



Thermodynamic Analysis of the Solubility of Propranolol-HCl in Ethanol + Water Mixtures

Daniel R. DELGADO & Fleming MARTÍNEZ *

*Grupo de Investigaciones Farmacéutico-Fisicoquímicas,
Departamento de Farmacia, Facultad de Ciencias,
Universidad Nacional de Colombia, A.A. 14490, Bogotá D.C., Colombia.*

SUMMARY. Propranolol-HCl (PPN-HCl) is a non selective β -adrenergic blocker widely used in therapeutics. Nevertheless, their physicochemical properties in aqueous media have not been adequately studied. In this context, by using the van't Hoff and Gibbs equations the thermodynamic functions Gibbs energy, enthalpy, and entropy of solution for this drug in ethanol (EtOH) + water (W) cosolvent mixtures, were evaluated from solubility data determined at several temperatures. The solubility was the greatest in the mixtures with 0.60 or 0.70 in mass fraction of EtOH and the lowest in neat W (or neat EtOH, as well) at almost all the temperatures studied. This behavior shows the cosolvent effect present for this electrolyte drug in this solvent system. By means of enthalpy-entropy compensation analysis, non-linear $\Delta H_{\text{soln}}^{0-\text{app}}$ vs. $\Delta G_{\text{soln}}^{0-\text{app}}$ plot with negative slope from water up to 0.10 in mass fraction of EtOH and positive slope from 0.10 to 0.60 in mass fraction of EtOH. Accordingly to this result, it follows that the dominant mechanism for the solubility of PPN-HCl in water-rich mixtures is the entropy, probably due to water-structure loosening around the drug's non-polar moieties by EtOH molecules, whereas, between 0.10 and 0.60 in mass fraction of EtOH the dominant mechanism is the enthalpy probably due to drug solvation increase by EtOH molecules. Ultimately, beyond this composition the behavior was more complex, and therefore, the ionic and molecular events involved in the drug dissolution in ethanol-rich mixtures are unclear.

KEY WORDS: Cosolvency, Ethanol, Solubility, Solution thermodynamics, Propranolol-HCl.

* Author to whom correspondence should be addressed. *E-mail:* fmartinezr@unal.edu.co