Research in Pharmaceutical Sciences, 2012;7(5)
School of Pharmacy and Pharmaceutical Sciences
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Thermodynamic studies of ketoconazol solubility in water + ethanol mixtures at different temperatures

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Background and Aims: Solubility data of drugs is required in developing synthesize, extraction and crystallization media and formulation as an oral or parenteral solution. Therefore, Solubility is one of the important physicochemical properties in drug discovery and development. The cosolvency (solvent mixing) is the most common technique to increase the aqueous solubility of drugs. Ethanol is one of the common cosolvents which, are used in the pharmaceutical industry. Ketoconazole (KTCZ) is a highly effective broadspectrum antifungal agents. In this study solubility of KTCZ in water + ethanol mixtures at various temperatures were investigated along correlation and prediction of solubility data using different cosolvency and thermodynamic models.
Methods: The solubility of KTCZ in water + ethanol mixtures were determined at 298.2 ,303.2 ,308.2 and 313.2 K after reaching the equilibrium condition, the saturated solutions were filtered, then diluted and samples were analysed by UV-spectrophotometer at 244 nm. Data is used to calculate thermodynamic properties and the prediciton capability of different cosolvency models were compared.
Results: The solubility of KTCZ in binary water + ethanol mixtures at 298.2 ,303.2 ,308.2 ,313.2 K is increased in ethanol concentration reached the maximum value and then decrease with further increase in ethanol concentration. The Gibbs energy, enthalpy, and entropy of solution and of mixing were computed using the generated solubility data. Thermodynamic properties show the dissolution mechanism of KTCZ in water + ethanol mixtures and data is correlated and predicted within an acceptable error range.
Conclusions: Mixing solvents of water + ethanol mixtures to create a solvent system can be used to increase the solubility of ketoconazol and thermodynamic data is useful tool to study of cosolvency mechanism in pharmaceutical engneering and industry.

Keywords: Ketoconazol; Solubility; Cosolvency; Thermodynamic; Modeling