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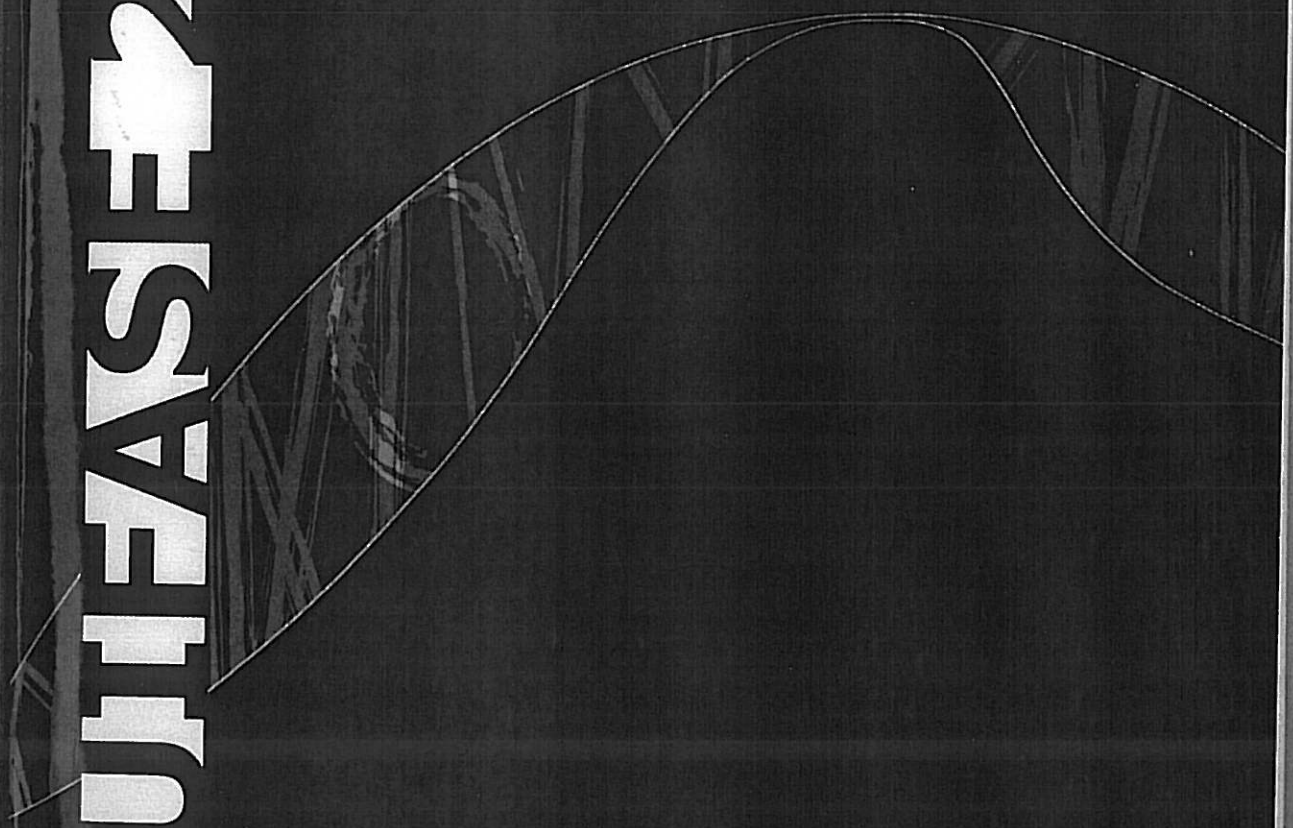

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Temperature and Solvent Effects in the Solubility of Some Drugs: Experimental and Modeling

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New drugs are always appearing during the development of new therapies or the improvement of existing ones. The effects of these drugs in the organism are dependent on the techniques used by the pharmaceutical industry to make them more soluble [1]. Solubility data involving new drug candidates are frequently not available in the open literature and, although predictive thermodynamic models can be used, the availability of experimental data is still fundamental for an appropriate model development and evaluation. One of the most recent and successful models is the Nonrandom Two Liquid Segment Activity Coefficient (NRTL-SAC) model [2-5], which gives reasonable results in the prediction of drug solubilities and has been widely applied to correlate and predict phase equilibria of highly nonideal systems, both in pure and mixed systems, both at academic and industrial level.

In this work, solubilities of four pharmaceutical compounds were addressed, namely paracetamol, allopurinol, budesonide and furosemide [5]. These drugs with specific therapeutic effects have different functional groups leading to multiple interactions with solvents. The selection of solvents was made to cover several types of surface interaction characteristics. Aqueous solubilities were measured between 298.2 and 315.2 K and, solubilities in acetone, carbon tetrachloride, ethanol, ethyl acetate and n-hexane were measured at 298.2, 310.2 and 313.2 K. The analytical shake-flask method was used to generate the saturated solutions followed by composition analysis by HPLC. Melting properties were measured by differential scanning calorimetry or predicted by a group-contribution method [6], if the substance decomposes before melting. These properties provide a broader understanding about the solubilization process and are required for modeling purposes. Solubility data as function of temperature were also used to determine the properties of dissolution like Gibbs energy, enthalpy and entropy. For modeling purposes the NRTL-SAC model was applied in the correlation of the experimental drug solubilities in organic solvents, and the same fitted drug parameters used to predict their solubility in water and mixed solvents. The results obtained were very satisfactory.

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