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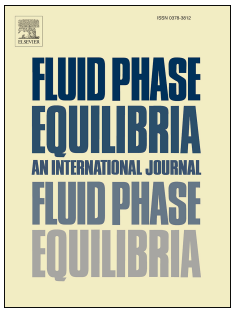

A junction between molecular dynamics simulation and local composition models for computation of solid-liquid equilibrium-A pharmaceutical solubility application

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A Junction between Molecular Dynamics Simulation and Local Composition Models for Computation of Solid-Liquid Equilibrium-A Pharmaceutical Solubility Application

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ABSTRACT

A connection is established between molecular level phenomena (molecular dynamics simulation) and macroscopic properties to obtain the solubility of solutes in a solvent. Condensed phase Optimized Molecular Potential for Atomistic Simulation Studies (COMPASS) was applied as a force field in Molecular Dynamics (MD) simulation. Radial distribution function (RDF) is used to calculate the interaction parameters of the local composition (LC) activity coefficient models, so that a specific range of RDF was considered. Using the present approach, the solubility of pharmaceuticals in the various solvents are calculated and compared with the experiment. The results demonstrate that the interaction parameters are radius dependent, but from engineering and practical point of view, the averaged interaction parameters are used in calculation of solid-liquid equilibrium. The upper limits of the integral for the average interaction parameters are determined at the specified radius which the slope of its tangent was zero. The important feature of the present study is that using RDF through MD simulation gives a pair of interaction parameter that could well predict the experimental solubility data. To validate the present method, the solubility of pharmaceutical solutes such as aspirin, acetaminophen, defriprone, and ephedrine were simulated in the selected solvents at 298.15 K and 1 atm. Thus, the MD simulations of these pharmaceutical systems are simulated and their RDFs are obtained to calculate the energy parameters of the LC models so that their solubility in a given solvent are calculated. The calculated solubility

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