論文の要旨

題 目 A novel approach to estimate the solubilities of non-steroidal anti-inflammatory drugs (NSAIDs) in supercritical carbon dioxide by PC-SAFT equation of state
(PC-SAFT 状態式による超臨界二酸化炭素中の非ステロイド性抗炎症薬(NSAIDs)の溶解度推算に向けた新規手法)

氏 名 Mahmoud Magdy Mahmoud Sadek Abdelazim

Supercritical carbon dioxide holds several advantages over conventional solvents such as being in-toxic, non-flammable, non-polar, and available solvent. It also has mild critical temperature and pressure, low surface tension, and low viscosity and is easy to remove and recycle making it an environmentally friendly material. Owing to these characteristics, supercritical carbon dioxide has found applications in the pharmaceutical industry such as in particle formation, recrystallization, adsorption processes, and the production of sustained delivery devices for controlled release applications.

The knowledge of solubility data is fundamental to understanding any industrial process that employs supercritical carbon dioxide. However, the study of solubility is challenging due to multiple obstacles like the difficulty of conducting the necessary experimental work owing to high cost, the huge number of pharmaceutical materials involved, and their complex structural formula, in addition to their thermal sensitivity that leads to their degradation at high temperatures. Thermodynamic modeling is also challenging due to the limited experimental data present in literature, and the limitations of the popular modeling approaches as they either require experimental solubility data or prior knowledge of the values of some physicochemical properties of the drugs that are hard to measure.

In this study, we suggest a novel thermodynamic method to investigate the solubility of pharmaceutical compounds in supercritical carbon dioxide that combines both

experimental and simulation work. This method uses the perturbed chain statistical associating fluid theory (PC-SAFT) which has higher predictive potential than the commonly used methods that employ cubic equations of state or semi-empirical density equations. The values of the needed three pure component parameters for the investigated drugs are determined using the more readily available and easier-to-measure solubility data in organic solvents. After then, these parameters are used to estimate the solubility of three model non-steroidal anti-inflammatory drugs (ibuprofen, ketoprofen, and salsalate) in supercritical carbon dioxide.

Calculations with PC-SAFT were performed over an extended range of pressures and temperatures for each of the investigated drugs with the binary interaction parameter k_{ij} once set to zero, and once used as an additional adjustable parameter. It was found that PC-SAFT was able to reproduce the experimental values satisfactorily. Additionally, a generalized equation for k_{ij} was derived and then used successfully to describe the isobaric solubility of the studied drugs in supercritical carbon dioxide.