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ORIGINAL PAPER

Solubility and micronisation of phenacetin in supercritical carbon dioxide

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The rapid expansion of a supercritical solution (RESS) process represents an attractive prospect for producing sub-micron and nano-particles of medical compounds with low solubility. The solubility of phenacetin in supercritical carbon dioxide was measured by the analytical-isothermal method at pressures ranging from 9.0 MPa to 30.0 MPa and temperatures ranging from 308.0 K to 328.0 K. The results show that the mole fraction solubility of phenacetin in supercritical carbon dioxide is up to 10^{-5}. Four density-based semi-empirical models were introduced to correlate the experimental data. Agreement between the model predictions and experimental data is greater with the Adachi–Lu-modified Chrastil model than with the Chrastil model, Méndez-Santiago–Teja model, and the Bartle model and the average absolute relative deviation (AARD) observed is 0.0483. The preparation of fine phenacetin particles by the RESS process under different conditions of extraction temperatures (308.0–328.0 K), extraction pressures (9.0–30.0 MPa), nozzle temperatures (373.0–393.0 K), nozzle diameters (0.1–0.8 mm), and collection distance (20.0–40.0 mm) was investigated. The size and morphology of the resultant particles were analysed by SEM. A remarkable modification in size and morphology can be obtained by condition-optimisation.

Keywords: RESS, micronisation, phenacetin, solubility, solubility models

Introduction

With ever greater emphasis being placed on environmental protection in the chemical process, and increasing demand for more advanced and safer products, supercritical fluids technologies have been widely investigated for use in industrial applications such as ceramics, catalysis, and pharmaceuticals (Cocero et al., 2009; Dohrn et al., 2010; Fages et al., 2004). In recent years, the applications of supercritical fluids technologies in the controlled production of fine drug powders with the requisite physical and surface properties for delivery have attracted considerable attention in the pharmaceutical industry (Kawashima, 2001; Kawakami, 2012; Tong et al., 2002; Yasuji et al., 2012). Many new technologies based on the use of supercritical fluids to obtain fine particles were investigated, such as SAS (Supercritical anti-solvent), SAA (Supercritical-assisted atomisation), GAS (Gas anti-solvent), ASES (Aerosol solvent extraction system), and RESS (Rapid expansion of supercritical solutions) (Fages et al., 2004; Jung & Perrut, 2001). Due to the attractive advantages offered by the RESS process, such as products without residual solvents, controllable particle size and mild operating conditions, the RESS process has been widely applied to the micronisation of drug particles. Precipitation from a supercritical solution as one of the basic mechanisms for material processing is often limited by the solute solubility (Palakodaty & York, 1999). To study these technologies, knowledge of the equilibrium solubility of the solute in the supercritical fluids is required. Many data on the solubility of pharmaceutical compounds in supercritical carbon dioxide have been reported (Lucien

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