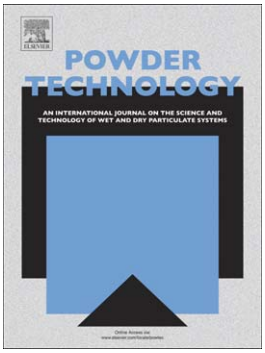

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Palmitoylethanolamide sub-micronization using fast precipitation followed by supercritical fluids extraction

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Abstract

Sub-micronization of palmitoylethanolamide (PEA) was successfully performed using fast precipitation coupled with supercritical fluid extraction. Different solvents were tested: acetone, ethyl acetate, isopropanol, dimethyl sulfoxide and ethanol; water was used as the antisolvent. PEA precipitated in all cases as crystals of hexagonal morphology. The best result in terms of control of dimension of the crystals was obtained using ethanol as solvent. Moreover, varying the concentration of PEA in the solution from 5 to 9 mg/mL, it was observed an increase of crystal dimensions. The effect of other process parameters, such as the solvent/antisolvent ratio and the concentration of surfactant in the antisolvent phase, was investigated to better control the crystallization process. Micronized crystals with controlled and regular dimensions (about 1 µm) and nanometric thickness (about 100 nm) were obtained at the optimized process conditions. A mass reduction of PEA particles of about ten times was obtained with respect to jet milling micronized particles.

The supercritical extraction process, performed at 120 bar, 44 °C and at a liquid to gas ratio of 0.05, allowed the selective extraction of ethanol from the water suspensions with a final solvent residue of 88 ppm; i.e. well below the pharmacopeia limit. Particles characterization was also performed using X-ray diffraction, differential scanning calorimetry and Fourier transform infrared spectroscopy. PEA fast precipitated particles were characterized by a reduced degree of crystallinity with respect to unprocessed PEA.

Keywords: palmitoylethanolamide, micronization, antisolvent, supercritical fluids

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