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Supercritical Antisolvent Precipitation Process

Fundamentals, Applications and Perspectives

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Introduction

The use of supercritical fluids has emerged in different fields. Supercritical fluid technologies to precipitate target compounds offer several advantages over conventional ones, such as low energy requirements, low thermal and chemical degradation of products, and the production of solvent-free particles with narrow size distributions. Microparticles and nanoparticles can be formed directly from substance solutions in a single-step supercritical fluid process based on its use as an antisolvent. This could be an excellent alternative since milling, grinding, and crushing process can lead to contamination of the product, batch variation, downstream processing difficulties, degradation of heat-sensitive materials during grinding, chemical degradation due to exposure to the atmosphere, long processing times, and high energy consumption. Thus, this book provides deep insights into the fundamentals, applications, and perspectives of the supercritical antisolvent (SAS) precipitation, and correlated processes.

Chapter 1, entitled “A Detailed Design and Construction of a Supercritical Antisolvent Precipitation Equipment,” presents the key procedures on the building of SAS precipitation equipment, besides the evaluation of the parts' acquisition costs, and the stages of construction along with the importance of each component in the equipment. An equipment design was presented as a result of the current work that serve as a basis for consulting future works on the development of new SAS precipitation equipment.

Chapter 2, entitled “Effect of Process Conditions on the Morphological Characteristics of Particles Obtained by Supercritical Antisolvent Precipitation,” presents experimental results regarding the validation of the supercritical particle formation equipment, designed and constructed by our research group, which was described in Chap. 3. It was validated using supercritical CO_2 as an antisolvent and Ibuprofen sodium salt as substance. Ethanol was used as solvent, and the effect of the operating conditions on the precipitation yield, residual organic solvent content, and particle morphology was evaluated using a split-plot experimental design and the analysis of variance (ANOVA) method.

Chapter 3, entitled “Recent Developments in Particle Formation with Supercritical Fluid Extraction of Emulsions Process for Encapsulation,” discusses another variant of the SAS precipitation process called Supercritical Fluid Extraction of Emulsions (SFEE). SFEE is a strategy to process natural target compounds, because it is suitable to encapsulate poorly water-soluble drugs in an aqueous suspension, providing products with controlled particle size and increased shelf life. The rapid extraction of organic solvent favored by SFEE causes supersaturation of dispersed organic phase, which favors the precipitation of target compounds encapsulated by the polymers and surfactants. Recent reviewed data (2016 to 2018) on the feasibility of SFEE to encapsulate compounds of great interest to the food and non-food industry were provided in this chapter.

The Chap. 4, entitled "Precipitation of Particles Using Combined High Turbulence Extraction Assisted by Ultrasound and Supercritical Antisolvent Fractionation" proposes for the first time the use of combined High Turbulence Extraction Assisted by Ultrasound (HTEAU) and Supercritical Antisolvent Fractionation (SAF) of semi-defatted annatto seeds (model raw material plant) on the possibility to obtain particles with enhanced bixin and total phenolic content. The HTEAU combines two types of commercial equipments and technologies. The first is the ULTRA-TURRAX® rotor–stator technology, which produces high turbulence in the plant material bed by high extracting solvent circulation flow rate (until 2000 cm^3/min), and the second is ultrasound technology, which is recognized to improve the extraction rate by the increasing the mass transfer and possible rupture of cell wall due the formation of microcavities. The SAF produces particles with increased composition of target compounds, by the removal of solvent from the actives solution with the use of supercritical carbon dioxide as antisolvent.

Extending the new proposed designs of SAS precipitation-based process, Chap. 5, entitled "Supercritical Fluid Extraction of Emulsion Obtained by Ultrasound Emulsification Assisted by Nitrogen Hydrostatic Pressure Using Novel Biosurfactant," shows experimental results regarding the process that we named Ultrasound Emulsification Assisted by Nitrogen Hydrostatic Pressure (UEANHP), during the emulsification preparation step of the Supercritical Fluid Extraction of Emulsions (SFEE) process, one of the options of the SAS precipitation-based process. Thus in this work, first it was evaluated the influence of hydrostatic pressure levels (up to 10 bars applying nitrogen), oily phase type, and surfactant type was evaluated. In addition, the effect of an alternative biosurfactant based on saponin-rich extract obtained from Brazilian Ginseng (*Pfaffia glomerata*) roots using hot pressurized water as extracting solvent was also evaluated to further processing of this emulsion by Supercritical Fluid Extraction of Emulsions (SFEE) process, using an oily bixin-rich extract from annatto seeds (*Bixa orellana* L.) as core material (extracting solution from pressurized hot ethyl acetate extraction).

Finally, Chap. 6, entitled "Economical Effects of Supercritical Antisolvent Precipitation Process Conditions," presents simulation results regarding of the effects of several operational parameters (pressure, temperature, CO_2 flow rate, solution flow rate, injector type, and concentration of solute in the ethanol solution) during supercritical antisolvent (SAS) precipitation process on the energy consumption cost per unit of manufactured product. For this study, Ibuprofen sodium salt, as in Chap. 3, was used as a model solute and CO_2 was used as antisolvent.

Focusing on energy saving, an SAS precipitation process was simulated using the SuperPro Designer simulation platform. The effect of temperature versus concentration of ethanolic solution and pressure versus solution flow rate interactions on the energy consumption cost per unit of manufactured product was demonstrated. Thus, the present work reports a systematic energetic-economic study of the supercritical antisolvent micronization process, aiming to increase knowledge about this process and its further incorporation by the food and pharmaceutical industries.

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