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Continuous supercritical fluid extraction of emulsions to produce nanocapsules of vitamin E in polycaprolactone

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ABSTRACT

Vitamin E in polycaprolactone nanoparticles was continuously produced by supercritical fluid extraction of emulsions using a high-pressure packing column in countercurrent mode. This operating mode reduces the amount of solvent required, increases production capacity and enables lower residual organic solvent concentrations in the raffinate. At 8.0 MPa and 313 K, with a packing height of 2 m, and a solvent to feed ratio of 5 kg L^{-1}, the residual acetone concentration was 1400 ppm, far below 5000 ppm, and therefore suitable for pharmaceutical applications. The process was also simulated with Aspen Plus. It would be necessary to increase the packing height to 3.5 m or the CO_2 flow rate to 60 g min^{-1} in order to get a residual acetone concentration suitable for food applications (50 ppm). The nanoparticles produced were non-aggregated spheres, which had an encapsulation efficiency higher than 70% and particle size at the nanoscale.

1. Introduction

Supercritical fluid extraction of emulsions (SFEE) is a novel encapsulation technology [1] that combines conventional emulsion processes with the unique properties of supercritical fluids to produce tailored micro- and nanoparticles. The basis of this process relies on the use of supercritical CO_2 to rapidly extract the organic phase of an emulsion in which a bioactive compound and its coating polymer have been previously dissolved. By removing the solvent, both compounds precipitate, generating a suspension of particles in water. The produced particles have controlled size and morphology [1], due to the use of the emulsion and to the fast kinetics of the supercritical CO_2 extraction. Particle agglomeration in the aqueous phase is avoided since the particles are stabilized by a surfactant. In addition, this technology is very versatile. It is possible to encapsulate hydrophilic and lipophilic compounds by changing the starting emulsion. An oil-in-water (O/W) emulsion can be used to encapsulate lipophilic compounds, while a water-in-oil-in-water (W/O/W) emulsion can be used to encapsulate hydrophilic compounds.

In an earlier work, we have investigated the encapsulation of the vitamin E in polycaprolactone using this technology in a batch apparatus at lab scale [2]. Yielded particles had very high encapsulation efficiency (around 90%), narrow particle size distribution (polydispersity index was between 0.24 and 0.54) and sizes at the nanoscale (between 8 and 276 nm). Morphology analysis showed that they were true spherical nanocapsules and they were non-aggregated. Stability testing showed that they remained unchangeable even at long storage times (6 and 12 months).

Such promising results made it interesting to scale-up the technology. Earlier studies have demonstrated that this process is easily scalable by means of a high-pressure packing column operating in countercurrent mode [3,4]. The supercritical extraction process of liquid mixtures in countercurrent packed columns has some resemblance to gas–liquid extraction processes due to the gas-like transport properties of supercritical fluids and to the liquid–liquid extraction processes, because of its liquid-like density [5]. The high-pressure packing column provides certain advantages over other gas–liquid extraction equipment, bubble columns or spray columns, such as the increase in mass transfer efficiency due to the presence of the packing, which provides a tortuous path for the dispersed phase [6]. In addition, the countercurrent operation in a separation device reduces the amount of solvent required, increases production capacity and enables higher extract concentrations in the solvent and lower residual concentrations in the raffinate than a cocurrent or crosscurrent operation does [7].

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Table 1
Composition and density of the two formulations used in the study.

Sample	Water (g)	Tween 80 (g)	Acetone (g)	PCL (g)	Vitamin E (g)	Density (kg m^{-3})
A	716	0.71	284	1.78	1.44	930
B	800	100	100	1.78	1.44	970

There is an extensive knowledge of the fundamentals of the liquid-supercritical fluid extraction in a packed column [8]. However, published data on the performance of packed columns applied to supercritical fluid extraction of liquid mixtures at large scales are limited, although this information is essential for a successful design and operation of such contactors [5]. The design and optimization of operating variables requires fundamental data on phase equilibria, mass transfer and hydrodynamics of the packed column [9].

The aim of this work was to study the SFEE process in continuous operation using a high-pressure packing column to produce nanocapsules of vitamin E in PCL. First, the hydrodynamics of the column were studied as well as its dependence on the density difference between phases, and on the solvent to feed ratio. Secondly, the best operating conditions were determined in order to maximize acetone extraction. Thirdly, nanocapsules of vitamin E were produced using two formulations with different colloid size. Nanoparticle characteristics were studied in terms of encapsulation efficiency, particle size distribution, residual acetone concentration and morphology. Finally, the process was simulated with a commercial process simulator, Aspen Plus, in order to evaluate the performance of supercritical CO_2 extraction on acetone removal.

2. Materials and methods

2.1. Materials

Vitamin E (α-tocopherol, ≥95%), polycaprolactone (PCL) (MW = 10,000), Tween 80 (polyoxyethylene (20) sorbitan monooleate), and acetone (≥99.5% (GC)) were all from Sigma Aldrich. Acetonitrile (gradient 240 nm/far UV HPLC grade) was from Scharlab. Sodium phosphotungstic acid solution (1%) was from Panreac. Carbon dioxide (99.98%) was from Air Liquide. All materials were used as received. Millipore water was used throughout the study.

2.2. Preparation of the starting emulsions

The system for the encapsulation of vitamin E consisted of acetone, water, Tween 80 as a surfactant, and PCL as the encapsulating polymer. PCL and vitamin E were dissolved in acetone. The aqueous phase was prepared by dissolving Tween 80 in water. The organic phase was added dropwise to the aqueous phase using a peristaltic pump (Masterflex 7524-10, Cole-Palmer) and stirred with a high speed homogenizer at 9500 rpm (Ultraturrax T-25, IKA) for 10 min to guarantee a homogeneous dispersion. Two formulations with a different colloid size were used. Compositions of these two formulations are shown in Table 1 and were taken from [2].

Although acetone is completely water-miscible, the presence of vitamin E increased the viscosity of the organic phase, allowing the formation of stable emulsions. When PCL was also present in the organic phase, the slow diffusion of the acetone into the water initiated PCL precipitation; however, particles were not formed until acetone was extracted by the supercritical CO_2 [2].

2.3. Installation description

The apparatus consisted of a 3 m long column with an internal diameter of 0.03 m, packed with random stainless steel packing (1889 m^{-1} specific surface, 0.94 of voidage; Propak, Canon Instrument Company). Two high-pressure pumps (Thar-SCF CO_2 Pump P-50) were used to deliver the aqueous solution and fresh supercritical CO_2 to the column, countercurrently. Supercritical CO_2 was preheated in a heat exchanger (Thar SFC) before entering the extraction column from the bottom. The temperature inside the column was controlled by eight heating jackets and recorded within ±0.1 K through the use of two type T thermocouples inside the column. The pressure inside the column was controlled by an automated BPR within ±0.1 MPa and read via the computer control system. CO_2 and the extract were depressurized down to atmospheric pressure in a separator and the gas stream was vented in the hood. CO_2 was not recycled. A scheme of this equipment is shown in Fig. 1.

2.4. Determination of the hydrodynamic behavior of the column

The maximum flow rate for the light and dense phases was determined as follows. The column was first preheated. The packing of the column was then wetted with a solution of water and surfactant with the same concentrations as the aqueous phase of the starting emulsion. Afterwards, the column was pressurized with CO_2, the BPR was opened and the CO_2 flow rate was adjusted. A synthetic mixture of acetone–water of the same composition as in the starting emulsion was used as the dense phase, since no significant difference was observed between the densities and viscosities of the emulsion and the acetone–water mixture. At a fixed operating pressure and temperature, and CO_2 flow rate, liquid flow rate ranged between 1 and 10 mL min^{-1}. Then, CO_2 flow rate was increased from 10 to 30 g min^{-1}. CO_2 density ranged between 280 and 630 kg m^{-3} by changing the pressure and temperature between 8.0 and 8.5 MPa and between 305.5 and 313 K, respectively. The maximum flow rate that produced entrainment was identified when water was found in the separator. Flooding was identified when no raffinate was withdrawn from the column.

2.5. Nanoparticle production

First, the column was preheated and wetted as explained earlier. Then, operation was carried out in countercurrent mode, with the emulsion entering near the top of the column, and the supercritical carbon dioxide entering near the bottom. The light phase (mainly CO_2 and acetone) was removed from the top. The nanoparticle suspension was recovered by opening a needle valve at the bottom of the column at constant time intervals to keep the level of the dense phase inside the column constant. It was necessary to wait until steady state was reached to take a sample of the nanoparticle suspension. Each experiment ended when a sufficient amount of raffinate had been recovered. Samples were stored in the refrigerator until analysis.

2.6. Product characterization

2.6.1. Encapsulation efficiency

The encapsulation efficiency was determined as the percentage of vitamin E entrapped in the particle. It was calculated by Eq. (1).

$$\text{Encapsulation efficiency } (\%) = \frac{T_E - F_E}{T_E} \times 100 \quad (1)$$

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