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Formation of hollow solid lipid micro- and nanoparticles using supercritical carbon dioxide

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ABSTRACT

Hollow solid lipid micro- and nanoparticles were formed from fully hydrogenated soybean oil (FHSO) using atomization of the carbon dioxide (CO_2)-expanded lipid. Melting point of FHSO decreased from 68.5 °C to 57 °C (0.096 °C/bar) above 120 bar in pressurized CO_2. Processing conditions of 50 μm nozzle diameter and 200 bar CO_2 pressure yielded smaller ($d_{50\%}$ = 278 nm) hollow solid lipid particles. Increasing nozzle diameter and pressure affected the particle morphology and size negatively. Shell thickness of the particles decreased with increasing pressure at the same nozzle diameter. Decreasing the nozzle diameter yielded the polymorphism of the particles from β to α. Melting point of the particles shifted to a lower melting range and broadened the melting range compared to FHSO. The results showed that the reported supercritical CO_2-assisted atomization process is a promising method to form hollow solid lipid micro- and nanoparticles to develop bioactive delivery systems.

1. Introduction

The growing pursuit of natural and "green" consumerism along with the increase of prevalence in diet-related illnesses such as obesity, type-2 diabetes, cardiovascular disease and cancer have led the food industry prioritize the development of health and wellness promoting foods by incorporating bioactive components into foods and beverages. A number of researches have verified that by incorporating functional ingredients into consumers' daily diet could have a significant positive effect on health promotion as well as relief of the above-mentioned illnesses (Qin et al., 2004; Shu et al., 2009; Bradford and Awad, 2007). However, many bioactives are lipophilic, resulting in poor water solubility that requires extra processes such as emulsification to make their addition into water possible, and result in poor absorption through gastrointestinal tract and limited bioavailability due to various physiochemical transformations during digestion (Ting et al., 2014). In addition, many of these bioactives are chemically sensitive, prone to degrade or decompose when exposed to light, oxygen, and heat during processing and storage. Therefore, inclusion of lipophilic bioactives in foods and beverages to produce functional foods and beverages has been a main challenge in the food industry. Lipids are promising delivery vehicles for lipophilic bioactives due to their biocompatibility and enhanced absorption (Dolatabadi et al., 2015; Severino et al., 2012). The utilization of solid lipids rather than liquid oils has the advantages of achieving controlled bioactive release and bioactive stability against thermal and mechanical stress (Dolatabadi et al., 2015; Scalia et al., 2015), thus solid lipid nanoparticles have become one promising lipid-based delivery system for bioactives and drugs. Nevertheless, to some extent, current conventional methods in producing solid lipid nanoparticles have restricted the full potential of developing an efficient delivery system. Safety concerns due to solvent use in solvent emulsification/evaporation method; bioactive instability in hot homogenization and high shear homogenization methods, and potential metal contamination

Abbreviations: FHSO, fully hydrogenated soybean oil; SC-CO_2, supercritical carbon dioxide; SEM, scanning electron microscopy; DSC, differential scanning calorimetry; XRD, X-ray powder diffraction.

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and particle physical instability in ultrasonication method are the limitations of the current methods (Beh et al., 2012; Ekambaram et al., 2012). Moreover, solid lipid nanoparticles possess poor loading capacity, also may expel the loaded bioactive during crystallization, because it is a full solid lipid particle (Mukherjee et al., 2009).

A promising strategy to overcome above-mentioned problems in manufacturing fine solid lipid particles can be realized by using supercritical fluid technology, which has been considered as an effective and green alternative to process materials in the pharmaceutical, chemical and food industries (Subramaniam et al., 1997; Fahim et al., 2014; Campardelli et al., 2013). Among many substances that can be used as supercritical fluids, carbon dioxide (CO_2) is the most common one since it has a relatively mild critical temperature (31 °C) and pressure (74 bar), and also it is nontoxic, nonflammable, environmental friendly, cheap, and safe. SC-CO_2 has a substantial impact on the properties of components with which they are mixed, including increasing solubility, affecting phase behavior, drastically decreasing the viscosity of condensed phases and surface tension of liquid (Brunner, 2010), thus serving as the most important phenomenon used to optimize process parameters to generate ideal particles with preferred size and morphology (Hakuta et al., 2003; Knez and Weidner, 2003; Nalawade et al., 2006; Mishima, 2008).

Though have been recognized as an efficient alternative to liquid oils and/or colloidal systems, the potential of solid lipid carrier systems for food applications has not yet been fully explored. In this study, we investigated the formation hollow solid lipid micro- and nanoparticles that can be used as bioactive carrier systems using supercritical fluid technology. The hollow structure can increase the loading capacity significantly compared to solid lipid nanoparticles, and solve the bioactive expelling problem. There are few reports on the formation of solid lipid particles using supercritical fluid technology reporting formation of only microsize particles using a technique called Particles from Gas Saturated Solutions (PGSS) (Sampaio de Sousa et al., 2007; Mandžuka and Knez, 2008; García-González et al., 2010; Lubary et al., 2011). Previously, Bertucco et al. (2007) reported a similar process for the formation of solid lipid nanoparticles using a similar process called Gas Assisted Melting Atomization (GAMA). In their process, molten mixture was pressurized with CO_2, and then a semisolid or liquid mixture was created with a second gas (air) which did not completely dissolve into the mixture, and then the mixture was expanded with evaporation of CO_2 to form solid lipid micro- and nanoparticles (Bertucco et al., 2007). Production of solid lipid submicron particles for protein delivery (Salmaso et al., 2009) and bioactive-containing solid lipid microparticles (Vezzù et al., 2010) were also reported. To the best of our knowledge, there is no report on the formation of hollow solid lipid particles at both micro- and nanosize using supercritical CO_2 (SC-CO_2).

The main objective of this study was to form hollow solid lipid micro- and nanoparticles (nanospheres) from fully hydrogenated soybean oil (FHSO) that will be used as biocompatible bioactive delivery systems using SC-CO_2. The specific objectives were to investigate the effects of pressure and nozzle diameter on the particle morphology, size and size distribution, melting properties, and polymorphism.

2. Materials and methods

2.1. Materials

FHSO was kindly provided by ConAgra Foods Inc., Omaha, NE, USA. CO_2 (dry 99.99% pure) was purchased from Matheson, Lincoln, NE, USA.

2.2. Determination of melting behavior in pressurized CO_2

Melting behavior of the FHSO in pressurized CO_2 was studied according to Ciftci and Temelli (2014) in a jacketed high pressure vessel equipped with two sapphire windows, microscope and camera systems, refrigerated circulator (model 1162A, VWR Inc., Radnor, PA, USA). The temperature of the vessel was controlled by circulating water through the jacket of the vessel. The molten FHSO was placed into a glass gas chromatograph vial insert (200 μL) between two windows, then the vessel was pressurized with CO_2 using a syringe pump (Model 250D, Teledyne Isco Inc., Lincoln, NE, USA). After 1 h stabilization time, the temperature of the vessel was decreased to 5 °C below the solidification temperature of the FHSO that was observed via the microscope-camera system. Then, the temperature of the vessel was increased at a rate of 0.3 °C/min until first melting of the sample was observed. The melting temperature and pressure of the lipid under pressurized CO_2 were recorded as the pressure and temperature at which the first melting was observed.

2.3. Production of hollow solid lipid micro- and nanoparticles using SC-CO_2

The hollow solid lipid particles were produced from FHSO using the particle formation system shown in Fig. 1. The system consisted of a high-pressure syringe pump, pre-heating section, 100 mL high-pressure expansion vessel, magnetic drive, magnetic drive controller, pressure gauge, thermocouple, sampling port, rupture disk, depressurization valve, and nozzle. The expansion vessel, depressurization valve, and nozzle were heated with heating tapes, and digital temperature controllers were used to control temperature of the heating tapes. Temperature of the expansion vessel was maintained at 57 °C that is the melting point of FHSO under CO_2 at 120 bar (Fig. 2). Temperature of the depressurization valve and nozzle was set to 5 °C above the melting point of the FHSO under atmospheric conditions.

The FHSO sample was firstly melted on a heater at 130 °C and then 20 mL of molten FHSO was injected into the expansion vessel through the sampling port. Then, the CO_2 inlet valve was slowly opened, and the expansion vessel was pressurized with CO_2 with the syringe pump until the set pressure was reached. The magnetic drive was turned on at 1000 rpm to mix the pressurized CO_2 and the FHSO to obtain the maximum expansion of SC-CO_2-dissolved solid lipid for 1 h. Then, the magnetic drive was turned off and waited for 10 min for stabilization of the SC-CO_2-expanded solid lipid. The pressure of the syringe pump was set to 10 bar above the pressure of the expansion vessel, and CO_2 inlet valve was opened, then depressurization valve was opened. Upon opening depressurization valve, CO_2-expanded lipid was atomized through the nozzle, solid lipid particles were formed and collected in the