

Encapsulation of Food Compounds Using Supercritical Technologies: Applications of Supercritical Carbon Dioxide as an Antisolvent

Eric Keven Silva, M. Angela A. Meireles*

LASEFI/DEA (Department of Food Engineering), FEA (School of Food Engineering), UNICAMP (University of Campinas), Campinas, Brazil

Abstract The application of supercritical technologies as an alternative to conventional methods for encapsulating food compounds is an area of research that can lead to significant innovations in various segments of industrial food processing. The existing supercritical techniques are classified as follows according to the function of the supercritical fluid used in the process: solvent; antisolvent; cosolvent or solute; nebulization compound; extractor and antisolvent techniques. Supercritical carbon dioxide (scCO₂) is the substance most widely used for obtaining micro/nanoparticles due to its unique characteristics, and among the existing encapsulation supercritical techniques, those using scCO₂ as the antisolvent are more likely to be successful because food compounds are generally less soluble or even insoluble in scCO₂. In this context, this review presents and discusses the applications of supercritical processes using scCO₂ as the antisolvent for the encapsulation of substances of interest to the food industry.

Keywords Supercritical Fluids, SAS, SEDS, Phase equilibria, Wall material

1. Introduction

Various foods and nutrients, such as antioxidants, vitamins, flavorings and colorings, are naturally unstable under normal conditions of temperature and relative humidity, which restricts their availability and their application in food processing.

Encapsulation technologies have recently been developed to create procedures and formulations for the stabilization, solubilization and release of active components of interest to the food industry, which have incorporated and been applied to various products, thus improving their stability and maintaining their viability [28, 20].

Among the numerous conventional encapsulation processes, those based on supercritical technologies have attracted the food industry due to the possibility of working with thermolabile products and the ability to conduct particle engineering, i.e., to obtain new natural powdered additives, such as flavorings, colorings and antioxidants, with controlled characteristics, such as their size and size distribution. In particular, there is great interest in the preparation and application of nanometer-sized materials because they can possess new properties of industrial

value [2, 60, 44].

Supercritical carbon dioxide (scCO₂) is the supercritical fluid that is most widely used in precipitation and encapsulation processes due to its favorable characteristics, such as its low toxicity, low cost, easy removal and non-flammability, and among the existing supercritical encapsulation techniques, those using scCO₂ as an antisolvent are more likely to be successful in industrial applications because food compounds are generally poorly soluble or even insoluble in scCO₂ [9, 47, 60].

The use of scCO₂ as the antisolvent has been explored for different materials, such as polymers, pharmaceuticals, dyestuffs, explosives, inorganic compounds and catalysts. This review presents and discusses the application of supercritical processes using scCO₂ as the antisolvent for the encapsulation of substances of interest to the food industry.

2. Encapsulation

Encapsulation is a physical coating process in which a substance (small solid particles, liquid droplets or a gas) which is called the active or core material, is surrounded by a material called the encapsulating agent or wall material, the function of which is to completely or partially isolate the active material in the form of capsules [25]. The goals of encapsulation are stabilizing the encapsulated materials, controlling its oxidative reactions, controlling its release,

* Corresponding author:
maameireles@gmail.com (M. Angela A. Meireles)
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masking its taste, color and/or odor, prolonging its lifetime, reducing its volatility and reactivity and protecting the components against nutritional losses, as well as increasing its stability under adverse environmental conditions, such as the presence of light, oxygen and pH extremes [14, 1, 25, 10, 11].

The obtained particles may have different morphologies and structures, such as that of a simple roofing membrane, a spherical or irregular morphology, a multiwalled structure or numerous cores in the same structure (Figure 1) [15]. The structures and morphologies of the particles are dependent on the materials (active and encapsulant) and the technique used in their preparation.

Several techniques have been developed for encapsulating active substances, such as spray-drying, spray-chilling, freeze-drying, coacervation, fluidized bedding, gelification, emulsion polymerization, extrusion and supercritical fluid processes, among others, and choosing the proper technique depends on the expected particle size, the biocompatibility and biodegradability of the particles, the physicochemical properties of the core and the encapsulant, the applications of the particles, the proposed mechanism for the release of the active material and the processing costs [40, 50].

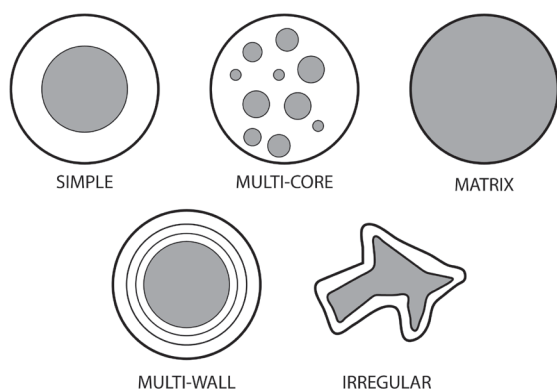


Figure 1. Morphologies of particles obtained using encapsulation processes (adapted from Gibbs *et al.* [15])

3. Supercritical Fluids

The advantages of using supercritical fluids (SCFs) rather than other solvents are primarily due to their physical and chemical properties being intermediate between those of liquids and gases and being easily adjustable with changes in temperature and pressure. SCFs have densities similar to those of liquids, viscosities near those of gases and diffusion coefficients greater than those of liquids, in addition to having a surface tension that is nearly zero [5].

Due to these transport properties, SCFs are applied for different purposes, such for extracting bioactive compounds, chromatographic analyses and particle formation [57, 47]. The mixing properties of liquid-gas are particularly useful in many applications related to nanotechnologies [44].

3.1. scCO_2 in the Particle Formation Process

scCO_2 is the SCF that is most widely used in precipitation processes because its critical properties, due to its T_c of 304.2 K and its P_c of 7.38 MPa, are relatively easily achieved (Figure 2) [53, 2]. These characteristics make scCO_2 an attractive alternative material for a variety of applications, particularly for the processing of labile compounds.

scCO_2 has other significant advantages, such as being available and therefore of low-cost. It exhibits moderate solubility in organic solvents and is nonflammable, nontoxic and environmentally safe, with the potential for use in developing new environmentally friendly processes. An important advantage of scCO_2 is that it leaves no residue in the treatment medium, i.e., it is easily removed [5, 57]. Moreover, as for all SCFs, the rates of mass transfer in scCO_2 are considerably higher than those in liquid solvents, and scCO_2 can easily penetrate highly porous nanostructures [47, 2].

The solvent power of a supercritical fluid is a function of its density, which increases with increasing pressure at a constant temperature [5]. Nonpolar compounds are generally highly soluble in scCO_2 because it is a nonpolar solvent. However, polar molecules can also be dissolved in scCO_2 . The solvating power of scCO_2 can be increased by adding modifiers or co-solvents, such as ethanol, methanol and hexane [42].

scCO_2 is completely miscible in water and in H_2 , O_2 or CO at temperatures above 304.1 K, whereas these gases are only slightly soluble in organic solvents. Higher concentrations of gases can be achieved in scCO_2 than in other SCFs, which may be advantageous in producing nanostructured materials. For example, in reactive processes involving these gases, having them at high concentrations in the fluid phase may increase the reaction rates and overcome the limitations of the mass transfer rate across the gas-liquid interface [47].

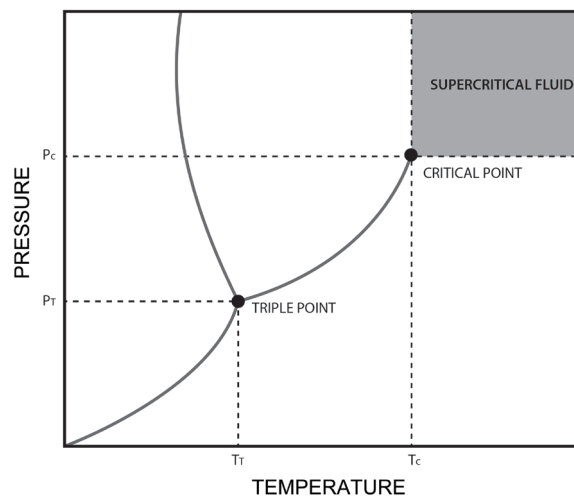


Figure 2. Pressure-temperature phase diagram for pure substances

The abovementioned properties of scCO_2 make it attractive for the processing and production of particles with controlled properties. The properties can be controlled by adjusting the kinetic and thermodynamic parameters of the system through adding surfactants or applying a specific configuration of the production process [57, 53, 9, 47, 30].

4. Supercritical Encapsulation Process

The selection of the supercritical process for encapsulating active compounds must be initially based on the solubility of the substrate and the polymer matrix in the supercritical fluid, which is one of the limiting factors of supercritical techniques. The size, shape and structure of the desired particles, the production scale and the processing costs must also be considered [22, 2].

The techniques are classified according to the function of the supercritical fluid in the process, as follows: solvent; antisolvent; cosolvent or solute; nebulization compound; extractor and antisolvent techniques. scCO_2 is the substance most often used to obtain pure or composite micro/nanoparticles due its unique characteristics. Table 1 presents the supercritical precipitation processes.

4.1. Solvent Techniques

The supercritical encapsulation techniques that are based on the solubilization of active compounds and wall materials in supercritical fluids are relatively simple. In the Rapid Expansion of a Supercritical Solution (RESS)

process, the solutes are dissolved in scCO_2 and then the homogeneous mixture is rapidly expanded in a container at atmospheric pressure using a suitable nozzle. With the sudden change in pressure, scCO_2 loses its solvent power and the dissolved material precipitates [22].

To overcome the limitation of the RESS technique being suitable only for products of low polarity or moderate solubility in scCO_2 , patents that proposed changes to the process were developed, which included the following: adding a cosolvent to increase the solubility of the solute in scCO_2 , which is the Rapid Expansion of a Supercritical Solution with a Nonsolvent (RESS-N) process; applying a liquid solvent in the precipitation container to prevent the growth of particles during jet expansion and thus obtain smaller particles, which is the Rapid Expansion of a Supercritical Solution in a Liquid Solvent (RESOLV) process; and specifically using an aqueous solution containing a surfactant rather than a liquid solvent as a stabilizing agent, which is the Rapid Expansion of a Supercritical Solution in an Aqueous Solution (RESSAS) process (RESSAS) [57, 2, 47].

The application of the supercritical encapsulation process using scCO_2 as a solvent is restricted in the area of food products because substances such as fats, vegetable oils and vitamins are only moderately soluble in scCO_2 [60]. A few food compounds, such as rutin and a jabuticaba-skin extract rich in anthocyanins, have been encapsulated via RESS-N using polyethylene glycol (PEG) as the wall material and ethanol as a cosolvent [51, 48].

Table 1. Functions of scCO_2 in the process of forming composed particles

scCO_2 function	Process	Acronym	Reference
Solvent	Rapid Expansion of Supercritical Solution	RESS	[22]
	Rapid Expansion of Supercritical Solution into a Liquid Solvent	RESOLV	[57]
	Rapid Expansion of Supercritical Solution into an Aqueous Solution	RESSAS	[47]
	Rapid Expansion of Supercritical Solution with a Nonsolvent	RESS-N	[22]
Antisolvent	Gas Antisolvent	GAS	[31]
	Supercritical Antisolvent	SAS	[53]
	Aerosol Solvent Extraction System	ASES	[2]
	Particles by Compressed Antisolvent	PCA	[2]
	Solution Enhanced Dispersion by Supercritical Fluids	SEDS	[22]
	Supercritical Antisolvent Precipitation with Enhanced Mass Transfer	SAS-EM	[6]
	Atomized Rapid Injection for Solvent Extraction	ARISE	[35]
Solute	Particles from Gas-Saturated Solutions	PGSS	[22]
	Particles from Gas-Saturated Solutions-Drying	PGSS-Drying	[36]
	Gas-Assisted Melting Atomization	GAMA	[57]
	Depressurization of an Expanded Liquid Organic Solution	DELOS	[53]
	Pressure Reduction of Gas-Expanded Liquids	PPRGEL	[57]
Nebulization Compound	Carbon Dioxide Assisted Nebulization with a Bubble Dryer	CAN-BD	[31]
	Supercritical Fluid-Assisted Atomization	SAA	[47]
Extractor and Antisolvent	Supercritical Fluid Extraction of Emulsions	SFEE	[9]

4.2. Antisolvent Techniques

The antisolvent gas (GAS) technique is a batch process in which the active substance and the wall material are solubilized in an organic solvent (primary solvent), characterizing an active solution (Figure 3). In this process, the solubilizing power of the encapsulant and the active compound in the primary solvent are reduced through the expansion of the active solution due to mixing it with a dense gas or supercritical fluid that is called the antisolvent [31].

The antisolvent saturates the active solution through the mass transfer process, which is rapid for CO₂ due to its high diffusion rate, reducing the density of the mixture (active solution + CO₂), increasing the volume of the solution and reducing its viscosity. The solvent power of a liquid is a function of its density, and thus the solubility of the solute (active compound + wall material) significantly decreases, reaching saturation and then supersaturation, at which point nucleation and the formation of fine particles occurs [47, 2, 30].

The greatest advantage of the GAS technique is the ability to micronize and encapsulate polar components, i.e., components that are not soluble in CO₂. However, because an organic solvent is used (primary solvent), traces quantities of the solvent can be detected in the particles obtained [3, 8].

Supercritical Antisolvent (SAS), Particles by Compressed Antisolvent (PCA), Aerosol Solvent Extraction System (ASES), Solution-Enhanced Dispersion by Supercritical Fluids (SEDS), Supercritical Antisolvent Precipitation with Enhanced Mass Transfer (SAS-EM) and Atomized Rapid Injection for Solvent Extraction (ARISE) processes were designed based on the GAS process, similarly to how other processes for supercritical encapsulation arose as the initial configurations were improved using the latest known methods through patent development [53]. These techniques differ mainly in that the active solution and the antisolvent come into contact [24]. These processes and their applications in food-compound encapsulation are presented in the following sections of this review.

4.3. Cosolvent or Solute Techniques

The Particles from Gas Saturated Solutions (PGSS) technique is particularly suitable for polymers and waxes because the dissolution of CO₂ considerably reduces the melting point of these substances. The process does not require that the active substance or the polymer encapsulant be dissolved in the supercritical fluid. The method exploits the cooling phenomenon that occurs due to the Joule-Thomson effect during depressurization and the ability of CO₂ to dissolve in organic compounds at high concentrations. The supercritical fluid is dissolved in a substrate, a substrate(s) solution in a solvent or a substrate(s) suspension in a solvent, followed by the rapid expansion of the saturated solution through a nozzle using a moderate pressure, which causes the formation of solid or liquid

particles due to the intense cooling effect caused by the release of CO₂ [22, 9, 2].

This process has long been used for micronization of foods and their derivatives, such as citric acid, chocolate, fatty acids and rosemary extracts [60], for menthol encapsulation in beeswax [26] and for the stabilization of the volatile compounds derived from several essential oils [33].

Among the variations of the PGSS process, the Particles from Gas Saturated Solutions-Drying (PGSS-Drying) technique is highlighted due to its application in encapsulating food compounds.

This technique relies on the use of scCO₂ as a propellant solute and drying medium [36]. β -carotene was encapsulated in soy lecithin via PGSS-drying, yielding spherical particles (10 - 500 μ m) at an encapsulation efficiency of 60% [41].

4.4. Compound-Nebulization Techniques

In the Carbon Dioxide-Assisted Nebulization with a Bubble Dryer (CAN-BD) and Supercritical Fluid-Assisted Atomization (SAA) processes, scCO₂ is used to promote the nebulization of the active solution. The main difference between the two techniques the limitation of the CAN-BD process to aqueous solutions, whereas SAA also works with organic solvent solutions. The mode of contact between the solution and scCO₂ is another difference. In CAN-BD, contact is achieved using a simple T-mixer and a short residence time, and in the SAA process, a saturator is used [57, 31].

These techniques have been used to produce particles using a range of substances but particularly pharmaceutical compounds [60]. The CAN-BD technique was used to obtain particles of α -lactose [55] and palmitic acid [54]. Particles of bovine serum albumin were obtained using the SAA technique [59].

4.5. Extractor and Antisolvent Techniques

Supercritical Fluid Extraction of Emulsions (SFEE) technique combines the efficiency of using a supercritical fluid as the antisolvent for the formation of particles with the effect of emulsification processes on the formation of nanoparticles [9]. The method is an extension of the SAS technique, in which scCO₂ is used to extract the organic solvent from the droplets of oil-in-water (o/w) or water-in-oil (w/o) emulsions [34]. The ability to control the particle size is associated with the control of the size of the droplets in the dispersed phase in which the substance active is dissolved [31, 34]. The main disadvantage of the process is that the final product generally consists of a suspension of the active component in water and not dry particles [17].

A shrimp-residue extract enriched with astaxanthin was encapsulated via the SFEE technique using the modified starch Hi-Cap 100 as the wall material and dichloromethane (DCM) as the primary solvent [37]. Lycopene and β -carotene solubilized in DCM were encapsulated using OSA modified starch as the encapsulant [49].

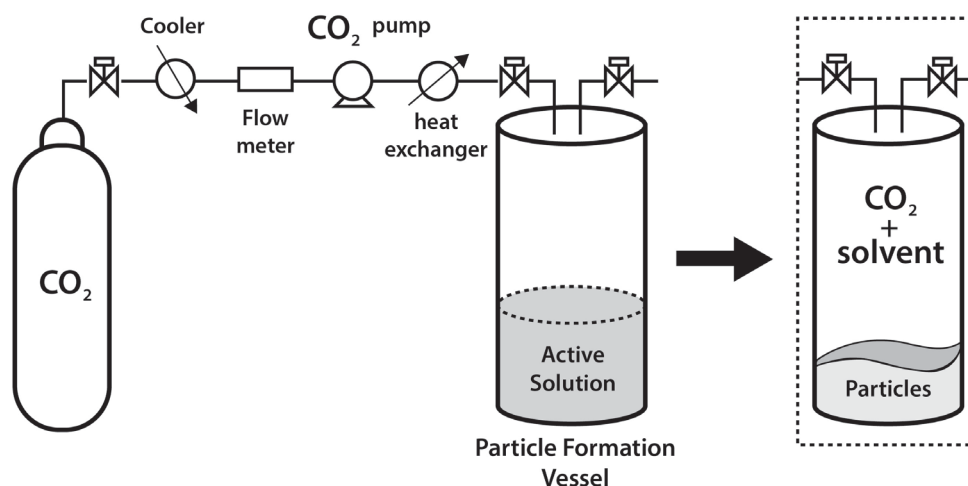


Figure 3. Simplified scheme of the GAS process

5. SAS, PCA, ASES, SEDS, SAS-EM and ARISE Processes

The SAS method is based on the same principle as the GAS process, but in a semi-continuous operation [44]. The processes also differ in that in the former, the active solution and the antisolvent fluid are continuously injected into the precipitation vessel through nozzles and their contact occurs with the vessel and with mixing so that supersaturation is achieved, leading to the formation of particles that accumulate within the container and are collected at the end of the operation [34]. According to Tabernero et al. [57], the SAS, PCA and ASES methods are similar processes. Figure 4 shows a simplified scheme of the SAS process.

The main advantages of the SAS process are associated with a reduced particle size due to supersaturation being caused by the rapid mixing of the supercritical fluid with the active solution [63]; the ability to prepare particles with high polymorphic purity, a higher solubility rate and an acceptable level of residual solvent [29]; the ability to control the size and size distribution of the obtained particles by varying the concentration of the active solution and other process parameters, including the temperature, pressure, feed rates of the solution and antisolvent and injector configuration [7]; the ability to encapsulate thermosensitive substances by choosing the appropriate antisolvent [38, 7]; the feasibility of adapting the technique for continuous operation and, therefore, its favorability for large-scale production of encapsulated food compounds [63].

The main factor distinguishing the SEDS and SAS procedures is that in the SEDS technique, scCO_2 is used not only as an antisolvent but also as a dispersing agent [2, 22]. The SEDS process involves a specific configuration of the nozzle (Figure 5), which was developed to promote intense mixing of the supercritical fluid (antisolvent) and the active

solution, with the aim of increasing the mass transfer rates and providing uniform conditions for crystallization, and thus the precipitation of particles with smaller sizes [57, 53]. Figure 5 shows the configuration of the nozzle used in the SEDS process as described in the patent of Hanna and York [18].

In addition to being used for its chemical properties, the antisolvent may also be used to enhance the mechanical effect of a nozzle designed for the coaxial passage of the feed fluids, which has a mixing chamber in its extremity that allows the simultaneous introduction and initial mixing of the antisolvent and the active solution. Mixing is terminated inside the particle-formation vessel. The high speed of the antisolvent spray breaks the solution into small droplets. Moreover, the processing conditions can be configured so that the supercritical fluid will extract the organic solvent from the solution while dispersing it [22, 2].

The technique in which an ultrasonic field is coupled to the SAS equipment to decrease the droplet size and improve mixing was called SAS-EM by Chattopadhyay and Gupta [6]. The SAS-EM system consists of an ultrasonic precipitation vessel maintained at high pressure, which increases the rates of mass transfer and turbulence so that the droplet size is decreased, leading to the precipitation of particles smaller than those produced using the original method [2, 57]. The contact between the active solution and the antisolvent is standardized based on the cross-flow properties [6].

Although adjustments to the nozzle configuration and the implementation of ultrasonic waves increase the control of the morphology of the particles, the SAS-EM process has some drawbacks, such as the need for operation at low flow rates to prevent clogging of the nozzle. The ARISE process was developed to overcome this limitation by eliminating the necessity of using a capillary injector [35].

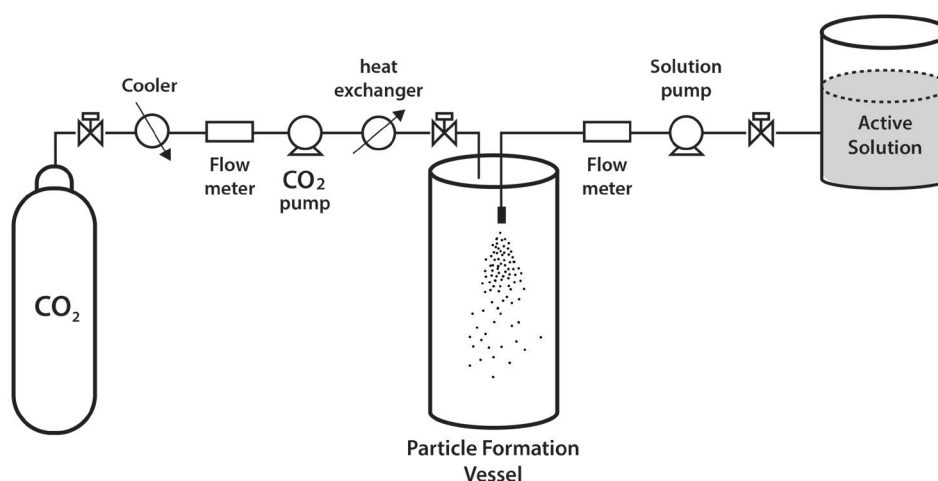


Figure 4. Simplified scheme of the SAS process

6. Process Parameters and the Particle Size

Process parameters, such as the pressure, temperature, rate of active solution flow, rate of antisolvent flow, the chemical and physical properties of the active compound, encapsulant and the organic solvent, intermolecular interactions between the scCO₂-solvent and the scCO₂-active compound/encapsulant, concentration of the active substance and the encapsulant in the solution and the nozzle geometry directly affect the encapsulation characteristics, such as the relation among supersaturation, nucleation and particle growth, the particle size and distribution of sizes and the particle morphology in the processes that utilize a supercritical fluid as the antisolvent. Therefore, optimizing these parameters is fundamental for obtaining particles with controlled characteristics [23, 30, 47, 57, 22, 46]. The size and size distribution of particles can also be adjusted changing the mode in which the antisolvent is added, in a batch or semi-continuous manner [47].

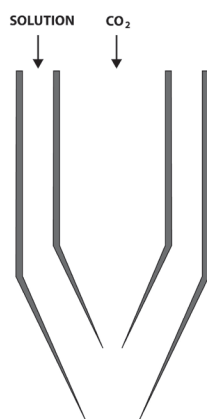


Figure 5. Coaxial nozzle used in the SEDS process

In their review of the application of the supercritical-antisolvent method in drug encapsulation, Kalani and Yunus

[23] discussed in detail the effect of each process parameter on the size of the particles obtained. However, the effects of the process variables are often contradictory and furthermore, there are no generally valid rules for the use of different types of active compounds, wall materials and organic solvents [45].

Hu *et al.* [19] studied the co-precipitation of lutein and zein solubilized in acetone and dimethyl sulfoxide (7:3, v/v) using scCO₂ as an antisolvent in a SEDS process. Process parameters, such as the temperature, pressure, lutein/zein ratio and the flow rate of the solution significantly affect the morphology (spherical) of the particles, the encapsulation efficiency (34.44 – 83.15%) and the average particle size (198 – 355 nm).

7. Organic Solvent

The use of various organic solvents provides benefits, such as increasing the number of active compounds and the types of wall materials that can be processed in procedures that techniques use scCO₂ as an antisolvent, although the application of toxic solvents, such as dichloromethane, dimethyl sulfoxide and others, is a factor that may limit their applications in the food-products encapsulation due to the presence of toxic residues in the final product [16]. According to Kalani and Yunus [23], the presence of residual toxic solvents in the obtained particles is the only drawback is associated with such processes.

Visentin *et al.* [58] encapsulated rosemary extracts with Pluronic® F 88 and Pluronic® F 127 via the SAS method and used ethanol, which is a food-grade solvent, as the primary solvent in the process.

8. Encapsulant Material

Selecting the appropriate wall material is an extremely important factor in the encapsulation of active compounds

because the material must meet criteria such as having a particular mechanical strength, being compatible with the food product, protecting the core material from factors that could cause its deterioration, limiting the loss of volatile compounds, allowing controlled release, and having thermal properties compatible with the designated application of the product [14].

Cocero et al. [9] listed the biopolymers that are often used in supercritical encapsulation. Among the classes shown are polysaccharides and starch-based polymers, such as dextrin, cyclodextrin, modified starch and inulin. Although these materials are commonly used in processing various foods, there are no reports of their application in encapsulating food substances via a supercritical technique in which the scCO_2 was used as the antisolvent.

9. Phase Equilibria

Most research on the encapsulation of food compounds using scCO_2 as the antisolvent focused on the effects of the operating conditions (temperature, pressure, active solution and antisolvent flow rate, among others) on the size distribution and morphology of the particles. However, to assess the feasibility of the process and optimize the choice of the operating variables, it is important to understand the phase equilibrium of the systems because it plays a fundamental role in the mechanism of precipitation, nucleation, growth kinetics and mass transfer [52].

Importantly, studying the thermodynamic equilibria reached using these techniques is complex because they involve more than two substances (active compound,

encapsulant, solvent and supercritical fluid) at different stages of aggregation, which may hamper determining the limits [60].

Franceschi et al. [13] studied the encapsulation of β -carotene using biocompatible poly (3-hydroxybutyrate-*co*-hydroxyvalerate) (PHBV) as the wall material and DCM as the primary solvent. They evaluated the phase equilibrium of the ternary systems $\text{CO}_2 + \text{DCM} + \beta$ -carotene and $\text{CO}_2 + \text{DCM} + \text{PHBV}$. The experiments were performed at high pressure using a variable-volume cell that allowed visualization and were based on the static synthetic method. The temperature range investigated was 303 K – 343 K. The authors concluded that the adding solutes (β -carotene and PHBV) to the binary system ($\text{CO}_2 + \text{DCM}$) had no significant effect on the transition pressures.

10. Applications in Encapsulating Food Compounds

The class of food compounds for which the largest number of studies of encapsulation via SAS processes is the carotenoids, such as lutein, which is found in some vegetables, such as spinach, cauliflower, peas, broccoli, and some fruits, such as oranges, papayas, peaches and kiwis, as well as in egg yolk [39, 32, 21, 61], bixin, the main pigment found in annatto seeds [51], β -carotene, an antioxidant pigment found in foods such as apricots, carrots, squash, beets, papayas, mangos and sweet potatoes [32], and astaxanthin, which is derived of the residues of shrimp processing [37].

Table 2. The application of the SAS and SEDS methods for encapsulating food compounds

Process	Core material	Wall material	Solvent	Operating parameters	Results and observations	Reference
SAS	Polyphenols (green tea extract)	Poly (epsilon-caprolactone)	Acetone	Pressure: 8 - 12 MPa Temperature: 284 - 307 K CO ₂ flow rate: 5.56E-5 - 1.11E-4 kg/s Solution flow rate: 3.95E-4 - 1.98 E-3 kg/s Polymer to solutes concentration (w/w) ratio: 4–58 Nozzle type: coaxial	Scanning electron microscopy (SEM) images of the products showed small particles (3–5 μm) with a narrow size distribution and a high degree of agglomeration	[56]
SAS	Lutein	PEG	DCM	Pressure: 8 - 10 MPa Temperature: 288 K CO ₂ flow rate: 2.5 and 3.5 kg/h Solution flow rate: 1.7 kg/h Lutein concentration: 1 – 3 g/L PEG concentration: 12 g/L Nozzle type: coaxial	The products obtained were spheres of PEG of approximately 50 μm in diameter, in which lutein was almost completely covered	[32]
	β -Carotene			Pressure: 8 MPa Temperature: 288 K CO ₂ flow rate: 2.5 and 3.5 kg/h Solution flow rate: 1.7 kg/h β -Carotene concentration: 1.2 g/L PEG concentration: 12 and 16 g/L Nozzle type: coaxial	Prismatic particles of 100–200 μm were produced.	

SAS	Bixin (annatto seed extract)	PEG	DCM	Pressure: 10 MPa Temperature: 313.15 K Solution flow rate: 1 mL/min CO ₂ flow rate: 0.6 and 1.5 kg/h Mass ratio of bixin-rich extract and PEG: 1:2 and 1:10 Nozzle type: coaxial	The higher CO ₂ flow rate (1.5 kg/h) employed resulted in an excessive loss of particles. The particle size was 33 ± 2 µm	[51]
SAS	Rosemary antioxidants	Pluronic® F 88 and Pluronic® F 127	Ethanol	Pressure: 8 - 10 MPa Temperature: 298 - 323 K Solution flow rate: 1 mL/min CO ₂ flow rate: 0.7 kg/h Mass ratio between rosemary extract and polymer: 1:2.5 Nozzle type: coaxial	The size of the particles of rosemary extracts encapsulated in Pluronic were less than 1 µm based on SEM analysis	[58]
SAS	Astaxanthin (Shrimp extract)	Pluronic® F 127	Acetone	SMALL SCALE Pressure: 10 - 12 MPa Temperature: 308.15 – 318.15 K Solution flow rate: 1 - 3 mL/min CO ₂ flow rate: 1.0 kg/h Extract concentration in the solution: 2 - 12 mg/mL Nozzle type: coaxial LARGE SCALE Pressure: 10 MPa Temperature: 308.15 and 313.15 K Solution flow rate: 4 and 5 mL/min CO ₂ flow rate: 4.0 and 5.0 kg/h Extract concentration in the solution: 6 - 12 mg/mL Nozzle type: coaxial	The SEM results showed that the SAS procedure was adequate for producing microparticles (greater than 1 µm in diameter) for all conditions evaluated. The highest efficiency of astaxanthin encapsulation (74%) in a small-scale unit was obtained at 10 MPa, 308.15 K and at a ratio between the solution and the CO ₂ flow rate of 1 (mL/min)/(kg/h). Similar encapsulation efficiencies were achieved using large-scale SAS assays using the same operational conditions used for the small-scale unit	[37]
SAS	Vitamin D ₃	Hydrogenated phosphatidylcholine (HPC)	Ethanol and <i>n</i> -hexane	Pressure: 8 - 12 MPa Temperature: 308 - 328 K Solution flow rate: 0.5 mL/min CO ₂ flow rate: 6.0 kg/h HPC concentration in the solution: 40 mg/mL Vitamin D ₃ /HPC: 5 - 15 % Nozzle type: coaxial	Nanoparticles of Vitamin D ₃ in an HPC matrix were formed. The optimal conditions of preparation were a temperature of 318 K, a pressure of 8 MPa and a mass ratio of vitamin D ₃ and HPC of 15%.	[62]
SAS	Quercetin	Pluronic® F 127	Acetone	Pressure: 10 MPa Temperature: 313 K Solution flow rate: 2 mL/min CO ₂ flow rate: 2 kg/h Solution concentration: 0.005 - 0.02 g of quercetin/mL acetone Quercetin/carrier mass ratios: 2:1 - 1:9 Nozzle type: coaxial	Using a quercetin/polymer mass ratio of 1:1 yielded a highly homogeneous product consisting of spherical particles of approximately 1 µm in diameter	[12]
SAS	Lutein	Poly-lactic acid (PLA)	Ethyl acetate	Pressure: 10 MPa Temperature: 290 K Solution flow rate: 1000 mL/h CO ₂ flow rate: 3.5 kg/h Lutein concentration: 350 and 700 ppm PLA concentration: 24000 ppm Nozzle type: coaxial	Spherical particles with diameters between 1 µm and 5 µm were produced	[39]

SAS	Lutein	Hydroxypropylmethyl cellulose phthalate (HPMCP)	Acetone	Pressure: 11 - 15 MPa Temperature: 313 - 323 K Solution flow rate: 1 and 2 mL/min CO ₂ flow rate: 0.88 – 2.00 kg/h Lutein concentration: 0.1 and 0.8 mg/mL HPMCP concentration: 1 - 8 mg/mL Nozzle type: coaxial	The optimal condition for the highest lutein loading and encapsulation efficiency is 11 MPa, 313 K and the ratio of 4.0:0.8 (mg/mL) of HPMCP:Lutein. The mean diameter of the nanocapsules, being nearly spherical, was in the range of 163 -219 nm	[21]
SAS	Lutein	HPC	DCM and ethanol	Pressure: 8 - 16 MPa Temperature: 308 - 328 K Solution flow rate: 0.5, 1.0 and 1.5 mL/min CO ₂ flow rate: 30 mL/min Weight ratio of lutein/HPC: 10%. Lutein concentration: 0.73 mg/mL Nozzle type: coaxial	The optimal conditions for preparing lutein/ HPC are a temperature of 308 K, the pressure of 8 MPa and the solution flow rate of 1 mL/min, at which the highest lutein loading of 55 mg/g was obtained	[61]
SEDS	Lutein	Zein	Acetone and dimethyl sulfoxide	Pressure: 10 - 15 MPa Temperature: 305 - 318 K Solution flow rate: 0.5 - 1.25 mL/min CO ₂ flow rate: 4 kg/h Lutein/zein (w/w): 1:12, 1:24 and 1:18	The lutein/zein nanoparticles in narrow size range were obtained at a pressure of 10 MPa, a lutein/zein ratio of 1:18 (w/w) and a solution flow rate of 1.0 mL/min at 318 K	[19]
SEDS	β -Carotene	PHBV	DCM	Pressure: 8 - 12 MPa Temperature: 313 K Solution flow rate: 1.0 mL/min CO ₂ flow rate: 20 - 40 mL/min β -carotene concentration: 4 - 8 mg/mL PHBV concentration: 10 - 40 mg/mL	The co-precipitation tests indicated that encapsulation of β -carotene in PHBV at up to 80% efficiency was achieved at a mass ratio of 1:3 (β -carotene to polymer) in the organic solution	[13]
SEDS	β -Carotene	PHBV	DCM	Pressure: 8 - 20 MPa Temperature: 313 K Solution flow rate: 1.0 mL/min CO ₂ flow rate: 40 mL/min β -Carotene concentration: 4 and 8 mg/mL PHBV concentration: 30 mg/mL	The encapsulation data showed that increasing the concentration of β -carotene while maintaining a fixed PHBV content resulted in a higher percentage of solute being encapsulated, increasing the encapsulation efficiency	[43]
SEDS	Grape seed extract	PHBV	DCM	Pressure: 8 - 12 MPa Temperature: 308 - 318 K Solution flow rate: 1.67×10^{-8} m ³ /s CO ₂ flow rate: 3.33×10^{-7} m ³ /s Grape seed extract to PHBV mass ratio: 1:1, 1:2 and 1:3 Extract concentration: 6.67 - 20.02 kg /m ³ PHBV concentration: 20.00 - 20.03 kg /m ³	The temperature had the greatest effect on particle morphology. Lower temperatures led to less agglomeration and smaller particles. The best conditions resulted spherical particles with the smallest size, 0.70 μ m, obtained at a pressure of 8 MPa, a temperature of 308 K, a 1:1 mass ratio and concentration of the extract and PHBV, both at 20 kg m ⁻³ , while maintaining all of the other processing variables at the fixed values	[4]
SEDS	Astaxanthin	PHBV	DCM	Pressure: 8 and 10 MPa Temperature: 308 K Solution flow rate: 1.0 mL/min CO ₂ flow rate: 20 mL/min Biomass containing astaxanthin: dichloromethane at 5, 8 and 10 mg/mL PHBV concentration: 20.00 mg/mL	The precipitation pressure had the strongest effect on the size of the particles formed, and the smallest mean particle size, 0.128 μ m, was obtained using the highest pressure tested, 10 MPa.	[27]

Other studies of encapsulating food compounds have involved an extract of the fresh roots of green tea plants that is rich in polyphenols and catechins [56], rosemary extracts that are rich in antioxidants, such as butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) [58], cholecalciferol (vitamin D3) [62], and quercetin, a natural flavonoid that is found mainly in apples, grapes, onions and broccoli [12].

Boschetto *et al.* [4] encapsulated a grape-seed extract that is rich in unsaturated fatty acids and antioxidant compounds via the SEDS technique using biocompatible PHBV as the encapsulant, DCM as the primary solvent and scCO₂ as the antisolvent. They obtained spherical particles with the small size of approximately 0.7 µm at an encapsulation efficiency of 66.01%.

Table 2 presents a summary of the investigations in which SAS and SEDS techniques were utilized for encapsulating compounds of interest to the food industry, as indicated by the authors of the respective studies. There are no records of studies that applied the SAS-EM or ARISE processes to food-compound encapsulation.

11. Conclusions

This review has shown that using scCO₂ as the antisolvent is a viable technique for encapsulating compounds of interest to the food industry. To date, there are few reports in the literature regarding this technique, with approximately 15 such articles found in the journals that are indexed in the Web-of-Science and Scopus databases reporting the encapsulation of compounds such as carotenoids [39, 32, 13, 21, 51, 37, 61], antioxidants [58], flavonoids [12] and polyphenols [56].

The SAS and SEDS techniques were the only processes used in the reported studies. These processes are good alternatives encapsulating thermosensitive substances and are suitable for applications in which particle engineering is desired. In all of the studies that applied the SAS configuration, the pattern of contact between the supercritical fluid and the active solution was the same, with feeding conducted in the coaxial mode [51, 32, 56, 58, 37, 62, 12, 39, 21, 61]. Due to the paucity of relevant studies, it was not possible to clearly establish the effect of the process parameters on encapsulation via the SAS and SEDS techniques.

In particular, further studies that use food-grade organic solvents that are generally recognized as safe (GRAS), such as ethanol, and wall materials that are derived from natural sources, such as modified starches, dextrins and inulin, may result in major innovations in the field of food engineering.

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