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UNIVERSITAT POLITÈCNICA DE CATALUNYA

INSTITUT DE CIÈNCIA DE MATERIALS DE BARCELONA –
CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS

DISSERTATION PRESENTED TO OBTAIN THE PhD DEGREE IN
CHEMICAL PROCESS ENGINEERING

USE OF THE SUPERCRITICAL FLUID TECHNOLOGY FOR THE PREPARATION OF NANOSTRUCTURED HYBRID MATERIALS AND DESIGN OF THE INTERFACE

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SHORT ABSTRACT

The use of nanostructured composites is a promising solution for the design of multifunctional materials. However, the lack of coupling or bonding between the organic and inorganic components of most nanostructured hybrid composites often leads to anisotropic macroscopic properties, limiting the use of these materials. Hence, the interaction at the components interphase must be engineered to enhance materials performance. In this PhD Thesis, the sustainable supercritical carbon dioxide ($scCO_2$) technology is used for both the surface modification of inorganic nanoparticles and the preparation of nanostructured hybrid materials.

Bifunctional alkoxysilanes, acting as adhesion promoters, are herein investigated for the surface modification of inorganic nanoparticles; particularly, titanium dioxide (TiO_2). For the silanization process, $scCO_2$ is used as the solvent of choice for alkoxysilanes. Fundamental studies on the solubility of octyltriethoxysilane in compressed CO_2 and on the kinetics of the TiO_2 silanization process are performed. Silanization experiments are conducted to ascertain the influence of pressure and temperature in the tunable physicochemical properties of $scCO_2$ and in the process. This information is needed for the engineering control of the characteristics of the silane coatings. Extension of the supercritical silanization process to other sets of alkoxysilanes and inorganic nanoparticles are presented.

Further, nanostructured hybrid materials are prepared using $scCO_2$ technology. Prior to obtain the composite materials, the inorganic nanoparticles are surface silanized in order to facilitate the homogeneous distribution of the nanoparticles within the matrix and to improve the filler-organic matrix interaction. Firstly, biopolymeric matrices of either poly(L-lactic acid) or the blend poly(methylmethacrylate)/poly(ε-caprolactone) loaded with nanometric TiO_2 or hydroxyapatite, respectively, are processed employing $scCO_2$ as an anti-solvent and the Particles from a Compressed Anti-Solvent technique. Precipitated materials have potential applications in tissue engineering. Secondly, lipid blend matrices of hydrogenated castor oil/glyceryl monostearate loaded with nanometric TiO_2 and caffeine are prepared employing $scCO_2$ as a solute and the Particles from Gas Saturated Solutions technique. Precipitated materials have potential applications in sunscreens and pharmaceutical dermal products.

Finally, the extension of the silanization $scCO_2$-assisted process to multiscale complex hybrid materials is assessed. The technology is presented for the two-step carbonation-silanization process of cement-based materials. Firstly, the carbonation of cement is accelerated by using $scCO_2$ as the carbonation agent. The carbonation process is followed by the hydrophobic treatment of the carbonated cement using the supercritical silanization method. The supercritical silanization of the carbonated cement confers water repellence to the material. Prepared materials may be potentially used for the confinement of hazardous wastes in a humid environment or as durable construction materials.

RESUMEN

Los materiales compuestos nanoestructurados son considerados una opción prometedora para la concepción de materiales multifuncionales. Sin embargo, la falta habitual de interacción entre los componentes orgánicos e inorgánicos en los materiales híbridos nanoestructurados comporta unas propiedades macroscópicas anisotrópicas que limitan su uso. Por ello, se hace necesario el diseño de la interfase formada entre los componentes mencionados a fin de mejorar sus prestaciones. En esta Tesis Doctoral se ha optado por el uso de dióxido de carbono supercrítico ($scCO_2$) para la modificación superficial de nanopartículas inorgánicas y para la preparación de materiales híbridos nanoestructurados. Estos procesos supercríticos, diseñados como sostenibles, se proponen como sustitutos de técnicas convencionales que empleen disolventes orgánicos.

El tratamiento superficial de nanopartículas de dióxido de titanio (TiO_2) con octiltrietoxisilano se ha empleado como sistema de estudio para evaluar el uso de recubrimientos de alcoxisilanos bifuncionales como promotores de adhesión de partículas inorgánicas nanométricas. El $scCO_2$ se emplea como disolvente del alcoxisilano para la silanización del TiO_2. También se han llevado a cabo estudios fundamentales de solubilidad de octiltrietoxisilano en CO_2 y de la cinética del proceso de silanización del TiO_2. La modulación de las propiedades fisicoquímicas del $scCO_2$ con la presión y la temperatura permite el control de las características del recubrimiento con silano. El proceso de silanización supercrítico se ha extendido a diferentes sistemas alcoxisilano-nanopartículas inorgánicas.

Asimismo, se ha evaluado la tecnología de $scCO_2$ para la preparación de materiales híbridos nanoestructurados que contengan nanopartículas inorgánicas silanizadas. El tratamiento superficial de las nanopartículas favorece la distribución homogénea de éstas en el material híbrido y mejora la interacción relleno-matriz orgánica. Se han procesado matrices biopoliméricas de interés en ingeniería tisular, compuestas de ácido poliláctico o la mezcla

polimetilmetacrilato/policaprolactona, con adiciones de nanopartículas de TiO_2 o hidroxiapatita, respectivamente. Para su procesado, se ha empleado $scCO_2$ como no-disolvente utilizando la técnica *Particles from a Compressed Anti-Solvent* (PCA). Además, se han preparado partículas híbridas formadas por una mezcla lipídica de aceite de ricino hidrogenado y glicerilmonoestearato con adiciones de TiO_2 y cafeína, con posibles aplicaciones en cremas para uso tópico. Estas partículas sólidas lipídicas se han obtenido usando la técnica *Particles from Gas Saturated Solutions* (PGSS) que emplea $scCO_2$ como soluto.

Por último, el proceso de silanización supercrítico se ha ensayado para materiales híbridos complejos multiescalados. Se han procesado materiales de base cemento empleando un proceso supercrítico de carbonatación-silanización en dos etapas. Primero, el cemento se carbonata de manera acelerada usando $scCO_2$ como agente de carbonatación. Este cemento, ya carbonatado, se somete, finalmente, a un tratamiento hidrofóbico mediante silanización supercrítica, para su posible aplicación en confinamiento de residuos peligrosos en ambientes húmedos o como material de construcción duradero.

ABSTRACT

Nowadays, society is asking for a global changing in the way of manufacturing goods in a more sustainable manner. Indeed, the weight of the classical factors (cost, quality, appearance) influencing the acceptance of a certain good in the market have currently changed. Manufacturing requirements and regulations concerning environment protection (e.g., resource consumption, sustainability, toxicity, CO_2 footprint, recycling potential) and quality features (e.g., product guarantees, durability against aggressive environments, corporate vision) are aspects of increasing concern. The competitive position of a company is influenced by seizing the opportunities and challenges and by managing the risks that the changeable market has. As a consequence, the industry is continuously looking for smart and innovative solutions for the design and manufacturing of materials with novel properties and increased added value, and for the production of materials already existing in the market in a more efficient manner.

Nanostructured hybrid composites have emerged as a promising class of innovative materials for many industrial sectors (e.g., energy, optoelectronics, biomedicine, cosmetics). The multicomponent composition of these materials provides them with unique properties arising from the synergistic combination of the characteristics of their individual components structured at the nanolevel. Nevertheless, in numerous hybrid materials, the lack of coupling or bonding between the components often leads to anisotropic macroscopic properties, limiting their use. Hence, the interaction at the interphase between hybrid components must be properly engineered to enhance materials properties. In this PhD Thesis, the quest for sustainable and environmentally friendly processes led to the use of supercritical carbon dioxide ($scCO_2$) for both the surface modification of nanometric inorganic particles and the preparation of nanostructured hybrid materials. These processes are designed for the replacement of conventional methods using organic solvents.

Bifunctional alkoxysilane molecules, acting as adhesion promoters, are, herein, investigated for the surface modification of nanometric inorganic particles. The surface treatment of titanium dioxide (TiO_2) nanoparticles with octyltriethoxysilane is taken as the model system for study. In terms of processing, $scCO_2$ is used as the solvent of choice for alkoxysilanes for the surface modification of TiO_2. Fundamental studies on the solubility of the used silane in CO_2 in the pressure range 8-18 MPa at two different temperatures (318 and 348 K) and on the kinetics of the TiO_2 silanization process are performed. For the $scCO_2$-aided silanization process, studies are conducted to ascertain the effects and interactions of the operating variables on the properties of the final material. Results show that the tunable physicochemical properties of $scCO_2$ with pressure and temperature (e.g., density, solvation power) allows the engineering control of the characteristics of the silane coating. Examples of the extension of the application of the supercritical silanization process to other sets of alkoxysilanes and inorganic nanoparticles are also presented.

The preparation of hybrid materials including silanized inorganic nanoparticles and organic matrices is further tested using $scCO_2$ technology. Surface treated nanoparticles are used to facilitate the homogeneous distribution of the nanoparticles within the matix and to improve the inorganic filler-organic matrix interaction. Biopolymeric matrices of either poly(L-lactic acid) (L-PLA) or the blend poly(methylmethacrylate)/poly(ε-caprolactone) (PMMA/PCL) loaded with nanometric titanium dioxide or hydroxyapatite, respectively, are prepared. To obtain these hybrid materials, $scCO_2$ is employed as an anti-solvent, using the Particles from a Compressed Anti-Solvent (PCA) technique. Studies are performed to pursue the effect of the processing conditions on the morphology of the precipitated hybrid materials. The resulting material, obtained in the form of fibers, has suitable properties for its potential application in tissue engineering. In a different system, hybrid particles composed of a lipidic matrix (hydrogenated castor oil/glyceryl monostearate) loaded with silanized titanium dioxide and caffeine are prepared. The Particles from Gas Saturated Solutions (PGSS) technique, assisted by the use of $scCO_2$ as a solute, is employed for the production of these solid lipid particles. The obtained hybrid material is evaluated concerning the drug carrier and release ability and the UV-shielding capacity. The UV-light protection and photoaging prevention capacity of the lipid-based hybrid material provide excellent properties for the use of these particles in the formulation of sunscreens and pharmaceutical dermal products.

Finally, the possibility of extending the supercritical silane treatment to multiscale complex hybrid materials is assessed. The technology based on the use of $scCO_2$ is presented for the two-step carbonation-silanization process of cement-based materials. In the first step, the carbonation of cement is accelerated using $scCO_2$ as the carbonation agent. The effects of the cement formulation and process operation conditions on the microstructure and physicochemical properties of carbonated samples are evaluated. The carbonation process is followed by the hydrophobic treatment of the carbonated samples using a supercritical silanization method. The surface modification of carbonated cement with octyltriethoxysilane confers water repellence to the material. The carbonation-silanization process is scheduled and integrated to mitigate the consumption of raw materials and the use of facilities.

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Chapter 0

INTRODUCTION

Nanostructured hybrid composites are multicomponent materials with novel and unique properties arising from the synergistic combination at the nanoscale of their dissimilar constituents. However, the components of these composites may be incompatible, and the formed interphase must be often engineered to induce interaction between the dissimilar constituents. The main goal of this PhD Thesis is the development of sustainable and environmentally friendly processes based in the use of supercritical carbon dioxide for the preparation of hybrid composite materials of designed interphase. The main goal is attained after accomplishing the specific objectives described in Section 0.3. In this Chapter, the overall structure of this PhD Thesis is also outlined.

0.1. Nanostructured organic-inorganic hybrid materials

Nanostructured hybrid materials are an especial class of composite systems comprised of organic and inorganic components distributed at the nanometric scale. The synergistic combination of both components in a single material at the nanosize level provides novel properties for the development of multifunctional materials [1-4]. There are two key approaches for the creation of composite structures at the nanometer scale: self-aggregation and dispersion. By using the self-aggregation approach, normally ordered hybrid materials are obtained; while disordered composites are often prepared by dispersing nanoparticles in a matrix. Nanostructured self-aggregated hybrid composites are materials with spatially well-defined domains for both the organic and inorganic components and with control of their mutual arrangement at the nanolevel. On the other hand, the combination by dispersion of low dimensional dispersed nanoparticles (fillers) with soft matter, particularly polymers, allows the easy preparation of hybrid materials with improved properties. The fascinating properties of these unique structural nanocomposites enable a wide range of applications in the fields of energy, biomedicine, optoelectronics, etc. [1-4].

Fillers are small particles (usually of less than 1000 μm length) added to matrices as admixtures, usually at high loadings, for the formulation of composites. Inorganic particles are used widespread as fillers, with a market value in Europe of 2.3 billion Euros in 2007 [5]. Fillers are basically divided into inactive and functional fillers. The term inactive is related to the primary use of fillers focused in reducing final material cost; while the term of functional is applied to emphasize the modern use of fillers that are employed to modify specific properties of the final composite product, such as density, shrinkage, expansion coefficient, conductivity, permeability, mechanical properties or thermal behaviour [4,6]. The addition of fillers to matrices to form composite materials has very different purposes, ranging from fire retardant effects to the hardening of soft matter (polymers, plastics) [5,7].

The use of nanoparticles as fillers has attracted the interest of scientists and engineers. On one side, nanotechnology has developed to a stage that allows the large-scale production of different tailored single-component nanosized entities, ranging from metal nanoparticles to carbon nanotubes. Hence, at this stage, a major challenge is to demonstrate the feasibility of the fabrication of complex nanostructured products or devices, such as nanostructured composites. However, the actual bottom-up mass-production methods (vapor-related physical routes or liquid-related chemical bulk processes) to further develop heterostructures of various nanoentities have severe limitations related to high cost and reduced purity. On the other hand, in order to effectively explore the remarkable properties of nanocomposites and to manipulate nanoparticles to form nanostructured hybrid composites, one essential step is the surface functionalization of the nanoparticles. The reason is that as-prepared inorganic fillers are often incompatible with organic-soft matrices, due to the low interfacial interaction between both phases [8]. This fact is especially relevant for nanometric fillers, which have a large surface area to volume ratio [9]. The lack of filler-matrix coupling or bonding often leads to the preparation of hybrid materials with non-isotropic properties and relatively poor mechanical behavior that limited their applications [10,11]. Therefore, the dispersion enhancement of nanometric fillers in the bulk of diverse organic matrices through their surface modification is technically needed [12]. Moreover, effects of weathering (e.g., wetting, permeability, fouling and corrosion) in the formed composite can be suppressed, or at least mitigated, by treating the surface of the inorganic filler, which increases the durability of the final material. The high surface reactivity of most inorganic nanoparticles facilitates their surface modification and functionalization.

By using the unique properties of compressed gases and supercritical fluids, which are intermediate between liquids (high density) and gases (high diffusivity, low viscosity and null surface tension), these fluids can be used to design innovative processes for the production of heterostructures, taking advantage of both abovementioned fabrication bottom-up approaches (physical & chemical). In this respect, this Thesis aims at demonstrating that the supercritical fluid technology can be used for the production of complex high purity nanoproducts fulfilling the majority of the Twelve Green Chemistry Principles [13].

0.2. Principles of Supercritical Fluids

Fluids turn supercritical when both temperature and pressure are above the value of the critical point (Figure 0.1) [14,15]. Besides, in the supercritical region, an isothermal pressure increase above the critical pressure (P_c) or an isobaric temperature increase above the critical temperature (T_c) maintains the fluid at supercritical conditions.

Supercritical fluid technology often uses supercritical carbon dioxide ($scCO_2$) as the fluid for materials processing. Supercritical fluids in general and $scCO_2$ in particular, have a set of characteristics that facilitates the processing of materials:

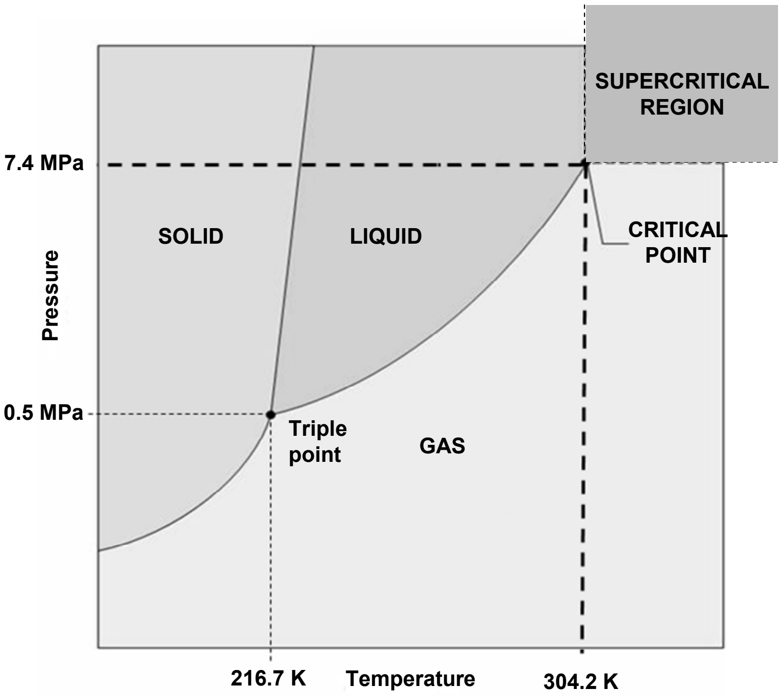

Figure 0.1. **Phase diagram of carbon dioxide.**

- The density of supercritical fluids can be tuned with pressure and/or temperature changes, providing new solvent power characteristics to the them (Figure 0.2). Due to the additional degree of freedom related to the density of supercritical fluids, the technology is able to carry out simultaneous control of the composition and the (nano)structure, allowing the design of one-stage processes.

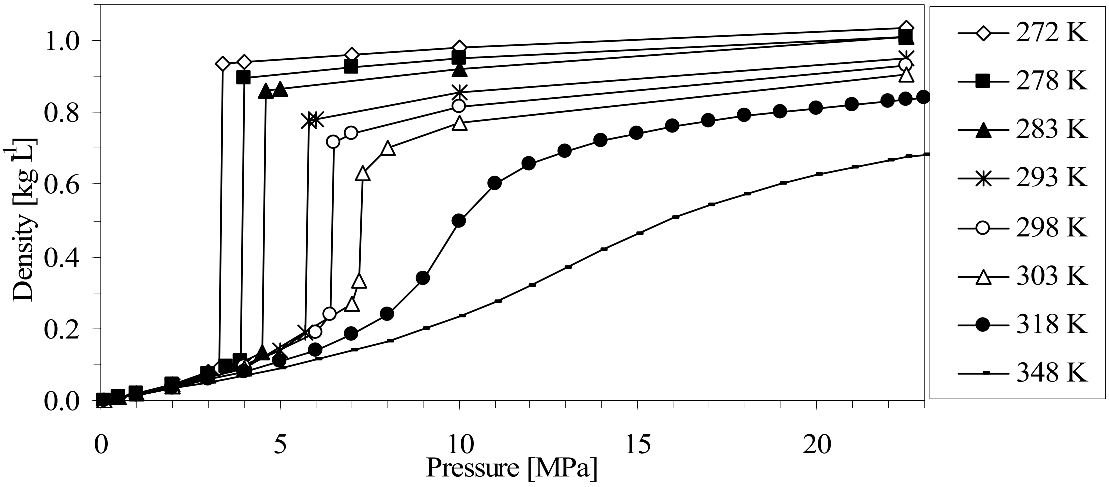

Figure 0.2. **Isothermal pressure-density projections of carbon dioxide between 272 and 348 K. CO_2 density data are taken from Span and Wagner [16,17].**

- Supercritical fluids have high diffusivity that facilitates mass transfer with the subsequent reduction in processing times.
- The null surface tension of supercritical fluids allows the complete wetting of substrates with intricate geometries, including microporous substrates and the internal surface of agglomerated nanoparticles [18].
- The $scCO_2$ is a non-damaging solvent adequate for processing nanostructures. This is an important effect, since with size reduction to nanoscale, classical solvent approaches may be destructive for the production of complex nanostructures. Due to the undesired effects of liquid viscosity and surface tension, liquid solvents can damage the extremely reactive surfaces that, on the other hand, they are helping to create.
- The $scCO_2$ has a pressure-tunable heat capacity which can be exploited for the absorption of the heat generated in exothermic reactions and to achieve a better temperature control of the process [19].
- The CO_2 preference as a supercritical fluid relies on its easily accessible critical point (7.38 MPa, 304 K in Table 0.1) along with its nontoxicity, nonflammability, relative inertness and low cost [20].

Table 0.1. **Critical points of some selected fluids.**

Fluid	T_c (K)	P_c (MPa)	Fluid	T_c (K)	P_c (MPa)
Neon	44	2.76	Sulfur hexafluoride	319	3.76
Nitrogen	126	3.39	n-propane	370	4.25
Argon	151	4.87	Ammonia	406	11.4
Xenon	290	5.92	Methanol	514	7.99
Carbon dioxide	304	7.38	Ethanol	517	6.38
Ethane	306	4.89	Water	647	22.1

- The CO_2 has a low critical temperature (304 K), allowing the processing of thermally labile materials.
- The $scCO_2$ standard working conditions are 10-25 MPa, which can be upscaled in a straightforward way, since they are in the boundary of the low limit region of high pressure systems.

- The CO_2 is gaseous at ambient conditions and the produced materials are isolated by depressurization, resulting in dry products.
- The CO_2 is considered a GRAS substance (Generally Recognized As Safe) by FDA and EMEA [15,21-24].
- The CO_2 can be obtained from natural sources or as a by-product in industrial processes [25]. Therefore, the use of $scCO_2$ do not lead to an additional contribution to greenhouse effect.

The range of current roles of supercritical fluids in the industry is wide, including extracting agents of valuable compounds [26-30], solvents for chemical reactions (e.g., for polimerization or enzimatic reactions) [20,31], mobile phases in chromatography [32,33], impregnation agents [9], assistance in particle design and size control [34-36] and reagents (e.g., in carbonation reaction) [37-39].

0.3. Objectives

On the basis of the main goal of this PhD Thesis and the potentials of the $scCO_2$ technology, the following scientific objectives are formulated:

- To develop a generic and versatile $scCO_2$ process as the manufacturing technology for the surface silanization of nanoparticles with improved composition control, enhanced grafting quality and high thermal stability.
- To extend the $scCO_2$ technology to the preparation of hybrid composite products involving silanized nanoparticles dispersed in liquid and solid organic matrices.
- To overcome technical barriers from more fundamental $scCO_2$ research to engineering processes designed for applications in bulk low-cost materials.
- To convey the knowledge between engineering and materials research contributing to the deployment of clean technologies with a more efficient life cycle and sustainability benefits upon substitution of organic solvents by $scCO_2$.

The following technical achievements need to be reached to meet the abovementioned objectives:

- Engineering of flexible bench-scale facilities for products preparation (preferably one-step) using $scCO_2$ as a solvent, anti-solvent or solute.
- Engineering of high pressure instrumentation for phase equilibria and solubility measurements.
- Process optimization by application of experimental design.
- Development of protocols for designing and evaluating surface modification (silanization) processes using $scCO_2$ as a solvent.
- Development of protocols for manufacturing hybrid nanostructured composite materials of the type inorganic nanoparticles dispersed in organic matrices using $scCO_2$ either as an antisolvent or as a solvent.
- Development of protocols and methods for off-situ materials characterization in solid (X-ray diffraction, infrared spectroscopy, Raman spectroscopy, low-temperature N_2 adsorption-desorption, mercury intrusion porosimetry, thermogravimetry, differential scanning calorimetry, scanning electron microscopy, transmission electron microscopy, UV-Vis spectroscopy, energy dispersive spectrometry, solid ^{29}Si nuclear magnetic resonance, water permeability test, static contact angle), dissolved (^{1}H nuclear magnetic resonance, high performance liquid chromatography) or dispersed mode (laser scattering and dynamic light scattering).

0.4. Strategies for $scCO_2$ technology

The physicochemical properties of $scCO_2$ offer a widespread set of alternatives for novel processing protocols and strategies. Moreover, some post-processing steps (e.g., grinding, milling, solvent removal by evaporation or extraction) needed in some specific industries (e.g., coating, drug delivery systems) using conventional technologies are usually avoided when using $scCO_2$. Strategies of the use of $scCO_2$ for materials processing purposes are, herein, classified in four main groups (Figure 0.3):

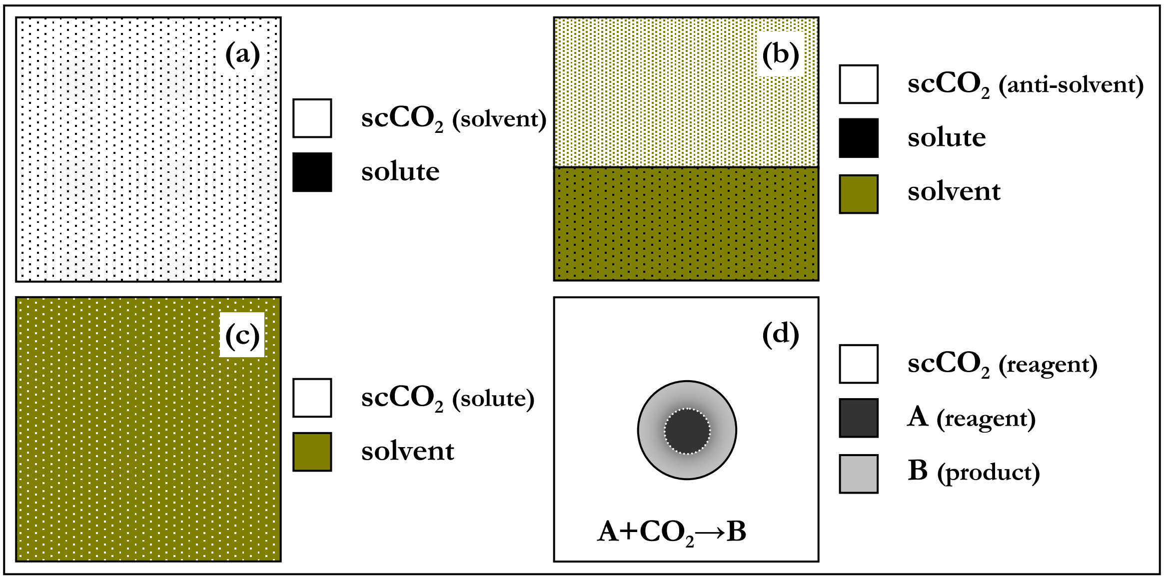

Figure 0.3. **Strategies for materials processing using supercritical fluid technology: (a) $scCO_2$ as a solvent, (b) $scCO_2$ as an anti-solvent, (c) $scCO_2$ as a solute, and (d) $scCO_2$ as a reagent.**

Strategy I: Use of $scCO_2$ as a solvent

Carbon dioxide has a low dielectric constant and no dipole moment, but a substantial quadrupole moment (-1.4 10^{-34} $J^{0.5}m^{2.5}$). Hence, $scCO_2$ can only solubilize small organic compounds of low polarity (e.g., esters, ethers, lactones, epoxides, hydrocarbons, aromatics) [15,40]. Moreover, a large solubility enhancement in $scCO_2$ is reported for fluorinated compounds and silicon atom-containing molecules [14,41]. On the other hand, the addition of small amounts (5-10 wt%) of cosolvents (e.g., acetone, ethanol) to $scCO_2$ is used to increase the solubility of polar nonvolatile molecules in the resulting mixture [42,43]. Extraction of natural compounds, particle formation processes (e.g., Rapid Expansion of a Supercritical Solution, RESS), polymer impregnation, cleaning of impurities, solvent removal and reaction medium (e.g., in Diels-Alder, silanization, hydrogenation, hydroformilation, oxidation, polymerization and enzimatic reactions) are among the most promising applications exploiting the solvent power of $scCO_2$ [21,44-64]. In the RESS process, the precipitation of the compound dissolved in $scCO_2$ is achieved by the rapid expansion of the supercritical solution, caused through a mechanical perturbation (e.g., using a nozzle), into a low pressure vessel at which the solvent becomes a gas.

Strategy II: Use of $scCO_2$ *as an anti-solvent*

The lack of solubility of certain solutes in $scCO_2$ may be exploited for the processing of these materials by using the $scCO_2$ as an anti-solvent added to a conventional liquid solution containing the solute. $scCO_2$ must be partially or totally miscible with the liquid solvent and a non-solvent for the solute. Under these conditions, a simultaneous two-way mass transfer, caused by the rapid diffusion of CO_2 into the liquid solution and the solvent into the CO_2 phase, takes place. The diffusion of the $scCO_2$ anti-solvent into the liquid solvent reduces the solvent power of the liquid, thus, causing solute precipitation. A vast number of technical processes take profit of this double mechanism for particle formation with $scCO_2$, being the most recognized the Gas Anti-Solvent (GAS), the Supercritical Anti-Solvent (SAS), the Precipitation with Compressed Anti-Solvent (PCA), and the Aerosol Solvent Extraction System (ASES) processes [48,50-52,55,57,65-70]. In the GAS process, $scCO_2$ is added to the precipitation vessel previously charged with the liquid solution. However, high amounts of solvent inclusions are usually incorporated in the formed powder. Conversely, in the SAS, PCA and ASES processes, $scCO_2$ is first pumped into the precipitation vessel and, then, the liquid solution is sprayed into the vessel through a restrictor (e.g., nozzle). The ASES process can be considered as a modification of the SAS process with simultaneous spraying through a nozzle of the liquid solution and the anti-solvent into the precipitation vessel.

Strategy III: Use of $scCO_2$ *as a solute*

Technologies based on the use of $scCO_2$ as a solute and, in particular, the from Particles Gas Saturated Solutions (PGSS®) process, have emerged as alternative one-step methods to obtain solvent-free polymer or lipid particles at low processing temperatures [65,66,71]. Active substance-loaded particles and particles with encapsulated liquid are also processed by the PGSS® process [72-76]. The technique consisted in dissolving high concentrations of $scCO_2$ in the bulk of a melted solid and the subsequent quick expansion through a nozzle, causing the complete evaporation of the gas and the solidification of the liquid into fine particles. The PGSS® process operates at lower pressures than other $scCO_2$-asssisted particle formation processes (e.g., RESS) and no organic cosolvents are needed for processing. Moreover, it can be operated in the continuous mode, giving excellent process yields. Equipment for materials processing using this technique is commercially available at industrial scale, with capacities of hundreds of kilograms per hour [57]. However, the control of particle size and particle size distribution of the obtained powder has to be improved. $scCO_2$ is also used in extrusion processes, since the dissolution of

$scCO_2$ in amorphous polymers reduces the melting point and, thus, the working temperature. The process is particularly important for the processing of immiscible polymers, because the addition of $scCO_2$ lowers the viscosity of the blend leading to a better mixing of the components [77]. Finally, $scCO_2$ acts as a porogenic agent for amorphous polymers. Pores are formed when the $scCO_2$ solubilized in the polymeric matrix is released upon depressurization. The foaming of biopolymers using $scCO_2$ is being investigated with the aim of preparing scaffolds for tissue engineering [78-82]. Moreover, these polymeric scaffolds can also be loaded with bioactive compounds using the supercritical technology (e.g., drugs, growth factors or proteins) [79,81-83].

Strategy IV: Use of $scCO_2$ *as a reagent*

Much research is focused on the use of carbon dioxide as a green feedstock for the sustainable synthesis of chemicals [84-91]. It is estimated that *ca.* 110 Mt per year of CO_2 are consumed worldwide to produce low molecular weight products (e.g., urea, salicylic acid, carbonates) [92]. To date, however, the economics of such processes are not very promising, since in most of the applications the CO_2 technology competes with the existing routes/plants using the highly reactive and effective, but toxic, carbon monoxide (CO) [21]. Nonetheless, the high concentration of CO_2 when $scCO_2$ is used may accelerate some of these reactions and make the use of $scCO_2$ more effective than CO. Moreover, the high solubility of many gases in $scCO_2$ (e.g., H_2) is a chemical advantage for using $scCO_2$ as a reagent (e.g., in the hydrogenation of CO_2 to make formic acid, and in the synthesis of alkyl formates or alkyl and dialkyl formamides using CO_2 and H_2 as the reagents) [87,93]. The use of $scCO_2$ as a carbonation agent may also reduce the mass transfer limitations in diffusion-controlled reactions, such as in the synthesis of inorganic carbonates [38,56,94-97]. Finally, the simultaneous use of $scCO_2$ as both a reaction medium and reactant is being prospected, since it is regarded as a smart reaction strategy for synthesis [98]. This approach is being evaluated for the synthesis of organic chemicals, such as ureas, carbamates and isocyanate carbodiimides [99].

0.5. Remarks on the use of $scCO_2$ technology

The viability of the application of any of the abovementioned supercritical processes must be subjected to a detailed case-by-case study. Further, the assessment of the potential of a certain technology using $scCO_2$ for the processing of a specific product should take into account the environmental and economical advantages of the process compared to the traditional method established in the industry. In this respect, green chemistry encourages innovation and promotes the creation of products that are both environmentally and economically sustainable. The 12 Principles of Green Chemistry [13] provide a road map for engineers to implement $scCO_2$ technology and have been applied in the PhD Thesis:

1. **Design chemical processing to prevent waste:** leaving no waste to treat.
    - ✓ CO_2 fluid technology incorporates environmental considerations into the process design from the beginning by avoiding or minimizing the use of persistent organic solvents.
    - ✓ In this PhD Thesis, the engineered nanostructures prepared using $scCO_2$ fluid technology needed no additional final drying steps.
    - ✓ Processes are designed to be closed-loop: after final product fabrication the CO_2 is recycled back to the pressure vessel. It is considered a zero waste technology.
2. **Design safer products:** preserving efficacy of function while reducing toxicity.
    - ✓ CO_2 has GRAS status.
3. **Design less hazardous processes:** no toxicity to humans / environment.
    - ✓ Health hazards are minimized by reducing the use of organic solvents in the fabricated nanostructures, thus reducing risks of adverse effects.
4. **Use renewable raw materials and feedstock:** rather than depletion.
    - ✓ Used CO_2 is a by-product of other processes. Shifting from organic solvents use must decrease the total CO_2 output.
    - ✓ A more efficient use of current resources is performed by decreasing the degradation rate of final products during storage through elimination of solvent inclusions.
5. **Use catalysts:** accelerating the reactions.
    - ✓ Reactive processes studied in this PhD Thesis (i.e., silanization) are accelerated in $scCO_2$, even without the addition of a catalyst.
6. **Avoid chemical derivatives and blocking or protecting groups.**
    - ✓ $scCO_2$ is mostly a non-reactive solvent and the protection of functional groups is not necessary.

7. **Maximize the incorporation of materials** used in the process into the final product.

- ✓ Products recoveries in the single-stage supercritical processes is generally enhanced (*ca.* 80-90%), offering significantly higher yields than the conventional multi-stage processing (*ca.* 30-50%).
- ✓ The used compressed fluid is easily recycled, and the remaining high value raw materials are simply recovered by lowering the pressure of the CO_2.

8. **Use safer solvents:** innocuous.

- ✓ In the chemical and pharmaceutical industry, major advances are needed to reduce the use of organic solvents (methanol, toluene, xylene, methyl ethyl ketone, and dichloromethane), which account for 27% of total Toxics Release Inventory Chemicals. This PhD Thesis mainly uses CO_2, an environmental friendly solvent.

9. **Increase energy efficiency:** energy and economic impacts should be minimized.

- ✓ Produced materials are isolated by CO_2 depressurization resulting in a dry product. This eliminates the cost of the energy-intensive filtration and drying procedures.
- ✓ The energy usage is reduced in the designed one-stage process due to the minimization in volume of waste disposal, recycling or destruction.

10. **Design chemicals and products to degrade after use:** do not persist.

- ✓ This principle implies the use of polymers *vs.* metals, since polymers are more easily recycled. $scCO_2$ is an adequate solvent to process polymers either pure or as a part of a composite.

11. **In-process monitoring and control:** analyze in real time to prevent pollution.

- ✓ In-process chemical monitoring for high-pressure equipment is difficult. However, the PhD Thesis intends the development of in-situ (phase behavior) high pressure and off-situ analytical instrumentation for the understanding of CO_2 fluid technology and nanoscale effects.

12. **Minimize the potential for accidents:** releases to the environment, explosions.

- ✓ CO_2 is a friendly solvent that improves working conditions when replacing organic solvents, by avoiding exposure of workers to hazardous, flammable and toxic materials.
- ✓ High pressure risks are limited by taking correct established engineering measures.

0.6. Scope and Structure of the Thesis

This Chapter has given an overview of the state-of-the-art of supercritical carbon dioxide technology and its use in materials processing. In the following Chapters, a rigorous study of the effects of the operation parameters on the studied supercritical processes and on the characteristics of the obtained end products is presented.

Chapter 1 – Processing using scCO$_2$ technology, contains the description of the general aspects and some rules-of-thumb to take into account when designing equipment working with scCO$_2$. Then, the components of the supercritical equipment, the process flow diagrams and the technological aspects of the different equipment used for materials processing in this PhD Thesis are described.

Chapter 2 - Use of scCO$_2$ as a solvent: Supercritical silanization reaction, contains the study of the surface treatment of inorganic nanoparticles with alkoxysilanes using scCO$_2$ as the reaction medium. Firstly, studies of the solubility of octyltriethoxysilane in compressed CO$_2$ and the kinetics of the silanization process of the surface of titanium dioxide nanoparticles, used as a model material, are undertaken. Then, the screening of the feasible set of the operating conditions in the supercritical silanization process to obtain silanized TiO$_2$ particles with the desired characteristics is carried out using chemometric tools. Finally, the compilation of all these data provides enough information for the engineering control of the degree and quality of the silane coating and for the implementation of the process to other combinations of inorganic nanoparticles and alkoxysilanes.

Chapter 3 – Use of scCO$_2$ as an anti-solvent: preparation of hybrid materials, contains the description of a scCO$_2$-assisted process designed for the preparation of fibers of biopolymers (poly(methylmethacrylate)/poly(ε-caprolactone) and poly(L-lactic acid)) loaded with inorganic nanometric fillers (titanium dioxide and hydroxyapatite). The effects of the operating parameters on the properties of the final material and the potential applicability of the fibers in tissue engineering are assessed.

Chapter 4 – Use of scCO$_2$ as a solute: preparation of lipid-based particles, contains the experimental data and the development of a scCO$_2$-assisted process for the preparation of particles composed of the lipid blend hydrogenated castor oil/glyceryl monostearate loaded with titanium dioxide nanoparticles and caffeine. The choice of the feasible region for the supercritical processing is assessed through the measurements of the variations in the lipids melting point in contact with $scCO_2$. The properties of the resulting lipid-based particles are determined for their potential applicability in topical cosmetics.

Chapter 5 – Use of $scCO_2$ as a reagent: accelerated cement carbonation, contains the study of the accelerated carbonation of Portland-cement based materials with $scCO_2$. Changes in composition, porosity and microstructure of supercritically carbonated cement samples without and with admixtures (silica fume and fly ash) are analyzed and compared to those of atmospherically carbonated samples. The supercritical silanization of the carbonated cement samples is performed with the objective of conferring water repellence and enhanced durability to the material. The silane treatment of cement-based samples also acts as an evaluation test for the implementation of the supercritical silanization process to multiscale complex composite materials. Finally, a detailed study on scheduling, processing time reduction and process integration is performed for the carbonation-silanization process of cement-based materials.

0.7. References

[1] C. Sanchez, G.J. de A.A. Soler-Illia, F. Ribot, T. Lalot, C.R. Mayer, V. Cabuil, *Designed hybrid organic–inorganic nanocomposites from functional nanobuilding blocks*. Chemistry of Materials 2001, 13(10), 3061-3083.

[2] P.M. Ajayan, L.S. Schadler, P.V. Braun, *Nanocomposite science and technology*. Wiley-VCH: Weinheim, 2003.

[3] P. Gómez-Romero, C. Sanchez, *Functional hybrid materials*, 6th edition. Wiley-VCH: Weinheim, 2004.

[4] G. Kickelbick, *Hybrid materials: Synthesis, characterization, and applications*, 1st edition. Wiley-VCH: Weinheim, 2007.

[5] R.N. Rothon, *Fillers and their surface modifiers for polymer applications*. Plastics Informations Direct: Bristol, 2007.

[6] L.E. Nielsen, R.F. Landel, *Mechanical properties of polymers and composites*, 1st edition. CRC: New York, 1993.

[7] P.R. Hornsby, *Fire retardant fillers for polymers*. International Materials Reviews 2001, 46(4), 199-210.

[8] Y. Liu, R. Yang, J. Yu, K. Wang, *Investigation of interfacial structure of coupling agent treated fillers by Fourier transform infrared spectroscopy and attenuated total reflection-FTIR spectroscopy*. Polymer Composites 2002, 23(1), 28-33.

[9] C. Domingo, E. Loste, J. Fraile, *Grafting of trialkoxysilane on the surface of nanoparticles by conventional wet alcoholic and supercritical carbon dioxide deposition methods*. The Journal of Supercritical Fluids 2006, 37(1), 72-86.

[10] Y. Zhou, K. Cooper, Y. Li, Z. Li, *Use of coupling agents to improve the interface in absorbable polymer composites*. U.S. Patent 20,090,149,873 (2009).

[11] P.C. Wernett, *Surface treated inorganic particle additive for increasing the toughness of polymers*. WO Patent 2,009,077,860 (2009).

[12] M.Z. Rong, M.Q. Zhang, W.H. Ruan, *Surface modification of nanoscale fillers for improving properties of polymer nanocomposites: A review*. Materials Science and Technology 2006, 22(7), 787–796.

[13] P.T. Anastas et al., *Green chemistry: Theory and practice*. Oxford University Press: New York, 1998.

[14] M.A. McHugh, V.J. Krukonis, *Supercritical fluid extraction: principles and practice*. Butterworth-Heinemann: Boston, 1994.

[15] Y. Sun, *Supercritical fluid technology in materials science and engineering*. Marcel Dekker: New York, 2002.

[16] R. Span, W. Wagner, *A new equation of state for carbon dioxide covering the fluid region from the triple-point temperature to 1100 K at pressures up to 800 MPa*. Journal of Physical and Chemical Reference Data 1996, 25(6), 1509-1596.

[17] L.W. Diamond, N.N. Akinfiev, *Solubility of* CO_2 *in water from -1.5 to 100ºC and from 0.1 to 100 MPa: evaluation of literature data and thermodynamic modelling*. Fluid Phase Equilibria 2003, 208(1-2), 265-290.

[18] J. García-Carmona, M.A. Fanovich, J. Llibre, R. Rodríguez-Clemente, C. Domingo, *Processing of microporous VPI-5 molecular sieve by using supercritical* CO_2*: stability and adsorption properties*. Microporous and Mesoporous Materials 2002, 54(1-2), 127-137.

[19] H. Jin, B. Subramaniam, *Exothermic oxidations in supercritical* CO_2*: effects of pressure-tunable heat capacity on adiabatic temperature rise and parametric sensitivity*. Chemical Engineering Science 2003, 58(9), 1897-1901.

[20] S.P. Nalawade, F. Picchioni, L.P.B.M. Janssen, *Supercritical carbon dioxide as a green solvent for processing polymer melts: Processing aspects and applications*. Progress in Polymer Science 2006, 31(1), 19-43.

[21] E.J. Beckman, *Supercritical and near-critical* CO_2 *in green chemical synthesis and processing*. The Journal of Supercritical Fluids 2004, 28 (2-3), 121-191.

[22] C. Vemavarapu, M.J. Mollan, M. Lodaya, T. E. Needham, *Design and process aspects of laboratory scale SCF particle formation systems.* International Journal of Pharmaceutics 2005, 292 (1-2), 1-16.

[23] A.R. Sampaio da Sousa, *Development of functional particles using supercritical fluid technology: Fundamentals, processing and applications.* PhD Thesis. Oeiras, 2007.

[24] P. Tundo, A. Perosa, F. Zecchini, *Methods and reagents for green chemistry.* Wiley: New Jersey, 2007.

[25] T. Clifford, *Fundamentals of Supercritical Fluids.* Oxford University Press: New York, 1999.

[26] O.J. Catchpole, P. Simoes, J.B. Grey, E.M.M. Nogueiro, P.J. Carmelo, M. Nunes da Ponte, *Fractionation of Lipids in a Static Mixer and Packed Column Using Supercritical Carbon Dioxide.* Industrial & Engineering Chemistry Research 2000, 39(12), 4820-4827.

[27] M. Fullana, F. Trabelsi, F. Recasens, *Use of neural net computing for statistical and kinetic modelling and simulation of supercritical fluid extractors.* Chemical Engineering Science 2000, 55(1), 79-95.

[28] S.J. Park, C.J. Kim, B.S. Rhee, *Fractionation of aromatic heavy oil by dynamic supercritical fluid extraction.* Industrial & Engineering Chemistry Research 2000, 39(12), 4897-4900.

[29] K.C. Zancan, M.O.M. Marques, A.J. Petenate, M.A.A. Meireles, *Extraction of ginger (Zingiber officinale Roscoe) oleoresin with* CO_2 *and co-solvents: a study of the antioxidant action of the extracts.* The Journal of Supercritical Fluids 2002, 24(1), 57-76.

[30] E. Reverchon, I. De Marco, *Supercritical fluid extraction and fractionation of natural matter.* The Journal of Supercritical Fluids 2006, 38(2), 146-166.

[31] Z. Knez, M. Habulin, *Compressed gases as alternative enzymatic-reaction solvents: a short review.* The Journal of Supercritical Fluids 2002, 23(1), 29-42.

[32] K. Sato, S.S. Sasaki, Y. Goda, T. Yamada, O. Nunomura, K. Ishikawa, T. Maitani, *Direct connection of supercritical fluid extraction and supercritical fluid chromatography as a rapid quantitative method for Capsaicinoids in placentas of Capsicum.* Journal of Agricultural and Food Chemistry 1999, 47(11), 4665-4668.

[33] T. Aro, C. Brede, P. Manninen, H. Kallio, *Determination of semivolatile compounds in Baltic herring (Clupea harengus membras) by supercritical fluid extraction-supercritical fluid chromatography-gas chromatography-mass spectrometry.* Journal of Agricultural and Food Chemistry 2002, 50(7), 1970-1975.

[34] J. Jung, M. Perrut, *Particle design using supercritical fluids: Literature and patent survey.* The Journal of Supercritical Fluids 2001, 20(3), 179-219.

[35] P. Chattopadhyay, R.B. Gupta, *Supercritical CO_2 based production of magnetically responsive micro- and nanoparticles for drug targeting*. Industrial & Engineering Chemistry Research 2002, 41(24), 6049-6058.

[36] C.G. Kalogiannis, C.M. Michailof, C.G. Panayiotou, *Microencapsulation of amoxicillin in poly(L-lactic acid) by supercritical antisolvent precipitation*. Industrial & Engineering Chemistry Research 2006, 45(25), 8738-8743.

[37] J.B. Rubin, C.M.V. Taylor, *Partial replacement of Portland cement with fly ashes and kiln dusts using supercritical carbon dioxide processing*. Los Alamos National Laboratory: Los Alamos, USA, 1998.

[38] C.A. García-González, A. Hidalgo, C. Andrade, M.C. Alonso, J. Fraile, A.M. López-Periago, C. Domingo, *Modification of composition and microstructure of Portland cement pastes as a result of natural and supercritical carbonation procedures.* Industrial & Engineering Chemistry Research 2006, 45(14), 4985-4992.

[39] G. Rimmelé, V. Barlet-Gouédard, O. Porcherie, B. Goffé, F. Brunet, *Heterogeneous porosity distribution in Portland cement exposed to CO_2-rich fluids.* Cement and Concrete Research 2008, 38 (8-9), 1038-1048.

[40] Y.J. Sheng, P.C. Chen, Y.P. Chen, D. Shan, *Calculations of solubilities of aromatic compounds in supercritical carbon dioxide*. Industrial & Engineering Chemistry Research 1992, 31(3), 967-973.

[41] C.A. García-González, J. Fraile, A. López-Periago, J. Saurina, C. Domingo, *Measurements and correlation of octyltriethoxysilane solubility in supercritical CO_2 and assembly of functional silane monolayers on the surface of nanometric particles.* Industrial & Engineering Chemistry Research, In Press (doi: 10.1021/ie900775z).

[42] R.K. Roop, A. Akgerman, *Entrainer effect for supercritical extraction of phenol from water*. Industrial & Engineering Chemistry Research 1989, 28(10), 1542-1546.

[43] S.S.T. Ting, D.L. Tomasko, S.J. MacNaughton, N.R. Foster, *Chemical-physical interpretation of co-solvent effects in supercritical fluids*. Industrial & Engineering Chemistry Research 1993, 32(7), 1482-1487.

[44] C. Domingo, E.M. Berends, G.M. van Rosmalen, *Precipitation of ultrafine benzoic acid by expansion of a supercritical carbon dioxide solution through a porous plate nozzle*. Journal of Crystal Growth 1996, 166(1-4), 989-995.

[45] C. Domingo, E. Berends, G.M. van Rosmalen, *Precipitation of ultrafine organic crystals from the rapid expansion of supercritical solutions over a capillary and a frit nozzle*. The Journal of Supercritical Fluids 1997, 10(1), 39-55.

[46] A. Roig, I. Mata, E. Molins, C. Miravitlles, J. Torras, J. Llibre, *Silica aerogels by supercritical extraction*. Journal of the European Ceramic Society 1998, 18(9), 1141-1143.

[47] C. Domingo, F.E. Wubbolts, R. Rodríguez-Clemente, G.M. van Rosmalen, *Solid crystallization by rapid expansion of supercritical ternary mixtures.* Journal of Crystal Growth 1999, 198-199(1), 760-766.

[48] M. Perrut, J.-Y. Clavier, *Supercritical Fluid Formulation: Process Choice and Scale-up.* Industrial & Engineering Chemistry Research 2003, 42(25), 6375-6383.

[49] E. Loste, J. Fraile, M.A. Fanovich, G.F. Woerlee, C. Domingo, *Anhydrous supercritical carbon dioxide method for the controlled silanization of inorganic nanoparticles.* Advanced Materials 2004, 16(8), 739-744.

[50] P. Subra, P. Berroy, A. Vega, C. Domingo, *Process performances and characteristics of powders produced using supercritical* CO_2 *as solvent and antisolvent.* Powder Technology 2004, 142(1), 13-22.

[51] S.-D. Yeo, E. Kiran, *Formation of polymer particles with supercritical fluids: A review.* The Journal of Supercritical Fluids 2005, 34 (3), 287-308.

[52] J.L. Martínez, *Supercritical fluid extraction of nutraceuticals and bioactive compounds.* CRC Press, Taylor & Francis Group: Boca Raton, 2007.

[53] E. Reverchon, A. Antonacci, *Polymer microparticles production by supercritical assisted atomization.* The Journal of Supercritical Fluids 2007, 39 (3), 444-452.

[54] A. Santana, M.A. Larrayoz, E. Ramírez, J. Nistal, F. Recasens, *Sunflower oil hydrogenation on Pd in supercritical solvents: Kinetics and selectivities.* The Journal of Supercritical Fluids 2007, 41(3), 391-403.

[55] K. Byrappa, S. Ohara, T. Adschiri, *Nanoparticles synthesis using supercritical fluid technology – towards biomedical applications.* Advanced Drug Delivery Reviews 2008, 60(3), 299-327.

[56] C.A. García-González, N. El Grouh, A. Hidalgo, J. Fraile, A.M. López-Periago, C. Andrade, C. Domingo, *New insights on the use of supercritical carbon dioxide for the accelerated carbonation of cement pastes.* The Journal of Supercritical Fluids 2008, 43(3), 500-509.

[57] I. Pasquali, R. Bettini, *Are pharmaceutics really going supercritical?* International Journal of Pharmaceutics 2008, 364(2), 176-187.

[58] S. Rodríguez-Rojo, J. Marienfeld, M.J. Cocero, *RESS process in coating applications in a high pressure fluidized bed environment: Bottom and top spray experiments.* Chemical Engineering Journal 2008, 144(3), 531-539.

[59] C.A. García-González, J.M. Andanson, S.G. Kazarian, C. Domingo, J. Saurina, *Application of principal component analysis to the thermal characterization of silanized nanoparticles obtained at supercritical carbon dioxide conditions.* Analytica Chimica Acta 2009, 635(2), 227–234.

[60] C.A. García-González, J.M. Andanson, S.G. Kazarian, J. Saurina, C. Domingo, *Preparation of nanostructured organic–inorganic hybrid materials using supercritical fluid technology*. Composite Interfaces 2009, 16(2-3), 143–155.

[61] C.A. García-González, J. Fraile, A. López-Periago, C. Domingo, *Preparation of silane-coated TiO_2 nanoparticles in supercritical CO_2*. Journal of Colloid and Interface Science 2009, 338(2), 491-499.

[62] C.A. García-González, J. Saurina, J.A. Ayllón, C. Domingo. *Preparation and characterization of surface silanized TiO_2 nanoparticles under compressed CO_2: Reaction kinetics*. The Journal of Physical Chemistry C 2009, 113(31), 13780-13786.

[63] A. López-Periago, C.A. García-González, C. Domingo, *Impregnation of a triphenylpyrylium cation into zeolite cavities using supercritical CO_2*. J. Supercritical Fluids 2009, 50(3), 305-312.

[64] A. López-Periago, C.A. García-González, C. Domingo, *Solvent- and thermal-induced crystallization of poly-L-lactic acid in supercritical CO_2 medium*. Journal of Applied Polymer Science 2009, 111(1), 291-300.

[65] R. Marr, T. Gamse, *Use of supercritical fluids for different processes including new developments – a review*. Chemical Engineering and Processing 2000, 39(1), 19-28.

[66] E. Weidner, M. Petermann, Z. Knez, *Multifunctional composites by high-pressure spray processes*. Current Opinion in Solid State and Materials Science 2003, 7(4-5), 385-390.

[67] F. Miguel, A. Martín, T. Gamse, M.J. Cocero, *Supercritical anti solvent precipitation of lycopene: Effect of the operating parameters*. The Journal of Supercritical Fluids 2006, 36(3), 225-235.

[68] P. Subra-Paternault, C. Roy, D. Vrel, A. Vega-González, C. Domingo, *Solvent effect on tolbutamide crystallization induced by compressed CO_2 as antisolvent*. Journal of Crystal Growth 2007, 309(1), 76-85.

[69] A. Vega-González, P. Subra-Paternault, A.M. López-Periago, C.A. García-González, C. Domingo, *Supercritical CO_2 antisolvent precipitation of polymer networks of L-PLA, PMMA and PMMA/PCL blends for biomedical applications*. European Polymer Journal 2008, 44(4), 1081-1094.

[70] C.A. García-González, A. Vega-González, A.M. López-Periago, P. Subra-Paternault, C. Domingo, *Composite fibrous biomaterials for tissue engineering obtained using a supercritical CO_2 antisolvent process*. Acta Biomaterialia 2009, 5(4), 1094-1103.

[71] E. Weidner, Z. Knez, Z. Novak, *Process for preparing particles or powders*, WO Patent WO95/21,688 (1995).

[72] M. Rodrigues, N. Peiriço, H. Matos, E. Gomes de Azevedo, M.R. Lobato, A.J. Almeida, *Microcomposites theophylline/hydrogenated palm oil from a PGSS process for controlled drug delivery systems*. The Journal of Supercritical Fluids 2004, 29(1-2), 175-184.

[73] A.R. Sampaio de Sousa, A.L. Simplício, H.C. de Sousa, C.M.M. Duarte, *Preparation of glyceryl monostearate-based particles by PGSS®—Application to caffeine*. The Journal of Supercritical Fluids 2007, 43(1), 120-125.

[74] A.R. Sampaio de Sousa, R. Silva, F.H. Tay, A.L. Simplício, S.G. Kazarian, C.M.M. Duarte, *Solubility enhancement of trans-chalcone using lipid carriers and supercritical* CO_2 *processing*. The Journal of Supercritical Fluids 2009, 48(2), 120-125.

[75] M.J. Cocero, A. Martín, F. Mattea, S. Varona, *Encapsulation and co-precipitation processes with supercritical fluids: Fundamentals and applications*. The Journal of Supercritical Fluids 2009, 47 (3), 546-555.

[76] C.A. García-González, A.R. Sampaio da Sousa, A. Argemí, A. López Periago, J. Saurina, C.M.M. Duarte, C. Domingo, *Production of hybrid lipid-based particles loaded with inorganic nanoparticles and active compounds for prolonged topical release*. International Journal of Pharmaceutics 2009, 382(1-2), 296-304.

[77] S.P. Nalawade, F. Picchioni, L.P.B.M. Janssen, *Supercritical carbon dioxide as a green solvent for processing polymer melts: Processing aspects and applications*. Progress in Polymer Science 2006, 31(1), 19-43.

[78] H.M. Woods, M.M.C.G. Silva, C. Nouvel, K.M. Shakesheff, S.M. Howdle, *Materials processing in supercritical carbon dioxide: surfactants, polymers and biomaterials*. Materials Chemistry 2004, 14(11), 1663-1678.

[79] A. Argemí, A. López-Periago, C. Domingo, J. Saurina, *Spectroscopic and chromatographic characterization of triflusal delivery systems prepared by using supercritical impregnation technologies*. Journal of Pharmaceutical and Biomedical Analysis 2008, 46(3), 456-462.

[80] A.M. López-Periago, A. Vega, P. Subra, A. Argemí, J. Saurina, C.A. García-González, C. Domingo, *Supercritical* CO_2 *processing of polymers for the production of materials with applications in tissue engineering and drug delivery*. Journal of Materials Science 2008, 43(6), 1939-1947.

[81] J.M. Andanson, A. López-Periago, C.A. García-González, C. Domingo, S.G. Kazarian, *Spectroscopic analysis of triflusal impregnated into PMMA from supercritical* CO_2 *solution*. Vibrational Spectroscopy 2009, 49(2), 183-189.

[82] A. López-Periago, A. Argemí, J.M. Andanson, V. Fernández, C.A. García-González, S.G. Kazarian, J. Saurina, C. Domingo, *Impregnation of a biocompatible polymer aided by supercritical* CO_2*: evaluation of drug stability, drug-matrix interactions*. The Journal of Supercritical Fluids 2009, 48(1), 56-63.

[83] C. Elvira, A. Fanovich, M. Fernández, J. Fraile, J. San Román, C. Domingo, *Evaluation of drug delivery characteristics of microspheres of PMMA–PCL–cholesterol obtained by supercritical-*CO_2 *impregnation and by dissolution–evaporation techniques*. Journal of Controlled Release 2004, 99(2), 231-240.

[84] A. Behr, *Carbon dioxide as an alternative C_1 synthetic unit: activation by transition-metal complexes*. Angewandte Chemie International Edition in English 1988, 27(5), 661-678.

[85] M.T. Reetz, W. Könen, T. Strack, *Supercritical carbon dioxide as a reaction medium and reaction partner*. CHIMIA International Journal for Chemistry 1993, 47(12), 493.

[86] D.H. Gibson, *The organometallic chemistry of carbon dioxide.* Chemical Reviews 1996, 96(6), 1063-2095.

[87] P.G. Jessop, Y. Hsiao, T. Ikariya, R. Noyori, *Homogeneous catalysis in supercritical fluids: hydrogenation of supercritical carbon dioxide to formic acid, alkyl formates, and formamides.* Journal of the American Chemical Society 1996, 118(2), 344-355.

[88] T. Ikariya, P.G. Jessop, Y. Hsiao, R. Noyori, *Method for producing formic acid or its derivatives*. US Patent No. 5,763,662 (1998).

[89] C.S. Pomelli, J. Tomasi, M. Solà, *Theoretical study on the thermodynamics of the elimination of formic acid in the last step of the hydrogenation of CO_2 catalyzed by rhodium complexes in the gas phase and supercritical CO_2*. Organometallics 1998, 17(15), 3164-3168.

[90] A.-A.G. Shaikh, S. Sivaram, *Organic carbonates*. Chemical Reviews 1996, 96(3), 951-976.

[91] C. Vieville, J.W. Yoo, S. Pelet, Z. Mouloungui, *Synthesis of glycerol carbonate by direct carbonation of glycerol in supercritical CO_2 in the presence of zeolites and ion exchange resin.* Catalysys Letters 1998, 56(4), 245-247.

[92] H. Arakawa et al., *Catalysis research of relevance to carbon management: Progress, challenges, and opportunities*. Chemical Reviews 2001, 101(4), 953-996.

[93] P.G. Jessop, *Homogeneous catalysis using supercritical fluids: Recent trends and systems studied*. The Journal of Supercritical Fluids 2006, 38(2), 211-231.

[94] C. Domingo, J. García-Carmona, E. Loste, A. Fanovich, J. Fraile, J. Gómez-Morales, *Control of calcium carbonate morphology by precipitation in compressed and supercritical carbon dioxide media*. Journal of Crystal Growth 2004, 271(1-2), 268-273.

[95] C. Domingo, E. Loste, J. Gómez-Morales, J. García-Carmona, J. Fraile, *Calcite precipitation by a high-pressure CO_2 carbonation route*. The Journal of Supercritical Fluids 2006, 36(3), 202-215.

[96] C.A. García-González, A. Hidalgo, J. Fraile, A.M. López-Periago, C. Andrade, C. Domingo, *Porosity and water permeability study of supercritically carbonated cement pastes involving mineral additions*. Industrial & Engineering Chemistry Research 2007, 46(8), 2488-2496.

[97] A. Hidalgo, C. Domingo, C. Garcia, S. Petit, C. Alonso, C. Andrade, *Microstructural changes induced in Portland cement-based materials due to natural and supercritical carbonation.* Journal of Materials Science 2008, 43(9), 3101-3111.

[98] P.G. Jessop, W. Leitner, *Chemical synthesis using supercritical fluids*. VCH/Wiley: Weinheim, 1999.

[99] A. Scondo, F. Dumarcay-Charbonnier, A. Marsura, D. Barth, *Supercritical* CO_2 *phosphine imide reaction on peracetylated β-cyclodextrins*. The Journal of Supercritical Fluids 2009, 48(1), 41-47.

Chapter 1

PROCESSING USING SCCO$_2$ TECHNOLOGY

The design of equipment for processes involving the use of scCO$_2$ implies some special features that must be taken into account before construction. Some important rules-of-thumb for high-pressure equipment design, selection of building materials and safety procedures are, herein, summarized. These principles have been applied in the supercritical equipment used in this PhD Thesis (multi-purpose supercritical batch equipment, multi-purpose supercritical equipment with a continuous flow of scCO$_2$, supercritical-assisted anti-solvent equipment and Particles from Gas Saturated Solutions equipment). In this Chapter, a detailed description of the process flow diagrams (PFD), the technical aspects and the running procedures are presented for all the used supercritical equipment.

1.1. Introduction

Inherent physicochemical properties of supercritical fluids imply special aspects to be considered for the design and selection of equipment involving the use of these compressed fluids. The first available off-the-shelf supercritical fluid apparatus in the market were designed and intended to be used for extraction purposes, mainly for the commercialization of the supercritical technology for the extraction of caffeine and flavors [1-4]. Nowadays, numerous suppliers of equipment for several specific applications of supercritical fluid technology are currently in the market [5-11]. For multi-purpose design, the general practice is to adapt or reconfigure already existing high-pressure components or equipments for the intended end application using supercritical fluids.

Materials selection for the supercritical equipment must take into account the used supercritical fluid, the operating conditions (pressure, temperature), as well as the chemical nature of the reagents used in the process. An initial approach to equipment materials choice should be performed using a decision table on chemical resistance of materials to solvents and aggressive chemicals. These tables give essential information regarding the risk for deterioration of the material and potential chemical accidents [12-18]. In general, AISI-316 stainless steel is the typical construction material employed for vessels, valves, piping and fittings using supercritical CO_2, due to the chemical inertness and sturdiness of this material, able to withstand both the operating temperatures and pressures intended for the equipment [3,16]. Maximum allowable working pressure of any AISI-316 stainless steel pressure vessel must be stated in terms of the temperature at which it applies. As a rule-of-thumb, the design pressure should be at least 10% higher than the maximum allowable working pressure, and the safety factor between the bursting pressure of the equipment and the design pressure is typically 2.4-3.0 [19-21]. Tables of the pressure rating factors as a function of the material permit the calculation of the maximum allowable working pressures at different operating temperatures.

The choice of the closure system type in the vessels and the material to be used for the assembly of the different components of the supercritical equipment depend on the operating conditions, the bore diameter and on the frequency of opening. Metallic seals are generally preferred for the assembly of fittings (e.g,, Swagelok®, A-Lok®, Gyrolok®, NPT, CPI, ANSI/ASME B1.20.1, BS21 (ISO 7-1), BSPP, SAE) [22,23]. The type of closure of pressure vessels may vary from metallic rings or polymeric o-rings to finger tight closures of graphite reinforced Teflon rings containing a self-energizing spring [24]. Metallic seals are usually made of stainless steel, brass or Inconel®, while there is a wide range of materials for polymeric o-rings (e.g., Teflon®, Viton®, Vespel®, Kalrez®, polyaryletheretherketone –PEEK–, ethylene propylene rubber –EPR–, polyimide C, chlorotrifluoroethylene –CTFE–, ethylene propylene diene monomer rubber –EPDM–) [22,25]. The selection of the elastomer is influenced by the operating pressure and temperature and the desired durability of the seal. Furthermore, leakages can be caused by the sorption of $scCO_2$ in the polymeric o-rings producing swelling, the ring extrusion due to high loadings (e.g. fluid hammer and pressure surges), heating-chilling cycles or the ring wear. The severity of these phenomena in the process influences the choice of the seal material.

The most common practice of achieving the supercritical conditions for CO_2 is in two steps: from the compressed gas (CO_2 supply lines are usually at 5.0-7.0 MPa under ambient temperature) to the liquid state (i.e., condensation) and, then, from liquid to supercritical conditions. The condensation of CO_2 is achieved by passing the gas through cooling lines (e.g., chiller or cryostat). The pumping of CO_2 in the liquid state ensures the successful pressurization of the fluid without cavitation problems. Syringe, liquid driven and air driven plunger pumps are the most common choice for CO_2 pumping. Syringe pumps are mainly limited to laboratory scale applications in the batch mode. Among the liquid driven plunger pumps, membrane pumps are usually preferred. From them, despite their relative high cost, pumps with metallic membranes are usually chosen to assure an acceptable CO_2-tightness, rather than Teflon or other elastomeric membrane pumps. In terms of the economy of the process, air driven plunger pumps are the choice for services needing high pumping flow capacity (f.i., circulation pumps). For these purposes, the reduced price of the air driven plunger pumps compensates their lower energy efficiency in comparison to membrane pumps. For air driven pumps, special care should be taken to the compatibility of CO_2 with all materials used in the plunger part of the pump, especially the materials for sealing. To avoid pressure fluctuations with both liquid- and air-driven plunger pumps, the strategy to be adopted is to use several pumps not working in phase. Otherwise, an alternative and economical method for reducing pressure fluctuations and flow variations is to install a pulsation dampener in the pipeline. Finally, the pressurized liquid coming from the pump is heated and brought to supercritical conditions using a heat exchanger [26].

Ball, needle and check valves are the most common choices to put in contact or to isolate lines pressurized with $scCO_2$. Ball valves are used for on-off or switching services. Needle valves can provide a certain capacity of flow regulation and are even used as backpressure regulators (i.e., devices intended for avoiding the loss of pressure upstream of the point where compressed CO_2 is depressurized). The flow regulation capacity of the valve depends on its intrinsic flow coefficient (C_v) [27]. In general, low C_v values allows a fine capacity of regulation at low fluid flow rates. Finally, check valves are used to ensure the CO_2 flow in only one direction.

The relatively high pressures that accompanied supercritical fluid technology using scCO_2 may lead to possible hazards for both personnel and equipment integrity [4]. Hence, a detailed protocol of operation during start-up, processing and shut-down procedures should be meticulously prepared [28]. For supercritical fluids, process control engineering is of special concern in the risk assessment of the equipment, since small variations in temperature and/or volume in the system lead to dramatic changes in pressure (see f.i., Figure 0.2). The measurement of the main operating parameters would help to the control and troubleshooting of the supercritical process. The use of off-the-shelf instrumentation for the follow-up of temperature (e.g., J- or K-type thermocouples and resistance temperature detectors), pressure (e.g., Bourdon pressure gauges and piezoresistive transducers), level (e.g., sapphire or quartz view windows) and fluid mass flow (e.g., rotameters, thermo flow meters or Coriolis flow meters) of the process should be foreseen in the design of the supercritical equipment [29].

Finally, safety procedures should include not only the use of hardware rated for high pressures but also pressure-relief mechanisms in the supercritical equipment. A partial or fully depressurization of the system must take place in case an unexpected event lead to an uncontrolled pressure increase above the limit value of the operating pressure fixed for the pressure-relief mechanism. For these purposes, rupture discs and relief or safety valves are the most common choices. Rupture discs are pressure relief devices providing instantaneous full-opening in case of an overpressure situation. Burst pressure of rupture discs are rated between a minimum and a maximum value. Normal operating pressure of the supercritical equipment should not exceed 70% of the rated minimum burst pressure. Rupture discs have different designs (flat or angle) and are available in several materials providing a broad operating service in a wide range of temperature, pressure and corrosion conditions [30-33]. Relief valves are devices with a spring designed to allow partial evacuation of the flow through the valve above a certain pressure value (cracking pressure) proportionately to the increase in upstream pressure [30,34-37]. Once the overpressure ceases and the normal operating conditions are reestablished, the upstream pressure is lower than the closing force exerted by the spring of the safety valve and the relief stops. The choice of either rupture discs or relief valves or both together relies on several factors, like margin between operating pressure and desired relief pressure, expected pressure fluctuations or use in an aggressive environment. Rupture discs are generally selected when the supercritical or gaseous stream contains solids or sticky compounds, since their presence may infer failures in the relief valves. The design of these relief devices must have inner and outer exhaust sections with dimensions at least equal to the sum of the sections of all the piping inlets of the operating unit at which they are giving service [30,32,33,38-40].

1.2. Supercritical processing equipment

1.2.1. Multi-purpose supercritical batch equipment

The PFD of the equipment used in this PhD Thesis for the experiments performed under $scCO_2$ in the batch mode is shown in Figure 1.1. The unit basically consists of three parts: cooling, compression and reaction sections.

The CO_2 (T1) initially enters in the equipment pipelines at 5-7 MPa and laboratory temperature. Then, the CO_2 is liquified using a 6-liter poly(ethylene glycol) (PEG) / water bath (EX1, Polyscience 9102). The used refrigeration system provides enough chilling and contact area between CO_2 and the circulating refrigeration fluid to achieve the temperature needed for getting liquid CO_2 before fluid pumping, even working with a continuous CO_2 flow at the low flow rate of 1-2 g min^{-1}. Needle valves with a Teflon sealing are used in the equipment (valves V1-V5 from HiP), since they provide a certain capacity of flow rate regulation.

A syringe pump with a body of 240 mL (P1, Thar Designs SP240) is used to raise the pressure of CO_2 up to the desired working value. The plunger movement of the pump can be controlled by setting either a constant displacement rate or a pressure set-point value (PIC-101). In the latter case, the plunger displacement rate remains constant until the difference between the set-point value and the system pressure is less than 1 MPa, and, then, the rate slows down so that the desired pressure can be precisely attained and overshoots are prevented. The pumping automatically stops in case the outlet pressure goes beyond the pre-set maximum pressure alarm (PAH-101). Additionally, a rupture disc (1/4” angle of Inconel rated at a burst pressure of 51 MPa at 295 K, Autoclave Engineers) is placed in the discharge line of the pump as a safety procedure in case of overpressure.

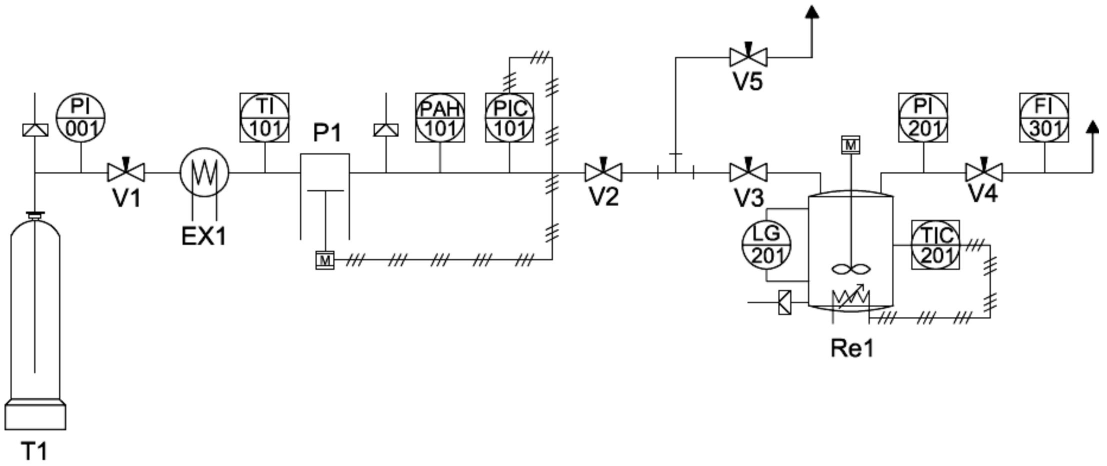

Figure 1.1. **PFD of the multi-purpose supercritical batch equipment.**

The reactor, previously charged with the reagents, is filled with the CO_2 coming from the pump through a 1/8" piping by opening valves V2 and V3 until the desired pressure is reached. During operation, the temperature and stirring of the stainless steel reactor (Thar Design, 100 mL) are set by using temperature-controlled electric resistances and a stirring-controlled device respectively. ¼" NPT ports located in the reactor cap are used for the CO_2 inlet and outlet. Two out of the three additional ports located in the reactor body are used for a thermocouple (TIC-201) and a rupture disc (1/4" angle of Inconel rated at a burst pressure of 41.3 MPa; Autoclave Engineers). The remaining port is capped. A finger tight closure of 2.12"-outer diameter of Polyimide C cup-type ring containing a self-energizing spring is used to seal the reactor. Moreover, two single-crystal sapphire windows (LG-201, 7/8" diameter), placed 180° apart in the reactor body, allow the visual follow-up of the process taking place inside of the reactor.

At the end of each experiment, the system is depressurized by means of valve V4 at a known CO_2 mass flow rate measured with a thermo flow meter (FI-301, Bronkhorst Hi-Tec F-111C-HBD-20-V).

1.2.2. Multi-purpose supercritical equipment with a continuous flow of $scCO_2$

The PFD of the equipment used in this PhD Thesis for processes involving a continuous flow of $scCO_2$ is shown in Figure 1.2. This equipment has an on-line data logger for the acquisition of the values of the main process parameters (pressure, temperature, flow, alarms). Customized software was developed in the laboratory for the computer-control of both the pressure and safety of the equipment.

The CO_2 feedstock (T1) at 5–7 MPa and laboratory temperature is cooled using a 6–meter counter-flow heat transfer coil (EX1), so that the fluid is delivered as a liquid to the pump. Cooling is necessary to ensure the effective pressurization of the fluid. The circulating refrigeration fluid is a PEG/water mixture, which is cooled at 265 K using a cryostat (Haake D8). A rupture disc (1/4" angle of AISI 316 stainless steel rated at a burst pressure of 13.0 MPa at 295 K, Autoclave Engineers) is placed in the pipeline of the CO_2 cooling section, in order to prevent the risk of overpressure caused by an unexpected boiling of the liquid CO_2 due to refrigeration failure. The liquid CO_2 is compressed using a hydraulic positive-displacement volumetric pump of the membrane-type (P1, Lewa EK-M-210). The head of the pump is cooled with the same refrigeration fluid. In this way, the warming up of the pump chamber during compression causing fluid cavitation is avoided. To safeguard the pump, it has a pressure-limiting relief valve on the hydraulic side at the pre-set cracking pressure of 25.0 MPa. The rest of the compression section is protected from a pressure surge with a rupture disc (1/4" angle of Inconel rated at a burst pressure of 42.7 MPa at 295 K, Autoclave Engineers). Ball check valves are placed in the inlet and outlet ports of the pump to avoid the flow of the fluid backward.

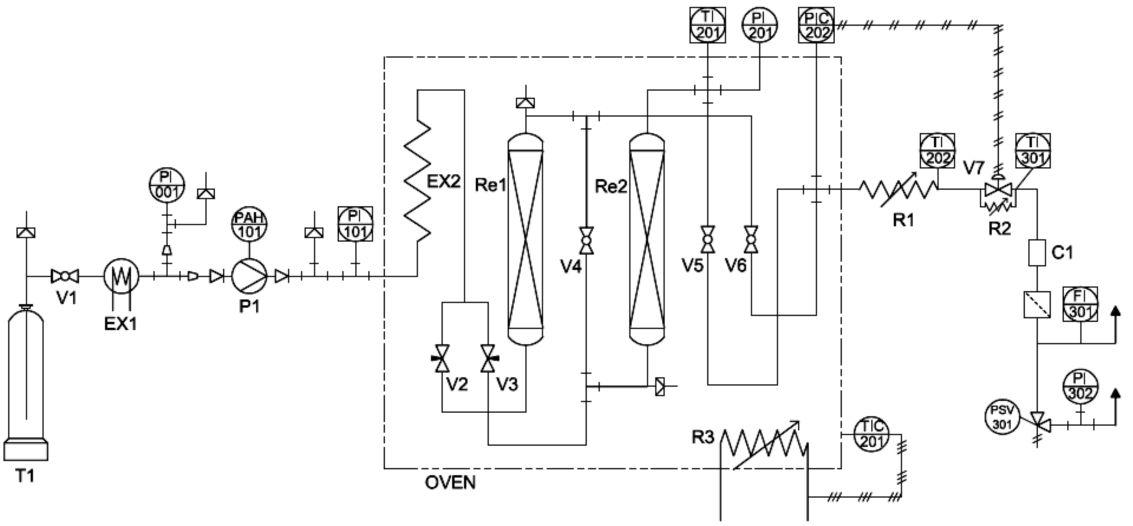

Figure 1.2. **PFD of the multi-purpose supercritical equipment with a continuous flow of $scCO_2$.**

The processing section of the equipment is placed in an air circulating oven (Selecta), able to heat the system up to the desired operating temperature. A piece of ¼" stainless steel 5–meter length coiled tubing (EX2) located inside the oven provides enough residence time to the fluid to achieve the desired operating temperature before entering the reactors [23].

The CO_2 at supercritical conditions is fed to two 10-mL stainless steel tubular reactors (Re1 and Re2) through two needle valves (V2 and V3, Autoclave Engineers), allowing the gradual pressurization of the reactors. The reactors are previously charged with the reagents/materials. Teflon filters (Supelco, 100 μm pore diameter) are placed on both extremes of the reactors to avoid solid particles entrainment. Silk wool or stainless steel fiber mesh is used within the reactors to assure a correct contact of the supercritical fluid with the material to be processed [41,42]. Thus, channelling and by-passing of $scCO_2$ are avoided and the fluid flow pulsations are damped by reducing the free volume in the reactor [3]. The design of the equipment is engineered with a set of on-off service ball valves (V4-V6, with an AISI 316 SS ball and a PEEK seat, Parker) conferring flexibility and versatility to the apparatus: in series, parallel and single-reactor operation are all possible arrangements of the equipment. The pressure in the reactors is regulated by means of a feed-forward loop through a computer-controlled neumatic backpressure (V7, Tescom) placed at the system exit. The backpressure regulator is heated (R1 and R2) to avoid clogging due to the precipitation of reagents escaping from the reactors or by formed dry ice as a result of the CO_2 Joule-Thomson effect. As a rule of thumb, for working pressures in the range of 7.4-68.9 MPa and CO_2 flow rates of 3-35 g min^{-1}, the temperature in the backpressure regulator should be 50 K higher than the temperature at the processing vessel [3].

Finally, CO_2 is decompressed up to atmospheric pressure in the backpressure regulator, passes through a Teflon collection chamber (C1), where entrained solid particles are collected in a filter, and, finally, the gas is released. The CO_2 flow rate is measured at atmospheric pressure using a gaseous flow meter (FI-301, Bronkhorst Hi-Tec) located downstream of the collection chamber. A relief valve rated at 0.2 MPa (PSV-301, Parker) is placed before the mass flow meter to avoid overpressure in the low pressure line. Finally, samples are recovered after the full depressurization of the processing section.

1.2.3. Supercritical-assisted anti-solvent equipment

Experiments using $scCO_2$ as an anti-solvent are carried out in the supercritical apparatus shown schematically in Fig. 1.3. The PCA (Particles from a Compressed Anti-Solvent) technique operating in the batch mode is used. The experimental set-up consists on a CO_2 supply line, a solution delivery line, a high-pressure collector vessel and an evacuation line. Briefly, in the PCA technique, components to be processed are first dissolved or dispersed in a suitable liquid organic phase. Next, the organic liquid phase is put in contact with the $scCO_2$ anti-solvent, and the latter rapidly diffuses into the organic liquid phase simultaneously to the diffusion of the organic solvent into scCO2. This double-mechanism leads to the supersaturation of the dissolved components in the organic phase, causing their precipitation. The dispersed components in the organic solution are expected to be embedded within the precipitated particles during their formation.

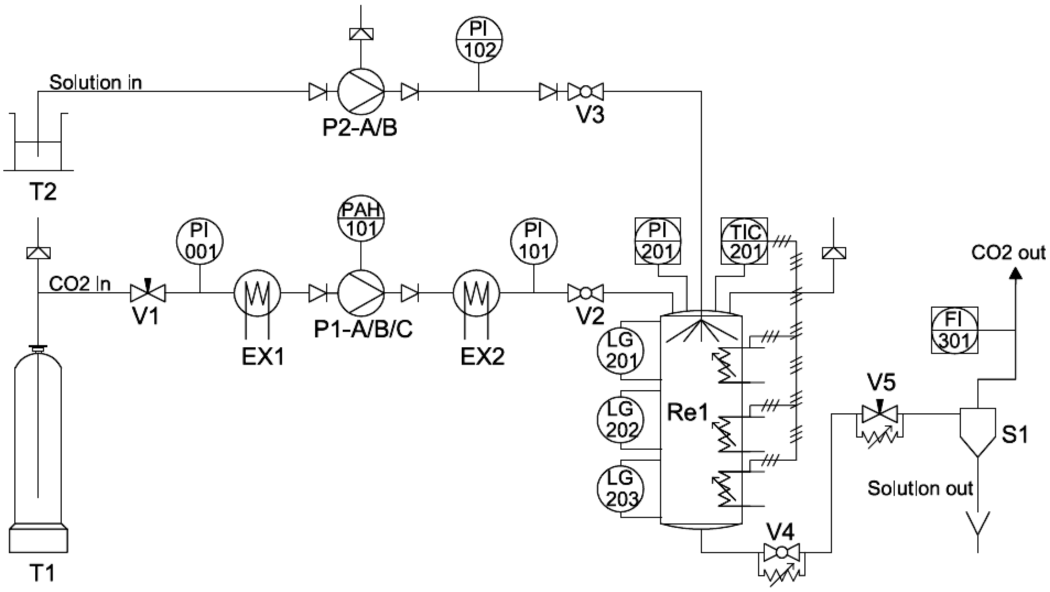

Figure 1.3. **PFD of the supercritical-assisted anti-solvent equipment.**

In a typical experiment, the CO2 at 5-7 MPa (T1) is first cooled at 273 K using a cryostat (EX1, Haake) and, then, pressurized to the desired operating pressure using three hydraulic positive-displacement volumetric pumps of the membrane-type arranged in parallel (P1-A/B/C, Lewa EK3). The fluid is compressed and, then, heated (EX2), and introduced into the collector vessel (Re1, Autoclave Engineers) by opening the needle valve V2 (HiP). The three pumps have similar protections against overpressure and cavitation as has pump P1 in the equipment described in Section 1.2.2 (head pump cooling, high pressure alarm and rupture discs). The precipitation vessel has 0.5 L of capacity of and a clamp closure with a Teflon O-ring sealing. The vessel is equipped with three pairs of sapphire windows at three different levels (LG-201, LG-202, LG-203), used for the visual follow-up of the process taking place inside. The vessel is heated with heating jackets (Watlow) and the temperature is controlled using a thermocouple (TIC-201). A rupture disc (1/4” angle of Inconel rated at a burst pressure of 32.0 MPa at 333K, Autoclave Engineers) is placed in one of the ports of the vessel as a safety procedure in case of overpressure. In a normal procedure, once the pressure and the temperature of the precipitation vessel are stabilized, the liquid is injected into it. This liquid contains dispersed solid compounds to be sprayed together with dissolved species. A double-piston liquid metering pump (P2-A/B, Milton Roy CP300), typical off-the-self item for liquid chromatographic systems, is used to deliver the liquid suspension into the processing vessel against the head pressure of the compressed fluid. The liquid metering pump has a rupture disc. A check valve is placed in the line delivering the suspension upstream of the needle valve V3 (HiP) to avoid CO_2 entry in the liquid line. The suspension is injected into the vessel through a conical spray (swirl) nozzle (Lechler, 100 μm diameter). The stainless steel nozzle is a restriction device that generates the expansion of the fluid. At the bottom of the vessel, a membrane filter placed on the top of a stainless steel frit (ColoChrom, 2 μm porosity) allows the collection of the precipitated solids.

Before solid collection, the ball valve V4 (Parker) is opened to remove the organic solvent by rinsing with a continuous flow of CO_2, remaining in the vessel Re1 the precipitated product. The micrometering needle valve V5 (Autoclave Engineers) is used as a backpressure regulator to maintain constant the working pressure employed during the rinsing period. A sudden pressure decrease of the fluid to atmospheric conditions takes place in the micrometering valve V5. The outlet pipeline and valves V4 and V5 are heated to prevent clogging due to CO_2 Joule-Thomson effect. The low solvation power of CO_2 at atmospheric pressure favors the liquid solvent separation from the stream and the collection of the liquid fraction in the separator S1 (Pirex). When the rinsing step is completed, the high-pressure vessel is slowly depressurized and the processed material is collected.

1.2.4. Supercritical-assisted PGSS® equipment

Experiments using $scCO_2$ as a solute in the Particles from Gas Saturated Solution (PGSS®) process are carried out in the equipment shown in the PFD of Figure 1.4. The unit basically consists on a CO_2 supply line, a high pressure vessel (Re1), a collector vessel (Re2) and an evacuation line [43]. Briefly, in the PGSS® technique, the solid components to be processed are first charged in the high pressure vessel. Then, compressed CO_2 is fed into the vessel. After heating, the mixture melts and the $scCO_2$ is solubilized in large quantities in the melt. Optionally, solid admixtures can be dispersed in the melt. After homogenization of the mixture, the CO_2-saturated melted solid is rapidly expanded through a restrictor (typically, a nozzle). The sudden change from supercritical pressure to ambient pressure causes the supersaturation of the CO_2 in the mixture and the quick expansion of the nucleated gaseous CO_2 bubbles. As a result, the melt cools down due to the Joule-Thomson effect. This effect, together with the volume expansion of the compressed CO_2 cause the solidification of the melted mixture, which usually precipitates in the form of micronized particles. The dispersed solid particles in the admixture are expected to be embedded within the solid particles formed during precipitation.

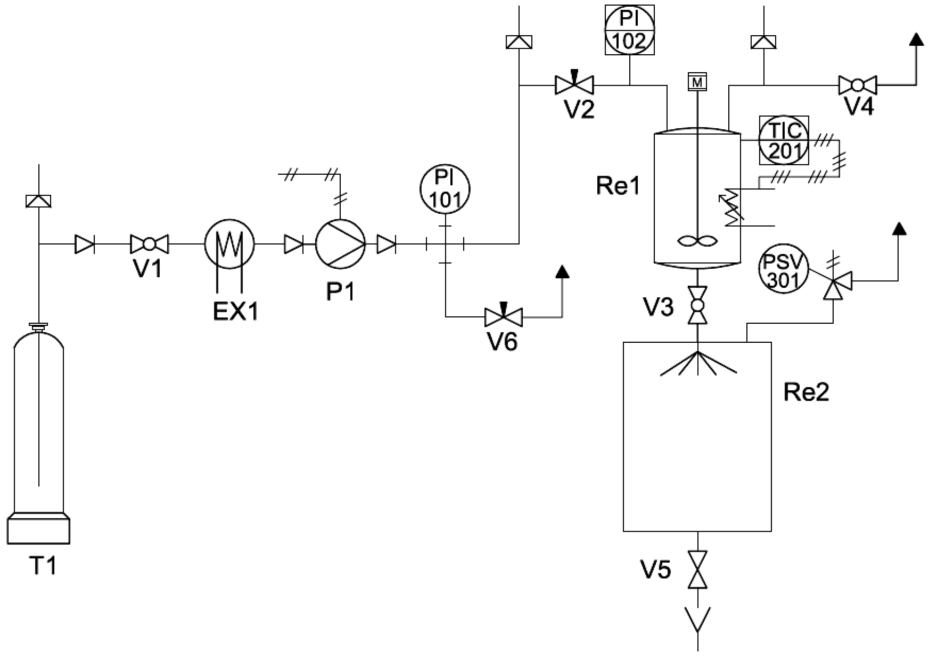

Figure 1.4. **PFD of the supercritical-assisted PGSS equipment.**

In a typical experiment, the CO_2 feedstock (T1) supplied at 5-7 MPa is first cooled using a cryostat (EX1, Haake), and, then, pressurized to the desired operating pressure using a high-pressure air-driven piston pump (P1, Haskel MCPV-71). Ball check valves are placed in the inlet and outlet ports of the pump to avoid the flow of the fluid backward. The maximum outlet pressure of CO_2 depends on the compressed air-driven pressure supplied to the pump [44]. The compression line is protected against pressure surge eventualities by means of a rupture disc (1/4" angle of Inconel rated at a burst pressure of 25.0 MPa at 295 K, Autoclave Engineers). The compressed CO_2 is fed to the high-pressure stirred vessel (Re1, Parr Instrument), containing the substances to be processed, by opening the needle valve V2 (HiP). The vessel Re1 has a capacity of 0.5 L and a clamp closure with a Teflon O-ring sealing. Two out of the six ports located in the reactor cap are used for the CO_2 inlet and purge. A thermocouple and a rupture disc (1/4" angle of Inconel rated at a burst pressure of 35.0 MPa, Autoclave Engineers) are inserted in other two ports. The two remaining ports are capped. The autoclave is heated by a temperature controlled electrical band heater (TIC-201) and agitated using a four-blade stirrer (Parr Instrument

A1120HC). In a normal procedure, once the pressure and the temperature of the vessel are stabilized and the materials are homogenized, the mixture is rapidly depressurized through a nozzle by opening the ball valve V3 (Parker). A stainless steel 600 μm-diameter cone nozzle (Spraying Systems Co) is used to generate the expansion of the melted mixture in a controlled way. The precipitated particles are collected in a 10-L vessel (Re2, Pirex). The vessel Re2 is equipped with a venting system to avoid overpressure.

1.3. Conclusions

Good performance and safety of processes involving the use of $scCO_2$ may be compromised without the assumption of a set of rule-of-thumbs and technical aspects related to materials selection, specifications of the equipment and health and safety practices. These recommendations are fulfilled in the design of the equipment used in this PhD Thesis for the supercritical processing of materials. A multi-purpose supercritical batch equipment, a multi-purpose equipment with a continuous flow of $scCO_2$, a supercritical-assisted anti-solvent equipment and a supercritical-assisted Particles from Gas Saturated Solution equipment are optimized for the preparation of the desired end-products. Customized protocols of operation are established for the high pressure equipment. Follow-up and control of the operating parameters (pressure, temperature, CO_2 flow, stirring rate) are carried out at different points of the equipment through the proper installation of measuring devices.

1.4. References

[1] K. Zosel, *Process for the decaffeination of coffee*, US Patent 4,247,570 (1981).

[2] G.F. Woerlee, *Process and device for separating a mixture or extracting a material*, WO Patent 013,377 (1994).

[3] C. Vemavarapu, M.J. Mollan, M. Lodaya, T.E. Needham, *Design and process aspects of laboratory scale SCF particle formation systems.* International Journal of Pharmaceutics 2005, 292 (1-2), 1-16.

[4] J.L. Martínez, *Supercritical fluid extraction of nutraceuticals and bioactive compounds*. Ed. CRC Press, Taylor & Francis Group: Boca Raton, 2007.

[5] FeyeCon Development & Implementation B.V. Information available on the website: www.feyecon.com. Accessed on July 2009.

[6] High Pressure Equipment Co. Information available on the website: www.highpressure.com. Accessed on July 2009.

[7] Iberfluid Instruments, S.A. Information available on the website: www.iberfluid.com. Accessed on July 2009.

[8] NATEX Prozesstechnologie GesmbH. Information available on the website: www.natex.at. Accessed on July 2009.

[9] Parr Instrument Co. Information available on the website: www.parrinst.com. Accessed on July 2009.

[10] SEPAREX S.A. Information available on the website: www.separex.fr. Accessed on July 2009.

[11] Thar Technologies, Inc. Information available on the website: www.thartec.com. Accessed on July 2009.

[12] Boc Edwards Group plc., *Product data – Carbon dioxide*. Publication No. Z023-01-895. 2002. Available on the website: www. bocedwards.com. Accessed on July 2009.

[13] ColePalmer Instrument co., *Chemical compatibility tester*. Available on the website: www.coleparmer.com/techinfo/ChemComp.asp. Accessed on July 2009.

[14] Eldon James Corp, *Chemical resistance of plastic & stainless steel*. Available on the website: www.eldonjames.com/html/chemical.html. Accessed on July 2009.

[15] Georg Fischer Piping Systems, *Chemical resistance of plastics and elastomers*. Available on the website: www.georgfischer.es. Accessed on July 2009.

[16] C.W. Kovach, *High performance stainless steels*. Available on the website: www.stainless-steel-world.net. Accessed on July 2009.

[17] N.A., *HELCOM Manual on co-operation in response to marine pollution within the framework of the convention on the protection of the marine environment of the Baltic sea area (Helsinki convention)*, Volume 2, Annex 2: Chemical resistance of materials, 2002. Available on the website: www.kbv.se/ra/volume2/start.htm. Accessed on July 2009.

[18] N.A., *HAM-LET, Advanced control technology. Corrosion data. Technical Information Bulletin.* Available on the website: www.accutech.com.sg/Images/Products/Reference/CATALOGE_PDF/CORROSION_DATA.pdf. Accessed on July 2009.

[19] D.M. Fryer, J.F. Harvey, *High pressure vessels*, 1st edition. Chapman & Hall: New York, 1998.

[20] S. Chattopadhyay, *Pressure vessels – Design and practice*, 1st edition. CRC Press: Boca Raton, 2004.

[21] J.R. Farr, M.H. Jawad, *Guidebook for the design of ASME Section VIII pressure vessels*, 3rd edition. ASME Press: New York, 2006.

[22] R.K. Flitney, *Seals and sealing handbook*, 5th Edition. Elsevier Science: Oxford, 2007.

[23] D. Green, R. Perry. *Perry's chemical engineers' handbook*, 8th edition. McGraw-Hill Professional: New York, 2007.

[24] L.M. Kumar, *Pressure vessel seal with self-energizing seal*. US Patent 5,850,934. (1998).

[25] N.P. Cheremisinoff, P.N. Cheremisinoff, *Elastomer technology handbook*, 1st edition. CRC-Press: Boca Raton, 1993.

[26] M. van der Kraan, M.M.W. Peeters, M.V. Fernandez Cid, G.F. Woerlee, W.J.T. Veugelers, G.J. Witkamp, *The influence of variable physical properties and buoyancy on heat exchanger design for near- and supercritical conditions*. The Journal of Supercritical Fluids 2005, 34(1), 99-105.

[27] Swagelok Co., *Valve Sizing – Technical Bulletin*. USA, 2002. Available on the website: www.swagelok.com. Accessed on September 2009.

[28] J. García-Serna, J.L. Martínez, M.J. Cocero, *Green HAZOP analysis: incorporating green engineering into design, assessment and implementation of chemical processes*. Green Chemistry 2007, 9, 111-124.

[29] B.G. Liptak, *Instrument engineers' handbook - Process measurement and analysis*, 3rd Edition. Butterworth-Heinemann. Boca Raton, 1995.

[30] Ministerio de Industria, Comercio y Turismo, *Código español de recipientes y aparatos a presión (CERAP)*. Madrid, 1992.

[31] LAMOT Corporation, *Rupture discs - Product selection guide*. USA, 2002. Available on the website: www.lamot.com. Accessed on July 2009.

[32] E. Turmo Sierra, *NTP 456: Discos de ruptura (I): Características*. Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.

[33] E. Turmo Sierra, *NTP 457: Discos de ruptura (II): Dimensionado*. Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.

[34] C.F. Parry, *Relief systems handbook*. Institution of Chemical Engineers: Rugby, 1992.

[35] American Institute of Chemical Engineers (AIChE), *Guidelines for engineering design for process safety*. AIChE: New York, 1993.

[36] J.M. Storch de Gracia, *Manual de seguridad industrial en plantas químicas y petroleras. Fundamentos, evaluación de riesgos y diseño*. McGrawHill/Interamericana de España: Madrid, 1998.

[37] Parker Instrumentation, *Relief valves (RH4 Series). Catalog no. 4131-RH*. USA, 2001.

[38] A. Cejalvo Lapeña, *NTP 342: Válvulas de seguridad (I): Características técnicas*. Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.

[39] A. Cejalvo Lapeña, *NTP 346: Válvulas de seguridad (II): Capacidad de alivio y dimensionado*. Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.

[40] E. Turmo Sierra, *NTP 510: Válvulas de Seguridad: Selección*. Instituto Nacional de Seguridad e Higiene en el Trabajo. Ministerio de Trabajo y Asuntos Sociales.

[41] T.H. Kim, D.Y. Lim, B.S. Yu, J.H. Lee, M. Goto, *Effect of stirring and heating rate on the formation of* TiO_2 *powders using supercritical fluid*, Industrial & Engineering Chemistry Research 2000, 39(12), 4702–4706.

[42] B.Y. Shekunov, J. Baldyga, P. York, *Particle formation by mixing with supercritical antisolvent at high Reynolds numbers*, Chemical Engineering Science 2001, 56(7), 2421–2433.

[43] A.R. Sampaio da Sousa, *Development of Functional Particles using Supercritical Fluid Technology: Fundamentals, processing and applications*. PhD Thesis. Oeiras, 2007.

[44] Haskel International, Inc., *Liquid Pump Catalog*. USA, 2002. Available on the website: www.haskel.com. Accessed on September 2009.

Chapter 2

USE OF SCCO2 AS A SOLVENT:

SUPERCRITICAL SILANIZATION REACTION

In this Chapter, the use of $scCO_2$ as the solvent of choice for alkoxysilanes for the surface treatment of inorganic nanoparticles is assessed. The silanization of nanometric titanium dioxide (TiO_2) particles with octyltriethoxysilane is taken as the model system. Chemometric analysis (2^3 full factorial design and Principal Component Analysis (PCA)) [1-3] is used to ascertain the feasible region of pressure and temperature for the $scCO_2$-aided silanization process and the effects and interactions of the operating variables on the properties of the final material. The characterization of the silanized materials is performed regarding the chemical structure of the silane on the surface, the silane content and the thermal stability of the coating, and the microstructure of the hybrid composite (porosity and dispersibility). The solubility measurements of octyltriethoxysilane in compressed CO_2 and the kinetic study of the TiO_2 silanization process allow the engineering control of the silane coating procedure. Finally, the conclusions obtained from the full study of the octyltriethoxysilane-TiO_2 model system are implemented to different silane molecules and inorganic substrates.

2.1. Introduction

Considerable research has been focused on nanostructured materials comprising nanoparticles, such as polymer composites [4,5], ceramic composites [6,7] and self-aggregated structures [8,9]. A significant proportion of hybrid inorganic-organic composites is compounded with particles and fibres used as fillers to improve various physical and mechanical properties of a matrix, such as the mechanical strength and the modulus, the rigidity or the heat-resistance [10]. Additionally, the use of inorganic fillers in hybrid materials compounded with polymeric matrices could reduce total costs [11]. These composites should meet many requirements for being used in different industrial applications such as adhesives, sealing materials, optical devices, sensors and artificial membranes [12].

The dispersion of most inorganic fillers into polymeric matrices is technically challenging, due to the low interfacial interaction between both phases [10,13,14]. For nanostructured hybrid composites, the large surface area to volume ratio of nanoparticles increases the relevance of the boundaries dividing the components [15].

The interfacial interaction between the dissimilar organic and inorganic phases can be increased by the surface modification of the inorganic nanoparticles. Many bifunctional organic molecules acting as coupling agents or adhesion promoters have been investigated for the surface modification of inorganic phases (e.g., organosilanes, organotitanates, aluminates, zirconates, zircoaluminates) [15-22]. These molecules are bifunctional chemical additives that interact with both the inorganic filler and the organic matrix, providing a molecular bridge between both components of the composite. Bifunctional organotrialkoxysilanes, a group of low toxicity and environmentally compliant chemicals, are the dominant coupling agents and adhesion promoters in the market [11,23,24]. Surface coating by silanization is also used in other applications such as surface protection against corrosive environments [25], water repellency (Fig. 2.1) [26-28], protection of labile biomolecules [29], metal recovery [30,31] or chromatographic stationary phase design [32].

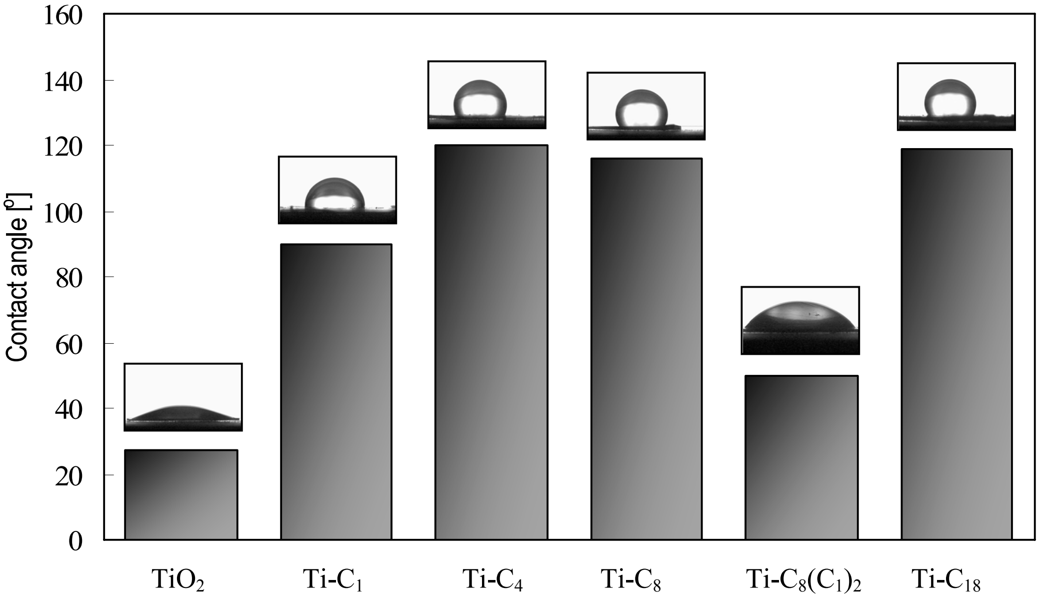

Figure 2.1. **Contact angle of a 1 μL-water droplet applied on the surface of compacted pellets of raw (TiO_2) and supercritically silanized TiO_2 particles with methyltrimethoxy- (Ti-C_1), isobutyltriethoxy- (Ti-C_4), octyltriethoxy- (Ti-C_8), octyldimethylmethoxy- (Ti-$C_8(C_1)_2$) and octadecyltrimethoxysilane (Ti-C_{18}).**

Organosilanes ($R_{(4-n)}SiX_n$) with one to three (n=1-3) hydrolyzable groups (X) in the molecule are used for the surface modification of inorganic particles. The hydrolyzable groups in the silane molecule may be of different nature (X=OR', Cl, H, NR'_2, $NHSiR_{(4-n)}$), being the alkoxysilanes (X=OR') the most common choice due to their availability, low cost and low toxicity of the generated by-products. Bifunctional organotrialkoxysilanes ($RSi(OR')_3$) are comprised of a silicon atom linked to three hydrolizable alkoxy groups (e.g., OR'= MeO, EtO or AcO) and a non-hydrolizable organofunctional group (e.g., R= alkyl, amine, methacryloxy or epoxy groups). The choice of the R group depends on each specific application of the silane treatment.

For trialkoxysilanes, the initiation of the silanization reaction [15,33-38] occurs by hydrolysis of the alkoxy groups promoted by water molecules either added to the reaction medium or present as a moisture adsorbed on the powder surface (reaction (1) in Fig. 2.2). The trivalent silanol head group can participate in multidirectional and interchangeable intra- and interlayer modes of coupling, which can be either covalent (siloxane bonds) or due to physical interaction (hydrogen bonds). The inorganic reactivity of silanols acts for hydrogen bonding with the hydroxyl groups from either other silanol molecules (reaction (2)) or placed on the inorganic substrate (reaction (3)). Finally, a polysiloxane layer on the surface of the particles is formed (reaction (4)), where hydrogen bridges with the surface are the predominant binding mode [36,39-41]. Additionally, the formation of siloxane bonds due to the condensation of silanol molecules may also lead to the production of highly branched polycondensed structures (reaction (5)). The robust chemical nature of the obtained silane coatings may offer extensive mechanisms for the engineering of the surface chemistry at the nanoscale [42-46] in processes of chemical modification, such as immobilization of organic molecules, metal cations and proteins or polymer grafting on silanized nanoparticles [47-50].

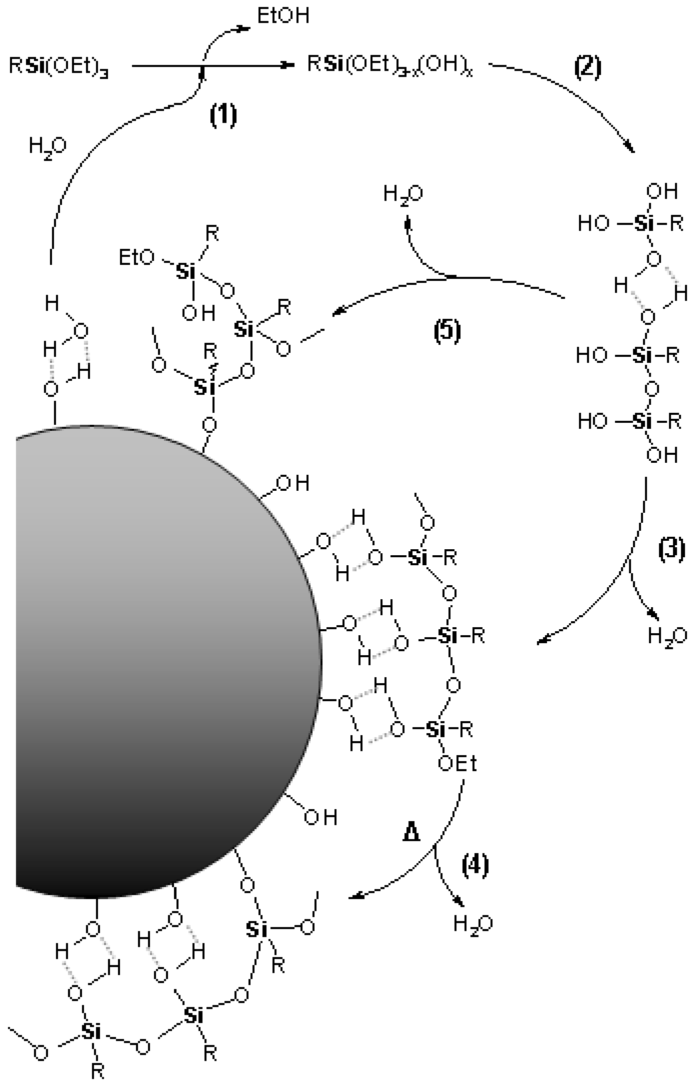

Figure 2.2. **Schematic representation of the different steps (1-5) of the silanization reaction with a triethoxysilane occurring on the surface of inorganic nanoparticles.**

The thickness of the silane coating is largely determined by the silane concentration in the used solution [35]. For most applications, monolayer deposition is usually preferred (reaction (4)). However, polycondensed multilayer coating (reaction (5)) and particle agglomeration are difficult to avoid employing conventional methods based in the use of liquid solvents (e.g., methanol, ethanol, toluene, tetrahydrofurane) [15,51-56]. For silanizations performed in solution, it is needed a precise control of the amount of water added to the liquid solvent to initiate the reaction in order to prevent polycondensation and multilayer formation. The anhydrous vapor phase deposition is a potential method used for monolayer formation [57]. Nevertheless, this deposition technique usually requires long-lasting reaction times (4-24 h), high temperatures (330-400 K), and it is limited to the deposition of volatile silane compounds (e.g., molecules with high vapor pressure and thermal stability). Further, in these vapor processes, only the methoxysilanes can be used without the presence of catalysts [51].

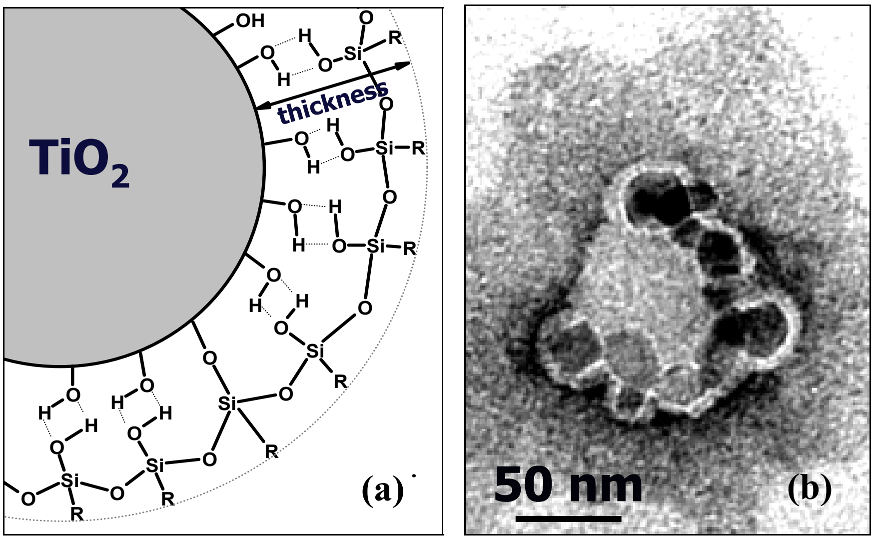

Figure 2.3. **Silane monolayer formation: (a) schematic representation, and (b) TEM picture of an octadecylsilane monolayer on TiO_2 nanoparticles obtained by the supercritical silanization process [68].**

In the search for an alternative sustainable process to overcome problems encountered for silane monolayer deposition, the use of supercritical carbon dioxide [58] has been proposed as an alternative [21,38,57,59]. The low viscosity, the absence of surface tension and the inert behavior of $scCO_2$ makes it adequate to manipulate complex surfaces, very small pieces of matter and nanostructured materials. Synthesis of inorganic nanoparticles in $scCO_2$ reaction medium is even reported in the literature [60,61]. These properties of $scCO_2$ allow the complete wetting of substrates with intricate geometries, including the interparticle surface of mesoporous agglomerates and the inner surface of microporous materials [62-64]. Further, in the anhydrous supercritical silanization process, water comes from moisture adsorbed on the powder surface. Thus, the hydrolysis step takes place preferentially near the surface of the inorganic nanoparticles, promoting monolayer formation (Fig. 2.3) through horizontal polymerization (reaction (4) in Fig. 2.2) [65].

The aim of this research is to optimize a generic method of silanization using $scCO_2$ [15,21,38,57,59] for the surface modification of inorganic nanoparticles in order to obtain new hybrid materials or to enhance the properties of already existing ones. The research is first focused on the silanization of TiO_2 nanoparticles with octyltriethoxysilane. This model system corresponds to a material of interest in pharmaceutical and cosmetic industries [66,67]. Firstly, the study of the solubility of the silane in compressed CO_2, and the kinetics of the silanization reaction under compressed CO_2 are carried out. This study is performed to control the degree and the quality of the silane coating [68,69]. The next step is the screening of the properties of the silanized TiO_2 particles obtained at different operating conditions through a chemometric analysis [70,71]. Finally, the process is implemented for other substrates (maghemite) and different mono- and trialkoxysilanes in order to assess the versatility of the supercritical silanization method [72].

2.2. Materials and methods [68-72]

2.2.1. Materials

Bare TiO_2 (20 nm, TiO_2 P25, Degussa) and γ-Fe_2O_3 (maghemite, 5 nm, lab synthesized) [73] nanoparticles are the inorganic substrates used for silane treatment. The silane molecules used are: methyltrimethoxysilane ($CH_3Si(OCH_3)_3$, Aldrich), isobutyltriethoxysilane ($(CH_3)_2CHCH_2Si(OCH_2CH_3)_3$, Fluka), octyltriethoxysilane (CH_3 $(CH_2)_7Si(OCH_2CH_3)_3$, Fluka), octyldimethylmethoxysilane ($CH_3(CH_2)_7Si(CH_3)_2(OCH_3)$, ABCR) and octadecyltrimethoxysilane ($CH_3(CH_2)_{17}Si(OCH_3)_3$, Fluka). CO_2 (Carburos Metálicos S.A.) is used as solvent.

2.2.2. Process

Inorganic nanoparticles are silanized using the batch equipment described in Section 1.2.1 of Chapter 1. The reactor was charged with the powder and the liquid silane in an arrangement in which there is no direct contact between both components (Fig. 2.4). The vessel is heated at the chosen operating temperature (T, 318-348 K) and the CO_2 is pumped into the reactor up to the operating pressure (P, 5.0-22.5 MPa). The system is stirred at 300 rpm during the complete running time (t, 5-240 min). At the end of each experiment, the system is depressurized at a CO_2 flow rate of *ca.* 1.2 g min^{-1} and cooled to room temperature.

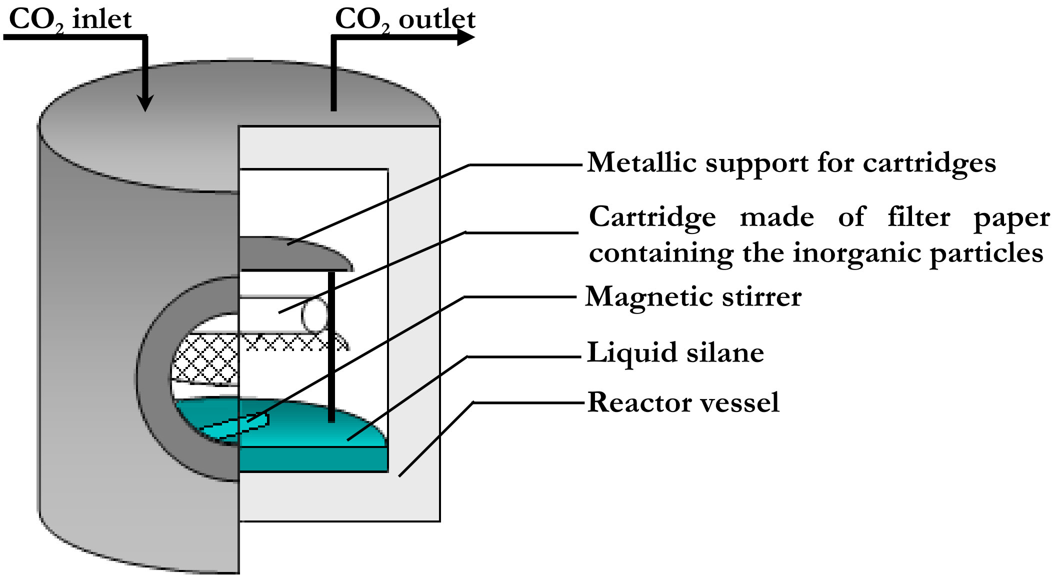

Figure 2.4. **Schematic drawing of the initial set-up of the reactor used for the supercritical silanization experiments.**

Silanized samples are further washed to remove the excess of silane by using the supercritical equipment described in Section 1.2.2 of Chapter 1, running with a continuous flow of CO_2 at a flow rate of 1.5-3.5 g min^{-1}, 318-348 K and 10.0-20.0 MPa, during different periods of time (15-120 min).

2.2.3. Characterization

The solubility measurement of octyltriethoxysilane in compressed CO_2 (8-18 MPa) is performed using a variable volume cell at two different temperatures (318 and 348 K). The properties of the silane coating deposited on the nanometric particles are studied by infrared and Raman spectroscopies, ^{29}Si nuclear magnetic resonance, energy dispersive spectrometry and thermogravimetric analysis. Textural characteristics of the silanized inorganic particles are analyzed by low-temperature N_2 adsorption-desorption, scanning electron microscopy and transmission electron microscopy. Laser scattering and dynamic light scattering methods are used to study the dispersibility of the silanized samples in an oleophilic medium (petroleum special). Finally, the static contact angle of a water droplet deposited on the surface of pellets made of compacted silanized nanoparticles is measured using a goniometer.

2.3. Results

Article no. 1

Title: Measurements and correlation of octyltriethoxysilane solubility in supercritical CO_2 and assembly of functional silane monolayers on the surface of nanometric particles

Authors: C. A. García-González, J. Fraile, A. López-Periago, J. Saurina, C. Domingo

Journal: Ind. Eng. Chem. Res., In Press (doi: 10.1021/ie900775z)

Article no. 2

Title: Preparation and Characterization of Surface Silanized TiO_2 Nanoparticles under Compressed CO_2: Reaction Kinetics

Authors: C. A. García-González, J. Saurina, J. A. Ayllón, C. Domingo

Journal: J. Phys. Chem. C, 113 (2009) 13780-13786

Article no. 3

Title: Preparation of Nanostructured Organic–Inorganic HybridMaterials Using Supercritical Fluid Technology

Authors: C. A. García-González, J.-M. Andanson, S. G. Kazarian, J. Saurina, C. Domingo

Journal: Compos. Interfaces 16 (2009) 143–155

Article no. 4

Title: Application of principal component analysis to the thermal characterization of silanized nanoparticles obtained at supercritical carbon dioxide conditions

Authors: C. A. García-González, J. M. Andanson, S. G. Kazarian, C. Domingo, J. Saurina

Journal: Anal. Chim. Acta 635 (2009) 227–234

Article no. 5

Title: Preparation of silane-coated TiO_2 nanoparticles in supercritical CO_2

Authors: C. A. García-González, J. Fraile, A. López-Periago, C. Domingo

Journal: J. Col. Inter. Sci., 338 (2009), 491-499

2.4. Conclusions

The optimization of a generic method of silanization using $scCO_2$ for the surface modification of inorganic nanoparticles is, herein, developed. The obtained silane coating using the supercritical silanization approach is thermally stable up to *ca.* 520 K, regardless of the operating conditions (pressure, temperature and reaction time) [71]. Free unbounded silane on the surface of the inorganic particles is completely removed by means of a continuous flow of $scCO_2$. A significant interaction of the variables operating pressure and temperature, influencing the properties of the final silanized materials, is revealed using chemometric analysis [70]. The combination of these two variables tunes the CO_2 density, varying the silane concentration in the reaction medium (i.e., silane solubility) and, subsequently, the quality of the silane coating on the inorganic particles [69]. The silanization process under compressed CO_2 can be described using a Langmuir-like kinetics model, which is largely influenced by the solubility of the silane in compressed CO_2 [68]. A fast silane monolayer formation on the TiO_2 surface is obtained by using CO_2 at supercritical conditions. Conversely, the degree of silane coating can be time-controlled if CO_2 at near-critical conditions is used. Compilation of the characterization data allows the definition of an objective function used to choose the operating conditions that lead to optimal material performance for two areas of potential application of TiO_2 nanoparticles silanized with octyltriethoxysilane: cosmetics and plastics industries. Finally, the process is implemented for other inorganic substrate (maghemite) and different mono- and tri-alkoxysilanes [72]. Hence, the versatility of the supercritical silanization method is demonstrated for its application in the preparation of hybrid materials.

2.5. References

[1] G.E.P. Box, W.G. Hunter, J.S. Hunter, *Statistics for experimenters: An introduction to design, data analysis, and model building*. John Wiley and Sons: New York, 1978.

[2] H. Martens, T. Naes, *Multivariate calibration*, John Wiley & Sons: New York, 1989.

[3] P. Subra, P. Berroy, J. Saurina, C. Domingo, *Influence of expansion conditions on the characteristics of cholesterol crystals analyzed by statistical design*. Journal of Supercritical Fluids 2004, 31(3), 313-322.

[4] H. Zhang, Z. Cui, Y. Wang, K. Zhang, X. Ji, C. Lü, B. Yang, M. Gao, *From water-soluble CdTe nanocrystals to fluorescent nanocrystal-polymer transparent composites using polymerizable surfactants*. Advanced Materials 2003, 15(10), 777-780.

[5] H. Althues, R. Palkovits, A. Rumplecker, P. Simon, W. Sigle, M. Bredol, U. Kynast, S. Kaskel, *Synthesis and characterization of transparent luminescent ZnS:Mn/PMMA nanocomposites*. Chemistry of Materials 2006, 18(4), 1068-1072.

[6] P. Limthongkul, H. Wang, H.Y.–M. Chiang, *Nanocomposite Li-ion battery anodes produced by the partial reduction of mixed oxides*. Chemistry of Materials 2001, 13(7), 2397-2402.

[7] X. F. Zhang, G. Harley, L .C. DeJonghe, *Co-continuous metal–ceramic nanocomposites*. Nano Letters 2005, 5(6), 1035-1037.

[8] F. Caruso, M. Spasova, V. Salgueiriño-Maceira, L.M. Liz-Marzán, *Multilayer assemblies of silica-encapsulated gold nanoparticles on decomposable colloid templates*. Advanced Materials 2001, 13(14), 1090-1094.

[9] E.V. Shevchenko, D.V. Talapin, N.A. Kotov, S. O'Brien, C.B. Murray, *Structural diversity in binary nanoparticle superlattices*. Nature 2006, 439, 55-59.

[10] Y. Liu, R. Yang, J. Yu, K. Wang, *Investigation of interfacial structure of coupling agent treated fillers by fourier transform infrared spectroscopy and attenuated total reflection-FTIR spectroscopy.* Polymer Composites 2002, 23(1), 28-33.

[11] N.A., *Bridging the gap with coupling agents*. Plastics, Additives and Compounding 2003, 5(3), 40-45.

[12] C. Sánchez, B. Julián, P. Belleville, M. Popall, *Applications of hybrid organic–inorganic nanocomposites*. Journal of Materials Chemistry 2005, 15(35-36), 3559 – 3592.

[13] P.C. Wernett, *Surface treated inorganic particle additive for increasing the toughness of polymers*. WO Patent 2,009,077,860 (2009).

[14] Y. Zhou, K. Cooper, Y. Li, Z. Li, *Use of coupling agents to improve the interface in absorbable polymer composites*. US Patent 20,090,149,873 (2009).

[15] C. Domingo, E. Loste, J. Fraile, *Grafting of trialkoxysilane on the surface of nanoparticles by conventional wet alcoholic and supercritical carbon dioxide deposition methods.* The Journal of Supercritical Fluids 2006, 37(1), 72-86.

[16] R. Rothon, *Particulate-filled polymer composites*. Longman Scientific & Technical: Harlow, 1995.

[17] Z. Demjén, B. Pukánszky, E. Földes, J. Nagy, *Interaction of silane coupling agents with* $CaCO_3$. Journal of Colloid and Interface Science 1997, 190(2), 427-436.

[18] H. Fujimatsu, K. Iyo, H. Usami, S. Ogasawara, K. Kajiwara, *Adhesion between polyethylene molding and metal surface-modified with silane coupling agents by use of polyethylene gels*. Composite Interfaces 2002, 9(3), 259-272.

[19] M.-I. Baraton. *Synthesis, functionalization and surface treatment of nanoparticles.* American Scientific Publishers: Los Angeles, 2003.

[20] G.A. Holmes, E. Feresenbet and D. Raghavan, *Using self-assembled monolayer technology to probe the mechanical response of the fiber interphase-matrix interphase interface*. Composite Interfaces 2003, 10(6), 515-546.

[21] E. Loste, J. Fraile, M.A. Fanovich, G.F. Woerlee, C. Domingo, *Anhydrous supercritical carbon dioxide method for the controlled silanization of inorganic nanoparticles.* Advanced Materials 2004, 16(8), 739-744.

[22] Z.X. Jiang, L.H. Meng, Y.D. Huang, L. Liu, C. Lu, *Influence of coupling agent chain lengths on interfacial performances of polyarylacetylene resin and silica glass composites.* Applied Surface Science 2007, 253(9), 4338-4343.

[23] N.R. Jana, C. Earhart, J.Y. Ying, *Synthesis of water-soluble and functionalized nanoparticles by silica coating*. Chemistry of Materials 2007, 19(21), 5074-5082.

[24] R.D. Palma, S. Peeters, M.J.V. Bael, H. Van den Rul, K. Bonroy, W. Laureyn, J. Mullens, G. Borghs, G. Maes, *Silane ligand exchange to make hydrophobic superparamagnetic nanoparticles water-dispersible*. Chemistry of Materials 2007, 19(7), 1821-1831.

[25] V. Palanivel, D. Zhu, W.J. van Ooij, *Nanoparticle-filled silane films as chromate replacements for aluminum alloys*. Progress in Organic Coatings 2003, 47(3-4), 384-392.

[26] D.-H. Park, N. Nishiyama, Y. Egashira, K. Ueyama, *Enhancement of hydrothermal stability and hydrophobicity of a silica MCM-48 membrane by silylation*. Industrial & Engineering Chemistry Research 2001, 40(26), 6105-6110.

[27] C.A. García-González, N. El Grouh, A. Hidalgo, J. Fraile, A.M. López-Periago, C. Andrade, C. Domingo, *New insights on the use of supercritical carbon dioxide for the accelerated carbonation of cement pastes*. The Journal of Supercritical Fluids 2008, 43(3), 500-509.

[28] S.A. Kulkarni, S.B. Ogale, K.P. Vijayamohanan, *Tuning the hydrophobic properties of silica particles by surface silanization using mixed self-assembled monolayers*. Journal of Colloid and Interface Science 2008, 318(2), 372-379.

[29] I. Gill, *Bio-doped nanocomposite polymers: sol-gel bioencapsulates*. Chemistry of Materials 2001, 13(10), 3404-3421.

[30] P. Wu, Z. Xu, *Silanation of nanostructured mesoporous magnetic particles for heavy metal recovery*. Industrial & Engineering Chemistry Research 2005, 44(4), 816-824.

[31] Y. Turhan, P. Turan, M. Doan, M. Alkam, H. Namli, Ö. Demirbaş, *Characterization and adsorption properties of chemically modified sepiolite*. Industrial & Engineering Chemistry Research 2008, 47(6), 1883-1895.

[32] N.M. Scully, L.O. Healy, T. O'Mahony, J.D. Glennon, B. Dietrich, K. Albert, *Effect of silane reagent functionality for fluorinated alkyl and phenyl silica bonded stationary phases prepared in supercritical carbon dioxide*. Journal of Chromatography A 2008, 1191(1-2), 99-107.

[33] E.P. Plueddemann, *Silane adhesion promoters in coatings*, Progress in Organic Coatings 1983, 11(3), 297-308.

[34] E.P. Plueddemann, *Silane coupling agents*, 2nd ed. Plenum Press: NewYork, 1991.

[35] G.L. Witucki, *A silane primer: Chemistry and applications of alkoxy silanes*. Journal of Coatings Technology 1993, 65(822), 57-60.

[36] C.P. Tripp, M.L. Hair, *Reaction of methylsilanols with hydrated silica surfaces: The hydrolysis of trichloro-, dichloro-, and monochloromethylsilanes and the effects of curing*. Langmuir 1995, 11(1), 149-155.

[37] C.P. Tripp, J.R. Combes, *Chemical modification of metal oxide surfaces in supercritical CO_2: The interaction of supercritical CO_2 with the adsorbed water layer and the surface hydroxyl groups of a silica surface*. Langmuir 1998, 14(26), 7348–7352.

[38] C. Cao, A.Y. Fadeev, T.J. McCarthy, *Reactions of organosilanes with silica surfaces in carbon dioxide.* Langmuir 2001, 17(3), 757-761.

[39] R. Maoz, J. Sagiv, D. Degenhardt, H. Möhwald, P. Quint, *Hydrogen-bonded multilayers of self-assembling silanes: Structure elucidation by combined Fourier transform infra-red spectroscopy and X-ray scattering techniques*. Supramolecular Science 1995, 2(1), 9-24.

[40] A.Y. Fadeev, R. Helmy, S. Marcinko, *Self-assembled monolayers of organosilicon hydrides supported on titanium, zirconium, and hafnium dioxides*. Langmuir 2002, 18(20), 7521-7529.

[41] S. Marcinko, A.Y. Fadeev, *Hydrolytic stability of organic monolayers supported on TiO_2 and ZrO_2*. Langmuir 2004, 20(6), 2270-2273.

[42] S.R. Wasserman, Y.T. Tao, G.M. Whitesides, *Structure and reactivity of alkylsiloxane monolayers formed by reaction of alkyltrichlorosilanes on silicon substrates*. Langmuir 1989, 5(4), 1074–1087.

[43] N. Balachander, C.N. Sukenik, *Monolayer transformation by nucleophilic substitution: Applications to the creation of new monolayer assemblies*. Langmuir 1990, 6(11), 1621–1627.

[44] R. Maoz, S.R. Cohen, J. Sagiv, *Nanoelectrochemical patterning of monolayer surfaces: toward spatially defined self-assembly of nanostructures*. Advanced Materials 1999, 11(1), 55–61.

[45] R. Maoz, E. Frydman, S.R. Cohen, J. Sagiv, *"Constructive nanolithography": Inert monolayers as patternable templates for in-situ nanofabrication of metal-semiconductor-organic surface structures - A generic approach*. Advanced Materials 2000, 12(10), 725–731.

[46] A.S. Killampalli, P.F. Ma, J.R. Engstrom, *The reaction of tetrakis(dimethylamido)-titanium with self-assembled alkyltrichlorosilane monolayers possessing* $-OH$*,* $-NH_2$*, and* $-CH_3$ *terminal groups*. Journal of the American Chemical Society 2005, 127, 6300–6310.

[47] H.H. Weetall, *Preparation of immobilized proteins covalently coupled through silane coupling agents to inorganic supports*. Advances in Molecular and Cell Biology 1996, 15(1), 161-192.

[48] G.-J. Kim, J.-H. Shin, *The catalytic activity of new chiral salen complexes immobilized on MCM-41 by multi-step grafting in the asymmetric epoxidation*. Tetrahedron Letters 1999, 40(37), 6827-6830.

[49] C.D. Nunes, A.A. Valente, M. Pillinger, A.C. Fernandes, C.C. Romao, J. Rocha, I.S. Gonçalves, *MCM-41 functionalized with bipyridyl groups and its use as a support for oxomolybdenum(VI) catalysts*. Journal of Materials Chemistry 2002, 12(6), 1735–1742.

[50] K. Matsuyama, K. Mishima, *Preparation of poly(methyl methacrylate)–*TiO_2 *nanoparticle composites by pseudo-dispersion polymerization of methyl methacrylate in supercritical* CO_2. The Journal of Supercritical Fluids 2009, 49(2), 256-264.

[51] S.R. Wasserman, Y.T. Tao, G.M. Whitesides, *Structure and reactivity of alkylsiloxane monolayers formed by reaction of alkyltrichlorosilanes on silicon substrates*. Langmuir 1989, 5(4), 1074–1087.

[52] N.R.E.N. Impens, P. van der Voort, E.F. Vansant, *Silylation of micro-, meso- and non-porous oxides: a review*. Microporous and Mesoporous Materials 1999, 28(2), 217-232.

[53] T. Jesionowski, *Modification and characterization of titanium dioxide surface*, Pigment & Resin Technology 2001, 30(5), 287-295.

[54] A.M. Almanza-Workman, S. Raghavan, P. Deymier, D.J. Monk, R.J. Roop, *Water dispersible silanes for wettability modification of polysilicon*. Journal of The Electrochemical Society 2002, 149(1), H6-H11.

[55] C. Santos, R.L. Clarke, M. Braden, F. Guitian, K.W.M. Davy, *Water absorption characteristics of dental composites incorporating hydroxyapatite filler*. Biomaterials 2002, 23(8), 1897-1904.

[56] E. Ukaji, T. Furusawa, M. Sato, N. Suzuki, *The effect of surface modification with silane coupling agent on suppressing the photo-catalytic activity of fine* TiO_2 *particles as inorganic UV filter*. Applied Surface Science 2007, 254(2), 563-569.

[57] W. Gu, C.P. Tripp, *Reaction of silanes in supercritical CO_2 with TiO_2 and Al_2O_3.* Langmuir 2006, 22(13), 5748-5752.

[58] Y. Sun, *Supercritical fluid technology in materials science and engineering.* Marcel Dekker: New York, 2002.

[59] Y. Shin, T.S. Zemanian, G.E. Fryxell, L.-Q. Wang, J. Liu, *Supercritical processing of functionalized size selective microporous materials.* Microporous and Mesoporous Materials 2000, 37(1-2), 49-56.

[60] E. Alonso, I. Montequi, S. Lucas, M.J. Cocero, *Synthesis of titanium oxide particles in supercritical CO_2: Effect of operational variables in the characteristics of the final product.* The Journal of Supercritical Fluids 2007, 39(3), 453-461.

[61] E. Alonso, I. Montequi, M.J. Cocero, *Effect of synthesis conditions on photocatalytic activity of TiO_2 powders synthesized in supercritical CO_2.* The Journal of Supercritical Fluids 2009, 49(2), 233-238.

[62] C. Domingo, J. García-Carmona, J. Llibre, R. Rodríguez-Clemente, *Organic-guest/microporous-host composite materials obtained by diffusion from a supercritical solution.* Advanced Materials 1998, 10(9), 672-676.

[63] C. Domingo, J. García-Carmona, M.A. Fanovich, J. Llibre, R. Rodríguez-Clemente, *Single or two-solute adsorption processes at supercritical conditions: an experimental study.* The Journal of Supercritical Fluids 2001, 21(2), 147-157.

[64] J. García-Carmona, M.A. Fanovich, J. Llibre, R. Rodríguez-Clemente, C. Domingo, *Processing of microporous VPI-5 molecular sieve by using supercritical CO_2: Stability and adsorption properties.* Microporous and Mesoporous Materials 2002, 54(1-2), 127-137.

[65] E. Loste, J. Fraile, M.A. Fanovich, G.F. Woerlee, C. Domingo, *Supercritical carbon dioxide anhydrous method for the controlled silanization of inorganic nanoparticles.* Advanced Materials 2004, 16(8), 739-744.

[66] N.J. Lowe, N.A. Shaath, M.A. Pathak, *Sunscreens: Development, evaluation, and regulatory aspects*, 2nd edition. Cosmetic Science and Technology Series, Vol. 15. Marcel Dekker: New York, 1997.

[67] S.C. Gad. *Pharmaceutical manufacturing handbook: Production and processes*, 1st edition. Wiley-Interscience: Hoboken, 2008.

[68] C.A. García-González, J. Saurina, J.A. Ayllón, C. Domingo. *Preparation and characterization of surface silanized TiO_2 nanoparticles under compressed CO_2: Reaction kinetics.* The Journal of Physical Chemistry C 2009, 113(31), 13780-13786.

[69] C.A. García-González, J. Fraile, A. López-Periago, J. Saurina, C. Domingo, *Measurements and correlation of octyltriethoxysilane solubility in supercritical CO_2 and*

assembly of functional silane monolayers on the surface of nanometric particles. Industrial & Engineering Chemistry Research, In Press (doi: 10.1021/ie900775z).

[70] C.A. García-González, J.-M. Andanson, S.G. Kazarian, J. Saurina, C. Domingo, *Preparation of nanostructured organic–inorganic hybrid materials using supercritical fluid technology*. Composite Interfaces 2009, 16(2-3), 143–155.

[71] C.A. García-González, J.M. Andanson, S.G. Kazarian, C. Domingo, J. Saurina, *Application of principal component analysis to the thermal characterization of silanized nanoparticles obtained at supercritical carbon dioxide conditions.* Analytica Chimica Acta 2009, 635(2), 227–234.

[72] C.A. García-González, J. Fraile, A. López-Periago, C. Domingo, *Preparation of silane-coated TiO_2 nanoparticles in supercritical CO_2.* Journal of Colloid and Interface Science 2009, 338(2), 491-499.

[73] P. Tartaj, M. P. Morales, T. González-Carreño, S. Veintemillas-Verdaguer, C.J. Serna, *Advances in magnetic nanoparticles for biotechnology applications*. Journal of Magnetism and Magnetic Materials 2005, 290-291(1), 28-34.

Chapter 3

USE OF SCCO$_2$ AS AN ANTI-SOLVENT:

PREPARATION OF HYBRID MATERIALS

This Chapter focuses on the assessment of the use of scCO$_2$ as an anti-solvent for the preparation of biopolymer-based materials organized in a three-dimensional network of fibers containing inorganic nanometric fillers. Either poly(L-lactic acid) (L-PLA) or the blend poly(methylmethacrylate)/poly(ε-caprolactone) (PMMA/PCL) is chosen as the biopolymer to be processed. The preparation of these materials is carried out by a supercritical anti-solvent technique, named Particles from a Compressed Anti-solvent (PCA). The polymeric matrices are loaded with *ca.* 15-20 wt% of the inorganic phase (either titanium dioxide or hydroxyapatite) distributed throughout the composite. The enhancement of the interaction at the filler-polymer interface and the homogeneous distribution of the filler in the polymeric matrix are achieved through the previous surface modification of the nanometric inorganic particles using the supercritical silanization process described in Chapter 2. Finally, the incorporation of an anti-inflammatory drug (ketoprofen) to the hybrid matrix during composite precipitation is also attempted. The incorporation of this drug can provide local inflammatory treatment early upon transplantation of the synthetic scaffold [1].

3.1. Introduction

In regenerative biomedicine, cell transplantation has emerged as an alternative treatment to the traditional replacement with biostable implants of damaged parts in the body [2-6]. Tissue engineering embraces the research on this topic and is defined by Langer and Vacanti as "an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ" [4]. From a materials engineering point of view, tissues are regarded as cellular composites where living cells are building blocks to be assembled into a three-dimensional (3D) support (scaffold). Thus, research is currently focused on the engineering of suitable scaffolds able to mimic the natural extracellular matrix and to induce both *in vivo* and *in vitro* tissue growth [7-9]. Main requirements for these scaffolds are a high mechanical strength, an interconnected 3D macroporous structure necessary for cell proliferation, a high microporosity essential for neovascularization, and a high surface area required for cell attachment and growth [10,11]. The synthetic polymers used for tissue engineering applications are typically biodegradable compounds (e.g., L-PLA, PCL, PGA —poly(glycolic acid)—) and, only in some cases, non-biodegradable materials (e.g., PMMA, EVA —ethylene vinyl-acetate—). Moreover, the combination of both types of polymers provides final materials with specific advantages in regard of the degradation rate and mechanical properties [12,13]. However, designed polymeric 3D-scaffolds to be used in load-bearing applications (e.g., bones and cartilages) lack of the appropriate mechanical strength and rigidity in comparison to metallic implants [5]. The dispersion of relatively low amounts of nanosized inorganic particles in the polymeric matrix constituting the scaffold improves the mechanical properties (e.g., strength, stiffness) of the material, maintaining at the same time the ductile properties (i.e. toughness and elongation-to-break ratio) [14,15]. The hybrid composite engineered in this Chapter (Figure 3.1) is expected to allow the conception of materials with novel properties arising from the synergic combination of the dissimilar characteristics of the constituents.

The most important techniques for the fabrication of polymeric scaffolds include chemical fiber gluing and/or thermal treatment forming meshes constituted by woven or nonwoven fibers, solvent methods forming blown films, sintering of polymer particles, etc [5,16-19]. Conventional techniques used for their fabrication often involves the use of organic solvents (e.g., solvent casting, foaming, phase separation, freeze drying). As a consequence, the residual solvent molecules within the polymeric matrix remaining after processing can be harmful to the transplanted cells. Clean technology based on the use of supercritical carbon dioxide ($scCO_2$) has emerged as a breakthrough to overcome some of the problems linked with the use of traditional organic solvents for pharmaceuticals and biomaterials preparation [20-22]. In particular, supercritical anti-solvent spray processes have achieved considerable success in producing polymers with different morphologies [23-29].

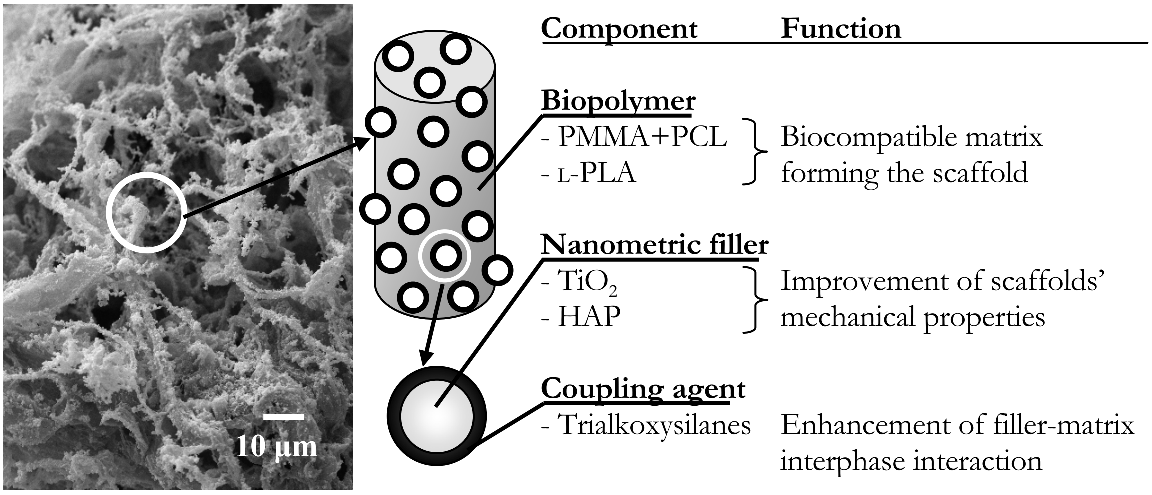

Figure 3.1. **Sketch of the prepared polymeric fibers loaded with inorganic fillers**

The aim of this Chapter is to explore the possibilities of using the $scCO_2$ anti-solvent process for the preparation of intermingled fibers with controlled morphology of either L-PLA or the blend PMMA/PCL containing ultrafine mineral particles of hydroxyapatite or titanium dioxide, respectively. The fillers are previously surface treated with a silane coupling agent using a supercritical silanization process (see Chapter 2). The use of silane coupling agents has the double purpose of facilitating the dispersion of the fillers in the hydrophobic liquid medium (dichloromethane) used for spraying in the supercritical process and improving the affinity between the polymer and the filler in the final material. Moreover, the effect of the polymer molecular weight on composite microstructure is studied. Finally, incorporation of a drug (ketoprofen) in the polymer blend is attempted using a similar PCA technique.

3.2. Materials and Methods [30]

3.2.1. Materials

Several polymers are selected as matrices for the hybrid materials: L-PLA (Biovalley, 100,000 g mol^{-1}), PCL (Aldrich, 14,000 g mol^{-1}) and two kinds of PMMA ($PMMA_1$: Bonar, 300,000 g mol^{-1}; $PMMA_2$: Aldrich, 120,000 g mol^{-1}). Bare TiO_2 (TiO_2 P25S, Degussa) and lab-synthesized nanometric hydroxyapatite (HAP) are used as fillers [31]. Using a supercritical silanization procedure (see Chapter 2), TiO_2 is functionalized with octyltriethoxysilane ($CH_3(CH_2)_7Si(OCH_2CH_3)_3$, Fluka). Commercially silanized TiO_2 (TiO_2 T805, Degussa) is used for comparison. HAP nanoparticles are silanized with γ-methacryloxypropyltrimethoxysilane ($H_2C{=}C(CH_3)CO_2(CH_2)_3Si(OCH_3)_3$, Sigma) following a similar supercritical silanization approach than that used for TiO_2 [31]. Ketoprofen (K, Aldrich) is used as the model drug. Carbon dioxide (CO_2, Air Liquide) and dichloromethane (DCM, Prolabo) are used as the anti-solvent and the solvent, respectively.

3.2.2. Process

Experiments are carried out in a PCA equipment (see Section 1.2.3 of Chapter 1). For the preparation of the fibers, CO_2 is introduced in a high pressure vessel (Re1 in Fig. 1.3) until a pressure of 11.0 MPa and a temperature of 312 K are reached. Then, a DCM suspension containing the nanoparticles and the dissolved polymer is injected into the vessel through a swirl nozzle at a rate of 1.5-2 mLmin^{-1}. The fibers are precipitated and deposited on the walls and at the bottom of the vessel. Once the injection of the DCM solution is finished, the precipitated hybrid material is dried using a continuous flow of $scCO_2$ of 65 gmin^{-1} during 10 min at 312 K and 11.0 MPa. Finally, the high-pressure vessel is slowly depressurized, and samples are collected for characterization.

3.2.3. Characterization

Obtained hybrid fibers or particles are analyzed using thermogravimetric analysis, differential scanning calorimetry, scanning electron microscopy with energy dispersive spectrometry, low-temperature N_2 adsorption-desorption analysis and ^1H nuclear magnetic resonance.

3.3. Results

Article no. 1

Title: Composite fibrous biomaterials for tissue engineering obtained using a supercritical CO_2 antisolvent process

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3.4. Conclusions

Networks of fibers of the L-PLA homopolymer and several PMMA/PCL blends (85:15 wt%) loaded with HAP and TiO_2 (15-20 wt%), respectively, are prepared using the anti-solvent PCA process. The silanization of the fillers facilitates nanoparticles dispersion in the DCM solution injected in the high-pressure vessel. Using the silane surface modification method, silanized TiO_2 particles incorporated in the PMMA/PCL fibers are homogeneously distributed throughout the hybrid material. Instead of the fibers obtained when processing either L-PLA or high molecular weight PMMA, agglomerated microparticles are prepared when low molecular weight PMMA is used in the PMMA/PCL blend. Hence, the viscosity of the polymeric solution influences the formation of either fibers or microparticles. Under the used experimental conditions, the incorporation of ketoprofen within the polymeric matrix is not achieved, due to the removal of the drug from the polymer during the drying of the fibers with $scCO_2$.

3.5. References

[1] M. Ricci, P. Blasi, S. Giovagnoli, C. Rossi, G. Macchiarulo, G. Luca, G. Basta, R. Calafiore *Ketoprofen controlled release from composite microcapsules for cell encapsulation: Effect on post-transplant acute inflammation*. Journal of Controlled Release 2005, 107(3), 395-407.

[2] L.G. Cima, D. Ingber, J.P. Vacanti, *Hepatocyte culture on biodegradable polymeric substrates*. Biotechnology and bioengineering 1991, 38(2), 145-158.

[3] L.G. Cima, J.P. Vacanti, C. Vacanti, *Tissue engineering by cell transplantation using degradable polymer substrates*. Journal of Biomechanical Engineering 1991, 113(2), 143-151.

[4] R. Langer, J.P. Vacanti, *Tissue engineering*. Science 1993, 260(5110), 920-926.

[5] S. Yang, K.-F. Leong, Z. Du, C.-K. Chua, *The design of scaffolds for use in tissue engineering. Part I. Traditional factors*. Tissue Engineering 2001, 7(6), 679-689.

[6] D. Shi, *Biomaterials and tissue engineering*, 1st edition. Springer: Heidelberg, 2004.

[7] L.G. Griffith, *Polymeric biomaterials*. Acta Materialia 2000, 48(1), 263-277.

[8] D.W. Hutmacher, *Scaffolds in tissue engineering bone and cartilage*. Biomaterials 2000, 21(24), 2529-2543.

[9] H. Shin, S. Jo, A.G. Mikos, *Biomimetic materials for tissue engineering*. Biomaterials 2003, 24(24), 4353-4364.

[10] K. Whang, C.H. Thomas, K.E. Healy, G. Nuber, *A novel method to fabricate bioabsorbable scaffolds*. Polymer 1995, 36(4), 837-842.

[11] T. Tateishi, G. Chen, T. Ushida, *Polyfunctional scaffolds for tissue engineering.* Journal of Biomechanical Science and Engineering 2006, 1(1), 8-15.

[12] G.A. Abraham, A. Gallardo, A. Motta, C. Migliaresi, J. San Román, *Microheterogeneous polymer systems prepared by suspension polymerization of methyl methacrylate in the presence of poly(ε-caprolactone).* Macromolecular Materials and Engineering 2000, 282(1), 44-50.

[13] G.A. Abraham, K. Kesenci, L. Fambri, C. Migliaresi, A. Gallardo, J. San Román, *Microcomposite of poly(ε-caprolactone) and poly(methyl methacrylate) prepared by suspension polymerization in the presence of poly(ε-caprolactone) macromonomer.* Macromolecular Materials and Engineering 2002, 287(12), 938-945.

[14] W.-Y. Yeong, Ch.-K. Chua, K.-F. Leong, M. Chandrasekaran, *Rapid prototyping in tissue engineering: challenges and potential.* Trends in Biotechnology 2004, 22(12), 643-652.

[15] Y. Zhou, K. Cooper, Y. Li, Z. Li, *Use of coupling agents to improve the interface in absorbable polymer composites.* US Patent 20,090,149,873 (2009).

[16] A.G. Mikos, J.S. Temenoff, *Formation of highly porous biodegradable scaffolds for tissue engineering.* Electronic Journal of Biotechnology 2000, 3(2), 1-6.

[17] D.W. Hutmacher, *Scaffold design and fabrication technologies for engineering tissues—State of the art and future perspectives.* Journal of Biomaterials Science: Polymer Edition 2002, 12(1), 107–124.

[18] L. Moroni, J.R. de Wijn, C.A. van Blitterswijk, *3D fiber-deposited scaffolds for tissue engineering: Influence of pores geometry and architecture on dynamic mechanical properties.* Biomaterials 2006, 27(7), 974–985.

[19] S.H. Park, T.G. Kim, H.C. Kim, D.Y. Yang, T.G. Park, *Development of dual scale scaffolds via direct polymer melt deposition and electrospinning for applications in tissue regeneration.* Acta Biomaterialia 2008, 4(5), 1198–1207.

[20] E. Reverchon, G. Della Porta, I. De Rosa, P. Subra, D. Letourneur, *Supercritical antisolvent micronization of some biopolymers.* The Journal of Supercritical Fluids 2000, 18(3), 239-245.

[21] R.A. Quirk, R.M. France, K.M. Shakesheff, S.M. Howdle, *Supercritical fluid technologies and tissue engineering scaffolds.* Current Opinion in Solid State and Materials Science 2004, 8(3-4), 313-321.

[22] A.R.C. Duarte, J.F. Mano, R.L. Reis, *Perspectives on: Supercritical fluid technology for 3D tissue engineering scaffold applications.* Journal of the Bioactive and Compatible Polymers 2009, 24(4), 385-400.

[23] K.J.L. Burg, S. Porter, J.F. Kellam, *Biomaterial developments for bone tissue engineering.* Biomaterials 2000, 21(23), 2347-2359.

[24] N. Elvassore, A. Bertucco, *Production of protein-loaded polymeric microcapsules by compressed CO_2 in a mixed solvent*. Industrial & Engineering Chemistry Research 2001, 40(3), 795–800.

[25] A.J. Salgado, O.P. Coutinho, R.L. Reis, *Bone tissue engineering: State of the art and future trends*. Macromolecular Bioscience 2004, 4(8), 743-765.

[26] A. Vega-González, C. Domingo, C. Elvira, P. Subra, *Precipitation of PMMA/PCL blends using supercritical carbon dioxide*. Journal of Applied Polymer Science 2004, 91(4), 2422-2426.

[27] S.-D. Yeo, E. Kiran, *Formation of polymer particles with supercritical fluids: A review*. The Journal of Supercritical Fluids 2005, 34(3), 287-308.

[28] F. Miguel, A. Martín, F. Mattea, M.J. Cocero, *Precipitation of lutein and co-precipitation of lutein and poly-lactic acid with the supercritical anti-solvent process*. Chemical Engineering and Processing: Process Intensification 2008, 47(9-10), 1594-1602.

[29] A. Vega-González, P. Subra-Paternault, A.M. López-Periago, C.A. García-González, C. Domingo, *Supercritical CO_2 antisolvent precipitation of polymer networks of L-PLA, PMMA and PMMA/PCL blends for biomedical applications*. European Polymer Journal 2008, 44(4), 1081-1094.

[30] C.A. García-González, A. Vega-González, A.M. López-Periago, P. Subra-Paternault, C. Domingo, *Composite fibrous biomaterials for tissue engineering obtained using a supercritical CO_2 antisolvent process*. Acta Biomaterialia 2009, 5(4), 1094-1103.

[31] C. Domingo, E. Loste, J. Fraile, *Grafting of trialkoxysilane on the surface of nanoparticles by conventional wet alcoholic and supercritical carbon dioxide deposition methods*. The Journal of Supercritical Fluids 2006, 37(1), 72-86.

Chapter 4

USE OF SCCO$_2$ AS A SOLUTE:

PREPARATION OF LIPID-BASED PARTICLES

This Chapter focuses on the use of scCO$_2$ as a solute in the Particles from Gas Saturated Solutions (PGSS®) process for the preparation of solid lipid hybrid particles containing active compounds. A lipid blend composed of glyceryl monostearate and hydrogenated castor oil is used as the carrier. The influence of the lipid composition and the presence of CO$_2$ in the melting point depression of the mixture are studied from atmospheric pressure to 16 MPa. Particles consisting in a lipidic matrix loaded with *ca.* 6 wt% of nanoparticles of titanium dioxide are obtained using the PGSS® technique. TiO$_2$ nanoparticles are previously surface hydrophobized using a supercritical silanization method (see Chapter 2) to improve their dispersibility in the lipidic matrix. The UV-shielding ability of TiO$_2$ after its incorporation in the lipid particles is assessed by solid UV-Vis spectroscopy. Finally, lipid particles loaded with *ca.* 6 wt% of TiO$_2$ and *ca.* 4 wt% of caffeine are prepared using a similar PGSS® process. The water dissolution profile of the caffeine loaded in the lipid particles is studied.

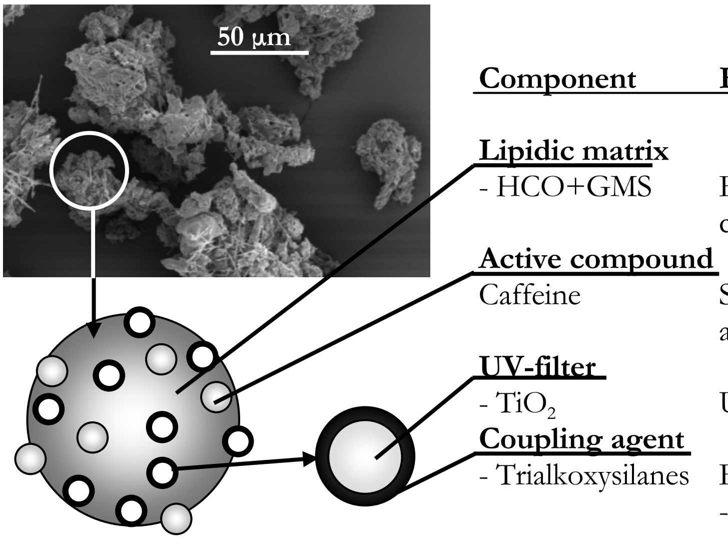
4.1. Introduction

Pharmaceutical and cosmetic industries are working on the development of new strategies for the formulation and processing of new products for topical applications containing active compounds [1]. When possible, topical treatment of skin diseases is preferred to oral or parenteral administration of drugs, since high drug concentrations can be achieved at the site of application with reduced systemic side effects [2]. Among the different studied systems, lipid-based drug delivery systems have become an attractive carrier for the formulation of pharmaceuticals and cosmetics. Most lipids, typically saturated and unsaturated fatty acids and derivatives, are well tolerated by the human body due to their quick metabolization into non-toxic products [3,4]. Lipid-based carriers can be obtained in the form of emulsions, liposomes or solid particles depending on the processing technique, the mixture of lipids used and the composition of the formulation. As a carrier, solid lipid particles (SLP) are particularly advantageous in terms of physical stability, drug protection against chemical degradation and cost [5]. The research activity on SLP is especially intensified for cosmetic and pharmaceutical dermal applications [2,6,7].

The development of sunscreens with SLP containing inorganic UV-blockers (e.g., titanium dioxide, zinc oxide) and organic UV-absorbers (e.g., avobenzone, oxybenzone, octinoxate, octocrylene, homosalate) for the prevention of skin damages inferred by UV radiation in humans is being investigated [2,8,9]. In these formulations, the lipid matrix can act as a complementary UV-filter [2,8,9]. Among the used inorganic UV-blockers, nanoparticulate titanium dioxide (TiO_2) is widely employed in the industry of cosmetics as an effective and transparent UVA-light and UVB-light blocker [10]. The entrapping of the TiO_2 nanoparticles into SLP may provide an excellent medium for the incorporation of this UV-filter in the formulation of sunscreens. In this way, the dispersion of the TiO_2 particles into the oil phase of sunscreens is facilitated and the segregation of the inorganic component is minimized [2]. Moreover, the encapsulation of nanoparticles into larger particles often minimizes the potential negative environmental and health impact of the nanoparticles [10,11]. However, owing to the intrinsic hydrophilic character of non-treated TiO_2 surfaces, the dispersion of the nanoparticles in the lipid matrices and in the organic media used in cosmetics is not easily achieved. A hydrophobic surface treatment of the TiO_2 nanoparticles facilitates particles dispersion and mitigates their tendency to agglomeration [12].

SLP loaded with active compounds are already used in formulations of pharmaceutical dermal products. The incorporation of the drug within the lipid-based particles confers enhanced controlled release ability to the formulation. The lipid matrix can also boost the chemical stability of drugs that are sensitive to light, oxidation or hydrolysis [2]. The choice of the composition of the lipidic matrix compromises its drug loading capacity and the release profile of the active compound. In general, the dispersion of the active compound inside the particles is facilitated by solid lipid particles with low crystallinity and many lattice defects or imperfections. Therefore, the use of complex mixtures of lipids that have different chemical composition and chain length is usually preferred for the preparation of SLP [13].

The quest for the development of a robust technology for the production of SLP with controlled properties (e.g., particle size distribution, crystallinity, purity and morphology) under mild and environmentally friendly conditions has promoted an intense research on this topic. Current technologies for SLP production include multi-step fusion processes (cold or hot high pressure homogenization), emulsification and ultrasonication [5]. Supercritical fluid-assisted processes are regarded as a feasible option for the preparation of particulate drug delivery systems. Particularly, the use of $scCO_2$ in the PGSS® (see Section 0.4 of Chapter 0) process is considered an alternative one-step method to obtain solvent-free SLP at low processing temperatures [14-21]. Briefly, the applied technique consisted in the dissolution of $scCO_2$ into the melted lipid until its saturation, followed by the expansion of the mixture through a nozzle. The fast cooling of the lipid mixture during the expansion is due to a sudden pressure drop (i.e., Joule-Thomson effect), and induces the generation of a dry powder.



Component	**Function**
Lipidic matrix	
- HCO+GMS	Encapsulating agent and controlled release carrier
Active compound	
Caffeine	Skin photoaging prevention and anticellulite activity
UV-filter	
- TiO_2	UVA and UVB radiation filter
Coupling agent	
- Trialkoxysilanes	Enhancement of UV-filter-matrix interphase interaction

Figure 4.1. **Sketch of the prepared lipid-based particles loaded with an inorganic UV-filter and an active compound.**

In this Chapter, the use of the PGSS® process is assessed for the production of particulate hybrid carriers consisting of a complex lipid matrix (Lumulse® GMS K / Cutina® HR blend) containing nanometric particles of TiO_2 and caffeine. Firstly, the effects of the lipid mixture composition and the presence of CO_2 on the extent of the melting point depression of the lipid blend are studied. Pure SLP are primarily produced using the PGSS® technique. Obtained particles are analyzed regarding physical state, thermal stability and morphology. The production of SLP loaded with a physical UV-blocker (TiO_2) is then carried out. TiO_2 is previously surface treated with two different silane adhesion promoters (octyltriethoxysilane and octadecyltrimethoxysilane) using a supercritical silanization process (see Chapter 2). The effects of the presence of TiO_2 on the properties of the obtained lipid-based particles are analyzed. Finally, composite particles are loaded with an active agent (caffeine) using a similar PGSS® technique (Figure 4.1).

4.2. Materials and Methods [21]

4.2.1. Materials

The selected lipid blend matrix is composed of Lumulse® GMS K (GMS; Lambent Technologies) and Cutina® HR (HCO, José M. Vaz Pereira S.A.) in a 1:1 weight ratio. Bare TiO_2 (TiO_2 P25, Degussa) is used as the inorganic UV-blocker. Using a supercritical silanization procedure (see Chapter 2), TiO_2 is coated with either octyltriethoxysilane ($CH_3(CH_2)_7Si(OCH_2CH_3)_3$, Fluka) or octadecyltrimethoxysilane ($CH_3(CH_2)_{17}Si(OCH_3)_3$, Fluka). Caffeine (Sigma-Aldrich) is used as the active compound to be incorporated in the lipid matrix. Carbon dioxide (CO_2, Air Liquide) is used in the PGSS® materials processing.

4.2.2. Process

Experiments are carried out in the PGSS® (Particles from Gas Saturated Solutions) equipment described in Section 1.2.4 of Chapter 1. For the preparation of the solid lipid-based particles, a 0.5-L high pressure vessel (Re1 in Fig. 1.4) is first charged with the lipids, the TiO_2 and the caffeine. Then, CO_2 is supplied to the vessel Re1 until a pressure of 13.0 MPa and a temperature of 345 K are reached. The mixture is stirred during 1 h, time after which the system is depressurized through a nozzle. A free-flowing powder is collected in a 10-L vessel (Re2).

4.2.3. Characterization

Melting point measurements of HCO:GMS blends (1:1 and 3:1 weight ratios) under compressed CO_2 (0.1-18.0 MPa) are performed using a 4-mL view cell. The obtained hybrid particles are analyzed using thermogravimetric analysis, differential scanning calorimetry, transmission electron microscopy, scanning electron microscopy with energy dispersive spectrometry, X-ray diffraction and UV-Vis spectroscopy. The caffeine dissolution profile in water is determined by high performance liquid chromatography.

4.3. Results

Article no. 1

Title: Production of hybrid lipid-based particles loaded with inorganic nanoparticles and active compounds for prolonged topical release

Authors: C. A. García-González, A. R. Sampaio da Sousa, A. Argemí, A. López Periago, J. Saurina, C. M. M. Duarte, C. Domingo

Journal: Int. J. Pharm. 382 (2009) 296-304

4.4. Conclusions

The supercritically aided PGSS® method is used for the incorporation of inorganic nanoparticles (TiO_2) and active compounds (caffeine) into a lipid blend matrix (HCO/GMS weight ratio= 1:1). Using this one-step supercritical technique, a decrease in the processing temperature is achieved. Moreover, a solvent-free product is obtained. The use of a blend instead of a pure lipid provides a reduction in the crystallinity of the mixture which increases the capacity of the lipidic matrix for drug incorporation. The silanization of the TiO_2 surface facilitates the homogeneous distribution of the inorganic nanoparticles within the lipidic matrix. Negative effects of silane coating and lipid encapsulation on the UV-shielding ability of the TiO_2 are not noticeable. A two-step dissolution profile was obtained for the caffeine loaded in the lipid particles.

4.5. References

[1] R. Liu, *Water-insoluble drug formulation*. Interpharm/CRC Press: Boca Raton, 2000.

[2] J. Pardeike, A. Hommoss, R.H. Müller, *Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products*. International Journal of Pharmaceutics 2009, 366(1-2), 170-184.

[3] K. Westesen, *Novel lipid-based colloidal dispersions as potential drug administration systems: expectations and reality*. Colloid and Polymer Science 2000, 278(7), 608-618.

[4] V. Jannin, J. Musakhanian, D. Marchaud, *Approaches for the development of solid and semi-solid lipid-based formulations*. Advanced Drug Delivery Reviews 2008, 60(6), 734-746.

[5] R.H. Müller, K. Mäder, S. Gohla, *Solid lipid nanoparticles (SLN) for controlled drug delivery – A review of the state of the art*. European Journal of Pharmaceutics and Biopharmaceutics 2000, 50(1), 161-177.

[6] R.H. Müller, M. Radtke, S.A. Wissing, *Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations*. Advanced Drug Delivery Reviews 2002, 54(1), S131-S155.

[7] C. Puglia, P. Blasi, L. Rizza, A. Schoubben, F. Bonina, C. Rossi, M. Ricci, *Lipid nanoparticles for prolonged topical delivery: An in vitro and in vivo investigation*. International Journal of Pharmaceutics 2008, 357(1-2), 295-304.

[8] G. Yener, T. Incegül, N. Yener, *Importance of using solid lipid microspheres as carriers for UV filters on the example octyl methoxy cinnamate*. International Journal of Pharmaceutics 2003, 258(1-2), 203-207.

[9] J.R. Villalobos-Hernández, C.C. Müller-Goymann, *Novel nanoparticulate carrier system based on carnauba wax and decyl oleate for the dispersion of inorganic sunscreens in*

aqueous media. European Journal of Pharmaceutics and biopharmaceutics 2005, 60(1), 113-122.

[10] A. Grobe, O. Renn, A. Jaeger, *A report for IRGC: Risk governance of nanotechnology applications in food and cosmetics*. International Risk Governance Council: Geneva, 2008.

[11] W. Klöpffer, *Nanotechnology and life cycle assessment: A systems approach to nanotechnology and environment*. Nanotechnology and Life Cycle Assessment: Washington, 2007.

[12] C.A. García-González, J. Fraile, A. López-Periago, C. Domingo, *Preparation of silane-coated* TiO_2 *nanoparticles in supercritical* CO_2. Journal of Colloid and Interface Science 2009, 338(2), 491-499.

[13] A.R. Sampaio de Sousa, M. Calderone, E. Rodier, J. Fages, C.M.M. Duarte, *Solubility of carbon dioxide in three lipid-based biocarriers*. The Journal of Supercritical Fluids 2006, 39(1), 13-19.

[14] E. Weidner, Z. Knez, Z. Novak, *Process for preparing particles or powders*, WO Patent WO95/21,688 (1995).

[15] M. Rodrigues, N. Peiriço, H. Matos, E. Gomes de Azevedo, M.R. Lobato, A.J. Almeida, *Microcomposites theophylline/hydrogenated palm oil from a PGSS process for controlled drug delivery systems*. The Journal of Supercritical Fluids 2004, 29(1-2), 175-184.

[16] M. Calderone, E. Rodier, J.-J. Letorneau, J. Fages, *Solidification of Precirol® by the expansion of a supercritical fluid saturated melt: From the thermodynamic balance towards the crystallization aspect*. The Journal of Supercritical Fluids 2007, 42(2), 189-199.

[17] A.R. Sampaio de Sousa, A.L. Simplício, H.C. de Sousa, C.M.M. Duarte, *Preparation of glyceryl monostearate-based particles by PGSS®—Application to caffeine*. The Journal of Supercritical Fluids 2007, 43(1), 120-125.

[18] A.R. Sampaio da Sousa, *Development of functional particles using supercritical fluid technology: Fundamentals, processing and applications*. PhD Thesis. Oeiras, 2007.

[19] A.R. Sampaio de Sousa, R. Silva, F.H. Tay, A.L. Simplício, S.G. Kazarian, C.M.M. Duarte, *Solubility enhancement of trans-chalcone using lipid carriers and supercritical* CO_2 *processing*. The Journal of Supercritical Fluids 2009, 48(2), 120-125.

[20] F. Temelli, *Perspectives on supercritical fluid processing of fats and oils*. The Journal of Supercritical Fluids 2009, 47(3), 583-590.

[21] C.A. García-González, A.R. Sampaio da Sousa, A. Argemí, A. López Periago, J. Saurina, C.M.M. Duarte, C. Domingo, *Production of hybrid lipid-based particles loaded with inorganic nanoparticles and active compounds for prolonged topical release*. International Journal of Pharmaceutics 2009, 382(1-2), 296-304.

Chapter 5

USE OF $scCO_2$ AS A REAGENT:

ACCELERATED CEMENT CARBONATION

The carbonation of Portland cement increases the density and reduces the macroporosity, the water permeability and the pH of the material, which enhances its durability in certain applications. Cement carbonation not only generates a high added value product, but also could help to CO_2 capture and storage and, therefore, it is regarded as a sustainable process. Nevertheless, natural carbonation is a very slow process and feasible alternatives for accelerated carbonation are being prospected. Cement carbonation may be greatly accelerated if $scCO_2$ is used as the carbonating agent. In this Chapter, the carbonation of several cementitious materials of different compositions and admixtures with $scCO_2$ is described. The effects of the supercritical process on the microstructure and physicochemical properties of the prepared samples are studied. On the other hand, the durability of cement-based materials is usually compromised by weathering and problems related with water ingress (coming from percolated ground water and infiltrated rainwater) in the cementitious matrix. Therefore, a surface treatment consisting in the supercritical silanization of the carbonated cement-based materials with octytriethoxysilane as the hydrophobic agent is assessed. The objective is to prevent the water ingress in the bulk of the cementitious material. Finally, some of the tools for the management of resources and process integration are applied to the supercritical carbonation-silanization process.

5.1. Introduction

Cement is a worldwide mainstream material with an annual consumption of $1.7 \cdot 10^9$ tones in 2004 [1] and with a trend of increasing by 3% per year [2]. Moreover, there is a major concern in producing cementitious material with longer durability than the current ones and in a more energetically efficient manner (the energy consumption of cement industry was of 7-10 10^9 GJ in year 2004 [3] and is responsible for 6% of total anthropogenic CO_2 emissions and for 4% of planet global warming effect) [2].

Natural carbonation is a well-known phenomenon associated with cement-based materials placed in natural environments, which progressively occurs over time owing to the reaction of calcium-containing phases in the cement with atmospheric CO_2 [4,5]. The overall carbonation reaction of cement-based materials results in the crystallization of calcium carbonate ($CaCO_3$) in the cement pores (eq. 5.1.). The carbonation reaction takes place in both Portland and calcium aluminate cements [6-8]. For cured Portland cement, the sources of Ca^{2+} cations are the hydrated compounds, mainly portlandite ($Ca(OH)_2$ or CH, eq. 5.2.), calcium silicate hydrate gel (CSH or $2CaO \cdot SiO_2 \cdot nH_2O$, eq. 5.3.) and ettringite ($3CaO \cdot Al_2O_3 \cdot 3CaSO_4 \cdot 32H_2O$) [6,9,10].

$$CO_{2(aq)} + Ca^{2+}{}_{(aq)} + 2OH^{-}{}_{(aq)} \rightarrow CaCO_{3(s)} + H_2O \qquad (5.1.)$$

$$Ca(OH)_2 + CO_2 \rightarrow CaCO_3 + H_2O \qquad (5.2.)$$

$$2CaO \cdot SiO_2 \cdot nH_2O + 2CO_2 \rightarrow 2CaCO_3 + 2SiO_2 + nH_2O \qquad (5.3.)$$

In general, carbonation increases the cement paste density, reduces the macroporosity, the water permeability and the pH of the pore water [11-16]. In spite of the detrimental effect of the carbonation process on structural steel-reinforced concrete [17,18], the procedure can influence positively the recycling of demolished concrete structures [19], the incorporation of non-expensive reinforcement products to the cement paste [20] and the production of materials for the immobilization of hazardous products (waste management) [21-23]. Further, carbonated concrete has been proposed for its use as a barrier, liner and encasement in engineered long-term deep geological repositories of high-level nuclear wastes in a humid environment (Figure 5.1) [24-29].

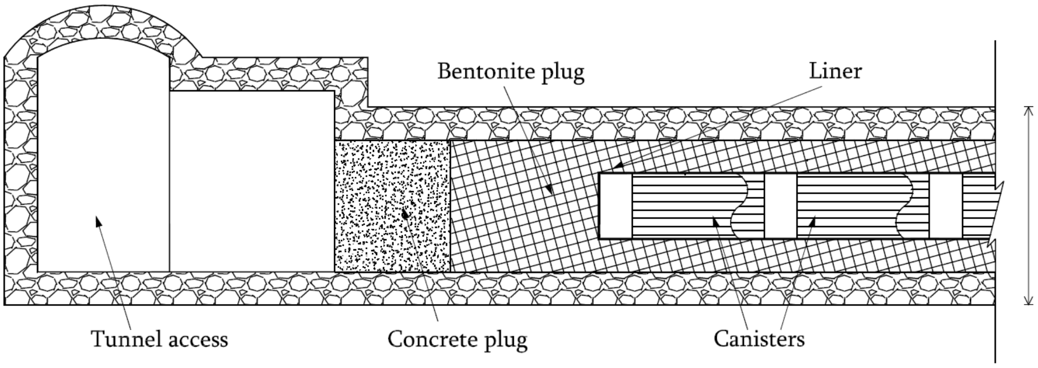


Figure 5.1. **Sketch of a deep geological repository placed in a granitic rock.**

Cement carbonation may be also considered a potentially feasible method for the sequestration of CO_2 [30,31], since a kilogram of fully-carbonated Portland cement sequesters around 0.23 kg of CO_2 (i.e., 130 L of CO_2 at 298 K and 0.1 MPa) [32,33]. Carbonation of alkaline minerals [34-36], mimicking natural rock weathering, leads to the permanent storage or sequestration of CO_2. Nevertheless, CO_2 sequestration technology through mineral carbonation has not been fully developed, due to the increased operation costs in CO_2-emitting industries if this technology is integrated [37]. However, this drawback may be mitigated if cement-based compounds are used, since in this case the carbonation process leads to high added-value materials with promising potential applications. Finally, cement carbonation plants may be hypothetically integrated in a coal-fired power plant with subsequent environmental and operational cost benefits (Figure 5.2).

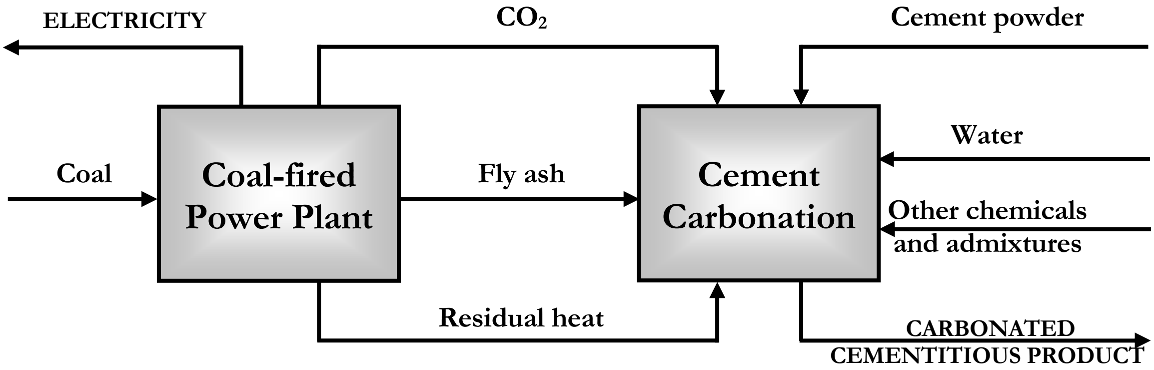


Figure 5.2. **Sketch of an integrated cement carbonation/coal-fired power plant. Adapted from Rubin and Taylor [32].**

The concentration of the CO_2 reagent plays an important role in cement carbonation processes. The natural carbonation process is too slow (in the order of months) to be implemented for any of the industrial applications already mentioned. The low carbonation rate is due to the low CO_2 concentration in the atmosphere (0.03-0.06 vol. %) and the slow diffusion velocity of CO_2 into the cement pores [38]. Thus, the aim is to develop a controlled accelerated carbonation method in order to obtain a carbonated cementitious material in a reasonable period of time. Cement carbonation in a gaseous CO_2 enriched atmosphere reduces the duration of the process from months up to weeks, due to the high CO_2 content in the gas phase [39-41]. In this case, the difussion of CO_2 inside the cement pores is the rate-limiting step of the carbonation process.

Cement carbonation may be greatly accelerated if $scCO_2$ is used as the carbonation agent [7,13-15,22,23,32,42]. Hyper-stoichiometric CO_2 concentration and enhanced CO_2 solubility in water is obtained when working with $scCO_2$. Further, the reaction acceleration is also due to the ease of penetration and diffusion of the $scCO_2$ into the micropores of the cement paste, providing continuous availability of fresh reactant. In this Chapter, the effects of supercritical carbonation on the physicochemical properties of different types of hardened Portland cement pastes are studied. Results are compared with those obtained from natural carbonation.

Additionally, a water repellency treatment confers high-added value to some construction materials (e.g., concrete, bricks, wood, stone, marble) [43-47]. Although water is very important to concrete during hardening stages, it could cause severe damages with time. For instance, some water-associated problems of the concrete are freeze–thaw damage, alkali silica reaction or sulphate attack [45,48-52]. Consequently, the next step of this research is to achieve an increase in the durability of concrete by preventing water ingress in the bulk of the matrix. Various hydrophobic treatments are currently used to prevent or minimize water penetration into concrete; among them, barrier systems are the most used ones [53]. Moreover, durability enhancement and graffiti prevention of cement-based materials have been reported using silane solutions as the hydrophobic agents [54]. In this Chapter, cement silanization using $scCO_2$ as a solvent (see Chapter 2) is performed [14,45]. Octyltriethoxysilane is used as the water-repellent agent [55] by forming a polysiloxane network on the surface of the inorganic material: the ethoxy groups hydrolize to produce silanols that bond with the surface hydroxyl groups of the cement, while the long-chain alkyl groups of the organic silane confer hydrophobicity to the surface.

5.2. Materials and Methods [13-15]

5.2.1. Materials

Conventional [56] and sulphate resisting [57] Portland cement (CEMI and CEM I-SR, respectively), a class F fly ash [58] (FA with a mean particle size of 18 μm), all from Cia. Valenciana de Cementos Portland S.A. (Alcalá de Guadaira, Spain), and silica fume [59] (SF with a mean particle size of 26 μm) from Ferroatlántica S.L. (A Coruña, Spain) are the ingredients used in the different cement and mortar formulations. FA and SF are puzzolanic admixtures commonly used in the cement industry, coming from subproducts of the coal-fired power plants and siderurgic industry, respectively. These mineral fillers are able to reduce the curing time of the cement and can also enhance the mechanical and chemical resistance of produced cement-based material [1,3,60-64]. Formulations of the studied pastes are: 100% CEM I (CEMI), 100% CEM I-SR (CEM), 56% CEM I-SR + 35% FA + 9% SF (CEM-35FA9SF), 83% CEM I-SR + 17% SF, (CEM-17SF) and 83% CEM I-SR + 8% FA + 9% SF (CEM-8FA9SF). Cement pastes are fabricated with a 0.4 water to cement ratio, and hydrated during 7 days in sealed conditions (98% relative humidity at 293±2 K). Moreover, cylinders (30 mm diameter x 20 mm height) of mortars of the CEM-35FA9SF sample are prepared with a 0.5 sand to cement ratio. The sand is a standard material (UNI ENV 196-1) with particle sizes of 80-2000 μm. The cement and mortar are mainly employed as granulated powders, although some monolithic pieces (0.2 cm^3) are also processed using the supercritical method. Octyltriethoxysilane (Fluka) is used for the hydrophobic treatment of the mortar. CO_2 (99.995 % purity) is supplied by Carburos Metálicos S.A. (Spain).

5.2.2. Process

Supercritical carbonation of the cementitious formulations is performed in the supercritical equipment described in Section 1.2.2 of Chapter 1, running with a continuous flow of $scCO_2$ of 1.5-3.5 g min^{-1} at 318 K and 20.0 MPa, during different periods of time. For the natural carbonation experiments, the cement samples are stored at 291 and 318 K during 200 and 30 days, respectively.

Monolythic mortar samples are carbonated using the supercritical equipment described in Section 1.2.1 of Chapter 1, running in the batch mode, at 318 K and 20.0 MPa, during 3 h and, subsequently, supercritically silanized using 2 mL of octyltriethoxysilane at 343 K and 8.5 MPa, during 3 h.

5.2.3. Characterization

Cement-based samples are analyzed using X-ray diffraction, thermogravimetric analysis, low-temperature N_2 adsorption-desorption analysis, mercury intrusion porosimetry, scanning electron microscopy with backscattered electron imaging, water permeability test, particle size distribution by light scattering, and Fourier transform infrared spectrometry.

5.3. Results

Article no. 1

Title: Modification in Composition and Microstructure of Portland Cement Pastes as a Result of Natural and Supercritical Carbonation Procedures

Authors: C. A. García-González, A. Hidalgo, C. Andrade, M. C. Alonso, J. Fraile, A. M. López, C. Domingo

Journal: Ind. Eng. Chem. Res. 45 (2006) 4985-4992

Article no. 2

Title: Porosity and Water Permeability Study of Supercritically Carbonated Cement Pastes Involving Mineral Additions

Authors: C. A. García-González, A. Hidalgo, J. Fraile, A. M. López-Periago, C. Andrade, C. Domingo

Journal: Ind. Eng. Chem. Res. 46 (2007) 2488-2496

Article no. 3

Title: New Insights on the Use of Supercritical Carbon Dioxide for the Accelerated Carbonation of Cement Pastes

Authors: C. A. García-González, N. El Grouh, A. Hidalgo, J. Fraile, A. M. López-Periago, C. Andrade, C. Domingo

Journal: J. Supercritical Fluids 43 (2008) 500-509

5.4. Process optimization

5.4.1. Scheduling

Modern manufacturing processes require organization and management of the resources for cost optimization. Scheduling provides detailed short-mid term decisions regarding unit assignment, sequencing and timing [65-67]. This information is extremely useful for a mid-term foresight of the process, i.e., planning, and in some cases leads to reassignment of resources, i.e., re-scheduling. As an example, the scheduling of the batch supercritical carbonation and silanization processes of cement-based materials using the supercritical batch equipment (see Section 1.2.1. of Chapter 1) is, herein, exposed. The equipment is considered to be operated a maximum of 12 working h per day. The overall process basically consists in ten tasks divided in two steps (carbonation and silanization) with the following five tasks each:

- Task #1: system preparation (i.e. loading of the processing vessels with the cementitious material and/or silane, start-up of the refrigeration system, CO_2 replenishment of the pump P1).
- Task #2: CO_2 filling of the processing vessels; heating of the processing vessels up to the operation temperature (318 K and 343 K for the carbonation and silanization processes, respectively); and pressurization of the processing vessel up to the desired operation pressure (20 MPa for the carbonation step and 8.5 MPa for the silanization step).
- Task #3: operation period (carbonation during 3 h, silanization plus washing with a $scCO_2$ flow during 3 h).
- Task #4: system (compression plus processing sections) depressurization.
- Task #5: cooling of the 100-mL reactor and unloading of the processed materials.

The overall process is sketched by means of the Gantt diagram in Figure 5.3. The black bars correspond to the carbonation process and the grey bars to the silanization process. The completion time of the process is around 15-16 working hours.

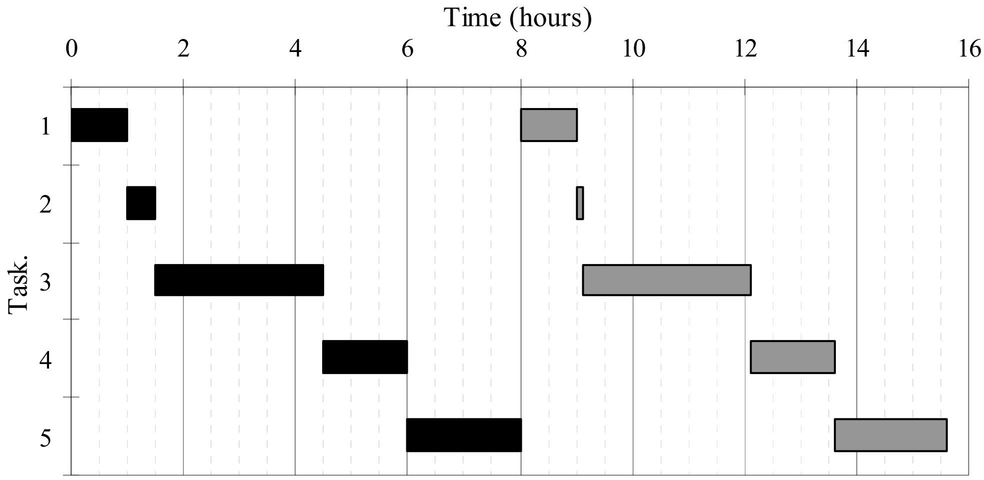


Figure 5.3. **Gantt diagram of the process of carbonation-silanization of cementitious materials.**

5.4.2. Process integration

In order to reduce the cycle time and operation costs, a modification of the batch process is proposed (Figure 5.4), consisting in the use of an additional 10-mL vessel (C1) acting as a silane reservoir. At the beginning of the process (task #1), the reactor Re1 is loaded with the material to be carbonated. When the carbonation process (task #3) is finished, the vessel Re1 is directly depressurized and heated up to the operating conditions for the silanization step (8.5 MPa and 343 K) without previous unloading (task #5). Then, the reservoir C1 is filled with the required amount of silane (task #1), heated and pressurized with CO_2 (task #2), and finally contacted with the carbonated material by opening the valve V7 (start of task #3).

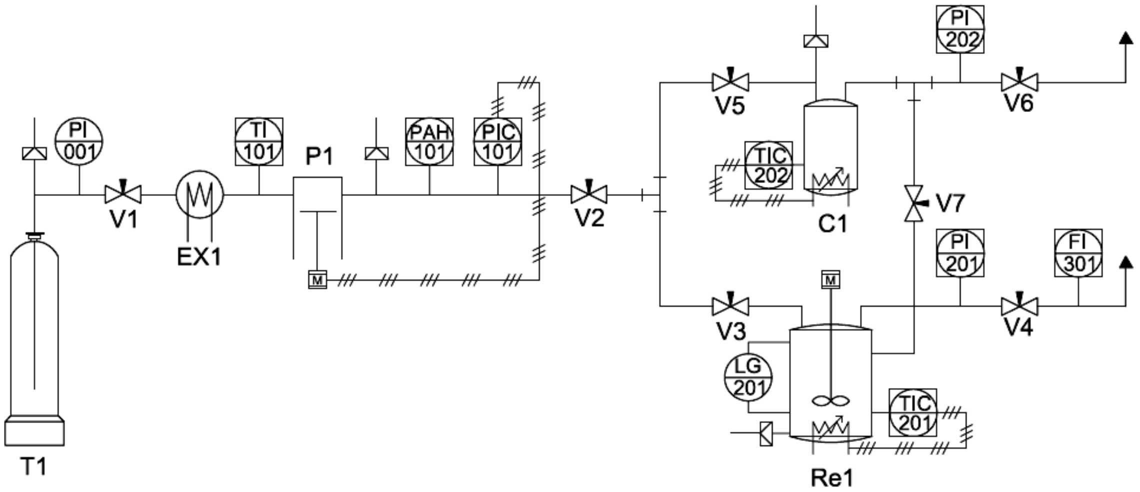


Figure 5.4. **Modified equipment for the integrated batch carbonation-silanization process.**

With the described process modification, it is possible to reduce the energy consumption (refrigeration, heating and pumping) and the use of added feedstock (CO_2 consumption). This upgrade of the process allows the elimination of task #5 in the carbonation process (Figure 5.5), since the reactor Re1 does not need to be opened before the beginning of the silanization step. Tasks #2 and #4 are shortened in the silanization and carbonation processes, respectively. The reason relies on the fact that less amount of CO_2 needs to be pumped and released in tasks #2 and #4, respectively. The time needed for process completion is reduced to *ca.* 11-12 h, i.e. a process time reduction of 26% with respect to the previous configuration is achieved. Furthermore, with the new configuration the amount of CO_2 used in the process is reduced in a percentage of 19%, as no total depressurization of the reactor Re1 is needed previous to the addition of the silane into the system.

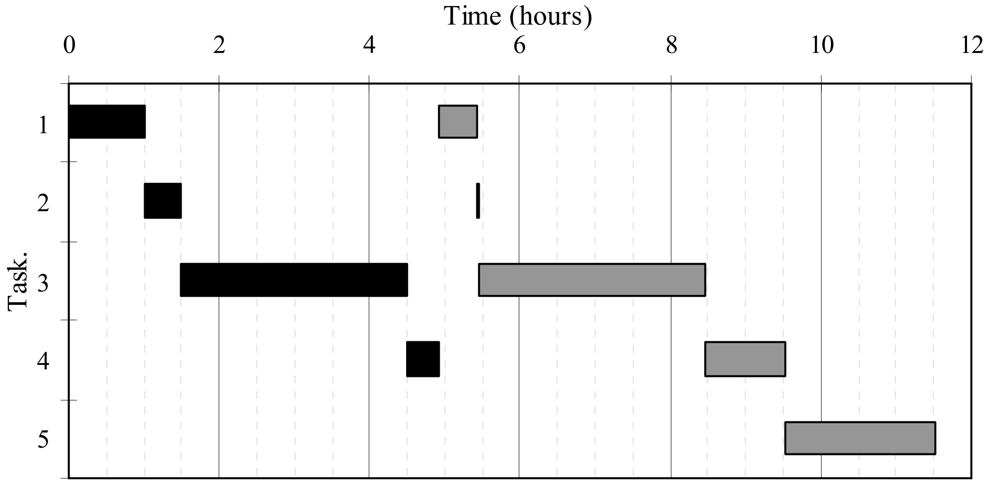


Figure 5.5. **Scheduling of the integrated carbonation-silanization process.**

5.4.3. Study of the regime change in the semicontinuous processing

A semicontinuous process configuration may be performed by means of the use of two extra vessels, Re2 and C2 arranged in parallel with the already existing Re1 and C1 (Figure 5.6), respectively, and with the same volume (100 mL and 10 mL, respectively). For the semicontinuous processing, follow-up and manipulation of the equipment is considered to be performed under shift work with one operator at a time. The modification of the process leads to the Gantt diagram shown in Figure 5.7, where a material lot can be produced every 8 h. Using this configuration, task #4 of the silanization step is shortened, since only the processing section (from valve V2 downstream) is depressurized, whereas the compression section (valve V2 upstream) can be reused for the next run. Thus, the CO_2 consumption is dramatically reduced in *ca.* 62% with respect to the configuration of Section 5.4.2.

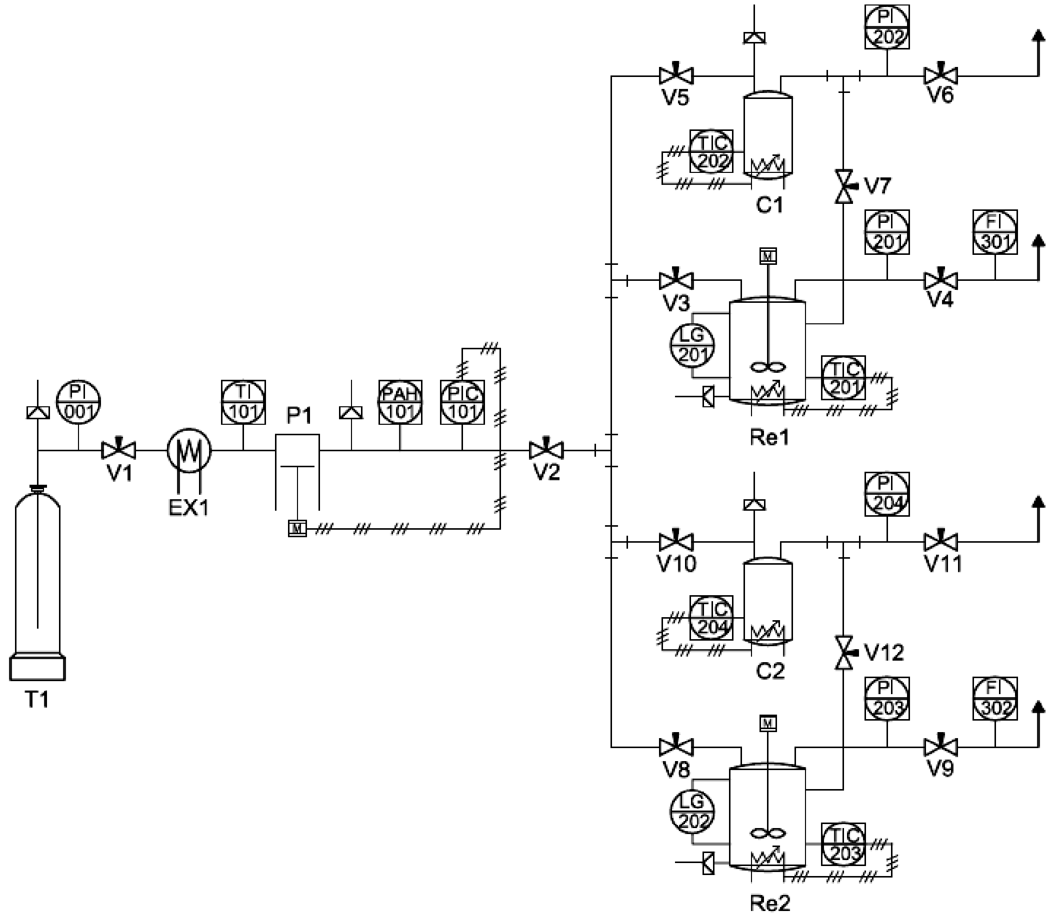


Figure 5.6. **Modified equipment for the semicontinuous carbonation-silanization process.**

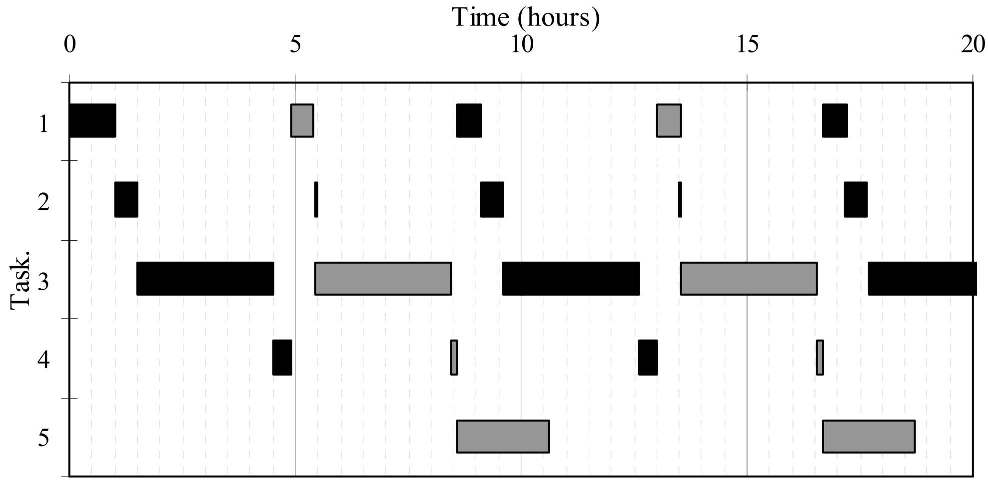


Figure 5.7. **Gantt diagram of the semicontinuous carbonation-silanization process.**

On the other hand, in the configuration of Figure 5.7 it is only considered the overlapping of the unloading of the processed material (task #5) with the start of a new run (task #1). Moreover, the overlapping of the depressurization of the processing vessels (task #4) with the beginning of the next step (i.e., task #1 of the silanization step) or a new run (i.e. task #1 of the carbonation step) can be also envisaged as a technically feasible solution, with the subsequent time reduction between material lots production (up to a duration of *ca.* 6.5 h).

Finally, in order to enhance the mass and energy integration of the process, the supercritical carbonation-silanization process can be further modified according to the PFD shown in Figure 5.8. The material to be processed is placed in the processing vessels Re1, Re2 and Re3; when one vessel is under carbonation conditions, the second is under silanization conditions, and the third is being unloaded, cleaned and then filled again to be ready for the next run. The alkyltriethoxysilane is placed in the silane reservoirs C1 and C2. During the period that one of the vessels (either C1 or C2) is being filled, the other (either C2 or C1) is under operation. This configuration can be also used for processes of discrete supercritical silanization or supercritical carbonation of materials (see Chapters 2 and 5).

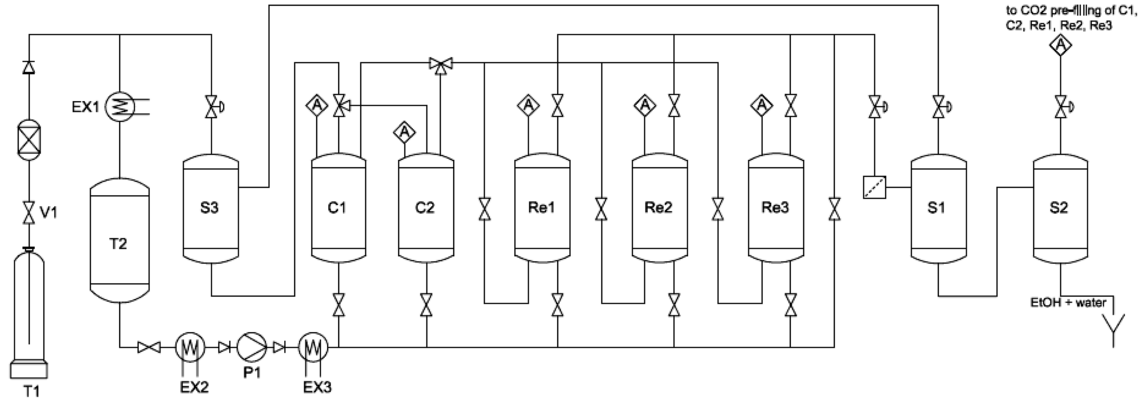


Figure 5.8. **PFD of the semicontinuous supercritical carbonation-silanization process with mass and energy integration.**

In Figure 5.8, the liquid CO_2 coming from a reservoir (T2) is pumped and heated in order to acquire the desired pressure and temperature in the silane reservoirs and processsing vessels. After the carbonation step, the processing vessels and silane reservoirs are contacted by opening the proper valves, and the silanization reaction takes place. Finally, a continuous flow of $scCO_2$ (f.i., at 318 K and 22.5 MPa) passes through the reaction vessel in order to perform the cleaning step, where the unreacted silane is eliminated of the silanized material. Neither the use of cosolvents nor a further treatment with organic solvents is necessary.

Small amounts of water and ethanol (EtOH) are obtained as by-products of the silanization process and should be removed. The separation of the majority of these chemicals from the main stream of the process can be performed by means of the use of gas-liquid separators (S1 and S2). EtOH and water are removed from the CO_2 in these separators by decreasing the solubilizing power of the solvent through a change in the operating conditions (i.e., pressure and temperature) [68]. Thus, CO_2 and unreacted silane can be both recycled and used again in the next runs. EtOH coming from the hydrolysis of the silane molecules (see Chapter 2) can be removed in a separator by reducing the pressure below 10.0 MPa and raising the temperature above 353 K. Under these operating conditions and with enough residence time, a fluid-liquid equilibrium is obtained with a CO_2-rich fluid phase (CO_2 molar fraction of 0.95) and a liquid phase containing water, EtOH and CO_2 (f.i., at 10.0 MPa and 353K, and for a system with a negligible content of water, the EtOH:CO_2 molar ratio is 3:2) [69-71]. By a further pressure reduction and a temperature decrease, the majority of the CO_2 can be separated from water and EtOH and recycled (f.i., at 2.0 MPa and 333 K). For a system with a negligible content of water, the EtOH:CO_2 molar ratio is 10:1 in the liquid phase and the CO_2 molar fraction in the gaseous phase is 0.97 [70,71].

As far as the residual silane separation from the flow of CO_2 is concerned, it should be taken into account that the silane has low solubility in gaseous CO_2 [72]. Therefore, the silane can be separated from the CO_2 by means of the gas-liquid separator S3 by reducing the pressure below the critical point of the CO_2. The collected silane can be recycled and used in the next run. This fact is extremely important, taking into account the large amount of silane excess used in the supercritical process and the cost of this chemical (Chapter 2).

5.5. Conclusions

The natural carbonation process is strongly accelerated by using $scCO_2$ as the carbonating agent for Portland cement powder and complete carbonation can be attained in less than 2 h. The tunability of the physicochemical properties of $scCO_2$ with pressure, its low viscosity and its high diffusivity allow the penetration of this fluid into very fine pores and increase the depth of carbonation of cement pastes. $Ca(OH)_2$ is the main source of Ca^{2+} ions during the carbonation process. Meanwhile, the partial decalcification of CSH gel indicates that this component is a secondary Ca^{2+} ion source for calcite formation. Complete disappearance of ettringite due to the supercritical carbonation process is also noticed. Calcium carbonate is mainly obtained in the form of the calcite polymorph. The massive precipitation of calcium carbonate inside the cement pores after supercritical treatment causes the refinement of the microstructure, thus reducing water permeability to a large extent (more than 4 orders of magnitude with respect to uncarbonated samples, measured at 0.02 MPa of water). Moreover, supercritical carbonation led to partial neutralization of the pore water alkalinity in the cement-based materials. Surface modification of the cement-based samples through the supercritical silanization process conferred weathering resistance to the material. The silane layer formed on the surface of the cementitious material led to a dramatic change in the hydrophobic behaviour of the sample, leading to an important reduction in the absorption of liquid water through the concrete. Finally, scheduling is a valuable tool for the management of resources and is applied for assisting the implementation and integration of the supercritical carbonation-silanization process.

5.6. References

[1] E. Gartner, *Industrially interesting approaches to "low-CO_2" cements*. Cement and Concrete Research 2004, 34(9), 1489-1498.

[2] R. McCaffrey, *Climate Change and the Cement Industry*. Global Cement and Lime Magazine 2002, Environmental Special Issue, 15-19.

[3] J.W. Phair, *Green chemistry for sustainable cement production and use.* Green Chemistry 2006, 8(9), 763-780.

[4] T.K.H. Al-Kadhimi, P.F.G. Banfill, S.G. Millard, J.H. Bungey, *An accelerated carbonation procedure for studies on concrete.* Advances in Cement Research 1996, 8(23), 47-59.

[5] J. Khunthongkeaw, S. Tangtermsirikul, T. Leelawat, *A study on carbonation depth prediction for fly ash concrete*. Construction and Building Materials 2006, 20(9), 744-753.

[6] H.F.W. Taylor, *Cement chemistry.* Academic Press: New York, 1990.

[7] L. Fernández-Carrasco, J. Rius, C. Miravitlles, *Supercritical carbonation of calcium aluminate cement.* Cement and Concrete Research 2008, 38(8-9), 1033-1037.

[8] A. Hidalgo, C. Domingo, F.J. Huertas, C. García González, J.L. García Calvo, M. Rozalén, C. Alonso, *Supercritically carbonation of concretes based in calcium aluminate cement and silica fume. Application to a high level nuclear waste repository.* Journal of Hazardous Materials. Under Revision.

[9] J.J. Chen, J.J. Thomas, H.F. W. Taylor, H.M. Jennings, *Solubility and structure of calcium silicate hydrate.* Cement and Concrete Research 2004, 34(9), 1499-1519.

[10] B.G. Kutchko, B.R. Strazisar, D.A. Dzombak, G.V. Lowry, N. Thaulow, *Degradation of well cement by CO_2 under geologic sequestration conditions.* Environmental Science & Technology 2007, 41(13), 4787-4792.

[11] A.C. Garrabrants, F. Sánchez, D.S. Kosson, *Changes in constituent equilibrium leaching and pore water characteristics of a Portland cement mortar as a result of carbonation.* Waste Management 2004, 24(1), 19-36.

[12] D.J. Anstice, C.L. Page, M.M. Page, *The pore solution phase of carbonated cement pastes.* Cement and Concrete Research 2005, 35(2), 377-383.

[13] C.A. García-González, A. Hidalgo, C. Andrade, M.C. Alonso, J. Fraile, A.M. López-Periago, C. Domingo, *Modification of composition and microstructure of Portland cement pastes as a result of natural and supercritical carbonation procedures.* Industrial & Engineering Chemistry Research 2006, 45(14), 4985-4992.

[14] C.A. García-González, A. Hidalgo, J. Fraile, A.M. López-Periago, C. Andrade, C. Domingo, *A porosity and water permeability study of supercritically carbonated cement pastes involving mineral additions.* Industrial & Engineering Chemistry Research 2007, 46(8), 2488–2496.

[15] C.A. García-González, N. El Grouh, A. Hidalgo, J. Fraile, A.M. López-Periago, C. Andrade, C. Domingo, *New insights on the use of supercritical carbon dioxide for the accelerated carbonation of cement pastes.* The Journal of Supercritical Fluids 2008, 43(3), 500–509.

[16] A. Hidalgo, C. Domingo, C. Garcia, S. Petit, C. Alonso, C. Andrade, *Microstructural changes induced in Portland cement-based materials due to natural and supercritical carbonation.* Journal of Materials Science 2008, 43(9), 3101-3111.

[17] S.K. Roy, K.B. Poh, D.O. Northwood, *Durability of concrete-accelerated carbonation and weathering studies.* Building and Environment 1999, 34(5), 597-606.

[18] J. Khunthongkeaw, S. Tangtermsirikul, T. Leelawat, *A study on carbonation depth prediction for fly ash concrete.* Construction and Building Materials 2006, 20(9), 744-753.

[19] L. Liu, J. Ha, T. Hashida, S. Teramura, *Development of a CO_2 solidification method for recycling autoclaved lightweight concrete waste*. Journal of Materials Science Letters 2001, 20(19), 1791-1794.

[20] P. Purnell, J. Beddows, *Durability and simulated ageing of new matrix glass fibre reinforced concrete.* Cement and Concrete Composites 2005, 27(9-10), 875-884.

[21] L.C. Lange, C.D. Hills, A.B. Poole, *Effect of carbonation on properties of blended and non-blended cement solidified waste forms*. Journal of Hazardous Materials 1997, 52(2-3), 193-212.

[22] T. Van Gerven, D. Van Baelen, V. Dutré, C. Vandecasteele, *Influence of carbonation and carbonation methods on leaching of metals from mortars*. Cement and Concrete Research 2004, 34(1), 149-156.

[23] L. Van Ginneken, V. Dutré, W. Adriansens, H. Weyten, *Effect of liquid and supercritical carbon dioxide treatments on the leaching performance of a cement-stabilised waste form*. The Journal of Supercritical Fluids 2004, 30(2), 175-188.

[24] W.L. Clarke, *Safe disposal of nuclear waste*. Science & Technology Review 1996, 3, 6-16.

[25] N.A., *Origen y gestión de residuos radiactivos.* 3rd edition. Ilustre Colegio Oficial de Físicos: Madrid, 2000.

[26] A. Pastor, *El almacenamiento geológico profundo de los residuos radiactivos de alta actividad. Principios básicos y tecnología*. Enresa: Madrid, 2001.

[27] N.A., *Engineered barrier systems and the safety of deep geological repositories.* Organization for Economic Co-operation and Development: Paris, 2003.

[28] A. Agüero, P. Pinedo, D. Cancio, I. Simón, M. Moraleda, D. Pérez-Sánchez, C. Trueba, *Spanish methodological approach for biosphere assessment of radioactive waste disposal.* Science of The Total Environment 2007, 384(1-3), 36-47.

[29] F.J. Huertas, A. Hidalgo, M.L. Rozalén, S. Pellicione, C. Domingo, C.A. García-González, C. Andrade, C. Alonso, *Interaction of bentonite with supercritically carbonated concrete*. Applied Clay Science 2009, 42(3-4), 488-496.

[30] O.L. Shtepenko, C.D. Hills, N.J. Coleman, A. Brough, *Characterization and preliminary assessment of a sorbent produced by accelerated mineral carbonation*. Environmental Science and Technology 2005, 39(1), 345-354.

[31] J. Stolaroff, H. Ecke, *Demobilization of critical contaminants in four typical waste-to-energy ashes by carbonation*. Waste Management 2006, 26(4), 430-441.

[32] J.B. Rubin, C.M.V. Taylor, *Partial replacement of Portland cement with fly ashes and kiln dusts using supercritical carbon dioxide processing*. Los Alamos National Laboratory: Los Álamos, 1998.

[33] A. Iizuka, M. Fujii, A. Yamasaki, Y. Yanagisawa, *Development of a new* CO_2 *sequestration process utilizing the carbonation of waste cement*. Industrial & Engineering Chemistry Research 2004, 43(24), 7880-7887.

[34] K.S. Lackner, *Carbonate chemistry for sequestering fossil carbon*. Annual Review for Energy and the Environment 2002, 27, 193-232.

[35] Intergovernamental Panel on Climate Change (IPCC), *IPCC special report on carbon dioxide capture and storage*. Cambridge University Press: Cambridge, 2005.

[36] W.J.J. Huijgen, R.N.J. Comans, *Carbonation of steel slag for* CO_2 *sequestration: leaching of products and reaction mechanisms*. Environmental Science and Technology 2006, 40(8), 2790-2796.

[37] W.K. O'Connor, D.C. Dahlin, G.E. Rush, S.J. Gerdermann, L.R. Penner, D.N. Nilsen, *Aqueous mineral carbonation: mineral availability, pretreatment, reaction parameters, and process studies*. Albany Research Center: Albany, 2005.

[38] J.M. Bukowski, R.L. Berger, *Reactivity and strength development of* CO_2 *activated non-hydraulic calcium silicates.* Cement and Concrete Research 1979, 9(1), 57-68.

[39] R.K. Dhir, M.R. Jones, J.G.L. Munday, *A practical approach to studying carbonation on concrete.* Concrete 1985, 19(10), 32-34.

[40] L. Liu, J. Ha, T. Hashida, S. Teramura, *Development of a* CO_2 *solidification method for recycling autoclaved lightweight concrete waste*. Journal of Materials Science Letters 2001, 20(19), 1791-1794.

[41] G. Costa, R. Baciocchi, A. Polettini, R. Pomi, C. Hills, P.J. Carey, *Current status and perspectives of accelerated carbonation processes on municipal waste combustion residues.* Environmental Monitoring and Assessment 2007, 135(1-3), 55-75.

[42] T. Hartmann, P. Paviet-Hartmann, J.B. Rubin, M.R. Fitzsimmons, K.E. Sickafus, *The effect of supercritical carbon dioxide treatment on the leachability and structure of cemented radioactive waste-forms.* Waste Management 1999, 19(5), 355-361.

[43] R.L. Cuthbert, E.P. Plueddemann, *Aqueous silane water repellent compositions*. US Patent 5,073,195 (1991).

[44] I.J. de Vries, R.B. Polder, *Hydrophobic treatment of concrete*. Construction and Building Materials 1997, 11(4), 259-265.

[45] A. Frattolillo, G. Giovinco, M.C. Mascolo, A. Vitale, *Effects of hydrophobic treatment on thermophysical properties of lightweight mortars*. Experimental Thermal and Fluid Science 2005, 29(6), 733–741.

[46] C. Ricci, C. Miliani, B.G. Brunetti, A. Sgamellotti, *Non-invasive identification of surface materials on marble artifacts with fiber optic mid-FTIR reflectance spectroscopy*. Talanta 2006, 69(5), 1221–1226.

[47] C. Domingo, M. Álvarez de Buergo, S. Sánchez-Cortés, R. Fort, J.V. García-Ramos, M. Gómez-Heras, *Possibilities of monitoring the polymerization process of silicon-based water repellents and consolidants in stones through infrared and Raman spectroscopy*. Progress in Organic Coatings 2008, 63(1), 5-12.

[48] M. Pigeon, J. Prevost, J.M. Semard, *Freeze–thaw durability versus freezing rate*. Journal of the American Concrete Institute 1985, 82(5), 684-692.

[49] B. Mather, *How to make concrete that will not suffer deleterious alkali–silica reaction*. Cement and Concrete Research 1999, 29(8), 1277-1280.

[50] E.E. Hekala, E. Kishar, H. Mostafa, *Magnesium sulfate attack on hardened blended cement pastes under different circumstances*. Cement and Concrete Research 2002, 32(9), 1421-1427.

[51] A. Al-Otoom, A. Al-Khlaifa, A. Shawaqfeh, *Crystallization technology for reducing water permeability into concrete*. Industrial & Engineering Chemistry Research 2007, 46(16), 5463-5467.

[52] F. Tittarelli, G. Moriconi, *The effect of silane-based hydrophobic admixture on corrosion of reinforcing steel in concrete*. Cement and Concrete Research 2008, 38(11), 1354-1357.

[53] A. Barbucci, M. Delucchi, G. Cerisola, *Organic coating for concrete protection. Liquid water and water vapor permeabilities*. Progress in Organic Coatings 1997, 30(4), 293-297.

[54] N.A., *Protectosil Antigraffiti SP: Solutions for preventing surface damaging effects*. Technical information from Evonik industries.

[55] A. Be, D.T. Liles, F.G.P. Wilhelmi, D.J. Romenesko, *Storage-stable water-repellent composition for masonry materials*. US Patent 5,919,296 (1999).

[56] N.A., *UNE-EN 197-1:2000. Cemento. Parte I: Composición, especificaciones y criterios de conformidad de los cementos comunes*. AENOR: Madrid, 2000.

[57] N.A., *UNE 80303-1:2001. Cementos con características adicionales. Parte 1: Cementos resistentes a los sulfatos*. AENOR: Madrid, 2001.

[58] N.A., *UNE-EN 450:1994. Cenizas volantes como adición al hormigón. Definiciones, especificaciones y control de calidad*. AENOR: Madrid, 1995.

[59] N.A., *UNE 83460-1/2. Adiciones al hormigón: Humo de sílice*. AENOR: Madrid, 2005

[60] S.K. Malhotra, N.G. Dave, *Investigations into the effect of addition of fly ash and burnt clay pozzolana on certain engineering properties of cement composites.* Cement and Concrete Composites 1999, 21(4), 285-291.

[61] A. Guerrero, S. Goñi, A. Macias, M.P. Luxan, *Effect of the starting fly ash on the microstructure and mechanical properties of fly ash-belite cement mortars.* Cement and Concrete Research 2000, 30(4), 553-559.

[62] X. Fu, Z. Wang, W. Tao, C. Yang, W. Hou, Y. Dong, X. Wu, *Studies on blended cement with a large amount of fly ash.* Cement and Concrete Research 2002, 32(7), 1153-1159.

[63] M.I. Khan, C.J. Lynsdale, *Strength, permeability, and carbonation of high-performance concrete.* Cement and Concrete Research 2002, 32(1), 123-131.

[64] I. Janotka, T. Nurnbergerova, *Effect of temperature on structural quality of the cement paste and high-strength concrete with silica fume.* Nuclear Engineering and Design 2005, 235(17-19), 2019-2032.

[65] J. Blazewicz, K.H. Ecker, E. Pesch, G. Schmidt, J. Weglarz, *Scheduling computer and manufacturing processes.* Springer: Berlin, 2001.

[66] M.L. Pinedo, *Planning and scheduling in manufacturing and services.* Springer: New York, 2005.

[67] J.W. Herrmann, *Handbook of production scheduling.* Springer: New York, 2006.

[68] K. Zosel, *Verfahren zur Trennung von Stoffgemischen, die organische Verbindungen und/oder organische Gruppen aufweisende Verbindungen enthalten*, German Patent 1,493,190 (1965).

[69] M.L. Gilbert, M.E. Paulaitis, *Gas-liquid equilibrium for ethanol-water-carbon dioxide mixtures at elevated pressures.* Journal of Chemical & Engineering Data 1986, 31(3), 296-298.

[70] K. Suzuki, H. Sue, M. Itou, R.L. Smith, H. Inomata, K. Arai, S. Saito, *Isothermal vapor-liquid equilibrium data for binary systems at high pressures: carbon dioxide-methanol, carbon dioxide-ethanol, carbon dioxide-1-propanol, methane-ethanol, methane-1-propanol, ethane-ethanol, and ethane-1-propanol systems.* Journal of Chemical & Engineering Data 1990, 35(1), 63-66.

[71] Ž. Knez, M. Škerget, L. Ilič, C. Lütge, *Vapor–liquid equilibrium of binary* CO_2*–organic solvent systems (ethanol, tetrahydrofuran, ortho-xylene, meta-xylene, para-xylene).* The Journal of Supercritical Fluids 2008, 43(3), 383-389.

[72] C.A. García-González, J. Fraile, A. López-Periago, J. Saurina, C. Domingo, *Measurements and correlation of octyltriethoxysilane solubility in supercritical* CO_2 *and assembly of functional silane monolayers on the surface of nanometric particles.* Industrial & Engineering Chemistry Research, In Press (doi: 10.1021/ie900775z).

SUMMARY OF RESULTS

With the aim of preparing nanostructured hybrid composites using dispersion methods, first the surface modification of the fillers by silanization has been carried out using a supercritical carbon dioxide ($scCO_2$ method). Then, the Particles from a Compressed Anti-Solvent (PCA) and the Particles from Gas Saturated Solution (PGSS) methods have been used to disperse the treated filler in a polymeric or lipidic matrix. Finally, the process has been extended to the modification of complex structures, such as cements.

The supercritical silanization process, where $scCO_2$ is used as a solvent for alkoxysilanes, has proven to be an excellent route for the surface modification and functionalization of inorganic nanoparticles. The designed $scCO_2$ silanization process has been optimized using fundamental studies of the solubility of octyltriethoxysilane in $scCO_2$. The solubility values of the said silane in $scCO_2$ under working pressures and temperatures (8.0-18 MPa and 318, 348 K, respectively) increased with pressure. The measured data have been correlated using the Chrastil equation ($S_{C8}=\rho_{CO2}^{k}$ exp(a/T+b), with fitting parameters a = -6373, b = -12.31 and k = 5.517; AARD ~8 %). The solubility values, expressed as a mole fraction, are in the range 8 10^{-5} - 2 10^{-2}. A considerable fast silanization (few minutes) of titanium dioxide (TiO_2) was obtained when working with CO_2 at supercritical conditions (10.0-22.5 MPa, 318-348K), leading to high grafting densities (~2.8-3.0 molecules per nm^2). On the other hand, the degree of silane surface coverage could be tuned when compressed CO_2 gas was used, simply by controlling the reaction time. For near-critical CO_2 (6.0 MPa, 348 K), the found silanization kinetic equation resembled the Langmuir adsorption model for monolayer formation (r_P=k'[OH_{Ti}], with fitting constant k'=0.0426 min^{-1}; $R^2 > 0.98$). A chemometric analysis (2^3 full factorial design and Principal Component Analysis) has revealed a significant effect of CO_2 density (operating pressure-temperature interaction) on the aggregates porosity and dispersibility properties of the silanized

TiO_2 nanoparticles. Moreover, the supercritical silanization process has produced a chemical and thermally stable silane coating (*ca.* up to 520 K), regardless of the used operating conditions (pressure, temperature and reaction time). Densely packed monolayers (~3.0 molecules per nm^2) have also been successfully prepared by reacting different chain length (from methyl to octadecyl) alkyltrialkoxysilanes with TiO_2 nanoparticles in a $scCO_2$ medium. In contrast, the grafting density decreased (~1.5 molecules per nm^2) when a trialkylmonoalkoxysilane was used. Finally, it is shown that the silane surface treatment with trialkoxysilanes intensifies the compatibility of hydrophilic TiO_2 or maghemite (γ-Fe_2O_3) nanoparticles with hydrophobic organic phases.

The first class of prepared nanostructured hybrid materials consisted in polymers with dispersed inorganic fillers, and was prepared using the PCA technique, where $scCO_2$ acted as an anti-solvent. Networks of fibers consisting of biopolymeric matrices of either poly(L-lactic acid) (L-PLA) or the blend high molecular weight-poly(methylmethacrylate)/poly(ε-caprolactone) (PMMA/PCL) loaded with *ca.* 15-20 wt.% of nanometric hydroxyapatite (HAP) or TiO_2, respectively, have been obtained. The inorganic fillers dispersed in the hybrid materials were previously surface treated through the supercritical silanization process. The silanization of HAP and TiO_2 has facilitated the dispersion of the nanoparticles in the dichloromethane solution of the biopolymer prepared before the addition of $scCO_2$ as the anti-solvent. Silanized nanoparticles incorporated in the biopolymeric fibers are homogeneously distributed throughout the hybrid material. The viscosity of the polymeric solution influences the morphology of the precipitated material. Hence, agglomerated microparticles, instead of fibers, have been obtained when low molecular weight PMMA was used in the blend PMMA/PCL. The prepared materials have potential applications in tissue engineering.

A second class of studied composites was solid lipid hybrid particles prepared using the PGSS technique, assisted by the use of $scCO_2$ as a solute. Using this process, the rapid cooling of a lipid-based mixture during expansion promoted the formation of a low ordered lipidic blend. The low order in the blend crystals facilitated the incorporation of inorganic nanoparticles and drugs within the matrix. The studied system was formed by a lipid matrix of hydrogenated castor oil/glyceryl monostearate (1:1 weight ratio) loaded with nanometric TiO_2 (*ca.* 6 wt.%) and caffeine (*ca.* 4 wt.%). Again, the previous surface treatment of the nanometric TiO_2, using the described supercritical silanization process, facilitated the dispersion of the nanoparticles throughout the bulk of the lipid matrix. The UV-shielding ability of the TiO_2 was preserved after the silanization and its subsequent incorporation in the lipid particles. The dissolution profile in water of the caffeine contained in the lipid particles had two steps: an initial burst of 60 wt.% occurring in *ca.* 1-2 h, corresponding to the caffeine deposited on the surface of the particles, followed by a slow release of residual caffeine entrapped within the lipid core. The obtained lipid-based particles encompassed the UV-light protection of the TiO_2 and the photoaging prevention properties of the caffeine, and can be potentially exploited for topical cosmetic and pharmaceutical purposes.

Finally, the possibility of extending the silane treatment under $scCO_2$ conditions to multiscale complex materials has been tested. Thus, the use of the $scCO_2$ technology has been evaluated in the two-step carbonation-silanization processing of cement-based materials. The supercritical carbonation step was compared to natural carbonation with atmospheric air under ambient conditions. The use of supercritical CO_2 accelerated the carbonation reaction (from months to hours) due to the huge rise of CO_2 solubility in water (near 100-fold) when increasing the pressure from 0.1 to 20 MPa and to the ease of penetration and diffusion of the $scCO_2$ into the cement paste pores. Cement paste densification and total pore volume reduction of the carbonated cement were observed in both carbonation scenarios (natural and accelerated), due to the deposition of calcium carbonate. However, there was a shift of the pore volume values to fractions with small pores when cement samples were processed with $scCO_2$, which resulted in a significant reduction in the water permeability of the carbonated material. In a second step of the process, the surface modification of the carbonated cement with octyltriethoxysilane using $scCO_2$ as a solvent has conferred to the material water repellence and reduced the water absorption due to capillary rise (from 3 wt.% to 0.5 wt.%). Finally, for the efficient management of resources, the scheduling and the process integration were applied to the carbonation-silanization process, leading to reductions in CO_2 consumption of *ca.* 62% and in processing time of *ca.* 30%.

CONCLUSIONS

- $scCO_2$ is a convenient solvent of alkoxysilanes used for silane monolayer deposition on the surface of nanoparticulate materials. The system TiO_2 nanoparticles/octyltriethoxysilane has been used as the model system for the development of a generic and versatile $scCO_2$ silanization process. High grafting densities (~2.8-3.0 molecules per nm^2) and robust thermal stability (*ca.* 520 K) were obtained after a few minutes of supercritical silanization. The acidic conditions of water in contact with CO_2 accelerated the kinetics of the silanization process. The quality of the layer of deposited silane was largely influenced by the $scCO_2$ density related with the concentration of the silane in the supercritical fluid. Monolayer formation was obtained by working in the silane mole fraction range of $3.9\ 10^{-4}$-$1.5\ 10^{-3}$. On the other hand, silane polycondensation and multilayer deposition on the TiO_2 surface took place when the octyltriethoxysilane concentration in $scCO_2$ was higher than $1.5\ 10^{-3}$ mole fraction. The solubility of the silane in $scCO_2$ was successfully correlated by the Chrastil equation (fitting parameters a = -6373, b = -12.31 and k = 5.517; AARD~8 %).

- The silanization of TiO_2 nanoparticles with octyltriethoxysilane under near-critical CO_2 (6.0 MPa, 348 K) followed a Langmuir adsorption-like kinetic model (fitting constant k'=0.0426 min^{-1}, $R^2 > 0.98$). In this case, the control of the reaction time allowed for the tailor-made degree of silane coverage of TiO_2 nanoparticles. Maximum grafting densities (~2.7 molecules per nm^2) were obtained after 2 h.

- Closely packed silane monolayers (*ca.* 3 molecules per nm^2) deposited on TiO_2 nanoparticles were also successfully prepared using alkyltrialkoxysilanes with different chain lengths of the alkyl group (from isobutyl to octadecyl) in a $scCO_2$ medium (22.5 MPa, 318 K). In contrast, covalently attached monolayers prepared from trialkylmonoalkoxysilane had a grafting density of only *ca.* 1.5 molecules per nm^2 due to sterical hindrance. Moreover, the supercritical silanization process was successfully extended to other inorganic nanoparticles, such as maghemite and hydroxyapatite.

- The supercritical hydrophobic treatment of inorganic nanoparticles with octyltriethoxysilane enhanced the dispersibility of the surface-treated powder in hydrophobic liquids (e.g., petroleum, dichloromethane, avocado oil) and the homogeneous distribution of the particles in solid hydrophobic matrices (e.g., PMMA/PCL and HCO/GMS blends). The supercritical silanization treatment of TiO_2 nanoparticles would facilitate the dispersion of this UV-blocker in the formulations used in cosmetics.

- Networks of fibers of PMMA/PCL polymer blend loaded with TiO_2 (18-23 wt%) and L-PLA biopolymer loaded with HAP (7-14 wt%) were prepared using the PCA supercritical technique. The proper choice of the physicochemical properties of the biopolymers (molecular weight, blend composition) and the PCA operating conditions (pressure, temperature, polymer concentration in the liquid solution) allowed the production of fibers with an interconnected 3D macroporous structure and high microporosity, valid as materials for tissue engineering purposes. Solid lipid microparticles of the HCO/GMS lipid blend loaded with silanized TiO_2 (*ca.* 6 wt%) and caffeine (*ca.* 4 wt%) were prepared using the PGSS supercritical technique. The rapid lipid solidification taking place in the PGSS process during expansion diminished the crystallinity of the lipid blend, which facilitated the loading of the particles. Caffeine was both deposited on the solid surface (60 %) and entrapped within the lipid core (40%), resulting in a characteristic two-step dissolution profile in water. The material found applications in cosmetic and pharmaceutical products.

- The accelerated carbonation of Portland cement-based materials using $scCO_2$ (20.0 MPa, 318 K, 1.5-3.5 g min^{-1}) was performed in few hours, while the carbonation under atmospheric air (natural carbonation) could take several months. The process evolved from the diffusion of CO_2 inside of the pores as the rate-limiting step for natural carbonation to the detachment of calcium cations from the cement matrix for the supercritical carbonation. The supercritical silanization process was also applied to the surface treatment of the supercritically carbonated Portland cement. The coating of the material with octyltriethoxysilane conferred water repellence and reduction of water absorption due to capillary rise (from 3 wt% to 0.5 wt%). Cement paste densification, reduction in total pore volume and in water permeability are consequences of the supercritical treatment. The developed properties allowed the use of these bulk low-cost cementitious materials for hazardous waste confinement purposes.

- The combined contribution of $scCO_2$ processes design and fundamentals, based on engineering concepts, and end-products characteristics, based on materials research concepts, moves forward on the launching of sustainable solutions for the preparation of advanced materials with null or minimized consumption of organic solvents.

7.1. Future work

Open lines of research related to the topic of this PhD Thesis are the preparation of other complex hybrid materials using the supercritical silanization process. The large catalogue of silane molecules with a broad range of functional groups opens the possibility to the engineering of composite materials fitting the requirements of many industrial applications (e.g., plastics, biomedical devices, drug carriers, water repellent materials or gas sensors).

Finally, further investigation on the scale-up of the supercritical silanization process applied to inorganic nanoparticles will provide essential information for the potential implementation of the process in a larger scale.