

INFLUENCE OF INJECTION PRESSURES UP TO 100 MPa AND VESSEL PRESSURES ABOVE THE CRITICAL POINT ON THE PARTICLE FORMATION IN A SUPERCRITICAL ANTISOLVENT PROCESS.

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The supercritical antisolvent (SAS) process is used to generate particles in the micro- and nanometer scale with a defined size, a narrow size distribution, and a defined morphology. A liquid solution of a solvent and a solute is injected into a supercritical fluid which acts as an antisolvent. By varying the process parameters such as pressure, temperature, type of solvent, solute concentration, and the flow rate ratio of solution and antisolvent the properties of the produced particles can be strongly influenced.

To explain the particle generation and phase behaviour of the processed mixtures, existing theories use a pseudo binary system without solute as a base framework. As the influence of the solute cannot be neglected at higher concentrations and in certain material systems, these models are no longer applicable. One of the reasons is that the mixture critical point shifts to higher pressure values [1, 2]. Therefore high vessel pressures, which means fully developed supercritical conditions, have to be achieved for the formation of nanoparticles.

This contribution deals with the particle formation at precipitation vessel pressures up to 30 MPa and injection pressures up to 100 MPa at different nozzle diameters ranging from 15 µm to 200 µm. These variables have a significant influence on the corresponding mixing characteristics, the phase behaviour and on the essential time scales of particle generation and therefore determine the particle properties mentioned above. Moreover, injection pressures up to 100 MPa and the corresponding high jet velocities at a given nozzle diameter have neither been realised before nor have they been subjected to a closer examination.

INTRODUCTION

The supercritical antisolvent (SAS) process is a suitable way to generate fine particles at moderate conditions, without nearly any residual solvent [3]. Therefore it is ideally suited for pharmaceutical products. The produced particles have a defined size and a very small size distribution depending on the process parameters chosen. This makes the SAS process also advantageous for other substances like superconductor precursors, polymers, or biological active substances [4, 5]. By just slightly varying the process parameters such as pressure, temperature, type of solvent and solute concentration, the properties of the produced particles can be strongly influenced.

Furthermore it is also possible to adjust the desired shape, e.g. crystalline or amorphous, of the generated particles. In case of crystals, even the polymorphism of the precipitate can be manipulated by changing the process parameters [6]. Existing theories about the particle generation and the phase behavior of the processed mixtures use a pseudo binary system without solute as a base framework. This is only valid for certain material systems and process conditions [7].

MATERIALS AND METHODS

In this work, Dimethylsulfoxid (ROTIDRY® 99,5%, purchased at Carl Roth) was used as solvent, Yttrium Acetate (99.9% META, purchased at Sigma Aldrich) as solute and carbon dioxide (CO₂ 99.9%, purchased at Linde) as antisolvent.

Figure 1 shows the schematic representation of the SAS-plant. The central part of the plant is the optically accessible high pressure chamber, where the precipitation occurs. The liquid solution and the supercritical antisolvent are continuously delivered to the vessel. The antisolvent is pressurised by a compressor. The liquid solution is pumped with a syringe pump and is injected into the precipitator via a nozzle. The precipitated particles are separated at a filter, located downstream of the vessel. Behind the filter, the mixture of solvent and antisolvent passes through a pressure control valve and gets depressurised. The whole plant is fully automated and can be controlled by a single operator.

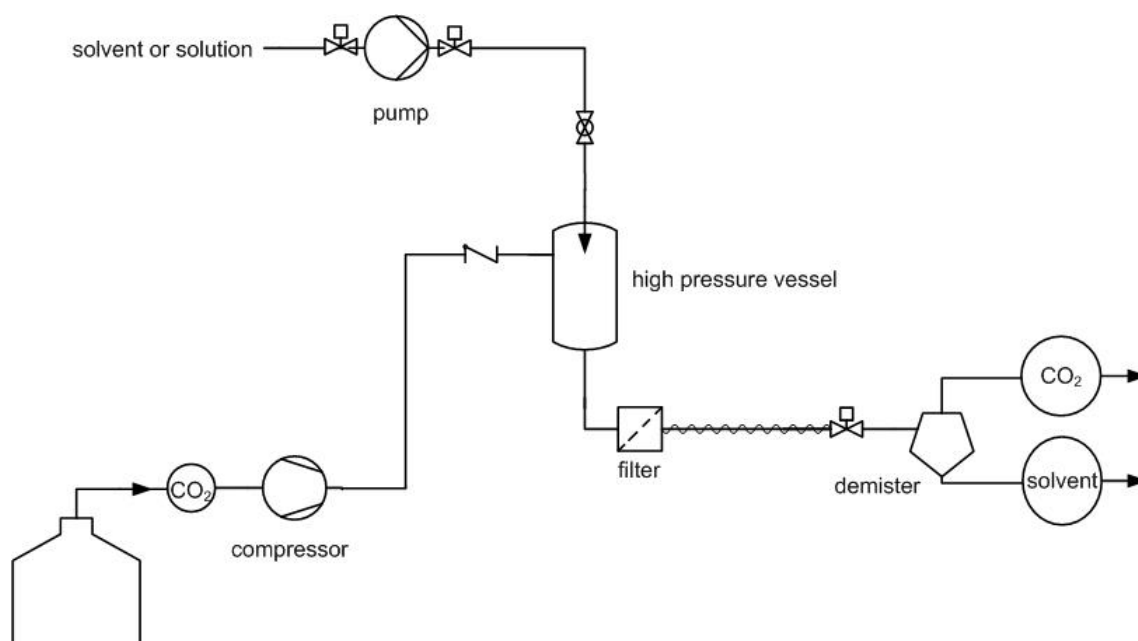


Figure 1: Schematic representation of the fully automated SAS plant

An experiment usually follows the same procedure. First of all, the vessel is pressurised to the desired value at a constant antisolvent flow rate. After that, pure solvent is injected into the chamber. The ratio of solvent and antisolvent flow is set to achieve a certain molar fraction within the precipitator. Thereafter the injection of pure solvent is stopped and the liquid

solution is injected. At the end of the solution injection and the following precipitation, the whole plant is washed with supercritical CO₂ to remove the residual solvent from the precipitator.

The windowed high pressure vessel also makes it possible to optically analyse the mixing, phase behaviour and particle formation in the SAS process. The optical measurement technique developed for this purpose and used at this plant is the topic of a further current conference proceeding by Dowy et. al [8].

RESULTS

This contribution deals with the variation of the vessel pressure, from values near the mixture critical point up to 30 MPa. The injection pressure at different nozzle diameters was set from slightly above the vessel pressure right up to 100 MPa. The molar fraction and the solute concentration were also varied.

Depending on the position in the vapour liquid equilibria of the antisolvent and the solvent, different mixing regimes can be characterised [9]. A pressure composition (Px)-diagramm for the processed material system DMSO and CO₂ is given in Figure 2.

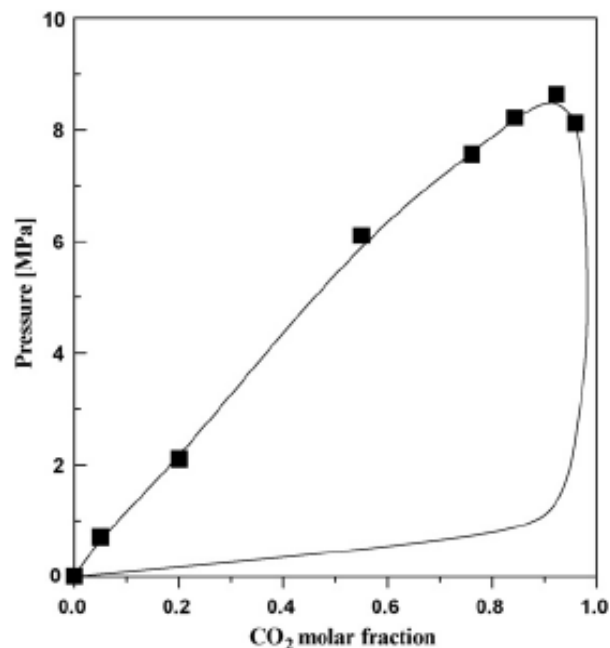


Figure 2: Px-diagramm of DMSO and CO₂ at 313 K [10]

In the following exemplary figures, only some SEM images of generated particles for certain process parameters are shown. Further results and images will be given on the poster. In figure 3, SEM images of generated Yttrium acetate (YAc) particles are displayed.

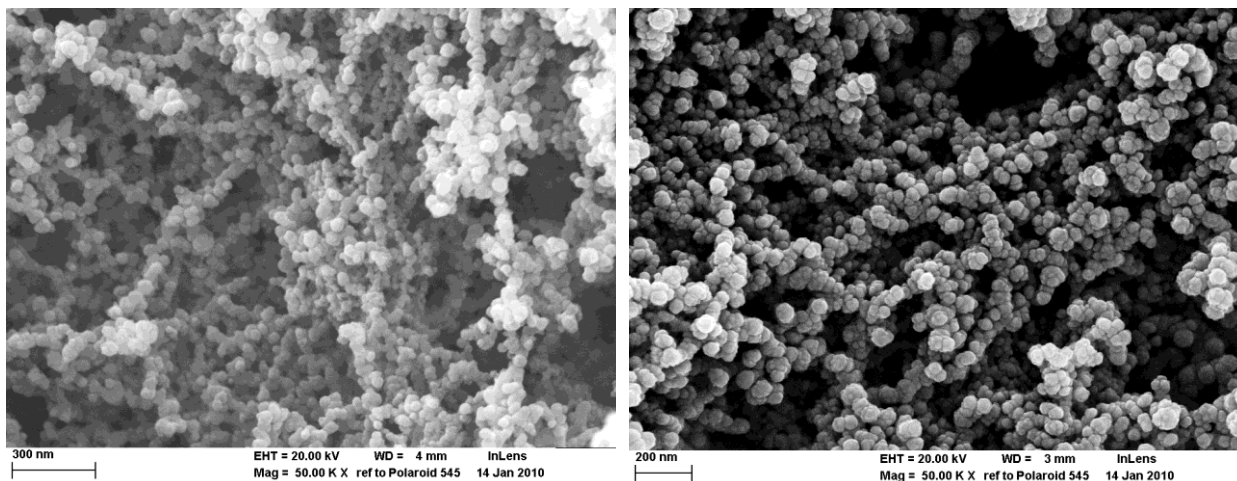


Figure 3: SEM images of YAc nanoparticles, generated at 12 MPa vessel pressure, 0.91 molar fraction of CO₂ and injection pressures of 28 MPa (left) respectively 41 MPa (right).

The process parameters for these images were a temperature of 40°C, a vessel pressure of 12 MPa, a CO₂ molar fraction of 0.91, and an injection pressure of 28 MPa (left) respectively 41 MPa (right). The nozzle diameter was 40 μm and the YAc concentration in the solution was 15 mg/ml. The corresponding volumetric flow rate of the solution through the nozzle was 11 ml/min (left) respectively 16 ml/min (right).

SEM images of generated YAc-particles, generated at different process conditions are displayed in figure 4. The vessel pressure was 9.5 MPa, the CO₂ molar fraction 0.91, and the injection pressure 25 MPa (left) respectively 42 MPa (right). The temperature was set to 40°C. The nozzle diameter was 40 μm and the YAc concentration in the solution was 15 mg/ml. In this case, the volumetric flow rate of the solution through the nozzle was 11 ml/min (left) respectively 17 ml/min (right).

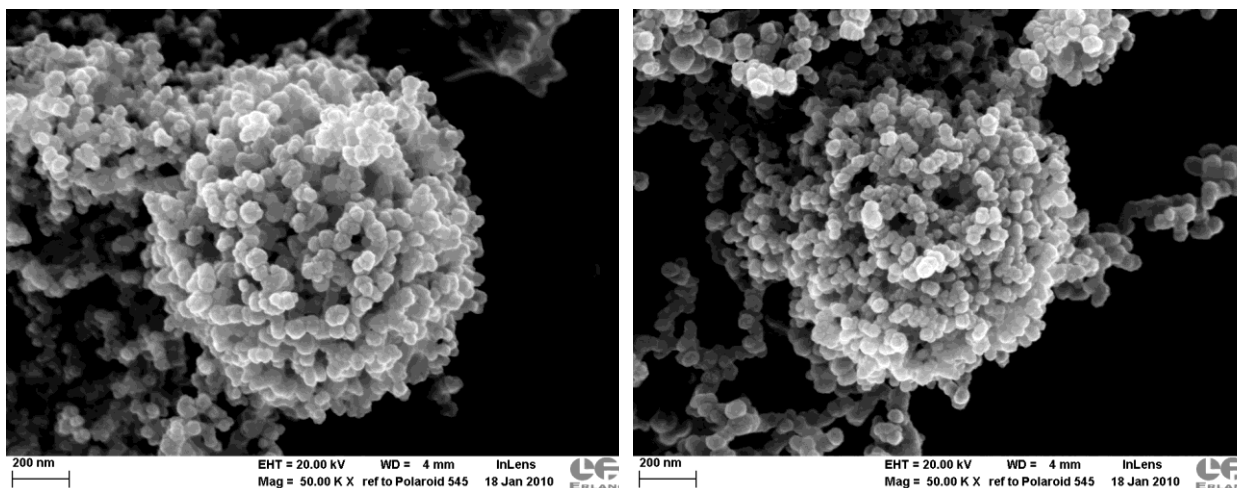


Figure 4: SEM images of YAc particles, generated at 9.5 MPa vessel pressure, 0.91 molar fraction of CO₂ and injection pressures of 25 MPa (left) respectively 42 MPa (right).

Considering the phase diagram for the binary mixture in figure 2, the particles in figure 3 and figure 4 were generated in different mixing regimes. In case of the vessel pressure at 12 MPa the mixing and precipitation took place above the mixture critical point (MCP), in the supercritical one phase mixing regime. For the particles in figure 4, the particle generation took place in the vicinity of the mixture critical point.

In both cases, for a constant vessel pressure no big difference in the generated particles, concerning the different injection pressures, can be identified. In figure 3, for both images, nanoparticles with about the same size were generated. In figure 4, irrespectively of the different injection pressures, micro-agglomerates consisting of nanoparticles were generated. Explanations on the particle characteristics illustrated in figure 4 are given in [11].

CONCLUSION

The influence of the injection pressure on the particle formation at different vessel pressures was investigated. For the parameters chosen in figure 3 and figure 4, was found that the injection pressure does not have a large influence on the particle size. For these experiments, the mixing took place in the supercritical one phase regime respectively in the vicinity of the MCP, corresponding to the binary mixture. This agrees with results published by other workgroups [7]. Further investigation will focus on different solute materials and varying solute concentrations.

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