ECO-EFFICIENT PARTICLE DESIGN WITH DELOS PROCESS, USING 1,1,1,2-TETRAFLUOROETHANE (R-134A) EXPANDED SOLVENTS

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R-134a-expanded liquids have been used, as solvent media, for the straightforward crystallization of micron sized crystalline powders using DELOS procedure. The results show that R-134-expanded liquids are suitable solvent media for material synthesis and processing at much lower working pressures (< 1 MPa) than those required with compressed CO_2 (> 15 MPa) and even CO_2-expanded solvents (≈10 MPa).

INTRODUCTION

Compressed CO_2 has been intensively investigated in the past decades as a compressed fluid (CF) in a wide range of materials synthesis and processing in the practice of the so–called 'green chemistry' [1]. The use of compressed CO_2 has been proved profitable, however, the relatively high-pressure equipment required and the low solubility of many substrates in this inorganic fluid, specially polar compounds, challenge its applications. On the other hand, the adequate miscibility of compressed CO_2 with common organic solvents promoted the development of CO_2 (liquid or supercritical) expanded solvent systems, which provided significant advantages in some processes [2]. For example, in previous works dealing with the preparation of finely divided materials by the DELOS process, it has been proved that this process is able to produced fine particles at lower pressures that the ones necessaries to perform other micronisation techniques such as the PCA and the RESS process [3,4].
In this work it is shown that the possibility to design processes using other sub-critical CF expanded solvent mixtures enabling to work at even lower pressure values, lead to test alternative fluids such as the hydrofluorocarbons (HFC). In particular, the environmentally benign, non-toxic, and non-flammable 1,1,1,2-tetrafluoroethane, known in industry as Freon R-134a, is selected as a promising CF solvent due to the low pressure at which it becomes liquid (<20bar, RT), along with its adequate physical properties [5]. As well, liquid R-134a is perfectly miscible with common organic solvents, and similarly to compressed CO_2, it has both low viscosity and low surface tension, which allows the rapid solute diffusion through the solvent. Herein, we compare the use of R-134a expanded liquid solvents with the use of CO_2 expanded solvents for powder processing by the DELOS process. The common pharmaceutical drugs acetylsalicylic acid (aspirin), 1,3,5,7,-tetraazatricyclo[3.3.1.-1^{3,7}]decane (hexamethylenetetramine-HMT) and colorant 1,4-bis-(n-butylamino)-9,10-anthraquinone (solvent blue 35) were chosen as model compounds to perform this study, using ethanol as the organic solvent.

MATERIALS AND METHODS

Aspirin (99.5%), hexamethylenetetramine (99%) and solvent blue 35 (98%) were purchased from SIGMA-ALDRICH (Steinheim, Germany). Concerning solvents, ethanol (99.5%) was bought from PANREAC (Barcelona, Spain) and CO_2 (purity 99.995%) was supplied by Carburos Metálicos S.A. (Barcelona, Spain). All chemicals were employed without further purification.

In Figure 1, DELOS procedure is schematized. The operational procedure used in these experiments is summarized as follows. A known volume of a solution of the compound to be crystallized in ethanol, with an initial supersaturation ratio, β_I, ($\beta_I = C/C^S$; where C is the initial material concentration in the non-pressurized solvent and C^S is the saturation limit of the material in that solvent) was loaded into a high-pressure vessel, at atmospheric pressure and at a given working temperature, T_W. The compressed fluid, either CO_2 or R-134a, was then pumped into this vessel producing a gas expanded solution with a given molar fraction of compressed fluid, X_W, at a given working pressure, P_W. The concentration of the substrate in the expanded mixture at this stage must remain below the saturation limit to avoid unwanted anti-solvent precipitation. The depressurization of this expanded solution, from P_W to atmospheric pressure through a non-return valve, causes evaporation of the compressed fluid from the solution, which induces a large, fast and extremely homogeneous decrease in the solution temperature, from T_W down to the final temperature, T_F, producing the precipitation of small size crystalline particles with a narrow particle size distribution, which are collected in a filter.

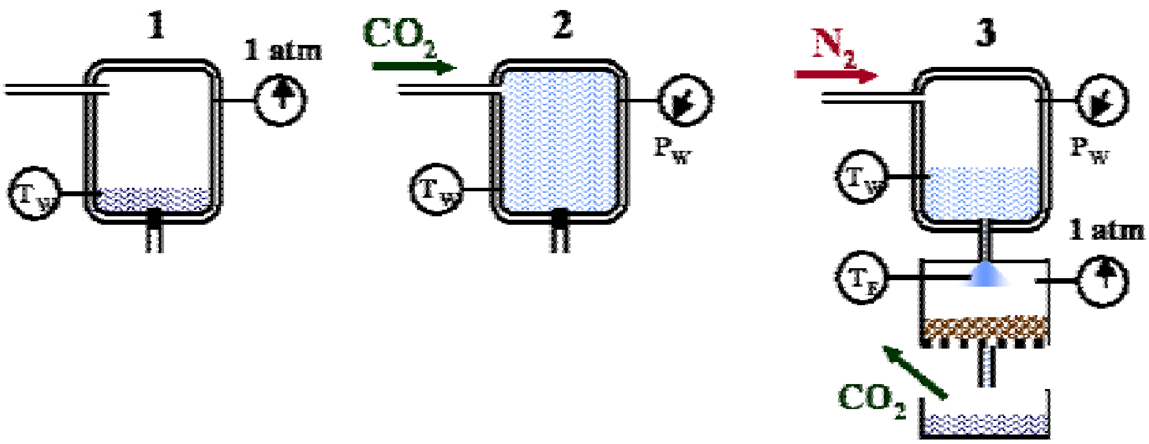

Figure 1: Scheme of DELOS procedure

Scanning electron microscopy (SEM) was used to characterize the particle morphologies of the processed powders. The particle size characteristics of the processed compounds, using both expanded solvents, were measured by light scattering (LS).

RESULTS AND DISCUSSION

Table 1 presents the operational parameters and the results obtained from the crystallization of the three model compounds using R-134a-expanded ethanol, by the DELOS method. In this Table, results with R134a are compared with those achieved when using CO_2-expanded ethanol as solvent. As previously reported in earlier works with CO_2 [3,7], the yield and the characteristics of crystalline particles resulting from the DELOS process with R-134a are mainly controlled by β_I and X_W, and they do not show any significant dependence on the working pressure P_W.

Table 1 : Operational parameters and results obtained with DELOS crystallization from R-134a-expanded ethanol and CO_2-expanded ethanol mixtures.

DELOS crystallizations from R-134a-expanded ethanol (from CO_2-expanded ethanol)									
							diameter of particles (µm)[b]		
compound	P_W **(MPa)**	T_W **(K)**	β_I	X_W	ΔT **(K)**[a]	**Yield**	$X_{10\%}$	$X_{50\%}$ [c]	$X_{90\%}$
aspirin	1 (7)	303 (295)	1 (0.8)	0.68 (0.8)	-57 (-91)	60 (65)	8.9 (3.6)	37.0 (12.5)	65.6 (23.2)
HMT	1 (10)	303 (313)	5 (4)	0.68 (0.8)	-55 (-98)	75 (80)	7.3 (5.1)	10.8 (15.5)	18.2 (33.6)
solvent blue 35	1 (10)	303 (303)	1 (0.8)	0.55 (0.7)	-55 (-72)	60 (50)	0.5 (1.8)	1.9 (3.5)	5.1 (6.5)

[a] Temperature decrease, $\Delta T=T_F-T_W$, where T_W is the solution temperature before the depressurization valve and T_F is the solution temperature after this valve. [b] Volumetric particle size distributions, measured with the light scattering technique (Beckman Coulter, model LS13320, USA) , are given as 10, 50 and 90% quantiles. [c] These values correspond to the medians of the particle distributions. The average diameters of particles were confirmed by SEM images.

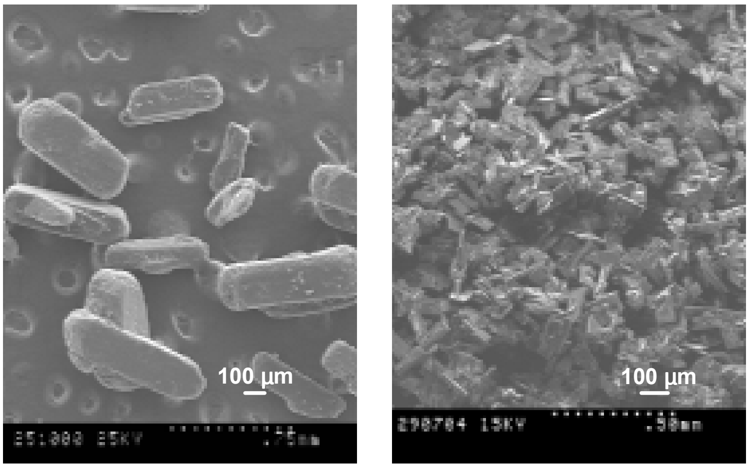

Figure 2. SEM micrograph image of the unprocessed aspirin powder precursor (image on the left). SEM micrograph image of DELOS crystallized aspirin from R-134a-expanded ethanol at P_W= 1MPa (image on the right).

The SEM micrograph image of the processed particles of aspirin from R-134a-expanded ethanol solution at P_W= 1 MPa (Figure 2, right) shows very homogeneous micron sized tablets, in comparison to the unprocessed substance (Figure 2, left). Similar results were obtained in the processing of hexamethylenetetramine and solvent blue 35.

As observed in Table 1, the nature of the compressed fluid does not significantly influence the yield of the DELOS process. Concerning particle characteristics, particle sizes for hexamethylenetetramine and solvent blue 35 are slightly smaller when using R-134-expanded ethanol rather than CO2-expanded ethanol. Contrarily, aspirin median particle size achieved is three times smaller when using CO_2-expanded ethanol.

CONCLUSIONS

The results obtained from this work, encourage the use of R-134a-expanded solvents as solvent media in synthesis and material processing, as they provide significant advantages over conventional media, and the working pressures are one order of magnitude less than those required with CO_2-expanded solvents. Research is currently in progress investigating the processing and testing of other compounds using other common organic solvents expanded with R-134a.

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