MELTING TEMPERATURE DEPRESSION OF SOLID LIPID UNDER HIGH PRESSURE GASES

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Abstract

The effects of high pressure gases on solid lipids were investigated by high-pressure differential scanning calorimeter (DSC). In particular, the influence of a high-pressure gas on solid-liquid and solid-solid transitions were investigated for pure tristearin and a mixture of lipids (tristearin-phosphatidylcoline-dioctilsolfosuccinate). Both of these substances are commonly used for the production of solid-lipid-nano-particles by high-pressure processes. The investigations were carried out in the presence of CO_2, $CHClF_2$ and CH_2FCF_3 at different operating pressures up to 7.0 MPa. The melting and solidification temperatures were measured for six different systems.

As regards the experiments under CO_2, the results indicate a melting point depression as function of the gas pressure, with a maximum 25 K at 6 MPa. The same performances of CO_2 were reached using $CHClF_2$ at maximum pressure of 0.45 MPa. CH_2FCF_3 exhibits lower melting temperature depression.

These results highlight the possibility of processing liquid lipids and thermosensitive compounds at mild temperature condition below 313 K and at moderate gas pressure.

Introduction

In the recent years, the interest in the production of micrometric or nanometric particles of low volatile substances through the use of compressed gases or supercritical fluids [1-3] has been growing. The most successful and important techniques are the gas antisolvent precipitation (GAS), particles from gas saturated solution (PGSS), rapid expansion of supercritical solution (RESS), (DELOS), supercritical assisted atomisation (SAA), supercritical carbon dioxide assisted nebulization bubble drying (CAN-BD).

In all these cases, the knowledge of both equilibrium and volumetric properties of the pure substances and their mixture at the process conditions are of fundamental importance for verifying the economical and practical feasibility of these processes.

An effective application of a high pressure process has need of a rational understanding of the phase behaviour of mixtures of low volatile compounds and high-pressure gasses. Among various thermodynamic data, the solid-liquid-fluid coexistence curve (SLF) may provide a general perception of the phase behaviour of these systems: the melting point as a function of the pressure, the solute solubility in the supercritical fluids and solubility of supercritical fluid or the compressed gas in the saturated liquid phase.

For the PGSS, the SLF coexistence curve restricts the choices of the operative conditions [4].

The aim of the present work is providing useful informations to apply the PGSS process for the production of solid-lipid-nanoparticles: in this regard, the behaviour of the SLF curves for gas-lipid system by a high-pressure differential scanning calorimeter (DSC) is investigated. Experimental results are presented for lipid and mixture of lipids generally involved in the production of solid-lipid-nanoparticles by PGSS process.

Experimental

The sample material was both pure tristearin (Fluks Chemie AG) and a mixture obtained from two lipids, tristearin and phosphatidylcoline (PC, Degussa Texturant System, Italy), and a surfactant, dioctilsolfosuccinate (DSS) (Sigma Aldrich Srl, Italy). 99.95% CO_2, 99% $CHClF_2$ and 99% CH_2CF_4 was purchased from Air Liquide (Padova, Italy). The pure components were used as received without further purification.

The mixture of lipids was obtained by adding a 10 mg of lipids in 10 mL of dichloromethane (DCM) (Carlo Erba Reagenti, Italiy) in an stirred vessel. The solution was dried for 12 hours in a vacuum system. A lipid mixture, without a residual solvent contents, was obtained. The presence of solvent was detected by DSC analysis.

The DSC measurements were performed by a high-pressure differential scanning calorimeter (HPDSC, mod. Q10, TA Instruments) and an acquisition software (Thermal Analysis System) was used to record the data. The dynamic scans were recorded at a heating rate of 5°C/min for the measurements at atmospheric pressure and of 2°C/min for the measurements under gas pressure. The samples were analysed in the temperature range of 30-70 °C and the experimental runs were repeated for three times.

Result and discussion

The present work focuses on the determination of the different phase-behaviour of three gases CO_2, $CHClF_2$ and CH_2FCF_3 in lipid and lipid-mixture systems. They are atoxic, inexpensive, available in large amounts, environmentally safe, and they posses peculiar properties. Table 1 shows the chemicophysical properties of CO_2, $CHClF_2$ (R22) and CH_2FCF_3 (R134A).

These three substance were chosen in order to rationally understand the influence of molecular weight, polarizability and dipole moment on the solubility in lipid systems (Tab 1).

Table 1. Properties of gas used as solvent this study: critical temperature T_c, critical pressure P_c, Polarizability ψ, Dipole moment δ and Molecular Weight of the three gases used in the study.

Gas	T_c (°C)	P_c (bar)	y (Å^3)	d (Debye)	*M.W.* gr/mol
CO_2	31.0	73.8	2.65	0	44
$CHClF_2$	96.2	49.7	4.44	1.42±0.03	86
CH_2FCF_3	101.1	40.7	4.38	1.80±0.22	102

Notice that the CO_2 has zero dipole moment and low polarizability because it posses a quadrupole moment. The dipole moments of $CHClF_2$ and CH_2FCF_3 are identical, however, these two substances differ in the polarizability and in number of carbon atoms, i.e., in the molecular volume. In order to determine the different impact of dipole moment and polarizability on the phase behaviour, it was interesting to compare the SLF coexistence curves of lipids in presence of CO_2 with those of the fluorinated compounds. Since the polarizability and, in particular, the dipole moment of $CHClF_2$ and CH_2FCF_3 are very close, a difference in melting point depression of lipids in presence of these two solvents implies a different impact of molecular volume on phase behaviour.

Figure 1 shows a typical isobaric differential scanning calorimeter analysis of pure tristearin under high pressure CO_2 at tthree different pressures. Similar diagrams were found for the other gases.

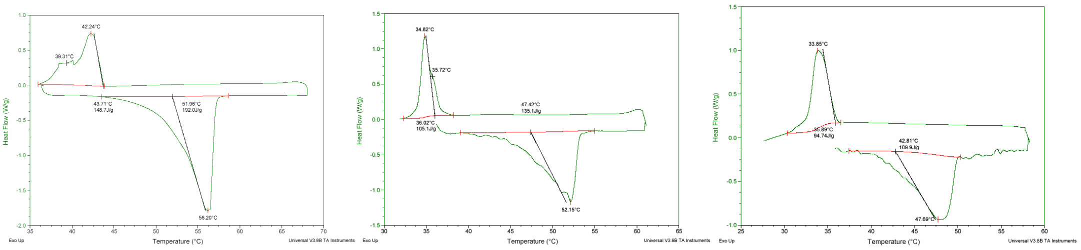

Figure 1. Typical isobaric differential scanning calorimeter analysis of pure tristearin under high pressure CO_2: Figure 2a at 1.0 MPa; Figure 2b at 4.0 MPa, Figure 1c at 5.8 MPa.

The melting and the solidification temperatures correspond in the DSC analysis to the negative and positive peak, respectively; the values for the tristearin at 1.0 MPa, shown in figure 2a, is evaluated at 56.2 and 42.24°C, at 4 MPa, shown in figure 2b, is evaluated at 52.15 and 34.82°C while at 5.8 MPa, shown in Fig. 1c, at 33.85°C and 47.69°C.

From the analysis of DSC spectra two important features can be easily observed, function of pressure of the system and types of gas: the depression of the lipid melting temperature, the hysteresis between melting and solidification temperature.

Tables 2, 3 and 4 show all the experimental data for the pure tristearin (indicated as system A) and the mixture of lipids (indicated as system B) in the presence of CO_2, $CHClF_2$ and CH_2FCF_3, respectively. Note that the maximum operating pressure for the different gases corresponds to their vapor pressure at ambient temperature of 25°C.

Table 2. Temperature of liquid-solid transition as a function of CO_2 pressure for the system A (pure tristearin) and B (tristearin/PC/DSS weight ratio of 40/40/20).

System	P (bar)	T_{melt} (°C)	T_{solid} (°C)	T_{solid} (°C)
A	10	56.20	39.31	42.24
A	20	54.57	37.58	40.20
A	30	53.87	35.30	36.88
A	40	52.15	34.82	35.72
A	50	50.43	34.65	-
A	58	49.49	33.48	-
B	10	59.68	41.25	42.51
B	20	58.19	39.55	40.30
B	30	54.92	36.39	-
B	40	54.82	36.65	-
B	50	53.29	35.54	-
B	58	51.60	34.10	-

First of all it must be observed that the melting point for both pure lipid and lipid mixture decreased by the presence of any gas under pressure as a function of the operating pressures: in the case of CO_2 the minimum in the melting point (49.9°C and 51.6°C for system A and B respectively) corresponds to 58 bar; in the case of $CHClF_2$, the melting point results 50.5°C and 55.4 °C (system A and B, respectively) at a pressure of 0.75 MPa while for the CH_2FCF_3 55.78 °C and 58.56 °C (system A and B, respectively) at 0.45 MPa.

Table 3. Temperature of liquid-solid transition as a function of $CHClF_2$ pressure for the system A (pure tristearin) and B (tristearin/PC/DSS weight ratio of 40/40/20).

System	P (bar)	T_{melt} (°C)	T_{solid} (°C)	T_{solid} (°C)
A	1.5	56.11	37.73	41.09
A	3.0	53.56	36.36	37.92
A	4.5	53.42	35.98	37.49
A	6.0	52.48	34.90	-
A	7.5	50.50	33.97	-
A	9.2	47.77	31.22	-
B	1.5	59.63	41.04	
B	3.0	59.37	38.87	
B	4.5	55.40	37.02	
B	6.0	55.35	36.98	
B	7.5	55.40	35.38	

Table 4. Temperature of liquid-solid transition as a function of CH_2FCF_3 pressure for the system A (pure tristearin) and B (tristearin/PC/DSS weight ratio of 40/40/20).

System	P (bar)	T_{melt} (°C)	T_{solid} (°C)	T_{solid} (°C)
A	1.5	56.78	39.19	43.24
A	3	56.67	38.67	42.85
A	4.5	55.78	38.04	41.55
B	1.5	59.50	41.60	
B	3	61.15	40.76	
B	4.5	58.56	39.77	

It is evident that a largest melting temperature depression was obtained for pure tristearin in presence of both CO_2 and $CHClF_2$, however, the $CHClF_2$ leads to tristearin melting point of about 48°C at a mild pressure condition of 9.0 MPa.

The differences in the phase behaviour of the system in the presence of different gases are related to the chemicophysical properties of the solvents and therefore to the intermolecular interactions between the solvent and the lipid-system considered.

High-pressures are needed to solubilize CO_2 in the tristearin; at these conditions, the CO_2 dissolve the apolar aliphatic chain of the lipid and the quadrupole moment of CO_2

is expected to interact favorably with the polar moment of the ester linkage in the tristearin.

The $CHClF_2$ shows higher solubility in tristearin than CO_2, probably, because it has a dipole moment and large polarizability than CO_2. In addition, $CHClF_2$ has an acidic proton that is capable of hydrogen bonding with the ester group, whereas, CO_2 is not expected to form any type of complex with tristearin.

On the other hand, even if the CH_2FCF_3 has slightly higher polarizability of $CHClF_2$, it has the hydrogen that are probably less acid than $CHClF_2$ and a larger molecular volume. This latter aspect probably influences the low solubility of CH_2FCF_3 in the pure tristearin that results in a melting point depression of only 5 K.

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