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Solid-liquid equilibrium measurements for the ternary system PCL + chloroform + nonsolvents (n-hexane, ethanol, methanol, isopropanol) at 303.15 K

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ABSTRACT. This work reports experimental data of polycaprolactone (PCL) polymer solubility in chloroform as solvent and n-hexane, methanol, ethanol and isopropanol as nonsolvents, at atmospheric pressure (about 1,0 bar) and temperature of 303.15 K. It was used PCL with 70000-90000 and 2000 molar mass (MM). The experiments of solubility were performed using a jacketed-cell with temperature controlled by an ultrathermostatic bath, in which a turbidity method was adopted and used. From the obtained results it should be observed that the n-hexane presented a more pronounced anti-solvent effect in the PCL solubility, where the heterogeneous region (solid phase presence) was broader than when other nonsolvent. It was also observed that the binodal curves measured with the high molar mass polymer showed similar results compared to the low molar mass one.

Keywords: solid-liquid equilibrium, polycaprolactone, microencapsulation.

Medidas de Equilíbrio Sólido-Líquido para os sistemas ternários PCL + clorofórmio + não solvente (n-hexano, etanol, metanol e isopropanol) a 303,15 K

RESUMO. O presente trabalho apresenta dados experimentais de solubilidade do polímero policaprolactona (PCL) em clorofórmio como solvente e n-hexano, metanol, etanol e isopropanol como não-solventes a pressão ambiente e temperatura de 303,15 K. Foi utilizado PCL com massa molecular (MM) de 70000-90000 e 2000. O método de turbidez para a determinação da solubilidade foi realizado em células encamisadas de equilíbrio. Os resultados obtidos indicaram que o n-hexano possui um efeito antisolvente mais pronunciado na solubilidade do PCL, pois a região heterogênea (presença da fase sólida) foi mais ampla do que os demais não-solventes avaliados. Verificou-se também, que as curvas binodais obtidas com o polímero de alta massa molecular apresentaram resultados similares com o de baixa massa molecular.

Palavras-chave: equilíbrio sólido-líquido, Policaprolactona, Microencapstulação.

Introduction

Microencapsulation techniques have been applied in the food, chemical, pharmaceutical, medical, printing and cosmetics industry (SILVA et al., 2003) for the production of micro and nanoparticles. In the chemical and food industry substances as acidifiers, flavorings, paints, enzymes, microorganisms, minerals, lipids, vitamins and amino acids the microencapsulation has been useful and important technique to protect them from temperature, oxidation, moisture and undesirable reactions (ALVIM; GROSSO, 2010; BAKAN, 1973; KAREL, 1990).

Microencapsulation is defined as the packaging technology of particles in capsules. This is a physical process that can be used to produce a coated or encapsulated active compound in a polymeric matrix. This material normally is found forming beads called microparticles or microcapsules. This fined material can then release their content under controlled rates in a specific application medium (AZEREDO, 2005; GHARSALLAOUI et al., 2007; KAREL; LANGER, 1988; MATIOLI; RODRIGUEZ-AMAYA, 2003).

The material used in the coating of the active substance, forms a three-dimensional network, wherein the compound can be adsorbed, embedded or attached covalently to the inside or particle surface (CECHINEL FILHO; BRESOLIN, 2003; SENHORINI et al., 2012).

In a general way, one of the most used microencapsulation technique in the chemical, pharmaceutical and food industry is the emulsification followed the appropriated separation processing, in which normally solvent evaporation or extraction are employed. In this process the active compound and polymer are dissolved or dispersed in an organic phase solvent. The organic solution is then mixed with a nonsolvent phase and this solution is emulsified. Following, the emulsion is treated under continuous stirring for extracting or evaporating solvent system. The formation of solid phase occurs during this evaporation/extraction process. The solid material containing the active compound micro or nanoencapsulated in the polymer phase are subjected to further purification (BORDES et al., 2010, ZANETTI, et al., 2002).

The polymers are the most employed materials in the microencapsulation process (JAIN et al., 1998). These polymers can be natural, synthetic or semisynthetic and several of them are biodegradable, however few of them are biocompatible (JAIN et al., 1998; SALTZMAN, 2001).

The polymers obtained from poly (α-hydroxy acids) are promising in food and pharmaceutical area due to their high biocompatibility (REZWAN et al., 2006). Considering polymers biodegradable and biocompatible from poly (α-hydroxy acids) the poly (ε-caprolactone) (PCL) can be highlighted. It is semi-crystalline aliphatic polyester with hydrophobic character. The PCL presents good mechanical properties, ability to form blends with other polymers, in addition to being biodegradable and bioresorbable (CÉSAR et al., 2009). However, an important issue in the polymer processing with solvents and nonsolvents is the phase behavior and the solubility of them in the ternary system. To the best of our knowledge there are few experimental data presented in the literature nowadays. In the work from Bordes et al. (2010), experiments of solubility were carried out with several solvents where chloroform, methylene chloride, 1,2-dichloroethane, methylene chloride and chloroethano were identified as good solvent for PCL14000 (0.5 g in 5 mL), in addition formamide, ethanol, hexane, heptane and water were characterized as nonsolvent. Considering mixed solvents the PCL solubility is not presented in the literature.

From this context, the aim of this work to provide fundamental information concerning on the phase behavior of solid-liquid equilibrium (SLE) for the system PCL + solvent + nonsolvents such as n-hexane and alcohols methyl, ethyl and isopropyl.

Material and methods

Polycaprolactone MM 70000-90000 (PCL 1) was purchased from Sigma-Aldrich and Polycaprolactone MM 2000 (PCL 2) from Acros Organics. Chloroform, n-hexane and ethanol were purchased from Carlo Erba. Methanol and isopropanol were purchased from Biotec. All chemicals were used without further purification. In Table 1 some properties of the material are presented.

Apparatus and experimental procedure

The SLE measurements for the ternary system PCL + chloroform + nonsolvent (n-hexane, methanol, ethanol and isopropyl alcohol) were carry out using a jacketed-cell, with temperature controlled by an ultrathermostatic bath (521D Nova Ética). The jacketed-cell was made of Pyrex glass with 60 mL volume. The measurements were performed at a fixed temperature of 303.15 K due to the high volatility solvents used. For the SLE measurements the turbidity point method was used. This method consists, at a constant temperature, in a titration of the homogeneous mixture, formed by a miscible two components (PCL + solvent) by a third known component (nonsolvent) until the turbidity of the solution is observed, due to the solid (polymer) phase formation. The cell was provided with a mechanical stirrer (RW 20 Digital IKA), that was kept at 400 rpm in all experiments. The nonsolvent was titrated using a glass syringe. The syringe was weighed before and after the titration to evaluate amount of nonsolvent used.

Table 1. Properties of pure compounds.

Compound	CAS	Impurities	Melting Point (°C)	Density (g mL^{-1})	Polydispersity Index
PCL 1	24980-41-4	< 1 %	60	1.145	< 2
PCL 2	36890-68-3	NA	NA	NA	NA
n-Hexane	110-54-3	< 1 %	NA	0.66 (20°C)	NA
Ethanol	64-17-5	< 1 %	NA	0.79 (20°C)	NA
Methanol	67-56-1	< 1 %	NA	0.79 (25°C)	NA
Isopropanol	67-63-0	< 1 %	NA	0.79 (20°C)	NA
Chloroform	67-66-3	< 1 %	NA	1.48 (20°C)	NA

NA – Not available or not applicable.

Results and discusion

The PCL 1 (PCL MM 70000-90000) solubility with chloroform was performed, at ambient conditions, and was 1.2949 g polymer g^{-1} chloroform (56.17 wt%). This solution was used in the SLE curves determination with nonsolvents.

In Table 2 the experimental data of SLE for the ternary systems PCL 1, chloroform a nonsolvents (n-hexane, methanol, ethanol, isopropanol) are presented.

Table 2. Solid-liquid equilibrium (experimental data) for PCL 1(1) + chloroform(2) + nonsolvents(3) system at 303.15 K.

X_1	X_2	X_3	Equilibrium type
PCL 1(1) + chloroform(2) + n-hexane(3)			
0.0074	0.5246	0.4680	SLE
0.0132	0.5335	0.4532	SLE
0.0274	0.5324	0.4402	SLE
0.0347	0.5268	0.4385	SLE
0.0742	0.5235	0.4023	SLE
0.1373	0.5261	0.3366	SLE
0.2070	0.5078	0.2852	SLE
0.2652	0.5194	0.2155	SLLE
PCL 1(1) + chloroform(2) + methanol(3)			
0.0119	0.4504	0.5377	SLE
0.0269	0.4525	0.5205	SLE
0.0503	0.4549	0.4948	SLE
0.0579	0.4523	0.4899	SLE
0.1092	0.4488	0.4420	SLE
0.1749	0.4322	0.3929	SLE
0.2228	0.4280	0.3492	SLLE
PCL 1(1) + chloroform(2) + ethanol(3)			
0.0093	0.3729	0.6178	SLE
0.0190	0.3846	0.5964	SLE
0.0418	0.3837	0.5745	SLE
0.0520	0.3826	0.5654	SLE
0.0948	0.3833	0.5219	SLE
0.1448	0.3875	0.4677	SLE
0.1968	0.3820	0.4212	SLLE
PCL 1(1) + chloroform(2) + isopropanol (3)			
0.0067	0.2364	0.7569	SLE
0.0133	0.2439	0.7428	SLE
0.0257	0.2480	0.7263	SLE
0.0338	0.2506	0.7156	SLE
0.0682	0.2612	0.6706	SLE
0.1017	0.2622	0.6361	SLE
0.1531	0.2827	0.5642	SLE
0.1808	0.2726	0.5466	SLE
0.2181	0.2515	0.5304	SLLE

Xi – mass fraction of component i; SLLE – solid-liquid-liquid equilibria

In Figure 1 the SLE curves measured for the ternary system PCL 1(1) + chloroform(2) + nonsolvents(3) at 303.15 K are presented. It can be observed that the homogeneous phase, one liquid phase with all charge of polymer dissolved in the solvent-nonsolvent mixture, occur at right of the experimental points presented. On the other hand, the homogeneous region on the triangular diagram was lower when n-hexane was used as nonsolvent and this complete solubility region was larger as the alcohol polarity was increased.

Regarding yet on the Figure 1, where the SLE of PCL 1 with solvent (chloroform) and different nonsolvents is presented, it can be seen from this figure that the n-hexane presents the most pronounce anti-solvent action in the system, viewed as larger heterogeneous region in the ternary diagram. Minor homogeneous region indicate that the lower miscibility of the components after the separation-microencapsulation is favored. Then, results observed in Figure 1 are indicating that the n-hexane as an anti-solvent in a separation-microencapsulation process is better in contrast with alcohols. Soon after, the comparison between alcohols, the results obtained wherein are indicating that the methanol has a larger heterogeneous region when compared with ethanol and isopropanol.

It is important to mention that the in all SLE experiments a second liquid phase was observed depending on the composition of the mixture. It can be seen that the SLE line is interrupted with a liquid-liquid equilibrium occurrence, as indicated as closed symbol. The solid phase presence with a two liquid phase is indicated in Table 2.

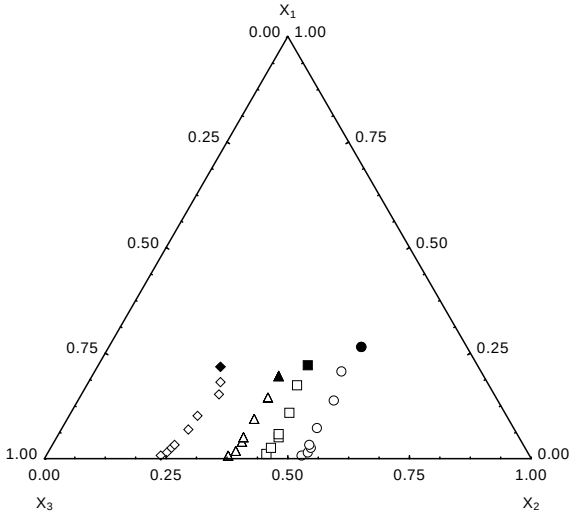

Figure 1. Experimental SLE curves for the ternary system polymer PCL 1(1) + chloroform(2) + nonsolvents(3) (○) n-hexane, (□) methanol, (△) ethanol and (◇) isopropanol at 303.15 K (mass fraction). Closed points represent SLLE.

In order to provide a better understanding the solid phase formation (polymer) process, with a solvency point of view, Figure 2 presents the solid-liquid phase behavior of the polymer in the solvents/nonsolvent mixture. Where X_{PCL}, $X_{solvent}$ and $X_{nonsolvent}$ are the mass fraction of PCL, solvent and nonsolvent in the ternary mixture, respectively.

It can see from Figure 2 that two liquid phases coexisting with the solid phase was from PCL 1 to solvent mass ration of 0.5 for all alcohols, however the amount of nonsolvent used to induce the polymer precipitation, from binary solution PCL solvents^{-1}, was greater according to the polarity

nonsolvent was increased. In other words, from Figure 2 it can seem that, at fixed polymer (PCL 1) to solvent (chloroform) mass ratio to get the polymer precipitation in the system the nonsolvent to solvent mass ratio a little amount of n-hexane is needed when compared with the isopropanol necessary in the same process.

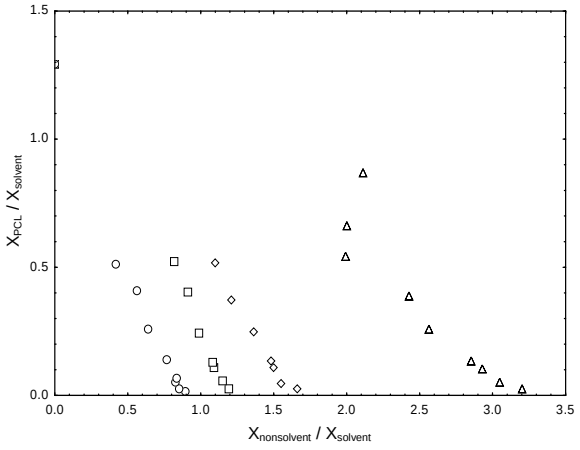

Figure 2. PCL 1 solubility in terms of PCL to solvent (chloroform) mass ratio versus nonsolvent (○, n-hexane; □, methanol; ◇, ethanol and, Δ, isopropanol) to solvent mass ratio, at 303.15 K.

In order to evaluate the influence of polymer molar mass, SLE data were obtained using the nonsolvent hexane, which presented more pronounced anti-solvent effect in the system. The solvent chloroform was maintained. And in this study a PCL with MM 2000 (PCL 2) was used (Table 3). Figure 3 shows the curves of ternary systems polymer PCL 2(1) + chloroform (2) + n-hexane(3). The results presented in this figure show that heterogeneous region is widely when compared with PCL 1 (Figure 4). This information indicates that the polymer with a lower molar mass is more soluble in the chloroform/n-hexane mixture. It can be explained due the PCL 2000 presented solubility more accentuated in the chloroform that PCL 70000-90000.

Table 3. Solid-liquid equilibrium (experimental data) for PCL 2(1) + chloroform(2) + n-hexane(3) system.

X_1	X_2	X_3	Equilibrium type
0.3904	7.435	7.4049	SLE
0.8341	7.4174	6.8282	SLE
1.1746	8.6445	6.6393	SLE
1.6039	7.8586	5.5404	SLE
2.0004	7.4916	5.1730	SLE
3.0524	7.8085	4.2667	SLE
6.1175	7.6996	3.7286	SLE
9.1768	8.695	4.4403	SLE
11.9389	7.1228	3.9847	SLLE

Xi – mass fraction of component i; SLLE – solid-liquid-liquid equilibria.

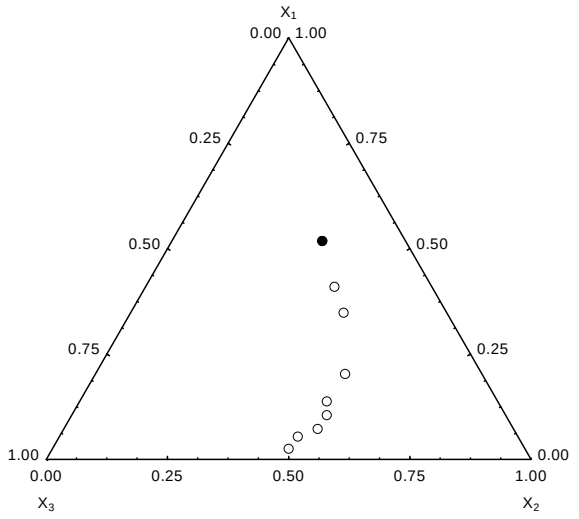

Figure 3. Experimental SLE curve for the system PCL 2(1) + chloroform(2) + n-hexane(3) at 303.15 K.

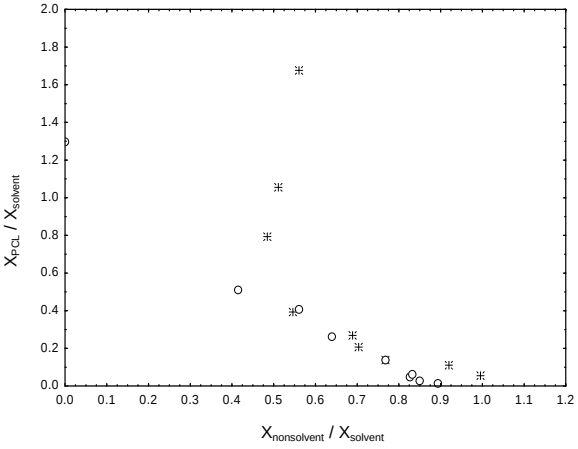

Figure 4. Graphical comparison between the solubility of PCL 1(○) and PCL 2(⋇) in terms of PCL to solvent (chloroform) mass ratio versus nonsolvent (n-hexane) to solvent mass ratio, at 303.15 K.

Conclusion

In this study we used the turbidity method to determine the solubility curves in mixed solvent (chlroform) and nonsolvents (n-hexane, methanol, ethanol and isopropanol), at a constant temperature (303.15 K). The anti-solvent effect of nonsolvents was evaluated. As expected, the n-hexane presented more pronounce nonsolvent effect in the PCL + chloroform system. Considering a solid (polymer) phase formation, e.g., micro or nanoparticles production from an anti-solvent process, the n-hexane would be more adequate as anti-solvent in the process, however a short chain alcohol would be possible, in which the alcohol amount in process depends on the alcohol chain length. The results of this study can be used in microencapsulation, when it is necessary an anti-solvent to the process to PCL micro or nanoparticles production.

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