**Phase inversion temperature of polymeric surfactant-based emulsions for the formation of nanoemulsions**

Martin Meulders, André Barrizzelli Murino, Véronique Sadtler, Cécile Nouvel\*

*LRGP Laboratoire Réactions et Génie des Procédés, UMR CNRS-Université de Lorraine 7274, Nancy F-54000, France*

*\* cecile.nouvel@univ-lorraine.fr*

***Highlights***

* Nanoemulsions were obtained with polymeric surfactants through PIT process
* Cycling the process decreases the droplets sizes and narrows the size distribution
* PIT process heavily depends on the copolymer architecture to achieve nanoemulsions

**1. Introduction**

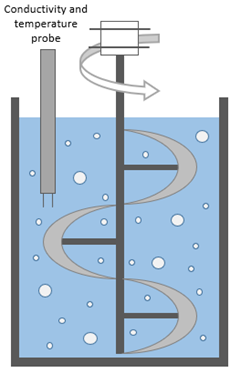
Nanoemulsions are remarkable for their high specific area and kinetic stability among others. They have many pharmaceutical or cosmetic applications for their high performances in drug delivery [1] and are often required as an intermediate for the formulation of nanocapsules [2]. Nevertheless, their making requires high mechanical energy input through traditional emulsification methods also called “high energy methods” [3]. Therefore, low-energy methods such as Phase Inversion Temperature (PIT) can be cost-effective alternatives for the production of nanoemulsions [4]. The principle of the PIT relies on the ability of a temperature-sensitive surfactant to shift its overall affinity from the aqueous phase of the emulsion [5] to the hydrophobic one with increasing temperature. Examples of PIT are reported with small commercially available surfactants but almost never for polymeric surfactants [6]. In this work, we have studied the PIT process on a dodecane/water system using various polystyrene-b-poly(oligo(ethylene glycol) methyl ether methacrylate) (PS-b-POEGMA) as surfactants. The influence of different process parameters was investigated to evaluate the potential of such surfactants to produce nanoemulsions.

**2. Methods**

A two-step synthetic pathway using the Atom Transfer Radical Polymerisation was adapted from the literature [6, 7] to synthesize PS-b-POEGMA copolymers with various molecular weights and POEGMA/PS weight ratios. The copolymers were solubilized at 8 wt% in aqueous solution, which was mixed with dodecane (80 v/v% water and 20 v/v% dodecane)and then used in the PIT process, monitored both by viscosimetry and conductimetry. Emulsification was carried out under a constant temperature rise at 0.5°C/min and under gentle stirring in a rheometer with a helical ribbon, equipped with conductivity and temperature probes (figure 1 a) as set up before in our laboratory [8]. Once the emulsion was inversed, highlighted by a dramatic conductimetry drop and viscosity increase, the system was rapidly cooled with an ice bath and the droplet size distribution was measured by laser granulometry. The procedure was cycled several times.

**3. Results and discussion**

The synthesis of the PS-b-POEGMA surfactants allowed us to design the molecular weight of each block, resulting in copolymers with various POEGMA/PS weight ratios (from 10 to 17) and total molecular weights ranging from 17 500 to 34 000 g/mol with a reasonable dispersity. The influence of the surfactant concentration, the number of cycles and the surfactant design on the PIT process was studied and compared to small surfactants (Brij30 and various Igepals). The conductivity dropped to zero because of the transition from a conductive oil-in-water emulsion to a water-in-oil emulsion (figure 1 b). Simultaneously, the viscosity increased rapidly due to the switchover from an aqueous continuous phase which was 80% of the emulsion volume to a more viscous oily continuous phase that only represented 20% of the system’s volume. The local maximums for conductivity and viscosity can be attributed to a transitional bicontinuous phase. Submicron emulsion could be produced with the polymeric surfactant through the PIT process. Cycling the procedure significantly facilitated the phase inversion resulting in lower droplet sizes (down to 150 nm). The shortest copolymers were the most efficient to achieve nanoemulsions (smaller droplet sizes and fewer PIT cycles) which was attributed to their faster diffusion at the water-oil interface.

a) b)

**Figure 1.**Conductivity and viscosity monitoring of the PIT a) Experimental setup b) Example of results with dodecane/water system using one PS-b-POEGMA surfactant (Mw = 17 500 g/mol, D=1.4).

**4. Conclusions**

This work has paved the way to the use of polymeric surfactants to produce nanoemulsions through the PIT process. The design of the copolymer (molecular weight, hydrophilic/hydrophobic ratio) has shown to be a crucial parameter to control the performances of the PIT process.

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