



## **Nano-emulsions and nanocapsules by the PIT method: an investigation on the role of the temperature cycling on the emulsion phase inversion**

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Résumé en  
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This paper focuses on the phenomenological understanding of temperature cycling process, applied to the phase inversion temperature (PIT) method. The role of this particular thermal treatment on emulsions phase inversion, as well as its ability to generate nano-emulsions have been investigated. In order to propose a general study, we have based our investigations on a given formulation of nano-emulsions classically proposed in the literature [Heurtault, B., Saulnier, P., Pech, B., Proust, J. E., Benoit, J.P., 2002. A novel phase inversion-based process for the preparation of lipid nanocarriers. *Pharm. Res.* 19, 875; Lamprecht, A., Bouligand, Y, Benoit, J.P., 2002. New lipid nanocapsules exhibit sustained release properties for amiodarone. *J. Control. Release* 84, 59-68], using a polyethoxylated model nonionic surfactant, a polyoxyethylene-660-12-hydroxy stearate, stabilizing the emulsion composed of caprylic triglycerides (triglycerides medium chains), salt water (and also phospholipidic amphiphiles neutral for the formulation). Characterization of nano-emulsions was performed by dynamic light scattering (DLS) which provides the hydrodynamic diameter, but also the polydispersity index (PDI), as a fundamental criteria to judge the quality of the dispersion. Another aspect of the characterization was done following the emulsion inversion and structure by electrical conductivity through the temperature scan. Overall, the role such a temperature cycling process on the formulation of nano-emulsions appears to be relatively important, and globally enhanced as the surfactant concentration is lowered. Actually, both the hydrodynamic diameter and the PDI decrease as a function of the number and temperature cycles up to stabilize a steady state. Eventually, such a cycling process allows the generation of nano-emulsions in ranges of compositions largely expanded when compared with the classical PIT method. These general and interesting trends emerge from the results, are discussed and essentially explained by regarding the behavior of the nonionic surfactants towards the water/oil interface, linking partitioning coefficients, temperature variation, and surfactant water/oil interfacial concentration. In that way, this paper proposes new insights into the phenomena governing the PIT method, by originally investigating the temperature cycling process.

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