Formation and characterization of perfluorocarbon nanocapsules as promising microbubble precursors for blood-brain barrier opening

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Microbubbles (MB) are used in the clinical field for a variety of applications such as ultrasound contrast agents, lithotripsy, etc. Recently it has been shown that MB can be used to open the blood-brain barrier (BBB) in a non-invasive, reversible and local manner when stimulated by focused ultrasound (FUS) [1, 2]. The preparation of suitable MB formulations is challenging, as they show short half-lifes and usually large and polydisperse particle sizes, which condition their biodistribution. In this context, nanocapsules containing a liquid perfluorocarbon which can phase shift to gas giving rise to expanded gas MB upon ultrasound stimulation are a promising approach [3].

The formation of polymeric perfluorocarbon nanocapsules prepared from nano-emulsion templates by the phase inversion composition method has been investigated in an aqueous solution / non-ionic surfactant / [polymer + non-fluorinated solvent + fluorinated solvent] system. It has been found that perfluorocarbon nano-emulsions can be formed at high oil-to-surfactant ratios and show sizes typically around 250 nm. Nanocapsules are obtained from the nano-emulsion templates by dialysis and show sizes below 150 nm. The presence of the highly volatile perfluorocarbon in the nano-emulsion template and further in the nanocapspules was confirmed by ^{19}F-NMR. The vaporization temperature of the perfluorocarbon once entrapped in the nanocapsules has been found to be higher (above 75ºC) than that of the no-encapsulated pure substance (around 58ºC). The as prepared perfluorocarbon nanocapsules show suitable features for their use as MB precursors.

References

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[2] Husseini GA, Diaz de la Rosa MA, Richardson ES, et al. J Control Release 107 (2005) 253
[3] Sheeran PS, Luois SH, Mullin LB, Matsunaga TO, Dayton PA. Biomaterials 33 (2012) 3262