Department of Chemical and Biomolecular Nanotechnology Seminars

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Preliminary studies on the preparation of polymeric perfluorohexane nanocapsules as microbubble precursors for blood-brain barrier opening applications

Date
9:30 am
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Location
"Sala d'Actes" room
Institute of Advanced Chemistry of Catalonia (IQAC-CSIC)
C/Jordi Girona 18-26, 08034 Barcelona

Abstract
In the last years, it has been shown that endovenously administered microbubbles can be used to increase the permeability of brain vessels by local stimulation with focused ultrasounds. Although respiratory gases such as O2 or CO2 at suitable concentrations are biocompatible, their half-life in blood is short . In this context, we propose the preparation of microbubbles from perfluorocarbon nano-emulsion templates. Perfluorocarbons show a very low solubility in aqueous media, reducing their diffusion from the dispersed droplets into the blood. However their formulation into stable colloidal systems is challenging because of their high density, hydrophobicity and lipophobicity. Due to the nanometric droplet size of perfluorocarbon nano-emulsion precursors, they may access easily fine capillaries and may be vapourized at the target site to form microbubbles. The formation of polymeric perfluorocarbon nano-emulsions (NE) has been investigated in an aqueous solution / non-ionic surfactant / [polymer + perfluorocarbon + organic solvent] system in the presence and absence of an apolar low density oil. Fluorocarbon nano-emulsions have been obtained at a high oil-to-surfactant ratio with hydrodynamic droplet sizes typically below 300 nm and improved colloidal stability when the apolar low-density oil is present in the oil phase of the NE. Further, globular-shaped perfluorocarbon-loaded polymeric nanocapsules (NC) have been obtained from the NE templates with sizes below 250 nm by DLS, suitable for endovenous administration. Perfluorocarbon encapsulation in the NC has been evidenced both, by spectral angle mapper classification of hyperspectral images and fluor elemental microanalysis. Interestingly, cytotoxicity tests revealed improved cell viability of perfluorocarbon-loaded NC as compared to NC without the perfluorocarbon. Preliminary analyses suggest successful vapourization after mild heating and/or sonication of the perfluorocarbon-loaded NC, although the ultrasound attenuation in the frequency range between 0.4 and 6.6 MHz was low. This may be attributed to the high polymer content in the microbubble shell. New research is ongoing for ultrasound response optimization, while the overall features of the perfluorocarbon nanocapsules studied encourage further research in this field.