Pluronics based host-guest systems for drug delivery

Nonionic pluronic triblock copolymers received considerable attention as modern drug delivery carriers [1]. They have the general formula PEOx-PPOy-PEOx, and are composed of a hydrophobic poly(propylene oxide) (PPO) block and two units of a hydrophilic poly(ethylene oxide) (PEO) block [2]. Their amphiphilic character results into surfactant properties, which includes the ability to interact with hydrophobic surfaces and biological membranes. Above their critical micelle concentration (cmc), these copolymers self-assemble into micelles. Due to their unique core−shell structure, polymeric micelles such as those based on the F127 pluronic (x= 65; y= 100) have the ability to solubilize hydrophobic drugs enhancing their solubility in water media. Because these polymeric micelles are also nontoxic in nature, they can be safely used for the controlled release of drugs [3]. Copolymers are efficient in intracellular delivery because of the presence of the PEO groups in the corona which prevents aggregation, protein adsorption and inactivation in biological media [4], while the hydrophobic PPO incorporates lipophilic drugs [3].

The stability of pluronic micelles is however low due to their high cmc (~1 mM for F127) resulting in their disaggregation by dilution or interaction with the blood components. The mixture of pluronic micelles with other polymers/surfactants enhances the stability of the resulting micelles thus increasing the bioavailability of the encapsulated drugs.

The aim of this project is to evaluate the loading efficiency of pluronics toward the fluorescent anticancer antibiotic doxorubicin (DX). It will be also studied the effect of bile salts (BS) or of bile salts derivatives (BSD) as well as polypeptide surfactants on the stability of the pluronics micelles and on their loading efficiency and release. Particular attention will be paid to the DX self-assembly properties when incorporated into pluronics mixed systems. It is known that DX forms supramolecular aggregates when solubilized into lecithin liposomes [5] or in the presence of salts [6]. Such behaviour could be enhanced or inhibited by the hosting matrices. The joint use of scattering (DLS, SAXS), spectroscopic (CD, steady state and time resolved fluorescence) and imaging (SEM, cryoTEM, confocal) techniques together with MD simulations will be used to investigate the systems.

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