Polymeric micelles nanovectors for photodynamic therapy applications: From the structure to the activity

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Abstract

The recent development of light irradiation systems has facilitated the emergence of new therapies based on light-sensitive drugs. However, photosensitizers have a tendency to self-associate in physiologic environment, leading to a loss of their physical properties. Hence, nanometric formulations have been assessed, because this limits self-association and enables accumulation in solid tumors owing to enhanced permeability and retention effect (EPR).

In this study, we present first a thorough characterization of polymeric micelles based on light scattering and Asymmetrical Flow Field Flow Fractionation. In a second step, we examine their efficiency as photosensitizer vectors using 2D or 3D tumor model namely spheroids.

Polymeric micelles were formed from 4 different amphiphilic block copolymers: poly(ethylene oxide-b- ε-caprolactone) 2000-2800, poly(ethylene oxide-b-ε-caprolactone) 5000-4000, poly(ethylene oxide-b-polystyrene) 3100-2200 and poly(ethylene oxide-b-(D,L)-lactide) 2400-2000. The micelles have been characterized by static and dynamic light scattering, electron microscopy and asymmetrical flow field-flow fractionation. This showed that all systems led to polymeric self-assemblies having a size close to 20nm and a neutral surface. They were shown to be stable upon ageing and dilution, even in the presence of various blood components such as globulins or albumin, which is essential for a possible application as vectors. Cytotoxicity and phototoxicity in the presence of Pheophorbide a as photosensitizer were then characterized both on 2D and 3D cell culture. PDT on spheroids enabled to corroborate results from 2D, showing that encapsulation of Pheophorbide yielded a strong increase of photocytotoxicity.

However, small differences for the nanovectors were highlighted: PEO-PCL 2000-2800 being the most efficient in 2D, whereas PEO-PDLLA 2400-2000 was the best for 3D tests. The obtained results will be discussed in relation with the ones obtained in physical chemistry characterizations.

Only a thorough physico-chemical characterization coupled to in vitro experiments may enable a critical analysis of possible vectors. The polymeric micelles chosen in this study were observed to yield a strong efficiency in PDT, but the differences observed between 2D and 3D systems show that a great care should be taken when testing such vectors.

References

Figures

Polymers and PS used

Example of tumor spheroid macroscopic aspect after PDT procedure with PEO-PS micelles loaded with pheophorbide a.