Tailor-made amphiphilic copolymers for the design of smart drug delivery systems

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Since many years, polymer materials are more and more applied in the pharmaceutical field, particularly in controlled drug delivery systems. Indeed, amphiphilic block copolymerspossess the remarkable property to self-assemble in water with formation, in most cases, of spherical micelles characterized by a hydrophobic core and a hydrophylic corona which are particularly well-suited as drug carriers. The availability of amphiphilic copolymers exhibiting an additional property of being responsive towards environmental changes such as pH, redox potential, temperature, fastly stressed the development of smart nanomedecines.

This work aims at reporting on the synthesis of novelamphiphilicand biodegradable block copolymers made ofa reactive block of aliphatic polyesters or polycarbonate initiated from a hydrophilic bioeliminable poly(ethylene oxide) macroinitiator. These azide bearing amphiphilic block copolymers were found quite suited for a post-modification of the hydrophobic blockby the copper azide-alkyne cycloaddition (CuAAC), without degradation.[1,2]This has been advantageously used to cross-linkthe core of the micelles by adding a bis-alkyne compoundwith the purpose to avoid apremature realease of the drug due to micelles destabilization uponinjection in the bloodstream. By choosing a bis-alkyne bearing an internal disulfide bond,thecore cross-linking is advantageously made reversible by the cleavage of the disulfide bond in presence of a reductive agent, such as glutathione.[3] Only the high cytoplasmic glutathione concentration is able to reduce this bond so that the drug release is triggered intracellularly after internalisation of the carrier in the cancer cell.

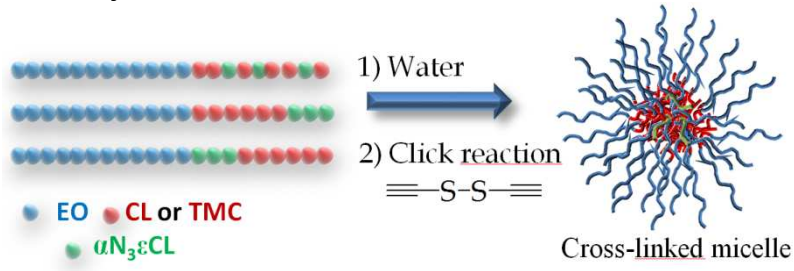

Figure 1. Developped strategy for the synthesis of reversibly cross-linked micelle by CuAAC

Beside, the azide pendant groups were used to covalently graft a drug also by CuAAC. As model molecules, the grafting of alkyne bearing fluorescent dyes was investigated leading to the synthesis of fluorescent micelles. The effect of the architecture of the copolymer on the efficiency of the coupling reaction,performeddirectly inside the micelle's core, and the fate of the carrier after internalisation were investigated.[4]

References

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