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Exploitation of hydrazone bond to deliver Doxorubicin

Azzurra Agostini and Davide Moscatelli
Polytechnic University of Milan, Italy

Statement of the Problem: Drug delivery systems based on polymeric nanoparticles (NPs) have shown interesting results in their applications for many diseases due to their improved pharmacokinetics and biodistribution profiles compared to the standard formulation of many active compounds. In particular, micellar carriers are one of the most widely used system due to their easy preparation and versatile properties. According to their structure with an internal hydrophobic core and an external hydrophilic shell, they can be used to encapsulate a hydrophobic drug in their core so as to obtain a formulation with improved bioavailability. A possible limitation of these systems is related to the possibility of a fast release after the injection in the bloodstream. Even if the NPs could target a specific diseased tissue, the targeting benefit will decrease in proportion of the burst extent.

Methodology & Theoretical Orientation: A strategy to avoid these drawbacks is to produce a prodrug by the covalent conjugation of the drug to the material which forms the NPs through a cleavable linker. The main advantage of this approach is the opportunity to exploit the chemical stability of the linker in order to trigger the release of the drug in determinate physiological conditions. This work focuses on the synthesis of materials in which there is a pH-sensitive hydrazone bond between polymer and Doxorubicin, an anticancer drug. The chosen linkage allows the controlled delivery of the drug in acid conditions and ensures the release of the intact Doxorubicin structure, confirmed via HPLC spectrum.

Findings: The drug release kinetics was studied in aqueous buffers at pH 5.2 (close to pH in endosomes) and 7.4 (pH of blood plasma).

Conclusion & Significance: The collected data show a real dependence to the pH values. In fact, the amount of Doxorubicin is higher at low pH value.

Biography

Azzurra Agostini is a Project Engineer and she is attending PhD in Chemical Engingeering at Politecnico di Milano. She works at the same time on materials suitable for both drug delivery systems and oil and gas applications. She was a visiting student at ETH in Zurich during August, 2016. She went to European Conferences during her first year of PhD. She is interested in teaching Thermodynamics and Electrochemistry. Actually she is working deeply on cationic nanoparticles, oral delivery and tissue engineering.

azzurra.agostini@polimi.it

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