Synthèse et caractérisation de nanoparticules magnétiques répondantes pour des applications en thérapie cancéreuse

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Abstract:

One of the major challenges in nanomedicine is to develop nanoparticulate systems able to serve as efficient diagnostic and/or therapeutic tools against sever diseases, such as infectious or neurodegenerative disorder. The most powerful diagnosis toll in medical science is MRI (magnetic resonance imaging). To enhance MRI images interpretation, contrast agents were developed to clarify images. Among them Superparamagnetic iron oxide (SPIO) nanoparticles have received a great attention since their development as a liver contrasting agent 20 years ago1. Furthermore, their nanoparticulate properties represented by the nanosized dimension and shape allow different biodistribution and opportunities beyond the conventional imaging of chemical agents. The opportunity to coat those biocompatible NPs by a polymer shell that can ensure a better stability of the new materials in the body, enhance their biodistribution and gives them new functionalities appear as very challenging for medicinal applications2.We have thus in this work developed new responsive SIONPs that are able carry the anticancer drug doxorubicin (DOX)and release it in physiological media at physiological temperature. Two family of nanoparticles were synthesized, the first one consist in superparamagnetic Fe3O4 nanoparticules were functionalized by a biocompatible responsive copolymer based on2-(2-méthoxy) éthylméthacrylate (MEO2MA), oligo (éthylène glycol) méthacrylate (OEGMA), which lead to Fe3O4@P(MEO2MAx-OEGMAy). The second family consists in the same nanoparticles as previously mentioned, but we have covalently grafted biological cancer targeting molecule at the chain end, i.e the folic acid. For the first time, P(MEO2MAx-OEGMAy)was grown by activator regenerated by electron transfer–atom

transferring radical polymerization (ARGET-ATRP) from Fe_3O_4 by surface-initiated polymerization. The core/shell nanostructures were fully characterized by the combination of transmission electron microscopy (TEM), thermogravimetric analysis (TGA), and by the physical properties of the nanostructures studied. We demonstrate the efficiency of the Atom Transfer Radical Polymerization with activators Regenerated by electron Transfer (ARGET-ATRP) process to graft polymers and copolymers at the surface of Fe3O4 nanoparticles. The influence of the polymer chain configuration (which lead to the aggregation of the NPs above the collapse temperature of the copolymer (LCST)) We could show that the magnetic properties of the core/shell Fe_3O_4 based nanostructures, only the amount of the grafted polymer plays a role on the saturation magnetization of the NPs, and no influence of the aggregation was evidenced. This simple and fast process developed in this work is efficient for the grafting of various co-polymer from any surfaces and the derived nanostructured display the combination of the physical properties of the core and the macromolecular behavior of the shell. The drug release experiments confirmed that only the DOX largely released above the co-polymer LCST. From the results obtained, it can be concluded that our new nanomaterials can be considered for further use as multi-modal cancer therapy tools.

(1) Semelka, R. C.; Helmberger, T. K. G. Contrast Agents for MR Imaging of the Liver1. Radiology**2001**, 218 (1), 27–38.

(2) Orringer, D. A.; Koo, Y. E.; Chen, T.; Kopelman, R.; Sagher, O.; Philbert, M. A. Small Solutions for Big Problems: The Application of Nanoparticles to Brain Tumor Diagnosis and Therapy. Clin. Pharmacol. Ther.**2009**, 85 (5), 531–534.

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