

Design and synthesis of nanoparticles based chitosan for improving drug delivery across blood-brain barrier

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We prepared nanoparticles based on chitosan grafted with poly (ethylene glycol) (PEG) methacrylate. These nanoparticles were then loaded with doxorubicin. The nanoparticles have been fully characterized: laser diffraction, electron microscopy, kinetic of swelling of nanoparticles. The size distribution curve of the nanoparticles attests that the average diameter is 450 nm. The analysis of the morphology of the nanoparticles proved the obtaining of spherical particles, well individualized. The process of loading and releasing the drug into the particle is based on diffusion through the hydrogel matrix. As a result, it depends on the swelling rate of the particles in aqueous solutions. The pH of the solution is also an important factor influencing the swelling degree. The kinetics of the particle swelling process was studied in an aqueous medium at acid pH (3.3) and weakly basic (7.4). The

swelling degree in both media is high enough, so the particles may fall into the category of superabsorbent gels. The effect is due to the high hydrodynamic volume of macromolecules that are branched by PEG on chitosan chains. To determine if these nanoparticles could be used as vehicle molecules to treat neurodegenerative diseases, we then investigated their toxicity using an *in vitro* model of the human blood-brain barrier (BBB). Free doxorubicin nanoparticles did not modify BLECs (Brain Like Endothelial Cells) permeability meaning that these molecules do not show any toxic effects at the BBB level. These nanoparticles could therefore be used after functionalization with anti-transferrin antibodies to cross the BBB and thus deliver doxorubicin in brain tumors.

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