Polymeric nanoparticle uptake studies for nanocarrier-based drug delivery in cancer treatment.

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Engineered nanoparticles (NPs) are a key point in new drug nanocarrier development for cancer treatment. Synthesized NPs must access the tumoral cell so the drug can be properly delivered and must not generate a toxic response that kills healthy cells. The goal of 7th Framework Program funded NANOTHER project is to develop these types of NPs to improve cancer treatment. Among many types of NPs synthesized in this project, poly(trimethylene carbonate)-b-poly(L-glutamic acid) (PTMC-b-PGA) polymersome nanoparticles were prepared. Rhodamine B was covalently attached to polymersome surface in order to track the system in the cell by specific fluorescence detection methods. HepG2 hepatocarcinoma cell line was used for the study. These cells grow in complete medium in the form of colonies of cells in a monolayer. The toxicity of PTMC-b-PGA NPs was assayed using Alamar blue. Apoptosis and necrosis studies were carried out by annexin V and propidium iodide stains using a flow cytometer. The polymersomes were non toxic at the concentrations assayed (0.1 and 0.5 mg/ml) at 24 and 72 h. The uptake rate and localization of the fluorescent nanoparticles were both studied using flow cytometry and confocal microscopy. The flow cytometry assays indicated that 5 hours after Red-PTMC-b-PGA NPs addition in cell medium, 50% of cells contained fluorescent NPs. However, more than 90% of cultured cells showed red fluorescence 24 hours after NPs addition. Confocal microscopy studies supported these data and also provided information of the cellular localization of the nanoparticles. In the case of this cell line, Rhodamine labelled polymersomes appeared to be located in the cytoplasm, in the proximity of the nucleus, inside small internal cellular vesicles. The data here presented together with previous results of doxorubicin (a well-known anticancer drug) high loading capacity [1] indicate that PTMC-b-PGA seems to be a good candidate system for drug delivery in cancer treatment.

References

[1] Sanson C, Schatz C, Le Meins JF, Soum A, Thévenot J, Garanger E, Lecommandoux S. "A simple method to achieve high doxorubicin loading in biodegradable polymersomes". *J Control Release.* 2010, 147(3):428-35.