"*Core-shell*" lipid-based nanosystems for mitochondrial targeting of cancer cells

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In this work, we designed and investigated "*core-shell*" drug delivery nanosystems featuring a mitochondriotropic liposomal "*core*" and a biocompatible polymeric "*shell*", formed by two layers: an outer cationic layer consisting of chitosan functionalized with transferrin to promote the interaction with cancer cells and an anionic inner one constituted by dextran, directly in contact with the liposome surface. Liposomes were prepared with a cationic triphenylphosphonium bolaamphiphile, developed for mitochondrial targeting, and a phospholipid (DPPC, DMPC or DOPC), in order to explore the influence of the different fluidity and organization of the "*core*" on the arrangement of the two polymers on the surface and, consequently, on the physico-chemical and biological properties of the nanosystem as a whole.
The formulations were prepared by the *layer-by-layer* technique and were characterized by Dynamic Light Scattering (DLS), Laser Doppler Electrophoresis (LDE), Fluorescence Anisotropy and Transmission Electron Microscopy (TEM). The cytotoxic effect of the formulations was investigated on human breast adenocarcinoma cells, MDA-MB231, by Electric Cell-substrate Impedance Sensing technique (ECIS) while the uptake, internalization and mitochondrial colocalization were investigated through flow cytometry and confocal microscopy measurements. In addition, the antioxidant Resveratrol (RSV), due to its chemosensitizing and anticancer activity, was included in liposomes as a model drug.

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