

Multifunctional iron oxide nanoparticles for targeting metastatic breast cancer cells

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Breast cancer results like one of the most common malignant tumors in females until now [1]. Advancement in next generations of cancer therapy modalities involving nanocarriers and nanoformulations is currently a crucial requirement of oncology. Early diagnosis and targeted treatment are important goals for increasing the survival rate of breast cancer patients. Last discoveries in nanomedicine are providing the development of dual and multifunctional nanoparticles that merge diagnostic and treatment agents. Associated studies have shown that iron-oxide nanoparticles can be used for diagnosis, as well as a good carrier of drugs and induced therapeutic for magnetic hyperthermia. Distinctive physicochemical features make iron-oxide magnetic nanoparticles as a multifunctional nanosystem (NS) for the targeted delivery of therapeutic agents. In the present study, we engineered conjugated superparamagnetic iron-oxide nanoparticles (SPIONs) for the targeted delivery of doxorubicin (DOX) to the breast cancer cells.

The aim of this work was to investigate the *in vitro* effect of the loading of doxorubicin (DOX) on negatively charged polycarboxylic iron-oxide nanoparticles (SPIONs) and Rhodamine B functionalized SPIONs on breast carcinoma cell lines. For proper analysis and understanding of cell behavior after administration of DOX-SPIONs compared with free DOX, a complex set of *in vitro* tests, including production of MTT assay, 3D cell toxicity and cell cycle determination, and cellular uptake, were utilized. In summary, we have developed a magnetic nanoparticle-based drug delivery system that sequentially delivers the cytotoxic drug doxorubicin to breast cancer cells (MCF-7 and MDA-MB-231). The drug-coated nanoparticles, DOX-NPs, were assembled stepwise, with doxorubicin adsorbed to bare iron oxide nanoparticles first, by electrostatic reaction and allowed for the complexation of doxorubicin. DOX-NPs were stable in solution at 37 °C and physiological pH (7.4). Rapid *in vitro* release of doxorubicin followed by gradual release of doxorubicin was triggered in aqueous solution by low pH (5.4) and heating. As a result of minimal internalization, the particles were not significantly toxic to noncancerous cells (MCF-10A). In contrast, they were internalized to a much greater extent in MCF-7 and MDA-MB-231 cells and were cytotoxic due to the synergistic action of the two drugs and the effects of hyperthermia. The drug-coated particles were able to inhibit growth and proliferation of breast cancer cells *in vitro*, indicating that the system has potential to act as an antimetastatic chemothermotherapeutic agent.