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Synthesis, functionalization and characterization of mesoporous silica nanoparticles for intravenous doxorubicin delivery to cancer cells

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Chemotherapy treatment of cancer has proved beneficial in increasing survival rate compared to radiation therapy, surgery, and photodynamic therapy because the drugs are spread all over the body. However, conventional chemotherapy is toxic to normal cells and requires very long treatment periods and cycles. Curative chemotherapy of human malignancies is also hindered mainly by multi-drug resistance (MDR) and other chemo-resistance properties exhibited by the body. The purpose of this study is to develop multifunctional drug carriers that can encapsulate, prevent premature drug release, and actively and specifically release the drugs in a stimuli-responsive way. Mesoporous silica nanoparticles were synthesized by the sol-gel method, functionalized by double bilayers of alginate and chitosan using the layer-by-layer technique and finally conjugated with folic acid. Drug loading, *in vitro* drug release in phosphate buffered saline and acetate buffers, *in vitro* cytotoxicity assay, intracellular uptake and drug internalization by living cells were investigated. Relatively high drug encapsulation efficiency and loading capacity of 53% and 2.3% were achieved at pH 5. *In vitro* drug release confirmed absence of doxorubicin release by the carrier at blood pH of 7.4 while an initial burst release was observed at acidic pH followed by a sustained drug release over a 36 hour period. MTT assay showed the biocompatibility of the drug carrier while confocal laser scanning microscopy proved the hyper uptake and internalization of the multifunctional drug carrier. Exposure of free doxorubicin drug, drug loaded carrier with and without folic acid on the surface to tumour cell line and normal HeLa cells, before and after folic acid blocking, showed the efficient folic acid receptor assisted drug internalization by the tumour cells. The investigation offered a practical route to the fabrication of biocompatible, pH responsive targeted active and sustained doxorubicin delivery to tumour cells.

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