Dual Targeted Polysaccharide/Lipid Nanoparticles for Oral Combination Therapy Delivery against Colon Cancer

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This work aims to develop functionalized solid lipid nanoparticles (SLNs) as an oral drug delivery system for improving the efficacy of colon cancer therapy. Doxorubicin (DOX)/superparamagnetic iron oxide nanoparticle (SPION)-loaded SLNs were prepared by double emulsion method and sequentially coated with folate-modified D-α-Tocopherol polyethylene glycol 1000 succinate (TPGS) and octadecanol-conjugated dextran. The dextran/folate-coated SLNs (DFSLNs) loaded with DOX and SPION had a particle size of ca. 132 nm. The loading contents of DOX and SPION were ca. 9.27 and 0.72 wt%, respectively. Compared to the uncoated SLNs, the folate-containing SLNs were significantly internalized by CT26 cancer cells with overexpressed folate receptor, thus increasing the intracellular DOX concentration by 2-fold. Similarly, the DFSLNs with dextranase pre-treatment exhibited an identical increase of DOX concentration within the cancer cells, indicating that the exposed folate ligands upon the detachment of the outer dextran layers due to enzymatic degradation appreciably promoted the cellular uptake of DFSLNs by folate-receptor mediated endocytosis. The in vivo characterization showed that the orthotopic CT26 tumor-bearing mice orally administrated with DFSLNs and treated with high frequency magnetic field exhibited the best colorectal drug accumulation and tumor growth inhibition. Moreover, the abdominal metastasis of CT26 colon tumor was also reduced by the chemo/thermal combination therapy of DFSLNs. These results demonstrate that the developed DFSLNs employed as an oral drug delivery system has great potential for colon cancer therapy.