
Research paper

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# Sugar-decorated mesoporous silica nanoparticles as delivery vehicles for the poorly soluble drug celastrol enables targeted induction of apoptosis in cancer cells

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Cancerous cells have a rapid metabolism by which they take up sugars, such as glucose, at significantly higher rates than normal cells. Celastrol is a traditional herbal medicine known for its anti-inflammatory and anti-cancer activities. The poor aqueous solubility and lack of target selectivity of celastrol, results in low therapeutic concentration of the drug reaching subcellular compartments of the target tissue, making it an interesting candidate for nanoparticulate delivery. The goal of this study was to utilize glucose as an affinity ligand decorated on mesoporous silica nanoparticles (MSNs), with the aim of delivering these celastrol-loaded MSNs with high specificity to cancer cells and inducing minimal off-target effects in healthy cells. MSNs were thus functionalized with sugar moieties by two different routes, either by conjugation directly to the MSN surface or mediated by a hyperbranched poly(ethylene imine, PEI) layer; the latter to increase the cellular uptake by providing an overall positive surface charge as well as to increase the reaction sites for sugar conjugation. The effect of surface functionalization on the target-specific efficacy of the particles was performed by analyzing the uptake in HeLa and A549 cells as cancer cell models, as compared to mouse embryonic fibroblasts (MEF~~s~~) as representative for normal cells. To this end a comprehensive analysis strategy was employed, including flow cytometry, confocal microscopy, and spectrophotometry. When the apoptotic effect of celastrol was evaluated, the anti-cancer activity of celastrol was shown to be significantly enhanced when it was loaded into the specifically designed MSNs. The particles themselves did not induce any toxicity, and normal cells displayed minimal off-target effects. In summary, we show that glucose-functionalized MSNs can be used as highly efficient carriers for targeted celastrol delivery to achieve specific apoptosis in cancer cells.

*Keywords: targeted drug delivery, celastrol, surface functionalization, mesoporous silica nanoparticles, glucose consumption, cancer therapy*