Combine drug delivery of Thymoquinone-doxorubicin by cockles shell derived pH-sensitive Aragonite CaCO3 nanoparticles

ABSTRACT

Background: Cockleshell-derived aragonite calcium carbonate nanoparticles were prepared by the top-down approach for combine delivery of two types of drugs. Objective: The aim of this study was to synthesize and characterize thymoquinone-doxorubicin loaded cockle shell-derived aragonite calcium carbonate nanoparticle. Aragonite calcium carbonate nanoparticles encapsulating thymoquinone and doxorubicin alone were also prepared. Methods: The blank and drug-loaded nanoparticles were characterized by field emission scanning electron microscopy, transmission electron microscopy, Zeta potential, Fourier transformed infrared and X-ray diffraction. Drug delivery properties, in vitro drug release study at pH 7.4, 6 and 4.8, and effect of blank nanoparticles on MCF10A, 3T3, MDA MB231 cells were also analyzed. Results: The blank and drug-loaded nanoparticles were pleomorphic and their sizes varying from 53.65 ± 10.29 nm to 60.49 ± 11.36 nm with an overall negative charge. The entrapment efficiency of thymoquinone and doxorubicin were 41.6 and 95.8, respectively. The FTIR showed little alteration after loading thymoquinone and doxorubicin while XRD patterns revealed no changes in the crystallizations of nanoparticles after drug loading. The drug release kinetics of doxorubicin and thymoquinone from the nanoparticles showed a continuous and gradual release after an initial burst release was observed. At pH 4.8, about 100% of drug release was noticed, 70% at pH 6 while only 50% at pH 7.4. The cell viability was 80% at a concentration of 1000 ug/ml of blank nanoparticle. Conclusion: The cockle shell-derived pH sensitive aragonite calcium carbonate nanoparticle provides an effective and simple means of multiple drug delivery and function as a platform for pH controlled release of loaded therapeutic agents.

Keyword: Cockleshell; Nanocarrier; Thymoquinone; Doxorubicin; Combine drug delivery; CaCO3 nanoparticles