

In vitro evaluation of a novel pH sensitive drug delivery system based cockle shell-derived aragonite nanoparticles against osteosarcoma

ABSTRACT

Background: Osteosarcoma (OS) is a highly malignant primary bone cancer. Severe side effects and multidrug resistance are obstacles faced with chemotherapy against OS. With the hope to overcome the obstacles of the conventional chemotherapy, various targeted drug delivery systems using nanotechnology have been explored in the past few decades. Biogenic calcium carbonate (CaCO_3) has great potential to be a smart drug delivery system. **Results:** In this study, cockle shells-derived aragonite nanoparticles (ANPs) were developed and loaded with doxorubicin (DOX). The physicochemical properties of the DOX-loaded ANPs (DOX-ANPs) were characterised by various techniques. The results of drug-loading study demonstrated that DOX was loaded onto ANPs at high loading and encapsulation efficiency (11.09% and 99.58%, respectively). The pH-sensitive release of DOX from DOX-ANPs was successful. At lower pH values (4.8), the release of DOX was much quicker than that at pH 7.4. Additionally, cellular uptake study using fluorescence microscopy showed obviously cellular uptake of DOX-ANPs through endocytosis. Moreover, the flow cytometric analysis revealed DOX-ANPs-induced cell cycle arrest, which was consistent with the mechanism of DOX. DOX-ANPs also showed an efficient cytotoxicity against OS cancer cells, close to the toxicity effect of free DOX at the same concentration. Morphological observations showed microvilli disappearance, chromatin condensation, cell shrinkage, membrane blebbing, and formation of apoptotic bodies, which confirmed both DOX-ANPs- and DOX-induced apoptosis of OS cancer cells *in vitro*. **Conclusion:** Our findings indicated that ANPs could act as a pH-sensitive drug delivery against OS.

Keyword: Cockle shell; Aragonite; Nanoparticles; pH-sensitive; Drug delivery; Doxorubicin; Osteosarcoma