

Ultrastructural changes and antitumor effects of doxorubicin/ thymoquinone-loaded CaCO₃ nanoparticles on breast cancer cell line

ABSTRACT

Background: Combination chemotherapy of anticancer drugs is extensively being researched since it could reduce multidrug resistance and side effects as a result of lower dosage of each drug. In this study, we evaluated the effects of doxorubicin-loaded (Dox-ACNP), thymoquinone-loaded (TQ-ACNP) and a combined doxorubicin/thymoquinone-loaded cockle shell-derived aragonite calcium carbonate nanoparticles (Dox/TQ-ACNP) on breast cancer cell line and compared with their free drugs counterpart. **Methods:** Cell viability using MTT assay, apoptosis with Annexin V-PI kit, morphological changes using contrast light microscope, scanning electron microscope and transmission electron microscope, cell cycle analysis, invasion assay, and scratch assay were carried out. The cell viability was evaluated in breast cancer cell line (MDA MB231), normal breast cells (MDF10A) and normal fibroblast (3T3). **Results:** MDA MB231 IC₅₀ dosages of drug-loaded nanoparticle were not toxic to the normal cells. The combination therapy showed enhanced apoptosis, reduction in cellular migration and invasion when compared to the single drug-loaded nanoparticle and the free drugs. Scanning electron microscope showed presence of cell shrinkage, cell membrane blebbing, while transmission electron microscope showed nuclear fragmentation, disruption of cell membrane, apoptotic bodies, and disruption of mitochondrial cistern. **Conclusion:** The results from this study showed that the combined drug-loaded cockle shell-derived aragonite calcium carbonate nanoparticles (Dox/TQ-ACNP) showed higher efficacy in breast cancer cells at lower dose of doxorubicin and thymoquinone.

Keyword: Doxorubicin; Thymoquinone; CaCO₃ nanoparticle; Breast cancer; Combination therapy