ABSTRACT

DETERMINATION OF THERAPEUTIC EFFECTS OF MULTIFUNCTIONAL ANTIBODY AND PEPTIDE MICELLE-BASED NANOCARRIERS ON BREAST CANCER CELLS

Breast cancer is the most prevalent type of cancer and a major cause of death among women globally. Currently, many treatments are developed to reduce breast cancer death risks. Targeting therapy represents an advanced and successful approach. It provides targeting specific tumor sites by using specific ligands and modifying physicochemical characterization of nanocarriers to increase drug efficiency.

In this study, we aim to determine and compare the therapeutic effects of doxorubicin (DOX)- loaded nanocarrier that was synthesized by using two properties a core cross-linked and pH sensitivity to increase drug stability and DOX releasing at the tumor site. The effects of DOX-loaded micelles (DM), HER2 targeting peptide (LTVSPWY)-conjugated-DOX-loaded micelles (DMP), and antibody (Herceptin) conjugated-DOX-loaded-micelles (DMA) on HER2 positive SKBR-3 cell line and HER2 negative MCF-10A normal epithelial breast cell line were determined by using cytotoxic, apoptotic, cytostatic, and genotoxic assays.

According to the cytotoxic assay, the IC50 value of DM, DMA, and DMP were 0.71-, 0.49-, 0.34-μM, respectively. Additionally, the fluorescence image showed higher DOX uptake by SKBR-3 cells treated with DMP. According to the apoptotic assays, the mitochondrial membrane potential on SKBR-3 cells with treated DMP decreased as well as higher apoptosis and necrosis rate that was regulated by Bcl-2, Pro-Caspase-3, PARP1, Bax, Bak, and Bcl-xL. Besides, the application of DMP caused cell cycle arrest at the G2/M phase. Lastly, DNA damage was observed in response to DMP determined by comet assay. This study provides a novel and effective therapeutic option for breast cancer through using this nanocarrier system with targeting properties.