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GSH -responsive nanoparticles in the treatment of tumor cells

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Cancer cells which develop resistance toward chemotherapeutic drugs become highly adapted to intrinsic oxidative stress by up-regulating their antioxidant systems which, in turn, can increase their capacity for drug inactivation. The major player in oxidative adaptation of cancer cells is glutathione (GSH). Doxorubicin is one of the most widely used drugs for treatment of cancers which acts by poisoning Topoisomerase II, by forming adducts with DNA and by inducing oxidative stress. However, doxorubicin use is limited by cardiac and kidney toxicity and by drug resistance. We have recently developed a new class of cyclodextrin nanosponges that are GSH-responsive (GSH-NSs), and able to release anticancer drugs in the presence of high GSH concentrations, similar to those detected in cancer chemo-resistant cells. In the present paper, we loaded GSH-NSs with doxorubicin and tested its toxic effect in cells with various GSH concentrations. The obtained results demonstrated that doxorubicin loaded GSH-NSs inhibited cell viability, and topoisomerase activity, and induced DNA damage with higher effectiveness than free drug in the cells with high GSH content, whereas in the cells with low GSH-content their action was similar to that displayed by the free drug. Furthermore, GSH-NSs, loaded with low doses of doxorubicin, inhibited clonogenic growth more than free doxorubicin, thus allowing the reduction of the effective doses. These characteristics indicate that GSH-NSs can be a suitable drug delivery carrier for future applications in cancer therapy.

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