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Enhanced anti-cancerous activity of dual drug loaded core-shell nanoparticles composed of fully alternating copolymer

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In recent years, polymeric nanoparticles have revolutionized the field of biomedical science with the development of novel drug carriers for increasing the solubility and stability of hydrophobic drugs. These nano drug-carriers have augmented the number of formulations in clinical trials. The polymeric nanoparticles are generally composed of different types of copolymers, which are usually synthesized from monomers using organometallic catalyst. The metal components of such catalysts are very toxic to healthy cells at higher concentration. In this study, we synthesized a metal-free fully alternating copolymer of ~9.3 kDa size, composed of tert-butyl glycidyl ether (t-BGE) and phthalic anhydride (PA) as monomeric units. Further, this fully alternating copolymer was used to prepare the core-shell nanoparticles loaded with single and dual drug using doxorubicin (DOX) and curcumin (CUR). The average diameter of these monodispersed nanoparticles ranged between ~200 to 300 nm. Moreover, these spherical nanoparticles showed sustained drug release behavior for both drugs in a defined physiological environment. Anti-tumor efficacy of these nano-drug carriers were examined on several cancer cell lines of different origins and exhibited higher toxicity on pancreatic cancer cells (MIA PaCa-2) with very low IC50 value suggesting the enhanced synergistic action of CUR with DOX drug on MIA PaCa-2 cells *in vitro*. In addition, these drug loaded NPs also inhibited the proliferation of MIA PaCa-2 cells due to the cell cycle arrest in G2/M phase that induced apoptosis with increased production of ROS and significant changes in mitochondrial membrane potential. Overall, this approach may open up novel avenues for the applications of metal-free fully alternating copolymers in biomedical sciences and as a therapeutic intervention for different cancers.

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