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Active nontargeted drug delivery in cancer therapy

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Cancer is one of the major causes of mortality in the worldwide and innovative methods for cancer therapy are urgently required. Nanoparticles, by using active targeting strategy, can enhance the intracellular concentration of drugs in cancerous cells while avoiding toxicity in normal cells. In our studies, the aims were developing a biodegradable polymeric drug delivery system for improving the therapeutic index of potent anticancer such as methotrexate, gemcitabine and 9-nitrocamptothecin, today on epirubicin. To achieve these goals, PLGA and PLGA-PEG nanoparticles were prepared by nanoprecipitation method and chitosan nanocarriers produced based on the ionic gelation method. The optimum loaded nanoparticles were evaluated by in vitro cytotoxicity and in vivo antitumor activity in breast tumor xenografted Balb/c compared to free drug and their ability to induce apoptosis compared to free drug by examining of caspase-3 activity. The encapsulation efficiency of the prepared PLGA-Fol nanoparticles was found to be 57%. In vitro release profile indicated that nearly 80% of the drug was released in the first 50hrs for both PLGA and PLGA-Fol NPs. The methotrexate loaded PLGA NPs increased caspase-3 activity to 33.3±4.1% in MCF7 cells compare to free drug ($p<0.05$). The results indicated that the drug formulated in the NPs significantly increased caspase-3 activation compared to alone MTX. The average IC50 values of Gem in chitosan nanoparticles for 4T1 and MDA-MB-231 cells were 0.2±0.05 and 0.28±0.04μg/ml and in free drug were 0.18±0.02, 0.2±0.04μg/ml, respectively.

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