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NANOCARRIERS MODIFIED WITH POLYETHYLENE GLYCOL FOR ANTICANCER DRUG DELIVERY

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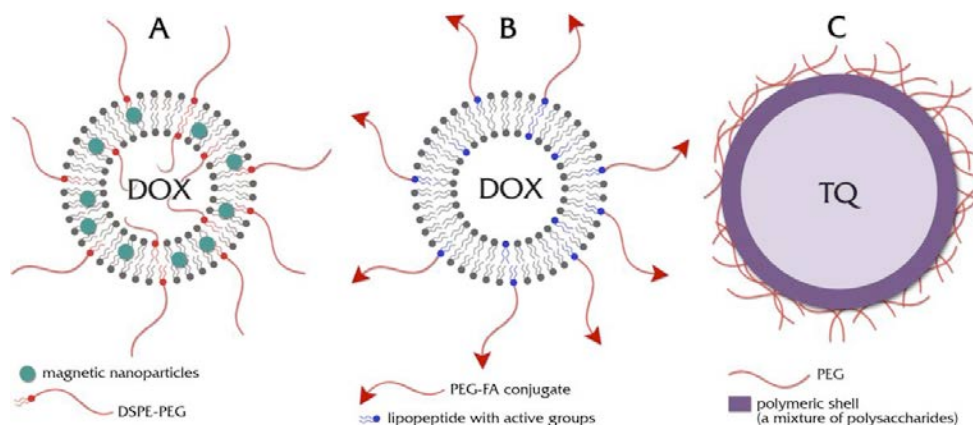
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The design of antitumor drug delivery systems (DDS) is a challenge of biomedicine. Conventional DDS have a number of disadvantages, including low stability in the blood stream. Recently, to enhance DDS longevity, various modifications have been proposed. Polyethylene glycol (PEG) is known as one of the most frequently used polymers for DDS stabilization due to its biocompatibility, solubility, hydrophilicity and high chain flexibility. The aim of the current study was to develop nanocarriers (NCs) modified with PEG and to evaluate their *in vitro* cytotoxicity in 2D (monolayer culture) and 3D (tumor spheroids) models.

Three types of NCs have been modified with PEG by different techniques. Doxorubicine (DOX)-loaded magnetic liposomes (A) were developed to provide controlled drug release under a low-frequency magnetic field. To modify the liposome surface, PEG was added at the thin film formation stage by mixing lipids with DSPE (1,2-Distearoyl-sn-glycero-3-phosphoethanolamine)-PEG conjugates. For active targeted drug delivery, DOX-loaded cationic liposomes associated with folic acid (FA) vector molecules (B) have been developed. In this case, to provide covalent PEG binding to FA and orientation of the obtained PEG-FA complex only at the liposome outer surface, an original “click”-chemistry approach has been proposed. Finally, polymer NCs based on polyelectrolyte complex of oppositely charged polysaccharides, namely xanthan gum and DEAE-dextran (C), have been proposed for encapsulation of lipophilic drug thymoquinone (TQ). For this purpose, previously prepared NCs were coated with PEG by adsorption. All NCs were characterized in terms of their physical-chemical properties (mean size, ζ -potential, storage stability etc.) and *in vitro* cytotoxicity. In this study, MCF-7 (human breast adenocarcinoma), U-87 MG (human brain glioma) and C6 (rat brain glioma) cells were used. The NCs accumulation and localization in 2D and 3D models were evaluated by confocal microscopy and flow cytometry, while MTT-test was used for cytotoxicity assay. Thus, three different NCs were successfully modified with PEG and their cytotoxicity was evaluated *in vitro*.



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