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Breast Tumor Targeting with PAMAM-PEG-5FU- ^{99m}Tc As a New Therapeutic Nanocomplex: In In-vitro and In-vivo studies

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Abstract

Dendrimer-based targeted drug delivery, as an innovative polymeric drug-delivery system, is promising for cancer therapy. Folate receptors (FR) are overexpressed in many types of tumor cells, such as breast cell carcinomas, which allow folate-targeted delivery. Therefore polyethylene glycol (PEG) modified-PAMAM G4 dendrimers were functionalized with folic acid (FA), as targeting agent. Then, 5-FU (5-fluorouracil) and ^{99m}Tc (technetium-99 m) as therapeutic agents were respectively loaded and conjugated to previous nano-complex (PEG-PAMAM G4-FA-5FU-^{99m}Tc). The value of drug loading was calculated by TGA analysis (16.97%). Drug release profiles of PEG-PAMAM G4-FA-5FU-^{99m}Tc and PEG-PAMAM G4-FA-5FU were evaluated. The radiochemical purity of PEG-PAMAM G4-FA-5FU-^{99m}Tc and PEG-PAMAM G4-FA-^{99m}Tc was obtained at >95% with excellent in-vitro and in-vivo stabilities. PEG-PAMAM G4-FA-5FU-^{99m}Tc was synthesized and the stability studies were carried out by the ITLC methods in serum (86.67% and 83.75%) and PBS. Combinational therapy effects of 5-FU and ^{99m}Tc containing nano-complexes were evaluated on 4 T1 (mouse breast cancer) and MDA-MB-231 (human breast adenocarcinoma) cancer cell lines. Excellent uptake values were obtained for FA-decorated nano-complexes on 4 T1 and MDA-MB-231 cell lines. Subsequently, tumor inhibition effects of PEG-PAMAM G4-FA-5FU-^{99m}Tc and PEG-PAMAM G4-FA-5FU were evaluated using the breast tumor-bearing BALB/C mice. Graphical abstract Breast Tumor Targeting with PAMAM-PEG-5FU- ^{99m}Tc As a New Therapeutic Nanocomplex: in In-vitro and In-vivo Studies was presented. This targeted drug delivery system can significantly increase the efficiency of cancer therapy, and reduce the treatment cost and time.

Keywords: 5-FU delivery; ^{99m}Tc; Breast cancer; Folic acid targeting; PAMAM G4-PEG.

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