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Laser-responsive liposome for selective tumor targeting of nitazoxanide nanoparticles

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Abstract

Nitazoxanide [2-(Acetyloxy)-N-(5-nitro-2-thiazolyl)benzamide], usually referred as NTZ, is an antiparasitic drug with a potential anti-cancer reactivity. However, the bioavailability of nitazoxanide is limited due to its poor water solubility. In this study, nitazoxanide could be successfully incorporated in a stable biocompatible liposome (NTZ-LP) using a modified thin film hydration technique. Further, a novel lipophilic phthalocyanine star polymer R_4PcZn was prepared as photosensitizer and in situ incorporated with NTZ in the liposome formulation affording a laser-responsive liposome (NTZ-ZnPc-LP). Both (NTZ-LP) and (NTZ-ZnPc-LP) showed high entrapment efficiency (EE) and high in vitro drug release rates. Transmission electron microscope (TEM) images and dynamic light scattering (DLS) measurements of (NTZ-LP) and (NTZ-ZnPc-LP) showed unilamellar vesicles of mean diameter 192.2 and 87.4 nm, respectively. In addition, NTZ nanoparticles (NTZ NPs) were prepared via membrane extrusion method using DMF and water as solvents. All formulations were similarly prepared using radiolabeled nitazoxanide ^{125}I-NTZ. After induction of solid tumor in mice using Ehrlich Ascites Carcinoma, the prepared formulations were injected in the tail vein of the mice. Tumor sites of the animal injected with (^{125}I-NTZ-ZnPc-LP) were illuminated with a He-Ne laser (λ= 630 nm). Afterwards, the biodistriburtion of ^{125}I-NTZ was tagged using γ counter. Results showed that the light-responsive formulation (^{125}I-NTZ-ZnPc-LP) affords a higher accumulation of ^{125}I NTZ in the tumor sites after illumination. This can be attributed to the rupture of liposome lipid bilayer as a result of the photosensitization process and the singlet oxygen species resulted thereof. Despite (NTZ NPs) formulation showed a rapid accumulation of NTZ in tumor, it showed unfavoured rapid blood clearance rate.

Keywords

Nitazoxanide nanoparticles - phthalocyanine polymers - laser - liposomes - radiolabeling

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