

Answer 1:

Bibliographic Information

Poly(ethylene oxide)-modified poly(beta-amino ester) nanoparticles as a pH-sensitive system for tumor-targeted delivery of hydrophobic drugs: part 3. Therapeutic efficacy and safety studies in ovarian cancer xenograft model. Devalapally, Harikrishna; Shenoy, Dinesh; Little, Steven; Langer, Robert; Amiji, Mansoor. Department of Pharmaceutical Sciences, School of Pharmacy, Northeastern University, Boston, MA, USA. *Cancer Chemotherapy and Pharmacology* (2007), 59(4), 477-484. Publisher: Springer, CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 146:365355 AN 2007:57209 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Purpose: The objective of this study was to evaluate the anti-tumor efficacy and lack of systemic toxicity of paclitaxel when administered in pH-sensitive poly(ethylene oxide) (PEO)-modified poly(beta-amino ester) (PbAE) nanoparticles in mice bearing human ovarian adenocarcinoma (SKOV-3) xenograft. **Methods:** Paclitaxel-encapsulated PEO-modified PbAE (PEO-PbAE) nanoparticles were prep'd. by the solvent displacement method. PEO-modified poly(epsilon-caprolactone) (PCL) (PEO-PCL) nanoparticles were used as a non pH-responsive control formulation. Efficacy studies were conducted in SKOV-3 tumor-bearing athymic (Nu/Nu) mice at an equiv. paclitaxel dose of 20 mg/kg with the control and nanoparticle formulations. Safety of the drug when administered in the control and nanoparticle formulation was det'd. from blood cell counts and changes in body wt. of the animals. **Results:** The formulated paclitaxel-contg. PEO-PbAE and PEO-PCL nanoparticles had a particle size in the range of 100-200 nm and a surface charge of + 39.0 and - 30.8 mV, resp. After i.v. administration of paclitaxel in these formulations, the tumor growth was inhibited significantly. Both of the formulated nanoparticles tested have shown improved therapeutic efficacy as compared to the paclitaxel aq. soln. Addnl., significantly lower toxicity profile of paclitaxel was obsd. with PEO-modified nanoparticles as compared to the aq. soln. formulation. **Conclusion:** PEO-modified PbAE nanoparticles are a unique pH-sensitive drug delivery system that elicits enhanced efficacy and safety profile in solid tumor therapy.

Answer 2:

Bibliographic Information

Poly(Ethylene Oxide)-Modified Poly(beta-Amino Ester) Nanoparticles as a pH-Sensitive System for Tumor-Targeted Delivery of Hydrophobic Drugs: Part 2. In Vivo Distribution and Tumor Localization Studies. Shenoy, Dinesh; Little, Steven; Langer, Robert; Amiji, Mansoor. Department of Pharmaceutical Sciences, School of Pharmacy, Northeastern University, Boston, MA, USA. *Pharmaceutical Research* (2005), 22(12), 2107-2114. Publisher: Springer, CODEN: PHREEB ISSN: 0724-8741. Journal written in English. CAN 144:239618 AN 2005:1335780 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

This study was carried out to det. the biodistribution profiles and tumor localization potential of poly(ethylene oxide) (PEO)-modified poly(beta-amino ester) (PbAE) as a novel, pH-sensitive biodegradable polymeric nanoparticulate system for tumor-targeted drug delivery. The biodistribution studies of PEO-modified PbAE and PEO-modified poly(epsilon-caprolactone) (PCL), a non-pH-sensitive polymer, nanoparticle systems were carried out in normal mice using 111indium-oxine [¹¹¹In] as a lipophilic radiolabel encapsulated within the polymeric matrix, and the distribution of the nanoparticles was studied in plasma and all the vital organs following i.v. administration. Solid tumors were developed on nude mice using human ovarian carcinoma xenograft (SKOV-3) and the change in concns. of tritium [³H]-labeled paclitaxel encapsulated in polymeric nanoparticles was exam'd. in blood, tumor mass, and liver. Study in normal mice with a gamma-emitting isotope [¹¹¹In] provided a thorough biodistribution anal. of the PEO-modified nanoparticulate carrier systems, whereas ³H-paclitaxel was useful to understand the change in concn. and tumor localization of anticancer comp'd. directly in major sites of distribution. Both PEO-PbAE and PEO-PCL nanoparticles showed long systemic circulating properties by virtue of surface modification with PEO-contg. triblock block copolymer (Pluronic) stabilizer. Although the PCL nanoparticles showed higher uptake by the reticuloendothelial system, the PbAE nanoparticles effectively delivered the encapsulated payload into the tumor mass. PEO-modified PbAE nanoparticles showed considerable passive tumor targeting potential in early stages of biodistribution via the enhanced permeation and retention (EPR) mechanism. This prompts a detailed biodistribution profiling of the nanocarrier for prolonged

periods to provide conclusive evidence for superiority of the delivery system.