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Utility of Gamma Camera as an Effective Non-Invasive Imaging Modality for Docetaxel loaded Liposomal Chitosan Nanoparticles: Synthesis and the In-Vivo trafficking in Animal Model.

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Background: The physicochemical properties of drug loaded nanoparticles in physiological system are important determinants for their in vivo distribution and drug delivery efficiency. Stability of nanoparticles in blood serum remains a significant challenge for successful delivery to target tissue. Analysis of intra-biliary infusion of nanoparticles within two-compartmental pharmacokinetic modeling revealed efficient retention in the liver and minimal leakage from the liver to the blood stream. Our aim was to demonstrate the utility of Gamma camera as an effective noninvasive imaging modality for the biodistribution of docetaxel loaded liposomal chitosan nanoparticles.

Methodology: Folic acid thiolated chitosan was synthesized via EDAC coupling at pH-5.0 and purified by a dialyzing membrane. NPs were partially oxidized 1h with stirring at room temperature, tween 80 was added to make an emulsion. Folic acid was grafted to TCS. The docetaxel was loaded as cross linkage using TPP (1%) solution in 500ml DCM, the weighed amount of lyophilized liposomes were suspended in 1mg/ml solution of FA-TCS and stirred for 4 hours for proper coating through electrostatic interaction between liposomes and FA-TCS. The coated liposomes were separated through ultracentrifugation. The Docetaxel loaded liposomal Thioglycolated chitosan were characterized for hydrodynamic diameter and surface zeta potential and their Surface morphology was studied with electron microscope (FEI Nova NanoSEM 450). The encapsulation efficiency was calculated by ACN: MeOH: Buffer, and quantified by HPLC-PDA. The in-vivo pharmacodynamic study was prepared docetaxel loaded liposomal thioglycolated chitosan (FORM-A) with freshly eleuted Tc-99m and docetaxel labeled alone with Tc-99m and then loaded afterwards on liposomal thioglycolated chitosan (FORM-B), by an optimized protocol to retain their favorable physicochemical properties. Radio labeling efficiency was measured by TLC-SG and methanol using BIOSCAN-TLC scanner coupled with PMT detector. The radio labeled nanoparticle complexes (avg. dose = 58±10MBq) were orally given to the animal model. Planer and static gamma images were acquired at the interval of 30 minutes, 1, 2, 3, 4, 24 and 36 hours for the localization of drug absorption and delivery site. The docetaxel drug absorption rate was quantified by HPLC.

Results and Discussion: The drug loaded liposome were successfully coated with FA-TCS, confirmed by change in zeta potential. Encapsulation efficiency indicated that liposomal formulations showed higher value above 70% as compared to chitosan-TGA. The radio-labeling efficiency of both formulations measured by TLC was 99.2%. Gamma Camera acquisition quantified as activity versus time curve indicated that the FORM-A was localized in gut after 2 hours of administration and HPLC quantification confirmed that 63% of the drug was absorbed at 2 hours of administration, FORM–B images showed that the 68.2% of drug was localized in lungs, 23.2 % in liver and 8.6% was excreted through kidney, confirmation by HPLC quantification indicated slow release of drug till 36 hours.
Conclusion: The use of gamma imaging can help to locate the specific site of absorption of nanoparticles and drug release while HPLC helps to quantify accurate assessment of drug release in general body circulation.

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