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A novel anisamide anchored nanocarrier for site specific/ targeted lung cancer therapeutic interventions

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Gemcitabine (2',2'-difluorodeoxycytidine) is a deoxycytidine analog with significant antitumor activity against variety of cancers including non-small cell lung cancer. However, rapid metabolism and shorter half-life of drug mandate higher dose and frequent dosing schedule which subsequently results into higher toxicity. Therefore, there is a need to design a vector which can reduce the burden of frequent dosing and higher toxicity associated with the use of gemcitabine. In this study, we investigated the possibility of improving the targeting potential by employing the surface modification on CTS/PEG NPs. We demonstrate formulation and characterization of chitosan/poly (ethylene glycol)-anisamide (CTS/PEG-AA) and compared its efficiency with CTS/PEG and free gemcitabine. Our results reveal its sizeable compatibility, comparatively less organ toxicity and higher antitumor activity *in vitro* as well as *in vivo*. This wealth of information surfaces the potential of CTS/PEG-AA nanoparticles as a potent carrier for drug delivery. In brief, this novel carrier opens new avenues for drug delivery which better meets the needs of anticancer research.

A lung-targeted drug delivery NPs (CTS/PEG-AA) composed of PEG-AA and CTS could be prepared conveniently by the ionic gelation process. The results of the study indicate targeting prospective, spatial delivery, amplified bioavailability and elevated retention potential of the formulation in tumor tissues. The presence of sigma receptors presents an exclusive platform and accordingly manifold replica of ligand can be used to facilitate targeting. These NPs accumulated particularly in the tumor, and maintained at a high level. This is remarkably higher than that of the NPs without the AA. Moreover, the *in vitro* cell uptake results showed that the introduction of AA to the CTS/PEG NPs could significantly increase the affinity of particles and the content therein to human lung carcinoma cells. In addition, the GEM-loaded CTS/PEG-AA NPs showed remarkable cytotoxicity towards A549 cells (*in vitro*), and could effectively inhibit tumor growth in A549 cell-bearing mice. Finally the present study reveals the prospective of anisamylated CTS/PEG NPs as efficient vectors to ferry large doses of anti-cancer drug. *In vitro* studies depict the sustained release nature of formulation. The developed CTS/PEG-AA nanoparticulate system demonstrated minimal toxicity in the tested area. This indicates that AA facilitates targeted delivery of anti-cancer drug to tumor sites, with reduced access to non-tumor tissues. Thus optimal therapeutic response, improved therapeutic efficacy may be attained with the interception of minimal side effects.

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