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Et al.

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Pancreatic cancer (PanCa) has a dismal prognosis with five-year survival rates under 5%. PanCa is usally diagnosed at very late stages and even if diagnosed early, surgery is rarely an option. These factors contribute towards the bleak statistics for PanCa Chemo and radiation treatments having deleterious side-effects. There is therefore a clinical, unmet need for novel, targeted treatments with low morbidity in PanCa. Gemzar® (gemcitabine-HCl) is an FDA (Food and Drug Administration) approved chemotherapeutic drug that has been used to treat PanCa. However, intrinsic and acquired chemoresistance to gemcitabine contribute to the poor prognosis of PanCa. A combination of Abraxane® (albumin-stabilized paclitaxel nano-formulation) with gemcitabine has shown survival benefits and has now become the first line treatment for PanCa. Desmoplasia is a fundamental characteristic of PanCa that contributes significantly to its chemoresistance, making drug delivery to PanCa cells difficult. Nanomedicines combining multiple drugs can be designed to overcome this hurdle. This project aims at developing a targeted nanomedicine by using a combination of gemcitabine and paclitaxel encapsulated in polymeric nanoparticles for the treatment of PanCa. Oil/ water emulsion technique was employed for the preparation of poly (lactic-co-glycolic acid) (PLGA) nanoparticles encapsulating gemcitabine and paclitaxel. Synthesis protocols yielded drug-loaded PLGA nanoparticles with an average diameter less than 200 nm, with encapsulation efficiencies ranging from 40-70%. In vitro tests for cell viability studies using the MTT assay demonstrated lower cell viability in AsPC-1 cells when treated with these nano-formulations as compared to their free-drug counterparts. Current studies include conjugating drug-loaded PLGA-polyethylene glycol-Maleimide nanoparticles with transferrin peptide for targeted therapy, which is expected to prove more efficacious when tested for cell viability in vitro than its non-targeted formulations that have been obtained. These results therefore certify this nanotherapeutic approach as a potential therapy for PanCa.

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