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Co-delivery of squalenoyl-gemcitabine and paclitaxel by thermo-responsive polymeric micelles to pancreatic cells *in vitro*

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Pancreatic cancer is one of the most lethal malignancies with very low survival rate. Despite having low incidence rates it ranks as the fifth most common cause of cancer mortality. The aim of chemotherapy in pancreatic cancer is to increase the survival time and the quality of patient's life. However, systemic toxicity occurs due to the distribution of the drugs non-specifically in the body which affect both normal and tumor cells. Targeted chemotherapy can be achieved by protecting the anti-cancer drugs in systemic circulation and delivering them to the tumor site by the use of nanoparticles. Thermo-responsive polymeric micelles are nanoparticles that consist of a hydrophobic core in which lipophilic drugs can be encapsulated and a thermo-sensitive hydrophilic corona that prevents the interaction of the carriers with the blood proteins and also allows for thermally triggered drug release specifically at the tumor sites. In this research, novel thermo-responsive block copolymers, poly[(di(ethylene glycol) methyl ether methacrylate-co-poly(ethylene glycol) methyl ether methacrylate300)-b-poly(2-ethylhexyl methacrylate)] [poly(diEGMA-co-OEGMA300)-b-PEHMA], were prepared by reversible addition fragmentation chain transfer (RAFT) polymerization. Poly(diEGMA-co-OEGMA300)-b-PEHMA self-assembled into micelles which were co-loaded with two anti-cancer drugs, squalenoyl-gemcitabine [(Sq-GEM), a hydrophobized amino-protected derivative of gemcitabine (GEM)] and paclitaxel (PTX) in order to exert combined and synergistic anticancer activity. The drug loaded micelles had a low critical micelle concentration (20 mg/L) and showed high colloidal stability. The drug release studies showed a thermally controlled profile where the release increased 2 orders of magnitude above the polymers' lower critical solution temperature (LCST) at 40°C for both sq-GEM and PTX. *In vitro* cytotoxicity assays (MTT assay) on MiaPaCa-2 pancreatic cancer cell line showed a synergistic effect of combinational co-delivery of sq-Gem and PTX with significant decrease of cells' viability compared to cells treated with each drug separately or with drug loaded micelles below their LCST. Potentially, our proposed concept could pave the way for the further development of thermally activated nano-formulations for targeted therapies with drug cocktails of difficult-to-treat tumor types.

Biography

Mandana Emamzadeh (BPharm, MSc) is a PhD student of Cancer Nanomedicine at UCL School of Pharmacy, London. Her area of focus is thermo-responsive smart nano-carriers for drug delivery. She has her expertise in thermo-responsive polymeric micelles and polymer modified thermo-responsive liposomes. She has been synthesizing novel nano-carriers which are able to co-deliver combination of anti-cancer drugs. Her research is expanding by incorporation of gold nanoparticles to synthesize further stimuli-responsive nano-carriers.

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