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Gigi N C Chiu, J Pharm Drug Deliv Res 2017, 6:4 (Suppl)
DOI: 10.4172/2325-9604-C1-020

International Conference and Exhibition on

Nanomedicine and Drug Delivery

May 29-31, 2017 Osaka, Japan

Lipid-dendrimer hybrid nanosystems as smart carriers of anti-cancer agents

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Statement of the Problem: Developing novel nanohybrids of lipids and hyperbranched polymeric structures called dendrimers has been emerged as an attractive approach in the design of smart drug delivery systems for anti-cancer drugs, including both hydrophobic and hydrophilic agents. In this study, we aim to show the ability of such nanohybrid systems in improving the therapeutic activity of encapsulated drugs by controlling drug release that could yield synergistic cancer cell killing effect.

Methodology: The nanohybrids were made from PC-based lipids and the PAMAM dendrimers in appropriate mole ratios via a sonication step. Paclitaxel (PTX), gemcitabine (GEM) and cisplatin (CIS) was used in this study. Physical characteristics, including size, zeta potential, drug encapsulation efficacy, and drug release in simulated physiological fluids, were determined. Viability of human ovarian cancer cells post drug treatment was determined by MTT viability assay. The combination index (C.I.) was computed to determine synergistic anti-cancer activity of drug combinations. *In vivo* therapeutic activity was determined in a human ovarian tumor xenograft model in SCID mice.

Findings: The drug-loaded nanohybrids displayed diameters ranging 40-200 nm, depending on the type of dendrimer used. The polydispersity indices reflecting the size distribution were <0.50. The encapsulation efficiencies for PTX alone, PTX/CIS or GEM/CIS combinations were >70%. The potency of PTX could be significantly improved when presented in the nanohybrid system, whereby PTX and PAMAM G4.0 acted synergistically in killing the ovarian cancer cells. Despite a 10-fold lower PTX dose, a 50% increase in the median survival time was observed in mice treated with PTX-loaded nanohybrid system. Sequential release of drug combinations was observed from the nanohybrids, and such release properties resulted in synergistic anti-cancer cell killing, whereby the C.I. was <1.0.

Conclusion: The lipid-dendrimer nanohybrid systems could pave way for the development of multifunctional delivery systems for cancer therapy.

Biography

Gigi N C Chiu obtained her BSc (Pharm) and PhD from the Faculty of Pharmaceutical Sciences, University of British Columbia, Canada. She completed her 2-year Post-doctoral fellowship at the BC Cancer Research Center, and joined NUS Department of Pharmacy subsequently. Her research is focused on the design and development of various nanoscaled drug delivery platforms to improve the activity of therapeutic agents. These delivery platforms include: 1) Liposomes and lipid nanoparticles, 2) polymers and dendrimers, and 3) carbon-based nanomaterials, which are developed for applications in cancer therapy, modulation of drug transport and pharmacokinetics, and culturing of stem cells. She has received research funding from various national agencies, including National Medical Research Council, Economic Development Board, and Agency for Science, Technology and Research (A*STAR). She has published 50 research articles in the field of Drug Delivery and Nanomedicine, and received the NUS Faculty of Science Young Scientist Award in 2012.

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