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Core-shell solid lipid nanoparticles for the targeted delivery of paclitaxel: A proof-of-concept study in breast cancer cells

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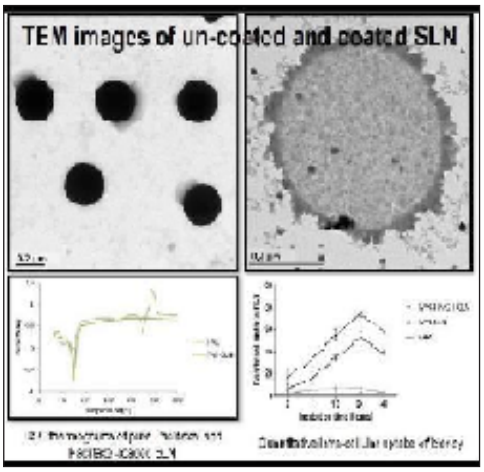

Statement of the Problem: Paclitaxel (PAX) is a chemotherapy agent, effective in the treatment of a broad range of human malignancies. PAX has an anti-angiogenic activity through inhibiting vascular endothelial-cell proliferation, motility and cord formation, at extremely low concentrations. Yet, side effects including hypersensitivity reactions, neurotoxicity, cardiotoxicity and nephrotoxicity, are common and are Carrier-Related/(CrEL) Multi-Drug Resistance (MDR) resulting in chemotherapeutic failure has been reported. Cost is an issue as well. Hence, it is necessary to develop an alternative formulation fit for controlled PAX delivery. SLN (solid lipid nanoparticles) as potential anti-cancer drug delivery nanocarriers, exhibit a great superiority to modulate drug release, improve anti-cancer activity and overcome MDR. We developed a novel natural polymer-lipid hybrid formulation consisting of SLN as core and chitosan-hyaluronic acid (CH-HA) as a shell, with HA as the outmost layer, to enhance selectivity towards HA receptors in MCF-7 cells.

Aim: To investigate the potential of modified SLN for the delivery of PAX.

Method: SLN loaded with PAX were prepared via high-pressure hot homogenization. Formulation parameters were optimized to obtain a high-quality delivery system. Selectivity towards HA receptors was tested in a breast cancer cell line.

Findings: Stable, reproducible and positively-charged nanoparticles resulted. Findings reveal that CH-HA-coated SLN facilitated the targeting, cellular uptake and the time-/dose-controlled delivery/release of PAX, enhancing intrinsic chemotherapeutic activities. CH exhibits increased uptake efficiency by negatively-charged cancer cell membranes due to electrostatic interactions. HA is a bio-adhesive compound capable of binding with high affinity to cell surface and intracellular receptors.

Conclusion: SLN are suitable carrier candidates for nano oncology given their localized and potent cytotoxic potential overcoming MDR cancer cells. CD44, an HA receptor, is overexpressed in cancer stem cells, therefore, targeting CD44 using HA seems as a fine strategy to eliminate cells accountable for treatment failure and cancer recurrence.

Biography

Ziyad S Haidar is a Full Professor of Biomaterials and Tissue Engineering and the Scientific Director of the Faculty of Dentistry, Universidad de los Andes in Santiago de Chile. Concurrently, he is the Founder and Head of the Biomaterials, Pharmaceutical Delivery and Cranio-Maxillo-Facial Tissue Engineering Laboratory/Research Group (BioMAT'X Chile). He also serves as the Head of Innovation at the Centre of Biomedical Investigation and Innovation and a Faculty Member in the Doctoral Program (BioMedicine) at the School of Medicine. He is a Visiting Professor at the Division of Maxillofacial Surgery at the Universidad de la Frontera in Temuco. He is a trained Dentist, Implantologist and an Oral and Maxillofacial Surgeon with a PhD in Nano biomaterials, Pharmaceuticals and Tissue Engineering from McGill University, Montreal, Canada. He is an international speaker with more than 125 publications, conference proceedings, text-books, patents and is an Editorial Board Member of several national and international peer-reviewed scientific journals.

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