Maria Manuela Gaspar et al., J Pharm Drug Deliv Res 2017, 6:3 (Suppl)
http://dx.doi.org/10.4172/2325-9604.C1.017

Therapeutic potential against metastatic melanoma of a copper-based aquaporin inhibitor nanoformulated

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Statement of Problem: Clinical and preclinical studies evidence the overexpression of aquaporin (AQPs) in a high number of cancers. In this sense, the development of selective AQP inhibitors represents an alternative therapeutic strategy for these pathologies. Metallodrugs of copper and gold are potential candidates to fulfill this need. However, to promote a preferential target to tumor sites *in vivo*, the design and development of novel technologies based on nanostructured materials such as liposomes acting mainly as vectors for metallodrugs delivery represents a stimulating research area. Cuphen, a potent copper-based aquaporin inhibitor, was selected as metallodrug in the present work to be nanoformulated in liposomes.

Methodology: Cuphen was incorporated in liposomes by the dehydration-rehydration method. Cuphen liposomes were characterized in terms of mean size, poly dispersion index, zeta potential and encapsulation parameters using different lipid compositions. The ability of Cuphen to induce cancer cell death was evaluated by MTS and ViaCount assays against several human and mouse cell lines (A431, MNT-1, HaCaT, B16F10 and C26). The hemolytic activity of Cuphen in free and liposomal forms using EDTA-preserved peripheral human blood from voluntary donors was carried out. *In vivo* toxicity studies were performed in healthy mice and the therapeutic effect was evaluated in a murine melanoma xenograft model.

Findings: *In vitro* studies illustrated the anti-proliferative effects of Cuphen in different cancer cell lines. *In vivo* studies revealed no toxic effects after parenteral administration in healthy mice. A higher anti-cancer effect in a murine melanoma xenograft model in terms of survival rate was observed for the metallodrug nanoformulated in long circulating liposomes.

Conclusion: Cuphen liposomes are considered as a very attractive nano-formulation with therapeutic potential against melanoma due to their preferential extravasation and accumulation in solid tumors.

Biography

Maria Manuela Gaspar has completed her PhD in 2005 in Pharmaceutical Technology at University of Lisbon and Post-doctoral studies at University of Dublin, Trinity College. She is a Researcher at Research Institute for Medicines, iMed.ULisboa, University of Lisbon. The area of research has been focused on "Design, development and biological evaluation of drug delivery systems for improving the therapeutic index of incorporated molecules in infectious, inflammatory and cancer animal models". She is a co-author of numerous patents, papers in peer-reviewed journals and book chapters.

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