Juliana Damasceno Oliveira et al., Nano Res Appl 2018, Volume 4
DOI: 10.21767/2471-9838-C3-015

Characterization, stability and cell viability tests on ionic-gradient liposomes designed for the delivery of etidocaine

Juliana Damasceno Oliveira, Ligia Nunes Moraes Ribeiro, Verônica Muniz Couto and **Eneida de Paula**
University of Campinas, Brazil

Statement of the Problem: Liposomes are lipid carriers widely used in drug-delivery, and a number of liposome-based products have been approved for clinical application, so far. Local anesthetics interact with liposomes, distributing themselves in the lipid bilayer and in the inner aqueous core, prolonging the anesthesia time. In ionic gradient liposomes (IGL) the ionizable drug is loaded in preformed vesicles that exhibit a trans-membrane ionic gradient leading to high drug upload and, subsequently, prolonged drug release.

Objectives: The objective of this work is to develop IGL for the sustained release of etidocaine (EDC).

Methodology: Large unilamellar vesicles (LUV, 20 mM) composed of soy phosphatidylcholine:cholesterol (6:4 mol%) plus 250 mM sulfate gradient, were prepared for the upload of 0.5% EDC. Dynamic light scattering (DLS), nanotracking analysis (NTA) and transmission electron microscopy (TEM) were used to characterize the liposomes' size, polydispersity (PDI), zeta potential (PZ) and number of particles. The *in vitro* release of EDC was measured in Franz diffusion cells, at 37°C. Cell-viability assays were done in primary cell cultures (Schwann or sciatic nerve cells from Wistar rats).

Results: IGL were successfully prepared with size, PDI, PZ and concentration in the range 500 nm, 0.2 and -20 mV, and 4-5.10^{12}, respectively, and they kept stable over 60 days at 37±37°C. TEM data revealed the spherical morphology of the liposomes that was able to encapsulate 41% of EDC. At 37°C, the time for 100% release of the anesthetic increased from 3 h (EDC in solution) to 24h in IGL_{EDC}. Cytotoxicity tests revealed that encapsulation into liposomes decreased the intrinsic toxicity of the anaesthetic.

Conclusions: IGL are very interesting carriers for the delivery of local anesthetics. In this study sulphate-gradient LUV (large unilamellar vesicles) were found promising increase the upload, and release of etidocaine. *In vivo* tests are under course to evaluate the antinociceptive effects of the formulation.

Recent Publications

1. Allen T M and Cullis P R (2013) Liposomal drug delivery systems: From concept to clinical applications. Advanced Drug Delivery Reviews. 65(1):36-48.
2. Bulbake U et al. (2017) Liposomal formulations in clinical use: An updated review. Pharmaceutics. 9(2).pii:E12.
3. de Paula E et al. (2010) Drug delivery systems for local anesthetics. Recent Patent on Drug Delivery Formulation. 4(1):23-34.
4. de Paula E et al. (2012) Micro and nanosystems for delivering local anesthetics. Expert Opinion on Drug Delivery. 9(12):1505-1524.
5. Grant G J et al. (2004) A novel liposomal bupivacaine formulation to produce ultralong-acting analgesia. Anesthesiology. 101(1):133-137.

Biography

Juliana Damasceno Oliveira completed her Bachelor's Degree in Pharmacy. She is currently a PhD student in the Department of Biochemistry and Tissue Biology at the Institute of Biology of University of Campinas (UNICAMP), Brazil. She has experience in the areas of pharmacology, biochemistry and pharmaceutical technology - working in the development of drug-delivery systems, DDS, mainly ionic gradient liposomes – and biophysical methods applied to the study of the structural, physicochemical, mechanical and biological properties of DDS.

damasceno.jufarmacia@gmail.com