PLGA nanoparticles as paclitaxel delivery system for the treatment of breast cancer

Laura Cabeza[1,2], Julia Jiménez-Lopez[1,2], Mazen El-Hammadi[3], Gloria Perazzoli[1,2], María Carmen Leiva[1,2], Lucia Martín-Balderas[3], Raul Ortiz[4], Jose Prados[1,2], Consolación Melguizo[1,2]

[1]Institute of Biopathology and Regenerative Medicine (IBIMER), 18100 Granada, Spain; [2]Biosanitary Institute of Granada (ibs.GRANADA), SAS-Universidad de Granada, Granada, Spain; [3]Department of Pharmacy and Pharmaceutical Technology, University of Sevilla, 41012 Sevilla, Spain; [4]Department of Health Science, University of Jaén, 23071 Jaén, Spain
Contact@E-mail: melguizo@ugr.es

Abstract

The treatment of breast cancer with the chemotherapeutic drug paclitaxel (PTX) is not entirely effective because of its low specificity for tumor tissues resulting in nonspecific toxicity [1]. Besides, the high PTX insolubility requires the use of the solvent Cremophor® EL which produces severe side effects [2]. Nanotechnology allows the use of nontoxic drug transporters that may enhance the specificity of drug for tumor tissues and avoid the use of toxic solvents. One example of these carriers are poly(lactic-co-glycolic acid) (PLGA) nanoparticles, one of the nanocarriers most studied in nanomedicine because of their biodegradability and good biocompatibility [3]. Thus, the aim of this study is to study the antitumor effect of drug PTX carried by PLGA nanoparticles and to compare with the free drug.

For this purpose toxicity studies were carried out by hemolysis assay with human erythrocytes exposed to PLGA blank nanoparticles. Furthermore, human breast cancer cell lines (MCF-7, MDA-MB-231) and a no tumor cell line (MCF-10A) were treated with PTX, PTX-PLGA, and PLGA for cytotoxicity and cell cycle assays. The cellular uptake of nanoparticles was studied with PLGA nanoparticles loaded with the fluorophore nile red (NR) by confocal microscopy and flow cytometry. Also, multicellular tumor spheroids were generated and exposed to the same treatments above for a preliminary study before the *in vivo* assays.

The results showed a good biocompatibility of PLGA nanoparticles in the hemolysis assay and the proliferation study with cell lines. It was also observed a higher cytotoxic activity of PTX when is loaded to PLGA nanoparticles. Tumor cells treated with PTX-PLGA showed a greater reduction of the PTX IC_{50} value (58,74% MCF-7, 23,5% MDA-MB-231), however the pattern of cell cycle was not altered. This higher antitumor effect was also observed in multicellular tumor spheroids. Cellular internalization studies showed a higher cell uptake of NR when is loaded to PLGA nanoparticles in comparison with a NR solution. These differences are greater with high exposure times.

From these preliminary results, we suggest that PTX-loaded nanoparticles could be a safe and useful tool to be used for the treatment of breast cancer because of their biocompatibility, good tumor cell uptake and higher drug cytotoxicity.

References

[1] Gornstein, E., and Schwarz, T.L., Neuropharmacology, **76** (2014) 175–183.
[2] Weiszhár, Z., Czúcz, J., Révész, C., Rosivall, L., Szebeni, J., Rozsnyay, Z., Eur. J. Pharm. Sci., **45** (2012) 492–498.
[3] Danhier, F., Ansorena, E., Silva, J.M., Coco, R., Le Breton, A., Préat, V., J. Control. Release, **161** (2012) 505–522.

Figures

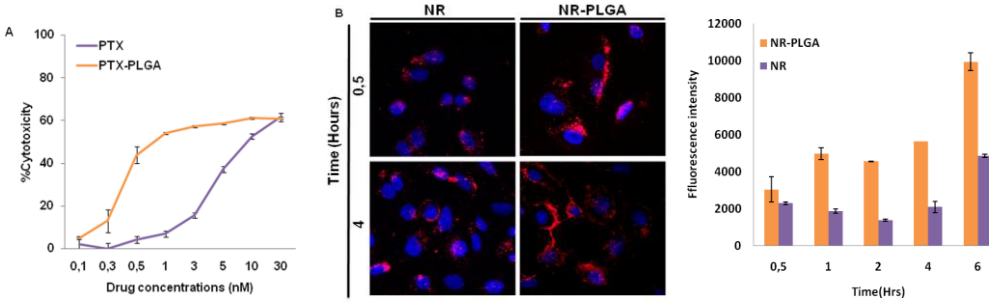

Figure 1. MDA-MB-231 prolifferation study (A), confocal images of MCF-7 cells treated with NR and NR-loaded PLGA nanoparticles (B) and MCF-7 cell uptake study by flow cytometry (C).