Tripalmitin and p4VP nanoparticles as PTX delivery systems for breast cancer treatment

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Paclitaxel (PTX) is one of the chemotherapics of election for the treatment of breast cancer. However, this drug presents some limitations as low solubility, poor tumor specificity and the appearance of side effects.[1] The use of nanoparticles (NPs) is an asset to improve PTX antitumor efficacy, avoid toxicity and target the drug action specifically on the tumor tissue.[2]

For these reasons, we have developed a delivery sistem, consisting on Tripalmitin solid lipid NPs (Tripalm-NPs) for PTX encapsulation (Tripalm-NPs-PTX). These NPs have been assayed in a wide range of breast tumor models, consisting on a human breast cancer cells (MCF7); multicellular tumor spheroids (MTS) derived from MCF7, that mimick a tumor mass; a resistant cells line through P-glycoprotein (P-gp) overexpression (HCT-15) and breast cancer stem cells (CSCs) obtained from MCF7, which are very often responsible for recurrences and recidives.

In order to asses the antitumor efficacy of these PTX-loaded NPs, treatments were added at increasing concentractions and a cytotoxicity assay was performed by the sulphorrodamine B method after 96 hours. MTS were obtained from MCF7, and their volume after being treated were monitored by microscopy at different times of the experience. Finally, for CSCs obtention, MCF7 were incubated with an induction medium for two weeks, treatments were administered for 48 hours, and the cytotoxicity assay was carried out using a Cell Counting Kit (CCK-8, Dojindo, Japan).

The results obtained prove an improvement in the antitumor efficacy of PTX after its incorporation in Tripalm-NPs-PTX over MCF7 cells and MTS. Further, they were also able to increase PTX effect against a resistant cell line, and CSCs, with a significant ($p<0.001$) decrease in cell viability in all the cases.

According to these results, Tripalm-NPs-PTX are very promising delivery systems to improve breast cancer treatment efficacy and avoid treatment failure.

References

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[2] Surapaneni, M. S.; Das, S. K.; Das, N. G., ISRN Pharmacol., 10 (2012) 12.

Figures

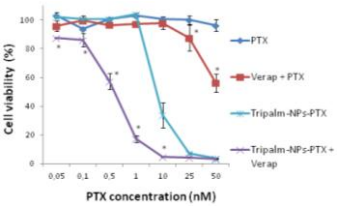

Figure 1: Cell viability (%) of HCT-15 resistant cells after exposure to PTX, Tripalm-NPs-PTX and their combination with verapamil, a P-gp inhibitor. *Significant differences ($p<0.001$) between treatments with or without verapamil.

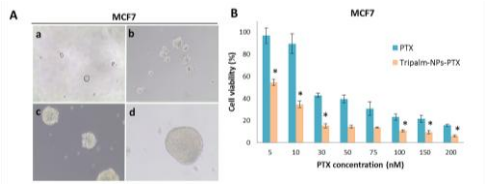

Figure 2: A) Images of breast CSCs after a)1, b)3, c)6, and d)13 days of induction (10x). B)CSCs viability (%) after treatment with increasing concentrations of PTX and Tripalm-NPs-PTX (48 hours). *Significant differences ($p<0.001$) between both treatments.