

Improve of the paclitaxel activity by the use of polymeric nanoparticles of lactic and glycolic acid: assay in multicellular spheroids from lung cancer cells

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Paclitaxel (PTX) is a cytotoxin used as a drug of choice for the treatment of various types of solid tumors, including breast and lung cancer. However, its commercial formulation (Taxol®) has been associated with several side effects such as hematologic toxicity, bone marrow depression, and painful peripheral neuropathy. In this work, a promising type of polymeric nanoparticles of lactic and glycolic acid loaded with this drug (PLGA-PTX) for the treatment of lung cancer is proposed to solve these limitations. The results of proliferation assays showed significant dose reduction IC₅₀ with PLGA-PTX up to 3.63 and 3.79 times lower in two human lung tumor cell lines A549 and NCI-H460, compared to free PTX. No inhibition was observed in the growth of any cell lines with blank nanoparticles. For cellular uptake studies with fluorescence microscopy, A549 was incubated with Nile red (NR) and NR-loaded NPs at different times. The results obtained suggest that NP-PTX facilitate the incorporation of NR into the cell compared with free NR. Finally, multicellular tumour spheroids (MTS) assays in A549 were performed and MTS were treated with PTX, PLGA-PTX and blank NPs at the IC₅₀ dose of free PTX. MTS growth was monitored with imaging microscopy the apoptosis induced was analyzed by a TUNEL assay. PLGA-PTX caused a significant reduction in the volume of MTS (73%) in comparison to free PTX (46%). In addition, the number of apoptotic cells was higher in MTS treated with PLGA-PTX than in those treated with PTX. The set of results presented in this work suggest that the association of paclitaxel with nanoparticles improves the antitumor effect of the drug and facilitates its incorporation into the tumor cells.

References

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Figures

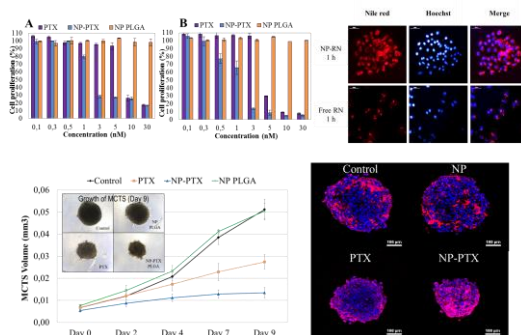


Figure 1: Proliferation assays in A549 (A) and NCI-H460 (B) cell lines. **Figure 2:** Intracellular uptake with RN and NP-loaded RN in A549 cells. **Figure 3:** Analysis of the PLGA-PTX effect in MCTs' growth of A549 cells. **Figure 4:** TUNEL assay in MCTs of A549 cells to detect apoptosis induced (in red).