Enhanced delivery of Paclitaxel using PLGA nanoparticles: therapeutic effect in lung cancer cell cultures

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Lung cancer is the main cause of death by cancer worldwide. Paclitaxel (PTX), an antimitotic drug which causes the kidnapping of the cell in the G2 phase of the cell cycle, is widely administered with carboplatin or cisplatin for the treatment of choice for this type of cancer and other solid tumours. However, PTX has many limitations such as the small amount of drug that reach the site of action, poor stability or low solubility and produces many undesirable effects like neutropenia, neurotoxicity or hypersensitivity reactions. These limitations require the development of new delivery systems to encapsulate PTX. In this study, proliferation assays were performed with two human lung tumor cell lines (A549 and NCI-H460) and a human non-tumor cell line (L132), comparing the antiproliferative efficacy of PTX-loaded PLGA nanoparticles (NPs) and the free drug. The results obtained in proliferation assays showed significant dose reduction IC50 with NP-PTX up to 3.63 and 3.79 times lower in A549 and NCI-H460, and 2.96 times lower in L132, compared to free PTX. Moreover, important accumulations in G2 phase were observed in cell cycle assays in all cell lines treated with PTX-loaded PLGA NPs. Also, intracellular uptake studies with Nile red (NR) and NR-loaded NPs by fluorescence microscopy showed that NPs improved the incorporation of NR inside the cells at different incubation times. Finally, the MCTS assays showed a significant reduction in the volume of spheroids when these were treated with free PTX (46%) and NP-PTX (73%). No significant difference was observed between MCTS untreated and treated with blank NPs. In short, PLGA NPs provide a potential strategy as a mechanism for PTX encapsulation and could allow increasing the therapeutic index of this drug.

References

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Figures

1. Proliferation assays in A549 (A), NCI-H460 (B) and L132 (C) cell lines. **2**. Cell cycle assays in A549 (A) and L132 (B) cell lines. **3**. Intracellular uptake with RN and NP-loaded RN in A549 cells**. 4**. Analysis of the NP-PTX effect in MCTs of A549 cells.