PACLITAXEL LOADED LIPID NANOEMULSIONS FOR THE TREATMENT OF BRAIN TUMOUR

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Background: Lipid nanoemulsions have been increasingly used as carriers for poorly soluble drugs owing to their biocompatibility and biodegradability. Paclitaxel (PTX) is an anticancer drug with wide activity against many types of cancer. However, the poor solubility in water is a serious limitation of this drug. Taxol is an established marketed formulation of PTX, which represents the drug dissolved in a vehicle consisting of ethanol and Cremophor EL (polyoxyethylated castor oil). Unfortunately, the toxic effects of Cremophor EL (nephrotoxicity, neurotoxicity, hypersensitivity, etc.) represent a significant drawback. In this study, we investigated commercially available Total Parenteral Nutrition (TPN) nanoemulsions, namely Intralipid 20% (Fresenius Kabi, Germany) and Clinoleic 20% (Baxter Healthcare, USA) nanoemulsions as vehicles and solubilizers of PTX and studied the efficacy of formulations against glioma cell lines and normal glial cells.

Methods: PTX was loaded into the nanoemulsions via vortex-mixing for 5 min followed by bath-sonication for 2 h at 40°C (Drug concentrations of 0-6 mg/mL). Size analysis and zeta potential measurements were performed using dynamic light scattering and electrophoretic mobility respectively. The entrapped fraction of PTX was calculated using UV by subtraction of the non-entrapped fraction from the total drug amount after forcing the emulsions through 400 nm syringe filters and quantifying the drug retained in the filter. MTT studies were conducted to investigate cytotoxicity of the formulations against U87-MG (grade 4 glioma) and SVG-P12 (normal glial) cell lines.

Results: Size was highly dependent on nanoemulsion type, being in the range of 254 – 264 nm for Clinololeic and 283 – 295 nm for Intralipid, depending on PTX concentration and polydispersity was generally higher for the Intralipid emulsion. Zeta potential values were negative for both emulsions with more intense charge for the Clinoleic formulations. Drug entrapment values were in the range of 70–80% and 44– 57% using for the Clinoleic and Intralipid formulations respectively. PTX-loaded Clinoleic decreased the viability of U87-MG glioma cells to 6.4%, compared to only 21.29% using PTX-loaded Intralipid nanoemulsion. Both nanoemulsions were less toxic to normal glial cells (SVG-P12), indicating selectivity of the emulsions against malignant cells. The higher entrapment in the Clinoleic emulsion correlated with the higher activity of its formulations against malignant cells. The difference in activity between the two emulsions is attributed to their different composition.

Conclusions: Nanoemulsions are applicable vehicles for solubilizing PTX and acting selectively against malignant glioma cells. Moreover, the enhanced cancer targetability of nanoemulsions might be attributed to the nutritive value of lipids present in the nanoemulsions.