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Cellular uptake of targeted nanostructured lipid carrier (NLC) and cytotoxicity evaluation of encapsulated paclitaxel in HT29 cancer cells

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Background and Aims: Nanostuctured lipid carriers (NLC) based on mixture of solid lipids with liquid lipids are a new type of lipid nanoparticles, which offer the advantages of improved drug loading capacity and release properties. In present study, cholesterol nanoparticles with various tocopherol (vitamine E) contents were prepared and loaded with paclitaxel for targeted delivery to cancer cells. Cholesterol-rich nanoparticles that bind to low-density lipoprotein (LDL) receptors are selectively taken up by malignant cells that overexpress those receptors. The cellular uptake of the NLC and cytotoxicity of encapsulated paclitaxel were investigated in HT29cancer cells.

Methods: the effect of tocopherol content on Size, zeta potential, entrapment efficiency (EE), drug loading (DL) and release percent of NLCs was measured. The conjugate of octadecylamine–fluorescein isothiocyanate (ODA–FITC) was synthesized, and used as a marker to prepare fluorescent NLC. The cellular uptakes of fluorescent NLC were evaluated by fluorescence microscopy and the measurement of fluorescence intensity.

Results: The size and surface morphology of nanoparticles were significantly influenced by tocopherol content. As tocopherol content increased up to 45 wt%, the obtained particles showed pronounced smaller size and more regular morphology in spherical shape with smooth surface. Paclitaxel was loaded to the solid cores at a 10 w/w. The particle sizes and zeta potentials of optimized NLCs were around 200 nm and -17 Mv, respectively, suggesting that they would be suitable as a parenteral formulation. Incorporation of cholesterol enhanced the cellular uptake of the NLC and the cellular cytotoxicity of paclitaxel by improved endocytosis mediated by LDL receptor. Treatment of the HT29 colon cancer cell with paclitaxel loaded NLC yielded cytotoxicities comparable to those of a commercially available Cremophor EL-based paclitaxel formulation.

Conclusions: our optimized NLC may have a potential as alternative delivery system for parenteral administration of paclitaxel.

Keywords: Nanostructure lipid carrier; Cholesterol; Paclitaxel; Targeted drug delivery