World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:18, No:05, 2024

Optimizing the Effectiveness of Docetaxel with Solid Lipid Nanoparticles: Formulation, Characterization, in Vitro and in Vivo Assessment

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Abstract : Background: Docetaxel (DTX), a potent anticancer drug derived from the European yew tree, is effective against various human cancers by inhibiting microtubule depolymerization. Solid lipid nanoparticles (SLNs) have gained attention as drug carriers for enhancing drug effectiveness and safety. SLNs, submicron-sized lipid-based particles, can passively target tumors through the "enhanced permeability and retention" (EPR) effect, providing stability, drug protection, and controlled release while being biocompatible. Methods: The SLN formulation included biodegradable lipids (Compritol and Precirol), hydrogenated soy phosphatidylcholine (H-SPC) as a lipophilic co-surfactant, and Poloxamer 188 as a non-ionic polymeric stabilizer. Two SLN preparation techniques, probe sonication and microemulsion, were assessed. Characterization encompassed SLNs' morphology, particle size, zeta potential, matrix, and encapsulation efficacy. In-vitro cytotoxicity and cellular uptake studies were conducted using mouse colorectal (C-26) and human malignant melanoma (A-375) cell lines, comparing SLN-DTX with Taxotere®. In-vivo studies evaluated tumor inhibitory efficacy and survival in mice with colorectal (C-26) tumors, comparing SLNDTX withTaxotere®. Results: SLN-DTX demonstrated stability, with an average size of 180 nm and a low polydispersity index (PDI) of 0.2 and encapsulation efficacy of 98.0 ± 0.1%. Differential scanning calorimetry (DSC) suggested amorphous encapsulation of DTX within SLNs. In vitro studies revealed that SLN-DTX exhibited nearly equivalent cytotoxicity to Taxotere®, depending on concentration and exposure time. Cellular uptake studies demonstrated superior intracellular DTX accumulation with SLN-DTX. In a C-26 mouse model, SLN-DTX at 10 mg/kg outperformed Taxotere® at 10 and 20 mg/kg, with no significant differences in body weight changes and a remarkably high survival rate of 60%. Conclusion: This study concludes that SLN-DTX, prepared using the probe sonication, offers stability and enhanced therapeutic effects. It displayed almost same in vitro cytotoxicity to Taxotere® but showed superior cellular uptake. In a mouse model, SLN-DTX effectively inhibited tumor growth, with 10 mg/kg outperforming even 20 mg/kg of Taxotere®, without adverse body weight changes and with higher survival rates. This suggests that SLN-DTX has the potential to reduce adverse effects while maintaining or enhancing docetaxel's therapeutic profile, making it a promising drug delivery strategy suitable for industrialization.

Keywords : docetaxel, Taxotere®, solid lipid nanoparticles, enhanced permeability and retention effect, drug delivery, cancer chemotherapy, cytotoxicity, cellular uptake, tumor inhibition
Conference Title : ICPNDD 2024 : International Conference on Pharma Nanotechnology and Drug Discovery
Conference Location : Montreal, Canada
Conference Dates : May 23-24, 2024