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Optimization and Detailed Evaluation of Efficacy and Toxicity of Topotecan Nanoparticles

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Abstract—*Engineering a dream nanoparticle with specific affinity and specificity for tumor tissues along with reduced toxicity to the biological environment is quite challenging, hence needs to be addressed specifically. A proper insight into these features needs careful design and construction of a biodegradable nanocarrier with acceptable formulation aspects including the composition and its physicochemical properties. Here we report the formulation and optimization of topotecan hydrochloride (TOPO) in poly lactide-co-glycolide polymer(PLGA) forming TOPO NPs for improving the therapeutic efficacy as well as reduce the toxicity issues associated with the use of the native therapeutics. The optimized nanoparticles had a mean particle size of 158 nm nm and an entrapment efficiency of 58.9±1.4% along with a smooth surface morphology as investigated by TEM micrography. The formulated nanoparticles were found to be absolutely stable in the presence of serum as well as in simulated physiological pH and the acidic microenvironment of tumors with a sustained release of the entrapped chemotherapeutics for a period of 25 days. The acceptable mean size of the optimized TOPO NPs led to better internalization as well as superior cytotoxicity in the Lewings lung carcinoma cells (LLC) as compared to native TOPO. Additionally the nanoparticles showed appreciable tumor regression pattern with reduced haematological toxicity.*

Conclusively, the superior internalization in the tumor microenvironment leading to obvious cytotoxic effects and improved antitumor efficacy along with a reduced hemotoxicity profile identifies the suitability of using TOPO NPs as a promising candidate for cancer treatment investigation.