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(57) Abstract :
The present invention provides a receptor-targeted dual-drug solid lipid nanoparticulate delivery system for the treatment of colorectal carcinoma. The system comprises irinotecan and daidzein co-encapsulated within a biocompatible solid lipid nanoparticle (SLN) matrix, wherein the nanoparticle surface is functionalized with hyaluronic acid and bovine serum albumin to achieve selective binding to CD44, GP60 and SPARC receptors overexpressed in malignant colon tissues. This multireceptor targeting facilitates receptor-mediated endocytosis and enhanced intracellular accumulation of the therapeutic agents. The formulation is prepared using a microemulsion-based high-shear homogenization process followed by ultrasonication and lyophilization, producing nanoparticles with controlled size distribution, low polydispersity and high entrapment efficiency. The dual-drug combination exhibits synergistic antiproliferative activity, induces mitochondrial membrane depolarization, elevates intracellular reactive oxygen species levels and arrests the cell cycle at the G2/M phase. The lipidic core enables biphasic, colon-specific sustained release. In-vivo studies demonstrate restoration of mucosal architecture, reduced dysplasia and downregulation of tumor biomarkers, indicating improved oral bioavailability, reduced systemic toxicity and enhanced therapeutic efficacy.

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