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ABSTRACT

Glioma is an aggressive and invasive brain tumor with limited treatment success due to the presence of the blood–brain barrier and resistance to conventional chemoradiation. To address these challenges, thermoresponsive solid lipid nanoparticles (T-SLNs) were developed for the targeted and temperature-triggered delivery of 5-Fluorouracil (5-FU). Stearic acid and oleic acid were employed as the lipid matrix, lecithin served as a biocompatible emulsifier, and Poloxamer F68 was incorporated to impart thermoresponsive behavior and stabilize the formulation. The T-SLNs were prepared by a hot homogenization-ultrasonication method and evaluated for particle size, polydispersity index (PDI), encapsulation efficiency, and phase transition behavior. Differential Scanning Calorimetry (DSC) and light transmission studies confirmed the thermoresponsive nature of the nanoparticles, with a marked transition occurring in the mild hyperthermic range (42–45°C). Scanning Electron Microscopy (SEM) revealed a smooth, spherical morphology. In vitro release studies demonstrated a temperature-dependent drug release pattern, with significantly enhanced 5-FU release at elevated temperatures, simulating localized tumor hyperthermia. Release kinetics followed Korsmeyer-Peppas and Higuchi models, indicating diffusion-dominated mechanisms. Importantly, the T-SLNs showed potential for integration with adjuvant hyperthermia and radiation therapy, wherein localized heating not only promotes nanoparticle-triggered drug release but may also sensitize glioma cells to radiotherapy. Formulations F9 (SA:OA:L = 4:6:1) and F10 (SA:OA:L = 2:2:1) exhibited >75% release at 45°C, making them ideal candidates for thermally targeted drug delivery during hyperthermia-enhanced radiotherapy.

This study presents T-SLNs as a promising multifunctional platform capable of overcoming therapeutic resistance in glioma by combining controlled chemotherapy, localized hyperthermia,