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Thermoresponsive poloxamer-based nanocomposite hydrogels containing docetaxel for local chemotherapy

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ABSTRACT

Introduction: Nanostructured lipid carriers have been reported as promising delivery systems for enhancing localized docetaxel therapy. However, nanoparticles are generally unable to remain confined to the tumor following direct injection. Combining them with hydrogels offers a practical strategy to improve retention. Compared with pre-formed systems, *in situ*-forming hydrogels are easier to administer and can adapt to irregular tumor geometries. The difference between room and body temperatures underlies the most straightforward mechanism of their formation. Among thermoresponsive polymers, poloxamer 407 is favored for its biocompatibility, gelation behavior, and regulatory approval.
Objectives: To develop and characterize an injectable thermoresponsive nanocomposite hydrogel based on docetaxel-loaded nanostructured lipid carriers and poloxamer 407 for intratumoral drug delivery.
Methodology: The nanostructured lipid carriers dispersions were gelled with poloxamer 407 to produce a nanocomposite hydrogel, which was characterized for rheological behavior, injectability, microstructure, and *in vitro* drug release and gel erosion.
Results: A rapid sol–gel transition at 37°C (~52 s) was achieved, yielding an elastic and mechanically stable gel. Injection forces through 18-gauge and 21-gauge needles were within acceptable

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limits (< 20 N). Drug release was slightly slower and more sustained than that from the nanostructured lipid carriers (13.5 ± 1.1% versus 18.7 ± 3.5% after 48 hours). Moderate resistance to dissolution was observed *in vitro* during the first hours (~68% remaining weight at 3 hours), which may help delay nanoparticle clearance from the tumor site.

Conclusion: Overall, the results support the potential of the developed nanocomposite hydrogel for intratumoral delivery of docetaxel, pending validation and performance assessment *in vivo*. If successfully translated to the clinic, it could enhance the efficacy of chemotherapy while minimizing systemic toxicity, enabling more effective and localized cancer treatment.