

Article

Versatile SI-ATRP Growth of Methacrylate Brushes on Superparamagnetic Iron Oxide Nanoparticles Enables Methotrexate-Mediated Antineoplastic Activity in MCF-7 Cells

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Abstract

Background/Objectives: Superparamagnetic iron-oxide nanoparticles (SPIONs) bearing poly(methacrylate) brushes were synthesized via surface-initiated atom-transfer radical polymerization (SI-ATRP) as magnetically responsive nanoplatforms. Three brush architectures, poly(2-hydroxyethyl methacrylate) (PHEMA) and poly(poly(ethylene glycol) methacrylate) with six ethylene-oxide units (PPEGMA6) and ten units (PPEGMA10), were grown from a dopamine-anchored initiator and covalently loaded with methotrexate (MTX). **Methods:** Physicochemical characterization confirmed successful polymer grafting, tunable hydrodynamic size (185–1320 nm before MTX conjugation and 427–694 nm after), retained superparamagnetic properties (22–69 emu g^{−1}), and high drug payloads, with PPEGMA6 achieving 131 µg mg^{−1}. MTX conjugation induced partial compaction of the polymer shell yet maintained ζ-potentials conducive to colloidal stability. **Results:** In vitro assays showed negligible toxicity toward primary human fibroblasts, whereas MTX-decorated formulations induced a pronounced concentration-dependent cytotoxic effect in MCF-7 breast cancer cells, reaching 69% loss of viability—significantly higher than free MTX. Structure–activity analysis attributes the superior performance of PPEGMA6-MTX to its balanced brush density, high payload, and favorable surface charge. **Conclusions:** These findings demonstrate that precise modulation of polymer brush architecture via SI-ATRP yields SPION-based nanocarriers that integrate MRI visibility and the potential for magnetic guidance and targeted chemotherapy. The PPEGMA6-MTX construct is highlighted as a promising platform for future preclinical investigations.



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