POLYDOPAMINE-COATED NANOCOMPOSITE THERANOSTIC IMPLANTS FOR LOCALIZED CHEMOTHERAPY AND MR IMAGING

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Background: Postoperative adjuvant chemotherapy has been proven to improve long-term prognosis compared to surgery alone in the treatment of early and localized tumors. However, systematic chemotherapy often fails to achieve desirable clinical outcomes owing to physiological barriers to drug delivery, or harmful effects on healthy organs. Alternative delivery approaches are required to enhance efficacy. One suitable option is the use of implantable drug delivery (IDD) systems. However, concerns arise associated with the safety and efficacy of IDD systems. It is important to monitor the implants to avoid any risks of displacement and/or deterioration.

Methods: Implantable fibres incorporating methotrexate (MTX) and magnetic resonance imaing (MRI) contrast agents were developed. To prolong the drug release profile and enhance MTX stability over a prolonged period, here MTX was firstly loaded into layered double hydroxide (LDH-MTX) carrier particles by anion exchange. IDD systems, biodegradable PCL-based core-shell fibres loaded with LDH-MTX, were then produced by electrospinning. Unlike the majority of electrospun platforms reported where functional agents are encapsulated inside the bulk of the formulation, MRI contrast agents, superparamagnetic iron oxide nanoparticles (SPIONs) were then incorporated onto the surface of the fibres via post-fabrication PDA coating. This should permit effective interactions with nearby water molecules, so as to provide high local contrast for MR imaging.

Results: Fibres were prepared by co-axial electrospinning and loaded with LDH-MTX nanocomposites in the core, yielding organic–inorganic hybrids with a diameter of 1.48 ± 0.58 μm. After surface coating with polydopamine and SPIONs, the hydrophilicity profoundly increased and the SPIONs were proven to be evenly distributed on the surface, providing high MRI contrast. *In vitro* drug release studies showed the PDA coated fibres gave sustained release of MTX over 18 days, and that the release profile is responsive to conditions representative of the tumor microenvironment such as slightly acidic pH values or elevated concentrations of the reducing agent glutathione (GSH). *In vitro* studies with Caco-2 and A549 cells showed highly effective killing with the PDA coated formulations, which was further enhanced at higher levels of GSH.

Conclusions: The fibres have the potential to act as an implantable drug-eluting platform for the sustained release of cytotoxic agents within a tumor site, providing a novel treatment option for post-operative cancer patients.