Novel approach for the local treatment of arthritis or osteoarthritis: magnetically retinable drug delivery systems

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To increase the duration of action of a model anti-inflammatory drug administered in the joint compared to conventional suspensions, we developed magnetic biodegradable microparticles, retinable by an external magnet (Fig. 1). This system gradually releasing the active component could also prevent crystal-induced pain. For this purpose, we incorporated superparamagnetic iron oxide nanoparticles (SPIONs) and dexamethasone acetate (DXM) into PLGA microparticles.

Aiming at high SPION content for an adequate magnetic retention and high DXM content for proper clinical response, we selected 10-μm microparticles, based on an experimental design (Fig. 2). The main features of these particles are:
- The encapsulation process does not change either the oxidation state of iron or magnetic properties.
- A good correlation between DXM in vitro and in vivo (over 5-6 days) release (as measured using a dorsal air pouch model in mice) was observed.

- In vivo imaging in mice demonstrated that the presence of a magnet near the knee improves the microparticle retention in the joint over 3 weeks.
- Microparticles are internalized by synovial fibroblasts (Prussian blue staining, confocal microscopy) through a phagocytic process (immunofluorescence actin staining).
- Intra-articular injection of microparticle suspensions elicited only minor inflammatory response (Fig. 3).
- Mice study using a model of antigen-induced arthritis evidenced efficacy of DXM and SPION-containing magnetically retinable microparticles.

These results validate the possibility of using this type of carrier for the local treatment of arthritis. Moreover, the system can advantageously be tailored by changing the polymer matrix for the intra-articular delivery of other anti-inflammatory drugs in view of clinical application.

References

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