Thematic area: Nanobiotechnology for pharmacy

New potential nanotechnology-based therapies for the treatment of rheumatoid arthritis

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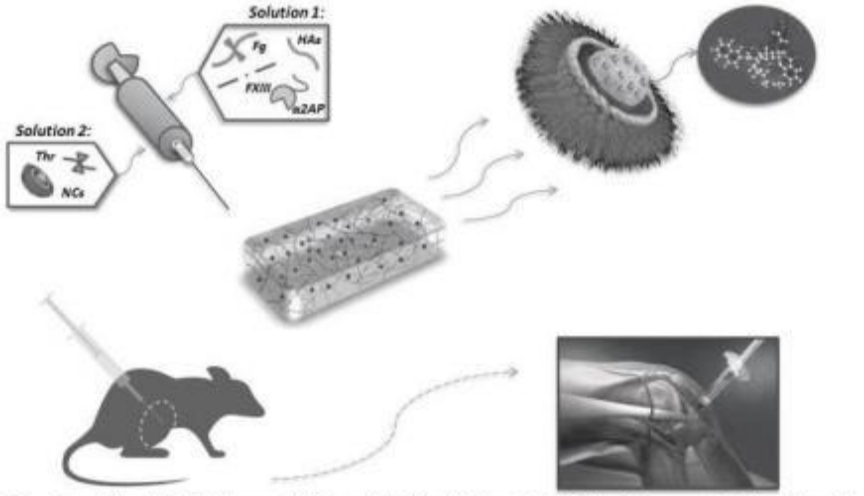
The development of controlled release drug delivery systems (DDS), easily injectable to the intra-articular (IA) cavity and displaying long residence time might have a significant benefit for the treatment of arthropathies [1]. Recently, have been found the roles of galectin-3 (Gal-3) in rheumatoid arthritis (RA), designing it as a new potential immunotherapeutic target [2, 3].

A graphical abstract



α2-AP - α2-antiplasmin, Fg- Fibrinogen, FXIII -Factor XIII, HAs - Hyaluronic acids, NCs – Nanocapsules, Thr – Thrombin.

The double aim of this work is the engineering of new biodegradable injectable nanotechnological platform for prolonged IA residence time and drug release, composed of *in situ* hydrogel with included nanocapsules (NCs) as multireservoirs for lipophilic anti-inflammatory drugs; synthesis of Gal-3 inhibitor (Gal-3i), encapsulation within this DDS and evaluation of its activity *in vivo*.

A novel highly affine, potent and selective Gal-3i with aromatic substituents introduced to type II lactosamine core [Gal-β(1→4)-GlcN] was obtained. The resulting compound had K_d = 590 nM to Gal-3 (4 °C) [4]. Thereafter, Gal-3i was firstly encapsulated within NCs prepared using a simple solvent displacement method, EE% was 11 ± 2 % (531 ± 5 μg/mL). NCs have nanometric size (122 ± 11 nm), negative surface charge and regular spherical shape. Then, an injectable *in situ* hydrogel composed of hyaluronic acid-fortified fibrin interpenetrating network, allowing 30% (v/v) NCs loading upon its self-assembly, was developed. The rheological properties and high resistance to deformation display the designed hydrogel suitable for IA application.

In vivo studies, performed at rat carrageenan-induced acute synovitis model, demonstrated a remarkable suppression of inflammation by Gal-3i at doses 55 and 200 μg/kg at histological level, in whole blood test and plasma levels of pro-inflammatory cytokines. These findings present Gal-3i as a lead compound for immunotherapeutic anti-RA drug candidate and the DDS showed good syringeability and a tendency to improve joints healing, by reducing the synovial inflammation.

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