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Intra-Articular Drug Delivery Systems for Osteoarthritis Treatment

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Cartilage lesions observed in osteoarthritis (OA) are related to an important release of cytokines. Current treatments though oral or systemic administration are suboptimal and not curative. Intra-articular administration of drugs is often proposed for localized forms of OA. MAPK inhibitors target important cytokines pathways and show promise for the treatment of OA [1].

The aim of the present work was to formulate nano- and microparticles loaded with a p38 MAPK inhibitor (VX-745) and to test their *in vitro* activity on human synoviocytes. We anticipated that this novel formulation will provide a high but local concentration of the active ingredient with a prolonged retention time.

Particles of different sizes were produced by a solvent evaporation method using a solution of PLGA and of VX-745 in dichloromethane and a solution of PVAL. The particles were characterized by laser diffraction, dynamic light scattering, scanning electron microscopy and reverse-phase HPLC.

In vitro studies were conducted by incubating nano- and microparticles with subconfluent human synoviocytes culture obtained from OA synovial samples. The ability of the particles to release the drug and consequently to inhibit the IL-6 biosynthesis was quantified by ELISA (eBioscience, San Diego, CA).

Spherical particles had a smooth surface and mean diameter of 300 nm, 2.5 µm and 25 µm. After 24 h of incubation with synoviocytes, IL-6 production was inhibited by VX-745-loaded nanoparticles in a dose-dependent and size-dependent pattern. For instance, the release of VX-745 from nanoparticles loaded at 100 nM inhibited IL-6 release to 52% compare to control and to 71% of control for a drug concentration of 800 nM.

To conclude, VX-745-loaded particles display extended release properties and inhibit significantly the production of IL-6 from human synoviocytes.

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