pH sensitive liposomes loading prednisolone for the treatment of rheumatoid arthritis

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Abstract

Rheumatoid arthritis is a chronic systemic inflammatory and autoimmune disease mainly characterized by the progressive inflammation of the synovial tissue of the body joints, destruction of cartilage and further bone erosion. Currently available treatment options include non-steroidal anti-inflammatory drugs, glucocorticoids and disease modifying anti-rheumatic drugs, either used as monotherapy or in combination therapy. However, all of these therapeutic strategies are associated with severe side effects resultant from limited selectivity and widespread biodistribution of drug molecules into non-target tissues. In order to overcome the drawbacks of conventional therapy, the aim of the following dissertation is to design pH-sensitive liposomes as suitable drug delivery nanosystems for the treatment of rheumatoid arthritis. Although these liposomes are stable at physiological pH, they undergo rapid liposomal destabilization under mildly acidic conditions as those presented in endosomes of target cells. Thus, promising to improve the therapeutic efficiency of a commonly used glucocorticoid - prednisolone disodium phosphate -, due to liposomes ability to mediate an intracellular, specific and controlled release of the drug molecules, while limiting adverse off-target unwanted effects. In this sense, designed pH-sensitive liposomes with specific targeting ligands, as the polyethylene glycol-folic acid or the hyaluronic acid, were developed to enhance the selective and efficient delivery of loaded drug into target synovial macrophages and fibroblast. Furthermore, the *in vitro* therapeutic performance of the designed pH-sensitive liposomes was evaluated, through the optimization of its lipid composition, physicochemical characteristics, drug release studies mimicking both biological conditions at pH 7.4 and pH 5.0, cellular studies and, as well as, the liposomal stability during storage. The selectivity and stability of the proposed targeted pH-sensitive liposomes increases the bioavailability of the drug molecules at the site of inflammation, once the liposomes specifically internalize into the target cells where they trigger the release of drug and thereby enhance the therapeutic effect, reducing the number of dosages and minimizing the well-known deleterious side effects of prednisolone.

Acknowledgments: We thank the financial support through the project PP-IJUP2011-279.