Elastin-like Polymers Enhance the Anti-inflammatory and Analgesic Properties of Semisynthetic Glycosaminoglycans

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Introduction

The bladder contraction poses an obstacle for intravesical delivery of water-soluble drugs due to short residence time after injection and barriers to diffusion.1 Thermoresponsive polymers can increase intravesical dwell time of water-soluble therapeutics and enhance their bioavailability profile in the bladder.2 We evaluated four distinct classes of polymers for their ability to enhance delivery of a semisynthetic glycosaminoglycan (SELP)15K, a novel anti-inflammatory anti-pain therapeutic, to the bladder via intravesical administration. Polysulfone 407, polyacrylic-co- glycolic and (PLGA-PEG-PLGA) (PLGA-PEG-PLGA 1500-1000-1500), a silk-elastin protein polymers (SELP) 815K, 12% SELP 815K, 12%, PLGA-PEG-PLGA 20%, Poloxamer 407 20% were selected for evaluation based on each of their distinct properties.

FIG. 3: Comparison of final release of SELP from thermoresponsive polymers, at 24h from release of the polymers in high temperature conditions. ***-, **-, and *- indicate p-values less than 0.001, 0.01, and 0.05, respectively for comparison of the high and low temperature conditions. 42°C (C) PFU-PLGA was statistically different compared to other polymers in high temperature conditions. °, °°, °°°-, °°°°-, °°°°°-, and °°°°°- indicate p-values less than 0.05, 0.01, 0.001, 0.0001, 0.00001, and 0.000001, respectively for comparison of the PBS and solution with 10 mg/ml GM-0111 in the absence and presence of SAGE, respectively.

Methods

In Vitro Characterization of Materials

In Vitro Evaluation of Intravesical Delivery

Effects on Pain and Inflammation

Discussion and Conclusions

These results show that thermoresponsive polymers enhance intravesical delivery of water-soluble therapeutics to the bladder. Matrix formation was not critical to enhanced accumulation but did improve residence time. Our results need to be taken in the context of the polymers themselves; such as the case with SELP 815K, but not SELP 415K and no effect with SELP 15K. Thermoresponsive effects while not causing any significant impairment to bladder function. 415K’s success over 815K can be attributed to slower gelation and greater biocompatibility, improved understanding of polymer properties and their potential to enhance intravesical delivery of drugs may improve intravesical treatments for bladder pain and painful bladder disease.

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References


In Vitro Evaluation of Intravesical Delivery

Statistical

In Vivo Assessment of Intravesical Delivery

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