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The Improvement of Disease-Modifying Osteoarthritis Drugs Model Uptake and Retention within Two Cartilage Models

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Abstract : Disease-modifying osteoarthritis drugs (DMOADs) are a new therapeutic class for OA, preventing or inhibiting OA development. Unfortunately, none of the DMOADs have been clinically approved due to their poor therapeutic effects in clinical trials. The joint environment has played a role in the poor clinical performance of these drugs by limiting the amount of drug effectively delivered as well as the time that the drug spends within the joint space. The current study aims to enhance the cartilage uptake and retention time of the DMOADs-model (licofelone), which showed a significant therapeutic effect against OA progression and is currently in phase III. Licofelone will be covalently conjugated to the hydrolysable, cytocompatible, and cationic poly beta-amino ester polymers (PBAE). The cationic polymers (A16 and A87) can be electrostatically attached to the negatively charged cartilage component (glycosaminoglycan), which will increase the drug penetration through the cartilage and extend the drug time within the cartilage. In the cartilage uptake and retention time studies, an increase of 18 to 37 times of the total conjugated licofelone to A87 and A16 was observed when compared to the free licofelone. Furthermore, the conjugated licofelone to A87 was detectable within the cartilage at 120 minutes, while the free licofelone was not detectable after 60 minutes. Additionally, the A87-licofelone conjugate showed no effect on the chondrocyte viability. In conclusion, the cationic A87 and A16 polymers increased the percentage of licofelone within the cartilage, which could potentially enhance the therapeutic effect and pharmacokinetic performance of licofelone or other DMOADs clinically.

Keywords : PBAE, cartilage., osteoarthritis, injectable biomaterials, drug delivery
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