Mucoadhesive Emulsion Microgels for Intravesical Drug Delivery: Preparation, Retention at Urothelium, and Biodistribution Study

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The intravesical instillation is a proven method used in the current urology practice for the treatment of bladder diseases. However, this method is limited by the low therapeutic efficiency and painfulness of the procedure. In this work we developed an approach to overcome these limitations by using micron-sized mucoadhesive macromolecular carriers based on whey protein isolate with the possibility of prolonged release of drugs as a drug delivery system. The whey isolated protein as mucoadhesive and emulsifier agent was used for the preparation of emulsion microgels. The drug release kinetics from the emulsion microgels was evaluated in saline and artificial urine *in vitro*. The effect of emulsion microgels on the morphology and viability of two cell lines was observed: L929 mouse fibroblasts (normal adherent cells) and THP-1 human monocytes (cancer suspension cells). Developed emulsion microgels showed sufficient mucoadhesion to a porcine bladder urothelium *ex vivo*. The biodistribution of emulsion microgels (5%, 1:3 and 1:5) in mice (n = 3) after intravesical (instillation) and systemic (intravenous) administration was assessed *in vivo* and *ex vivo* using near-infrared fluorescence live imaging for real time. It was demonstrated that intravesical instillation allows approximately 10 times more efficient accumulation of emulsion microgels in the mice urinary bladder in vivo 1 h after injection compared to systemic injection. The retention of the emulsion of mucoadhesive microgels in bladders after the intravesical instillation was observed for 24 h. Thus, the developed drug carriers based on the mucoadhesive emulsion microgels demontstrate the properties of sufficient mucoadhesion to the bladder urothelium, as well as the capability of prolonged drug release, which has perspectived for the future applications in urology.

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