

Injectable Biodegradable Hydrogels for Protein Delivery

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Injectable biodegradable hydrogels that are formed in situ from aqueous polymer solutions under physiological conditions are of particular interest for tissue engineering and protein delivery applications. In situ formed hydrogels provide many advantages. For instance, they allow easy homogenous encapsulation of cells and/or proteins, preparation of complex shapes, as well as minimally invasive implantation. However, current injectable hydrogels often require photo-irradiation, auxiliary crosslinking agents, and/or organic solvents, which may damage the cells or proteins of interest. In the past few years, we have developed several novel types of rapidly in situ forming biodegradable hydrogels.

Stereocomplexed hydrogels. Based on stereocomplex formation between enantiomeric PLLA and PDLA blocks, in situ forming hydrogels have been prepared from eight-arm poly(ethylene glycol)-poly(L-lactide) (PEG-PLLA) and poly(ethylene glycol)-poly(D-lactide) (PEG-PDLA) star block copolymers, wherein the gelation time (from instantaneous to 1 h) and storage modulus (up to 14 kPa in PBS at 37 °C) were shown to depend on PLA block length and polymer concentration [1, 2]. These stereocomplexed hydrogels have been used for in vitro and in vivo protein release [3, 4].

Michael addition hydrogels. Highly elastic hydrogels were rapidly formed in situ under physiological conditions by Michael type addition upon mixing aqueous solutions of dextran-vinyl sulfone (dex-VS) and multi-functional PEG-SH at a concentration of 10 to 20 w/v% [5]. These dextran hydrogels have a low initial swelling and are degradable under physiological conditions with degradation time varying from 3 to 21 days depending on the DS, concentration, dextran molecular weight and PEG-SH functionality. Dextran hydrogels with slower degradation (degradation time ranging from 3 to over 21 weeks) could be obtained from thiol functionalized dextran (dex-SH) and PEG tetra-acrylate [6].

Enzymatic hydrogels. Dextran-tyramine (Dex-TA) conjugates have been designed to prepare hydrogels via enzymatic oxidative crosslinking [7]. Interestingly, hydrogels were rapidly formed under physiological conditions from Dex-TA at or above a concentration of 2.5 wt% in the presence of H₂O₂ and horseradish peroxidase (HRP). The swelling/degradation studies showed that under physiological conditions, Dex-TA hydrogels are rather stable with less than 25% loss of gel weight in 5 months. Hydrogels with faster degradation could be achieved by linking tyramine to dextran via an ester group.

Keywords: hydrogels, biodegradable, drug delivery systems

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