Poly(ethylene glycol) based Diels-Alder hydrogels for biomedical applications

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Statement of Purpose: Over the last 20 years, cross-linked poly(ethylene glycol) (PEG) hydrogels have been developed as a versatile material for a variety of biomedical applications. They can be used as liquid-absorbing wound dressings, as injectable drug delivery systems, or as three-dimensional scaffolds for cell transplantation (1-3). Nevertheless, most of the existing cross-linking mechanisms are associated with disadvantages, such as the formation of potentially harmful radicals. A relatively unknown cross-linking mechanism for hydrogels is the Diels-Alder click reaction. Here, we present the influences of the polymer concentration, the branching factor and molecular weight of the macromers on the characteristics of the resulting hydrogels. The mechanical properties, such as gelation time, gel strength and swelling behavior, are quite important for biomedical applications.

Methods: PEG with branching factors of four and eight (4armPEG10k-OH and 8armPEG10k-OH) and different molecular weights (8armPEG10k-OH and 8armPEG20k-OH) were used as raw materials. Each polymer was modified either with furyl groups or maleimide groups according to previously established protocols. All compounds were characterized by ^{1}H-NMR spectroscopy. For hydrogel preparation, defined amounts of the two complementary macromers were separately dissolved in water. The two precursor solutions were mixed to initiate gel formation (Fig.1).

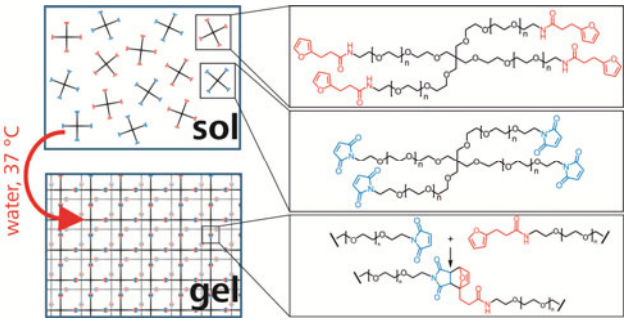

Fig.1: Mechanism of hydrogel formation

Gelation kinetics and gel strength were studied by performing oscillatory shear experiments on a TA Instruments AR 2000 rheometer with parallel plate geometry. For swelling studies, gel cylinders (Ø 7 mm) were incubated in 10 ml of phosphate buffer pH 7.4.

Results: Rheological studies showed that the gelation time and gel strength could be controlled by adjusting the overall polymer concentration and by varying the branching factor and the molecular weight of the macromers. The gelation time decreased with increasing polymer concentration and branching factor while the gel strength increased. The results indicated that in some cases, gelation time and gel strength could be controlled independently from each other. The swelling behavior of the different hydrogels is also influenced by the same factors. 5 % (w/v) 4armPEG10k-hydrogels dissolved after one day of swelling. By increasing the branching factor form four to eight, the gel cylinders (5 % polymer) were stable over four weeks. A prolonged stability of the gel cylinders was although observed when the total polymer concentration was increased from 5 % to 15 %. The dissolution of the hydrogels can be explained by a retro-Diels-Alder reaction and hydrolysis of the maleimide groups to maleamic acid derivatives that do not form hydrogels under the experimental conditions.

Conclusions: In summary, our studies showed a clear influence of the polymer concentration, the branching and molecular weight of the macromers on gelation time, gel strength, hydrogel swelling and degradation. Given their favorable gelation time and long-term stability, 8armPEG10k-hydrogels seem to be a promising biomaterial for various biomedical applications.

References:

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