

Hydrogels By Supramolecular Crosslinking Of Terpyridine End Group Functionalized 8-arm Poly(Ethylene Glycol)

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Introduction

Polymer gels are networks of polymer molecules that are either covalently or physically crosslinked and expanded throughout their volume by a fluid. Physically cross-linked polymer gels are based on supramolecular chemistry and examples are dipole-dipole interactions, host-guest complex, ionic bonding, hydrogen bonding, π - π stacking or combinations of these, such as ion-dipole interactions. Up to now only minor attention has been given to terpyridyl modified polymers that can be crosslinked into metallo-supramolecular hydrogels by third row transition metal ions. In this paper, we describe such supramolecular gels formed by the self-assembly of an 8-arm PEG end modified with terpyridyl groups via metal-ligand interaction using Ni^{2+} , Fe^{2+} , Co^{2+} and Zn^{2+} ions [1]. Moreover, we determined the cell viability of these hydrogels by incorporating the chondrocytes in the gels, by direct contacting the cells with the gels and by indirect contact using transwells.

Results and discussion

In dilute aqueous solutions the 8-armed PEG end-modified with terpyridyl groups (Figure 1) forms nano-particles with an average diameter of ~ 10 nm. Titration of the polymer with Fe^{2+} ions resulted in a distinct shift of the average particle size to ~ 200 nm (Fig. 2). The dissociation rate constant of the formed Fe^{2+} complexes is $\sim 8.1 \times 10^{-7} \text{ s}^{-1}$.

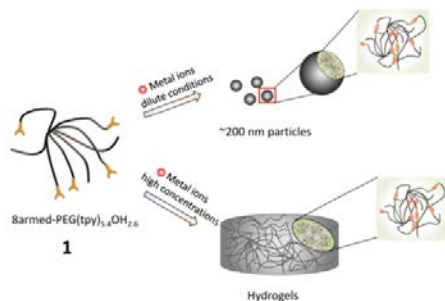


Figure 1. Complexion of transition metal ions with a terpyridyl end-group 8-arm poly(ethylene glycol) afforded either nano-particles or hydrogels at different concentrations.

At polymer concentrations higher than 3 wt%, addition of Fe^{2+} ions to the polymer at a 2:1 ratio of Fe^{2+} to terpyridyl units afforded hydrogels. Gelation took place instantaneously. The mechanical properties of the gels at different concentrations was studied. As depicted in Fig. 2 the storage moduli of the Fe^{2+} gels increases with an increase in concentration in line with the theory of rubber elasticity. The morphology properties of 8 wt% hydrogel was observed by scanning electron microscope in Fig. 3 (left).

Chondrocytes incorporated in the complexed hydrogels at different concentrations for 1, 7 and 14 days. Cell survival of the chondrocytes in the hydrogels was evaluated using a live-dead assay, in which living cells stained green and dead

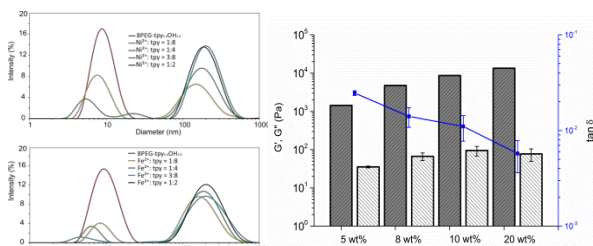


Figure 2. Nano-particle formation of **1** with $\text{Fe}(\text{II})$ chloride at different ratios probed by DLS (left). Storage modulus (G') and loss modulus (G'') as a function of time at different polymer concentrations.

cells red. As is shown in Fig 3, over 97% cells in this hydrogel were alive, similar to those embedded in an agarose gel which was used as a control.

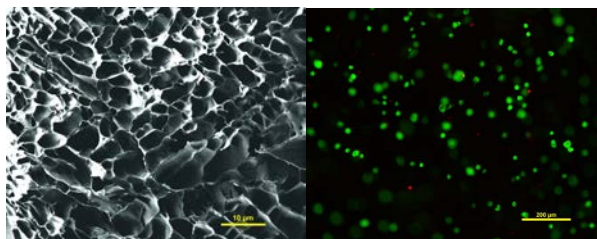


Figure 3. SEM image of the **1**- Fe^{2+} complex gels at 8 wt% (left). Live-dead assay showing chondrocytes incorporated in **1**- Fe^{2+} complex gels (8 wt%) after 14 days in culture (right).

Conclusions

The stability of the complexes of **1** with transition metal ions were followed: $\text{Ni}^{2+} > \text{Fe}^{2+} > \text{Co}^{2+} > \text{Zn}^{2+}$ in an aqueous environment at both dilute and higher concentrations. Increasing the concentration of polymer solutions resulted in increasing storage moduli. Chondrocytes incorporated in the hydrogels showed a high cell viability after 2 weeks and retained their round cell morphology.

Reference

[1] R. Wang, M. Geven, P. J. Dijkstra, P. Martens, M. Karperien, *Soft Matter* 2014.