Photocrosslinked Hydrogels from Thermoresponsive Dendritic Copolymers: Synthesis, Mechanical Property, Swelling, Protein Release and Cytotoxicity

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Introduction: Photocrosslinked hydrogels from thermoresponsive polymers can be used as advanced injectable biomaterials via a combination of physical interaction (in situ thermal gelation) and covalent cross-links (in situ photopolymerization). This can lead to gels with significantly enhanced mechanical properties compared to non-photocrosslinked thermoresponsive hydrogels. Moreover, they have attractive advantages over non-thermoresponsive photocrosslinked gels because thermal gelation upon injection allows easy handling and holds the shape of the gels prior to photopolymerization during clinical practice.

Materials: The (macro)monomers PEGMEMA (Mₙ = 475), PPGMA (Mₙ = 375) and EGDMA were purchased from Sigma-Aldrich. The methyl chloride (CuCl, 95 %, Acros), copper (II) chloride (CuCl₂, 99 %, Lancaster) and 2, 2'-bipyridine (bpy, Aldrich) were used as the solvent. Copper (I) chloride (CuCl, 95 %, Acros), copper (II) chloride (CuCl₂, 99 %, Lancaster) and 2, 2'-bipyridine (bpy, Aldrich) were used as the catalyst. Photoinitiator 2-hydroxy-4′-(2-hydroxy-ethoxy)-2-methyl-propiophenone (Ciba Irgacure 2959) was purchased from Sigma-Aldrich.

Results and Discussions: Water soluble thermoresponsive copolymers containing multiple methacrylate groups (Fig. 1) were synthesized via one-step deactivation enhanced atom transfer radical copolymerization (ATRP) of PEGMEMA (Mₙ = 475), PPGMA (Mₙ = 375) and EGDMA in butanone at 60 °C.¹,²

These dendritic copolymers were well characterized by GPC and NMR. They were used to form covalent cross-linked hydrogels by photocopolymerization (Fig. 2). The crosslinking density was found to have a significant impact on the mechanical and swelling properties of the photocrosslinked gels. The photocrosslinked gels prepared from these copolymers at a temperature above the LCST showed excellent mechanical properties. The swelling ratio and the lysozyme release rate of these gels could be controlled by simply adjusting the monomer composition within the polymers. Also, these materials were found to have low toxicity for mouse C2C12 myoblast cells as assessed with LDH, Alamar Blue and a live-dead assay at concentrations less than 1 mg/mL. Further structure modifications by introducing cell-adhesion functionality are needed to improve cyto compatibility of the photocrosslinked gels.

Conclusions: This study demonstrates that PEGMEMA-PPGMA-EGDMA dendritic copolymers offer potential as in situ thermoresponsive and photopolymerizable materials for tissue engineering and drug delivery applications through a combination of facile synthesis, enhanced mechanical properties, tuneable crosslinking density, adequate cytotoxicity and accessible functionality for further structure modifications.

References
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