FIRST EVER SOLID STATE CROSSLINKING OF HYDROGEL PRECURSORS: OPENING UP UNPRECEDENTED HYDROGEL PROCESSING AVENUES IN THE BIOMEDICAL FIELD

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Introduction

Hydrogels are biomaterials often obtained by incorporating a polymerizable double bond in a hydrophilic prepolymer enabling UV-curing. An important requirement for the curing is high mobility of the reactive groups. This is either achieved by dissolving or melting the prepolymers, which is a limiting step for many processing techniques e.g. electrospinning and 3D printing. Radicals initiating the crosslinking can be generated by adding a photo-initiator (PI). Drawbacks of a PI include toxicity, low solubility and mixing problems. To date, UV-curable urethane-based poly(ethylene glycol)(PEG) hydrogels have been described in literature [1,2]. Nonetheless, those materials do not exhibit the unique solid state UV reactivity without PI, as targeted for the novel hydrogel precursors developed in this work [3].

Materials and Methods

Acrylate-terminated, urethane-based PEG(AUP) was prepared by reacting PEG 2000 with isophorone diisocyanate(IPDI) and monoacrylate PEG(336 Da) in a 1:2:2 molar ratio. UV-curing was assessed using rheology and differential photocalorimetry(DPC). 1-Hydroxycyclohexyl-phenyl-ketone (HCPK), 0.2 wt% was used as PI. Cell tests were performed using human foreskin fibroblasts (HFF).

Results and Discussion

In a first part, the precursor was fully characterized using nuclear magnetic resonance spectroscopy, infrared spectroscopy and gel permeation chromatography. The material is solid at room temperature (Tmelt = 37°C) and has a remarkably high water compatibility: even for a AUP content of 90 wt%, a homogeneous solution is obtained. The water content prior to UV curing affects the final characteristics of the hydrogel. These were evaluated using rheology, tensile testing, DPC and swelling tests.
Secondly, and most importantly, the materials show unprecedented photo reactivity. Efficient crosslinking occurs both in the solid state and in absence of a photo-initiator. DPC results (FIG. 1) show that without PI, the maximal polymerization speed is about 50% higher in the solid state compared to the molten state.

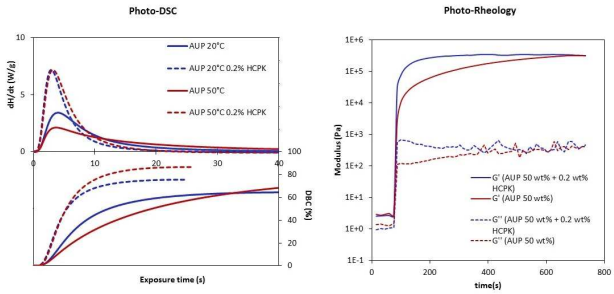

FIG. 1. Left: DPC: UV-curing in PI absence (full line) and presence (dotted line) and in the solid state (20°C, blue) and molten state (50°C, red). The bottom curves show the double bond conversion. Right: Rheology: The red curves are without PI and blue curves with PI.

UV-curing in the presence of water was characterized using rheology (FIG. 1). Adding a PI results in faster UV-curing, while similar final moduli are obtained. This is in line with the DPC results for samples in the molten state.
Some exciting applications of the materials are shown in FIG. 2. A first example is the production of UV-cured hydrogel fibers. As the microfibers are in a solid state post-processing, conventional electrospun hydrogel fibers cannot be UV-cured. However, due to the high solid state reactivity of this material this is possible. Secondly, the material was 3D-printed from melt. The effective UV curing was shown by swelling studies. Very interestingly, the obtained materials were highly flexible.

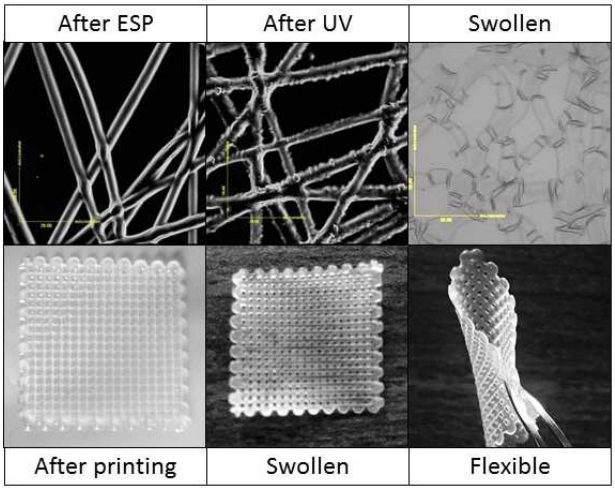

FIG. 2. Electrospun fibers (top), 3D printed scaffold (bottom).

In a final part, indirect and direct cell tests using HFF show good biocompatibility.

Conclusions

We for the first time report on the solid state UV-curing of hydrogel precursors for biomedical applications. The reactivity in the solid state opens up unprecedented possibilities towards material processing, while the absence of a photoinitiator can reduce cytotoxicity and eliminates preparation steps.

Acknowledgments

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References

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