BEHAVIOR OF DUAL-CROSSLINKED GELATIN AND ITS POTENTIAL INFLUENCE ON VASCULARIZATION

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INTRODUCTION

Vascularization remains a critical factor for the success of various applications in the biomedical field. Insufficient blood vessel systems often limit the availability of replacement tissues *via* TERM.[1] Hence, there is a great interest in materials that potentially improve vascularization. The mechanical properties of hydrogels strongly influence cell behavior and organization. A promising approach for tunable hydrogel stiffness is dual-crosslinking, *i.e.*, combining physical and chemical crosslinking by cooling and UV-irradiation.[2] This study investigated the influence of dual-crosslinked gelatin-methacryloyl (GM) on hydrogel material properties and HUVECs cell formation. Additionally, we employed mimicry of placenta extracellular matrix as a highly vascularized organ within the hydrogels to potentially improve vascularization and investigate the effect of hydrogel stiffness.

METHODOLOGY

Gelatin was synthesized with methacrylic anhydride, and formulations were prepared with varying macromer concentrations using lithium phenyl-2,4-6-trimethylbenzoylphosphinate (LAP) as photoinitiator in an aqueous solution. Human Placenta Substrate (hpS) was incorporated within the network (50 vol%) as a source of angiogenic factors. Crosslinking was performed either chemically with UV light at ~37 °C, or as dual-crosslinking (UV crosslinking of physically crosslinked GM at 4 °C). Gelation was monitored by photorheology, and *in vitro* analysis was performed using HUVECs.

RESULTS

The crosslinking mechanism significantly influences the stiffness of the gelatin-methacryloyl (GM) hydrogels. GM's dual-crosslinking increases hydrogel stiffness; however, double bond conversions do slightly decrease.[2] Hydrogel vascular network formation with HUVECs was observed when placenta-specific factors were incorporated, yet increased hydrogel stiffness resulted in confluency.

CONCLUSION

We suggest an explicit dependency between HUVEC behavior and hydrogel stiffness. Stiffer networks (due to higher macromer concentration or double-crosslinking) tend to confluence and less network formation. The crosslinking mechanism influences cell morbidity as well as behavior and should not be neglected, especially during the preparation process of GM hydrogels.

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LITERATURE

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