Thermosensitive, Biodegradable, and Cell Adhesive Pluronic Hydrogels for Tissue Engineering

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Introduction: Pluronics are nontoxic poly(ethylene oxide)-(polypropylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymers showing thermoreversible gels at high concentrations. These gels have received increasing attention over many years for drug delivery systems (DDS), implantable applications as well as biomaterials.[1,2] In particular, Pluronic F127 has been most widely used as proper block copolymers in pharmaceutical systems. For thermal behaviors in specific temperature, we have already synthesized META-F127 and META-F127-RGD using F127. In this study, F127 was further chemically modified to yield intelligent hydrogels for tissue regeneration. Temperature-sensitive, biodegradable, and cell adhesive triblock copolymer, META-F127-G5-RGD, was synthesized by subsequent grafting of functional 4-methacryloxyethyl trimellitic anhydride (4-META), biodegradable glycolide (G), and then Arg-Gly-Asp (RGD) peptide ligand to F127, and its characteristics were evaluated.

Methods: First, the mixture of Pluronic F127, glycolide, and Tin(Ⅱ) 2-ethylhexanoate was gently stirred. After the reaction, the reactant was precipitated in n-hexane to obtain F127-G5. Second, the mixture of F127-G5, 4-META, and anhydrous pyridine was stirred magnetically under dry nitrogen and the mixture was precipitated in diethylether to obtain META-F127-G5. Last, META-F127-G5 was activated by adding EDC. The mixture of peptide ligand (RGD) and the activated META-F127-G5 was stirred magnetically. After the reaction was completed, the product was dialyzed and freeze-dried finally to get META-F127-G5-RGD. The chemical structures of the resulting META-F127-G5-RGD block copolymers were analyzed by FTIR, ^{1}H and ^{13}C NMR, and GPC. Sol-gel transitions of the F127 derivatives were evaluated by tube tilting method (tilted the vial with 90° for 10 minutes). The critical micelle temperature (CMT) and particle size of the F127 derivatives in aqueous solution were measured by UV spectroscopy and dynamic light scattering, respectively. In addition, adipose-derived stem cell (ASC) culture using the F127 derivatives was performed for the predetermined period of times.

Results / Discussion: Thermosensitive, biodegradable, and cell adhesive META-F127-G5-RGD was successfully synthesized. From the results of thermal sol-gel transitions, the META-F127-G5-RGD showed the very similar thermosensitive behaviors to F127, META-F127, and META-F127-RGD (Fig. 1). The CMT of the META-F127-G5-RGD was lower than those of the F127, META-F127 and, META-F127-RGD (Table 1), whereas the micelle size of the META-F127-G5-RGD was a little larger than the others. The rate of biodegradation increased as the following order: F127 < META-F127 < META-F127-RGD < META-F127-G5-RGD. From the results of ASC culture using the META-F127-G5-RGD hydrogel, the order of ASC adhesion was F127 < META-F127-RGD = META-F127-G5-RGD.

Conclusion: This META-F127-G5-RGD, which has temperature-sensitive, biodegradable, and cell adhesive characteristics, is expected to be useful as a matrix for intelligent injectable tissue engineering and DDS.

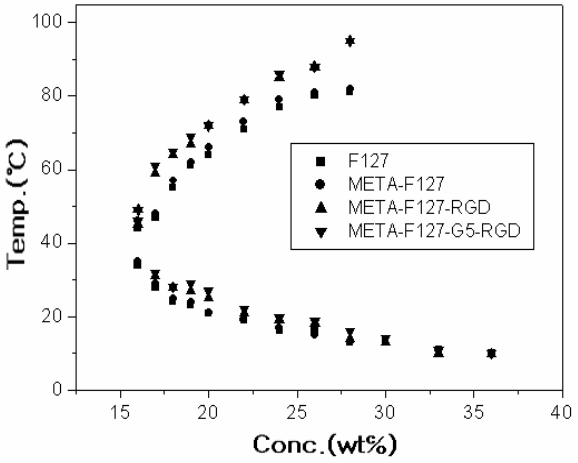

Fig. 1. Thermosensitive sol-gel behaviors of intelligent F127 derivatives.

Table 1. CMT of intelligent F127 derivatives

Concentration (wt%)	CMT (℃)			
	F127	META-F127	META-F127-RGD	META-F127-G5-RGD
0.5	46.4	35.6	29.7	20.3
2.0	39.1	30.6	25.6	16.0

Acknowledgement
This work was supported by MOST grants, 2V00940 and 2E18652.

References

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