Formation of Bundle-like Structured Gels Using the Co-flow Microfluidic Device

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Introduction

Bundle-like structures of the hydrogel expected to be useful to provide the biological tissues with multiple complex hierarchic structures, such as muscle fibers and tendons. To prepare the artificial bundle-like structures, we usually use the way of twisting a number of fibers. To reproduce these structures using hydrogels, it is necessary to establish complicated technologies such as (i) the preparation technique of a lot of high strength microfibers, and (ii) the twisting technique of microfibers. However, the technologies have not yet been implemented.

In this study, we propose a novel method to prepare the gel fibers consisting of multiple gels (bundle-like gel) simultaneously. To generate bundle-like gels, we utilized a combination of dynamic flow field with the microfluidic device and lower critical solution temperature (LCST)-type polymers.

Methods

Material selection: It is known that the LCST-type polymer expresses a strong intermolecular interaction in condensed phases by temperature change. We selected the cellulose ether (CE) as LCST-type polymers because of having some useful properties like biocompatibility, biodegradability, and non-toxicity. The CE is also used as cell scaffolds in tissue engineering application. Since CE requires long-term gelation (more than 6 hours), we use the sacrificial polymers (SP) that can be gelled instantly under the dynamic flow within the microfluidic device.

Gel fiber formation: We prepared the CE-SP composite fibers having frameworks of SP using a coaxial microfluidic device equipped with two inlets for the core and sheath flows (Figure 1). Pre-gel solution and gelling agents are introduced into Inlets A and B, respectively. Briefly, the mixed aqueous solution of SP and CE is introduced as a core flow from Inlet A, and the flow is covered by a sheath flow of the gelling agent of SP from inlet B. Pre-gel solution is gelled after combining with the gelling agent in the channel (Part of the red circle at Figure 1), and then the CE-SP composite fibers are generated. The resulting fiber is immersed in the gelling agent of CE for 17 hours, and then we finally remove the phase of SP by the dissolving agent for SP.

Results & Discussion

The microfluidic device allows preparation of gel fibers with various sizes depend on flow ratio between inlet A and B. In this study, we flowed the mixed aqueous solution of CE and SP at 2.5 mL/min in inlet A, and gelling agents of SP at 300 μL/min in inlet B. As a result, the CE-SP composite fibers were prepared (Figure 2: left).

The diameter of the composite fibers was about 350 μm. The resulting fibers have enough strength to handle with tweezers. By removing SP, CE-gel fibers with bundle-like structure were obtained (Figure. 2: right). We also confirmed that this CE bundle gel fibers are easy to handle.

We found that the bundle structures can be generated at a certain condition of the mixed solution of CE and SP. When the mixed solution of CE and SP is condensed, there was tendency to form bundle structures. It is known that the aqueous solution of CE is clouded by not only temperature change but also chemical potential changes of a solvent. The reason is, changing chemical potential of the solvent forms the condensed phase, and then aggregates are formed by intermolecular hydrophobic interactions in the phase. As a result, we revealed that it is necessary to form aggregates of CE for shaping bundle-like structure. In other words, it is considered that the bundle-like structure of CE has been formed by being stretched aggregates of CE because of share stress in microfluidic device.

Conclusions

We prepared the gel fiber of LCST-type polymers using SP by the micro fluidic device. The resulting fibers had a bundle-like structures consist of multiple microfibers. We expected the new method of gel formation bring about imitating of bundle-like structure in the body, building materials with new properties.

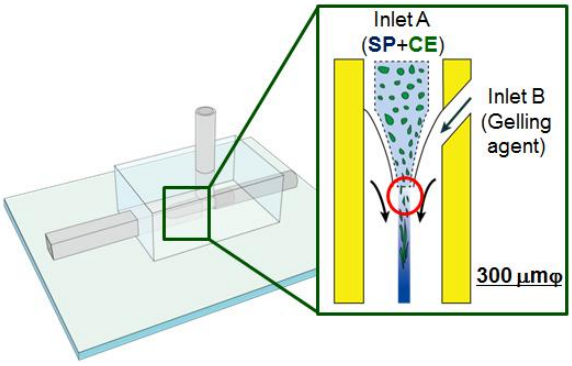

Figure 1. Diagram of the coaxial microfluidic device to prepare the gel fibers.

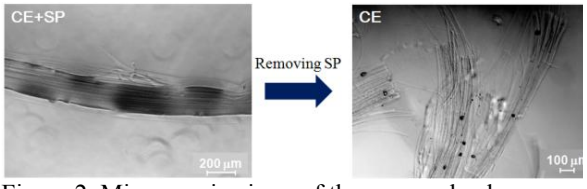

Figure 2. Microscopic views of the prepared gel fibers. The gels pre- (left) and post- (right) removal of the SP.