RAPID FORMATION OF ANISOTROPIC NON-SPHERICAL HYDROGEL MICROPARTICLES WITH COMPLEX STRUCTURES USING A TABLETOP CENTRIFUGE-BASED MICROFLUIDIC DEVICE

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ABSTRACT

We report an easy-to-use and versatile method for the synthesis of anisotropic non-spherical hydrogel microparticles with a various complex structures (e.g., two thirds of a sphere, triple-bladed turbines, etc.). The complex non-spherical microparticles were produced by partly dissolving specific parts of anisotropic spherical microparticles like colorful beach balls. Our method needs a tabletop mini centrifuge and common experimental supplies such as microtubes, glass capillaries, etc. and requires only 20 minutes for the whole process. This method will be useful for wide range of microparticle-based technologies such as self-assembled smart materials, drug delivery, and smart micro-machines, etc.

KEYWARDS: Anisotropic particle, Hydrogel, Microfluidics, Centrifuge

INTRODUCTION

Recently, anisotropic microparticles with complex structures have been attracting much attention because of their unique properties caused by their shapes. For example, anisotropic non-spherical microparticles can offer complex self-assembly with higher-order structures [1], and can also show translational and rotational motions under the certain conditions such as surface tension gradient and magnetic force field [2, 3]. Moreover, non-spherical microparticles can release much chemical drugs because their surface area is larger than that of spherical microparticles [4]. Those properties of anisotropic microparticles with complex structures are expected for applying various technologies such as self-assembled smart materials, drug delivery, and smart micro-machines, etc.

In order to realize such technologies, a synthesizing method for anisotropic microparticles with complex structures is required. To date, the micropartcle synthesis based on microfluidic channels has achieved producing anisotropic and non-spherical microparticles [5-7]. However, those approaches based on micro fluidic channels include some unfavorable works such as treating oils that induces serious pollutions, precise control of syringe pumps, etc. and also require much time and cost to fabricate microfluidic devices for the synthesis of those microparticles. Hence, it is highly desired to develop a simple and rapid method to synthesize anisotropic and non-spherical microparticles.

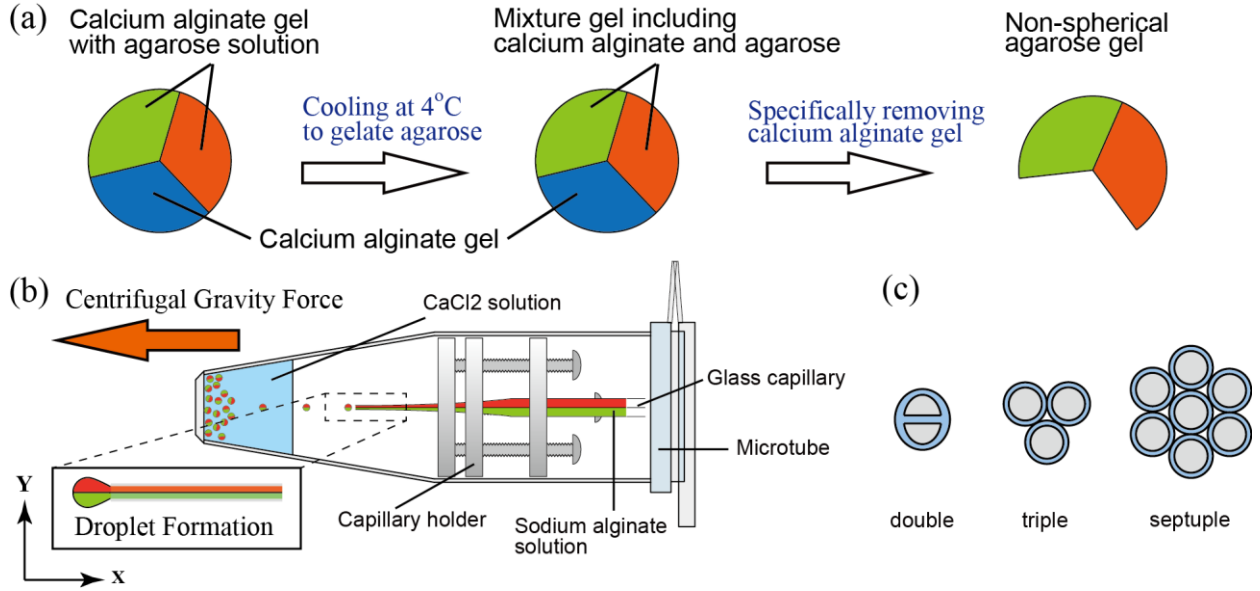

Figure1. (a) Synthesizing process of anisotropic non-spherical hydrogel microparticles with complex structures. The complex anisotropic non-spherical microparticles are produced by partly dissolving some parts of anisotropic spherical hydrogel microparticles. (b) Schematic image of Centrifuge-based Droplet Shooting Device. In the mini centrifuge, sodium alginate sol microdroplets were shot and gelated in a $CaCl_2$ solution. (c) Cross-section images of various shaped glass capillaries. Using those glass capillaries, anisotropic spherical microparticles composed of "calcium alginate gel parts" and "mixture gel including calcium alginate and agarose" were generated.

Here, we present a simple, versatile, and rapid synthesizing method for anisotropic non-spherical hydrogel microparticles with complex structures using a Centrifuge-based Droplet Shooting Device (CDSD) [8] and tabletop mini centrifuge. We report the synthesis of a variety of anisotropic non-spherical hydrogel microparticles with complex structures such as two thirds of a sphere and triple-bladed turbines with highly monodispersity in size.

MATERIALS AND METHODS

Figure 1a shows the procedure to generate anisotropic non-spherical hydrogel microparticles with complex structures. First, we formed anisotropic spherical microparticles composed of "calcium alginate gel parts" and "mixture gel parts including calcium alginate and agarose" using a centrifuge-based droplet shooting device (CDSD) (Fig. 1b). The CDSD is a tabletop centrifuge-based microfluidic device. In the CDSD, sol microdroplets were shot from the tip of a glass capillary (Fig. 1c) by ultra-high centrifugal gravity (about 1500 G) and the microdroplets gelated in a $CaCl_2$ solution. After centrifuge, spherical multi-compartmental microhydrogels were obtained. Then, the spherical microparticles were cooled at 4°C to gelate the agarose in the microparticles. Finally, we dissolved away calcium alginate gels by removing Ca^{2+} ions with a calcium-chelating agent, ethylenediamine-tetraacetic acid (EDTA); we obtained anisotropic non-spherical agarose gel microparticles. Those complex non-spherical microparticles were produced in approximately 20 minutes.

RESULTS AND DISSCUSION

Figure 2 shows the size distributions of two-compartmental microparticles (Janus microparticles) and three-compartmental spherical microparticles. Those anisotropic particles were composed of "calcium alginate gel parts" and "mixture gel parts: calcium alginate and agarose". They were synthesized from 3% (w/w) sodium alginate solutions and mixture solutions of 2% (w/w) sodium alginate and 1.5% (w/w) agarose in 3 M $CaCl_2$ solution. Each sol solutions contained 0.1% (w/w) 100 nm fluorescent nanobeads for optical visibility in microscopic observation. The mean diameters of Janus and three-compartmental spherical microparticles were 93 μm and 101 μm, respectively. The coefficient of variation (C.V.) of both the spherical microparticles was about 3%. We successfully obtained the anisotropic spherical microparticles composed of calcium alginate gels and mixture gels that had narrow size distributions.

Figure 3 shows the cross-section of applied glass capillaries and the formed anisotropic spherical/non-spherical hydrogel microparticles. The left images of each panel represent cross-sections of glass capillary and introduced sol solutions. We used mixture sol solutions of 2% (w/w) sodium alginate and 1.5% (w/w) agarose ("A") and 3% (w/w) sodium alginate sol solutions ("B"). As a gelling agent, 3 M $CaCl_2$ solution was used. The "B" parts were dissolved away by adding EDTA; anisotropic non-spherical hydrogel microparticles with complex structures were produced. The center and right images are confocal laser scanning microscope images of microparticles before and after removing calcium alginate gel parts, respectively. These results demonstrate the monodisperse production of two thirds of spheres (Fig. 3a) and triple-bladed turbines (Fig. 3b).

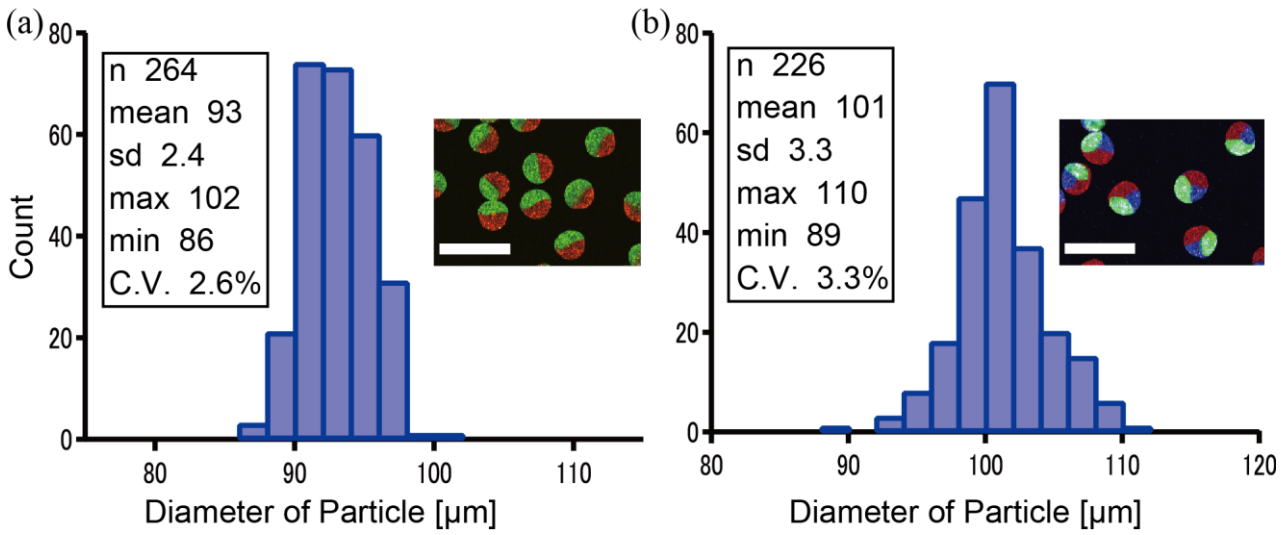

Figure2. Size distributions of anisotropic spherical microparticles (a) Janus spherical microparticles. (b) three-compartmental spherical microparticles. Both of them were made from 3% (w/w) sodium alginate sol solutions and mixture sol solutions of 2% (w/w) sodium alginate and 1.5% (w/w) agarose. Each sol solution contained 0.1% (w/w) fluorescent nanobeads and gelified in 3 M $CaCl_2$ solution. The mean diameters of the particles were 93 μm and 101 μm, respectively. Both the particles showed high-monodispersity: 2.6% and 3.3%, respectively. Scale bars represent 200 μm.

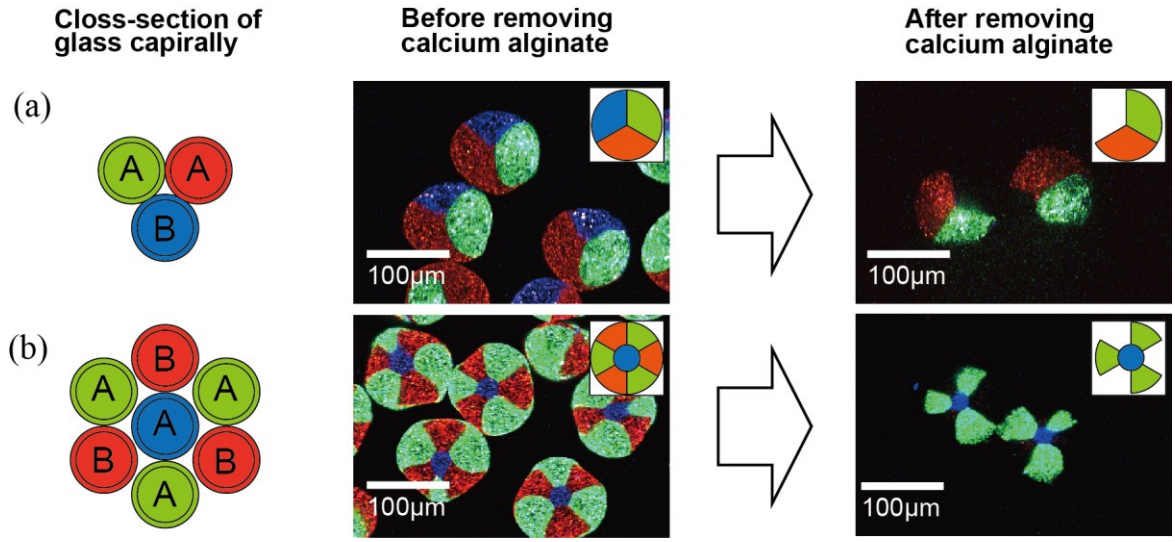

Figure3. The results of the synthesis of anisotropic non-spherical hydrogel microparticles with complex structures. (a) two thirds of a sphere. (b) triple-bladed turbines. The left images of each panel: cross-sections of glass capillary and introduced sol solutions. "A", "B" indicate the mixture sol solution of 3% (w/w) sodium alginate and 1.5% (w/w) agarose sols, and 3% (w/w) sodium alginate sol solution, respectively. Those sol solutions were gelified in 3 M $CaCl_2$ solution. The "B" parts were dissolved by adding a chelate agent, EDTA. Scale bars represent 100 μm.

CONCLUSION

In conclusion, we developed an easy-to-use and versatile method for the synthesis of anisotropic non-spherical hydrogel microparticles with a variety of complex structures by partly dissolving specific parts of anisotropic spherical microparticles. Moreover, our investigation indicated that those microparticles had high monodisperse. We believe that the anisotropic non-spherical hydrogel microparticles made by our method will promote the technologies for self-assembled smart materials, drug delivery, and smart micro-machines, etc.

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