단일 공정을 이용한 O/W/O 다중 에멀젼의 제조

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A one-step method to prepare O/W/O multiple emulsion

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1. Introduction

An emulsion is a significantly stable suspension of particles of liquid of a certain size within a second, immiscible liquid. It is obtained by dispersing one phase into the other in the presence of surface active materials (surfactants, polymers, etc.). If emulsifying agent is not used, two immiscible, pure liquids cannot form an emulsion. Direct emulsions are dispersions of oil droplets into continuous water phase whereas inverse emulsions consist of water droplets dispersed into continuous oil phase. At the present time, researchers in this field distinguish between three different types of emulsions, based upon the size of the dispersed droplets : macroemulsions (droplet size〉400nm), microemulsions(〈100nm), miniemulsion (100nm-400nm) [1,2]. They may maintain metastable and persist long enough to be utilized in many industrial fields of paints, suface coatings, and food products [3,4].

Recently, Multiple emulsions in which the dispersed particles are themselves emulsions, have been the subject of considerable investigation, particularly in the field of cosmetic, pharmaceutical, and separation sciences. Potential pharmaceutical applications, that take advantage of the presence of a reservoir phase inside droplets of another phase, include adjuvant vaccines, prolonged drug delivery systems, sorbent reservoirs in drug overdose treatment, and immobilization of enzymes [5,6]. Multiple emulsions may be either of the water-in-oil-in-water type (W/O/W) or of oil-in-water-in-oil type (O/W/O). They consist of two different interfaces which require two sets of different types of surfactants. In the case of O/W/O multiple-emulsions which were applied to our system, for the internal interface, the first set of surfactants must be hydrophilic, while the second set of surfactants, for the external interface, must be hydrophobic. In most recent emulsion formulations the emulsions are prepared in two steps. In the case of O/W/O multiple emulsion, at first, a high-shear homogenization is applied to the water that is added to the solution of the oil and the hydrophilic emulsifiers, to obtain a stable O/W emulsion. In the second step, the O/W emulsion is gently added with stirring (not homogenization) to the oil and hydrophobic emulsifiers solution. The droplet size distribution of a typical multiple emulsion ranges from 10 to 50 ㎛. Despite potential usefulness of muliple emulsions, their applications have been limited due to the inherent themodynamic instability and the complexity of their structures. To improve the stability of multiple emulsions, polymerizable emulsifiers, biopolymers, solid particles, and copolymers is used [7-9].

In this study, we prepare O/W/O multiple emulsion via a one-step emulsification process. O/W/O multiple emulsion was prepared by adding the aqueous phase containing polyethylene glycol and Tween20 to 1-octanol containing hydorxypropyl cellulose and Span80 while stirring with a magnetic mixer. Compared to two-step emulsification, this process is simple and efficient. Optical microscope equipped with camera was used to investigate formation of multiple emulsion and stability as time.

2. Experimental

2.1 Materials

1-octanol (supplied by Junsei Chemical Company) was used to prepare O/W/O multiple emulsion. The surfactant incorporated in the continuous oil phase was Span80. Span80 is a commercially available non-ionic surfactant manufactured by Sigma Chemical Company. The hydrophile-liphophile balance (HLB) value of this surfactant is 4.3. Hydroxypropyl cellulose (HPC, average Mw ca. 370,000) as a stabilizer of multiple emulsion was purchased from Aldrich Chemical Company. A water-soluble non-ionic surfactant, Tween20 (supplied by Aldrich Chemical Company), was used in the non-continuous aqueous phase. It has a high HLB value of 16.7. Also, TritonX-100 was purchased from Aldirich Chemical Company and NP-9, Span20 were supplied by Sigma Chemical Company. To control viscosity of aqueous phase, polyethylene glycol (PEG, average Mw. 18000-25000, supplied by Junsei Chemical Company) was used. All chemicals were used as received without further purification. The water in this study was deionized by Milli-Q Plus system (Millipore, France), having 18.2㏁ electrical resistivity.

2.2 Procedures

The O/W/O multiple emulsion was prepared by using a type of oil, 1-octanol and a one-step emulsification process. To make an external oil phase, HPC was solubilized in 1-octanol at 80℃ for 6hr. Then, with water bath, temperature of oil phase was dropped and maintained down to 40℃. After stirring with the use of magnetic stirrer for 1h, a low HLB surfactant, Span80 was added in 1-octanol containing HPC. Next, Internal aqueous phase was prepared. A high HLB surfactant, Tween20, and NH_4OH were solubilized in water. After stirring for a appropriate time, PEG was added to this solution. At last, 10 wt% water containing Tween20, NH4OH and PEG was added to 90 wt% continuous oil phase. Water phase was mixed with oil phase using the magnetic stirrer for 1h. After stirring, O/W/O multiple emulsion which internal oil phase was equal to external oil phase was prepared. Not only Tween20, but also TritonX-100, NP-9 and Span20 were evaluated for formation of multiple emulsion separately. The concentration of Tween20 in water was varied from 0 wt% to 18 wt% and the concentration of Span80 in 1-octanol was varied from 0.5 wt% to 1.4 wt%. Above 1.4 wt%, the solution was so viscouse that it was difficult to be handled.

2.3 Charaterization

Microslides and coverslips were rinsed with the external continuous oil phase of the O/W/O multiple emulsion before use. The O/W/O multiple emulsion samples were placed on a microslide with care to minimize possible destruction of the emulsion structures by shear stress. The samples were then covered with a coverslip. To estimate the droplet size and morphology of multiple emulsion, Optical microscope Optiphot-2 (Nikon, Japan) equipped with a camera was used. The O/W/O multiple emulsion was investigated at 200 magnification.

3. Result and discussion

3.1 Preparation of O/W/O emulsion using two mixed surfactant system

Generally, to prepare O/W/O multiple emulsion with Span80 and Tween20, a primary O/W emulsion was firstly made by adding oil phase to water containing Tween20. Secondly, the primary emulsion was dispersed in the external oil phase containing Span80. But because of complexity of two-step emulsification to prepare O/W/O multiple emulsion, the simplified process was introduced in this study. At first, to observe whether O/W/O multiple emulsion was formed, the emulsion which had two surfactants, Span80 in the oil continuous phase and Tween20 in the aqueous phase was prepared while stirring with a magnetic stirrer. In the frist trial, two polymers of hydroxypropyl cellulose (HPC) and polyethylene glycol (PEG) was not used. As shown in figure 1, O/W/O multiple emulsion was not formed but only W/O emulsion was observed. This result was same to the general phenomenon shown by two mixed surfactant system [10]. Although it was different that each surfactant was used in the different phase, oil and water, the results was very similar.

3.2 Preparation of O/W/O multiple emulsion utilizing two surfactants and two polymers

In the second trial, the polymers which can have the important role on the controll of viscosity and stability of emulsion was solubilized in each phase. Under the same condition of other experimental, only 1.4 wt.% HPC with respect to oil continuous phase was added to this system. Because above 1.4 wt.% the solution was difficult to be handled, this HPC concentration was the maximum soluble in oil phase. Although emulsion stability increased as viscosity increased, O/W/O multiple emulsion was not formed as shown in figure 2. In the next experimental, polyethylene glycol (PEG) of various concentration for the aqueous phase was utilized to prepare O/W/O multiple emulsion. As shown in figure 3, multiple emulsion droplets were not observed. Compared to the sample using HPC polymer in the oil phase, the water droplets became very smaller.

To prepare O/W/O multiple emulsion by one-step emulsification, HPC and Span80 in the oil phase and PEG and Tween20 in the water phase were added. When all of two polymers and two surfactants were added in the solution, O/W/O multiple emulsion with various shapes was observed by optical microscope equipped with camera as shown in figure 4. Through the experiment under the various condition, it was known that without one of two polymers and two surfactants, O/W/O muliple emulsion was not prepared. In this O/W/O multiple emulsion, three types of emulsion droplets were observed. : One type is droplets containing one large internal droplet, the other is droplets containing several small internal droplets with various size, and another is droplets entrapping large numbers of small internal droplets with narrow size distribution [11]. Water droplet size with internal oil droplets was ranging from 5 ㎛ to 10 ㎛. As the number of internal oil droplets within water droplet increases, the size of external water droplet grows larger.

The stability of multiple emulsion prepared under the condition of 1.4 wt.% HPC, 18 wt.% PEG, 5 wt.% Tween20, and 3 wt.% Span80, was investigated using optical microscope. Compared to initial morphology, the multiple emulsion was stable for 6h after preparing. After 8h, the reduction of the number of internal small oil droplets and the coalescences between internal oil droplets occurred. After the lapse of 24h, Most external water droplet containing one large internal droplet or large numbers of small internal droplets disappeared and only a small number of droplets entrapping several small internal dorplets remained.

4. Acknowledgements

The financial support for this work was partially provided by Center for Ultramicrochemial Process System (CUPS).

5. References

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Figure 1. Optical image of W/O emulsion prepared by Tween20 and Span80

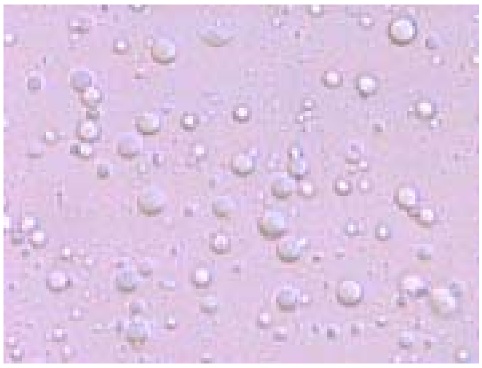

Figure 2. Optical image of W/O emulsion prepared by adding HPC polymer

Figure 3. Optical image of W/O emulsion prepared by adding PEG polymer

Figure 4. Optical image of O/W/O multiple emulsion prepared by adding HPC and PEG