Proceedings of Symposium on Ultrasonic Electronics, Vol. 33 (2012) pp. 221-222
13-15 November, 2012

Controlled Release of Internal Substances from Pluronic Micelles using Ultrasound as Trigger

超音波刺激によるプルロニックミセルからの内包物質の放出制御

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1. Introduction

Recently ultrasonic cavitation has been attracted in various fields; many researchers are studying about it. One of them is drug delivery system(DDS) in medical field. Liposomes or micelles of surfactant are used as drug carrier and internal drug release control with ultrasound for decreasing drug toxicity. We adapt this research for chemical reaction control; in brief spatial and temporal chemical reaction control by ultrasound cavitation. However it has also been pointed out in the study of the medical fields, knowledge on the effects conditions ultrasonic irradiation such as the operating frequency and structure of the surfactant molecules to form micelles consisting of a carrier will give the release of substance comprehension has not been obtained. In this research, to research about them, we use Pluronic for water-soluble polymer surfactant.

2. Experimental

2.1 Reagents

In this study, the Pluronic micelle and hydrophobic dye (NKX-1595) were used as the model reactant carrier and internal substances, respectively. Figure 1 shows structure of pluronic molecule that we use as surfactant to form micelles.

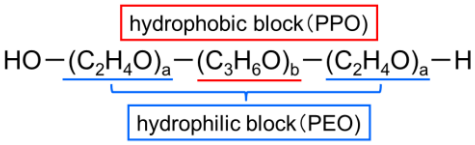

Fig.1 Structure of Pluronic

Pluronic block copolymers consist of polyethylene oxide (PEO) and polypropylene oxide (PPO) blocks arranged in the EOx=2–POy–EOx=2 structure. Table 1 shows the physical properties of the Pluronic using this study.

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Table 1 Physicochemical properties of Pluronic

Copolymer	PEO/PPO	Molecular weight	CMC [M]	HLB value
F-68	160/30	8350	4.8×10^{-4}	29
P-84	35/40	4200	7.1×10^{-5}	14
P-85	50/40	4600	6.5×10^{-5}	16
F-88	200/40	10800	2.5×10^{-4}	28
F-108	300/55	15500	2.2×10^{-5}	27

2.2 Experimental procedure

The Pluronic micelle solution containing NKX-1595 was prepared by a dialysis method. The Pluronic and NKX-1595 were dissolved in N,N-dimethylacetamide, at the concentrations of 0.5 and 2.1×10^{-5} wt %, respectively. To form the Pluronic micelle and remove organic solvent, the solution was dialyzed for 24 h in a cellulose membrane bag against ion exchanged water. Ultrasound was irradiated to the ion exchanged water solution including the Pluronic micelle containing dye for 10 min. The ultrasonic power in the reactor was measured by calorimetry,[1)] and power was changed in the range of 0 and 17 W. Figure 2 shows the experimental apparatus. The absorbance of the sample solution was measured before and after ultrasonication because the internal dye was released from the micelle after ultrasonication, and the released dye was separated from the micelle solution. The degree of dye release (DR) was defined by eq. (1). Here, I_0 and I represented the absorbance of the sample solution before and after ultrasonic irradiation at the wavelength of 480 nm.

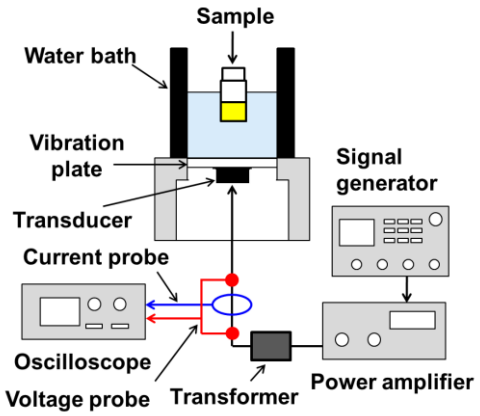

Fig.2 Experimental setup

$$\mathrm{DR}\ [\%] = \frac{I_0 - I}{I_0} \times 100 \qquad (1)$$

In this study, the relationship between the ultrasonic frequency and the type of Pluronic was investigated.

3. Results and Discussion

Figure 3 shows effect of ultrasonic frequency on DR on Pluronic F-108 micelle.

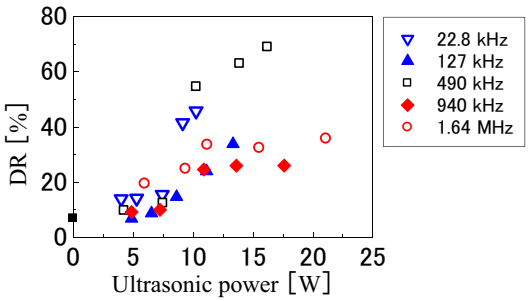

Fig.3 Effect of ultrasonic frequency on relationship between ultrasonic power and DR with Pluronic F-108.

This graph indicates that it is easy to promote release from micelle when we irradiate small frequency ultrasound. We considered that the physical effects of ultrasound such as the shock wave are affected.

In addition, the stability of Pluronic micelles is proportional to the CMC of Pluronic molecule[2], we organized by the change of the CMC of Pluronic effects of the structure of the molecule on the release with ultrasonic power 10 W in Figure 4. The graph shows that the release has been promoted in Pluronic micelles of all kinds in the 22.8 kHz low-frequency. From these results, to promote the release of internal substances by ultrasound, ultrasonic physical effect may have an impact. Moreover, the stability of Pluronic micelle is proportional to the CMC has been confirmed

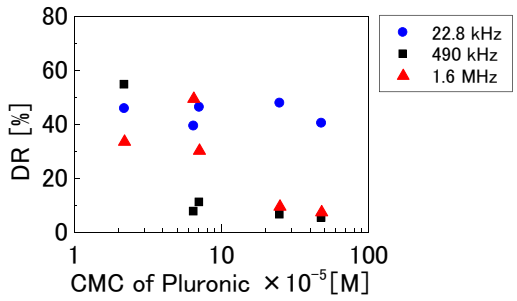

Fig.3 Effect of molecule structure of Pluronic on stability of Pluronic micelle.

because as the CMC of Pluronic micelle is small, release is promoted in a large frequency.

Based on the results of this time, we were carried out following discussion about the mechanism of release of encapsulated material from Pluronic micelles by ultrasonic stimulation. Micelle has been releasing material comprehension gradually even in the stable. When it is promoting the release by ultrasonic stimulation, it is necessary to cleave or ease the micelle and the core of the micelle expose. In this case, two processes are considered. First, micelle is cleaved by the shock wave caused by cavitation due to ultrasound irradiation. Another is promoted by the droplets to vibrate by the effect of acceleration at high frequencies. It considered that ultrasonic cavitation plays important role because release from the micelles of Pluronic of all kinds have been promoted on 22.8 kHz most low frequency.

4. Conclusion

When the ultrasound irradiate to aqueous solution of Pluronic micelles, the release of encapsulated material from the micelle has been promoted. In this case, the release of substances from inside the micelle is the contribution of the physical effects of ultrasound has been suggested because the release rate increases by more low-frequency ultrasonic irradiation.

References

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