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Effluence of Internal Substances from Pluronic Micelle using Ultrasound

超音波を用いたプルロニックミセルからの内包物質の放出

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1. Introduction

In a general chemical industrial process, the reactant is injected into the reactor with the progress of the reaction, and a reactor is different at each reaction. Therefore, many reactors, mixture operations, and separation operations are needed, and the design and maintenance become complex. On the other hand, high performance drug carrier has been investigated in the field of drug delivery system[1)]. The use of Pluronic block copolymers in experimental medicine and pharmaceutical has been investigated long time[2)]. And, the application of ultrasound for drug delivery system has been investigated[3)]. In this study, the application of the drug carrier to a chemical reaction process was investigated from the vier point of process intensification. Pluronic micelle and hydrophobic dye (NKX-1595) were used as a model reactant carrier and internal substances, respectively. The effects of ultrasonic irradiation on effulence of dye from Pluronic micelle were investigated. Especially, the relationships between ultrasonic frequency and type of Pluronic were investigated. In addition, the difference between the ultrasonic stimulation and thermal stimulation was compared.

2. Experimental

Fig. 1 shows the experimental apparatus. A stainless-steel vibration plate attached with PZT transducer (Honda Electronics Co., Ltd.) was installed at the bottom of the center of the water bath. The ultrasonic frequency was operated at 22.8 kHz and 490 kHz. The transducers were driven by a power amplifier (1040L, E&J). The power amplifier was driven by a continuous sinusoidal wave produced by a signal generator (WF1984, NF Corp.). The effective electric power input to the transducer was calculated from the voltage at both ends of the transducer and current measured using an oscilloscope (TDS3012C, Tektronix Inc.) and current probe (TCP202, Tektronix Inc.). The diameter of the glass reactor was 27 mm, and the temperature of the water bath was kept constant at 298 K. **Table 1** shows the experimental condition.

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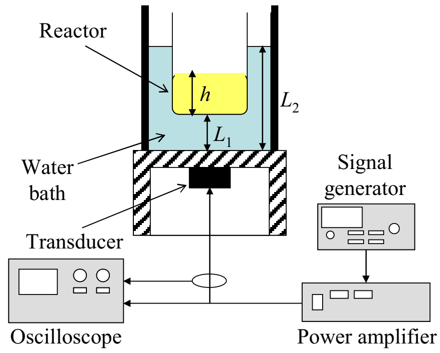


Fig. 1 Experimental apparatus

Table1 Experimental condition

f [kHz]	L_1 [mm]	L_2 [mm]	h [mm]	V [mL]	P [W]
22.8	47	90	18	10	0 - 10
490	60	90	18	10	0 - 17

Table 2 shows the physical property of Pluronic using this study. Pluronic block copolymers consist of ethylene oxide (EO) and propylene oxide (PO) blocks arranged in EO_x - PO_y - EO_x structure. The Pluronic micelle solution containing NKX-1595 was prepared by a dialysis method. Pluronic and NKX-1595 were dissolved in N,N-dimethylacetamide, and concentrations were 0.5 wt% and 2.1 × 10^{-5} wt%, respectively. To form Pluronic micelle and remove organic solvent, the solution was dialyzed for 24 h in a cellulose membrane bag against ion exchanged water.

Table 2 The physical property of Pluronic

Pluronic	EO units (x)	PO units (y)	Molecular weight	CMC [M]
F-68	153	29	8400	4.8×10^{-4}
F-88	207	39	11400	2.5×10^{-4}
P-103	34	60	4950	6.1×10^{-6}
F-108	265	50	14600	2.2×10^{-5}

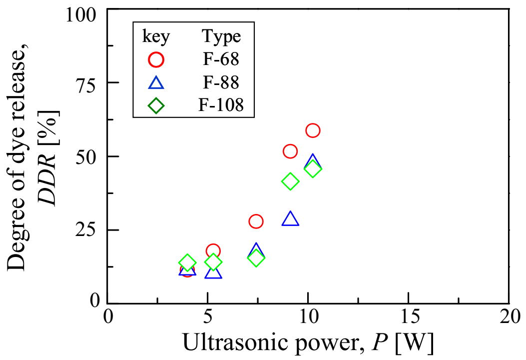
The ultrasound was irradiated to the micelle solution containing dye for 10 min. The ultrasonic power in the reactor was measured by calorimetry[4]. The effect of thermal stimulation on release was investigated for the comparison. The temperature of water bath was changed within 276.5 K and 313 K, and the micelle solution was set in the water bath for 24 h.

The absorbance of sample solution was measured before and after ultrasonic or thermal stimulation, and the degree of dye release (DDR) was defined as **Eq. (1)**. Here, I_0 and I represented absorbance of before and after ultrasonic irradiation sample solution at the wavelength of 480 nm.

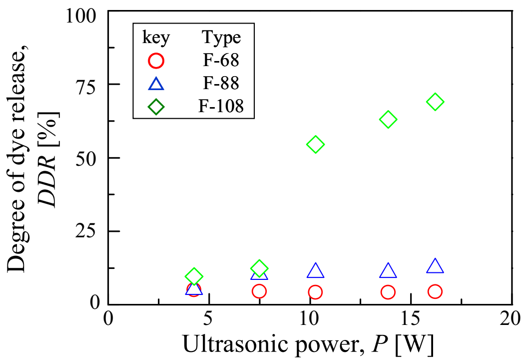
$$DDR = \frac{I_0 - I}{I_0} \times 100 \qquad (1)$$

3. Results and Discussions

Fig. 2 shows the effect of molecular weight of Pluronic on DDR at the frequencies of 22.8 kHz and 490 kHz. It is found that the dye release becomes easy at low ultrasonic frequency. The internal dye was considered to be released from the micelle by ultrasonic physical effect.



(a) f = 22.8 kHz



(b) f = 490 kHz

Fig. 2 Effect of molecular weight of Pluronic on DDR

Fig. 3 shows the effect of number of EO units on DDR at the frequency of 490 kHz. The dye was easy to release from P-108 micelle. Core size and corona thickness of Pluronic micelle have been reported[5]. Core size of P-103 and F-108 were 38.6 Å and 28.3 Å, respectively. Corona thickness of P-103 and F-108 were 21.5 Å and 76.6 Å, respectively. It is guessed that the core size of micelle influences DDR.

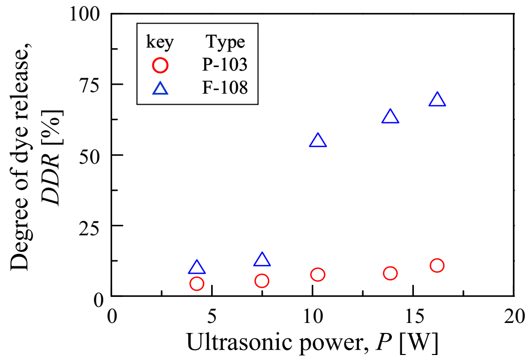


Fig. 3 Effect of number of EO units of Pluronic on DDR

Table 3 shows the effect of type of external stimulation on DDR. The ultrasonic stimulation was effective for the release of internal substance. And, DDR was considered to be controlled by the type of external stimulation.

Table 3 Effect of ultrasonic stimulation (10 min) and thermal stimulation (24 h) on DDR

Pluronic	22.8 kHz (10 min)	490 kHz (10 min)	303 K (24 h)	313 K (24 h)
F-68	58.7	4.4	4.54	27.8
F-88	47.6	12.5	10.8	63.4
F-108	45.8	69	61	51.8

4. Conclusion

The combination between ultrasonic frequency and type of Pluronic influenced the capability of effluence of internal substance from micelle. From the result of the comparison of ultrasonic stimulation and thermal stimulation, internal substance was able to release from the micelle rapidly using ultrasound in an appropriate condition. The possibility of new chemical reaction process using Pluronic micelle as a reactant carrier was found.

References

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