実験報告書様式（一般利用課題・成果公開利用）

（ ※本報告書は英語で記述してください。ただし、産業利用課題として採択されている方は日本語で記述していただいても結構です。 ）

CROSS TOKAI **Experimental Report** J-PARC	承認日 Date of Approval 2015/9/15 承認者 Approver Jun-ichi Suzuki 提出日 Date of Report 2015/5/22
課題番号 Project No. **2014B0279** 実験課題名 Title of experiment **Characterization of Stimuli-Responsive Magnetic Nanocomposites as Multifunctional Drug Delivery Systems** 実験責任者名 Name of principal investigator **Kuen-Song Lin** 所属 Affiliation **Department of Chemical Engineering & Materials Science, Yuan Ze University, Chung-Li City 320, Taiwan, R.O.**	装置責任者 Name of Instrument scientist **Dr. Jun-ichi Suzuki** 装置名 Name of Instrument/(BL No.) **Bl 15 TAIKAN** 実施日 Date of Experiment **19 - 21 December 2014**

試料、実験方法、利用の結果得られた主なデータ、考察、結論等を、記述して下さい。（適宜、図表添付のこと）

Please report your samples, experimental method and results, discussion and conclusions. Please add figures and tables for better explanation.

1. 試料 Name of sample(s) and chemical formula, or compositions including physical form.

No	物質名 Sample or reagent name	化学式 Chemical formula	形態(形状) Description	量 Quantity	性質 Hazards	用途 Purpose
1	Pluronic	PEO-PPO-PEO	Dissolved in water	25 samples Ten samples contain 0.2 g Five samples contain 20 mg Five samples contain 20 mg Three samples contain 50 mg Two samples contain 0.1 g	None	Experimental sample
2	Paclitaxel	$C_{47}H_{51}NO_{14}$	Dissolved in Pluronic	10 samples each contains 2 mg	Toxic if ingested	Experimental sample
3	Magnetite	Fe_3O_4	Dissolved in Pluronic	10 samples each contains 3 mg	None	Experimental sample
4	Doxorubicin hydrochloride	$C_{27}H_{29}NO_{11}$.HCl	Dissolved in Pluronic	5 samples each contains 1 mg	Toxic if ingested	Experimental sample
5	Deuterium oxide	D_2O	To dissolve Pluronic, magemite , Doxorubicin	20 samples Five samples contain 2 ml Five samples contain 5 ml Ten samples contain 20 ml	None	Experimental sample

2. 実験方法及び結果（実験がうまくいかなかった場合、その理由を記述してください。）

Experimental method and results. If you failed to conduct experiment as planned, please describe reasons.

Samples and experimental procedures

This work aimed to study the effect of temperature and addition of paclitaxel (PTX) as hydrophobic drug and superparamegnetic iron oxide nanoparticles (SIONs) on micelle formation and structural changes. In doing so, samples divided into three parts:

(a) Pluronic with different concentrations and hydrophobicity
(b) Pluronic in presence of SIONs
(c) Pluronic in presence of PTX
(d) Pluronic in presence of PTX and SIONs

The magnetic DDS in H_2O-rich and D_2O-rich solvents prepared to isolate scattering from the iron oxide core and polymer shell, respectively. To study the effect of the drug, SIONs, temperature, and magnetic field on the DDS structure, samples in presence and absence of these components investigated, respectively. Scattering experiments for each sample at continuous Q range of $0.005 < Q < 0.4$ Å^{-1} was performed. Selected samples were then measured at two different temperatures 37 and 50^{o}C. The exposure time for each sample was 1 hour. The raw data then processed using house made package. The experiments were started from 9 am on December 19 and ended on 10 am December 21and totally 30 samples have measured. After sample disposal and cleaning the quartz cell we took airport bus and returned to Taiwan midnight.

Summary of measurement and results

We really enjoyed learning small-angle neutron scattering (SANS) and discussion with beamline scientists. The data was as expected and we definitely gained a lot from doing SANS experiments at J-PARC not to mention and getting to meet and discussion on SANS techniques with experts was helpful to better manage and design SANS experiments in future. Pluronic micelles have been investigated at different temperatures and concentrations. There was correlation between SANS intensity and polymer concentration.

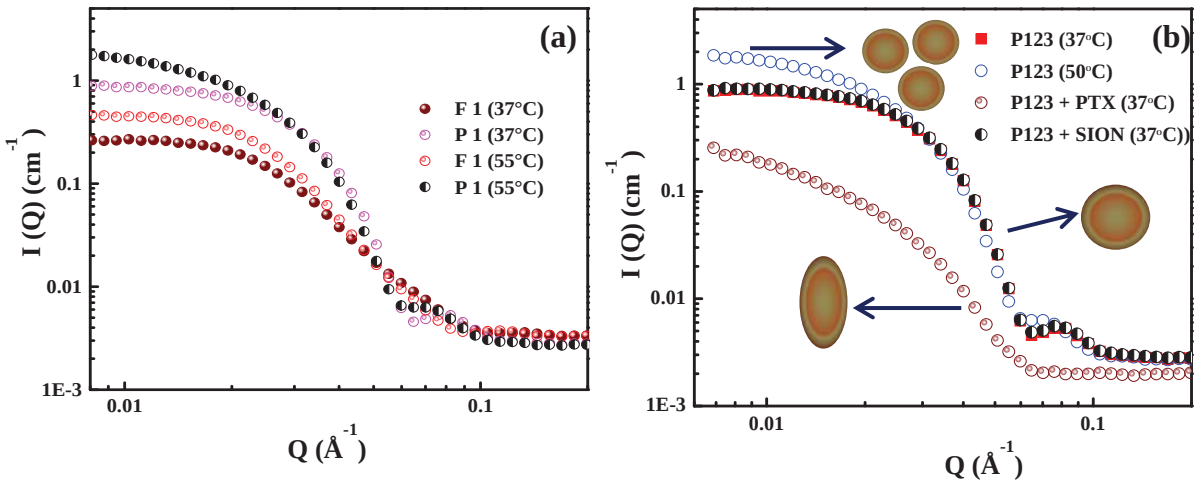

Figure 1. SANS from (a) Pluronic P123 and F127 at different temperatures (b) SANS from Pluronic P123 at different temperatures and in presence of SIONs and PTX.

2. 実験方法及び結果（つづき） Experimental method and results (continued)

As expected the micelle structure for 1 w/v% differs from 0.1 w/v%. The former exhibited core/shell structure however large aggregates are formed. The effect of temperature shown in Figure 1. At higher temperature due to dehydration of hydrophilic PEO and greater influence of hydrophobic interaction of PPO which is associated with a decrease in CMC of Pluronic. In comparison to 34ºC, aggregation number and size of spherical micelles became large at 50ºC. As shown in Figure 1(b), addition of drug resulted in change of micelle structures, but, presence of SIONs with the size of >6 nm did not influence the micelle structure. Furthermore, SANS experiment performed to better understand the effects of solubilized drugs on the micellar structure.

Results showed that the presence of higher concentrations of PTX in micelle structure leads to the larger core and corona size which are in good agreement with the findings of other studies. As can be seen in Figure 2, the SANS of P123-PTX at low Q increases slightly. This implies the presence of large aggregates, and it is believed to be due to the existence of dominant hydrophobic interaction of PPO core. Upon addition of drug, both Pluronic concentrations showed significant changes in their aggregation behavior indicating the uptake of the drug mainly by the hydrophobic PPO core, which gives rise to the larger core radius. In summary, results of SANS analyses showed that micelle structure and functions of nanocarriers can be influenced by its magnetic core and hydrophobic drug. As a result, presence of SIONs and PTX in hydrophobic core leads to the larger micelle core. The same trend was observed at higher temperature due to dehydration of hydrophilic PEO and greater influence of hydrophobic interaction of PPO, which is confirmed by Fourier transform infrared spectroscopy (FTIR). The volume fraction of solvent in the core (Φsol) decreases on addition of the drug, indicating the uptake of the drug by the hydrophobic PPO core. Accordingly, an increase in the aggregation number (Nagg), and the core radius (Rc) was observed. Moreover, comparison of the results between F127 and P123 also indicated that the hydrophobicity of the polymers influences micelle structure and drug uptake.

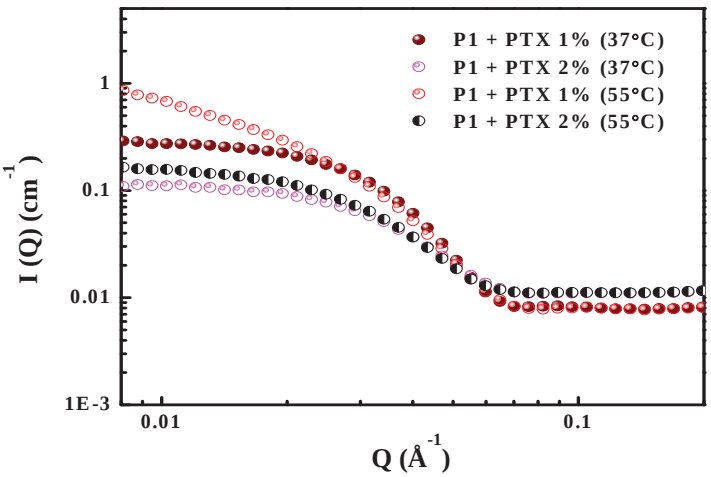

Figure 2. SANS from Pluronic P123 with 1% and 2 % PTX at different temperatures.

Acknowledgment

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