Fabrication of PEGylated Liposome using supercritical flow process in tube system

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1. Background and Purpose

Drug Delivery system (DDS) have an enormous amount of interest because Active Pharmaceutical Ingredient (API) are decomposed or absorbed in in-vivo system before reaching the target area, which caused the over dose API and the serious side effects for human body [1]. Liposome is one of the most promising API carriers in the pharmaceutical industry. In our work, liposome fabrication flow process (called as LipTube) using supercritical carbon dioxide ($scCO_2$) and microfluidic tube system has already been developed. However, the size control of liposome is not enough as a practical drug carrier. The retention time of the liposome in blood is needed to be increased by the surface modification with a functional chemical group. Poly- (ethylene glycol) (PEG) is widely used surface modifier of liposome due to biocompatibility, solubility in aqueous and organic media and very low immunogenicity. Therefore, we aimed to make PEGylated liposomes and to control the state of PEGylation using LipTube process.

2. Experiment

We compared the properties of PEGylated liposome fabricated by a batch-type process based on thin layer method [2] and LipTube process in this work. Figure 1 shows a schematic diagram of LipTube process used for PEGylated liposome. Timolol maleate (TM) was used as API, 1,2-Distearoyl-sn-glycero-3-phosphocholine (DSPC) and 1,2-Distearoyl-sn-glycero-3-phosphoethanolamine-PEG-2K-Amine (PEG-DSPE) were used as lipid forming liposome. In LipTube process, DSPC solution and TM solution mix to form $W/scCO_2$ emulsion. After formation of $W/scCO_2$ emulsion, $W/scCO_2$ emulsion was mixed with PEG-DSPE solution to form liposome in the microchannel. Size and surface zeta potential of liposome fabricated in LipTube process were measured using a dynamic light scattering (DLS) method. Encapsulation efficiency of TM in the liposome was measured using high performance liquid chromatograph. The zeta potential was used for the determination of the fixed aqueous layer thickness for PEGylated liposome from LipTube process. [3]

3. Results and Discussion

Figure 2 give the results of PEGylated liposome size. The results in figure2 revealed that LipTube process gives the PEGylated liposome with size distribution narrower than that from thin layer method. Additionally, the fixed aqueous layer thickness was successfully controlled by changing the concentration of PEGylated lipid. These results suggest that LipTube process is one of the promising process to fabricate the PEGylated liposome and to control the PEGylated surface liposome.

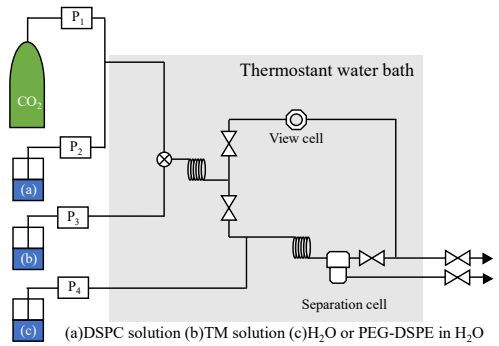

Figure 1. Experimental equipment for LipTube

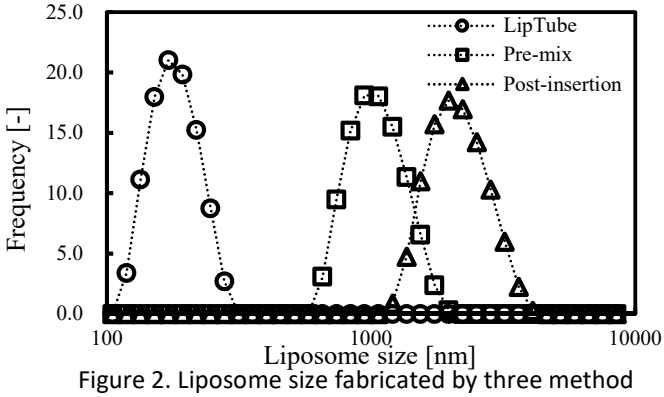

Figure 2. Liposome size fabricated by three method

Reference

[1] T. M. Allen et al., SCIENCE, 303, 1818-1822 (2004)
[2] A. D. Bangham et al., J. Mol. Biol., 13, 238-252 (1965)
[3] Y. Sadzuka et al., International Journal of Pharmaceutics, 234, 171-180 (2002)