Mechanism of Micelle-Vesicle Transformation and Control of Vesicular Sizes and Properties

○Hiroshi KASHIWAGI and Masaharu UENO
(Division of Pharmaceutical Sciences, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama)

Liposomes play important roles not only in reconstitution of proteins on lipid membranes but also in materials of drug delivery. Sizes are responsible for disposition of liposomes, while fluidities for orientation of proteins on the reconstituted membranes. Sizes of liposomes prepared on removal of detergents from mixed micelles were known to depend on the kinds and removal methods of the detergent. In this study, measurement of particle sizes by quasi-elastic light scattering, turbidity, and fluidity parameters monitored by ESR spectrum of 5-, 12-, or 16-doxylstearic acid, electron micrographs of binary aggregates of egg yolk phosphatidylcholine (EPC) and a detergent (octylglucoside, sodium cholate, or octaethyleneglycol mono-n-dodecylether ($C_{12}E_8$)) as functions of detergent concentrations and time resulted in the liposomal destruction mechanism (vesicles→SUV*(small particles containing large amounts of detergents)→intermediate structures→mixed micelles). Vesicle formation on removal of detergents from mixed micelles proceeded oppositely symmetrically. The sizes of SUV*, which were prepared by adding appropriate amount of a detergent to EPC small unilamellar vesicles, time-dependently increased in case of octylglucoside-containing aggregates, but slightly increased in case of sodium cholate-containing systems, suggesting the size determining step to be the stage of SUV* and involvement of net charges of detergent molecules in the liposomal size control. The membrane fluidities of EPC micelles containing small amounts of detergents possessing steroidal structures, such as sodium cholate, CHAPS, and sodium taurocholate, were small, while those of detergents without steroidal structures, such as octylglucoside and $C_{12}E_8$, were large, suggesting methods of regulation of a physical property (e.g., orderliness of hydrocarbon chains of liposomes) during preparation.