Monolayers of Poly(ethylene oxide)-Bearing Lipids at Air-Water Interface

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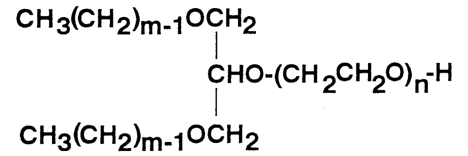
Monolayers of poly(ethylene oxide)-bearing lipids and their mixed monolayers with dimyristoylphosphatidylcholine at the air-water interface was investigated using surface pressure measurements. The surface pressure-area relationship revealed that the poly(ethylene oxide) moiety length significantly affected the interaction among the lipid molecules. This study provided a precise picture of the lipid membrane-water interface.

A modification of liposomal surface with poly(ethylene oxide) (PEO) affects interaction of liposome with intact cell membrane. Although in many cases the modification weakens the interaction,[1] we have shown that a specific modification of liposomal surface with PEO-lipids (Figure 1) can enhance the interaction as well: incorporation of PEO-lipid(12,13) to liposome induced fusion between the liposome and carrot protoplast[2,3] or HeLa[4] and promoted endocytosis of liposome by Jurkat cell.[5] To Jurkat cell, PEO-lipid(12,31) caused fusion of liposome.[6]



$$\begin{array}{l} CH_3(CH_2)_{m-1}OCH_2 \\ \quad\quad\quad\quad\quad\quad\ | \\ \quad\quad\quad\quad\quad\quad CHO\text{-}(CH_2CH_2O)_n\text{-}H \\ \quad\quad\quad\quad\quad\quad\ | \\ CH_3(CH_2)_{m-1}OCH_2 \end{array}$$

Figure 1. The structure of PEO-lipid(m,n).

The rationale of the apparently ambivalent effects of the modifications with PEO is yet to be clarified. Clearly here, the presence of PEO moieties at the lipid membrane-water interface intervenes in the original cell-liposome interaction. Knowledge of the precise behavior of PEO moieties at this interfacial region is essential to understand the effect of the modifications.

In this study, we focused on our own PEO-lipid system and investigated the interaction between PEO-lipid molecules or between PEO-lipid and DMPC molecules in a monolayer spread at the air-water interface using surface pressure measurements. This should provide valuable information on the interfacial region.

PEO-lipids (PEO-lipid(12,5), PEO-lipid(12,13), and PEO-lipid(12,31)) were synthesized as previously described.[7,8] Aliquots (2 μl) of dimyristoylphosphatidylcholine (DMPC) and the PEO-lipids dissolved in chloroform/methanol mixture (9:1 v/v) were successively spread on a triply distilled water subphase. The measurements of surface tension $\gamma(M)$ at constant area (38 cm^2) were performed by the Wilhelmy plate method at 25℃ ± 0.5℃.[9] From the values of water surface tension ($\gamma(H_2O) = 71.8$ mN/m at 25℃) and the surface tension values of the spread monolayers, $\gamma(M)$, the surface pressures of the monolayers, $\Pi = \gamma(H_2O) - \gamma(M)$, were deduced. All the surface pressure values reported are mean values of at least three measurements, and the standard deviation of the mean never exceeded ± 2 mN/m.

In Figure 2, the surface pressure was plotted against the surface density of either DMPC or PEO-lipids. The surface pressure (Π)-surface density ($1/A$, where A is the area per molecule) plots for the three PEO-lipids studied show that the surface property of these lipids is closely related to the PEO chain

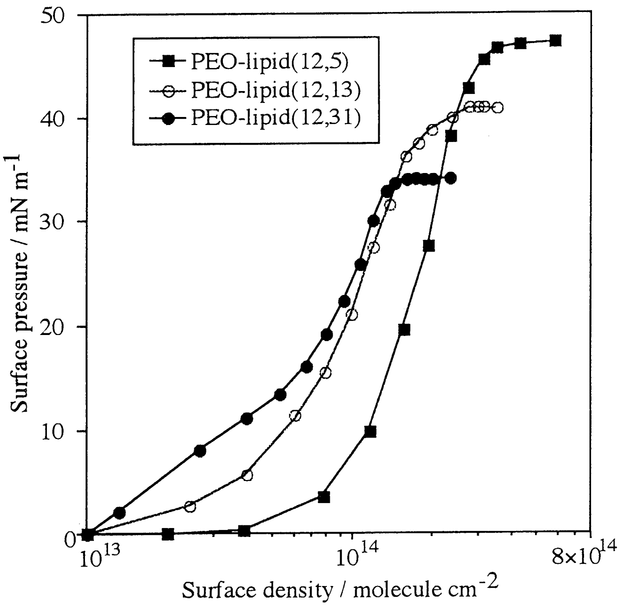


Figure 2. Surface pressure-surface density plots of PEO-lipid monolayers.

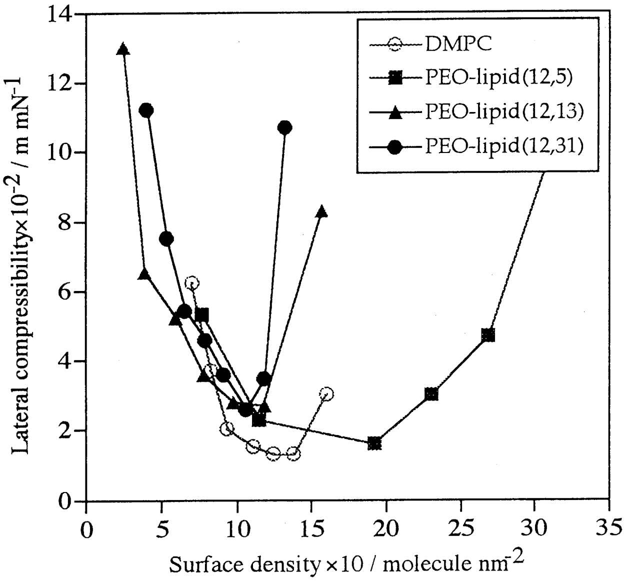


Figure 3. Lateral compressibilities of pure DMPC and PEO-lipidmonolayers.

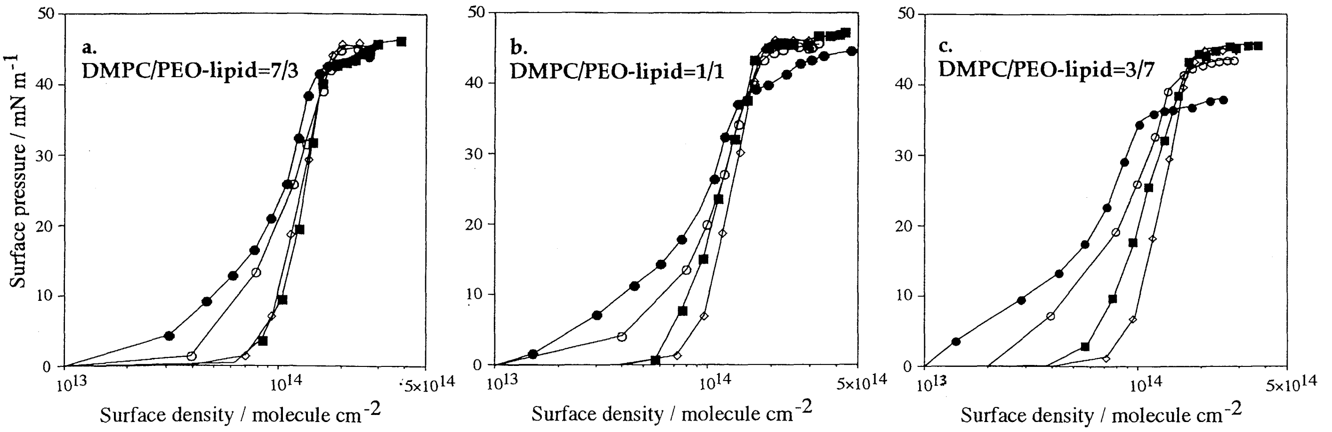


Figure 4. Surface pressure-surface density relationships for mixed DMPC/PEO-lipid monolayers. DMPC/PEO-lipid(12,5) (■), DMPC/PEO-lipid(12,13) (○), DMPC/PEO-lipid(12,31) (●) and DMPC only (◇).

length. The collapse pressure (∏c) decreased as the chain length increased; PEO-lipid(12,5) collapsed at 46.5 mN/m, PEO-lipid(12,13) at 41 mN/m, and PEO-lipid(12,31) at 34 mN/m. At the same time the limiting area increased; 36.8 × 10^{-2} nm^2 for PEO-lipid(12,5), 55 × 10^{-2} nm^2 for PEO-lipid(12,13), and 74 × 10^{-2} nm^2 for PEO-lipid(12,31). The larger molecular area observed for PEO-lipid(12,13) or PEO-lipid(12,31) is attributed to the larger area occupied by the PEO moiety of those PEO-lipids in the subphase compared to the case of PEO-lipid(12,5).

Also the contour of the isotherm changes with the PEO chain length. The steep slope displayed by PEO-lipid(12,5), which corresponds to condensed type behavior of this monolayer, contrasted with the moderate slope observed for the two other PEO-lipid monolayers, characteristic of expanded film behavior.

The change in the shape of the isotherms with the increase in the PEO chain length is better understood when one compares their lateral compressibilities, (1/A)(dA/d∏).[10] From the compressibility plots of the PEO-lipids and DMPC (Figure 3), it is clearly seen that the lowest compressibility is exhibited by DMPC (1.3 × 10^{-2} m/mN), followed by PEO-lipid(12,5) (1.6 × 10^{-2} m/mN). Increasing the chain length of the PEO moiety led to a sharp increase in the minimum of the compressibility (up to 2.6 × 10^{-2} m/mN for PEO-lipid(12,31)).

The low compressibility of PEO-lipid(12,5) suggests strong van der Waals interactions between the aliphatic moieties of the lipid molecules protruding into the air phase. The picture that the alkyl chain moieties, rather than the PEO moieties, control the lateral packing of the PEO-lipid(12,5) monolayer is consistent with the high collapse pressure and the low limiting area displayed by this monolayer. Such a behavior of PEO-lipid(12,5) is comparable to that of DMPC. Conversely, for PEO-lipid(12,13) and PEO-lipid(12,31) monolayers, the longer PEO chain immersed in the water subphase controls the packing at the interface. The PEO moiety occupies large area as indicated by the high limiting area and prevents a close contact between the hydrophobic moieties of the lipid molecules. This view is also supported by the higher compressibility and the relatively low collapse pressure.

The interfacial behavior of DMPC/PEO-lipid mixed monolayers with the high DMPC content (Figure 4a) is strongly controlled by the highly incompressible DMPC, while the PEO chain length affects the behavior less significantly. In Figure 4b, both DMPC/PEO-lipid(12,5) and DMPC/PEO-lipid(12,13) monolayers collapsed at 45.5 mN/m, the collapse pressure of DMPC. The control of the behavior of the whole by the single component indicates the existence of strong interaction between the two components. On the other hand, a kink in the isotherm of DMPC/PEO-lipid(12,31) in Figure 4b signifies that each of the two components tends to collapse at its own collapse pressure. Such independence of each component in a mixed monolayer (demixing) reveals that two components exist without that they strongly interact one with other. The weak interaction between DMPC and PEO-lipid(12,31) can be attributed to a larger distance between their hydrophobic chains. The compressibility of the mixed monolayers calculated from the data in Figure 4 (not shown) also supported the absence of strong interaction between the two lipids.

References and Notes

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