CHEMISTRY LETTERS, pp. 755-758, 1983.

SIGNAL RECEPTIVE CAPSULE MEMBRANE. Ca^{2+}-INDUCED PERMEABILITY CONTROL OF LARGE NYLON CAPSULE COATED WITH SYNTHETIC BILAYER MEMBRANE

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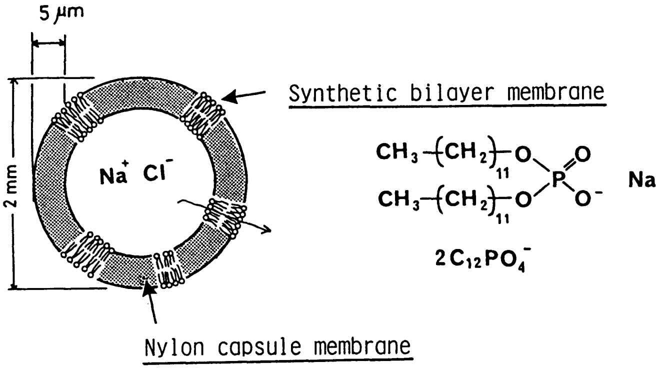
Nylon ultrathin capsules coated with sodium didodecyl phosphate bilayer membrane were prepared. Permeation of NaCl from the inner aqueous phase of the coated capsule was reversibly increased by treating with Ca^{2+}, and decreased to the original rate by washing with EDTA from outside.

In an previous paper$^{1)}$, we reported the permeation of NaCl from the inner aqueous phase of the synthetic dialkyl bilayer membrane-coated nylon capsule was controlled by the phase transition phenomenon of the coated bilayers. These amphiphile bilayer-coated capsule membranes have advantages of both nylon capsules and bilayer vesicles; a large inner aqueous phase, a physically strong wall and characteristics of bilayer membranes.

In this communication, we describe the signal receptive nylon capsule coated with sodium didodecyl phosphate ($2C_{12}PO_4^-$)bilayer membrane. A schematic illustration of the capsule is shown below.



Large nylon capsules (diameter; 2 mm, membrane thickness; 5 µm) were prepared by interfacial polymerization from ethylenediamine and 1,10-decanedicarbonyl chloride in the presence of a little amount of a cross-linking agent (trimesoyl chloride)$^{1)}$. Nylon capsules obtained were dialyzed against 0.2 M NaCl aqueous solution to get capsules containing NaCl in the inner aqueous core. They were transferred to a dodecane solution (3 ml) of $2C_{12}PO_4^-$ amphiphiles$^{2)}$ (50 mg) and submerged at 60°C for 10 min. Amphiphile-coated capsules were picked up and rolled on a filter paper to remove the excess dodecane solution. The amphiphile content on the capsule was estimated to be 0.15 ± 0.02 mg/capsule from the elemental analysis. Figure 1 shows scanning electron micrographs of the sectional view of the uncoated and $2C_{12}PO_4^-$-coated nylon capsule membrane. It was proved that the uncoated nylon capsule had an porous membrane structure and the amphiphile-coated capsule was entirely coverd with plates of $2C_{12}PO_4^-$ and clear pores were not seen in the intersection. Similar electron micrographs had been obtained from other amphiphile-coated capsules$^{1)}$.

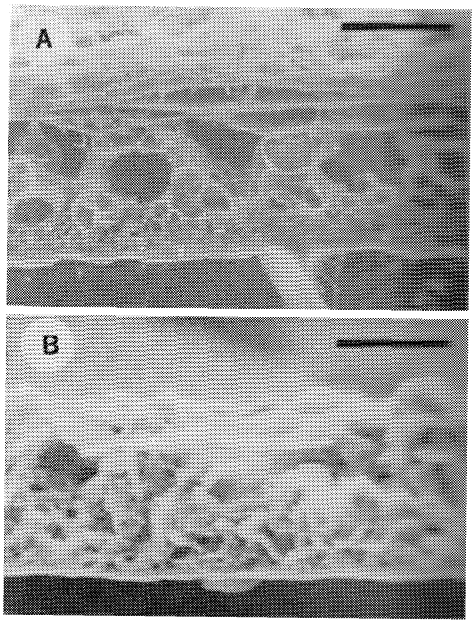


Figure 1. Scanning electron micrograph of sectional view of uncoated (a) and $2C_{12}PO_4^-$ coated (b) nylon capsule membrane. Scale is 5 μm

It is important whether the coating $2C_{12}PO_4^-$ amphiphile forms bilayer structures on the capsule or not. The presence of the phase transition between gel and liquid crystal is one of the fundamental physicochemical characteristics of bilayer structures, and has been inferred or proved for the coating amphiphiles on the capsule membrane by a differential scanning calorimetry (DSC), as well as aqueous bilayer vesicles$^{1)}$. The coating $2C_{12}PO_4^-$ bilayer on the capsule was confirmed to have the phase transition tempareture (T_c) at 45°C (ΔH = 15 kcal/mol) by DSC measurements.

The permeability of these capsules to NaCl was measured by detecting increases in the electrical conductance of the outer water phase, after dropping one capsule into the deionized, distilled water in a thermostated cell. Figure 2 shows typical examples of NaCl release to the outer water phase with time at 35°C. The permeability constant (P, cm/s) is calculated from an efflux (a slope of Fig.1), a diameter of the capsule (2 mm) and a concentration of NaCl incorporated in the inner aqueous phase (0.19 ± 0.01 M) which is estimated from the change of specific conductance after destroying the capsule$^{1)}$.

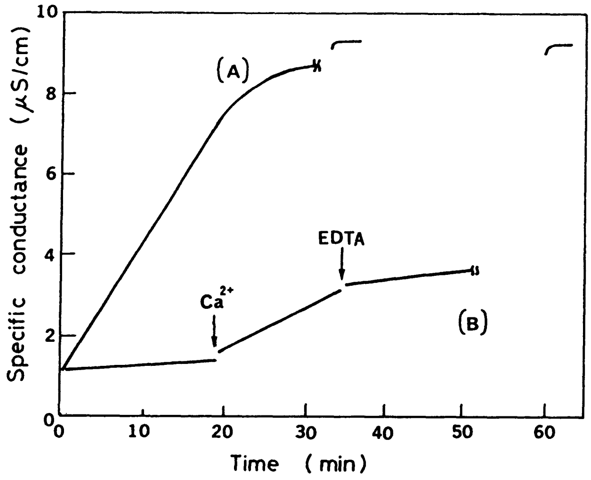
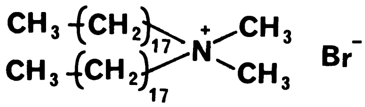


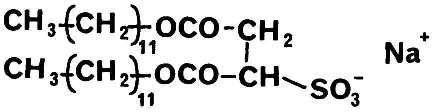
Figure 2. Ca^{2+}-induced permeation control of NaCl release from $2C_{12}PO_4^-$ coated nylon capsule (B) and uncoated (A) capsule at 40°C

Complete release of NaCl was achieved within 30 min when the uncoated, semipermeable capsule membrane was employed (curve A, P = 6.0×10^{-5} cm/s). A marked decrease in NaCl influx was observed with $2C_{12}PO_4^-$-coated capsule (curve B, P = 2.5×10^{-6} cm/s). When $2C_{12}PO_4^-$-coated capsule was picked up, immersed in 0.05 M $CaCl_2$ aqueous solution at 50°C for 1 min and returned to the cell, the permeability of NaCl increased about 8 times (P = 2.0×10^{-5} cm/s).

The permeability was reduced nearly to the original rate (P = 3.0 x 10^{-6} cm/s), when the Ca^{2+}-interacted capsule was picked up, immersed in 0.01 M EDTA (ethylenediaminetetraacetic acid disodium salts) aqueous solution at 50° C for 10 min and returned to the cell. Same phenomena were observed when $2C_{12}PO_4^-$-coated capsule was treated with other divalent cations (Mg^{2+}, Cu^{2+}, Ba^{2+}) and then EDTA, although the effect was not so drastic (2-4 times acceleration by adding metal ions). The treatment with alkali metal ions (Na^+, K^+) could not change the permeability. These divalent cation-induced permeability controls were not detected on cationic $2C_{18}N^+2C_1$-or anionic $2C_{12}$-suc-SO_3^--bilayer membrane coated nylon capsule[1].



$2C_{18}N^+2C_1$



$2C_{12}$-suc-SO_3^-

It has been reported that the permeability of amphiphile bilayer-coated capsule membrane, amphiphile bilayer-blended PVC polymer membrane and aqueous bilayer vesicles is drastically changed near the phase transition temperature (T_c) of bilayers [1,3]. Permeability constants (P) of the $2C_{12}PO_4^-$-coated capsule were measured at various temperature to study the effect of the phase transition and Ca^{2+} -coodination on NaCl release. Arrhenius plots are shown in Figure 3. In the case of the uncoated capsule (A), the plot of log P vs 1/T gave a straight line. On the contrary, the Arrhenius plot gave a inflection near 45° C in the case of $2C_{12}PO_4^-$-coated capsule (B). The drastic increase of NaCl release near 45° C is associated with the phase transition from a rigid gel to a disordered liquid crystalline state of $2C_{12}PO_4^-$ bilayers on the capsule membrane (T_c = 45° C from DSC measurements). When $2C_{12}PO_4^-$ bilayer membrane-coated capsule which was dipped in 0.05 M $CaCl_2$ aqueous solution was employed, the straight Arrhenius plot was obtained and the permeability constant was 5-10 times larger than the original $2C_{12}PO_4^-$-coated capsule (C).

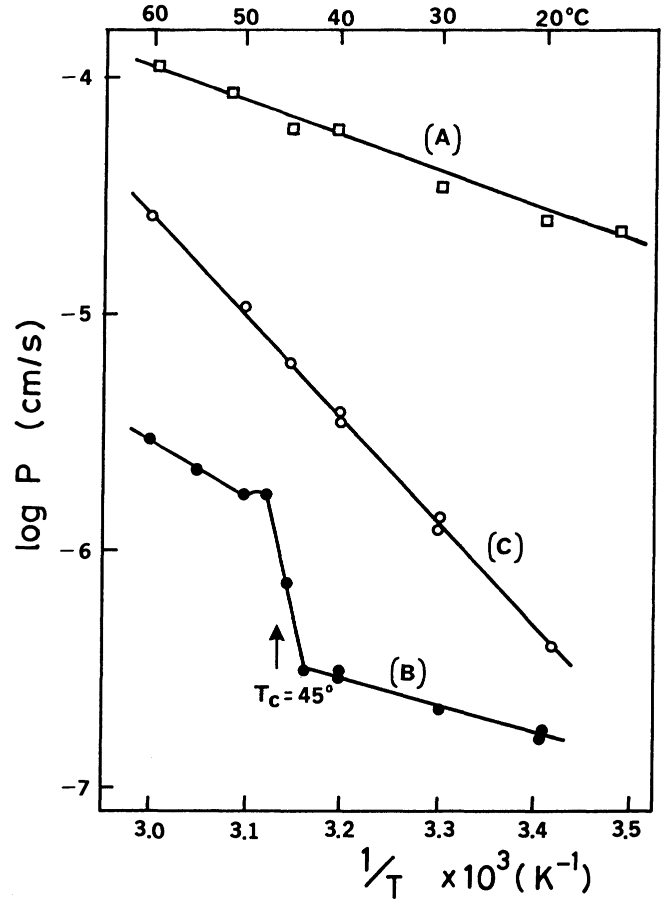


Figure 3. Arrhenius plot of NaCl release from uncoated (A), $2C_{12}PO_4^-$-coated (B) and $Ca^{2\pm}$-coordinated, $2C_{12}PO_4^-$-coated (C) nylon capsule membrane

It was confirmed that Ca^{2+}-treated capsule was still covered with plates of $2C_{12}PO_4^-$ amphiphiles by SEM observation, however, had no peak of T_c in the range of 5-80°C by DSC measurements. After washing the Ca^{2+}-coordinated capsule by EDTA aqueous solution, DSC measurement showed a relatively broad peak at 45° C which means the regeneration of bilayer structures on the capsule membrane. These findings indicate that the fast release of NaCl by treating with Ca^{2+} is due to the disturbed bilayer structure and/or the charge effect of the coordinated Ca^{2+} on the capsule membrane by the chelation of the phosphate head group of bilayers with divalent cations, and the permeation rate is reduced to the original on account of the regeneration of bilayer structures by removing Ca^{2+} ions with EDTA.

It is well known that divalent cations cause the release of encapsulated drugs and the fusion of negatively charged liposomes from acidic phospholipids such as diacyl phosphatidylserine and phosphatidic acid[4-6]. Ca^{2+}-coodination to phosphate head groups of bilayers is explained to cause the formation of a hexagonal structure in bilayers and strongly reduce the barrier ability of bilayer membranes[7]. It is difficult to realize the reversible permeability control induced by divalent cations in liposomal membranes because of the damage of the vesicle structure. On the contrary, acidic amphiphile-coated nylon capsule membrane is not damaged by repeated divalent cation treatments, because of the physically strong capsule wall.

In conclusion, although nylon capsule membrane are semipermeable, $2C_{12}PO_4^-$ bilayer membrane-coated nylon capsules can reversibly control the permeability of water soluble substances such as NaCl using the coordination with divalent cations. This is a simple model of the signal receptive capsule membrane which responds to a stimulas from outside.

The authors are grateful to Profs T. Kunitake (Kyushu Univ.) and T. Iijima for their encouragement.

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(Received March 3, 1983)