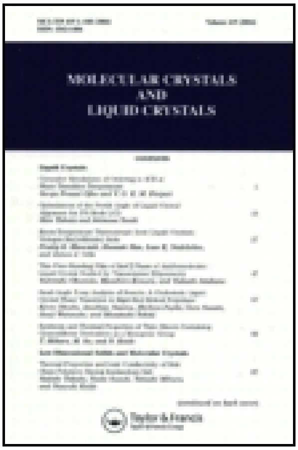

Molecular Crystals and Liquid Crystals Science and Technology. Section A. Molecular Crystals and Liquid Crystals

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gmcl19

Electrical Properties of Planar Bilayer Lipid Membranes

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Version of record first published: 24 Sep 2006

Mol. Cryst. and Liq. Cryst., 1999, Vol. 337, pp. 469-472
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Electrical Properties of Planar Bilayer Lipid Membranes

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Planar Bilayer Lipid Membrane (BLM) was used as a model of liposome drug delivery system. By establishing the relations between membrane electrical properties and liposome characters, the behavior of liposomes in various conditions can be predicted by means of measuring sensitive electrical properties of BLM. When different ratios of cholesterol incorporated into membranes, or various quantities of detergents added into solutions, membrane resistance (Rm) and capacitance (Cm) changed regularly. Results indicated that there exited obvious relations between membrane electrical properties and characters of liposomes, thus BLM can become a useful and simple method to study liposome drug delivery system.

Keywords: Bilayer Lipid Membrane(BLM); membrane electrical properties; liposome; phosphatidylcholine; cholesterol; detergents

INTRODUCTION

Both BLM and liposomes are biomembrane models. From 1960's, BLM was widely used in biosensors, energy transfer, ligand-receptor interaction as well as ion channel[1]. As a favorable drug delivery system, liposomes have great advantages in drug targeting[2], gene transfer and immunoassay. However, BLM formed by phosphatidylcholine and cholesterol had not been studied systematically, not to mention using BLM to study liposomes. We hoped to predict the behavior of liposomes in various conditions by membrane electrical properties. At first, relations between BLM electrical properties and liposomes should be established, which is the main purpose of this study.

EXPERIMENTAL DETAILS

Forming BLM

BLMs were formed from phosphatidylcholine (Epc) and cholesterol (Chol) in decane (20mg Epc/ml) by means of Mueller and Rudin[3]. Membranes were formed on a 1.0mm diameter hole in a polytetrafluoroethylene partition which separated two solutions. After a black membrane was seen under a microscope, electrical properties of BLM were measured using cyclic voltammetry. The instrument used was a Multi-function Analyzer (Model J1-100, Sino Jinke Electronics Co. ltd., Tianjing, China). The temperature was 23±1°C.

Experimental Procedure

Epc and Chol with different molar ratios were used as BLM forming materials. Different concentrations of detergents, anionic detergent sodium lauryl sulfate(SDS), cationic hexadecyltrimethylammonium bromide (HDTAB) and non-ionic detergent Tritonx-100 (Tx-100),Tween80 were added into solutions respectively. For detergent experiments, the molar ratio of Epc to Chol was 5:3. Rm, Cm and Vb were measured under the above conditions.

RESULTS AND DISCUSSION

Detergent Effect

All of the detergents caused Rm to decrease and Cm to increase. The drop of Rm caused by detergents accorded with liposome studies[4]. As concentration increased, the changing rates of Rm and Cm increased (see Figure 1 and 2). Except SDS, all of other detergents produced lower Vb values than that of pure 0.1N KCl. SDS had special effect on Vb. The value was high even in a high concentration (0.04%, 600mv), and Rm rose to $10^{10}\Omega$ in low concentration (0.0008%), which may be due to the stabilization effect of SDS. When the concentration reached a higher level, all detergents caused membrane rupture. However, this higher level was still lower than CMC of the detergent. The modes that detergents influenced membrane electrical properties were quite different. The effect of ionic detergent (HDTAB and SDS) on Cm were significant, while non-ionic detergents (Tritonx-100 and Tween80) were less effective. In the presence of HDTAB, Tritonx-100 or Tween80, Rm decreased slowly after forming BLM. As for SDS, Rm stayed in a stable value during the whole experiment, which may be also due to its stabilization effect. Rm fluctuated regularly with a cycle of 1000s when SDS and Tween80 were used. This was not observed with HDTAB .

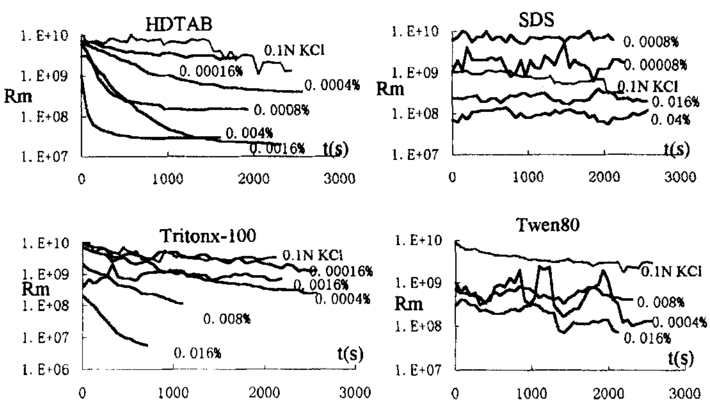

FIGURE 1 Effect of different concentrations of detergents on Rm of BLM .

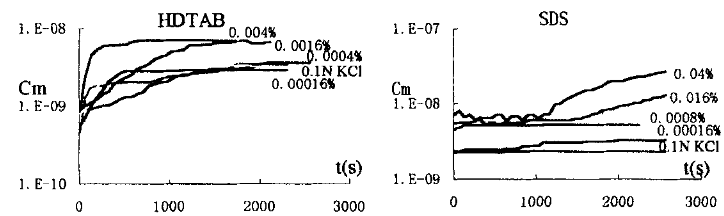

FIGURE 2 Effect of different concentrations of detergents on Cm of BLM.

Effect of Cholesterol on Electrical Properties

The effect of different concentrations of Chol incorporated into BLM is summarized in Table I. The changes was regular: when quantity of Chol increased, Rm became more stable. Membrane stability was enhanced and Vb also increased. At molar ratio 5:3 and 5:4 (Epc/Chol), Cm, Rm were very stable , even with no change during the time of observation. Vb reached the highest level. At the ratio of 5:5, though Vb was high, Rm was less stable with several stable stages. These results demonstrated that 5:3, 5:4 was the best ratio to form a stable membrane, fitting well with liposome leakage experiment[5].

TABLE I Electrical parameters of BLM composed of Epc and Chol.

Epc/Chol mol/mol	Cm $\mu F/cm^2$	Rm $10^6\Omega\ cm^2$	Vb mv	membrane electrical stability
5:0	0.495±0.039	3.2	266	Cm is stable. Rm descend rapidly
5:1	0.361±0.012	1.37±0.176	300	Cm is stable. Although Rm still descend, it is more stable.
5:2	0.362±0.014	4.215±0.461	314	Cm is stable.Rm is relatively stable. The time it come to steady delayed.
5:3	0.436±0.037	3.501±0.357	326	Both Cm and Rm are very stable, without any changes during the time.
5:4	0.636±0.066	0.514±0.106	360	Both Cm and Rm are very stable, without any changes during the time.
5:5	0.621±0.049	0.31 21.59*	338	Membranes are very stable,but the data repeated badly.There seem to be two stable stage during the course.

*: Rm stayed in this value for a long time, then it descended to 0.3 rapidly.

There is a close relationship between membrane electrical properties and chemical composition of membrane and solutions. The consistence of BLM electrical properties with characters of liposomes makes BLM a good model of liposome drug delivery system. By measuring sensitive electrical parameters rapidly, we can predict drug's effect on liposome leakage and stability, drug-liposome interaction and their behavior in various conditions. BLM will play an important role on this field. For this, plenty of data should be collected.

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