Biochimica et Biophysica Acta, 598 (1980) 189—192
© Elsevier/North-Holland Biomedical Press

BBA Report

BBA 71455

PHASE TRANSITIONS OF ALKYL ETHER ANALOGS OF PHOSPHATIDYLCHOLINE

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(Received December 13th, 1979)

Key words: Alkyl ether analog; Phase transition; Phosphatidylcholine analog; (Fluorescent probe)

Summary

The phase-transition temperatures of aqueous dispersions of diester, monoether and diether analogs of phosphatidylcholine were determined using *trans*-parinaric acid as a fluorescent probe. The diether analog of phosphatidylcholine has a higher phase-transition temperature, whilst the monoether analog has a lower phase-transition temperature than their diester counterpart.

The occurrence of thermotropic phase transitions is characteristic for phospholipid/water systems. The gel to liquid-crystalline phase-transition temperature depends strongly both on the chain length and degree of unsaturation of the fatty-acyl moieties and the nature of the phospholipid polar head groups [1]. It is known that alkyl and alk-1-enyl ether linkages are found in phospholipids of membranes of normal mammalian tissues (brain, heart, skeletal muscle, liver, etc.) [2,3] and, at even higher levels, in cancer cells [4,5]; yet little is known about their physical properties. The dipole moments of the ether-linked lipids differ from those of the corresponding diacyl compounds. Diether lecithin has been used as a model to study the interaction of cholesterol with diester lecithin [6—9]. Phase-transition temperatures of two species of diether lecithin (dihexadecyl and dioctadecenyl glycerophosphocholine) have been reported in the literature [10,11]. It is a prerequisite to gain more information

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on the physical properties of these phospholipids in order to understand their structural function.

1,2-Dipalmitoyl-*sn*-glycero-3-phosphocholine was purchased from Sigma Chemical Co., and α-palmitoyl-β-oleoyl-*rac*-glycero-α′-phosphocholine, α-hexadecyl-β-oleoyl-*rac*-glycero-α′-phosphocholine, α-hexadecyl-β-octadecenyl-*rac*-glycero-α′-phosphocholine and α,β-dihexadecyl-*rac*-glycero-α′-phosphocholine were obtained from R. Berchtold Biochemisches Labor, Bern, Switzerland. Each phospholipid was checked for purity by thin-layer chromatography in a solvent system of chloroform/methanol/acetic acid/water (50 : 25 : 8 : 4, v/v); when necessary they were purified using an identical chromatographic system. Fluorescent β-parinaric acid (all-*trans*-9,11,13,15-octadecatetraenoic acid) was used to monitor the phase transitions of lipid bilayers. Methods for isolation of β-parinaric acid, preparation of lipid dispersions and fluorescence measurements were the same as described by Sklar et al. [12].

Fig. 1 shows a typical plot of logarithmic fluorescence intensity of *trans*-parinaric acid as a function of the reciprocal of temperature (K^{-1}) for the aqueous dispersions of the various diradyl choline-containing glycerolipids. The phase-transition temperatures were then calculated from these curves as described [12] and are listed in Table I. Our transition temperature for dipalmitoyl phosphatidylcholine agrees quite well with that reported before [12] and with those determined by other methods [13—16]. We obtained a value for

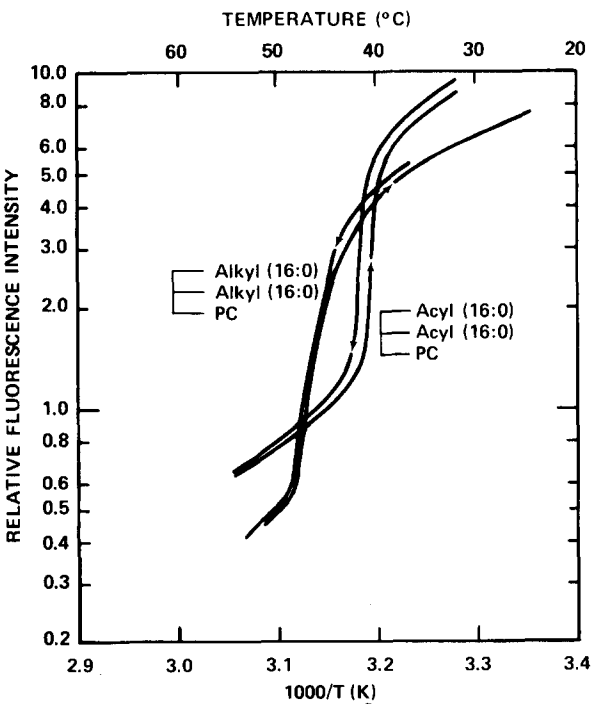

Fig. 1. The response of the fluorescence intensity of the *trans*-parinaric acid probe to the phase transitions of aqueous dispersions of dipalmitoyl or dihexadecyl glycerophosphocholine. Each sample was cooled to approx. 10°C below the lipid transition temperature and then heated at a rate not exceeding 2 K/min. This heating curve and a subsequent cooling curve are shown for each compound.

TABLE I

TRANSITION TEMPERATURES FOR VARIOUS DIRADYL GLYCEROPHOSPHOCHOLINE (GPC) DISPERSIONS

t_1 was calculated from the heating curve and t_2 was from the cooling curve of Fig. 1. Similar experiments, not presented, are also included.

Phospholipid	Transition temperature (°C)	
	t_1	t_2
Dipalmitoyl GPC	41.5	40.3
Dihexadecyl GPC	44.7	44.7
α-Palmitoyl-β-oleoyl GPC	11.0	11.0
α-Hexadecyl-β-oleoyl GPC	9.4	9.5
α-Hexadecyl-β-octadecenyl GPC	17.0	16.4

the transition temperature of the dihexadecyl analog of phosphatidylcholine comparable to that determined using differential scanning colorimetry [10]. Both diether analogs (dihexadecyl and α-hexadecyl-β-octadecenyl) of phosphatidylcholine display higher transition temperatures than their corresponding diester phospholipids. It is possible that in the diether analog the absence of the carboxyl groups in the region of the glycerol backbone brings closer packing and a more ordered state in the plane of the bilayer and thus produces higher transition temperatures. On the other hand, a single ether linkage in the phospholipid disrupts the packing of the bilayer and results in a lower transition temperature. Ether-linked glycerophospholipids are widespread in nature. A diether analog of phosphatidylglycerophosphate is the major component of polar lipids in extremely halophilic bacteria [17] and as mentioned earlier ether-linked phospholipids occur in both normal and cancerous mammalian cells. Since both the monoether- and diether-linked phospholipids have different transition temperatures from their ester- and diester-linked counterparts, the presence of these analogs of phospholipids in the membranes could play an important role in influencing the fluidity of the membranes.

This work was supported by the United States Department of Energy (Contract No. DE-AC05-760R00033) and the American Cancer Society (Grant No. BC-70J). We are grateful to Dr. Robert D. Simoni for the use of his laboratory where most of this work was performed. We also wish to thank Dr. Amy Lu for her assistance.

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