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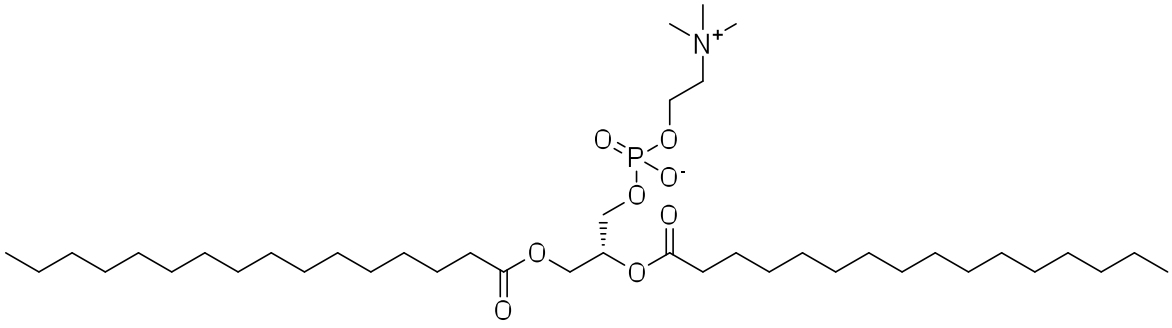
Phosphatidylcholine

Phosphatidylcholines are a class of glycerophospholipids which along with other phospholipids account for more than half of the lipids in most membranes. Phosphatidylcholines can further be divided into several subcategories[1] and one typical representative is [(2*R*)-2,3-di(hexadecanoyl-oxy)propyl] 2-(trimethylazaniumyl)ethylphosphate (Scheme 1), a molecule also known under many other names including 1,2-dipalmitoylphosphatidylcholine, 3,5,9-Trioxa-4-phosphapenta-cosan-1-aminium, 4-hydroxy-*N*,*N*,*N*-trimethyl-10-oxo-7-[(1-oxohexadecyl)oxy]-, hydroxide, inner salt, 4-oxide; Choline, hydroxide, dihydrogen phosphate, inner salt, ester with 1,2-dipal-mitin (8CI); Choline, phosphate, ester with 1,2-dipalmitin (6CI).[2] These phosphatidylcholines are predominantly found in the outer leaflet of the plasma membrane.[1] Recent studies suggest that the administration of 100 mg of egg phosphatidylcholine to mice with dementia increases brain acetylcholine concentration.[3] Related research suggests diet supplements of 2% phospha-tidylcholine improves memory in mice that are memory-deficient from gestation.[4] The toxi-cological properties of this compound have not been fully evaluated but it may be harmful by inhalation, ingestion, or skin absorption. Phosphatidylcholines may also cause eye, skin, or respiratory system irritation.[5]



Scheme 1. [(2*R*)-2,3-di(hexadecanoyloxy)propyl] 2-(trimethylazaniumyl)ethylphosphate.

(1) Cooper, G. *The Cell: A Molecular Approach. 2nd* ed. Sinauer Associates: Sunderland, MA, 2000. http://www.ncbi.nlm.nih.gov/books/NBK9898/.
(2) ScifFinder. https://scifinder.cas.org/scifinder/view/scifinder/scifinderExplore.jsf (accessed February 27, 2012).

(3) Chung, S.; Moriyama, T; Uezu, K; Hirata, R; Yohena, N; Masuda, Y; Kokubu, T; Yamamoto, S. Administration of Phosphatidylcholine Increases Brain Acetylcholine Concentration. *The Journal of Nutrition*. **1995**, *125*, 1484-1489.
(4) Moriyami, T; Uezu, K; Matsumoto, Y; Chung S.Y.; Uezu E; Miyagi S; Uza M; Masuda Y; Kokubu T; Tanaka T; Yamamoto S. Effects of Dietary Phosphatidylcholine on Memory in Memory Deficient Mice with Low Brain Acetylcholine Concentration. *Life Sciences* **1996**, 58, 111-118.
(5) *1,2-dipalmitoyl-sn-glycero-3-phosphorylcholine*; Material Safety Data Sheet No. 100009473; Cayman Chemical Company: Ann Arbor, MI, 2007, http://www.caymanchem.com/msdss/100009473m.pdf, (accessed Feb. 2012).

^{1}H-NMR and ^{13}C-NMR spectra were recorded of dipalmitoylphosphatidylcholine (DPPC, 41 mg in 0.5 ml $CDCl_3$) and they are shown in Figs. 1 and 2. The ^{13}C-NMR spectrum was recorded with a machine frequency of 100.54 MHz, and the ^{1}H-NMR spectrum was recorded at 399.65 MHz.[6] The DPPC methylene stretching mode (CH_2 or CD_2) was monitored by IR spectroscopy at various surface pressures. As the pressure increases, the intensity of the peak increases due to the reduction of the average surface area of each molecule (Fig. 3).[7] A Raman spectrum of DPPC was recorded by delivering the laser beam through a silica surface as opposed to focusing the beam through the collection optics. This method was employed to increase the angle at which the beam enters the sample above the critical angle for TIR. An electrical field builds up in the silica interface amd its strength decreases exponentially with distance from the surface. This is what causes the excitement of measureable Raman vibrations (Fig. 4).[8]

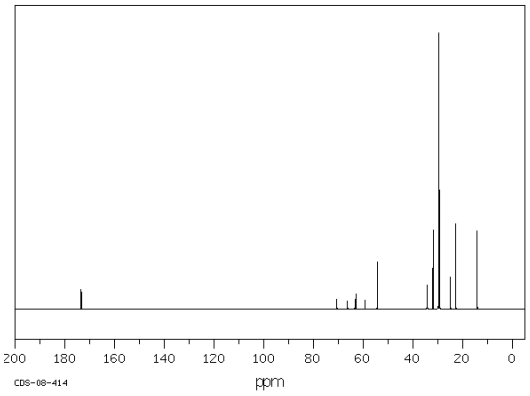


Figure 1. ^{13}C-NMR Spectroscopy of dipalmitoylphosphatidylcholine.[6]

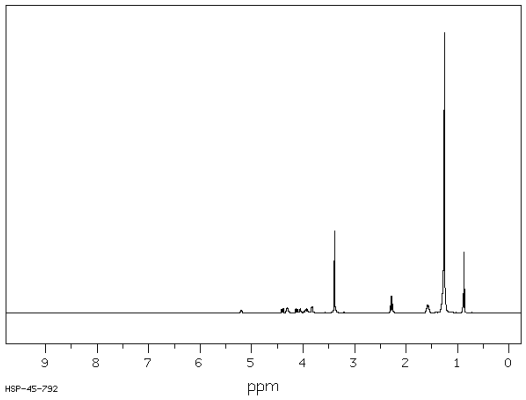


Figure 2. ^{1}H-NMR Spectroscopy of dipalmitoylphosphatidylcholine.[6]

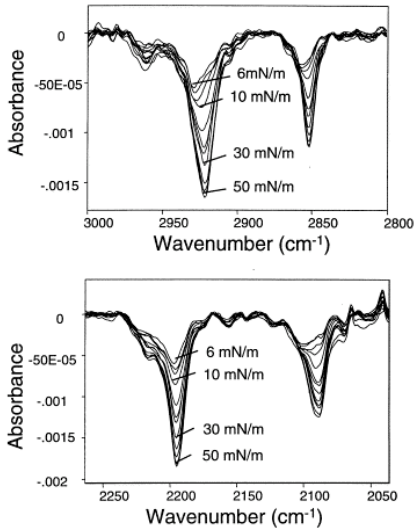


Figure 3. IR Spectra of DPPC at various pressures (top-C-H, bottom-C-D).[7]

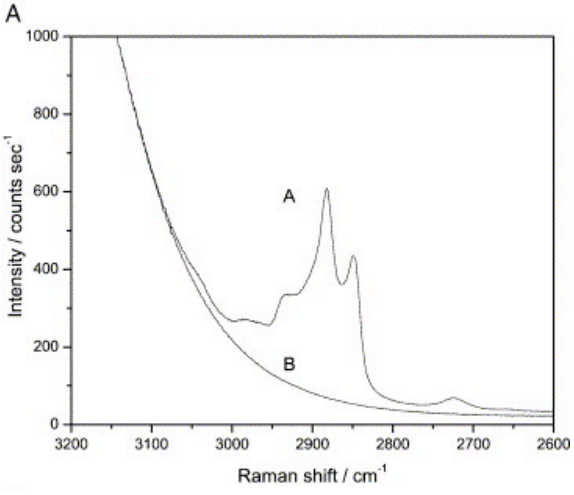


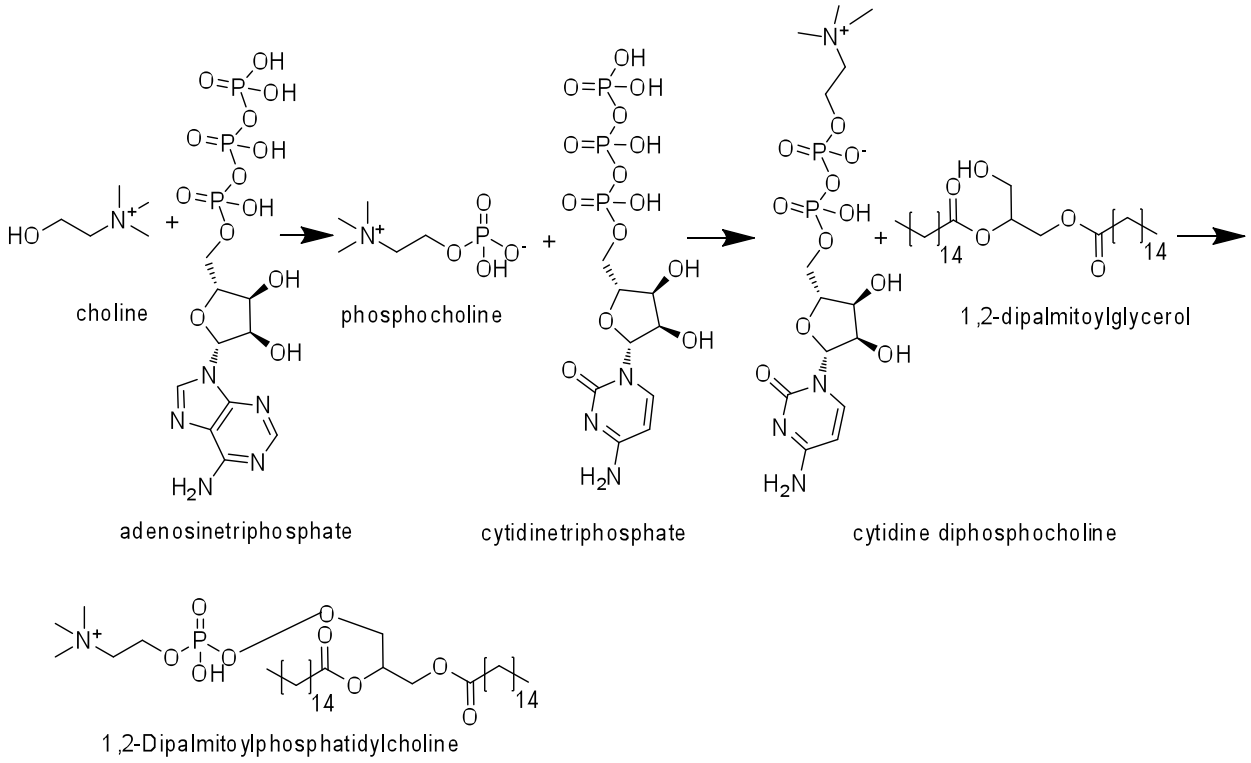
Figure 4. Raman spectrum of DPPC in H_2O (A; B shows pure H_2O).[8]

(6) 1H-NMR, 13C-NMR of dipalmitoylphosphatidylcholine. *Spectral Database for Organic Chemistry*. http://riodb01.ibase.aist.go.jp/sdbs/cgi-bin/direct_frame_top.cgi.

(7) Dluhy, R.; Zhao, P.; Faucher, K.; Brockman, J. Infrared Spectroscopy of Aqueous Biophysical Monolayers. *Thin Solid Films* **1998,** 327-329, 308-314.

(8) Lee, C.; Bain, C. Raman Spectra of Planar Supported Lipid Bilayers. *Biochimica et Biophysica Acta-Biomembranes* **2005**, *1711*, 59-71.

There are many syntheses for 1,2-dipalmitoylphosphatidylcholine and there are many pathways for biological synthesis in cells. The most common biosynthesis of this compound starts with the phosphorylation of choline by adenosine triphosphate (ATP). In animal cells, choline is not synthesized but is instead ingested through the animal's diet. The next step in this process is the addition of cytidine triphosphate (CTP) to phosphocholine to form cytidine diphosphocholine. Subsequent reaction with 1,2-dipalmitoylglycerol (a 1,2-diacylglycerol) forms the product 1,2-dipalmitoylphosphatidylcholine (Scheme 1) and cytidine triphosphate (CDP).[9] Bacteria also synthesize 1,2-dipalmitoylphosphatidylcholine and in several ways. The two main paths include the methylation of phosphatidylethanolamine (PE) and use a bacteria unique enzyme called phosphatidylcholine synthase. There are also two ways in which the PE can be methylated, one in a simple pathway and one in a complex pathway. The simple pathway involves one phosphoethanolamine *N*-methyltransferase (Pmt), whereas the complex pathway involves multiple types of this enzyme.[10]



Scheme 2. Biosynthesis of 1,2-Dipalmitoylphosphatidylcholine.[9]

(9) Christie, W. Phosphatidylcholine and Related Lipids. James Hutton Institute. The AOCS Lipid Library. http://lipidlibrary.aocs.org/lipids/pc/index.htm.

(10) Aktas, M., Wessel, M., Hacker, S., Klusener, S., Gleichenhagen, J., Narberhaus, F. Phosphatidylcholine Synthesis. *European Journal of Cell Biology* **2010**, *89*, 888-894.