from 4.23 ± 0.42 mμmole of histamine-C^{14} formed per gram of stomach per hour to 17.57 ± 2.94 mμmole after portacaval shunt ($P < .001$). A similar increase was also noted in the cardiac stomach of these animals (Table 1). The activity of the serotonin-synthesizing enzyme, 5-hydroxytryptophan decarboxylase (*15*), was normal in stomachs of rats with portacaval shunts, an indication of specific alteration in histamine synthesis.

If hypersecretion of acid in our experimental rats is secondary to an increased activity of histidine decarboxylase, it should be possible to reduce this acid secretion by an inhibitor of this enzyme. Acid in the stomach was measured by the administration of a test meal (*16*). Two months after portacaval shunt, gastric secretion of acid rose from 26.80 ± 2.98 μeq of HCl per 30 minutes to 115.1 ± 16.4 μeq ($P < .001$). Treatment with NSD-1055 (4-bromo-3-hydroxybenzyloxyamine) (*17*), a potent inhibitor of histidine decarboxylase reduced acid secretion to 38.55 ± 3.08 μeq, nearly normal.

Our data suggest that the hypersecretion of acid after portacaval shunt may be secondary to increased histamine synthesis in the stomach. The mechanism of the activation of histidine decarboxylase is not clear.

Treatment with corticosteroids often results in hypersecretion of acids and an increased incidence of peptic ulcers (*18*). Telford and West (*19*) have noted an increase both in activity of histidine decarboxylase and histamine content in the stomachs of rats after administration of prednisolone. We have confirmed these observations and have been able to inhibit this hypersecretion by treatment with NSD-1055.

Histamine has been proposed as the final common pathway in secretion of gastric acid (*20*). Stimuli resulting in acid secretion do so by way of local release of histamine. If the content of histamine in the stomach is increased, as after portacaval shunt or steroid therapy, a given stimulus may result in greater histamine release, thereby resulting in greater acid secretion. Thus, an increase in synthesis of histamine in the stomach may play a part in hypersecretion of acid and subsequent peptic ulceration in these conditions and in a variety of pathological states.

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Crystal and Molecular Structure of a Phospholipid Component: L-α-Glycerophosphorylcholine Cadmium Chloride Trihydrate

Abstract. *The structure of* L-α-*glycerophosphorylcholine cadmium chloride trihydrate has been determined by the conventional, single-crystal, x-ray diffraction technique. The phospholipid component displays the characteristic* gauche *conformation for the choline residue and the* gauche-gauche *conformation for the glycerol moiety. Therefore, a possible model for the structures of phospholipids is similar to that proposed by Finean.*

The phospholipids form a major constituent of cell membranes. Their structures have never been studied by the method of single crystal x-ray techniques primarily because of the difficulty of obtaining adequate crystals. Any information on the molecular structure of the constituents would provide a useful basis for postulating probable structures for the phospholipids. We have determined the crystal and molecular structure of the trihydrate of the cadmium chloride complex of L-α-glycerophosphorylcholine (GPC). Figure 1 shows the chemical formula of GPC, which is a hydrolytic product of phosphotidyl choline (lecithin) and occurs in mammalian tissues and fluids.

The cadmium chloride complex of GPC crystallizes from aqueous solutions as the trihydrate, yielding colorless needles elongated in the *c* direction. The crystals have orthorhombic symmetry. Unit cell parameters measured with a diffractometer are: a = 9.452 ± 0.001 Å, b = 27.038 ± 0.004 Å, and c = 7.391 ± 0.002 Å. For four molecules, chemical composition $PO_6NC_8H_{20} \cdot CdCl_2 \cdot 3H_2O$, per unit cell, the calculated density is 1.739 g cm^{-3}, which is in agreement with the value of 1.731 g cm^{-3} measured by the flotation method in a mixture of CCl_4 and CHI_3.

The systematically absent reflections were $h00$, $0k0$ and $00l$ for h, k and l odd except for the very weak 100 and 500 reflections. The space group was assumed, therefore, to be $P22_12_1$. However, the three largest peaks in the Patterson function cannot be interpreted to give Cd positions consistent with the symmetry of this space group. It was assumed that reflections 100 and 500 were spurious, probably Renninger reflections, and that the space group is in fact $P2_12_12_1$.

Intensities on unidimensionally inte-

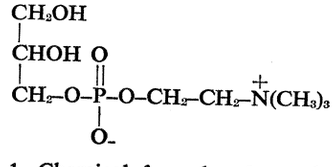
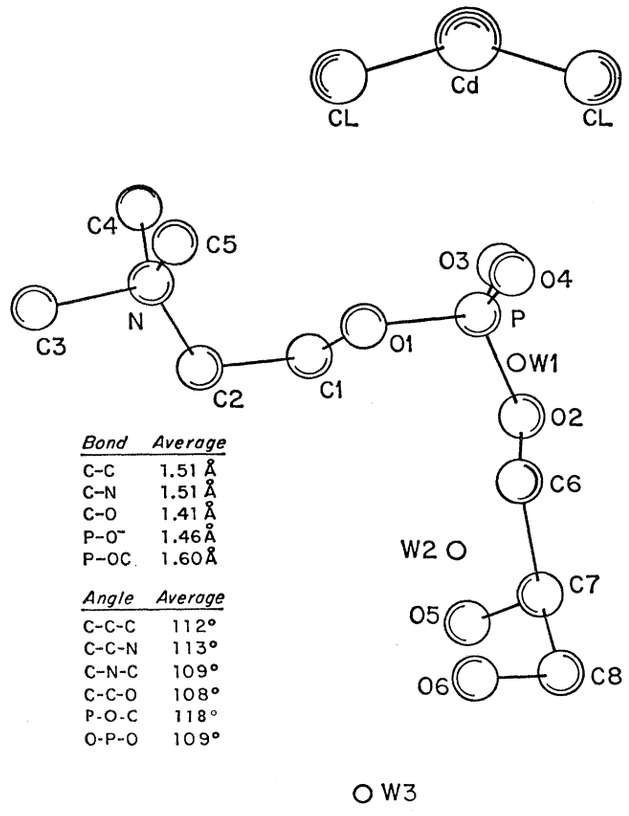


Fig. 1. Chemical formula of L-α-glycerophosphorylcholine.



Bond	Average
C-C	1.51 Å
C-N	1.51 Å
C-O	1.41 Å
P-O⁻	1.46 Å
P-OC	1.60 Å

Angle	Average
C-C-C	112°
C-C-N	113°
C-N-C	109°
C-C-O	108°
P-O-C	118°
O-P-O	109°

Fig. 2. A (001) projection of the asymmetric unit of glycerophosphorylcholine cadmium chloride trihydrate.

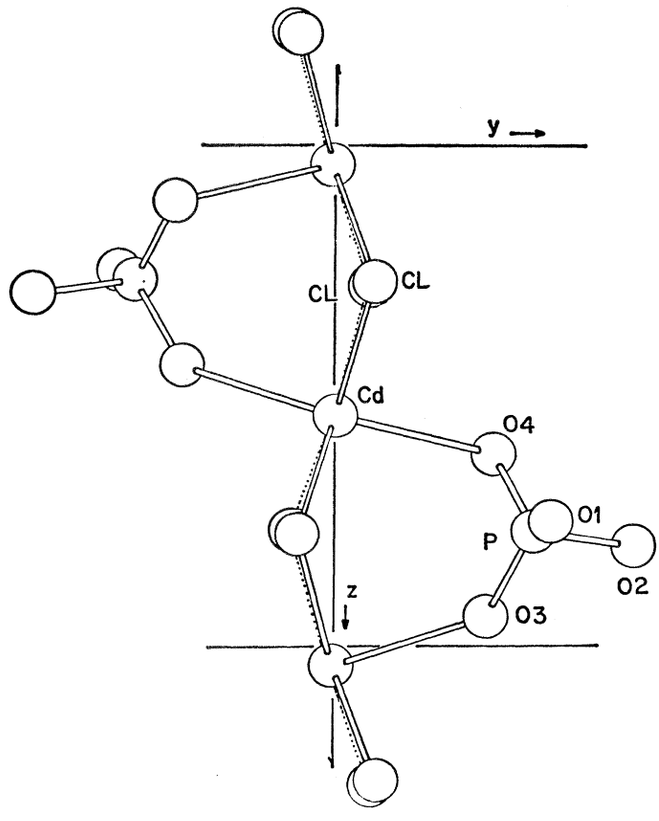


Fig. 3. A portion of the molecule, showing the coordination around Cd. Each phosphate is bound to two Cd atoms.

grated photographs were measured with a recording microdensitometer having a logarithmic response. Within the linear range of the film, area under the recorder tracing was taken as proportional to the integrated intensity. In all, about 1200 equi-inclination Weissenberg data were recorded for levels with l from 0 to 6 with CuKα radiation.

It proved possible to locate Cd, Cl, and P positions from the Patterson function. These were used for the trial structure and led in successive cycles of structure factors–Fourier syntheses to the location of all nonhydrogen atoms, including the O atoms of the three water molecules. The structure has been refined by full matrix least-squares, including individual atom isotropic thermal parameters, to a residual $R = \Sigma(|F_o| - |F_c|)/\Sigma|F_o|$ of 11.5 percent. An asymmetric unit of the structure in projection on (001) and the average bond lengths and bond angles in the phospholipid component are shown in Fig. 2. The structure has the L configuration.

The Cd atoms are nearly coincident with the screw axes at $x = \frac{1}{4}$, $y = 0$, and $x = \frac{3}{4}$, $y = \frac{1}{2}$. The environment of the Cd consists of four chlorine atoms in a square planar arrangement and two phosphate oxygen atoms which form the apices of a distorted octahedron, Fig. 3. The Cd-Cl and Cd-O distances are about 2.62 Å and 2.32 Å, respectively. The Cl atoms form bridges between the Cd atoms, resulting in a pleated arrangement of a cadmium chloride ($CdCl_4^{-2}$), as shown in Fig. 3. The phosphate oxygens O(3) and O(4) are bonded to two Cd atoms. Furthermore, O(3) of one phosphate and O(4) of an adjacent phosphate, related by c translation (that is, the phosphorus-phosphorus distance is 7.391 Å), are bridged by hydrogen bonds to the water molecules W(1). Interestingly, the phosphorus-phosphorus distance within a strand of DNA and RNA is similar to this value.

L-α-Glycerophosphorylcholine exists as a dipolar ion with the positive charge on the quaternary nitrogen neutralized by the negative charge on the phosphoric acid residue. The diester is approximately "L-shaped," with the phosphate at the corner of the L and the polar ends pointing outward. The projected angles between adjacent C-O bonds of the glycerol moiety are about 60°. Hence, the conformation of the glycerol residue is *gauche-gauche*. It is noteworthy that the choline residue exists in the *gauche* conformation rather than in the more extended (zig-zag) form.

It is of interest to compare the structure of glycerophosphorylcholine with that of proposed models of phospholipids (*1*, *2*). Finean (*2*) has proposed a "walking-stick" model for the phospholipids where the choline chain is in the extended conformation. It is important to note that the introduction of acyl (fatty acid residues) chains on C7 and C8 of GPC will give the phospholipids a configuration similar to that proposed by Finean (*2*), except for the difference in the conformation of the end group.

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