



# Polyenylphosphatidylcholine (PPC) and Mitochondria



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## Polyenylphosphatidylcholine (PPC) and Mitochondria

Mitochondria are organelles with unique characteristics. An organelle is a specialized subunit within a cell with specific functions that is usually separately enclosed within its own lipid bilayer.

A mitochondrion consists of an outer membrane and an inner membrane, composed of phospholipids and proteins. While the outer membrane encloses the entire organelle, the inner membrane is compartmentalized into numerous cristae (fig.1). These cristae expand the surface area of the inner mitochondrial membrane, enhancing its ability to produce adenosine triphosphate (ATP), an important source of chemical energy. Therefore, mitochondria are also described as “cellular power plants”.

For typical liver mitochondria, the area of the inner membrane is about five times greater than the outer membrane.

In addition to supplying cellular energy, mitochondrial membranes contain a large number of integral proteins. The proteins are involved in a wide range of important processes, such as cell signaling and complex cellular transitions, including development cues, mitosis, and apoptosis (1).

The mitochondria are essential to multicellular life. Without mitochondria, cells cease to respire aerobically and quickly die, a process exploited by some apoptotic pathways.

Depletion of phosphatidylcholine in the membranes of hepatic mitochondria is an early manifestation of decreased capacity of hepatic mitochondria to control cellular respiration, to oxidize substrates and form high energy phosphate metabolites.

During the last decade, several investigations have shown that PPC with its special ingredient 1,3-bis(sn-3'-phosphatidyl)-sn-glycerol-3 (BPPC) positively affects structure and function of mitochondria. These results can be summarized as follows:

### *Membrane Ultrastructure*

Electron microscopic examinations of hepatocytes demonstrated already in 1977 the positive effects of PPC in children with Kwashiorkor and in rats with ethyl alcohol or

carbon tetrachloride poisoning. The effectiveness of PPC was most strikingly seen at the structure of the mitochondria. Already a few days after the beginning of treatment, a practically total disappearance of osmiophilia, otherwise present in matrices, was conspicuous in the mal-nourished children. With the number of mitochondria increasing, the picture of the double membranes and cristae returned to normal, and the dense intramitochondrial granules became visible (2, 3).

The efficiency of PPC is not limited to the liver. Administered at a curative level, PPC facilitated the general repair process of mitochondrial membranes of spongicytes of the zona fasciculata of the adrenal cortex (4).

#### *Mitochondrial Respiration*

PPC and DLPC improved ethanol-induced impairments in the capacity of hepatic mitochondria to oxidize fatty acids and attenuated alcohol-induced fatty liver and hyperlipidemia. A likely mechanism for these preventive effects of PPC and DLPC was the lowering of the adenosine diphosphate to oxygen ratio (ADP/O), which is a measure of efficiency of coupling between oxidation and ATP production. The changes were particularly manifest when judged by the ratio between the ADP-stimulated and non-stimulated oxygen consumption with glutamate, succinate and palmitoyl-1-carnitine as substrates. Additionally, the phospholipids re-increased the activity of cytochrome c oxidase, a membrane-bound key enzyme of the mitochondrial electron transport chain, which requires a normal phospholipid milieu for optimal activity (5, 6).

#### *Mitochondrial Energization*

Mitochondrial membrane potential, measured by determining the retention of a dye, was significantly diminished in HepG2 cells by ethanol and corrected by DLPC. Glutathione, an antioxidant which prevents damage to important cellular components caused by reactive oxygen species such as radicals, was also partially restored in the mitochondria (7).

#### *Apoptosis*

Apoptosis is programmed cell death. Cytochrome c, released from mitochondria into cytosol, participates in the activation of the enzyme caspase-3, which in turn triggers apoptosis. DLPC and PPC decreased ethanol-induced increased hepatocyte apoptosis, cytochrome c leakage into cytoplasm, and the content and activity of the

cell degrading enzyme caspase 3. Furthermore, there was a trend for a re-increase of the anti-apoptotic protein Bcl-xL after PPC and DLPC supplementation (8, 9).

According to the published data, PPC with DLPC as its key component is of special value for the restructuring and functioning of the double membrane of mitochondria.

## References

1. Braschi E, McBride HM: Mitochondria and the culture of the Borg: understanding the integration of mitochondrial function within the reticulum, the cell, and the organism. *Bioessays* 2010; 32: 958-66
2. Théret CG et al: Phosphatidylcholines and hepatic steatosis. *Méd. Chir. Dig.* 1977; 6: 69-74
3. Théret et al: L'hépatostéatose de dénutrition chez l'enfant. *L'Ouest Médical* 1977; 22: 1595-1614
4. Théret CG et al: Ultrastructure de la cortico-surrénale et du foie dans l'alcoolisme expérimental: effets réparateurs membranaires de dilinoléoylphosphatidylcholines. *Revue Française De Gastroentérologie* 1979; 7: 5-26
5. Navder KP et al: Polyenylphosphatidylcholine attenuates alcohol-induced fatty liver and hyperlipidemia in rats. *J. Nutr.* 1997; 127: 1800-6
6. Navder KP, Lieber CS: Dilinoleoylphosphatidylcholine is responsible for the beneficial effects of polyenylphosphatidylcholine on ethanol-induced mitochondrial injury in rats. *Biochem. Biophys. Res. Commun.* 2002; 291: 1109-12

7. Xu Y et al: DLPC attenuates alcohol-induced cytotoxicity in HepG2 cells expressing CYP2E1. *Alcohol & Alcoholism* 2005; 40: 172-5
8. Mak KM et al: Dilinoleoylphosphatidylcholine reproduced the antiapoptotic actions of polyenylphosphatidylcholine against ethanol-induced hepatocyte apoptosis. *Alcohol. Clin. Exp. Res.* 2003; 27: 997-1005
9. Okiyama W et al: Polyenylphosphatidylcholine prevents alcoholic liver disease in PPAR $\alpha$ -null mice through attenuation of increases in oxidative stress. *J. Hepatol.* 2009; 50: 1236-46

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