ADVERSE REACTIONS

No major side effects have been reported. Mild side effects have been noted occasionally such as nausea, diarrhea and increased salivation in some. This holds for all forms of phosphatidylcholine.

INTERACTIONS

There are no known interactions.

OVERDOSAGE

There are no reports of overdosage.

DOSAGE AND ADMINISTRATION

There are several forms of phosphatidylcholine supplements. Typical commercial lecithin supplements contain 20 to 30% phosphatidylcholine. Softgel capsules containing 55% and 90% phosphatidylcholine are available. Liquid concentrates containing 3 grams of phosphatidylcholine per 5 milliliters (one teaspoon) are also available.

Recommended doses range from 3 to 9 grams of phosphatidylcholine daily in divided doses.

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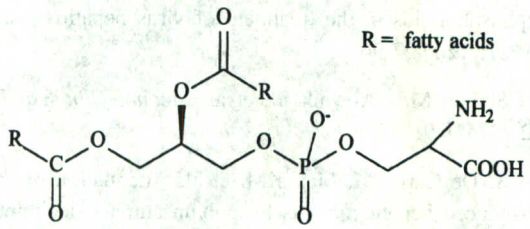
Phosphatidylserine

DESCRIPTION

Phosphatidylserine is a phospholipid that is a structural component of biological membranes of plants, animals and other life forms. Phosphatidylserine was first isolated from brain lipids called cephalins. The major cephalins are phosphatidylserine and phophatidylethanolamine. Another major phospholipid found in egg yolks and soya is phosphatidylcholine, also known, chemically, as lecithin. Phosphatidylserine is also isolated from soya and egg yolks.

Phosphatidylserine is made up of a glycerophosphate skeleton linked to two fatty acid molecules and the amino acid L-serine. It is an amphiphilic molecule because it is made up of the lipophilic fatty acid tails on one side and the hydrophilic head group containing phosphate and serine on the other side of the molecule. Phosphatidylserine is located in the internal layers of biologic membranes, facing the cytoplasm with its polar head group. In animal tissues, phosphatidylserine is formed from phosphatidylethanolamine by exchange of the ethanolamine head for L-serine. Phosphatidylethanolamine itself is synthesized from diacylglycerol and CDP-ethanolamine.

Phosphatidylserine is known chemically as 1,2-diacyl-sn-glycerol-(3)-L-phosphoserine. It is abbreviated as Ptd Ser, $Acyl_2$ Gro PSer and PS. Most commonly, it is called phosphatidylserine or PS. It has the following chemical structure:



Phosphatidylserine

The fatty acid composition of phosphatidylserine derived from bovine brain and soya lecithin differ. Phosphatidylserine from soya lecithin contains mainly polyunsatured fatty acids, while phosphatidylserine derived from bovine brain contains mainly saturated and monounsaturated fatty acids, as well as some docosahexaenoic acid.

Phosphatidylserine is involved in signal transduction activity as well as being a basic structural component of biologic membranes.

ACTIONS AND PHARMACOLOGY

ACTIONS

Supplemental phosphatidylserine may have cognition enhancing activity.

MECHANISM OF ACTION

Since the action of phosphatidylserine has not been established, any discussion of the mechanism of action is speculative. However, some findings from animal studies are of interest. Cholinergic hypofunction is thought to account in part for the cognitive deficits found in Alzheimer's disease. The most commonly used drugs for the treatment of Alzheimer's disease are reversible acetylcholinesterase inhibitors. The rationale of these drugs is to increase acetylcholine levels in the brains of Alzheimer's patients, and they may be somewhat effective in some cases. Animal studies indicate that phosphatidylserine restores acetylcholine release in aging rats by maintaining an adequate supply of the molecule and is able to increase the availability of endogenous choline for *de novo* acetylcholine synthesis.

The hippocampus of the brain is believed to be important for cognitive processes and is affected in those with Alzheimer's disease. The dendritic spines of pyramidal cells, the postsynaptic target of the excitatory input to the hippocampus, have been proposed as a substrate for information storage. Age-dependent dendritic spine loss in pyramidal neurons has been reported in the human brain, and the extent of synaptic loss appears to correlate with the degree of cognitive impairment. Rat experiments indicate that phosphatidylserine treatment prevents the age-related reduction in dendritic spine density in rat hippocampus. Protein kinase C facilitation of acetylcholine release has been reported in rats. Phosphatidylserine was found to restore protein kinase C activity in aging rats. Stimulation of calcium uptake by brain synaptosomes and activation of protein kinase C are yet other speculative mechanisms of phosphatidylserine's putative cognition-enhancing action.

PHARMACOKINETICS

Pharmacokinetic studies of phosphatidylserine have been performed in rats. Little is known of the pharmacokinetics of oral phosphatidylserine in humans. In rats, it appears that there is extensive digestion of phosphatidylserine in the small intestine, producing, among other things, lysophosphatidylserine, a substance that contains only one fatty acid, and phosphatidylethanolamine.

Following absorption, lysophosphatidylserine is metabolized in intestinal mucosa cells, and its metabolites, which include some phosphatidylserine, enter the lymphatics draining the small intestine. It appears that only a small fraction of ingested phosphatidylserine reaches the systemic circulation as part of the phospholipid pool. The amount that reaches the brain, after either intraperitoneal injection or oral administration, is very small. Most of the behavioral and neurochemical effects noted in animal studies have been observed only after repeated intraperitoneal and oral phosphatidylserine dosing.

INDICATIONS AND USAGE

Phosphatidylserine has demonstrated some usefulness in treating cognitive impairment, including Alzheimer's disease, age-associated memory impairment and some non-Alzheimer's dementias. More research is needed before phosphatidylserine can be indicated for immune enhancement or for reduction of exercise stress.

RESEARCH SUMMARY

Several double-blind studies suggest that phosphatidylserine can help maintain cognitive function in older individuals and may be able to improve memory and learning skill in some. These results, while encouraging, are not, to date, dramatic.

Various animal experiments have also demonstrated some benefits including stimulation of brain catechecholaminergic turnover and increased acetylcholine output from the cerebral cortex of adult and old rats, as well as enhanced neurotransmitter and central nervous system signal transduction. There is evidence that phosphatidylserine can help maintain the hippocampal dendritic spine population of aging rats. It has been suggested that these spines serve as a substrate for information storage. There are several studies demonstrating improved cognitive function in several animal models.

In the largest multicenter study to date of phosphatidylserine and Alzheimer's disease, 142 subjects aged 40 to 80 were given 200 milligrams of phosphatidylserine per day or

placebo over a three-month period. Those treated with phosphatidylserine exhibited improvement on several items on the scales normally used to assess Alzheimer's status. The differences between placebo and experimental groups were small but statistically significant. Researchers directing a smaller study, also achieving statistical significance with respect to several measures, characterized the therapeutic effects of phosphatidylserine in their Alzheimer's subjects as "mild."

Phosphatidylserine has also shown some efficacy in some non-Alzheimer's dementias, in age-associated memory impairment and general mental deterioration. More clinical trials need to be conducted before anything conclusive can be said about phosphatidylserine in the treatment of cognition impairment. But, given the results to date and the fact that there are so few side effects associated with phosphatidylserine and so few treatment options for Alzheimer's disease, one research group concludes that "the therapeutic possibilities offered by phosphatidylserine should not be dismissed." There are some animal studies demonstrating positive immunomodulatory effects but, as yet, no human studies showing similar effects. There is preliminary research indicating that phosphatidylserine, at doses of 400 to 800 milligrams per day, can inhibit exercise-induced increases in cortisol.

CONTRAINDICATIONS, PRECAUTIONS, ADVERSE REACTIONS

CONTRAINDICATIONS

Phosphatidylserine supplementation is contraindicated in those hypersensitive to any component of the preparation.

PRECAUTIONS

Because of lack of long-term safety studies, phosphatidylserine should be avoided by children, pregnant women and nursing mothers. Those with the antiphospholipid-antibody syndrome should exercise caution in the use of phosphatidylserine and only take it under medical supervision and monitoring.

ADVERSE REACTIONS

Occasional gastrointestinal side effects, such as nausea and indigestion, are reported.

INTERACTIONS

There are no reported drug, nutritional supplement, food or herb interactions with phosphatidylserine.

OVERDOSAGE

There are no reports of overdosage.

LD_{50} in rats is more than 5g/kg, and in rabbits is more than 2g/kg.

DOSAGE AND ADMINISTRATION

Phosphatidylserine supplements derived from both bovine brain and from soya lecithin are available. Phosphatidylserine derived from soya lecithin undergoes an enzymatic process that converts phosphatidylcholine to phosphatidylserine. Because of the hypothetical possibility of bovine spongiform encephalopathy, the soya-derived phosphatidylserine is preferred. Typical doses are 100 milligrams three time daily.

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