



➤ Product Review ◀

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TWO NEW PRODUCTS FROM MOSS NUTRITION – PHOSPHATIDYLSERINE AND DHA 710 SELECT™

We are very excited to announce to you the release of our two newest products, **Phosphatidylserine** and **DHA 710 Select™**. As you will see, it is not a coincidence that we are releasing these two products at the same time. Of course, as most of you know, these two nutrients have been important staples in the practice of clinical nutrition for several years now. However, most of the information on these two nutrients I have seen has tended to consider them individually and there is certainly much that can be said about the benefits of each when used as isolated supplements, as will be discussed in relationship to DHA later in this monograph. In contrast, what I would like to explore in detail is the much less well known interrelationship between the two, focusing in particular on how phosphatidylserine and DHA function synergistically to optimize various aspects of brain function. The impact of the two on brain function was touched upon briefly in the enclosed technical bulletin on **Phosphatidylserine** from Moss Nutrition. Because of its importance, though, I would like to explore the unique benefits of the phosphatidylserine/DHA combination in much more detail.

Basic information on the role of phosphatidylserine in brain function

The paper “Phosphatidylserine and the human brain” by Glade & Smith (Glade MJ & Smith K. *Nutrition*, Vol. 31, pp. 781-786, 2015) provides an excellent overview of the importance of phosphatidylserine in brain

function. Glade and Smith begin their paper by discussing the phosphatidylserine content of the body in general and the brain:

“Phosphatidylserine (PS) is the major acidic phospholipid in human membranes and constitutes 2% to 20% of the total phospholipid mass of adult human plasma and intracellular membranes. Within the healthy human brain, myelin is enriched with PS and the PS content of gray matter doubles from birth to age 80 y.”

Interestingly, the PS in the gray matter of the brain contains a significant amount of docosahexaenoic acid (DHA):

“About 20% to 30% of the PS in the human gray matter is in the form of 1-stearoyl-2-docosahexaenoyl-*sn*-glycero-3-phosphoserine. The docosahexaenoic acid (DHA) content of neuronal PS is of functional importance; in the cortex of the brain, a reduction in the DHA content of PS is associated with the progression of mild cognitive impairment to Alzheimer’s disease. Consequently, the incorporation of PS into human membranes is sensitive to the availability of both PS and DHA.”

Research on the impact of PS on various aspects of brain function

Neurotransmission – Glade states the following about PS and DHA:

“The incorporation of PS into neuronal cell membranes influences the metabolism of the neurotransmitters acetylcholine (ACh), norepinephrine, serotonin, and dopamine. Adequate amounts of DHA-enriched PS are required for the fusion of intraneuronal secretory granules with the presynaptic membrane, the subsequent release of neurotransmitter molecules into the synaptic cleft during the intracellular transmission of action potentials and proper postsynaptic neurotransmitter-receptor interactions.

Additionally, exogenous PS stimulates electroencephalographic (EEG) evidence of increased cholinergic neurotransmission in healthy men and women.”

Aging and deterioration of the human brain – As you might expect the PS content of the brain plays an integral role in brain health during aging:

“Aging of the human brain is associated with loss of neurons, dendritic atrophy, loss of synaptic connections, decreased synaptic density, decreased synthesis of Ach and other neurotransmitters, abnormal neuronal membrane lipid composition (especially decreased membrane PS content and increased membrane cholesterol content), and reduced sensitivity of postsynaptic membranes to ACh. A decrease in the ratio of PS to cholesterol within neuronal membranes causes neurochemical changes that can contribute to an increase in the viscosity of cellular membranes, thus reducing enzymatic activity that require optimum fluidity.”

Before continuing, I would like to comment on the statement made in the above about fluidity. A large body of research over the years has commented on optimal fluidity of various membranes in the body, particularly cell membranes. For optimal functioning of membranes in relationship to receptor activity and the ability of various constituents to pass through membranes, they must have the optimal amount of fluidity or bendability. If they are either too hard or too soft, improper function results. This fluidity is primarily dependent on the right balance of cholesterol, which brings the property of strength and “hardness,” and PS and DHA which bring the property of bendability and softness. As suggested in the above quote, this balance of PS and cholesterol is particularly important in the membranes of the brain in relationship to resisting the typical impact of aging.

With the above in mind, what does PS do for the deteriorating brain? Glade and Smith first state:

“In humans, the incorporation of exogenous PS into brain structures is functionally

relevant; for example, human studies using positron emission tomography (PET) to investigate brain glucose utilization in patients with Alzheimer’s disease have noted evidence of significantly increased glucose utilization in response to supplementation with PS, especially in temporoparietal areas that are specifically affected by this disease. Such biochemical responses to PS supplementation elicit physiological processes that produce functional manifestations reflecting the impact of exogenous PS on neuronal membranes in the central nervous system.

In open-label trials, older individuals with mild degrees of decline in cognitive function have responded to 60 d of dietary supplementation with 300 mg of oral PS (100 mg three times daily) with significantly improved performance on tests of verbal learning, verbal recall, verbal fluency, visual learning, attention, communication skills, initiative, socialization, and self-sufficiency. Similar results were obtained in similar individuals following 90 d of the same level of daily supplementation; additionally, the abilities to recall names and recognize faces also were improved.”

Depression – What about depression and use of PS? Glade and Smith point out:

“Patients exhibiting symptoms of chronic depression also have responded to PS supplementation (100 mg three times daily, for 1-6 mo) with decreased apathy, withdrawal, and sleep disturbances and increased motivation and interest in others.”

Alzheimer’s disease – Concerning research on the use of PS with patients with diagnosed Alzheimer’s disease, the authors mention the following:

“Older patients diagnosed with Alzheimer’s disease also have benefited from supplemental PS. For example, in one placebo-controlled randomized double-blind trial of older patients with severe cognitive impairments secondary to Alzheimer’s disease who were given supplemental PS (200 mg/d for 3 mo), the investigators reported significantly greater improvements in memory, information processing, and the ability to perform acts of daily living than those produced by placebo. In another trial in which oral PS (400 mg/d)

was administered to patients with Alzheimer's disease, the addition of PS supplementation to a cognitive training program for 16 wk resulted in significantly greater improvements in performance on neuropsychological tests than did cognitive training alone."

Unfortunately, despite the positive results reported above, PS did not halt progression of the disease:

"However, PS did not halt progression of the disease and deterioration of performance was noted in most patients 4 mo later despite continued PS supplementation."

Therefore, while PS can in no way be considered as a cure for Alzheimer's disease, supplementation may have a positive impact on progression.

Phosphatidylserine and stress responses

As with many of you, my first exposure to information on PS almost 20 years ago revolved around the impact of PS to optimize stress responses, especially in relation to cortisol production. As noted by Glade and Smith, increased levels of PS appear to optimize endocrine responses to stress:

"Increased circulating concentrations of PS also attenuate the endocrine responses to exercise-induced acute stress. When healthy men received single intravenous infusions of either placebo or PS just before the initiation of a strenuous workout on a stationary bike, the typical exercise-induced stress response (increases in plasma adrenocorticotrophin (ACTH) and cortisol concentrations) occurred only following infusions of placebo and not after acute administration of PS. Oral PS also attenuates the 'stress response'; supplementation of PS 300 mg/d for 1 mo, 400 mg for 21 d, 600 mg for 21 d, 600 mg for 10 d, 800 mg for 10 d, 800 mg for 21 d, or 800 mg for 14 d suppressed the typical exercise-induced spikes in the serum concentrations of ACTH and cortisol that accompanied the initiation of cycling exercise in healthy young physically conditioned men or exposure to acute psychological stress in healthy young men and women."

More research on the use of phosphatidylserine and DHA supplementation

As was discussed above in relation to the Glade and Smith study, several studies have highlighted the benefits on neurologic function of a combination of PS and DHA supplementation. What follows is two that are most applicable clinically. The first paper examines the impact of a PS-DHA combination on neurologic function.

In "The effect of phosphatidylserine-containing omega-3 fatty acids on memory abilities in subjects with subjective memory complaints: a pilot study" by Richter et al (Richter Y et al, *Clinical Interventions in Aging*, Vol. 5, pp. 313-316, 2010) 8 men and women aged 60 years or above were administered 300 mg PS and 37.5 mg EPA + DHA per day for six weeks. What were the findings?

"PS-omega-3 may have a favorable effect on memory in subjects with subjective memory complaints."

The second paper examines the other common use of a PS-DHA combination, as a supplemental regimen to optimize stress and cortisol levels. In "Omega-3 fatty acids administered in phosphatidylserine improved certain aspects of high chronic stress in men" by Hellhammer et al (Hellhammer J et al, *Nutr Res*, Vol. 32, pp. 241-250, 2012) a stress test was administered to 60 healthy nonsmoking men aged 30 to 60 years. The subjects were then divided into high or low responders:

"In this study, the stress test (Trier Social Stress Test) induced significant increases in cortisol, norepinephrine, epinephrine, and heart rate as well as in subjective stress perception. By assigning individuals to groups corresponding to their cortisol response (low/high responders), we found that low responders generally showed a blunted physiologic stress response, with respect to ACTH, cortisol in serum saliva, epinephrine levels, and heart rate."

Supplementation was the following:

“Participants took a daily dose of 300 mg (3 capsules) omega-3-rich PS...or 300 mg (3 capsules) soy oil (placebo; thereof 207 mg/d saturated fatty acids) for 12 weeks.”

What were the results? The authors state:

“Our results demonstrate possible beneficial effects of omega-3 supplementation related to cortisol response, depending from cortisol responsivity. In cortisol low responders, we observed a slight increase in cortisol after omega-3 PS supplementation, whereas in cortisol high responders, a decrease of cortisol was evident. Thus, the treatment effects of omega-3 PS may be best understood in terms of a normalization of the stress response. Chronic stress likely affects adrenal cortisol release in a biphasic mode. First, the HPA axis is permanently activated. In this stage, the overdrive of CRH/arginine vasopressin neurons results in a down-regulation of CRH receptors on the pituitary, which makes the HPA axis less responsive to psychologic or pharmacologic stimuli. In a second phase, the adrenals gradually reduce cortisol release in some but not all individuals. Not surprisingly, low responders were more likely to report high chronic stress levels than high responders.”

Of course, we have known for years that phosphatidylserine is very useful for both optimizing stress related symptoms plus optimizing the cortisol findings we tend to see with salivary cortisol testing. The quote above provides a good explanation as to how PS, along with DHA, accomplishes this.

DHA as an anti-inflammatory supplement

Certainly we have been hearing about DHA as part of the anti-inflammatory constituents in fish oil for years. However, we have also been hearing for years that the impact of DHA in fish oil is secondary to EPA in terms of an anti-inflammatory impact. Even though it is virtually dogma that EPA is the most important anti-inflammatory constituent in fish oil, should this long time clinical nutrition tenet be questioned? Interestingly, according to the study “A randomized, crossover, head-to-head comparison of eicosapentaenoic acid and docosahexaenoic acid supplementation to

reduce inflammation markers in men and women: the comparing EPA to DHA (ComparED) study” by Allaire et al (Allaire J et al, *Am J Clin Nutr*, Vol. 104, No. 2, pp. 280-287, August 2016), the answer is yes. It may surprise you as it did me that, according to the authors, no one has ever researched the claim we have heard for years that EPA is a better anti-inflammatory constituent than DHA:

“To the best of our knowledge, this is the first study that was designed specifically to provide a head-to-head comparison of the effects of EPA and DHA on inflammation markers as a primary outcome in both men and women.”

In this study, 48 men and 106 women aged 18 to 70 years who were determined to have metabolic syndrome based on the presence of abdominal obesity and low-grade inflammation were supplemented. The supplemental protocol occurred in three phases of 10 weeks with a 9 week washout period between each phase. The three phases were 1) EPA (2.7 g/d), 2) DHA (2.7 g/d), and corn oil as a control.

What were the findings? The authors state:

“Data indicated that DHA may be more effective than EPA in attenuating systemic inflammation and modulating plasma lipid risk factors in healthy men and women with abdominal obesity and subclinical systemic inflammation.”

What were the specific findings?

“Supplementation with DHA (2.7 g/d) for 10 wk decreased IL-18 and increased adiponectin significantly more than did supplementation with EPA (2.7 g/d). Also, the reduction in plasma CRP concentrations with DHA compared with control oil was almost 4-fold greater in magnitude than the reduction with EPA although this difference did not reach significance. The data confirm the indirect evidence from the meta-analysis by Li et al., which suggested that the anti-inflammatory effects of mixed LCn-3PUFAs seen in previous studies may have been attributable to DHA.”

To match the dose of DHA used in this study, the recommended dose of **DHA 710 Select™**

would be 4 caps per day. Of course, this recommendation should be kept in perspective because there was no suggestion in the Allaire et al study that a lower dose of DHA would be less effective.

What is the clinical significance of this study? I realize that it is tempting to conclude that we should stop using fish oil and just use DHA supplementation. In my opinion, this would be a mistake. Why? First, the study did not consider the synergistic effects of EPA and DHA that is found in fish oil. Second, in terms of cost/efficacy considerations, particularly for those patients who require long term supplementation, fish oil may still be the better choice in terms of the anti-inflammatory impact per dollar spent. Therefore, I feel that the clinical takeaway from this study is not that DHA should be used instead of fish oil when anti-inflammatory effects are desired. Rather, fish oil should be the starting point. Then, if additional anti-inflammatory effects are required, DHA supplementation should be added.

With the above in mind, we still recommend that **EPA/DHA Select®** or **EPA/DHA Select HP®** should be the starting point when considering a long-term, anti-inflammatory protocol for the many patients whose diets appear to be deficient in omega-3 fatty acids. Then, if necessary, add **DHA 710 Select™**. Because of the DHA content of **EPA/DHA Select®** and **EPA/DHA HP Select®**, dosage of **DHA 710 Select™** would only be 2-3 caps day in this scenario.

For further information, please visit the product pages on our website.

Phosphatidylserine – Moss Nutrition

Contents: 90 VC – 100 mg per capsule

DHA 710 Select™ – Moss Nutrition

Contents: 60 SG – 710 mg of DHA per Softgel

