



DOSSIER · SUBSTANCE

Phosphatidylserine

The database includes studies on **phosphatidylserine**, some of which involve human subjects. The controlled study evidence is methodologically diverse. The most notable finding: A significant portion of controlled studies investigates **cognitive effects**, though results are heterogeneous and often tied to specific combinations with omega-3 fatty acids.

371

STUDIES IN
TOTAL

115

IN HUMANS

28

OF WHICH
CONTROLLED

42

IN ANIMALS

43

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-04

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Phosphatidylserine at a glance

ORIGIN:
Phosphatidylserine is a phospholipid membrane component found in all animal and plant cells. It is primarily located in the inner layer of the cell membrane and plays a central role in signal transduction, apoptosis, and the interaction between cells and the immune system. As a dietary supplement, it is typically derived from soya or sunflower lecithin, with the fatty acid composition varying depending on the source.

EVIDENCE BASE:
371 evaluated studies · 28 controlled human trials · 87 observational studies · 12 review articles · 42 animal studies · 40 cell culture studies

- STRONGEST EVIDENCE:**
- **Cognition and mental health:** A randomised, double-blind study (2014) involving 36 children with ADHD demonstrated significant improvements in ADHD symptoms, attention deficit, and hyperactivity following two months of daily intake of 200 mg soya-derived phosphatidylserine.
 - **Cognition and mental health:** A randomised, double-blind study (2010) with 157 older participants experiencing subjective memory complaints suggests dose-dependent improvements in delayed recall and learning ability through a phosphatidylserine-omega-3 complex.
 - **Cognition and mental health:** A randomised, double-blind study (2014) involving 84 older participants with Alzheimer's dementia showed no deterioration in activities of daily living after two months of intake of a phosphatidylserine-phosphatidic acid complex.
 - **Stress reactivity** Studies (1990, 1992) indicate that phosphatidylserine may attenuate the neuroendocrine stress response and activation of the hypothalamic-pituitary-adrenal axis in healthy men.
 - **Safety** A randomised, double-blind study (2013) in children with ADHD confirmed the short-term safety of phosphatidylserine combined with omega-3 fatty acids.

- LIMITATIONS:**
- The isolated effect of phosphatidylserine cannot be demonstrated, as most studies test combinations with omega-3 fatty acids or phosphatidic acid.
 - The evidence base for clinically relevant effects on cardiovascular diseases or antioxidant effects is sparse or contradictory. For Alzheimer's dementia, studies are limited to combinations and show no progression rather than improvement.
 - Long-term studies with larger sample sizes investigating pure phosphatidylserine preparations at various dosages are lacking.

CLASSIFICATION:
Phosphatidylserine is a phospholipid membrane component with plausible neuroprotective mechanisms; however, its clinical efficacy in cognitive impairment and stress reactivity is predominantly supported in combination with other substances and with limited robustness.

1. What Phosphatidylserine Is

Phosphatidylserine is a **phospholipid membrane component** found in all animal and plant cells. Natural sources include soya, sunflower seeds, and animal tissues such as brain or liver. In the human body, it is primarily located in the **inner layer of the cell membrane** and plays a key role in **signal transduction**, **apoptosis**, and the **interaction between cells and the immune system**.

For understanding the evidence base, it is crucial that **phosphatidylserine** is rarely studied in isolation. It is frequently used in combination with **phosphatidic acid** or **omega-3 fatty acids**, which complicates the attribution of effects. Additionally, **bioavailability** and **metabolic utilisation** differ depending on the formulation (e.g., as powder, capsule, or in liposomes). Measuring **phosphatidylserine** in blood or tissue is methodologically challenging, as it is rapidly converted into other phospholipids or incorporated into cell membranes. Many studies therefore use **surrogate markers**, such as the **phagocytic activity of microglia** or **cognitive test batteries**, whose validity is limited.

2. What the Studies Show in Detail

The key human studies and most important reviews — by area of application, including population, duration, preparation, outcome measures, and results, as reported in the original publications. Numbers are only provided where the study specifies them.

Distribution of **controlled human trials** by area of application — the numbers are not additive, as a single study may be assigned to multiple areas:

AREA OF APPLICATION	CONTROLLED STUDIES
Metabolism	10
Fatigue and stress	10
Cognition and mental health	10
Cardiovascular system	7
Safety and tolerability	7
Immune system	5
Oncology	4

AREA OF APPLICATION	CONTROLLED STUDIES
Oxidative stress	2

Cognition and Psyche

In a randomised, double-blind pilot study (2016), 15 postmenopausal women (aged 60–84) received a multivitamin supplement (Efalex Active 50+) for 6 months, which included 60 mg of phosphatidylserine per day. The control group (N = 12) received a placebo. Cognitive performance was measured using computer-assisted tests, mobility via the VICON-9 camera system and force plates, and blood levels of fatty acids. The supplement led to significantly shorter reaction times in a motor screening test ($p < 0.05$) and improved word memory performance ($p < 0.03$). Additionally, habitual walking speed increased ($p < 0.05$). Limitations include the small sample size and the combination with other active ingredients (e.g., DHA, *Ginkgo biloba*), which precludes isolating the effect of phosphatidylserine within the multivitamin supplement.

A randomised, double-blind study (2010) investigated the effect of a phosphatidylserine-omega-3 complex (PS-DHA) in 157 non-demented older participants with subjective memory complaints. Over 15 weeks, participants received daily PS-DHA or placebo. Primary endpoints included cognitive tests (Rey Auditory Verbal Learning Test, Rey Complex Figure Test, computerised battery). A post-hoc analysis revealed that participants with relatively good baseline cognitive performance additionally benefited from improvements in delayed recall, learning ability, and the time taken to copy complex figures. The study suggests a dose-dependent effect of the PS-DHA complex, though the combination with omega-3 limits the generalisability to the specific effects of this complex ¹.

In a randomised, double-blind study (2014), the effect of a soy lecithin-derived phosphatidylserine-phosphatidic acid complex (PS+PA, 300 mg PS + 240 mg PA/day) was examined in 84 older participants with Alzheimer’s dementia over 2 months. The verum group (PP n = 53) showed no deterioration in 7 activities of daily living (ADL), whereas the placebo group (PP n = 39) exhibited a significant decline from 5.62 to 4.90 points ($p = 0.035$). The results provide a hint for the PS+PA complex but are not interpretable for phosphatidylserine alone due to the combination with phosphatidic acid ².

A randomised, double-blind study (2014) assessed the effect of 200 mg/day soy-derived phosphatidylserine in 36 children (aged 4–14) with ADHD over 2 months. The verum group (n = 19) demonstrated significant improvements in ADHD symptoms ($p < 0.01$), attention deficit ($p < 0.01$), and hyperactivity ($p < 0.01$), as well as in auditory short-term memory (Digit Span Test, $p < 0.05$). The placebo group (n = 17) showed no significant changes. The study suggests that phosphatidylserine may alleviate ADHD symptoms, though long-term data and differentiation by ADHD subtypes are lacking ³.

HYPOTHESIS The studies indicate a potential cognitive effect of phosphatidylserine, particularly in mild cognitive impairment, ADHD, and early-stage dementia. However, the effects are often only detectable in subgroups or in studies combining phosphatidylserine with other active ingredients (e.g., omega-3, phosphatidic acid). A clear dose-response relationship or a uniform mechanism of action is lacking. It remains unclear whether the observed effects in these combinations are attributable to phosphatidylserine, the additional substances, or their interaction.

What is lacking: Long-term studies with larger sample sizes examining pure phosphatidylserine preparations at various dosages and in specific cognitive deficits (e.g., executive functions, working memory). Additionally, studies directly measuring the influence of phosphatidylserine on neuronal plasticity or neurotransmitter systems (e.g., acetylcholine, dopamine) are needed.

Overall Picture

Phosphatidylserine and Cognition: Correlation or Causality?

The **MOST COMMON ASSUMPTION** in practice is that **phosphatidylserine** has been studied for **improving cognitive performance**; however, the controlled results are inconsistent. This claim is supported by controlled studies, most of which test **combined preparations**. For example, the most frequently cited works (2010, 2014, 2016) examine **phosphatidylserine in combination with omega-3 fatty acids or phosphatidic acid**. The **isolated effect of phosphatidylserine** is not demonstrable in these studies. Furthermore, the **effect sizes are small**, and the **target groups are heterogeneous** (e.g., older individuals with subjective memory complaints vs. patients with Alzheimer’s dementia). While **review articles** (e.g., 2022) emphasise the **theoretical benefit for neuroinflammation**, the **clinical evidence** remains **still emerging and contradictory**.

A further issue is the **METHODOLOGICAL QUALITY** of the studies. Many use **subjective endpoints** (e.g., self-reported memory performance) or **short-term test batteries**, the **clinical relevance of which is unclear**. Additionally, **comparisons with established therapies** (e.g., cognitive training or pharmacotherapy) are lacking. While **basic scientific research** shows that **phosphatidylserine influences microglial phagocytosis** (e.g., 2021, 2023), this **mechanism is not directly translatable to cognitive performance**. The **discrepancy between laboratory findings and clinical data** raises the question of whether **phosphatidylserine** crosses the **blood-brain barrier** in sufficient concentrations or whether the observed effects are due to **indirect mechanisms** (e.g., stress reduction).

3. How Robust the Research Is

Research on **phosphatidylserine** is divided into **three main areas**: **basic research**, **observational human studies**, and **controlled clinical trials**. The controlled trials focus on **three areas of application**: **cognition**, **metabolism**, and **fatigue**. Additional studies examine **cardiovascular effects**, **safety**, and **immune modulation**. Notably, **no area of application** is covered by a large number of controlled studies. The controlled studies from 2010–2024 primarily investigate **cognitive parameters** in older participants or **stress reactivity**.

The **robustness of the data** is limited by several factors. Firstly, the **number of controlled studies per area of application is small**, making quantitative syntheses challenging. Secondly, many studies are **combined with other substances** (e.g., omega-3 fatty acids), which complicates the **causal attribution** of effects. Thirdly, **long-term data** on safety and efficacy are lacking. Fourthly, the **target groups are often narrowly defined** (e.g., older individuals with subjective memory complaints), which limits **generalizability**. While **basic scientific studies** demonstrate plausible **mechanisms** (e.g., modulation of microglial activity), the **translation into clinical application** remains speculative.

4. Common Claims and the Evidence

STATEMENT	EVIDENCE
Phosphatidylserine in Alzheimer's Dementia	Controlled studies examine oncological or immunological effects , not specifically Alzheimer's dementia . One of the most frequently cited papers (2014)
Phosphatidylserine in ADHD	A controlled study (2014) examines phosphatidylserine in ADHD . The results are not generalisable , as the study found no replication and lacks long-term data
Phosphatidylserine and Cardiovascular Disease	Controlled studies examine cardiovascular parameters , typically in the context of microparticles or inflammatory markers . No study demonstrates clinical benefits
Phosphatidylserine as an Antioxidant	Controlled studies examine antioxidative effects , yet the methodology (e.g., measurement of surrogate markers) is not conclusive . While fundamental research suggests potential, clinical evidence is limited

5. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full evaluation includes significantly more studies; only the most robust are listed here.

Controlled Human Studies

- A High Omega-3 Fatty Acid Multinutrient Supplement Benefits Cognition and Mobility in Older Women: A Randomized, Double-blind, Placebo-controlled Pilo (2016)
- ¹ Phosphatidylserine containing omega-3 fatty acids may improve memory abilities in non-demented elderly with memory complaints: a double-blind placebo- (2010)
- ² Positive effects of soy lecithin-derived phosphatidylserine plus phosphatidic acid on memory, cognition, daily functioning, and mood in elderly patien (2014)
- ³ The effect of phosphatidylserine administration on memory and symptoms of attention-deficit hyperactivity disorder: a randomised, double-blind, placeb (2014)
- Ticagrelor attenuates the increase of extracellular vesicle concentrations in plasma after acute myocardial infarction compared to clopidogrel (2020)
- Randomised phase III study of docetaxel plus bavituximab in previously treated advanced non-squamous non-small-cell lung cancer (2018)
- ⁴ The phosphatidylserine-targeting antibody bavituximab plus pembrolizumab in unresectable hepatocellular carcinoma: a phase 2 trial (2024)
- ⁵ Effects of phosphatidylserine on the neuroendocrine response to physical stress in humans (1990)
- ⁶ Blunting of the stress-induced activation of the hypothalamic-pituitary-adrenal axis in healthy men by chronic phosphatidylserine administration (1992)
- ⁷ Omega-3 fatty acids administered in phosphatidylserine improved certain aspects of high chronic stress in men (2012)
- Effects of lipid-lowering treatment on circulating microparticles in patients with diabetes mellitus and chronic kidney disease (2016)
- ⁸ A soy-based phosphatidylserine/phosphatidic acid complex (PAS) normalises the stress reactivity of the hypothalamus-pituitary-adrenal axis in chronic stress (2014)
- Docetaxel combined with bavituximab in previously treated, advanced non-squamous non-small-cell lung cancer (2016)
- How to diagnose and manage antiphospholipid syndrome (2023)
- ⁹ Safety of phosphatidylserine containing omega-3 fatty acids in children with ADHD: a double-blind placebo-controlled trial followed by an open-label extension (2013)
- The effects of IQPLUS Focus on cognitive function, mood and endocrine response before and following acute exercise (2011)
- ¹⁰ Phosphatidylserine for the treatment of paediatric attention-deficit/hyperactivity disorder: a systematic review and meta-analysis (2021)
- ¹¹ A lecithin phosphatidylserine and phosphatidic acid complex (PAS) reduces symptoms of premenstrual syndrome (PMS): results of a randomised, placebo-controlled trial (2018)
- Profile of bavituximab and its potential in the treatment of non-small-cell lung cancer (2014)
- ¹² Phosphatidylserine enriched with polyunsaturated n-3 fatty acid supplementation for attention-deficit hyperactivity disorder in children and adolescents (2024)

- Acute supplementation with an amino acid mixture suppressed the exercise-induced cortisol response in recreationally active healthy volunteers: a randomised controlled trial (2020)
- Combining a high-DHA multi-nutrient supplement with aerobic exercise: protocol for a randomised controlled study assessing mobility and cognitive function (2019)
- ¹³ Effects of a food supplement containing phosphatidylserine on cognitive function in Chinese older adults with mild cognitive impairment: a randomised controlled trial (2025)
- Impact of a plant sterol food supplement on erythrocytic and associated cardiometabolic parameters: a randomised placebo-controlled trial in statin-treated patients (2024)

6. Summary

Controlled studies on phosphatidylserine primarily focus on cognitive effects, particularly in older participants with subjective memory complaints or mild cognitive impairment, as well as in children with ADHD. The most robust findings demonstrate improvements in cognitive test batteries, reaction times, and activities of daily living in studies combining phosphatidylserine with other substances such as omega-3 fatty acids or phosphatidic acid. The evidence on stress reactivity suggests a potential modulation of the hypothalamic-pituitary-adrenal axis in these combinations, while data on cardiovascular disease, immune modulation, or antioxidant effects remain insufficient to draw reliable conclusions. The methodological quality of the studies is limited by small sample sizes, heterogeneous populations, and the use of surrogate markers.

HYPOTHESIS The observed cognitive effects may be attributable to modulation of membrane fluidity or an indirect neuroprotective effect of phosphatidylserine, particularly when combined with omega-3 fatty acids. A role in regulating microglial activity and neuroinflammation also appears plausible, as suggested by basic science research. Should these mechanisms be confirmed, phosphatidylserine could in future play a role as a supportive measure in mild cognitive impairment or stress-related dysregulation. However, it remains unclear whether the substance crosses the blood-brain barrier in effective concentrations or whether the effects are due to systemic actions (e.g., stress reduction).

To clarify the clinical relevance of phosphatidylserine, long-term studies with larger sample sizes would be required, investigating pure phosphatidylserine preparations at various dosages and in specific cognitive deficits (e.g., executive function, working memory). Additionally, studies would need to directly measure the influence on neuronal plasticity, neurotransmitter systems (e.g., acetylcholine, dopamine), and the ability to cross the blood-brain barrier. Systematic investigations into combination effects with omega-3 fatty acids or phosphatidic acid, as well as comparisons with established therapies (e.g., cognitive training, pharmacotherapy), would be necessary to enable causal attribution of effects. Finally, data on long-term safety and potential interactions with chronic use are lacking.

7. Unresolved Questions

- **Blood-brain barrier:** It remains unclear whether phosphatidylserine crosses the blood-brain barrier in effective concentrations. Most studies do not measure CNS levels.
- **Long-term safety:** There are no long-term data on safety and potential interactions, particularly with chronic use.
- **Combination effects:** The interaction with omega-3 fatty acids or phosphatidic acid has not been systematically investigated. It remains unclear whether synergies or antagonisms exist.

Frequently Asked Questions

Can phosphatidylserine be used for chronic stress?

Controlled studies examine phosphatidylserine for exhaustion or stress, typically in combination with phosphatidic acid or omega-3 fatty acids. Results show minor effects on stress markers (e.g., cortisol), but the clinical relevance remains unclear. Studies are short-term and rely on subjective endpoints. A general recommendation cannot be derived.

Are there differences between plant-based and animal-derived phosphatidylserine?

The fatty acid composition varies depending on the source (e.g., soya vs. bovine brain). Animal-derived phosphatidylserine contains more long-chain omega-3 fatty acids, whereas plant-based versions are often enriched with omega-6 fatty acids. Controlled studies do not directly compare the sources, so no conclusion can be drawn regarding superiority. Bioavailability may differ, but clinical data are lacking.

What role does phosphatidylserine play in immune modulation**?

Controlled studies investigate immunological effects, primarily in the context of microparticles or inflammatory markers. Basic science research demonstrates that phosphatidylserine influences microglial phagocytosis (e.g., 2021, 2023). However, the clinical relevance of these findings is unclear, as no studies assess hard endpoints (e.g., infection rates). The evidence base is too limited for an evaluation.

Sources

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Vakhapova V, Cohen T, Richter Y, Herzog Y, Korczyn AD · 2010

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Positive effects of soy lecithin-derived phosphatidylserine plus phosphatidic acid on memory, cognition, daily functioning, and mood in elderly patients with Alzheimer's disease and dementia
Moré MI, Freitas U, Rutenberg D · 2014

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The effect of phosphatidylserine administration on memory and symptoms of attention-deficit hyperactivity disorder: a randomised, double-blind, placebo-controlled clinical trial
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The phosphatidylserine targeting antibody bavituximab plus pembrolizumab in unresectable hepatocellular carcinoma: a phase 2 trial
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Omega-3 fatty acids administered in phosphatidylserine improved certain aspects of high chronic stress in men
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A soy-based phosphatidylserine/ phosphatidic acid complex (PAS) normalizes the stress reactivity of hypothalamus-pituitary-adrenal-axis in chronically stressed male subjects: a randomized, placebo-controlled study
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A lecithin phosphatidylserine and phosphatidic acid complex (PAS) reduces symptoms of the premenstrual syndrome (PMS): Results of a randomized, placebo-controlled, double-blind clinical trial
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Phosphatidylserine enriched with polyunsaturated n-3 fatty acid supplementation for attention-deficit hyperactivity disorder in children and adolescents with epilepsy: A randomized placebo-controlled trial
Rheims S, Herbillon V, Gaillard S, Mercier C, Villeuve N, Villéga F et al. · 2024

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Effects of a food supplement containing phosphatidylserine on cognitive function in Chinese older adults with mild cognitive impairment: A randomized double-blind, placebo-controlled trial
Duan H, Xu N, Yang T, Wang M, Zhang C, Zhao J et al. · 2025

International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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