Phosphatidyl serine and phosphatidic acid complex (PSPA™)
New PS brain ingredient safe and efficacious for stress management and mitigation
**Abstract**

Stress kills. Literally. The World Health Organization declared (chronic) stress the “health epidemic of the 21st century.”[^10] Recent research, however, has brought to the forefront a naturally derived nutraceutical solution for mitigating, managing and normalizing the body’s reaction to physiological and social stress: Lipogen PSPA -- a complex of phosphatidylserine (PS) and phosphatidic acid (PA). PSPA is a new generation of PS brain ingredient for stress management, with efficacy and safety already proven in two separate clinical studies.[^2][^3] It is a patent-protected ingredient, providing Lipogen’s partners a clear-cut marketing edge (granted patent in USA, Canada & EU).

While common stress “cures” such as exercise, meditation, diet and management of the exogenous causes all are important, the endocrine impacts of stress must not be ignored. Traditionally, the reflexive response to this need has been pharmaceutical, bringing a wealth of side effects, expense and dependency.

Phosphatidylserine is a well-studied phospholipid previously notable for its role in memory and cognitive health. It is in particularly high concentration in brain and nerve tissue and has been shown to be integral to nerve cell functions, including conduction, neurotransmission and synaptic activity. It also allows for the accumulation, storage and release of neurotransmitter compounds, as well as the action of neurotransmitters on target cell surface receptors.[^7]

One phosphatide component in particular has stood out as having exemplary abilities that not only support mechanisms of brain function but actively participate in this reduction of stress: Phosphatidic acid (PA). As with PS itself, further scientific research has indicated that anti-stress capacities of PS+PA are effective across a broad demographic spectrum of age groups.

Phosphatidic acid is a key component of, and precursor to, the phospholipid compounds that are integral to cell membranes, and also acts as a signaling lipid. It helps determine the shape of the cell—specifically, its curvature. This shape determination can have an impact on the overall cellular function.[^7]

---

**PSPA™: The Natural Enemy of Stress**

Stress has become universal. According to the Centers for Disease Control (CDC) and the National Institute on Occupational Safety & Health[^4][^5], eight in 10 workers feel stress on the job. Surveys by the American Psychological Assn. (APA) and others[^6] show that the workplace is one of the top sources of life stress, along with money woes; family responsibilities; relationships; family and personal health concerns.

Health experts have shown that stress is linked to the six leading causes of death in America: heart disease, cancer, lung disease, accidents, liver disease (especially secondary to alcohol abuse) and suicide. Stress is also known to be a major source of memory and cognition impairment, depression, sleep deficit/sleep disorders and more. All these set off metabolic chain reactions that can culminate in physical disorders as well as obesity/metabolic syndrome and its accompanying disease states.

---

*Signs Displayed by Overly Stressed Individuals*

**Emotional symptoms:**
- Becoming easily agitated, frustrated, and moody

**Cognitive symptoms:**
- Forgetfulness, disorganization and Poor judgment

**Physical symptoms:**
- Insomnia, chest pains, aches and pains

Source: WebMD
Greater Synergy

The impressive ability of PS to act as an ingredient for brain health and cognition encouraged further research of its potential to alleviate stress response and support stabilization of the internal hormonal secretion. PS as a single-ingredient was not adaptable as a natural stress reliever due to the need to apply high dosages (and thus high costs) per serving (800mg).[3] However, when PS is combined with PA, the blend becomes a remarkable solution to support a healthy stress response, and at a competitive cost.

Research is pointing to the phosphatidylserine + phosphatic acid complex (PSPA) as perhaps being greater than the sum of the parts for effecting stress mitigation. One landmark study conducted last summer showed that supplementation with PSPA was able to normalize stress-induced dysregulations of the hypothalamic-pituitary-adrenal axis (HPAA).[8]

The randomized, double-blind, placebo-controlled study of 75 healthy male volunteers was published by Hellhammer, et al., in the peer-reviewed journal: Lipids in Health and Disease July, 2014. The researchers examined effects of daily oral supplementation of PSPA 400 (PAS 400), a complex containing 400mg PS and 400mg PA, for a 42-day period (6 weeks). This six week period of supplementation was followed by an acute stress test (Trier Social Stress Test, or TSST) to determine the effect of the complex on exogenously induced psychological and social stress.

Researchers looked at endocrine stress response—specifically, ACTH as well as both saliva and serum cortisol—to a psychosocial stressor. In the chronically high-stressed subjects, supplementation with daily PSPA 400 proved effective at normalizing the ACTH and both cortisol responses following the TSST, compared to the placebo.

While some studies, as previously mentioned, indicate EEG changes following supplementation with PSPA, in this study there were no statistically significant effects of supplementation with PSPA on heart rate, pulse transit time or psychological stress response. Still, researchers could state with confidence that, in chronically stressed subjects, supplementation with PSPA 400 can normalize the hyper-responsivity of the HPAA to an acute stressor.

Mechanisms of Action

As chronic stress results in a hyper-responsivity of the HPAA, the studied phospholipid compounds engage normalization of stress responsivity effects on the HPAA, thus can be expected to buffer the HPAA response to stress. Phospholipids can further restore normal ACTH and cortisol responses to stress in subjects with a reduced HPAA response.

Chronic stress has been shown to reduce cortisol binding globulin (CBG) in the blood, where it binds with a high affinity—but low capacity—to glucocorticoid hormones, such as cortisol. It’s well known that during stress, the concentration of glucocorticoids spikes and the free fraction increases even more as CBG becomes saturated.[7]

The observed pronounced increase of ACTH and cortisol in stress tests administered to PSPA subjects can possibly be explained by a drop of CBG in chronically stressed subjects. Researchers hypothesized that, if this is the case, PSPA 400...
could first cause a normalization of CBG levels under such conditions. This, then would result in the normalization of the activity and reactivity of the HPAA seen.

The findings in the 2014 PSPA study expand on a previous study in which young adult subjects aged 20-45 were provided soy lecithin-derived PSPA complex. Pituitary adrenal reactivity to a mental and emotional stressor was measured via ACTH, cortisol, as was psychological response on the Spielberger State Anxiety Inventory stress subscale. Four groups of 20 subjects were treated for three weeks with daily dosages of either 400mg, 600mg or 800mg PSPA or a placebo before exposure to the TSST. In this study, the treatment with 400mg PSPA resulted in a pronounced blunting of both serum ACTH and cortisol, and salivary cortisol responses to the TSST, but did not affect heart rate.[8]

Evaluation of the psychological response demonstrated that 400mg PSPA exerted a specific positive effect on emotional responses to the TSST. While the placebo group showed the expected increase in distress after the test, the group treated with 400mg PSPA showed decreased distress. These data provide initial evidence for a selective stress dampening effect of PSPA on the pituitary–adrenal axis, suggesting the potential of PSPA in the treatment of stress related disorders.

Formulating with PSPA

With such strong evidence for cognitive health and stress relief, the development of a plant source of PS made it an in-demand ingredient for supplements and its subsequent GRAS status (granted in 2006) opened the door for its use in functional foods and beverages targeting cognitive health.

Plant-derived PSPA complex has been scientifically designed to support not only the essential functions of the brain vis. cognition and memory but to work synergistically to counteract and mitigate the body’s reaction to stress and the metabolic imbalances wrought by that state.

In the studies outlined above, pronounced stress dampening effects of PSPA on HPAA responses have been observed for the 400mg treatment group. These results were highly consistent with previous findings, and are in line with other studies showing that both interim and sustained administration of PSPA can normalize cortisol responses to acute physical and mental stress.

Lipogen PSPA is the only proprietary, patent-protected, lecithin-derived PSPA phospholipid complex designed to naturally support a healthy response to stress. It is non-GMO, kosher certified plus all-natural. The unique and proprietary production methods result in a pure, high quality product which is well-tolerated by the body, safe for use with no known side effects, as demonstrated in multiple clinical studies.

With today’s demanding pace of life, stress is inevitable. Lipogen PSPA provides an alternative to powerful and sometimes dangerous pharmaceuticals and their side effects. Lipogen PSPA can help overworked and under-rested individuals perform better under daily stress, while maintaining a focused and uplifted state of mind.
References


4. Centers for Disease Control (CDC) and National Institute on Occupational Safety & Health (2011).


