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WHITE PAPER

ALPHA-GLYCERYL PHOSPHORYL CHOLINE FOR MENTAL & PHYSICAL PERFORMANCE

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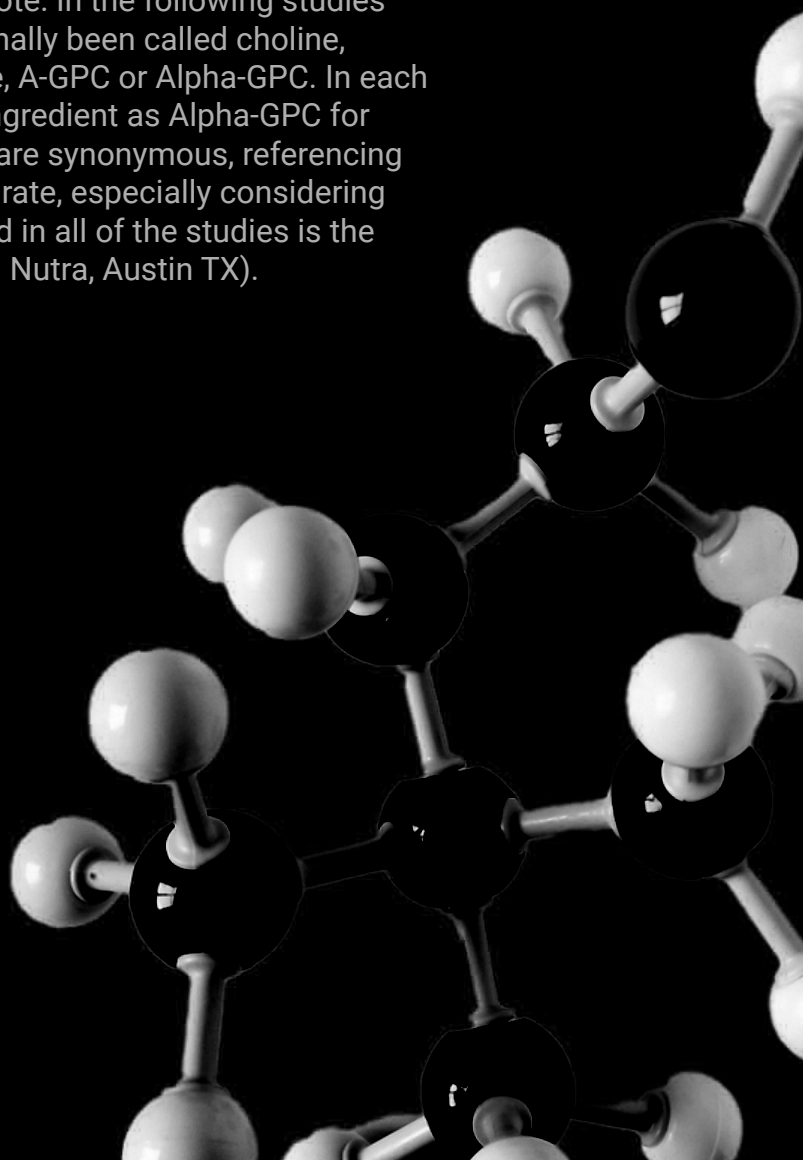
INTRODUCTION

Alpha-Glyceryl Phosphoryl Choline (Alpha-GPC), sometimes called choline alfoscerate (or choline alphoscerate) or A-GPC, is a water-soluble phospholipid, naturally occurring in the body and typically derived from plants such as soy. A source of the vitamin choline, Alpha-GPC is breakdown product of phosphatidylcholine, and a precursor to the neurotransmitter, acetylcholine precursor. This nutraceutical has a significant body of research behind it, attesting to its benefits for mental and physical performance. These benefits are largely due to its role as an acetylcholine precursor. Note: In the following studies cited, Alpha-GPC may have originally been called choline, alfoscerate choline alphoscerate, A-GPC or Alpha-GPC. In each instance, I have referred to the ingredient as Alpha-GPC for ease of reading. Since all terms are synonymous, referencing them thusly is scientifically accurate, especially considering that the Alpha-GPC material used in all of the studies is the same: AlphaSize® A-GPC (Chemi Nutra, Austin TX).



ACETYLCHOLINE

Acetylcholine (ACh) is an organic chemical that functions in the brain and body of many types of animals, including humans, as a neurotransmitter—a chemical released by nerve cells to send signals to other cells. Acetylcholine is the neurotransmitter that motor neurons of the nervous system release in order to activate muscles. It is also used in the autonomic nervous system, both as an internal transmitter for the sympathetic nervous system and as the final product released by the parasympathetic nervous system. In the brain, acetylcholine plays an important role in cognitive function, including arousal, attention, memory and motivation. Now let's take a look at how Alpha-GPC, as an acetylcholine precursor, provides benefits for autism, cognition, growth hormone, exercise performance and sleep.

AUTISM

In addition to behavioral issues, mental developmental delay and cognitive dysfunction are usually diagnosed in childhood autism. Children who receive only neuroleptic therapy (i.e. major tranquilizers) generally do not demonstrate significant improvement of cognitive functions. Consequently, it is important to include neuroprotective therapy as part of a strategy for treating autism. Since the cholinergic system plays an important role in the functioning of those parts of the brain affected in autism, and since research suggests that Alpha-GPC helps improve cognitive functions and behavioral reactions, a study was conducted to evaluate the therapeutic effects of Alpha-GPC during an eight-week course of supplementation using 400 mg/day in 20 children (aged 3 to 8 years) with autism. There were 10 patients with mild autism, three with moderate autism, and seven with moderate/severe autism. The patients were assessed twice: before (0 day) and after the therapeutic course (56th day). Results showed positive effects observed at the end of therapeutic course in 89 percent of the patients: significant improvement in 61 percent and minimal improvement in 28 percent. Statistically significant positive changes in the patients' state were observed in the general improvement of behavior ($p < 0.001$), development of social and communicative skills, as well as self-service, reduction of marked speech disturbances ($p < 0.001$) and motor sphere dysfunction ($p < 0.001$), enhancement of learning activity and productivity ($p < 0.05$). Improvement was also seen in concentration, imitation, social play activity, speech understanding, thinking and emotional response. The authors concluded that, overall, Alpha- GPC may be recommended for combined therapy with neuroleptics as an effective and safe medicine for the treatment of cognitive and behavioral disorders in patients with childhood autism.

COGNITION

Due to its ability to increase production of acetylcholine and phosphatidylcholine, Alpha-GPC has demonstrated value for improving memory in adults with dementia/ neurocognitive disorders. First of all, Alpha-GPC is also a precursor to membrane phospholipids. Therefore, it might improve neuronal functioning by improving neuronal membrane fluidity. In addition, levels of alpha-GPC-derived choline in the brain are thought to increase much more slowly, but also remain elevated for longer period of time. A multicenter, randomized, controlled study was conducted to compare the efficacy of Alpha-GPC and acetyl-l-carnitine among 126 patients with probable senile dementia of Alzheimer's type (SDAT) of mild to moderate degree. Patients received oral Alpha-GPC (800 mg at 8 a.m. and 400 mg at 4 p.m.) and acetyl-l-carnitine (1,000 mg at 8 a.m. and 500 mg at 4 p.m.) for six months. Efficacy was evaluated using behavioral scales and psychometric tests. The results showed significant improvements ($P<0.05$) in most neuropsychological parameters in the Alpha-GPC recipients. Improvements also occurred in the acetyl-l-carnitine recipients, but to a lesser extent. Tolerability was good in both groups. A comparative study was conducted to assess the effects of oxiracetam (a nootropic drug) versus Alpha-GPC in brain aging. Forty male patients (aged 55 to 65 years) with senile organic brain syndrome (an older term used to describe a neurocognitive disorder) were randomly assigned to 1 g/day of either therapy for 12 weeks. The clinical efficacy of the two agents was assessed by neuropsychological and clinical parameters, including measurements of reaction time. Treatment with oxiracetam was associated with early improvement that was maintained for the duration of therapy, but whose effects ceased following discontinuation of therapy. In contrast, the response to Alpha-GPC was slower but more sustained. Eight weeks after discontinuation of therapy, the clinical effects were as apparent as during the eighth week of treatment ($P<0.001$). Both agents were well tolerated and can be expected to be particularly effective in longterm patient management. In an open, uncontrolled clinical study, 817 elderly patients with the diagnoses of Alzheimer's disease (AD), multi-infarct dementia (MID) or mixed dementia (MD) weretreated with 1,200 mg/day of Alpha-GPC. Although an open label design makes it hard to reach final conclusions, results showed that both the dimensional changes in rating scale scores and the proportional changes in terms of number of patients showing improvement are well beyond the 20 percent range which have been reported with an inactive placebo. Furthermore, unlike temporary benefits seen with placebos, the improvement with Alpha- GPC continued throughout the study period and was not restricted to alleviation of psychopathology and improvement of performance, but extended to areas intimately linked to social behavior. There were also indications that patients with MID responded more favorably than patients with AD, and patients with moderate and moderately severe cognitive decline responded more favorably than patients with very mild and mild cognitive decline. To assess the efficacy and tolerability of Alpha-GPC in the treatment of cognitive impairment due to mild to moderate AD, a multicenter, double-blind, randomized, placebo-controlled trial was conducted. A total of 261 patients (age range, 60 to 80 years) were treated with 400 mg Alpha-GPC or placebo capsules, three times daily for 180 days. Outcome measures that were assessed at the beginning of the investigation and after 90 and 180 days of treatment, included scores of the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), the Mini-Mental State Examination (MMSE), the Global Deterioration Scale (GDS), the Alzheimer’s Disease Assessment Scale- Behavioral Subscale (ADAS-Behav), all items of the Alzheimer’s Disease Assessment Scale (ADAS-Total) and the Clinical Global Impression (CG) scale. The Global Improvement Scale (GIS) score was assessed after 90 and 180 days of treatment.

COGNITION CONT.

Results were that the average decrease in ADAS-Cog score in patients treated with Alpha-GPC was 2.42 points after 90 days of treatment and 3.20 points at the end of the study (the lower the score, the better) ($P < 0.001$). However, in patients receiving placebo, there was an average increase in ADAS-Cog score of 0.36 points ≤ 1 after 90 days of treatment and 2.90 points after 180 days of treatment. All other assessed parameters consistently improved after 90 and 180 days versus baseline in the Alpha-GPC group, whereas in the placebo group they remained unchanged or worsened. In conclusion, this study suggests that Alpha-GPC is clinical useful and tolerable in the treatment Alzheimer's disease. Cholinesterase inhibitors (ChE-Is), drugs that reduce the breakdown of acetylcholine in the body, are commonly used for the treatment of mild-to-moderate symptoms of AD, but their long-term effects on cognitive, functional, and behavioral symptoms are small and not always apparent in practice. To assess if the ChE-I donepezil (10 mg/day) with Alpha-GPC (1,200 mg/day) had a more favorable clinical profile than therapy with donepezil alone (+ placebo), a 12-month, double-blind multicenter trial was conducted, with data from 91 AD patients (aged 56 to 91 years) who also had ischemic cerebrovascular disease. Patients' cognitive functions, daily activities and behavioral symptoms were assessed by the Mini-Mental State Evaluation (MMSE), Alzheimer's Disease Assessment Scale Cognitive subscale (ADAS-cog), Basic Activities of Daily Living (BADL), Instrumental Activities of Daily Living (IADL) and Neuropsychiatric Inventory (NPI), of severity and of caregiver distress measures (NPI-F and NPI-D). The results were that patients receiving donepezil plus placebo showed a slight worsening of MMSE, ADAS-cog, IADL and NPI-D scores, and no changes in the BADL and NPI-F scores. By contrast, donepezil plus Alpha-GPC showed improvements in all scores ($P<0.05$) (except the BADL) to donepezil plus placebo. In addition to the beneficial effects of Alpha-GPC in patients with cognitive disorders, this phospholipid may also help with cognitive recovery in some situations. For, example stroke and transient ischemic attack patients who receive alpha-GPC within 10 days post-stroke might have improved outcomes. Preliminary evidence suggests that these patients who get alpha-GPC 1,200 mg/day intramuscularly for 28 days, followed by 400 mg three times daily (1,200 mg/day) orally for six months, have improved recovery including improved cognitive and behavioral function.

GROWTH HORMONE

In adults, growth hormone (GH), secreted during sleep and in response to exercise, stimulates protein synthesis in muscle, the release of fatty acids from adipose tissue (aka, fat), helps maintain boon health, and inhibits the uptake of glucose by muscle while stimulating uptake of amino acids, which can then be used in the synthesis of proteins and encourages muscle to shift to using fatty acids as a source of energy. However, GH secretion rates decline with age. In fact, compared to puberty, there is an 83 percent decline in GH by age 55. This decline in GH production is associated with alterations in body composition, hormonal status, and functional capacity that mimic the changes seen in adult GH deficiency or partial hypogonadism (diminished functional activity of the gonads—the testes in males or the ovaries in females—that may result in diminished sex hormone biosynthesis). In addition to deteriorating memory and cognitive function, the changes in body composition that are most pronounced in normal aging include a reduction in bone density and in muscle mass and strength, an increase in body fat, and adverse changes in lipoprotein profiles. These facts have led to the following statement by researchers from the VA Puget Sound Health Care System and University of Washington, School of Medicine: "Aging is not a disease. Rather, it is a physiological state of relative GH deficiency." It turns out that Alpha-GPC may help to promote GH release. Here's how it works. A hormone called growth hormone releasing hormone (GHRH) is released from the hypothalamus, which in turn stimulates GH secretion from the pituitary. On the other hand, the hypothalamic hormone somatostatin inhibits GH release. With aging, the imbalance between stimulatory (GHRH) and inhibitory (somatostatin) activities on GH secretion leads to an enhanced somatostatin action and decreased GH release. Part of the reason for this imbalance is a concurrent decrease in levels of acetylcholine, which plays an important role in the control of GH secretion. Anticholinergic drugs (or drugs that decrease acetylcholine activity) have been shown to diminish GH response, while drugs able to increase acetylcholine transmission are able to potentiate the stimulatory effect of GHRH through a decrease of somatostatin release. Increasing GHRH, by decreasing somatostatin release, is a novel approach to increasing GH levels. Alpha-GPC fits into the GH picture because, research has demonstrated that it increases acetylcholine release. Research suggests that both older and younger people can benefit from Alpha-GPC to promote GH secretion, but the difference will simply be more profound in older people since they have naturally lower levels of GH. In one study, GHRH was given to eight young and seven old human volunteers, with or without the addition of 1 gram of Alpha-GPC. The results were that the groups given the Alpha-GPC experienced a greater stimulatory effect of GHRH on HGH secretion in both young and old subjects—about 130 percent greater HGH in the case of the older subjects, and about 35 percent greater in the case of younger subjects. In a follow-up study, Alpha-GPC was tested in 10 normal elderly subjects (aged 79.4 ± 1.7 years). The subjects were given GHRH with 2 grams of Alpha- GPC. The results demonstrated that when the 2 grams of Alpha-GPC was administered with GHRH, the HGH responses were significantly higher than those found after GHRH alone, but not significantly different from those seen in the elderly subjects who received 1 gram of Alpha-GPC. This suggests that a maximal potentiation of GHRH-induced GH responses could be achieved by the lower dose.

The amounts of HGH released from the anterior pituitary are summarized in the table below:

Substance(s) given	Young Subjects (1g)	Old Subjects (1g)	Old Subjects (2g)
GHRH	1375 + 263	415 + 119	191 + 57
GHRH + A-GPC	1849 + 215	977 + 273	804 + 182

GROWTH HORMONE CONT.

More recently, a double-blind, randomized, crossover study was conducted to investigate acute the physiologic response to a single intake of 1,000 mg Alpha-GPC or placebo in eight healthy male subjects (25 ± 1 y old). Fasting blood samples were taken at baseline, as well as 60 and 120 minutes after administration. All subjects repeated the identical protocol using the placebo. The results were that plasma growth hormone secretion was increased significantly (see bar graph) 60 min after taking Alpha-GPC ($P<0.0167$), whereas no significant change was observed with the placebo. In addition, the serum free fatty acid was increased 120 min after Alpha-GPC ingestion ($P<0.0167$), but no changes were seen with the placebo. This increase suggests an increase in lipolysis (breakdown of fat) from fat cells. Moreover, indicators of fat oxidation in the liver were significantly increased at 120 minutes after taking Alpha-GPC ($P<0.0167$), whereas the placebo had no effect. In conclusion, a single dose of Alpha-GPC significantly increased growth hormone secretion, free fatty acids, and liver fat oxidation. Exercise Performance Another randomized, placebo-controlled, crossover study also examined the effects of Alpha-GPC on GH levels, as well as on explosive performance, and post-exercise substrate oxidation. Seven men with at least two years of resistance training experience were given supplement containing primarily 600 mg/day Alpha-GPC (or placebo). The supplement was taken 90 minutes prior to completing six sets times 10 repetitions of squats at 70 percent of their pre-determined one repetition maximum. Results were that, compared to baseline (pre) values, peak GH increased 44-fold during Alpha-GPC vs. 2.6-fold during placebo ($P < 0.03$). Likewise, peak bench press force was 14 percent greater in A-GPC vs. placebo ($P < 0.02$). These data indicate that a single 600 mg dose of Alpha-GPC, when administered 90 minutes prior to resistance exercise, increases post-exercise serum GH and peak bench force. To determine if six days of supplementation with Alpha-GPC would augment isometric force production, 13 college-aged males consumed either 600 mg per day of Alpha-GPC or placebo for six days in a double blind, placebo controlled, crossover study. At baseline, and at the end of six days, the participants performed isometric mid-thigh pull in a custom squat cage on a force platform and upper body isometric test against a high frequency load cell. Results were that the Alpha-GPC treatment resulted in significantly greater isometric mid-thigh pull peak force change from baseline ($P = 0.044$) compared with placebo. For the upper body test, the Alpha-GPC treatment trended towards greater change from baseline force production but failed to obtain statistical significance. In conclusion, Alpha-GPC enhanced muscle performance in speed and power athletes. To assess the efficacy of two doses of Alpha-GPC in comparison to placebo and caffeine for increasing countermovement jump performance, isometric strength, and psychomotor function, a double-blind, four arm study was conducted with 48 healthy, college-aged males who underwent baseline assessment of countermovement jump (CMJ), isometric mid-thigh pull (IMTP), upper body isometric strength test (UBIST) and psychomotor vigilance (PVT). The participants were randomly assigned to groups consisting of 500 mg/day Alpha-GPC, 250 mg/day Alpha-GPC, 200 mg/day caffeine or placebo. Blood samples were collected one and two hours after the initial dose, and then subjects returned after seven days of supplementation to repeat the physical tests. No differences were noted between groups for IMTP, UBIST or PVT performance. However, group differences were noted for maximum velocity and maximum mechanical power on the CMJ ($p < 0.05$) with the 250 mg Alpha-GPC group demonstrating the greatest improvements in result. The study authors concluded that Alpha-GPC should be considered as an emerging ergogenic supplement.

SLEEP

Rapid eye movement (REM) sleep is a unique phase of sleep during which the sleeper is likely to dream more vividly. This phase is characterized most notably by an abundance of the acetylcholine. The different theories about REM sleep's function are that it helps in forming new memories, stimulates the central nervous system and restores brain chemistry to a normal balance. A lack of REM sleep can result in mild psychological disturbances, such as anxiety, irritability, hallucinations and difficulty concentrating may develop and appetite may increase. It is now well known that rapid eye movement (REM) density, which is a measure of the frequency of REMs during REM sleep, increases over the course of the sleep episode in successive REM sleep episodes. Protocols utilizing extended sleep episodes have suggested that REM density increases with prolonged sleep duration and eventually saturates at a maximal level. It has even been proposed that REM density is an index of sleep satiety—that is, when you get good quality sleep, you don't need as much sleep. Accordingly, an inverse relationship between the depth of sleep and REM density has been observed. Consequently, there would seem to be an advantage to increasing REM density. Such an increase was seen with Alpha- GPC supplementation. A single-blind controlled study26 was conducted in eight healthy young male subjects to assess the effect of Alpha- GPC, on sleep. Alpha-GPC was supplemented in doses of 400 mg, three times daily (1,200 mg total). The study examined whether short-term treatment modified REM sleep parameters. The results were that REM density was increased, which returned to pre-study levels once supplementation ceased. Conclusion Alpha-GPC (AlphaSize® A-GPC, Chemi Nutra) has been extensively studied in human clinical research, with results showing significant benefits for autism, cognition, growth hormone, exercise performance and sleep. The fact is that this article has only scratched the surface of the body of research conducted on Alpha-GPC, and that continues to be conducted on this evidence-based nutraceutical.