



Exploring α -GPC - A Comprehensive Overview of Its Impact on Cognitive Health

Visit Umbrella Labs here: <https://umbrellalabs.is>

History

α -GPC is a precursor to the neurotransmitter acetylcholine (ACh), which is used in the central and peripheral nervous system but can also be considered as precursor to phosphatidylcholines, which are an essential part of animal cell membranes and high content in the human brain. α -GPC is naturally occurring in food and beverages, although in low amounts. It is also known as L- α -GPC, Alphoscerat or Cholin Asphoscerat.

Research on α -GPC is several decades old. When first test on patients suffering from cognitive decline showed that in these individuals neurons seem to have trouble to produce ACh and absorb it from their immediate environment. Hence, treatments were looked after that could provide these neurons with enough ACh to satisfy their

increased demand.

Despite encouraging early results, well-controlled clinical trials failed to show significant improvement of treatment with choline or lecithin and therefore, the clinical value of these drugs, if any, is controversial. The development of central inhibitors of enzymes that block breakdown of ACh, which have a therapeutic role in the treatment of Alzheimer's symptoms today, prompted scientists to focus their attention on the role of ACh loss as responsible for cognitive impairment which is a trait of the disease. From these efforts, α -GPC arose as a potential candidate.

α -GPC is a semi-synthetic derivative of phosphatidylcholine. Pre-clinical studies have demonstrated it increases the release of acetylcholine, facilitates learning and memory in experimental animals, improves brain transduction mechanisms

and decreases the age-dependent structural changes occurring in the rat brain. The compound also contributes to anabolic processes. Due to these promising results, it was subsequently trialed to treat symptoms of neurodegenerative diseases in humans starting in the early 1990's.

Preclinical Data

Preclinical data for α -GPC is abundant. It has been mostly evaluated as neuroprotective or neurostimulatory compound, but also in other roles, for example as a nephroprotectant.

The potential therapeutic effects of α -GPC on seizure-induced cognitive impairment were tested in rats. α -GPC (250 mg/kg) was injected into the intramuscular space once daily for one or three weeks from immediately after seizure, or from 3 weeks after the seizure onset for 3 weeks. The

authors found that administration of α -GPC starting at 3 weeks after seizure improved cognitive function through reduced neuronal death and blood brain barrier disruption, and increased neurogenesis.¹ An earlier study had already reported beneficial short-term effects.² Similar studies in mice have come to comparable conclusions.³ Oral administration of α -GPC 3 hours before cognitive test in rats prevented learning impairment induced by other drugs. Similarly, drug induced retrograde amnesia was also completely reversed by the drug. These effects were dose-dependent with a maximum at 300 mg/kg.⁴

A further study on rats exposed to stress has shown a neuroprotective effect under these conditions. Animals treated with α -GPC (400 mg/kg) administered orally after stress exposure showed better memory function, decreased immune response and a more favorable cytokine and hormone profile compared to the control group.⁵ Another study on hypertensive rats demonstrated α -GPC (150 mg/kg/day) and lipoic acid (125 μ mol/kg/day) resulted in a decrease in blood pressure and neuronal damage in these animals. In aged rats Injections of 100mg/kg/day α -GPC did increase learning and memory as well.⁶

Aging rats show a significant decrease in the number of muscarinic M1 receptors in some brain areas compared to young animals. Chronic treatment of aged rats with α -GPC restored the number of M1 receptors to levels found in young animals. The

metabolites of α -GPC showed the same influence in receptor density, indicating α -GPC is not a prodrug.⁷

Isoflurane, a widely used common inhalational anesthetic agent, can induce brain toxicity. α -GPC has been recognized for its neuroprotective properties against oxidative stress and inflammation, hence it was trailed to prevent damage from isoflurane in cell culture. However, the findings suggest that α -GPC treatment could potentially enhance the vulnerability of brain cells to isoflurane.⁸ Another study has pointed towards to conclusion, that α -GPC can be either protective or toxic, depending on the external circumstances in some cells.⁹

Clinical Data

As early as 1993, a study with 126 patients suffering from Alzheimer's disease explored the effects of α -GPC but also Acetyl L-Carnitine (ST200) in these individuals. The study participants received 800 mg of α -GPC at 8 am and 400 mg at 4 pm daily for 6 months. After 4 months significant improvements in the degree of dementia were observed, while there was no significant difference between the groups. The data overall showed a better effect of α -GPC compared to ST200 though. Both drugs were well tolerated. Adverse effects observed in the α -GPC-treated group were insomnia, gastric pain and restlessness in 1 patient each.

In 2002 a further clinical study assessed the efficacy and

tolerability of α -GPC in the treatment of cognitive impairment due to mild to moderate Alzheimer's disease in elderly individuals. 132 patients were treated with 400 mg α -GPC 3x times daily for 180 days. Similar to previous findings, cognitive function improved significantly in the group after 90 and 180 days of treatment compared to the control group. A longer treatment time corresponded to a higher increase in mental function. Fifteen drug-related adverse effects (10 episodes of constipation, 5 episodes of nervousness) were reported.¹⁰

α -GPC was also administered to 2044 patients who had suffered a recent stroke or transient ischemic attack. In the first 30 days, it was administered intravenously at a dose of 1000 mg/day. In the next 4 months, they would orally receive 1200 mg per day. The data show that α -GPC did effectively prevent the deterioration of the cognitive function due to the ischemic event. Adverse events were complained of by 44 patients (2.14%); in 14 (0.7%) the investigator preferred to discontinue therapy. The most frequent complaints were heartburn (0.7%), nausea-vomit (0.5%), insomnia-excitation (0.4%), and headache (0.2%). The trial confirmed the therapeutic role of α -GPC on the cognitive recovery of patients with acute stroke and the low percentage of adverse events confirms its excellent tolerability.¹¹

In 2021, 40 healthy volunteers aged 22-59 years were recruited to investigate the effects of α -GPC on human emotions. They received 400 mg α -GPC before bedtime for 2 weeks. A placebo had no effect on motivation, whereas the α -GPC group showed an increasing trend in motivation during the intervention period at nighttime. Effects on anxiety were not observed. The authors concluded that that α -GPC (400 mg/day) administration did not exhibit any side effects or addictions during the 2 weeks of intervention and at least 12 months after taking the medication.¹²

There are also a number of smaller clinical trials mostly published in Italian language. The trials focused in degenerative dementia disorders, vascular dementia and acute cerebrovascular diseases.^{13 14}

Degenerative dementia disorders

In four trials, α -GPC was administered orally at the dose of 1200 mg per day, while in the remaining studies it was administered intramuscularly at the dose of 1000 mg per day. The duration of the treatment was 3 or 6 months for oral administration and 3 months for parenteral administration. Overall, 505 patients were treated orally (466 for 6 months and 39 for 3 months) and 60 patients were treated intramuscularly. In general, in all trials treatment with α -GPC proved to improve the patients clinical condition, especially regarding memory and attention impairment.

A recent meta-analysis (2023), considering the most recent developments, has again confirmed the

positive effect of α -GPC on cognition of patients suffering from Alzheimer's disease.¹⁵

Vascular dementia

Overall, 789 patients with vascular dementia were enrolled in seven trials. In four trials, α -GPC was administered orally at the dose of 1200 mg per day for 3 or 6 months, while in three further studies it was administered by intramuscular injection at the dose of 1000 mg per day for 3 months. Of the 431 orally treated patients, 418 received the drug over 6 months and 13 over 3 months. Similarly, as observed in degenerative dementia disorders, treatment with choline, α -GPC improved overall clinical symptoms, such as memory and attention impairment, affective disorders and somatic symptoms (fatigue, dizziness) in all trials on vascular dementia. A different analysis of clinical data concluded that α -GPC provided some modest symptomatic relief primarily on memory and attention in dementia of vascular origin.¹⁶

Acute cerebrovascular diseases

All patients in three trials were subjected to intramuscular treatment with a daily dose of 1000 mg per day α -GPC in the 4 weeks following the acute event. This parenteral administration was followed by a 5-month oral administration of the drug at the

dose of 1200 mg per day. In all three trials, parenteral treatment with α -GPC favored cognitive, functional and motor recovery in the acute phase, while the subsequent oral treatment consolidated the clinical results obtained in the acute phase and positively influenced the whole clinical course.

A study investigating a change in electrical signaling in the brain in 17 patients with mild cognitive impairment found no statistically significant changes, but a tendency for faster signaling.¹⁷

As a result of these studies, α -GPC has been used extensively in some parts of the world as clinical treatment. In 2021, a study was published evaluating the subsequent risks of a stroke 10 years after α -GPC treatment. Data of over 100.000 participants were collected. Results showed users of α -GPC were about 40 % more likely to suffer a stroke in 10 years after initial treatment. It is however not clear whether this is due to α -GPC intake or to other factors.¹⁸

Performance in healthy subjects

Twenty participants 10 males, 10 females consumed 200 mg of α -GPC, 400 mg of α -GPC, 200 mg of caffeine and a placebo in a randomized, double-blind study. They reported mood and performed a serial subtraction test and tests for reaction time, hand-eye coordination, power, speed, and agility. Subtraction test scores were 18.1 % and 10.5 % faster in the α -GPC group compared to caffeine and PL, respectively. Vertical Jump Peak

Power was 8.5 % higher in the 200 mg α -GPC, 7.5 % higher in the 400 mg α -GPC and 2.0 % higher in the caffeine group in comparison to placebo. Mood changes in between the groups were not recorded, except jitteriness seemed to be lower in the 400 mg α -GPC group to all other groups.¹⁹ These findings demonstrate that α -GPC can increase mental and physical performance in healthy subjects, although the participant count was small.

α -GPC was also theorized to have an effect on dreams, but a study on 40 participants was not able to verify this hypothesis.²⁰ α -GPC does also not seem to influence body weight or composition and growth hormone level in humans.

Conclusion

The evidence for α -GPC as an effective treatment of Alzheimer's disease symptoms and in the attenuation of stroke damage has been documented extensively by a series of studies and meta-analyses. Hence, has been used to treat cognitive decline from various sources since decades on a large number of patients. There is also limited clinical data suggesting that not only certain groups of diseases may be treated with α -GPC, but that healthy subjects can profit from a supplementation of α -GPC on a physical and mental level as well. However, more data is needed to confirm this. In addition, some preclinical findings indicate a possible positive effect on kidney metabolism. A typical dose of α -GPC is 500-1500 mg per day in most clinical studies.

Due to its long-time clinical use, the data availability for the safety of α -GPC is excellent. For most individuals, no side effects are to be expected from a regular dose while few may experience mild side effects. It is considered as "Generally recognized as safe" by the US food and drug administration (FDA). One long-term study was found that use of α -GPC may increase the risk of strokes in a 10-year time period after α -GPC intake in patient that had already suffered a previous stroke, which is a concerning result. It is however not clear if this is due to α -GPC or if there were confounding factors in this singular study.

There are also some trials indicating there might be a toxic effect of α -GPC, however these results stem from experiments in cell culture and it is unclear if these findings can be transferred to a living organism.

References

- [1] Lee SH, Choi BY, Kim JH, Kho AR, Sohn M, Song HK, Choi HC, Suh SW. *Late treatment with choline alfoscerate (L-alpha glycerylphosphorylcholine, α -GPC) increases hippocampal neurogenesis and provides protection against seizure-induced neuronal death and cognitive impairment.* *Brain Res.* **2017**;1654:66–76. doi: 10.1016/j.brainres.2016.10.011.
- [2] Sigala S, Imperato A, Rizzonelli P, Casolini P, Missale C, Spano P. *L-alpha-glycerylphosphorylcholine antagonizes scopolamine-induced amnesia and enhances hippocampal cholinergic transmission in the rat.* *Eur J Pharmacol.* **1992**;211:351–358. doi: 10.1016/0014-2999(92)90392-H.
- [3] Yulong Zheng, Geum Duck Park. *Treatment with Soybean Lecithin-Derived A-Gpc (Shcog™) Improves Scopolamine-Induced Cognitive Declines in Mice Via Regulating Cholinergic Neurotransmission and Enhancing Neural Plasticity in the Hippocampus.* *Preprint.* **2024**.
- [4] Drago F, D'Agata V, Guidi G. *Effects of L- α -Glycerylphosphorylcholine on Drug-Induced Behavioral Alterations in Rats.* *Dement Geriatr Cogn Disord.* **1992**;3:7–9. doi: 10.1159/000106986.
- [5] Jeong Yu H, Lin Kim Y, Jung Kim M, Mee Park J, Young Park S, Nae Park S, Won Yang D. *The effect of choline alfoscerate on non spatial memory and neuronal differentiation in a rat model of dual stress.* *Brain Res.* **2022**;1786:147900. doi: 10.1016/j.brainres.2022.147900.
- [6] Drago F, Mauceri F, Nardo L, Valerio C, Lauria N, Rampello L, Guidi G. *Behavioral effects of L- α -glycerylphosphorylcholine: influence on cognitive mechanisms in the rat.* *Pharmacol Biochem Behav.* **1992**;41:445–448. doi: 10.1016/0091-3057(92)90124-X.
- [7] Muccioli G, Raso GM, Ghé C, Di Carlo R. *Effect of L-alpha glycerylphosphorylcholine on muscarinic receptors and membrane microviscosity of aged rat brain.* *Prog Neuropsychopharmacol Biol Psychiatry.* **1996**;20:323–339. doi: 10.1016/0278-5846(95)00313-4.
- [8] Lee HJ, Cho HR, Bang M, Lee YS, Kim YJ, Chong K. *Potential Risk of Choline Alfoscerate on Isoflurane-Induced Toxicity in Primary Human Astrocytes.* *J Korean Neurosurg Soc.* **2023**. doi: 10.3340/jkns.2023.0208.
- [9] Tuboly E, Gáspár R, Ibor MO, Gömöri K, Kiss B, Strifler G, Hartmann P, Ferdinandy P, Bartekova M, Boros M, et al. *L-Alpha-glycerylphosphorylcholine can be cytoprotective or cytotoxic in neonatal rat cardiac myocytes: a double-edged sword phenomenon.* *Mol Cell Biochem.* **2019**;460:195–203. doi: 10.1007/s11010-019-03580-1.
- [10] Jesus Moreno Moreno M de. *Cognitive improvement in mild to moderate Alzheimer's dementia after treatment with the acetylcholine precursor choline alfoscerate: a multicenter, double-blind, randomized, placebo-controlled trial.* *Clin Ther.* **2003**;25:178–193. doi: 10.1016/S0149-2918(03)90023-3.
- [11] Barbagallo Sangiorgi G, Barbagallo M, Giordano M, Meli M, Panzarasa R. *alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial.* *Ann N Y Acad Sci.* **1994**;717:253–269. doi: 10.1111/j.1749-6632.1994.tb12095.x.
- [12] Tamura Y, Takata K, Matsubara K, Kataoka Y. *Alpha-Glycerylphosphorylcholine Increases Motivation in Healthy Volunteers: A Single-Blind, Randomized, Placebo-Controlled Human Study.* *Nutrients.* **2021**;13. doi: 10.3390/nu13062091.
- [13] Parnetti L, Amenta F, Gallai V. *Choline alfoscerate in cognitive decline and in acute cerebrovascular disease: an analysis of published clinical data.* *Mech Ageing Dev.* **2001**;122:2041–2055. doi: 10.1016/S0047-6374(01)00312-8.
- [14] Kolykhalov IV, Androsova LV, Gavrilova SI. *Kliniko-immunologicheskie efekty kholina al'fostserata pri lechenii sindroma myagkogo kognitivnogo snizheniya amnesticheskogo tipa.* *Zh Nevrol Psikhiatr Im S S Korsakova.* **2022**;122:59–66. doi: 10.17116/jnevro202212211259.
- [15] Sagaro GG, Traini E, Amenta F. *Activity of Choline Alfoscerate on Adult-Onset Cognitive Dysfunctions: A Systematic Review and Meta-Analysis.* *J Alzheimers Dis.* **2023**;92:59–70. doi: 10.3233/JAD-221189.
- [16] Parnetti L, Mignini F, Tomassoni D, Traini E, Amenta F. *Cholinergic precursors in the treatment of cognitive impairment of vascular origin: ineffective approaches or need for re-evaluation?* *J Neurol Sci.* **2007**;257:264–269. doi: 10.1016/j.jns.2007.01.043.
- [17] Han S-H, Jeong H-B, Park K-Y, Shin H-W, Youn YC, Kim S. *P300 latency changes in patients with mild cognitive impairment after taking choline alfoscerate; A preliminary study.* *eNeurologicalSci.* **2018**;11:5–8. doi: 10.1016/j.ensci.2018.04.004.
- [18] Lee G, Choi S, Chang J, Choi D, Son JS, Kim K, Kim SM, Jeong S, Park SM. *Association of L- α -Glycerylphosphorylcholine With Subsequent Stroke Risk After 10 Years.* *JAMA Netw Open.* **2021**;4:e2136008. doi: 10.1001/jamanetworkopen.2021.36008.
- [19] Parker AG, Byars A, Purpura M, Jäger R. *The effects of alpha-glycerylphosphorylcholine, caffeine or placebo on markers of mood, cognitive function, power, speed, and agility.* *Journal of the International Society of Sports Nutrition.* **2015**;12. doi: 10.1186/1550-2783-12-S1-P41.
- [20] Kern S, Appel K, Schredl M, Pipa G. *No effect of α -GPC on lucid dream induction or dream content.* *Somnologie.* **2017**;21:180–186. doi: 10.1007/s11818-017-0122-8.
- [21] Maldonado WG. *The effects of α -GPC supplementation on growth hormone, fat loss, and body composition in overweight adults.*

To learn more information about **Alpha GPC**, visit:

<https://umbrellalabs.is/shop/nootropics/nootropic-powder/alpha-gpc/>