Reference List for Alpha-Glyceryl Phosphoryl Choline (Alpha-GPC)

2023.08.22

TABLE OF CONTENTS:

KEY:

Indicates Chemi Nutra's material utilized

OUTCOME: **Autism**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Krasnoperova	2005	Gliatilin In Childhood Autism Treatment	Trial	400 mg per day for 8 weeks	20 children (16 boys, 4 girls) with childhood autism aged 3–8 years	Positive effect on CGI scale was observed at the end of therapeutic course in 89% of the patients: significant improvement — in 61% and minimal efficacy — in 28%. 11% patients did not demonstrate any changes in their clinical state. 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 selfservice, reduction of marked speech disturbances ($p < 0.001$) and motor sphere dysfunction ($p < 0.001$), enhancement of learning activity and productivity ($p < 0.05$). Also improvement was seen in concentration, imitation, social play activity, speech understanding, thinking, emotional response. Good tolerability to the therapy without patient's state worsening was registered. Some patients exhibited strengthening of affective lability during the first 2–3 weeks of the treatment which attenuated to the 4th week as the Gliatilin dosages decreased to 400 mg every other day.	Krasnoperova M.G. Gliatilin In Childhood Autism Treatment. Psychopharmacol. Biol. Narcol. 2005. Vol. 5, N 2. P. 887–888.

OUTCOME: **Body Composition**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Maldonado	2019	The effects of α-GPC supplementation on growth hormone, fat loss, and body composition in overweight adults	Clinical Trial	1200 mg per day for 8 weeks	28 (10 male, 18 female) between ages 18 and 45, with BMI > 23, and body fat percentage >20% for men and 25% for women in good health.	The purpose of the current study was to investigate daily supplementation of 1200 mg α-GPC compared to a placebo in an overweight, moderately active population. We hypothesized that α-GPC supplementation would result in greater loss of FM, increased FFM, decreased BM, and increased GH levels when dietary and exercise habits were maintained during this eight-week intervention. There was a significant Time effect for body composition measures, however no significant differences were seen between groups for any variables over the intervention. These findings suggest α-GPC does not confer any additional benefits to weight loss, body composition, and GH level beyond placebo in this population.	Maldonado W. The effects of α-GPC supplementation on growth hormone, fat loss, and body composition in overweight adults. Rutgers, The State University of New Jersey. DOI 10.7282/t3-qggq-ff53.

OUTCOME: **Cognition**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Trabucchi	1986	Changes in the interaction between CNS cholinergic and dopaminergic neurons induced by L-alpha-glycerylphosphoryl choline, a cholinomimetic drug	Animal Study	Unknown dosage, Intraperitoneal injection and orally	Rats	alpha-GPC both i.p. and per os administered increased striatal dihydroxyphenylacetic acid (DOPAC) content. In addition, the in vitro K+ stimulated dopamine release was increased in rats treated in vivo with alpha-GPC. Since alpha-GPC has a weak displacing activity in QNB binding, the in vivo cholinergic activity might be due to the fact that this drug may increase the availability of choline for acetylcholine synthesis leading to increased acetylcholine production. This activity may be useful in those situations such as aging in which cholinergic activity is deficient.	Trabucchi M, Govoni S, Battaini F. Changes in the interaction between CNS cholinergic and dopaminergic neurons induced by L-alpha-glycerylphosphoryl choline, a cholinomimetic drug. Il Farmaco; Edizione Scientifica. 1986 Apr;41(4):325-334. PMID: 3709792
Abbati	1991	Nootropic Therapy of Cerebral Aging	Clinical Trial	1 gram intramuscular injection (IM) for 12 weeks	40 males (55 to 65 years of age)	On the whole, our results demonstrated the efficacy of pharmacologic therapy with oxiracetam or choline alphoscerate in brain aging, a condition characterized by cognitive and behavioral deficits of medium severity. An appropriate regimen for administration of these agents may also be inferred from our results. Between-group comparisons during the follow-up period suggest that treatment with choline alphoscerate can be suspended for a longer time than oxiracetam without affecting the clinical results. Such a treatment regimen can be expected to have a favorable effect on compliance of patients and relatives. The safety profiles of both treatments were good; no patients withdrew because of side effects or poor compliance. Such a result is of great interest in view of the long period of treatment and the route of administration of the test drugs.	Abbati, Claudia et al. “Nootropic therapy of cerebral aging.” Advances in Therapy 8 (1991): 268-276.
Ban	1991	Choline alphoscerate in Elderly Patients with Cognitive Decline Due to Dementing Illness	Open, Uncontrolled Clinical Trial	1200 mg orally for 6 months	817 patients aged 60 and older (61 to 95, with a mean age 73) fulfilling DSM-III-R criteria for dementia with a clinical diagnosis of primary degenerative dementia of the Alzheimer’s type, multi-infarct dementia, or mixed dementia	The favorable changes observed with a.-GPC treatment were consistent and detectable in all dimensional measures (ratig scales) and categorical proportions (number of patients showing improvement). Furthermore, improvement was not restricted to psychopathologic changes (SCAG), but extended to performance (GOS and MMSE) and social behavior (CRICHTON) as well. An examination of the changes in dimensional measures revealed that improvement was not restricted to the first 30 days of treatment, but continued throughout the , 80-day study. In all measures of assessment, improvement at Days 90 and , SO was well above the 12% placebo response rate of psychogeriatric patients (28) (Table VI). The same applies to categorical proportions: while at the time of the Day 30 assessment most patients fell into the group with 5% or less improvement, by the time of the Day 180 assessment most patients fell into the group with 20% or more improvement (Table VII).	Ban T. Choline alphoscerate in Elderly Patients with Cognitive Decline Due to Dementing Illness. New Trends in Clinical Neuropharmacology. Vol. V-n. ¾-1991.

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Canal	1991	Effect of L-alpha-glyceryl-phosphorylcholine on amnesia caused by scopolamine	Clinical Trial	1200 mg intramuscular injection (IM) for 10 days	Thirty-two healthy young volunteers (18 males, 14 females; mean age 26.5 ± 4.5).	In conclusion, our data confirm that L-α-GPC does act on memory-related cholinergic circuits. This finding and the lack of any significant side-effects indicates that further trials should be done, aimed at assessing the potential therapeutic role of L-α-GPC in Alzheimer's disease, a clinical condition characterized by memory disturbance associated with cortical cholinergic dysfunction.	Canal, N et al. "Effect of L-alpha-glyceryl-phosphorylcholine on amnesia caused by scopolamine." International journal of clinical pharmacology, therapy, and toxicology vol. 29,3 (1991): 103-7. PMID: 2071257
Di Perri	1991	A multicentre trial to evaluate the efficacy and tolerability of alpha-glycerylphosphoryl choline versus cytosine diphosphocholine in patients with vascular dementia	Clinical Trial	1 gram intramuscular injection (IM) for 90 days	120 patients with mild to moderate vascular dementia	Both treatments produced a definite symptomatic improvement and showed a very good tolerability. The results suggest that in most tests alpha-GPC possessed a statistical higher efficacy and an overall more satisfactory activity assessed by both patients and investigators compared with CDP.	Di Perri, R et al. "A multicentre trial to evaluate the efficacy and tolerability of alpha-glycerylphosphoryl choline versus cytosine diphosphocholine in patients with vascular dementia." The Journal of international medical research vol. 19,4 (1991): 330-41. doi:10.1177/030006059101900406
Frattola	1991	Multicenter Clinical comparison of the effects of Choline Alphoscerate and Cytidine Diphosphocholine in the treatment of Multi-Infarct Dementia.	Clinical Trial, Comparative	1 gram intramuscular injection (IM) per day for 90 days	126 patients	Both treatment produced positive effects on memory, cognitive and behavioural parameters. However, a.-GPC acted more swiftly and more completely than CDP-choline. Statistical analysis showed that the effects of a.-GPC on the parameters relative to spontaneous behaviour and those relative to stimulated behaviour were significantly better than those of CDPcholine. Both drugs were judged to be well tolerated.	Frattola L. Multicenter Clinical comparison of the effects of Choline Alphoscerate and Cytidine Diphosphocholine in the treatment of Multi-Infarct Dementia. Current Therapeutic Research Vol. 49, 4 (1991): 683-693

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Lopez	1991	Effect of a new cognition enhancer, alpha-glycerylphosphoryl choline, on scopolamine-induced amnesia and brain acetylcholine	Animal Study	100, 300, 600, 1000 mg/kg Immune globulin intravenous (IG) in I ml 5 hours before training.	Adult male Wistar rats	The present study investigates the effect of the administration of alphaglycerylphosphorylcholine (alpha-GPC) on scopolamine-induced amnesia and on brain acetylcholine (ACh) levels and release in rats. The results indicate that alpha-GPC, when administered orally, reverses the amnesia caused by scopolamine in passive avoidance. The peak effect is observed using 600 mg/kg IG, 5 h before training. The effect of the drug is long lasting (up 30 h) in accordance with its pharmacokinetic characteristics. Since, alpha-GPC administered IG is cleaved within the gut mucosal cells to glycerophosphate and free choline, it is tempting to speculate that this drug acts by increasing the ACh precursor pool. This view is supported also by the observation that alpha-GPC partially counteracts the decrease of brain ACh levels elicited by scopolamine administration. The effect is observed in the hippocampus and cortex, but not in the striatum. Moreover, in ex vivo experiments, alpha-GPC is able to increase the amount of ACh released by rat hippocampus slices following potassium stimulation.	Lopez, C M et al. “Effect of a new cognition enhancer, alpha-glycerylphosphoryl choline, on scopolamine-induced amnesia and brain acetylcholine.” *Pharmacology, biochemistry, and behavior* vol. 39,4 (1991): 835-40. doi:10.1016/0091-3057(91)90040-9
Sigala	1992	L-alpha-glycerylphosphoryl choline antagonizes scopolamine-induced amnesia and enhances hippocampal cholinergic transmission in the rat	Animal Study	100-600 mg/kg, oral, acutely	Male Sprague-Dawley rats	In conclusion, the present data suggest that α -GPC is able to prevent the scopolamine-induced impairment of learning and memory in the rat. These behavioural effects seem to be well correlated with the neurochemical properties of the drug. α-GPC may have an initial short-lasting stimulatory effect on ACh release paralleled by a significant and long-lasting increase of ACh synthesis, resulting in an increased storage of ACh and an increased secretion upon stimulation.	Sigala, S et al. “L-alpha-glycerylphosphoryl choline antagonizes scopolamine-induced amnesia and enhances hippocampal cholinergic transmission in the rat.” European journal of pharmacology vol. 211,3 (1992): 351-8. doi:10.1016/0014-2999(92)90392-h
Gatti	1992	A comparative study of free plasma choline levels following intramuscular administration of L-α-glycerylphosphoryl choline and citicholine in normal volunteers	Clinical Trial, Comparative	1 gram intramuscular injection (IM), acutely	12 male volunteers, aged 20–29 (mean age 26±2)	The administration of alpha-GPC was associated with a rapid rise in plasma choline, peak levels being usually observed at the first (0.25 h) or second (0.5 h) sampling time after the injection. Thereafter, the concentration of choline declined gradually and returned to near baseline values at the end of the observation period. After the administration of [citicoline], plasma choline levels showed a similar time course but were considerably lower than those observed after the administration of alpha-GPC.	Gatti, G et al. “A comparative study of free plasma choline levels following intramuscular administration of L-alpha-glycerylphosphoryl choline and citicoline in normal volunteers.” *International journal of clinical pharmacology,*

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
							therapy, and toxicology vol. 30,9 (1992): 331-5. PMID: 1428296
Govoni	1992	Chronic treatment with an acetylcholine synthesis precursor, alpha-glycerylphosphoryl choline, alters brain parameters linked to cholinergic transmission and passive avoidance behavior	Animal Trial	100 and 300 mg/kg i.g. per day for 22 days	Adult male Wistar rats (150–250 g)	The results obtained following repeated oral treatment with GPC show that the drug retains its ability to counteract scopolamine-induced amnesia following a prolonged adminis-tration period. Moreover the behavioral response was observed for a dose (100 mg/kg) that acutely is unable to antagonize scopolamine. Furthermore, the protective effect of the 300 mg/kg dose appears to be more robust than following the single administration. Also in the case of the chronic treatment the behavioral effect of GPC appears to be at least partially mediated by an effect on cholinergic transmission. In fact the chronic treatment with GPC (300 mg/kg) enhanced the K+ stimulated ACh release both in hippocampus and in cerebral cortex of treated rats. In contrast no effect on ACh release was observed using the 100 mg/kg dose, which was behaviorally active, once more stressing the partial dissociation of the two parameters.	Govoni S. Chronic treatment with an acetylcholine synthesis precursor, alpha-glycerylphosphoryl choline, alters brain parameters linked to cholinergic transmission and passive avoidance behavior. Drug Development Research. 1992. Issue 4, 439–447. Doi: 10.1002/ddr.430260407
Muratorio	1992	A neurotropic approach to the treatment of multi-infarct dementia using L-α-glycerylphosphoryl choline	Clinical Trial, Comparative	1 gram intramuscular injection (IM) per day for 90 days	112 patients (77 males, 35 females; mean age 68.5 ± 6.4) with mild to moderate multi-infarct dementia	The patients receiving L-α-GPC showed a significant improvement of cognitive functions, behavior, and personality at the end of the treatment, compared with baseline values. This improvement was still apparent at the end of the follow-up period. Only aphasia, as measured by the Word Fluency test, was significantly improved by the CDP-choline treatment. A comparison of the results obtained with L-α-GPC and CDP-choline shows that the performance of the patients treated with L-α-GPC was significantly better than that of the CDP-choline group on the Blessed Dementia Scale, WMS, RDRS 2, and SDC at the end of treatment and on the Blessed Dementia Scale, WMS, SCAG, and Token test at the end of the follow-up period. Both treatments were well tolerated.	Muratorio A. A neurotropic approach to the treatment of multi-infarct dementia using L-α-glycerylphosphoryl choline. Current Therapeutic Research, Volume 52, Issue 5, 1992, Pages 741-752, ISSN 0011-393X, Doi: 10.1016/S0011-393X(05)80518-1.
Parnetti	1993	Multicentre study of l-alpha-glyceryl-phosphorylcholine vs ST200 among patients with probable senile dementia of Alzheimer's type	Clinical Trial	1200 mg (800 mg AM, 400 mg afternoon) orally for 6 months	126 patients (48 males; 78 females; mean age 74.2 ± 5) with probable senile dementia of Alzheimer's type (SDAT) of mild to moderate degree	The results showed significant improvements in most neuropsychological parameters in the alpha GPC recipients. Improvements also occurred in the ST200 [acetyl-l-carnitine] recipients but to a lesser extent. Tolerability was good in both groups. These positive findings require replication in larger, double-blind, longitudinal studies coupling clinical and biological determinations.	Parnetti, L et al. "Multicentre study of l-alpha-glyceryl-phosphorylcholine vs ST200 among patients with probable senile dementia of Alzheimer's type." *Drugs &*

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
							aging vol. 3,2 (1993): 159-64. doi:10.2165/00002512-199303020-00006
Sangiorgi	1994	alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial	Clinical Trial	Phase 1: 1 g per day for 28 days. Phase 2: 1200 mg per day orally for 5 months.	2058 patients 45-85 years of age (1132 males; 908 females, 4 missing; mean age 70.3 ± 8.6), with diagnosis of cerebral ischemic attacks (stroke or TIA), within the previous 10 days.	The present results collected from a large patient population diagnosed for acute ischemic cerebral attacks confirm the efficacy of a-GPC on the mental recovery after stroke. At the end of the first part of the study, after 1 month of parenteral therapy with a-GPC, the results were very good both in tolerability and in efficacy: Mathew Scale reached a mean score equivalent to a less deteriorated neurological condition (> 65) and the tolerability was good: 34 events (1.66%) and 10 withdrawals (0.49%). The improvement was maintained in time during the following 5 months of oral therapy, and a further improvement in cognitive functions (by the Minimental State Test), in behavioral functions (by the Crichton Geriatric Rating Scale), and in medical conditions related to cognitive decline (by the GDS) was statistically evaluable. Tolerability was very good also in the second part: 17 events (0.33%) and 4 withdrawals (0.2%). These data confirm in a large patient population the efficacy and the therapeutic role of a-GPC on the cognitive enhancement of patients with an acute cerebrovascular attacks (stroke and/or TIA): the very low incidence of adverse events confirms that a-GPC can be safely administered also for a long period after the occurrence of stroke.	Barbagallo Sangiorgi, G et al. “alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial.” *Annals of the New York Academy of Sciences* vol. 717 (1994): 253-69. doi:10.1111/j.1749-6632.1994.tb12095.x
Ferraro	1996	Evidence for an in vivo and in vitro modulation of endogenous cortical GABA release by alpha-glycerylphosphoryl choline	Animal Study	3 – 300 mg/kg Intraperitoneal injection	Male Sprague Dawley rats	In conclusion, previous observations and the present findings indicate that α-GPC is able to simultaneously activate different neuronal systems, such as the cholinergic and the GABAergic ones. It will be possible to obtain a more complete view of the central beneficial effects of this drug by extending the analysis to other transmitters, such as noradrenaline and glutamate, most likely involved in age-linked cognitive deficits.	Ferraro, L et al. “Evidence for an in vivo and in vitro modulation of endogenous cortical GABA release by alpha-glycerylphosphoryl choline.” Neurochemical research vol. 21,5 (1996): 547-52. doi:10.1007/BF02527751

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Amenta	2001	Treatment of cognitive dysfunction associated with Alzheimer's disease with cholinergic precursors. Ineffective treatments or inappropriate approaches?	Review	Not applicable	Not applicable	The first attempts in the treatment of [Alzheimer's disease; AD] with cholinergic precursors did not confirm a clinical utility of this class of compounds in well controlled clinical trials. However, cholinergic precursors most largely used such as choline and phosphatidylcholine (lecithin) were probably not suitable for enhancing brain levels of ACh. Other phospholipids involved in choline biosynthetic pathways such as CDP-choline, choline alphoscerate and phosphatidylserine clearly enhanced ACh availability or release and provided a modest improvement of cognitive dysfunction in AD, these effects being more pronounced with choline alphoscerate. Although some positive results cannot be generalized due to the small numbers of patients studied, they probably would justify reconsideration of the most promising molecules in larger carefully controlled trials.	Amenta, F et al. "Treatment of cognitive dysfunction associated with Alzheimer's disease with cholinergic precursors. Ineffective treatments or inappropriate approaches?." Mechanisms of ageing and development vol. 122,16 (2001): 2025-40. doi:10.1016/s0047-6374(01)00310-4
Parnetti	2001	Choline alphoscerate in cognitive decline and in acute cerebrovascular disease: an analysis of published clinical data	Review	Not applicable	Not applicable	Thirteen published clinical trials, examining in total 4054 patients, have evaluated the use of choline alphoscerate in various forms of dementia disorders of degenerative, vascular or combined origin, such as senile dementia of the Alzheimer's type (SDAT) or vascular dementia (VaD) and in acute cerebrovascular diseases, such as transitory ischemic attack (TIA) and stroke. Analysis has assessed the design of each study, in particular with respect to experimental design, number of cases, duration of treatment and tests used to evaluate drug clinical efficacy. Most of the ten studies performed in dementia disorders were controlled trials versus a reference drug or placebo. Overall, 1570 patients were assessed in these studies, 854 of which in controlled trials. As detected by validated and appropriate tests, such as Mini Mental State Evaluation (MMSE) in SDAT and Sandoz Clinical Assessment Geriatric (SCAG) in VaD, administration of choline alphoscerate significantly improved patient clinical condition. Clinical results obtained with choline alphoscerate were superior or equivalent to those observed in control groups under active treatment and superior to the results observed in placebo groups. Analysis stresses the clear internal consistency of clinical data gathered by different experimental situations on the drug effect, especially with regard to the cognitive symptoms (memory, attention) characterising the clinical picture of adult-onset dementia disorders. The therapeutic usefulness of choline alphoscerate in relieving cognitive symptoms of chronic cerebral deterioration differentiates this drug from cholinergic precursors used in the past, such as choline and lecithin. Three uncontrolled trials were performed with choline alphoscerate in acute cerebrovascular stroke and TIA, totalling 2484 patients. The results of these trials suggest that this drug might favour functional recovery of patients with cerebral stroke and should be confirmed in future investigations aimed at establish the efficacy of the drug in achieving functional recovery of patients with acute cerebrovascular disease.	Lucilla Parnetti, Francesco Amenta, Virgilio Gallai, Choline alphoscerate in cognitive decline and in acute cerebrovascular disease: an analysis of published clinical data. Mechanisms of Ageing and Development, Volume 122, Issue 16,2001,Pages 2041-2055, ISSN 0047-6374. Doi: 10.1016/S0047-6374(01)00312-8.

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Moreno	2003	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	Clinical Trial	1200 mg per day for 180 days	261 patients (62 males, 199 females; mean age 76.9 ± 7.4) affected by mild to moderate dementia of the Alzheimer's type	Our study shows that compared with placebo, treatment with oral [Choline Alfoscerate; CA] significantly improved cognition and global function in our relatively small group of patients selected according to the enrollment criteria of the study protocol from the population affected with mild to moderate dementia of the Alzheimer type. Based on the results of different tests examined, the following points should be considered. The ADAS-Cog score, the primary end point of efficacy, showed a statistically significant improvement after 90 and 180 days of treatment with CA, demonstrating a comprehensive improvement of cognitive measures compared with the worsening observed in the placebo group. The analysis of patients responding to treatment was implemented only post hoc (by classification of each patient according to the improvement observed on this scale at the end of treatment) and therefore cannot be acknowledged as a major study finding. Nevertheless, this analysis allows us to classify 46.2% of total patients in the CA group as responders, and 35.6% as complete responders to treatment. Based on published data, mean ADAS-Cog score deteriorates up to 3.5 points over a 180-day period in untreated patients. In the current study, patients treated with CA had a mean improvement in ADAS-Cog score of 3.20 points, company with a decrease in score of 2.90 points in patients treated with placebo for 180 days; this suggest that the response to CA treatment, as assessed using the mean ADAS-Cog score, counteracts symptom progression.	De Jesus Moreno Moreno, Maria. "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." *Clinical therapeutics* vol. 25,1 (2003): 178-93. doi:10.1016/s0149-2918(03)90023-3
Doggrell	2003	Treatment of dementia with neurotransmission modulation	Review	Not applicable	Not applicable	There has been a small number of controlled clinical trials of choline alfoscerate (neurodegenerative dementia: three trials with 565 patients; VaD: four trials with 789 patients). In these trials, choline alfoscerate has been shown to consistently improve Mini-Mental State Examination (MMSE) scores. More recently, in a Mexican study of 261 out-patients with mild-to-moderate AD, choline alfoscerate was shown to have a marked beneficial effect in AD. Thus, in the patients given choline alfoscerate (400 mg t.i.d.) for 180 days, there was a difference in favour of choline alfoscerate over placebo in the primary efficacy end point of the cognitive-subscale score of the AD Assessment Scale (ADAS-cog) of 6.1 points, which evaluates memory, language and praxis. A 4-point improvement in this scale is considered clinically significant and 46% of patients treated with choline alfoscerate achieved this (placebo 10.1%). Choline alfoscerate also caused significant improvements in the MMSE scores (placebo: baseline = 17.6, 180 days = 17.1; choline alfoscerate group: baseline = 18.2, 180 days = 24.5) [13]. With choline alfoscerate there were also improvements on the Global Deterioration Scale (GDS) and Clinical Global Impression of Change (CGIC) scales. More adverse effects were reported in the choline alfoscerate group (8.3% of patients) than in the placebo group (2.3%) with the most common adverse effect with choline alfoscerate being constipation, which is not usually associated with enhancement of cholinergic transmission.	Doggrell, Sheila A, and Suzanne Evans. "Treatment of dementia with neurotransmission modulation." Expert opinion on investigational drugs vol. 12,10 (2003): 1633-54. doi:10.1517/13543784.12.10.1633
Amenta	2006	Association with the cholinergic precursor choline alphoscerate and the cholinesterase inhibitor rivastigmine: An approach for	Animal Study, Comparative	150 mg/kg Intraperitoneal injection per day with rivastigmine	Adult male Wistar rats (200–250 g body weight)	In summary, our data suggest that combination of the precursor in the biosynthesis of acetylcholine choline alphoscerate and of the cholinesterase inhibitor rivastigmine may represent an association worthwhile of being further investigated as a possible approach in cholinergic replacement therapy of AD. The advantage of the proposed association versus cholinesterase inhibitor as monotherapy is represented by the lower doses of cholinesterase inhibitor necessary for increasing brain levels of acetylcholine. This may be useful for reducing the probability of side or toxic effects (primarily gastrointestinal and	Amenta, Francesco et al. "Association with the cholinergic precursor choline alphoscerate and the cholinesterase inhibitor

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		enhancing cholinergic neurotransmission				hepatic) induced by cholinesterase inhibitors (Gauthier, 2002). Another potential advantage of the association could be in making available larger amounts of choline and consequently of acetylcholine in patients in which cholinesterase inhibition may be not effective due to low levels of neurotransmitter in cholinergic synapses.	rivastigmine: an approach for enhancing cholinergic neurotransmission." Mechanisms of ageing and development vol. 127,2 (2006): 173-9. doi:10.1016/j.mad.2005.09.017
Parnetti	2007	Cholinergic precursors in the treatment of cognitive impairment of vascular origin: ineffective approaches or need for re-evaluation?	Review	Not applicable	Not applicable	The first cholinergic precursor used phosphatidylcholine (lecithin) did not show any clear clinical benefit on symptoms of dementia disorders. The same is not true for other phospholipids involved in choline biosynthetic pathways such as cytidine 5'-diphosphocholine (CDP-choline) and choline alphoscerate for which a modest improvement of cognitive dysfunction in dementia of neurodegenerative and vascular origin is documented. Positive results obtained with selected cholinergic precursors cannot be generalized due to the small numbers of patients studied in appropriate clinical trials. However, they probably would justify reconsideration of the most promising molecules in larger carefully controlled studies.	Parnetti, Lucilla et al. "Cholinergic precursors in the treatment of cognitive impairment of vascular origin: ineffective approaches or need for re-evaluation?." Journal of the neurological sciences vol. 257,1-2 (2007): 264-9. doi:10.1016/j.jns.2007.01.043
Amenta	2008	Pathways of Acetylcholine Synthesis, Transport and Release as Targets for Treatment of Adult-Onset Cognitive Dysfunction	Review	Not applicable	Not applicable	Controlled clinical studies denied clinical usefulness of choline and lecithin (phosphatidylcholine), whereas for other phospholipids involved in choline biosynthetic pathways such as cytidine 5'-diphosphocholine (CDP-choline) or alpha-glyceryl-phosphorylcholine (choline alphoscerate) a modest improvement of cognitive dysfunction in adult-onset dementia disorders is documented. These inconsistencies have probably a metabolic explanation. Free choline administration increases brain choline availability but it does not increase ACh synthesis/or release. Cholinergic precursors to serve for ACh biosynthesis should be incorporate and stored into phospholipids in brain. It is probable that appropriate ACh precursors and other correlated molecules (natural or synthesized) could represent a tool for developing therapeutic strategies by revisiting and updating treatments/supplementations coming out from this therapeutic stalemate.	Amenta, F, and S K Tayebati. "Pathways of acetylcholine synthesis, transport and release as targets for treatment of adult-onset cognitive dysfunction." Current medicinal chemistry vol. 15,5 (2008): 488-98. doi:10.2174/092986708783503203
Tayebati	2011	Effect of choline-containing phospholipids on	Animal Study,	CDP-choline: 325 mg/kg/day; choline alphoscerate: 150	36 Wistar Rats	Choline alphoscerate stimulated significantly the neurotransmitter concentration in the frontal cortex, however, the levels were similar to the controls in both the striatum and cerebellum. In comparison to the controls, VAChT expression	Tayebati, Seyed Khosrow et al. "Effect of choline-

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		brain cholinergic transporters in the rat	Comparative	mg/kg/day administered Intraperitoneal injection for 7 days		following either CDP-choline or choline alphoscerate treatment, was enhanced greatly in the striatum and cerebellum. Also, ELISA measurements for VAChT showed significant increases in all choline alphoscerate treated brain areas. In contrast, in the CDP-choline treated rats the vesicular transporter amount was greater than the control only in the striatum. The cholinergic presynaptic transporters VAChT and CHT play a relevant role in sustaining new ACh synthesis and release. To sum up, CDP-choline and choline alphoscerate stimulated to a different extent the expression of VAChT and CHT primarily in a cognitive area such as frontal cortex. In the lack of novel therapeutic strategies, safe compounds developed since a long time such as the choline-containing phospholipids investigated would merit to be further investigated by new and adequate clinical studies. This for assessing their place if any in pharmacotherapy of dementia disorders characterized by diminished cholinergic tone.	containing phospholipids on brain cholinergic transporters in the rat." *Journal of the neurological sciences* vol. 302,1-2 (2011): 49-57. doi:10.1016/j.jns.2010.11.028
Tomassoni	2012	Effects of cholinergic enhancing drugs on cholinergic transporters in the brain and peripheral blood lymphocytes of spontaneously hypertensive rats	Animal Study	150 mg/kg perday	Male Spontaneously hypertensive rat (SHR)	Cholinergic hypofunction is a trait of Alzheimer's disease and vascular dementia and countering it is one of the main therapeutic strategies available for these disorders. Cholinergic transporters control cellular mechanisms of acetylcholine (ACh) synthesis and release at presynaptic terminals. This study has assessed the influence of 4 week treatment with two different cholinergic enhancing drugs, the cholinergic precursor choline alphoscerate (alpha-glyceryl-phosphorylcholine) or the acetylcholinesterase (AChE) inhibitor galantamine on high affinity choline uptake transporter (CHT) and vesicular ACh transporter (VAChT) expression in the brain of spontaneously hypertensive rats (SHR). … Treatment with choline alphoscerate increased CHT and to a greater extent VAChT expression. Treatment with galantamine countered the increase of CHT and VAChT. The different activity of the cholinergic precursor and of the AChE inhibitor on parameters investigated is likely related to their mechanism of action. Choline alphoscerate increases ACh synthesis and release. This requires an augmentation of systems regulating neurotransmitter uptake and storage. The effect of choline alphoscerate on CHT and VAChT observed in this study suggests an improved synaptic efficiency elicited by the compound. The AChE inhibitor slows-down ACh degradation in the synaptic cleft. A greater availability of neurotransmitter elicited by galantamine counters the enhanced activity of cholinergic transporters compensating cholinergic deficits. Differences in the activity of the cholinergic precursor and AChE inhibitor investigated on CHT and VAChT suggests that association between choline alphoscerate and AChE/cholinesterase inhibitors may represent a strategy for potentiating deficient cholinergic neurotransmission worthwhile of being investigated in clinical trials.	Tomassoni, Daniele et al. "Effects of cholinergic enhancing drugs on cholinergic transporters in the brain and peripheral blood lymphocytes of spontaneously hypertensive rats." Current Alzheimer research vol. 9,1 (2012): 120-7. doi:10.2174/156720512799015118
Amenta	2012	The ASCOMALVA trial: Association between the cholinesterase inhibitor donepezil and the cholinergic precursor choline alphoscerate in Alzheimer's disease with	Clinical Trial	Cholinesterase inhibitor (donepezil 10 mg/day)+ precursor cholinergic (choline alphoscerate 1200 mg/day) for 24 months	183 patients (78 males, 105 females; mean age 75 ± 10 years) with Alzheimer's Disease and concomitant ischemic cerebrovascular disease.	The first results of the ASCOMALVA trial suggest that association of choline alphoscerate to the standard treatment with a ChE-Imay represent an option to prolong beneficial effects of cholinergic therapies in AD with concomitant ischemic cerebrovascular injury.	Amenta, Francesco et al. "The ASCOMALVA trial: association between the cholinesterase inhibitor donepezil and the cholinergic precursor choline alphoscerate in

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		cerebrovascular injury: Interim results					Alzheimer's disease with cerebrovascular injury: interim results." *Journal of the neurological sciences* vol. 322,1-2 (2012): 96-101. doi:10.1016/j.jns.2012.07.003
Colucci	2012	Effectiveness of nootropic drugs with cholinergic activity in treatment of cognitive deficit: a review	Review, Comparative	Not applicable	Not applicable	Regarding cholinergic precursors, not all the data are positive. Lecithin does not seem to achieve significant improvement in cognitive functioning. The same is not true for citicoline or choline alfoscerate. Citicoline has neuroprotective effects, especially in patients with stroke and traumatic brain injury, probably by helping repair processes in the neural membrane, reducing the accumulation of lipids, and increasing acetylcholine levels. Citicoline also improves cognition, particularly motor and attentive functioning, in patients with dementia. Acetyl-carnitine is associated with an increase in energy and well-being by reducing physical and psychological fatigue. Further, acetyl-carnitine has demonstrated an antidepressive effect. Choline alfoscerate also enhances cognitive functioning and is, among several precursors, active in increasing acetylcholine levels in the brain. Therefore, it may represent a therapeutic option to improve the beneficial effects of cholinergic therapy in patients with Alzheimer's disease and concomitant cerebrovascular damage.	Colucci, Luisa et al. "Effectiveness of nootropic drugs with cholinergic activity in treatment of cognitive deficit: a review." *Journal of experimental pharmacology* vol. 4 163-72. 11 Dec. 2012, doi:10.2147/JEP.S35326
Scapicchio	2013	Revisiting choline alphoscerate profile: a new, perspective, role in dementia?	Review	Not applicable	Not applicable	In a number of clinical studies, alpha-GPC demonstrated benefit in patients with cognitive dysfunction. In light of the limited therapeutical results obtained in the past decades by the use of cholinesterase inhibitors in dementia, and of the relevance of their side effects in long-lasting therapies, it is desirable to reconsider alpha-GPC in larger carefully controlled studies not only as monotherapy but also in association with cholinesterase inhibitor drugs.	Scapicchio, Pier Luigi. "Revisiting choline alphoscerate profile: a new, perspective, role in dementia?." The International journal of neuroscience vol. 123,7 (2013): 444-9. doi:10.3109/00207454.2013.765870
Traini	2013	Choline Alphoscerate (Alpha-Glyceryl-Phosphoryl-Choline) An Old Choline-containing Phospholipid with a Still Interesting Profile As	Review	Not applicable	Not applicable	In summary, choline alphoscerate has significant effects on cognitive function with a good safety profile and tolerability. Although limited both in terms of size of the samples investigated and of the length of treatment, preclinical and clinical results presented suggest that cognitive enhancing capabilities of choline alphoscerate merit of being further investigated in appropriate trials.	Traini, Enea et al. "Choline alphoscerate (alpha-glyceryl-phosphoryl-choline) an old choline- containing phospholipid with a still interesting profile as cognition

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		Cognition Enhancing Agent					enhancing agent." *Current Alzheimer research* vol. 10,10 (2013): 1070-9. doi:10.2174/1567205013106660173
Parker	2015	The effects of alpha-glycerylphosphoryl choline,caffeine or placebo on markers of mood,cognitive function, power, speed, and agility	Poster Presentation	200 mg, 400 mg, or 200 mg caffeine, acutely (30 minutes)	Twenty participants (10 males, 10 females; mean age 22.0 ± 3.4)	[Serial Subtraction Test; SST] scores were 18.1% and 10.5% faster in the [200 mg aGPC] (6.19 ± 2.21 s) group compared to [caffeine] (7.32 ± 5.67 s) and [placebo] (6.85 ± 2.52 s), respectively. Vertical Jump Peak Power was 8.5% higher in the [200 mg aGPC] (2,041.3 ± 547.2 W), 7.5% higher in the [400 mg aGPC] (2,023.1 ± 942.8 W) and 2.0% higher in the [caffeine] group (1,920.4 ± 689.6 W) in comparison to [placebo] (1,881.9 ± 576.9 W). The group consuming [caffeine] had significantly higher scores on the [Visual Analog Scale; VAS] for jitteriness compared to [400 mg aGPC] (p = 0.019), but not [200 mg aGPC] (p = 0.849) or [placebo] (p = 0.086). There were no other statistically significant differences between supplement groups for any of the dependent variables.	Parker, A.G., Byars, A., Purpura, M. *et al.* The effects of alpha-glycerylphosphoryl choline, caffeine or placebo on markers of mood, cognitive function, power, speed, and agility. *J Int Soc Sports Nutr* **12** (Suppl 1), P41 (2015). https://doi.org/10.1186/1550-2783-12-S1-P41
Lee S.	2016	Late treatment with choline alfoscerate (l-alpha glycerylphosphoryl choline, α-GPC) increases hippocampal neurogenesis and provides protection against seizure-induced neuronal death and cognitive impairment	Animal Study	250 mg/kg intramuscularly once per day for 1 week or 3 weeks.	Male rats	Here we found that immediate 1-week treatment of α-GPC showed no neuroprotective effects and neurogenesis. Immediate 3-week treatment of α-GPC showed neuroprotective effect but no effect on neurogenesis. To evaluate the effect of late treatment of α-GPC on cognitive impairment following seizure, rats were injected α-GPC from 3 weeks after seizure for 3 weeks and subjected to a water maze test. In the present study, we found that administration of α-GPC starting at 3 weeks after seizure improved cognitive function through reduced neuronal death and BBB disruption, and increased neurogenesis. Therefore, α-GPC injection may serve as a beneficial treatment for improvement of cognitive function in epilepsy patients.	Lee, Song Hee et al. "Late treatment with choline alfoscerate (l-alpha glycerylphosphoryl choline, α-GPC) increases hippocampal neurogenesis and provides protection against seizure-induced neuronal death and cognitive impairment." *Brain research* vol. 1654,Pt A (2017): 66-76. doi:10.1016/j.brainres.2016.10.011
Han	2018	P300 latency changes in patients with mild cognitive impairment after taking choline	Preliminary Study	800 mg per day for 3 months	34 subjects with amnestic form mild cognitive impairment	Object of this preliminary study is to evaluate the change of the P300 latency as a biomarker for cognitive function after taking choline alphoscerate in patients with MCI. Event related evoked potential study were done in baseline (n=27) and 3 months after taking choline alphoscerate (n=17). When compared to our previous reported control database, the difference of the P300 latencies	Han, Su-Hyun et al. "P300 latency changes in patients with mild cognitive impairment after

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		alphoscerate; A preliminary study				between MCI and control group at baseline was statistically significant (P < 0.01). Although Followup P300 latencies after taking choline alphoscerate did not show the significant change, the tendency of shortened P300 latencies was identified. Even though there are some limitations, choline alphoscerate could improve the electrophysiological markers in MCI patients. To identify the effect of cholinergic precursor in MCI and the usefulness of electrophysiological biomarkers, well-designed further study is needed.	taking choline alphoscerate; A preliminary study." *eNeurologicalSci* vol. 11 5-8. 12 Apr. 2018, doi:10.1016/j.ensci.2018.04.004
Lee M.	2018	Unexpected Effects of Acetylcholine Precursors on Pilocarpine Seizure- Induced Neuronal Death	Review, Comparative	Not applicable	Male rats	From the Abstract: Early administration of CDP-choline immediately after seizure increased neuronal death, blood-brain barrier (BBB) disruption and microglial activation in the hippocampus. However, administration of α-GPC starting 3 weeks after seizure (late administration) improved cognitive function through reduced neuronal death and BBB disruption, and increased neurogenesis in the hippocampus. From the Discussion: Our previous study also tested the potential therapeutic effects of α-GPC on pilocarpine seizure-induced neuronal death when administered at later time points. Seizure was induced by injection of pilocarpine (25mg/kg) in male rats. α-GPC was injected once daily from 3 weeks after the seizure onset for 3 additional weeks. The rats were subjected to a water maze test and then sacrificed. In order to verify the beneficial effects for preventing neuronal death and BBB disruption, we performed NeuN and IgG staining at 6 weeks after seizure. A clear increase in the number of NeuNpositive neurons in the α-GPC late treatment group (compared to the vehicle group) indicated that the number of live neurons in the hippocampal area was enhanced with treatment (Fig. 3A-D). Moreover, the late α-GPC treatment group showed a significant decrease in IgG extravasation; a strong indicator that BBB disruption was reduced. Additionally, administration of α-GPC promoted improved performance in a standard water maze test protocol compared to the vehicle-treated group. These results suggest that late treatment of α-GPC improved cognitive function through reduced neuronal death and BBB disruption.	Lee, Minwoo et al. "Unexpected Effects of Acetylcholine Precursors on Pilocarpine Seizure- Induced Neuronal Death." *Current neuropharmacology* vol. 16,1 (2018): 51-58. doi:10.2174/1570159X15666170518150053
Traini	2020	Volume Analysis of Brain Cognitive Areas in Alzheimer's Disease: Interim 3-Year Results from the ASCOMALVA Trial	Randomized Controlled Trial	10 mg donepezil plus 1200 mg choline alphoscerate per day for 3 years.	56 male and female subjects with Alzheimer's disease treated with donepezil plus choline alphoscerate compared to 57 male and female subjects with Alzheimer's disease treated with donepezil alone.	Based on our finding we can suggest that cognitive impairment associated with cerebrovascular involvement may be more effectively countered, similarly as shown in preclinical studies, by combining a cholinergic precursor as choline alphoscerate to standard treatment with ChE-I. These two treatments in combination seem to exert synergistic effects and, consequently, could represent a therapeutic option to be considered in AD associated with cerebrovascular damage.	Traini, Enea et al. "Volume Analysis of Brain Cognitive Areas in Alzheimer's Disease: Interim 3-Year Results from the ASCOMALVA Trial." *Journal of Alzheimer's disease : JAD* vol. 76,1 (2020): 317-329. doi:10.3233/JAD-190623
Salvadori	2021	Efficacy and Safety of the Association of Nimodipine and	Randomized	90 mg nimodipine plus 1200 mg choline	48 male and female subjects with vascular	In the CONIVaD pilot study, the combined treatment with choline alphoscerate and nimodipine in patients with SVD and mild-to-moderate cognitive impairment resulted in low patient adherence to treatment, particularly for nimodipine, and	Salvadori, Emilia et al. "Efficacy and Safety of the

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		Choline Alphoscerate in the Treatment of Cognitive Impairment in Patients with Cerebral Small Vessel Disease. The CONIVaD Trial	Controlled Trial	alphoscerate per day for 12 months.	cognitive impairment (VCI) due to small vessel disease (SVD) and mild-to-moderate cognitive impairment.	no significant efficacy. Safety and tolerability were adequate. Further efforts are needed to find a specific treatment in patients with VCI.	Association of Nimodipine and Choline Alphoscerate in the Treatment of Cognitive Impairment in Patients with Cerebral Small Vessel Disease. The CONIVaD Trial." Drugs & aging vol. 38,6 (2021): 481-491. doi:10.1007/s40266-021-00852-8
Roy	2022	Effects of choline containing phospholipids on the neurovascular unit: A review	Review	Not applicable	Not applicable	Phosphatidylcholine was the first cholinergic precursor molecule used, but it did not demonstrate clear clinical benefits. The same is not true for other phospholipids, CDP-choline and α-GPC, involved in choline biosynthetic pathways. For these an uncertain improvement of cognitive dysfunction in neurodegenerative and vascular dementia is documented. Positive results obtained with selected cholinergic precursors cannot be generalized due to the small numbers of patients studied in appropriate clinical trials. However, they probably would justify reconsideration of the most promising molecules in larger carefully controlled studies. This can also contribute to better define the role of the NVU in the pathophysiology of brain disorders characterized by vascular impairment.	Roy, Proshanta et al. "Effects of choline containing phospholipids on the neurovascular unit: A review." Frontiers in cellular neuroscience vol. 16 988759. 23 Sep. 2022, doi:10.3389/fncel.2022.988759
Kansakar	2023	Choline supplements: An update	Review	Not applicable	Not applicable	In summary, preclinical and clinical investigations have shown that GPC and other forms of choline supplementation have beneficial effects especially in terms of improved endothelial function and cognitive performance. Notwithstanding, further dedicated studies are warranted to compare the different effects of the currently available forms of choline supplementation.	Kansakar, Urna et al. "Choline supplements: An update." *Frontiers in endocrinology* vol. 14 1148166. 7 Mar. 2023, doi:10.3389/fendo.2023.1148166
Sagaro	2023	Activity of Choline Alphoscerate on Adult-Onset Cognitive Dysfunctions: A Systematic Review and Meta-Analysis	Systematic Review and Meta-Analysis	Not applicable	Not applicable	A total of 1,326 studies and 300 full-text articles were screened. We included seven randomized controlled trials (RCTs) and one prospective cohort study that met our eligibility criteria. We found significant effects of α-GPC in combination with donepezil on cognition [4 RCTs, mean difference (MD):1.72, 95% confidence interval (CI): 0.20 to 3.25], functional outcomes [3 RCTs, MD:0.79, 95% CI: 0.34 to 1.23], and behavioral outcomes [4 RCTs; MD: –7.61, 95% CI: –10.31 to –4.91]. We also observed that patients who received α-GPC had significantly better cognition than those who received either placebo or other medications [MD: 3.50, 95% CI: 0.36 to 6.63].	Sagaro, Getu Gamo et al. "Activity of Choline Alphoscerate on Adult-Onset Cognitive Dysfunctions: A Systematic Review and Meta-Analysis." *Journal of Alzheimer's*

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
							disease : JAD vol. 92,1 (2023): 59-70. doi:10.3233/JAD-221189
Sagaro	2023	Choline-Containing Phospholipids in Stroke Treatment: A Systematic Review and Meta-Analysis	Systematic Review and Meta-Analysis	Not applicable	Not applicable	Our analysis of pooled patient data suggests that citicoline is not effective in improving neurological function, functional recovery, and independence or improvement in daily living activities in patients with acute stroke. There are also a number of RCT studies that support our findings, and the authors conclude that citicoline does not improve clinical outcomes in patients with acute stroke. Additionally, according to our findings, citicoline treatment does not show evidence of improving functional and neurological outcomes in patients with hemorrhagic stroke who received the drug. Choline alphoscerate, on the other hand, is effective in the improvement in neurological function, functional recovery, and positive outcomes in terms of everyday living activities in patients following an acute stroke. In order to confirm our findings, it is important that future studies make use of a pooled analysis that estimates the odds ratio (OR) for the effect of choline alphoscerate on patients with acute strokes.	Sagaro, Getu Gamo, and Francesco Amenta. "Choline-Containing Phospholipids in Stroke Treatment: A Systematic Review and Meta-Analysis." *Journal of clinical medicine* vol. 12,8 2875. 14 Apr. 2023, doi:10.3390/jcm12082875
Aguglia		Choline Alphoscerate in the treatment of mental pathology following acute cerebrovascular accident	Clinical Trial	Phase 1: 1 g per day intramuscular injection (IM) Phase 2: 1200 mg per day orally	425 patients with diagnosis of stroke, Transient Ischemic Attack (TIA), or Acute Cerebral Ischemia	Therapeutic changes during the period of treatment were statistically high significant and were detectable in all dimensional measures and categorical proportions. The improvement was not restricted to either the functional state of the patients or to the first month of treatment, but extended to changes in performance and social behaviour, and continued over the six-month investigational period. Moreover, these findings indicate that a.-GPC was well tolerated both parenterally and orally in the daily dosage of 1000 mg and 1200 mg respectively.	Aguglia E. Choline Alphoscerate in the treatment of mental pathology following acute cerebrovascular accident. 182.
Muiesan		Controlled clinical trial of α-GPC 400 mg i.m. administered in patients with senile mental decline	Clinical Trial, Comparative	800 mg intramuscular injection (IM) per day for 20 days compared to 1000 mg citicoline IM	30 patients in both groups. 15 patients in A-GPC group (3 males, 12 females; mean age 71.5)	At the beginning of the study the two treatment groups were comparable as for severity of mental deterioration. The results obtained in the two treatment groups showed no significant difference. Both drugs produced an appreciable increase in patient's capacity for attention and concentration (Toulouse Pieron Test), with a highly significant ($P < 0.01$) increase in correct answers, along with a reduction of wrong answers and of skipped responses. Cognitive functions (Cattel's test) showed an appreciable and highly significant ($P < 0.01$) improvement in both treatment groups. Last, the Gottfries test for mental deterioration showed a 25% mean improvement at termination in both treatment groups ($P < 0.01$). Treatment with a-GPC was consistently free of adverse side-effects, whether local (at the sites of injection) or systemic, subjective or objective. Nine out of the fifteen patients (60%) treated with a.-GPC received concomitantly one or more other drugs (such as digitalis, antihypertensives-diuretics, coronary vasodilators, aminophylline, and antiepileptic drugs with no sign of clinical interactions.	Muiesan G. Controlled clinical trial of α-GPC 400 mg i.m. administered in patients with senile mental decline.

OUTCOME: **Emotional State**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Tamura	2021	Alpha-Glycerylphosphoryl choline Increases Motivation in Healthy Volunteers: A Single-Blind, Randomized, Placebo-Controlled Human Study	Clinical Trial	400 mg per day for 2 weeks	40 (9 males, 31 females) healthy individuals aged 22–59	αGPC treatment show a tendency to increase motivation during the intervention period. Furthermore, motivation at night was significantly higher in the αGPC group than in the placebo group ($p < 0.05$). However, αGPC did not show any effects on anxiety. These data suggest that αGPC can be used to increase motivation in healthy individuals.	Tamura, Yasuhisa et al. "Alpha-Glycerylphosphoryl choline Increases Motivation in Healthy Volunteers: A Single-Blind, Randomized, Placebo-Controlled Human Study." Nutrients vol. 13,6 2091. 18 Jun. 2021, doi:10.3390/nu13062091
Rea	2015	Apathy Treatment in Alzheimer's Disease: Interim Results of the ASCOMALVA Trial	Randomized Controlled Trial	10 mg donepezil plus 1200 mg choline alphoscerate per day for 24 months.	56 male and female subjects with Alzheimer's disease treated with donepezil plus choline alphoscerate compared to 57 male and female subjects with Alzheimer's disease treated with donepezil alone.	In this study, we evaluated the severity of apathy in 113 subjects with mild-moderate [Alzheimer's disease; AD] included in the double-blind trial ASCOMALVA, and randomly allotted to the treatment with donepezil plus choline alphoscerate or with donepezil plus placebo. We found that, overall, the subjects treated with the combination had lower apathy after 12 and 24 months than patients in the reference group. A similar trend was found in the level of the caregiver distress, as it was lower in those taking care of patients treated with donepezil plus choline alphoscerate, than in those who were caring patients receiving donepezil alone. The effect of donepezil plus choline alphoscerate on apathy symptoms was unrelated to the cognitive impairment and its progression, measured by the MMSE and the ADASCog tests, but was related to [Frontal Assessment Battery; FAB] scores. In fact, the subjects having FAB scores at baseline in the normal range (FAB 13–18) were those showing lower apathy after 12, 18, and 24 months. This finding suggests that the treatment with donepezil plus choline alphoscerate counteracted the progression of apathy, and that providing more cholinergic stimulation to patients having still spared executive functions may be protective. This is not surprising, as apathy is largely related to dysfunctions of the frontal pathways, and in particular of the attention system, which are also implied in the performance of the FAB test. The cholinergic disruption causes attention deficits [40] and apathy also has been related to cholinergic dysfunctions [34]. Hence, apathy and attention are both related to the integrity of the cholinergic system.	Rea, Raffaele et al. "Apathy Treatment in Alzheimer's Disease: Interim Results of the ASCOMALVA Trial." *Journal of Alzheimer's disease : JAD* vol. 48,2 (2015): 377-83. doi:10.3233/JAD-141983
Carotenutoa	2022	Association Between the Cholinesterase Inhibitor Donepezil and the Cholinergic Precursor Choline Alphoscerate in the	Randomized Controlled Trial	10 mg donepezil plus 1200 mg choline alphoscerate per day for 24 months.	56 male and female subjects with Alzheimer's disease treated with donepezil plus choline alphoscerate	Depression symptoms were significantly lower ($p < 0.05$) in patients treated with donepezil plus choline alphoscerate compared to patients treated with donepezil alone. Subjects of the group having mild to moderate cognitive impairment were those more sensitive to the association treatment.	Carotenuto, Anna et al. "Association Between the Cholinesterase Inhibitor Donepezil and the Cholinergic Precursor Choline

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
		Treatment of Depression in Patients with Alzheimer's Disease			compared to 57 male and female subjects with Alzheimer's disease treated with donepezil alone.		Alphoscerate in the Treatment of Depression in Patients with Alzheimer's Disease." *Journal of Alzheimer's disease reports* vol. 6,1 235-243. 23 May. 2022, doi:10.3233/ADR-200269

OUTCOME: **Exercise Performance**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Ziegenfuss	2008	Acute supplementation with alpha-glycerylphosphoryl choline augments growth hormone response to, and peak force production during, resistance exercise	Poster Presentation	A supplement containing primarily A-GPC (600 mg*) *The supplement actually contained 100 mg of A-GPC per serving, acutely administered.	7 resistance trained males (mean age 30.1 ± 7.3)	Compared to baseline (pre) values, peak GH increased 44-fold during A-GPC (from 0.19 ± 0.06 to 8.4 ± 2.1 ng/ mL) vs. 2.6-fold during placebo (from 1.9 ± 0.8 to 5.0 ± 4.8 ng/mL, P < 0.03) (Figure 1). Peak bench press force was 14% greater in A-GPC (933 ± 89 N) vs. placebo (818 ± 77 N, P < 0.02). Trends toward higher peak bench press power (P < 0.13) and lower post-exercise RER (P < 0.12) were noted in the A-GPC trial.	Ziegenfuss, T., Landis, J. & Hofheins, J. Acute supplementation with alpha-glycerylphosphoryl choline augments growth hormone response to, and peak force production during, resistance exercise. J Int Soc Sports Nutr 5 (Suppl 1), P15 (2008). Doi: 10.1186/1550-2783-5-S1-P15
Hoffman	2010	The effects of acute and prolonged CRAM supplementation on reaction time and subjective measures of focus and alertness in healthy college students		A supplement called CRAM containing 150mg A-GPC, 125mg choline bitartrate, 50mg phosphatidylserine, 30mg vitamins B3, 30 mg B6, and 0.06mg B12, 4mg folic acid, 500mg L-tyrosine, 60mg anhydrous caffeine, 500mg acetyl-L-carnitine, and 20mg naringin for 4 weeks.	19 recreationally active subjects (17 males, 2 females; mean age 21.2 ± 0.7)	Results of this study indicated that acute ingestion of CRAM can maintain reaction time to both visual and auditory stimuli following a high-intensity bout of exhaustive exercise, while subjects consuming a placebo experienced significant reductions in performance. In addition, acute ingestion of CRAM resulted in maintained focus and alertness following exhaustive exercise, while subjects consuming a placebo experienced significant declines in focus and alertness. Following 4 weeks of supplementation both groups exhibited significant declines in reaction performance. However, subjects consuming CRAM were still able to maintain their focus following exhaustive exercise, while subjects consuming a placebo did not.	Hoffman, Jay R et al. "The effects of acute and prolonged CRAM supplementation on reaction time and subjective measures of focus and alertness in healthy college students." *Journal of the International Society of Sports Nutrition* vol. 7 39. 15 Dec. 2010, doi:10.1186/1550-2783-7-39
Bellar	2015	The effect of 6 days of alpha glycerylphosphoryl choline on isometric strength	Clinical Trial	600 mg per day for 6 days	13 healthy, college-aged males (mean age 21.9 ± 2.2)	The A-GPC treatment resulted in significantly greater isometric mid thigh pull peak force change from baseline (t = 1.76, p = 0.044) compared with placebo (A-GPC: 98.8. ± 236.9 N vs Placebo: −39.0 ± 170.9 N). For the upper body test the A-GPC treatment trended towards greater change from baseline force production (A-GPC: 50.9 ± 167.2 N Placebo: −14.9 ± 114.9 N) but failed to obtain statistical significance (t = 1.16, p = 0.127).	Bellar, David et al. "The effect of 6 days of alpha glycerylphosphoryl choline on isometric strength." Journal of the International Society of Sports Nutrition vol. 12 42. 17 Nov. 2015,

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
							doi:10.1186/s12970-015-0103-x
Marcus	2017	Evaluation of the effects of two doses of alpha glycerylphosphoryl choline on physical and psychomotor performance	Clinical Trial, Comparative	250 mg A-GPC, 500 mg A-GPC, or 200 mg caffeine for 7 days	48 healthy college aged males	Based upon the available evidence from this study, it appears that A-GPC may maintain some ergogenic effects in doses of 250 mg or greater, although lower doses have been found in other studies to offer various degrees of ergogenic effects [10–13]. It can be suggested that athletes and coaches looking to improve performance in events that emphasize velocity and power consider adding A-GPC to their nutritional strategy; however, based upon the total available literature dose of 600 mg or greater are more likely to provide performance results. While more evidence needs to be collected regarding the use of A-GPC, current results are positive particularly in the area of vertical or countermovement jump where a number of studies have been focused. Future research on A-GPC should focus on larger doses for significant performance benefits, while doses lower than this should focus perhaps on other neurological benefits.	Marcus, Lena et al. "Evaluation of the effects of two doses of alpha glycerylphosphoryl choline on physical and psychomotor performance." *Journal of the International Society of Sports Nutrition* vol. 14 39. 5 Oct. 2017, doi:10.1186/s12970-017-0196-5
Rickard	2017	α-GlycerylPhosphoryl Choline and the Effects on Anaerobic Indices	Clinical Trial	300 mg administered acutely (1 hour)	17 young, recreationally trained females.	The primary purpose of this study was to examine the acute effects of α-GPC ingestion on acute anaerobic performance as measured by the [counter movement jump; CMJ], 40-yd dash, and 30-second [Wingate anaerobic test; WAnT]. It was hypothesized that ingestion of α-GPC would improve CMJ height, 40-yd dash times, as well as peak and mean power during the 30-second WAnT. These hypotheses were developed around the claim that α-GPC has ergogenic potential (Ziegenfuss et al., 2008; Hoffman et al. 2010; Bellar et al., 2015). The primary findings were that α-GPC supplementation significantly improved CMJ height, while neither the 40-yd dash times nor the peak or mean power during the 30-second WAnT improved. Secondary findings show minimum power during the 30-second WAnT were trending towards significance, but failed to reach significance.	Rickard, Alex. α-GlycerylPhosphoryl Choline and the Effects on Anaerobic Indices. Department of Nutrition and Kinesiology University of Central Missouri. May 2017
Cruse	2018	The Acute Effects Of Alpha-Gpc On Hand Grip Strength, Jump Height, Power Output, Mood, And Reaction-Time In Recreationally Trained, College-Aged Individuals	Clinical Trial	600 mg acutely administered (25 min)	27 college-aged, recreationally trained individuals (15 males, 12 females; mean Age 21.66 ± 1.88)	This study provides support, similar to previous literature, that A-GPC maybe beneficial as a cognitive and power output supplement. Significance of the study reveals a 12% increase in power output during the plyometric push-up and accuracy during the reaction-time test. This study sheds new light on the potential benefits AGPC may have on young healthy adults and the ergogenic effects of A-GPC. Specifically, A-GPC may improve trained college-aged individuals' level of fatigue, mood, force production, and reaction time. For college students, the amount of time spent working and attending school may create challenges with expending and managing energy requirements. A-GPC could potentially serve as a reasonable supplement for young healthy adults attempting to deal with the stressors of everyday life or for the student looking for an advantage academically or with physical activity. Although future research is needed to give merit to these findings, A-GPC looks promising in supplementation as an ergogenic aid or to help facilitate cognitive function, promoting learning via enhanced memory recall.	Cruse, Joseph. "The Acute Effects Of Alpha-Gpc On Hand Grip Strength, Jump Height, Power Output, Mood, And Reaction-Time In Recreationally Trained, College-Aged Individuals." (2018).

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Jäger	2022	Paraxanthine Supplementation Increases Muscle Mass, Strength, and Endurance in Mice	Animal Study, Comparative	41.09 mg/kg/day, human equivalent dose 200 mg	Male Swiss Albino mice	Supplementation with alpha-GPC also led to significant increases in strength in the present study. These findings align with previous findings of Bellar et al. [13] who reported significant increases in isometric strength using a mid-thigh pull movement in college-aged males after 6 days of 600 mg/day alpha-GPC supplementation using a randomized, double-blind, crossover approach. A later study by Marcus and investigators [31] reported no changes in upper- and lower-body isometric strength in 48 healthy college-aged males who randomly supplemented with either 500 mg alpha-GPC, 250 mg alpha-GPC, 200 mg caffeine, or a placebo for 7 days. Maximum velocity and maximum mechanical power during countermovement jumps were found to be greater in the 250 mg alpha-GPC group. Additional research needs to be conducted using alpha-GPC to better understand its other ergogenic properties and associated mechanisms of action.	Jäger, Ralf et al. “Paraxanthine Supplementation Increases Muscle Mass, Strength, and Endurance in Mice.” Nutrients vol. 14,4 893. 20 Feb. 2022, doi:10.3390/nu14040893
Barzanjeh	2022	The Effects of Alpha-Glycerylphosphorylcholine on Heart Rate Variability and Hemodynamic Variables	Clinical Trial	1000 mg	12 overweight or obese women between 20 to 40 years of age.	We found the A-GPC consumption prior to [Sprint Interval Exercise; SIE] can attenuate the changes in [heart rate variability; HRV] and hemodynamic variables that typically occur during and after SIE and recovery. Therefore, it may be a useful strategy to reduce the risk associated with supramaximal exercise in individuals who are overweight or obese. Additionally, our study indicates that A-GPC could have ergogenic effects on performance by improving peak power, mean power, and fatigue index. However, more studies are required to determine the mechanisms responsible for A-GPC-induced modulations in ANS and hemodynamics following supramaximal exercise.	Barzanjeh SP, Pescatello LS, Figueroa A, Ahmadizad S. The Effects of Alpha-Glycerylphosphorylcholine on Heart Rate Variability and Hemodynamic Variables Following Sprint Interval Exercise in Overweight and Obese Women. Nutrients. 2022; 14(19):3970. https://doi.org/10.3390/nu14193970

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Harrington	2023	Effects of branched chain amino acids, l-citrulline, and alpha-glycerylphosphoryl choline supplementation on exercise performance in trained cyclists: a randomized crossover trial	Clinical Trial	A supplement containing 8 g BCAAs, 6 g L-citrulline, and 300 mg A-GPC administered for 7 days.	Thirty male trained cyclists (age: 43.7 ± 8.5 years)	There was a significant increase (p = .003) in peak power in the 20 km [Time Trial; TT] (354.27 ± 87.88 and 321.67 ± 63.65, for supplement and placebo trials, respectively) and a significant increase (p = .001) in time to fatigue in the HIEC test (0:19:49 ± 0:11:13 min and 0:14:33 ± 0:09:59 min, for supplement and placebo trials, respectively) with the test supplement compared to the placebo. With the test supplement, there was an average increase in TT peak power of 11% and an average increase in time to fatigue of 36.2% in the HIEC test compared to the placebo. There was no significant improvement in time to completion, average power, OMNI rating of perceived exertion, or VAS responses on perceived exertion in the TT test and no significant improvement in VAS measures of perceived exertion in the HIEC test.	Harrington, Renee Nicole. “Effects of branched chain amino acids, l-citrulline, and alpha-glycerylphosphoryl choline supplementation on exercise performance in trained cyclists: a randomized crossover trial.” *Journal of the International Society of Sports Nutrition* vol. 20,1 (2023): 2214112. doi:10.1080/15502783.2023.2214112

OUTCOME: **Gaming**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Redacted	2020	The Effects of aGPC on Virtual Reality Video Game Performance	Clinical Trial	300 mg per day for 7 days	13 (10 males, 3 females; mean age 22.7 + 2.2)	aGPC supplementation increased the number of levels completed by 24.9% (PL: 1.85 +0.98 levels, aGPC: 2.30 + 1.1 levels; p = 0.190), reduced the number of attempts per level by13.8% (PL: 17.2 + 8.6 attempts, aGPC: 14.8 + 7.9 attempts, p = 0.316), and reduced time to complete each level by 0.64% (PL: 17.19 + 2.2 s, aGPC: 17.08 + 2.54 s, p = 0.896) compared to PL. aGPC supplementation indicated a positive trend for Vigor (PL: 53.8 + 22.2, aGPC: 64.2 +16.1, p = 0.079) and Focus (PL: 56.6 + 20.4, aGPC: 64.0 + 14.8, p = 0.241) in comparison to PL.There were no significant changes in regards to mood or VR video game performance in response to aGPC supplementation.	The Effects of aGPC on Virtual Reality Video Game Performance. 2020.

OUTCOME: **Hormone Effects**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Ceda	1991	Alpha-Glycerylphosphorylcholine Administration Increases the GH Responses to GHRH of Young and Elderly Subjects	Trial	IV infusion of 1 g	8 young (5 males and 3 females) aged 32.1 ± 1.9 and 7 healthy old subjects (4 males and 3 females) aged 80 ± 2 yrs.	GH secretion was greater in the younger subjects than in the old individuals, and both groups had a greater GH response to the GHRH + alphaGFC than to GHRH alone. The potentiating effect of alpha-GFC on GH secretion was more pronounced in the elderly subjects. These findings confirm the observation that aged individuals respond less well to GHRH than younger subjects, and provides further evidcence that increased cholinergic tone enhances GH release.	Ceda GP, Ceresini G, Denti L, et al. alpha-Glycerylphosphorylcholine administration increases the GH responses to GHRH of young and elderly subjects. Horm Metab Res. 1992;24(3):119-121. doi:10.1055/s-2007-1003272
Ceda	1994	Effects of an Acetylcholine Precursor on GH Secretion in Elderly Subjects	Trial	Three different protocols; all including IV infusion of 2 g	Three different protocols. Protocol 1: 10 normal elderly subjects 79.4 ± 1.7 yrs. Protocol 2: 13 normal subjects, 78 ± 1.5 yrs. Protocol 3: 8 elderly subjects, 80.6 ± 1.5 yrs.	Our results clearly demonstrate that after 14 days of treatment the pituitary responsiveness to the combined administration of these agents was maintained at the level seen before the therapy, suggesting that the use of an Ach precursor together with the GHRH could represent, in some patients, a useful tool in the treatment of the catabolic changes of aging.	Ceda, G.P. et al. Effects of an Acetylcholine Precursor on GH Secretion in Elderly Subjects. In: Bercu, B.B., Walker, R.F. (eds) Growth Hormone II. Serono Symposia USA Norwell, Massachusetts. Springer, New York, NY. 1994. doi: 10.1007/978-1-4613-8372-7_25
Ziegenfuss	2008	Acute supplementation with alpha-glycerylphosphorylcholine augments growth hormone response to, and peak force production during, resistance exercise	Poster Presentation	A supplement containing primarily A-GPC (600 mg*) *The supplement actually contained 100 mg of A-GPC per serving, acutely administered.	7 resistance trained males (mean age 30.1 ± 7.3)	Compared to baseline (pre) values, peak GH increased 44-fold during A-GPC (from 0.19 ± 0.06 to 8.4 ± 2.1 ng/mL) vs. 2.6-fold during placebo (from 1.9 ± 0.8 to 5.0 ± 4.8 ng/mL, P < 0.03) (Figure 1). Peak bench press force was 14% greater in A-GPC (933 ± 89 N) vs. placebo (818 ± 77 N, P < 0.02). Trends toward higher peak bench press power (P < 0.13) and lower post-exercise RER (P < 0.12) were noted in the A-GPC trial.	Ziegenfuss, T., Landis, J. & Hofheins, J. Acute supplementation with alpha-glycerylphosphorylcholine augments growth hormone response to, and peak force production during, resistance exercise. J Int Soc Sports Nutr 5

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
							(Suppl 1), P15 (2008). Doi: 10.1186/1550-2783-5-S1-P15
Kawamura	2012	Glycerophosphocholine enhances growth hormone secretion and fat oxidation in young adults	Trial	1000 mg, oral	Eight healthy male subjects (25 ± 1 year old)	Plasma free choline levels significantly increased at 60 and 120 min after GPC administration. Plasma growth hormone secretion was increased significantly 60 min after taking GPC, whereas no significant change was observed with the placebo. In addition, the serum free fatty acid was increased 120 min after GPC ingestion, but no changes were seen with the placebo. Moreover, serum acetoacetate and 3-hydroxybutyrate levels, which are indices of hepatic fat oxidation, were increased at 120 min after taking GPC, whereas the placebo had no effect	Kawamura T, Okubo T, Sato K, et al. Glycerophosphocholine enhances growth hormone secretion and fat oxidation in young adults. Nutrition. 2012;28(11-12):1122-1126. doi: 10.1016/j.nut.2012.02.011
Maldonado	2019	The Effects of α-GPC Supplementation on Growth Hormone, Fat Loss, And Body Composition In Overweight Adults	Trial	1200 mg per day for 8 weeks, oral	28 subjects (10 male, 18 female), between 18 and 45 yrs old	There were no significant differences between groups for any body composition, girth measurements, GH, caloric intake, or F-score from pre- to post-intervention (P>0.05). There were significant main Time effects for decreases in BF%, FM, and waist measurements (P<0.05) as well as trends for decreased BM (P=0.094) and increased FFM (P=0.064). No main effects were observed for any other variable (P>0.05). Univariate follow-ups showed a significant Time-by-Group interaction for an increase in SBP in the α-GPC group (P<0.05). A negative trend was seen for total daily caloric intake among all subjects over time (P=0.066, ES=0.136).	Maldonado, et al. The Effects of α-GPC Supplementation on Growth Hormone, Fat Loss, And Body Composition In Overweight Adults. Rutgers. 2019. Doi: 10.7282/t3-qggq-ff53

OUTCOME: **Pharmacokinetics**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Abbiati	1991	Absorption, tissue distribution and excretion of radiolabelled compounds in rats after administration of [^{14}C]-L-α-glycerylphosphoryl choline	Animal Study	10 mg/kg intravenous or 100 mg/kg or 300 mg/kg orally	Adult male and female Sprague Dawley rats	Both labelled compounds gave a wide distribution of radioactivity, particularly concentrated in the liver, kidney, lung and spleen compared to blood. Brain concentrations of [^{14}C]-GPC were comparable to ([^{14}G]-GPC) or lower than ([^{14}C]-GPC) total blood radioactivity. The metabolite profile in the perfused brain showed a small amount of choline and two unknown metabolites, probably the same as in blood. In addition, choline was incorporated into brain phospholipids in increasing amounts within 24 h of dosing. In all cases renal and fecal excretion of radioactivity was low and comparable for [^{14}G]-GPC and [^{14}C]-GPC. Mostly the administered radioactivity was exhaled as $^{14}CO_2$, this degradation being baster and more pronounced for the glycerol-labelled metabolites than for the choline-labelled metabolites for both routes of administration. In all cases the results were the same for male and female rats.	Abbiati G, Fossati T, Lachmann G, Bergamaschi M, Castiglioni C. Absorption, tissue distribution and excretion of radiolabelled compounds in rats after administration of [14C]-L-alpha-glycerylphosphoryl choline. Eur J Drug Metab Pharmacokinet. 1993 Apr-Jun;18(2) 173-180. doi:10.1007/bf03188793. PMID: 8243501.

OUTCOME: **Safety**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Brownawell	2011	Safety assessment of AGPC as a food ingredient	Safety Assessment	Various	Rats, mice, dogs	A series of studies were conducted to demonstrate the safety of AGPC. The oral LD50 was equal to or greater than 10,000 mg/kg in rats and mice. Deaths were preceded by convulsions in some animals. Dosing of dogs with up to 3000 mg/kg AGPC resulted only in reduced activity. Sub-chronic and chronic oral toxicity studies in rats (up to 1000 mg/kg/day) and beagles (up to 300 mg/kg/day) produced symptomology primarily consisting of reduced activity; slight decreases in food consumption and body weight gain; and slight reduction in liver weight, paralleled by significant decreases in plasma triglycerides, bilirubin, and alkaline phosphatase. There were no histopathological correlates. The in vivo and in vitro assays clearly indicated that AGPC was devoid of mutagenic activity. Based on these results, AGPC is not genotoxic in vitro or in vivo, exhibits low acute oral toxicity and, has an oral NOAEL of 150 mg/kg bw/day following 26 weeks oral exposure.	Brownawell, Amy M et al. “Safety assessment of AGPC as a food ingredient.” Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association vol. 49,6 (2011): 1303-15. doi:10.1016/j.fct.2011.03.012

OUTCOME: **Sleep**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Strambi	1991	Choline Alfoscerate: Short-Term Effect on Sleep in Healthy Subjects	Clinical Trial	400 mg for 1 week.	8 healthy young males (mean age 24.7 ± 3.8).	Sleep induction and maintenance in healthy subjects was not significantly modified by α-GPC, 400 mg, TID, for one week, although total time awake and number of awakenings showed a general trend toward reduction compared with baseline. Sleep efficiency increased after α-GPC treatment, but the difference was not statistically significant. These slight modifications in sleep parameters remained unchanged one week after α-GPC was stopped. No differences in sleep stages were found in the three experimental conditions. Of greatest interest is the fact that α-GPC did not modify percentage of REM or the latency of the first REM period, while it appeared to increase REM density. This parameter returned to baseline values after α-GPC withdrawal.	Strambi L. Choline Alfoscerate: Short-Term Effect on Sleep in Healthy Subjects. Current Therapeutic Research Vol. 49, 4 (1991): 610-615.

OUTCOME: **Trimethylamine N-oxide (TMAO)**

Author	Year	Title	Type	Dose & Duration	Subjects	Result	Citation
Davis	2021	Comparison of Serum Choline and Trimethylamine N-oxide after Ingestion of Alpha Glyceryl Phosphoryl Choline and Choline Salts	Clinical Trial, Comparative	225 mg choline from A-GPC or 150 mg of choline from A-GPC	40 healthy male subjects	Based upon the data in this paper, it appears that lower doses of A-GPC are as effective at providing bio-available choline at higher doses of other choline salts. Additionally, it does not appear that A-GPC or choline salts impact the circulating levels of TMAO with either acute or chronic ingestion. Further research should be directed at determining the doses of A-GPC that are necessary to impact human performance and cognition.	Davis, Greggory & Bellar, David & Aldret, Randy. (2021). Comparison of Serum Choline and Trimethylamine N-oxide after Ingestion of Alpha Glyceryl Phosphoryl Choline and Choline Salts. Current Nutraceuticals. 02. Doi: 10.2174/2665978602666210212115014.