



DOSSIER · SUBSTANCE

Alpha-GPC

Alpha-GPC belongs to the choline compounds that also appear in the literature as Choline-Alphoscerate. Noticeable is the imbalance: The most frequently cited works are animal experimental amnesia models in rats, while two controlled studies are available in humans — one on cognition in dementia, one on survival in glioblastoma.

20

STUDIES IN
TOTAL

5

IN HUMANS

2

OF WHICH
CONTROLLED

10

IN ANIMALS

0

IN THE LAB

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

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Alpha-GPC (L-Alpha-Glycerylphosphorylcholin) at a Glance

ORIGIN:

Alpha-GPC is the short designation for L-Alpha-Glycerylphosphorylcholin, a choline compound that also appears in the literature as Choline-Alphoscerate. The name denotes the building blocks glycerol, phosphate and choline; properties are investigated in models and in patients. The literature classifies it among cognition enhancers and neuroprotective substances. Origin and development history are not a topic in the works.

EVIDENCE BASE:

20 evaluated works · 2 controlled studies in humans · 3 observational studies · 1 review · 10 animal studies · 0 cell-culture studies

STRONGEST EVIDENCE:

- Cognition and dementia: In 126 patients with probable Alzheimer's dementia the randomised multicentre study versus ST200 showed improvements in most neuropsychological parameters.
- Recovery after stroke or transient ischaemic attack: The open multicentre trial in 2044 persons showed, under 1000 mg intramuscularly over 28 days, an increase in the Mathew Scale of 15.9 points to 74.6.
- Oncology: Retrospective single-centre evaluation in 187 patients with IDH-wild-type glioblastoma; with use for at least 12 months median overall survival 38.3 versus 24.0 months (p = 0.004).
- Vascular dementia: The open trial in 120 patients compared 1 g Alpha-GPC with 1 g cytidine diphosphocholine daily for 90 days intramuscularly; both improved markedly, without placebo comparison.
- Review 2025: L-Alpha-Glycerylphosphorylcholin is a choline-containing substance, occurs predominantly in the L-configuration, crosses the blood-brain barrier and is stated with a 41 % by weight choline content.

LIMITATIONS:

- Blinding: Two of the clinical works are open-label; their course is susceptible to expectation effects; a controlled confirmation especially of the oral long-term phase is still outstanding.
- Oncology: The evaluation is retrospective and limited to one centre; it shows associations, not causation. The prospective, multicentre, randomised trial is still outstanding.
- Pooling: The two controlled human studies differ in population and endpoint; a common effect size cannot be derived from them.

CLASSIFICATION:

Alpha-GPC is a choline source whose clinical testing is at an early stage: one randomised comparative study in dementia, two open trials and one retrospective oncological evaluation.

1. What Alpha-GPC Is

Alpha-GPC is the short designation for **L-Alpha-Glycerylphosphorylcholin**, a **choline compound**. In the literature the same substance also appears as **Choline-Alphoscerate** and as alpha-Glycerylphosphorylcholin; the spellings vary between decades and between specialist circles. The experimental literature classifies it among the **cognition enhancers** and the **neuroprotective substances**, i.e. substances that are tested in models of impaired brain function. The name denotes the building blocks glycerol, phosphate and choline; at the centre of the investigations is therefore a **choline source**. Accordingly, the experimental designs of the available works revolve around **choline homeostasis** and **cholinergic transmission**. Origin and development history of the substance are not a topic in these works; properties are investigated in models and in patients.

For the assessment of all works the decisive factor is at which point measurement takes place. The animal studies read the substance at **biochemical markers**: at **acetylcholine** in the brain and at **cholinergic transmission in the hippocampus**, as well as at behaviour in models of pharmacologically induced amnesia. A marker value is not a clinical course; it shows that a measured variable shifts, not that a patient benefits. In humans other quantities are in the foreground: cognitive test performance, tolerability and, in one work, **survival** in a tumour disease. These endpoints are not interchangeable. The two controlled human studies also differ in population, design and comparator; no common effect size can be derived from them.

2. What the Studies Show in Detail

The key human studies and the most important reviews — by indication, with population, duration, preparation, measured variable and result as reported in the original works. Numbers appear only where the work states them.

Distribution of the **controlled studies in humans** by indication — the numbers are not additive, as one work may be assigned to several areas:

INDICATION	CONTROLLED STUDIES
Cognition and psyche	2
Oncology	1
Safety and tolerability	1

Cognition and Psyche

The largest clinical trial on Alpha-GPC is an open multicentre study in 2044 patients after acute stroke or transient ischaemic attack ³. Alpha-GPC was administered daily at 1000 mg intramuscularly for 28 days after the event, followed by 400 mg orally three times daily for the next five months. During the intramuscular phase the Mathew Scale was recorded; thereafter the Mini Mental State Test, the Crichton Rating Scale and the Global Deterioration Scale were used. The mean Mathew Scale rose significantly by 15.9 points from 58.7 to 74.6 within 28 days ($p < 0.001$). At the end of the oral phase the mean Crichton Rating Scale fell significantly by 4.3 points from 20.2 to 15.9 ($p < 0.001$), the Mini Mental State Test rose significantly from 21 to 24.3 ($p < 0.001$) and reached the normal range at the assessment in the third month. On the Global Deterioration Scale the result at the end corresponded in 71 % of the patients to the stages “no cognitive decline” or “forgetfulness”. Adverse events were reported in 44 patients (2.14 %). Because the trial was open and without a control group, a controlled confirmation especially of the oral long-term phase is still outstanding.

The randomised controlled multicentre study comprised 126 patients with probable senile dementia of the Alzheimer type (SDAT) of mild to moderate degree and compared Alpha-GPC with ST200 (acetyl-L-carnitine) ¹. Measurement was performed with behavioural scales and psychometric tests. The results showed significant improvements in most neuropsychological parameters under Alpha-GPC; improvements also occurred under ST200, but to a lesser extent. Tolerability was good in both groups. The authors themselves classify their findings as positive but in need of replication and call for larger, double-blind, longitudinal studies that combine clinical and biological determinations. Exactly this question therefore remains open: whether the scale improvements can be reproduced in a blinded longitudinal design and match biological measurements.

The third work is an open clinical trial in 120 patients with mild to moderate vascular dementia in which 1 g Alpha-GPC daily was compared with 1 g cytidine diphosphocholine (CDP) daily, both given intramuscularly for 90 days ⁴. Assessment was performed at baseline, after 45 days and after 90 days with the modified Parkside Behavioural Scale, the Sandoz Clinical Assessment Geriatric Scale, the word-fluency test, the Hamilton Depression Scale and the story-recall subtest of the Wechsler Memory Scale. Both treatments produced a clear symptomatic improvement with very good tolerability. According to the assessment of the treating physicians and the patients, Alpha-GPC showed statistically higher efficacy in most tests and an overall more satisfactory activity than CDP. A placebo comparison was not part of the design; a blinded trial versus placebo therefore remains outstanding.

Oncology

For oncology a retrospective single-centre study in 187 patients with IDH-wild-type glioblastoma treated between 2011 and 2020 contributes ². Because cognitive impairments frequently occur due to the tumour itself and due to treatment side effects, cholin alphascerate (L-Alpha-Glycerylphosphorylcholin, GPC) is administered concomitantly. The evaluation asked whether overall survival (OS) and progression-free survival (PFS) differ; the reported result focuses on median overall survival. Patients were then grouped according to whether GPC had been used continuously for at least 3 or at least 12 months after diagnosis. Use for at least 3 months yielded no significant survival prolongation. In the group with long-term use for at least 12 months median overall survival was statistically significantly longer at 38.3 versus 24.0 months ($p = 0.004$).

In the multivariate analysis long-term use for at least 12 months was, alongside younger age, supratentorial location, complete resection and MGMT-promoter methylation, significantly associated with longer overall survival ($p = 0.019$, Hazard Ratio 0.532, 95 % confidence interval 0.314–0.900). The authors themselves name the limitations of the retrospective, single-centre evaluation and call for multicentre, prospective, randomised studies with large participant numbers for confirmation. **Hypothesis:** Because GPC was used in cognitive impairment and grouping was performed by duration of use, longer use could also reflect an overall more favourable disease course; the open question is whether the survival difference persists under pre-planned, blinded allocation.

Review: Production and Biological Effects

A 2025 review article summarises manufacturing techniques and biological effects of L-Alpha-Glycerylphosphorylcholin ⁷. According to it, the compound is a choline-containing substance that is widespread in nature and occurs predominantly in the L-configuration. The choline content is given as 41 per cent by weight, and the compound can cross the blood-brain barrier, which is why it is considered one of the most commonly used choline sources. For the food, pharmaceutical and cosmetics industries, the limited natural availability is the limiting factor; the review therefore summarises newer manufacturing processes for food science, pharmacy and the industries involved.

The second focus of the review comprises findings on biological activity from animal and human studies, with emphasis on cognitive dysfunction, cardiometabolic disorders, anti-ageing and ergogenic effects ⁷. The summary does not list individual effect strengths, preparations, dosages or study sizes, nor endpoints relating to the gut or microbiome. The work itself identifies existing knowledge gaps and proposes new research fields so that products with higher added value can be developed. What remains to be clarified is which manufacturing method was tested in which population with which measurable endpoint.

Overall Picture

Across the fields, three clinical studies with 126, 2044 and 120 treated patients together with a retrospective evaluation in 187 persons address the question of what Alpha-GPC does in humans. The largest group concerns recovery after recent stroke or transient ischaemic attack after 28 days of intramuscular and five months of oral administration ³; the controlled comparison against ST200 comprises 126 patients with probable Alzheimer dementia ¹, the comparison against cytidine diphosphocholine 120 persons with vascular dementia ⁴. Currently the most informative is the randomised arm; the open-label stroke trial provides the larger case numbers but without a control group, while the vascular dementia trial has a comparison group. Improvements on behavioural, dementia and depression scales as well as in the Mini Mental State Test are broadly supported; the oncological finding on overall survival and progression-free survival stands alongside ².

Blinding remains consistently absent. Two of the clinical studies are open-label; their course is therefore susceptible to expectation effects in both clinicians and patients; the authors of the controlled study themselves call for larger double-blind longitudinal investigations that combine clinical and biological determinations ¹. In oncology the prospective, multicentre, randomised trial is named as the next step ²; in the review, knowledge gaps regarding manufacturing and bioactivity are identified ⁷. The next point to clarify is whether the scale improvements are reproduced in blinded designs with pre-specified endpoints and whether they align with accompanying biological measures.

Methodology of the evidence base

The studies on Alpha-GPC comprise a randomised controlled multicentre trial against acetyl-L-carnitine in 126 patients ¹, an open-label, uncontrolled multicentre trial in 2044 persons after stroke or transient ischaemic attack ³, an open-label multicentre trial in 120 persons with vascular dementia against cytidine diphosphocholine ⁴, a retrospective single-centre evaluation in 187 glioblastoma patients ² and a 2025 review ⁷. Treatment duration ranges from 28 days intramuscularly followed by five months of oral administration, through 90 days, to classification after at least 3 or 12 months of continuous use. Recorded are behavioural, dementia and depression scales, the Mini Mental State Test, the Mathew Scale, the Global Deterioration Scale as well as overall and progression-free survival; blinded longitudinal data with pre-specified endpoints and accompanying biological determinations are outstanding.

Citation frequency measures the animal models, not the clinical trial

The most frequently cited works on Alpha-GPC date from 1991 and 1992 and are

ANIMAL-EXPERIMENTAL

: they examine reversal of scopolamine-induced amnesia and cholinergic transmission in the hippocampus. The 1992 study on young and aged rats and the later investigation into **mitochondrial dysfunction** also belong to the animal domain; a basic-research paper on neuroprotective substances in an experimental stroke model treats these substances as a group. These works shape the picture of the substance because they are frequently cited. Citation frequency, however, is a measure of attention, not of efficacy in humans.

On the clinical side there are two controlled studies whose results cannot be combined: one tested a cognitive endpoint against a comparator substance in dementia, the other retrospectively recorded survival of patients with glioblastoma at a single centre.

HYPOTHESIS:

That both reflect the same mechanism of action is plausible, yet it was not examined in the studies themselves. The decisive question is therefore not how often a substance is cited, but whether a **prospective, blinded and independent trial** with pre-specified endpoints confirms the findings.

3. How Robust the Research Is

Research is distributed clearly at the preclinical level: ten studies are animal-experimental, four are basic-research, and one review organises the mechanisms. Five studies exist in humans, of which three are observational and two are controlled. **Plausible:** That the emphasis lies so clearly in the animal model is linked to the good measurability of cholinergic parameters. The application areas follow the classic fields of choline and nootropic research: **dementia** and **cognition**, alongside vascular dementia, recovery after **ischaemic attacks** and **tolerability**. Added to these is a field that is rare in the remaining literature on choline compounds: **oncology**, with one study on survival in glioblastoma.

The most elaborate human study in this field is a 1993 multicentre comparison study in probable Alzheimer dementia that tested against an active comparator (ST200); an **active comparator arm** instead of placebo is methodologically demanding. The second controlled study from 2022 is a retrospective survey at a single centre. **Retrospective data** can show associations but cannot establish causation. The two multicentre studies from 1991 and 1994 on vascular dementia and recovery after ischaemic attacks are observational in design and do not support a controlled statement. A review on the mechanistic level is available; a meta-analysis is not. The clinical side therefore rests on individual studies with differing endpoints; investigation in humans is at an early stage.

4. What Is Frequently Claimed — and What the Data Support

STATEMENT	EVIDENCE BASE
Cognitive improvement in Alzheimer dementia	A multicentre controlled comparative study from 1993 against the comparator substance ST200. An indication; an independent replication with cognitive endpo
Longer survival in glioblastoma	A single-centre retrospective survey from 2022. Retrospective data show associations, not causation; a prospective examination is pending.
Vascular dementia and recovery after ischaemic attacks	Two multicentre observational follow-up studies from 1991 and 1994, set up as observational; they provide no controlled statement.
Cholinergic effect in the brain	Findings from animal experiments on acetylcholine and the hippocampus. Preclinical results cannot be directly transferred to humans.

5. Profile: Molecule and Charge

Alpha-GPC (L-Alpha-Glycerylphosphorylcholine) is not a single molecule but a **mixture** — there is no molecular formula and no fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; that is exactly what the next section addresses.

6. Interactions with Other Substances

With which other substances on the platform this compound has been **jointly** investigated or discussed in human studies and reviews — combination, comparison or shared pathway. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Cognitive behavioural therapy for insomnia (CBT-I)	3	1

7. Overdosage, Tolerability, Limits

The same work rates tolerability as good and attributes the low rate of adverse events to this ³. Both figures come from an observational study, not a controlled trial; a dose-response relationship or an upper limit cannot be derived from this. Data on pre-existing conditions and concomitant medication are lacking for any statement on contraindications.

Preclinically, a contradictory signal appears: in cardiac muscle cells of newborn rats, L-alpha-glycerylphosphorylcholine acted both cytoprotectively and cytotoxicity ⁵, and long-term administration can be cytotoxic over a wide concentration range ⁵. The authors recommend a comprehensive cardiac safety protocol ⁵. A safety assessment states a NOAEL of 1000 mg/kg body weight per day for a 90-day study and for maternal toxicity in a teratogenicity study, but points to limitations of the submitted animal data ⁶; identity, manufacturing process and specifications give no cause for safety concerns ⁶. It remains to be clarified whether the cardiac findings can be confirmed in humans and which dose is considered safe there.

8. The Most Robust Studies

Ordered by strength of evidence, not by familiarity: reviews and studies with many participants first. The complete evaluation comprises considerably more studies; the most robust ones are presented here.

Controlled Human Studies

- ¹ Multicentre study of l-alpha-glyceryl-phosphorylcholine vs ST200 among patients with probable senile dementia of Alzheimer's type (1993) — 126 participants
- ² Effect of Choline Alphoscerate on the Survival of Glioblastoma Patients: A Retrospective, Single-Center Study (2022)

Observational Human Studies

- ³ alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial (1994) — 2,044 participants
- ⁴ A multicentre trial to evaluate the efficacy and tolerability of alpha-glycerylphosphorylcholine versus cytosine diphosphocholine in patients with ... (1991) — 120 participants

9. Summary

Human testing is at an early stage. The randomised multicentre study in 126 patients with probable Alzheimer's dementia showed significant improvements in most neuropsychological parameters versus ST200; the authors rate the finding as positive but in need of replication. The open multicentre trial in 2,044 persons after stroke or transient ischaemic attack showed an increase in the Mathew Scale of 15.9 points and in the Mini Mental State Test from 21 to 24.3. The open trial in 120 persons with vascular dementia showed improvements under both substances. A retrospective evaluation in 187 glioblastoma patients shows longer median overall survival with use for at least 12 months.

PLAUSIBLE That the research focus lies so clearly in the animal model is linked to the good measurability of cholinergic parameters; acetylcholine and cholinergic transmission in the hippocampus are read there, not a clinical course. **Hypothesis:** That the cognitive finding in dementia and the survival finding in glioblastoma reflect the same mechanism of action is plausible, but has not been examined in the studies themselves. **Hypothesis:** Since GPC was given in the oncological evaluation for cognitive impairment and classification was made by duration of use, longer use could also reflect an overall more favourable disease course.

The next points to clarify are whether the scale improvements can be reproduced in blinded designs with pre-specified endpoints and whether they align with accompanying biological measures; the authors of the controlled study specifically call for such larger double-blind longitudinal studies. For oncology, the prospective, multicentre, randomised trial with a large number of participants is named as the next step; for the overview, knowledge gaps on

manufacturing and bioactivity remain open: it must be clarified which manufacturing method was tested in which population with which measurable endpoint. An independent replication supports the finding only when the endpoints are pre-specified.

10. What Remains Open

- **Endpoints:** Which cognitive target measure is suitable in which patient group to reflect a change under alpha-GPC?
- **Replication:** An independent, prospectively blinded replication of the 1993 dementia study against placebo or active comparator is still outstanding.
- **Long-term tolerability:** How longer-term use affects tolerability and course cannot yet be answered with the available studies.

11. Further Paths

Topics, mechanisms and pathways in which this substance occurs — for all those who wish to look beyond the substance.

- Interaction network

Frequently Asked Questions

How many studies in humans are there on Alpha-GPC?

In humans five studies are available, three of them observational and two controlled. The controlled studies examine different populations: a multicentre comparative study in probable Alzheimer's dementia from 1993 and a retrospective survey on survival in glioblastoma from 2022. In addition there are multicentre course observations in vascular dementia and after ischaemic attacks.

Why is Alpha-GPC so frequently tested in animal models?

The animal experimental works from 1991, 1992 and 2016 use models in which cholinergic transmission can be measured directly: scopolamine-induced amnesia, the behaviour of young and aged rats and mitochondrial function. Such models allow statements about mechanisms, not about clinical benefit. The majority of the available works are designed as animal experimental or basic research.

Are there data on tolerability?

Tolerability is one of the stated endpoints of the human studies; the comparative study in vascular dementia from 1991 already names it in the title. How longer-term use affects tolerability is not answered by this. Prospective surveys over longer periods with uniformly recorded adverse events would be required for that.

Sources

1

Multicentre study of l-alpha-glyceryl-phosphorylcholine vs ST200 among patients with probable senile dementia of Alzheimer's type
Parnetti L, Abate G, Bartorelli L, Cucinotta D, Cuzzupoli M, Maggioni M et al. · 1993

2

Effect of Choline Alphoscerate on the Survival of Glioblastoma Patients: A Retrospective, Single-Center Study
Kim YJ, Lee TK, Noh MG, Jung TY, Kim IY, Jung S et al. · 2022

3

alpha-Glycerophosphocholine in the mental recovery of cerebral ischemic attacks. An Italian multicenter clinical trial
Barbagallo Sangiorgi G, Barbagallo M, Giordano M, Meli M, Panzarasa R · 1994

4

A multicentre trial to evaluate the efficacy and tolerability of alpha-glycerylphosphorylcholine versus cytosine diphosphocholine in patients with vascular dementia
Di Perri R, Coppola G, Ambrosio LA, Grasso A, Puca FM, Rizzo M · 1991

5

L-Alpha-glycerylphosphorylcholine can be cytoprotective or cytotoxic in neonatal rat cardiac myocytes: a double-edged sw...
· 2019

6

The safety data in laboratory animals submitted by the applicant show several limitations; however, a no observed advers...
· 2026

7

L-Alpha-Glycerylphosphorylcholine (L-α-GPC): A Comprehensive Review of Its Preparation Techniques and Versatile Biological Effects
Li J, Zhang J, Wang Y, Yang Y, Su Y, Gu L et al. · 2025

International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
ih-research.com/en/knowledge/alpha-gpc/ · Last updated 2026-10-04