



DOSSIER · SUBSTANCE

Alpha-Ketoglutarate (AKG)

The database contains studies on **alpha-ketoglutarate (AKG)**, with only a few conducted in humans. Research primarily focuses on **basic science** and **animal models**, while controlled human studies are rare. The most notable finding: the limited clinical data available almost exclusively derive from **burn medicine** and **ageing research**, rather than from common areas of application.

46

STUDIES IN
TOTAL

8

IN HUMANS

3

OF WHICH
CONTROLLED

19

IN ANIMALS

1

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

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-Ketoglutarate (AKG) at a glance

ORIGIN:

Alpha-ketoglutarate (AKG) is a central intermediate of the citric acid cycle and plays a key role in cellular metabolism, particularly as a nitrogen acceptor in amino acid metabolism and as a precursor for glutamate and glutamine. It is endogenously produced from glutamate or the degradation of amino acids such as glutamine and is involved in the regulation of epigenetic processes. AKG occurs naturally in small quantities in fermented dairy products or meat. Industrially, it is typically produced as a calcium or ornithine salt, as the free acid is unstable.

EVIDENCE BASE:

46 evaluated studies · 3 controlled human trials · 5 observational studies · 2 review articles · 19 animal studies · 1 cell culture study

STRONGEST EVIDENCE:

- **Skin – Wound healing** A controlled human trial in burn medicine showed a significant reduction in wound healing time in severely burned patients treated with ornithine-alpha-ketoglutarate. Secondary endpoints, such as antibiotic use and nutritional status, were positively influenced, though the effect was not quantified in the abstract.
- **Metabolism – Amino acid and hormone profiles** A controlled observational study in healthy volunteers (n=6) showed that ornithine-alpha-ketoglutarate exerts specific effects on plasma amino acids (increases in proline, arginine, glutamate) and hormone levels (insulin, glucagon).
- **Biological age and gerotherapy** A recruitment study (ABLE) confirmed the feasibility of enrolling older participants for a placebo-controlled trial of delayed-release calcium-alpha-ketoglutarate. A cross-sectional study associated calcium-alpha-ketoglutarate intake with a biological age reduction of 1.8 years, though no causal conclusions could be drawn.

LIMITATIONS:

- Controlled human studies are small (n=6) or not designed for clinical endpoints. The applicability of animal models (e.g., lifespan extension, anti-inflammatory effects) to humans remains unclear, as these findings are preclinical.
- Dose-finding studies and long-term data on safety and efficacy are lacking. The bioavailability of AKG is low, and the use of different salts (ornithine-AKG vs. calcium-AKG) limits comparability.
- Applications such as sports performance, immunomodulation, or neuroprotection are not supported by controlled human trials. Observational studies often measure only surrogate parameters, and their clinical relevance is not established.

CLASSIFICATION:

Alpha-ketoglutarate salts (e.g., ornithine-alpha-ketoglutarate, calcium-alpha-ketoglutarate) showed effects on wound healing and amino acid profiles. However, the clinical potential of alpha-ketoglutarate itself in other applications is limited by the lack of controlled human studies and the use of different salt formulations.

1. What Alpha-Ketoglutarate Is

Alpha-ketoglutarate (AKG) is a central intermediate of the citric acid cycle and plays a key role in cellular metabolism. It is endogenously produced from glutamate or via the degradation of amino acids such as glutamine. AKG acts as a nitrogen acceptor in amino acid metabolism and serves as a precursor for the synthesis of glutamate and glutamine. Additionally, it is involved in the regulation of epigenetic processes, such as the inhibition of DNA and histone demethylases. AKG occurs naturally in small amounts in foods, including fermented dairy products and meat.

For the evidence base, bioavailability and metabolism of AKG are critical. Orally administered AKG is partially converted to glutamate and glutamine in the gut before exerting systemic effects. Plasma levels rise only briefly after administration, as AKG is rapidly incorporated into the citric acid cycle or metabolised into other compounds. This complicates the measurement of direct effects and explains why many studies rely on indirect markers, such as amino acid profiles or hormone levels. Furthermore, the salts used (e.g., ornithine-AKG vs. calcium-AKG) vary, limiting the comparability of data.

2. What the Studies Show in Detail

The pivotal human studies and key reviews—organised by application, including population, duration, preparation, measured outcomes, and results, exactly as reported in the original publications. Numbers are included only where the study provides them.

Distribution of controlled human studies by field of application — the figures are not additive, as a single study may be assigned to multiple fields:

FIELD OF APPLICATION	CONTROLLED STUDIES
Skin	1

Skin – Wound Healing

The primary endpoint was wound healing time. Secondary endpoints included antibiotic use, tolerability, duration of enteral nutrition, and nutritional status. Additionally, serum transthyretin, plasma phenylalanine, and urinary 3-methylhistidine excretion were measured on days 4 and 21 post-burn as biochemical markers. The study demonstrated a significant reduction in wound healing time in the ornithine α-ketoglutarate group compared to the control group. The exact magnitude of the effect was not quantified in the abstract. A limitation is that the study was conducted at a single centre (military hospital) and does not provide detailed information on potential confounders such as comorbidities or concomitant medication. The findings pertain to the combination of ornithine and alpha-ketoglutarate, and it remains unclear whether alpha-ketoglutarate alone would yield similar results.¹

The study provides an indication of the efficacy of ornithine α -ketoglutarate in clinical practice for patients with severe burns. However, it remains unclear whether the observed effects are attributable to the specific combination of ornithine and alpha-ketoglutarate or if alpha-ketoglutarate alone would yield similar results. Furthermore, data on long-term safety and efficacy beyond the three-month observation period are lacking. There is a need for replication studies with larger, multicentre cohorts to confirm the generalisability of the findings for ornithine α -ketoglutarate.

Gut and Microbiome

An older observational study from 1994 discusses the potential role of ornithine α -ketoglutarate as a precursor for arginine and its metabolites, which are involved in regulating intestinal permeability and adaptive responses of the gut. The study references preclinical animal data showing improved intestinal morphology following administration of ornithine α -ketoglutarate, potentially mediated by increased polyamine secretion. However, concrete human data on the effects of ornithine α -ketoglutarate on the gut are lacking. The authors emphasise that the role of enteral arginine or ornithine α -ketoglutarate supplementation urgently requires investigation in clinical studies, particularly regarding dosage, as high doses of arginine in animal models exacerbated the effects of experimentally induced sepsis, whereas low doses improved survival rates. ³

HYPOTHESIS The theoretical considerations regarding the effects of ornithine α -ketoglutarate on gut health are primarily based on animal experimental data and metabolic reasoning. Should the positive effects on intestinal integrity be confirmed in human studies, this could be particularly relevant for patients with inflammatory bowel disease or postoperative conditions. However, controlled clinical studies in humans to test these hypotheses are currently lacking.

Metabolism – Amino Acid and Hormone Profiles

A controlled observational study in six healthy, fasted male subjects examined the effects of ornithine α -ketoglutarate (10 g, equivalent to 3.6 g alpha-ketoglutarate and 6.4 g ornithine), ornithine hydrochloride (6.4 g ornithine), and calcium alpha-ketoglutarate (3.6 g alpha-ketoglutarate) on plasma amino acids as well as insulin and glucagon levels. Blood samples were taken over a period of five hours following oral administration. After administration of ornithine α -ketoglutarate and ornithine hydrochloride, plasma ornithine levels rose to $494 \pm 91 \mu\text{mol/L}$ and $541 \pm 85 \mu\text{mol/L}$, respectively, after 60–75 minutes. The increase in plasma alpha-ketoglutarate was, however, very slight. All three substances significantly increased glutamate concentration after 60 minutes (ornithine α -ketoglutarate: +43%, calcium alpha-ketoglutarate: +68%, ornithine hydrochloride: +68%, $p < 0.05$). Only ornithine α -ketoglutarate, however, led to a significant increase in proline (+35%, $p < 0.01$) and arginine levels (+41%, $p < 0.05$) after 60 minutes. Furthermore, the concentrations of glutamate, proline, and arginine correlated linearly with ornithine levels. Ornithine α -ketoglutarate also increased insulin (+24% after 15 minutes, $p < 0.05$) and glucagon levels (+30% after 60 minutes, $p < 0.01$). The study showed that ornithine α -ketoglutarate exerts specific metabolic effects on amino acid and hormone profiles that go beyond the effects of its individual components. Limitations include the small number of subjects ($n=6$) and the short observation period of five hours. ⁴

HYPOTHESIS Observed effects of alpha-ketoglutarate (AKG) on amino acid and hormone profiles in preclinical and small-scale human studies suggest a potential anabolic effect, which could be of clinical relevance in catabolic states such as postoperatively or in severe burns. However, long-term studies examining these effects over extended periods and in larger populations are lacking.

Viral Infections and Inflammation

An animal study in mice with type-2 diabetes (T2D) investigated the preclinical effects of alpha-ketoglutarate on inflammatory and thrombotic processes. The animals received a daily dose of 8 mg of alpha-ketoglutarate per 100 g of body weight over seven days. Supplementation significantly reduced the activation of platelets and leukocytes (neutrophils and monocytes), as well as the accumulation of the proinflammatory cytokines IL-1 β , TNF- α , and IL-6 in peripheral blood. Additionally, alpha-ketoglutarate decreased the infiltration of platelets and leukocytes into the lungs and the accumulation of inflammatory cytokines by inhibiting the pAkt and pP65 signalling pathways. These findings are preclinical and have not been confirmed in humans. A cross-sectional study in T2D patients demonstrated elevated platelet-leukocyte aggregates and proinflammatory cytokines in the blood. The study suggests that preclinical models *may* indicate a reduction of thromboinflammatory complications in T2D through alpha-ketoglutarate, but this remains to be investigated in clinical trials. A limitation is the unclear translatability of the mouse findings to humans. Furthermore, data on the long-term safety and efficacy of supplementation are lacking. ⁵

In preclinical models (mice with SARS-CoV-2 infection or hypoxia), alpha-ketoglutarate demonstrated significant inhibition of lung inflammation. These findings suggest a potential therapeutic window for alpha-ketoglutarate in viral infections in preclinical research, particularly in combination with inflammatory underlying conditions such as diabetes. However, clinical studies in humans confirming these effects are currently lacking, and the relevance for human therapy remains to be established.

Biological Age and Gerotherapy

A recruitment evaluation for the randomised, placebo-controlled ABLE study (Alpha-ketoglutarate Supplementation and Biological age) assessed the feasibility of recruiting 120 biologically older but healthy adults aged 40–60 years (with a maximum of one chronic condition) in Singapore. Participants were to receive 1 g of delayed-release calcium alpha-ketoglutarate or placebo over six months, followed by a three-month follow-up phase. The primary endpoint was the recruitment rate, with secondary endpoints including consent rate, eligibility rate, and the effectiveness of recruitment strategies. Of 467 interested individuals, 120 participants were recruited over 223 working days. The eligibility rate was 80.3% at pre-screening and 67.3% at screening. The study demonstrates that recruiting biologically older but healthy participants for gerotherapeutic studies is feasible. However, results on the efficacy of alpha-ketoglutarate on biological age are not yet available. ²

The intake of a delayed-release calcium alpha-ketoglutarate preparation (dAKG) in combination with a vitamin supplement ('Rejuvant') was associated with a biological age lower by an average of 1.8 years. This effect remained significant even after adjustment for age, sex, smoking, health status, and other covariates. In contrast, regular alpha-ketoglutarate showed a much smaller and statistically non-significant benefit. The study does not allow for causal inferences regarding the effects of alpha-ketoglutarate alone, as it was administered as part of a combination. Additionally, the cross-sectional design and the selective population of 'health enthusiasts' limit the generalisability of the findings.

HYPOTHESIS The association between delayed-release calcium alpha-ketoglutarate and a lower biological age suggests potential gerotherapeutic benefits. However, the observed effect stems from a cross-sectional study, and randomised, controlled long-term trials are needed to confirm these findings in larger, representative populations.

Oxidative Stress and Cellular Ageing

A 2024 review discusses the role of metabolic intermediates, including alpha-ketoglutarate, in the tricarboxylic acid (TCA) cycle and their importance for energy supply, regulation of oxidative stress, and cellular ageing. The review describes alpha-ketoglutarate as a central regulator influencing cell function through epigenetic modulation, potentially delaying cellular ageing, and maintaining immune homeostasis. However, this is a narrative review covering multiple compounds that presents no new experimental data on alpha-ketoglutarate. The statements are based on a synthesis of existing literature, the quality and validity of which vary. ⁶

HYPOTHESIS The theoretical considerations regarding the role of alpha-ketoglutarate in regulating oxidative stress and cellular ageing are promising, particularly concerning mitochondrial function and epigenetic regulation. However, concrete clinical studies in humans are lacking to test these hypotheses and investigate optimal dosing and long-term effects.

Bone and Joints – Biomaterials and Cell Differentiation

A 2026 review describes alpha-ketoglutarate as a central metabolic hub in the tricarboxylic acid cycle, whose role has expanded from a mere energy supplier to a proposed regulator of cell differentiation, epigenetic landscape, and immune homeostasis. The review, which covers multiple metabolic intermediates and biomaterial strategies, highlights that the clinical translation of alpha-ketoglutarate is hampered by pharmacokinetic limitations such as low bioavailability, short half-life, and lack of tissue specificity. It proposes a paradigm shift: alpha-ketoglutarate should no longer be viewed as a 'therapeutic molecule' but as a 'smart building block' for biomedical materials. Through covalent bonding to biomaterials, alpha-ketoglutarate could serve as an integral component of scaffolds for bone and cartilage regeneration. The review discusses three strategies—alpha-ketoglutarate as a protected 'cargo,' as a functionally synergistic 'adjuvant,' or as a structural 'framework' of the biomaterial—across various compounds. Applications in bone and cartilage regeneration, as well as wound healing, are particularly highlighted. However, this is a conceptual work that presents no new experimental data. ⁷

HYPOTHESIS The integration of alpha-ketoglutarate into biomedical materials could represent an innovative strategy to harness its regenerative properties in a targeted manner. However, preclinical and clinical studies are lacking to demonstrate the feasibility, safety, and efficacy of these approaches.

Overall Picture

The available studies demonstrate a broad but heterogeneous spectrum of effects of alpha-ketoglutarate and its derivatives. A randomised, controlled study showed that ornithine alpha-ketoglutarate significantly shortened healing time in severely burned patients. Additionally, preclinical models indicate metabolic effects of AKG in animals, particularly on amino acid and hormone profiles, as well as anti-inflammatory and thromboinhibitory effects. These findings have not yet been investigated in humans. Associative data suggest a potential gerotherapeutic benefit of delayed-release calcium alpha-ketoglutarate, although randomised, controlled studies in humans are lacking in this area.

The evidence base is still developing in many areas: long-term studies investigating safety and efficacy over months or years are still pending. Furthermore, most studies have been conducted either preclinically (animal models) or in highly selective populations (e.g., 'health enthusiasts'), which limits generalisability. Systematic investigations into optimal dosing, bioavailability, and tissue specificity are still pending, as are studies on potential interactions with medications or other dietary supplements.

Methodology of the evidence base

["The studies on alpha-ketoglutarate and its derivatives encompass a wide range of designs: from randomised, controlled trials (e.g., wound healing in burn patients) to observational studies (e.g., metabolic effects or biological ageing) and preclinical animal models (e.g., inflammation and thrombosis). The duration of interventions varies considerably, from acute stress tests lasting a few hours to six-month supplementation phases. Primary endpoints range from clinical parameters (wound healing time, inflammatory markers) to biochemical markers (amino acid and hormone profiles) and epigenetic ageing markers. However, long-term studies with clinically relevant endpoints, multicentre approaches to confirm generalisability, and standardised dose-finding studies are still pending. Additionally, many studies have been conducted in small, selective populations, which limits their applicability to broader patient groups."]

AKG and life extension: what the data actually support

The
POPULAR SCIENCE CLAIM

that AKG could **extend lifespan** is based almost exclusively on a **highly cited animal study**. In this study, AKG was investigated for its potential to extend the **lifespan of mice**; however, the results are inconsistent regarding translatability to humans. A **replication in humans** is lacking. The only **controlled human study** related to ageing is a **recruitment study** without clinical outcomes. The **mechanistic reviews** discuss AKG as an **epigenetic regulator**, but the **translation into clinical effects** remains speculative. Even the **animal studies** show **no consistent dose-response relationships**, and the **concentrations used** often **exceed physiological levels**.

A further issue is the
CONFUSION OF CORRELATION WITH CAUSATION

. The **observational study** associating AKG with a **lower biological age** cannot **demonstrate an effect**—it merely shows an **association** in a selected population. Such findings are susceptible to **confounding**. Additionally, **long-term data** on **safety and side effects** from chronic intake are lacking. The **burn study** is the **only controlled trial with a clinical endpoint**, yet even here it is unclear whether **wound healing** is attributable to AKG or to **nitrogen supply**. The

data do not support conclusions about long-term effects.

3. How Robust the Research Is

The research on AKG is heavily focused on basic science: a significant portion of the work consists of animal studies and in vitro or biochemical basic research. Only three controlled human studies exist, two from burn medicine (wound healing) and one recruitment study for an ageing research project. The observational human studies primarily examine amino acid profiles and hormonal changes following AKG administration, without assessing clinical endpoints. Preclinical animal studies suggest effects on lifespan extension and obesity, but these findings require validation in human trials. Applications in sports, immune modulation, or neuroprotection have not been covered by controlled human studies to date.

The data show methodological limitations. The controlled human studies are either old or not designed to assess clinical effects. The observational human studies typically measure surrogate parameters, not clinical outcomes. Furthermore, dose-finding studies are still pending, so it remains uncertain whether the amounts effective in animal models are physiologically relevant. The mechanistic reviews often rely on in vitro data or animal models, not on human findings. A systematic evaluation of clinical relevance is still pending.

4. What Is Often Claimed — and What the Data Actually Show

STATEMENT	EVIDENCE BASE
AKG in Sports	No controlled human studies available. Animal studies demonstrate effects on muscle catabolism, but their applicability to humans remains unclear. Observed effects are limited to short-term studies.
AKG in Neurodegenerative Diseases	Keine Humanstudien. Mechanistische Arbeiten diskutieren neuroprotektive Effekte in Zellkulturen, doch klinische Daten fehlen.
AKG as an Anti-Ageing Agent	The only controlled human study is a recruitment study without results. Animal studies have investigated AKG for life extension, but transferability has not been established.
AKG in Immune Modulation	Keine kontrollierten Humanstudien. Grundlagenarbeiten deuten auf Effekte im Darmmikrobiom hin, doch klinische Relevanz ist unklar.

5. Fact Sheet: Molecule and Charge

Alpha-ketoglutarate (AKG) is not a single molecule but a mixture—there is no molecular formula or fixed molecular mass. What can be described are its functional groups, charge behaviour, and redox properties; this is the focus of the next section.

6. Charge, Electrons, Radicals

As a dicarboxylic acid, it contains two carboxyl groups, which are deprotonated under physiological conditions, resulting in a net negative charge. In the TCA cycle, AKG acts as an electron acceptor during oxidative decarboxylation, where it is converted into succinyl-CoA and generates reducing equivalents (NADH) ^{6 10}. This reaction is associated with the production of reactive oxygen species (ROS), as electron transfers in mitochondrial metabolism can potentially release radicals ⁶. In animal models, AKG influences enzyme activities such as glutathione peroxidase and NAD(P)H quinone oxidoreductase 1 (NQO1), suggesting involvement in redox processes ⁹.

No direct electrochemical measurements in humans are available. However, animal studies have shown that AKG affects the metabolism of glutamate and ornithine, leading to a 10- to 16-fold accumulation of gamma-aminobutyric acid (GABA) in the intestinal mucosa ^{8 8}. These effects indicate a role in cation exchange (e.g., ammonium ions) and transamination, though the precise charge shifts or electron transfer mechanisms have not been quantified. Foundational research demonstrates that AKG serves as a substrate for reversible enzyme reactions (e.g., GPT2), linking the TCA cycle to neurotransmitter synthesis ^{11 12}. Whether these processes correlate with measurable electrochemical changes in the human organism remains to be investigated.

7. Interactions with Other Substances

Substances from this platform that have been jointly studied or discussed with this compound in human trials and review articles—whether in combination, comparison, or shared mechanistic pathways. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic Inflammation	2	0

Substance	Shared Studies	Of Which Controlled in Humans
Spermidine	2	0

8. Overdose, Tolerability, and Limits

No direct evidence regarding overdose, toxicity, or defined upper limits of alpha-ketoglutarate (AKG) is available from the studies reviewed. In one controlled human trial, ornithine alpha-ketoglutarate (a derivative) was described as 'safe and well-tolerated' at an unspecified dosage, with no reported adverse effects ¹. Animal studies suggest general safety for dietary interventions with AKG-like substances, though without specific dosage details or toxicity data. No adverse effects or contraindications were reported in these studies. Whether gastrointestinal effects, such as those observed with other metabolic interventions (e.g., bariatric surgery), are relevant for AKG has not been investigated.

The available data do not provide concrete dose-response relationships or thresholds for toxic effects of AKG or AKG-containing formulations. The human study ¹ lacks details on the administered quantity, precluding conclusions about potential upper limits. While animal studies emphasise safety, they do not provide quantitative toxicity parameters. It remains unclear whether interactions with other substances or contraindications exist. Further investigation is needed to determine whether high doses of AKG or AKG-containing formulations could induce metabolic imbalances (e.g., acidosis), particularly in individuals with pre-existing renal or hepatic dysfunction.

9. The Most Robust Studies

Ranked by evidential strength, not by prominence. The full analysis includes significantly more studies; only the most reliable are listed here.

Controlled Human Trials

- ¹ Ornithine alpha-ketoglutarate improves wound healing in severe burn patients: a prospective randomised double-blind trial versus isonitrogenous control (2000)
- ² Recruitment evaluation of a gerotherapeutic randomised controlled trial testing alpha-ketoglutarate in biologically older, middle-aged adults (ABLE) (2025)
- Supplements and Drugs Are Associated With Biological Age in a Cohort of Exceptionally Healthy Individuals (2026)

Observational Human Studies

- ³ Can arginine and ornithine support gut functions? (1994)
- ⁴ Action of ornithine alpha-ketoglutarate, ornithine hydrochloride, and calcium alpha-ketoglutarate on plasma amino acid and hormonal patterns in health (1990)
- ⁵ Alpha-ketoglutarate supplementation reduces inflammation and thrombosis in type 2 diabetes by suppressing leukocyte and platelet activation (2023)

10. Summary

What is established: The most robust human findings come from burn medicine, where ornithine alpha-ketoglutarate showed a shortened wound healing time in a controlled trial. Additionally, a small study demonstrated specific metabolic effects on amino acid and hormone profiles, suggesting an anabolic action in humans. In ageing research, an observational association between sustained-release calcium alpha-ketoglutarate and a lower biological age was reported, though without causal proof. Basic research underscores the central role of AKG in the citric acid cycle and epigenetic processes, yet clinical endpoints are largely lacking.

HYPOTHESIS The observed effects on wound healing and amino acid metabolism may indicate clinical relevance of AKG in catabolic states such as postoperative phases or severe burns. The association with a lower biological age suggests gerotherapeutic potential, which would, however, require validation through randomised controlled trials. Theoretical considerations regarding the role of AKG in gut health, anti-inflammatory effects, and cellular ageing are plausible but primarily based on preclinical animal models or in vitro data. These findings remain to be confirmed in human studies to establish relevance for patients with inflammatory bowel diseases, viral infections, or oxidative stress.

What a study would need to clarify: First, randomised, placebo-controlled trials with adequate participant numbers and clinical endpoints are required to confirm the efficacy of AKG in the postulated areas of application (e.g., wound healing, ageing research, gut health). Dose-finding studies should determine whether the effective amounts used in animal models are physiologically relevant and which formulation (e.g., ornithine-AKG, calcium-AKG, sustained-release preparations) offers the best bioavailability and tolerability. Long-term studies are necessary to evaluate safety and efficacy over extended periods. Furthermore, mechanistic studies in humans should examine the transferability of animal and in vitro data, particularly concerning epigenetic regulation, mitochondrial function, and anti-inflammatory effects. For the integration of AKG into biomedical materials, preclinical studies on feasibility and efficacy are needed.

11. Open Questions

- **Dose-response relationship:** Unclear which AKG quantities are systemically effective in humans. Animal studies often use supraphysiological doses.
- **Long-term safety:** No data on chronic intake. Potential interactions with medications or metabolic processes remain uninvestigated.
- **Epigenetic effects:** Mechanistic studies discuss AKG as a demethylase inhibitor, but its clinical relevance in humans is unproven.

12. Further Paths

Topics, mechanisms and chains in which this substance appears — for those who want to look beyond the substance.

- Interaction network

Frequently Asked Questions

Can AKG improve wound healing?

The **evidence base is limited**: Only **one controlled study** investigated AKG (as ornithine-AKG) in **severe burns**; the results on **wound healing** are inconsistent. It remains unclear whether the effect is attributable to AKG or to **nitrogen supplementation**. Other areas of application (e.g., postoperative wound healing) are **not supported by controlled studies**. The **applicability to non-burn-related wounds** is questionable.

Is there evidence of a life-extending effect in humans?

No. The **hypothesis of a life-extending effect** is based on a **single animal study** in which AKG was investigated for **extending lifespan in mice**. In humans, **no controlled study** with this endpoint exists. A **recruitment study** is examining AKG in an **ageing research project**, but it **provides no results**. Observational data show an **association** between AKG and biological age, but they **do not prove causality**. The **evidence base is too limited to make claims about life extension**.

What role does AKG play in amino acid metabolism?

AKG is a central metabolite in amino acid metabolism and acts as a **nitrogen acceptor** during transamination. Observational studies in humans show that AKG administration affects **plasma levels of glutamate, glutamine, and branched-chain amino acids**. Whether these changes are **clinically relevant** remains unclear. The **majority of data come from short-term observations**, not **long-term studies**. Furthermore, it is uncertain whether the effects are attributable to AKG itself or to its **metabolites**.

Sources

1

Ornithine alpha-ketoglutarate improves wound healing in severe burn patients: a prospective randomized double-blind trial versus isonitrogenous controls
Coudray-Lucas C, Le Bever H, Cynober L, De Bandt JP, Carsin H · 2000

2

Recruitment evaluation of a gerotherapeutic randomized controlled trial testing alpha-ketoglutarate in biologically older, middle-aged adults (ABLE)
Lim ZM, Chew YE, Guan L, Wang W, Mahadzir MDA, Dorajoo R et al. · 2025

3

Can arginine and ornithine support gut functions?
Cynober L · 1994

4

Action of ornithine alpha-ketoglutarate, ornithine hydrochloride, and calcium alpha-ketoglutarate on plasma amino acid and hormonal patterns in healthy subjects
Cynober L, Coudray-Lucas C, de Bandt JP, Guéchet J, Aussel C, Salvucci M et al. · 1990

5

Alpha-ketoglutarate supplementation reduces inflammation and thrombosis in type 2 diabetes by suppressing leukocyte and platelet activation
Agarwal S, Ghosh R, Verma G, Khadgawat R, Guchhait P · 2023

6

Individual components of these effects are postulated to be related to the energy supply by tricarboxylic acid (TCA) cyc...
· 2024

7

From metabolic node to smart building block: α-Ketoglutarate-empowered biomaterials for programmable cell fate. α-Ketogl...
· 2026

8

Surprisingly, with glutamate and putrescine, the products of ornithine transamination and decarboxylation, gamma-aminobu...
· 1995

9

HFFD or AKG lowered glutathione peroxidase and NAD(P)H-quinone oxidoreductase 1 (NQO1) activities in adipose tissue rela...
· 2025

10

Alpha-ketoglutarate is a key metabolite in the tricarboxylic acid (TCA) cycle, and its levels change upon fasting, exerc...
· 2020

11

GPT2 catalyzes a reversible reaction interconverting glutamate and pyruvate with alanine and alpha-ketoglutarate, a TCA ...
· 2024

12

GPT2 catalyzes a reversible reaction interconverting glutamate and pyruvate with alanine and alpha-ketoglutarate, a TCA ...
· 2024

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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-ketoglutarate/ · Last updated 2026-10-15