



DOSSIER · SUBSTANCE

Ergothioneine

Ergothioneine is a sulphur-containing natural compound with **antioxidant** and **cytoprotective** effects that has been studied for decades. The body of evidence reveals a significant imbalance: while basic research and observational studies predominate, robust controlled trials in humans are lacking. The most notable finding is that even for frequently discussed applications such as **inflammation** or **cognition**, the evidence has not progressed beyond pilot studies.

204

STUDIES IN
TOTAL

47

IN HUMANS

6

OF WHICH
CONTROLLED

6

IN ANIMALS

29

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

Ergothioneine at a glance

ORIGIN:
Ergothioneine is a sulphur-containing thiohistidine derivative with antioxidant and cytoprotective effects, synthesised by certain fungi, bacteria, and actinomycetes. The human body does not produce it endogenously but obtains it through the diet, particularly from mushrooms such as *Agaricus bisporus*, as well as from cereals, meat, and fish. It accumulates in tissues with high oxidative stress and is transported into cells via the specific transporter **OCTN1**.

EVIDENCE BASE:
204 evaluated studies · 6 controlled human trials · 41 observational studies · 33 review articles · 6 animal studies · 24 cell culture studies

- KEY FINDINGS:**
- **Bioavailability and uptake** Ergothioneine from mushrooms such as *Agaricus bisporus* is well absorbed and accumulates in erythrocytes. Plasma concentration depends directly on intake, with a half-life of approximately 30 days. Measurement is performed via HPLC-MS/MS, with intracellular concentrations often higher than in plasma. Studies showed trends in bioavailability, though long-term confirmation is still pending.
 - **Inflammation** Acute human studies show trends towards reduction in inflammatory markers such as NADPH oxidase 2 and iNOS following mushroom consumption. A pilot study (2012) observed a blunted postprandial triglyceride response but no significant changes in CRP.
 - **Oxidative stress** Observational studies link low ergothioneine levels to neurodegenerative diseases such as dementia. Preclinical studies suggest potential neuroprotective effects, though these findings have not been confirmed in humans. A randomised trial (2025) showed improved subjective sleep quality after 16 weeks of 8 mg/day, though without objective biomarkers or clinical endpoints.
 - **Gut and microbiome** A human study (2026) refuted the hypothesis that ergothioneine is a relevant source of trimethylamine-*N*-oxide (TMAO), a metabolite associated with cardiovascular risk. Supplementation increased plasma ergothioneine without affecting TMAO levels.
 - **Cognition** A 12-week intervention with *Pleurotus ostreatus* mushrooms (2026) showed improved delayed word recognition and reduced anxiety parameters in older adults. However, systemic inflammatory markers were not directly measured.

- LIMITATIONS:**
- **Clinical endpoints** There are no long-term studies with clinically relevant endpoints such as disease progression or mortality. The six controlled human trials include pilot trials with small sample sizes and short durations.
 - **Dose-response relationship** The optimal dosage for specific applications remains unclear. Studies typically tested only 1–2 dosages, and the translatability of *in vitro* findings to humans is limited.
 - **Isolating the effect** Ergothioneine is often administered as a mushroom extract, so the contribution of other compounds cannot be ruled out. Studies on the isolated effects of ergothioneine are still pending.

ASSESSMENT:
Ergothioneine is a promising sulphur-containing antioxidant with demonstrated bioavailability and potential anti-inflammatory effects, though its clinical relevance still requires confirmation through controlled long-term studies.

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1. What Ergothioneine Is

Ergothioneine is a **thiohistidine derivative** synthesised by certain fungi, bacteria, and actinomycetes. It does not occur naturally in the human body but is obtained through the diet—primarily from mushrooms such as *Agaricus bisporus*, as well as from cereals, meat, and fish. The compound accumulates in tissues with high oxidative stress, including the liver, kidneys, bone marrow, and the eye lens. Its chemical structure enables a **stable thiol-disulphide interaction**, distinguishing it from other antioxidants like glutathione. Ergothioneine is transported into cells via the specific transporter **OCTN1** (organic cation transporter novel 1), which significantly influences its bioavailability and tissue distribution.

Uptake and measurement of ergothioneine are central to interpreting all studies. Since humans do not produce the compound endogenously, **plasma concentration** depends directly on dietary intake. Bioavailability varies by source: while ergothioneine from mushrooms is well absorbed, uptake from plant sources such as cereals is lower. The **half-life** in plasma is approximately 30 days, indicating slow excretion. Measurement is typically performed via **HPLC-MS/MS** (high-performance liquid chromatography with tandem mass spectrometry), with **intracellular concentrations** often exceeding those in plasma. These characteristics complicate the comparability of studies, particularly when different dosages or routes of administration are investigated.

2. What the Studies Show in Detail

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

Distribution of **controlled human trials** by application—numbers are not additive, as a single study may be assigned to multiple categories:

APPLICATION	CONTROLLED STUDIES
Metabolism	5
Inflammation	4

APPLICATION	CONTROLLED STUDIES
Fatigue and stress	4
Cognition and mental health	3
Oxidative stress	3
Uptake and bioavailability	2
Gut and microbiome	1
Cardiovascular health	1

Inflammation

The controlled pilot study by Weigand-Heller et al. (2012) investigated the bioavailability of ergothioneine from *Agaricus bisporus* mushrooms and its acute effects on antioxidant capacity and inflammatory markers in 10 healthy men. Measurement of erythrocyte ergothioneine concentration showed significant cellular uptake. Among inflammatory markers, a trend towards a blunted postprandial triglyceride response was observed, while antioxidant capacity (ORAC(total)) decreased after both dosages. C-reactive protein (CRP) showed no significant changes. The study showed the bioavailability of ergothioneine from mushrooms but provides no clear evidence of an anti-inflammatory effect under acute conditions. Limitations include the small sample size and short observation period of a few hours ¹.

The planned ErgMS pilot project (2021) is designed as a randomised, double-blind, placebo-controlled trial with three arms (placebo, 5 mg/day, or 30 mg/day ergothioneine over 12 weeks) to assess the feasibility of a larger intervention study in individuals with metabolic syndrome. Primary endpoints include metabolic syndrome risk factors, while secondary endpoints cover oxidative stress (lipid peroxidation), inflammatory markers, platelet function, and liver enzymes. Additionally, the serum metabolome will be analysed. The study is not yet completed, so no results are available. The planned 12-week duration may provide initial insights into chronic effects if the dosages are adequate. A critical limitation is the lack of a dose-response relationship from prior studies to justify the selected dosages ².

The OYSCOG study (2026) investigated the effects of a 12-week intervention with *Pleurotus ostreatus* mushrooms (four portions per week, ergothioneine content not explicitly stated) on cognition, mood, and inflammatory markers in 80 healthy older adults (aged 60–80). Compared to the placebo group, the mushroom group showed improvements in delayed word recognition and recall (RAVLT), as well as reductions in anxiety (DASS-21) and negative mood parameters (PANAS-X). In a *preclinical* model using rodent microglial cells, inflammatory markers cyclooxygenase-2 (COX-2) and NADPH oxidase 2 decreased, indicating potential anti-inflammatory effects *in vitro*. However, systemic inflammatory markers in humans were not measured in this study, and the relevance of these *in vitro* findings to human physiology remains to be investigated. The study suggests potential benefits, though the contribution of other mushroom compounds cannot be ruled out.

The acute OYSACO study (2026) examined the effects of *Pleurotus* mushrooms (0.5, 1, or 2 portions in a noodle soup) on cognition, mood, and inflammatory markers in 33 healthy older adults using a crossover design. Postprandial inflammatory markers nitrite, NADPH oxidase 2, and inducible nitric oxide synthase (iNOS) were significantly lower after mushroom consumption compared to placebo. Mood (Positive Affect) deteriorated over the course of the day only in the placebo group, not following the mushroom intervention. Cognitive effects were inconsistent. The study showed acute effects on inflammatory markers in blood samples, though the clinical relevance of these surrogate parameters remains to be investigated. The short observation period (6 hours) and small sample size limit the conclusiveness of potential implications ⁴.

HYPOTHESIS The observed trends in reducing inflammatory markers (COX-2, NADPH oxidase 2, iNOS) in *in vitro* and acute *preclinical* studies suggest that ergothioneine or mushroom extracts may play a modulating role in inflammation *in these models*. However, whether these effects translate to long-term anti-inflammatory action in humans remains uninvestigated. The discrepancy between acute and chronic effects (e.g., ORAC decline vs. potential anti-inflammatory effects) remains an open question.

Oxidative Stress

The study by Nakamichi et al. (2025) used a physiologically based pharmacokinetic (PBPK) model to determine the effective dose of ergothioneine for influencing *subjective* sleep quality. In Study 1, participants received 5 or 10 mg/day of ergothioneine over 8 weeks, with plasma and blood concentrations measured. The optimised PBPK model showed that 8 mg/day over 16 weeks achieves an effective plasma concentration. In Study 2 (randomised, double-blind, placebo-controlled), administration of 8 mg/day over 16 weeks led to a significant improvement in *subjective* sleep quality ($p < 0.05$). This is the first study to propose a dose-finding strategy based on PBPK models, though objective sleep parameters or biomarkers for oxidative stress were not assessed ³.

The observational study by Yamazaki et al. (2021) compared metabolites in whole blood from dementia patients with those in healthy older adults using LC-MS. Ergothioneine was among the 26 metabolites significantly reduced in dementia (Group B: compounds with trimethylammonium structures, enriched in erythrocytes). The study shows that ergothioneine levels are reduced in dementia; whether this also holds for mild cognitive impairment and frailty was not examined. However, the design does not allow for causal inferences, and the contribution of other metabolites (e.g., glutathione, NADP+) remains unclear. The findings underscore ergothioneine's potential as a marker for oxidative stress in the context of neurodegenerative diseases ⁹.

The study by Servillo et al. (2015) investigated the redox behaviour of ergothioneine (ESH) in human neutrophils and cell-free systems. Upon activation of neutrophils with phorbol-12-myristate-13-acetate (PMA), the desulfurisation product hercynine (EH) and, unexpectedly, the sulfonated form ergothioneine sulfonate (ESO₃H)—previously undescribed—were formed. Similar oxidation products emerged from the reaction of ESH with hypochlorite, hydrogen peroxide, or peroxynitrite. The study demonstrates that ergothioneine forms specific metabolites under oxidative stress, which may exert cytoprotective effects. However, data on the biological activity of ESO₃H or its relevance *in vivo* are lacking ¹⁰.

HYPOTHESIS The consistent observation that ergothioneine is reduced under oxidative stress (e.g., dementia) suggests it may function as an endogenous protective mechanism. The formation of specific oxidation products such as ESO₃H could represent an underappreciated mechanism of cytoprotection. However, it remains to be demonstrated whether these metabolites themselves exert antioxidant effects or merely serve as markers of oxidative stress.

Gut and Microbiome

The study by Cheah et al. (2026) investigated whether ergothioneine is a significant source of trimethylamine-*N*-oxide (TMAO), a metabolite with a proven association with cardiometabolic and neurodegenerative diseases. Bioinformatic analyses revealed that the enzyme ergothionase—responsible for converting ergothioneine to trimethylamine (TMA)—is restricted to a few bacterial genera and is significantly less common than choline trimethylamine-lyase (TMA formation from choline). In a randomised, placebo-controlled human study, supplementation with 25 mg/day of ergothioneine over 7 days led to a significant increase in plasma ergothioneine concentrations *without* raising TMAO levels. In a cohort of heart failure patients, ergothioneine did not correlate with TMA or TMAO, whereas TMAO was clearly associated with TMA. The study provides no evidence that ergothioneine is a relevant source of TMAO and found no rise in TMAO in the context of microbial metabolism ⁵.

HYPOTHESIS The findings suggest that, despite its structural similarity to choline or carnitine, ergothioneine is *not* metabolised via the TMA/TMAO pathway. This is relevant because TMAO is associated with cardiovascular risks, whereas ergothioneine exhibits protective effects. The study addresses an important safety concern, though it remains unclear whether long-term ergothioneine supplementation influences microbiome composition.

Oncology

The observational study by Olsen et al. (2020) identified metabolites in the plasma of 3,236 participants from the Malmö Diet and Cancer Study that were associated with a health-conscious dietary pattern (HCFP). Five metabolites, including ergothioneine, were significantly linked to the HCFP ($p < 0.0004$).

Plausible: The study showed an inverse relationship between ergothioneine and cardiovascular events but provides no direct evidence regarding oncological endpoints. The association may be mediated by antioxidant or anti-inflammatory effects, though the design does not permit causal inferences (Olsen et al., 2020). What remains to be clarified is whether ergothioneine directly contributes to the observed health benefits or merely reflects other dietary or lifestyle factors.

HYPOTHESIS The inverse association between ergothioneine and mortality or cardiovascular diseases may indicate its role as an antioxidant and cytoprotective agent. Whether ergothioneine also exerts protective effects in oncology remains an open question, as the study did not examine specific cancer endpoints.

Overall Picture

Across multiple studies, ergothioneine consistently demonstrates evidence of bioavailability and antioxidant effects in preclinical and observational settings. Its absorption from dietary sources (e.g., mushrooms) is well-documented, and its accumulation in erythrocytes suggests targeted distribution within the body. Observational studies link higher ergothioneine levels to reduced risks of cardiovascular disease, mortality, and cognitive decline; however, *causal* evidence from interventional studies with clinically relevant endpoints is still lacking. Anti-inflammatory effects are primarily observed in *in vitro* models or as changes in inflammatory markers in acute human studies, while long-term data on chronic use in humans are still pending.

Evidence for a direct oncological or microbiome-modulating effect remains insufficiently investigated. While ergothioneine does not contribute to the formation of TMAO—a risk factor for cardiovascular disease—it remains unclear whether it influences microbiome composition in the long term. The role of ergothioneine as an antioxidant has been shown in multiple studies, though these often do not isolate its effects from other dietary components (e.g., mushroom compounds) or determine the optimal dosage for specific applications.

Methodology of the Evidence Base

["The available controlled human trials on ergothioneine (6 studies) encompass acute and chronic designs (6 hours to 16 weeks). Observational studies include large cohorts (up to 3,236 participants), and *in vitro* models are also represented. Typical endpoints include biomarkers for oxidative stress (ORAC, lipid peroxidation), inflammation (CRP, COX-2, iNOS), and cognitive function (RAVLT, PANAS-X). Systematic gaps exist in *long-term use* (beyond 16 weeks), *dose-response relationships* (usually only 1–2 dosages tested), and the *isolation of ergothioneine* (often administered as a mushroom extract). Additionally, studies with clinical endpoints (e.g., disease progression) and population-specific data (e.g., in pre-existing conditions) are lacking."]

Ergothioneine: An Antioxidant Without Clinical Proof of Efficacy?

The

DISCREPANCY BETWEEN BASIC RESEARCH AND CLINICAL EVIDENCE

is striking. While ergothioneine demonstrates strong **antioxidant** and **cytoprotective** effects in **cell cultures** and **animal models**, **blinded, placebo-controlled studies** with adequate sample sizes are lacking in humans. The few existing controlled studies are **pilot studies** with short intervention periods and small sample sizes. Even the most frequently cited study (2012) examines only **acute effects** after a single dose and provides no data on **long-term outcomes** or **clinically relevant endpoints**. **Review articles** emphasise the **therapeutic potential** but rely predominantly on **in vitro data** and **observational studies**, which cannot establish **proof of efficacy**.

A further issue is the

HETEROGENEITY OF THE STUDIES

. **Dosages** vary widely, and **routes of administration** (supplements vs. natural sources) are not standardised. **Bioavailability** from mushrooms is well-documented, but whether this applies to other sources remains unclear. Moreover, studies examining **clinical endpoints** such as **disease progression** or **quality of life** are lacking. Instead, **surrogate parameters** like **inflammatory markers** or **cognitive tests** are often measured, the **clinical relevance** of which is

questionable. Research in this area is still in its early stages: to draw robust conclusions, **long-term studies** with **hard endpoints** and **standardised dosages** would be necessary.

3. How Robust Is the Research?

Research on ergothioneine spans a substantial number of studies, including **basic research**, **observational studies**, and controlled trials. The applications in controlled studies focus on **metabolism**, **inflammation**, **fatigue**, **cognition**, and **antioxidant effects**. The most frequently cited works are review articles and mechanistic studies that highlight the **plausible therapeutic potential** of the compound. The six controlled human trials are predominantly pilot studies with small sample sizes, concentrating on **bioavailability**, **inflammatory markers**, and **cognitive parameters**.

The **methodological robustness** of the evidence base is limited. The few controlled human studies are **small**, **heterogeneous**, and often not blinded. The **most cited study (2012)** examines bioavailability from mushrooms and acute effects on **antioxidant capacity** and **inflammatory markers** but provides no long-term data. More recent studies (2025/2026) showed effects on **sleep quality**, **cognitive parameters**, and **metabolic parameters** in pilot designs, but these have not yet been cited and thus lack independent replication. **Observational studies** show associations between ergothioneine plasma levels and **ageing processes** or **neurodegenerative diseases** but cannot establish **causality**. Basic research provides robust data on **cellular uptake** and **antioxidant mechanisms**, yet the translation into clinical application remains outstanding.

4. Common Claims — and What the Data Show

CLAIM	EVIDENCE
Ergothioneine has been investigated for the prevention of oxidative stress and ageing; controlled results are inconsistent.	Observational studies demonstrate an association between higher plasma levels and reduced cognitive ageing , yet controlled studies are lacking. Whether erg
Ergothioneine has been studied for improving cognitive performance; the results are inconsistent.	Three controlled studies examine cognitive parameters , including two recent (2026) investigations into fungal interventions . The findings are preliminary and
Ergothioneine has been examined for anti-inflammatory effects; the results are inconsistent.	Four controlled studies examine inflammatory markers , including a pilot study (2021) on metabolic syndrome . The data are heterogeneous and do not allow fi
Ergothioneine has been tested for safety in small studies; long-term data are lacking.	Safety has been assessed in small-scale studies, but long-term data are still pending. One study (2026) examines the association with TMAO , a potentially ha

5. Profile: Molecule and Charge

Ergothioneine 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, which are the focus of the next section.

6. Charge, Electrons, Radicals

Ergothioneine exhibits electrochemical properties as a radical scavenger and chelator. In laboratory studies, regulation of the Nrf2 signalling pathway, which controls antioxidant defence mechanisms, has been demonstrated ^{11 22}. Direct measurements of electron transfer or cation exchange capacity in humans are not available.

No electrochemical parameters such as charge state or redox potential of ergothioneine have been directly determined in humans to date. The described effects are based on cell and tissue studies. These include the reduction of mitochondrial ROS (mROS) ^{20 21}, stabilisation of the mitochondrial membrane potential ($\Delta\Psi_m$) ^{20 21}, and inhibition of pro-inflammatory cytokines (TNF- α , IL-1 β , IL-6) ²². Animal or tissue models show activation of antioxidant enzymes such as superoxide dismutase (SOD). Whether these effects result from direct electron transfer or indirect signal modulation remains to be investigated.

7. Interactions with Other Substances

Substances from this platform that have been **jointly** investigated or discussed with ergothioneine in human studies and review articles — whether in combination, comparison, or shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	STUDIES FEATURING BOTH	OF WHICH CONTROLLED IN HUMANS
Stress, cortisol and inflammation	38	2
Chronic inflammation	34	4
NAC and glutathione	12	0
Gut microbiome	10	1
L-Carnitine	9	0
Iron	7	0
Beta-glucans	4	0
Betaine (trimethylglycine)	4	0
Hericium (lion's mane)	3	0
Selenium	3	0

Data on interactions between ergothioneine and pharmaceuticals or nutrients are limited. In cell cultures, synergistic effects with other antioxidants have been observed, such as when combined with neuronal induction media or glutathione-like compounds, suggesting an enhancement of antioxidant capacity ²⁸. A study in human cells indicates that ergothioneine acts intracellularly and does not interact through direct binding to external substances like 7-ketocholesterol (7KC) ²³. The biosynthesis of ergothioneine occurs via enzymatic reactions, including a PLP-dependent C-S-lyase (EgtE), which transfers sulphur from cysteine to histidine ^{25 27}. Whether these enzymes (e.g., CYP enzymes) are influenced by ergothioneine is not described. The absorption of ergothioneine from foods such as mushrooms (*Agaricus bisporus*) has been examined in controlled human studies, confirming its bioavailability ¹.

Combinations of ergothioneine with other active compounds have been evaluated in preclinical models. In cell cultures and animal studies, enhanced protective effects against UVB-induced skin damage were observed when used in conjunction with Guang Chenpi extract or polydeoxyribonucleotide (PDRN) ²⁶. Another study suggests potential synergistic effects with physical activity, such as promoting cognitive resilience in ageing, though without mechanistic clarification ²⁴. Interactions with the microbiome or the oxidation of trimethylamine (TMA) to TMAO have been discussed in review articles, albeit without direct reference to ergothioneine. Whether ergothioneine influences the pharmacokinetics of other substances (e.g., through enzyme induction or inhibition) remains to be investigated. Data on binding affinities or interactions with specific medications are lacking.

8. Overdose, Tolerability, and Limitations

Data on the toxicity and upper limits of ergothioneine are available from subchronic toxicity studies. A *No Observed Adverse Effect Level* (NOAEL) of 800 mg/kg body weight per day was determined ²⁹. Safety assessments using the *Margin of Exposure* (MOE) consistently showed values above the threshold of 300, with fewer than 0.3% of the general population and 1.3% of children aged 3 to 6 years falling below this level ²⁹. Natural dietary exposure in China was classified as safe, with no indications of risk ²⁹. Review articles reported no safety concerns with supplementation of up to 25 mg/day ³⁰. Animal studies (zebrafish) demonstrated low toxicity at concentrations of ≤ 0.63 mg/mL.

No adverse effects or contraindications have been documented in the available studies. Ergothioneine exhibited protective effects against doxorubicin-induced cardiotoxicity in mouse models without promoting tumour growth or impairing chemotherapy efficacy^{19,19}. Observations in humans suggest a potential role in neuroinflammatory processes, with no toxic effects reported¹². Long-term data, interactions with medications, and dose-dependent effects in various populations remain to be examined.

9. The Most Robust Studies

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

Controlled Human Studies

- ¹ The bioavailability of ergothioneine from mushrooms (*Agaricus bisporus*) and the acute effects on antioxidant capacity and biomarkers of inflammation (2012)
- ² Ergothioneine supplementation in people with metabolic syndrome (ErgMS): protocol for a randomised, double-blind, placebo-controlled pilot study (2021)
- ³ Estimation and Validation of an Effective Ergothioneine Dose for Improved Sleep Quality Using Physiologically Based Pharmacokinetic Model (2025)
- A randomised controlled study to investigate the cognitive, mood, metabolic and anti-inflammatory effects of chronic oyster mushroom intervention in healthy adults (2026)
- ⁴ A randomised controlled study to investigate the cognitive, mood, metabolic and anti-inflammatory effects of acute oyster mushroom intervention in healthy adults (2026)
- ⁵ Is Ergothioneine an Important Source of Plasma Trimethylamine *N*-Oxide in Humans? (2026)

Observational Human Studies

- ⁶ The biology of ergothioneine, an antioxidant nutraceutical (2020)
- ⁷ Administration of Pure Ergothioneine to Healthy Human Subjects: Uptake, Metabolism, and Effects on Biomarkers of Oxidative Damage and Inflammation (2017)
- ⁸ Ergothioneine is associated with reduced mortality and decreased risk of cardiovascular disease (2020)
- ⁹ Whole-blood metabolomics of dementia patients reveal classes of disease-linked metabolites (2021)
- ¹⁰ An uncommon redox behaviour sheds light on the cellular antioxidant properties of ergothioneine (2015)
- ¹¹ Ergothioneine: an underrecognised dietary micronutrient required for healthy ageing? (2023)
- ¹² Effect of Ergothioneine on 7-Ketocholesterol-Induced Endothelial Injury (2021)
- ¹³ Could Ergothioneine Aid in the Treatment of Coronavirus Patients? (2020)
- Plasma protein thiols: an early marker of oxidative stress in asthma and chronic obstructive pulmonary disease (2016)
- ¹⁴ Low Plasma Ergothioneine Predicts Cognitive and Functional Decline in an Elderly Cohort Attending Memory Clinics (2022)
- ¹⁵ Ergothioneine and its prospects as an anti-ageing compound (2022)
- ¹⁶ Clinical and biochemical correlates of serum L-ergothioneine concentrations in community-dwelling middle-aged and older adults (2014)
- Reflections of an ageing free radical (2020)
- Repeated double cross-validation applied to the PCA-LDA classification of SERS spectra: a case study with serum samples from hepatocellular carcinoma (2021)
- Trimethylamine *N*-Oxide (TMAO) Impairs Purinergic-Induced Intracellular Calcium Increase and Nitric Oxide Release in Endothelial Cells (2022)
- ¹⁷ Multiomics analysis to explore blood metabolite biomarkers in an Alzheimer's Disease Neuroimaging Initiative cohort (2024)
- ¹⁸ Mushroom intake and cognitive performance among US older adults: the National Health and Nutrition Examination Survey, 2011–2014 (2022)
- ¹⁹ Protection against Doxorubicin-Induced Cardiotoxicity by Ergothioneine (2023)

10. Summary

Ergothioneine is a well-documented antioxidant with established bioavailability from dietary sources, particularly mushrooms. Its uptake via the specific transporter OCTN1 and accumulation in tissues under high oxidative stress are shown in studies. Observational studies show associations between higher ergothioneine levels and markers linked to reduced risk for cardiovascular disease, mortality, and cognitive decline, though causality is not established. Acute human studies suggest inflammation-modulating effects, such as reductions in markers like NADPH oxidase 2 or iNOS. Safety in the context of microbial metabolism has been shown in studies, as ergothioneine does not contribute to the formation of the risk metabolite TMAO.

HYPOTHESIS The consistent evidence of antioxidant and inflammation-modulating effects suggests that ergothioneine may play a protective role in the prevention of oxidative stress and neurodegenerative diseases. The observed improvements in cognitive parameters and sleep quality could indicate a neuroprotective effect. However, it remains unclear whether these effects are directly attributable to ergothioneine or mediated by synergistic interactions with other mushroom constituents. The formation of specific oxidation products, such as ergothioneine sulphonate (ESO₃H), may represent an underappreciated mechanism of cytoprotection, though its biological relevance has yet to be clarified.

To confirm the clinical relevance of ergothioneine, controlled long-term studies with clinical endpoints are required. These should determine the optimal dosage for specific applications such as inflammation, cognition, or oxidative stress, and compare the effects of isolated ergothioneine versus mushroom extracts. Additionally, population-specific data should be collected, for example, in patients with pre-existing conditions such as metabolic syndrome or neurodegenerative diseases. Clarifying the dose-response relationship and isolating the effects of ergothioneine from other dietary components remain key open questions.

11. Open Questions

- **Long-term effects:** Whether ergothioneine exerts **clinically relevant** effects on **metabolism**, **inflammation**, or **cognition** over months or years remains unresolved. **Blinded long-term studies** with **hard endpoints** are needed.
- **Dosage and bioavailability:** The optimal **intake amount** and **source** (dietary vs. supplement) are unclear. Studies with **standardised dosages** and **comparable routes of administration** are lacking.
- **Clinical endpoints:** Whether ergothioneine influences **disease progression** (e.g., **neurodegeneration**, **cardiovascular disease**) has never been systematically investigated. **Interventional studies** with **clinically relevant parameters** would be necessary here.

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 ergothioneine be recommended as a dietary supplement?

The **evidence base** is insufficient to support a **recommendation**. Existing controlled studies are **pilot studies** with small sample sizes and short intervention periods. They show **no clinically relevant effects** but instead examine **surrogate parameters** such as **inflammatory markers** or **cognitive tests**. A **generalisable conclusion** regarding efficacy cannot be drawn. Furthermore, **long-term safety data** are lacking.

Are there differences between ergothioneine derived from mushrooms and synthetic preparations?

The **bioavailability** of ergothioneine from mushrooms (*Agaricus bisporus*) is well documented, whereas data on **synthetic preparations** are lacking. A 2012 study demonstrated that ergothioneine from mushrooms **acutely** increases **antioxidant capacity**, but whether this applies to **supplements** has not been investigated. **Dosage** and **absorption** may differ, complicating the **comparability** of studies.

What role does the OCTN1 transporter play in the effects of ergothioneine?

The **OCTN1 transporter** is critical for the **uptake** and **tissue distribution** of ergothioneine. It facilitates **accumulation** in cells under high oxidative stress, such as those in the **liver**, **kidney**, and **brain**. Genetic variants of the transporter may influence **individual efficacy**, but this has not been systematically examined in **clinical trials**. **Basic research** indicates that OCTN1 is essential for the **cytoprotective effect**, yet the **clinical benefit** remains unclear.

Sources

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