



DOSSIER · SUBSTANCE

Spermidine

Spermidine is a polyamine produced by the body itself and found in foods such as wheat germ; human studies show mainly marker effects, mostly in small groups.

444

STUDIES IN
TOTAL

87

IN HUMANS

9

OF WHICH
CONTROLLED

76

IN ANIMALS

50

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

Spermidine at a Glance

In a small placebo-controlled pilot study in older adults, oral spermidine lowered aging markers in immune cells, especially in people with a weak vaccine response ³⁴.

A combination product of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide lowered cholesterol and fasting blood glucose compared with placebo; the contribution of spermidine to this is unclear ¹. High-dose pure spermidine trihydrochloride did not change clinical and laboratory values compared with placebo in older men ⁵.

We evaluated 30 human studies on Spermidine, including 7 randomised controlled trials and 0 meta-analyses or systematic reviews; the controlled studies include 234 participants in total. As of 13 October 2026.

1. What Is Spermidine? Occurrence, Origin and Forms

Spermidine is a polyamine, a substance that occurs in the cells of humans, animals and plants. The body produces it itself and also takes it in through food. Spermidine is best known as a component of wheat germ, aged cheese, soy, mushrooms and legumes; in research it is studied in connection with cellular self-cleaning (autophagy) and with aging.

Spermidine occurs in almost all living cells, in the human body as well as in foods of plant and animal origin. Among the best-known sources are wheat germ, aged cheese, fermented soy products and mushrooms.

For preparations, spermidine is either obtained from wheat germ or produced chemically and supplied as spermidine trihydrochloride. Studies mainly examine wheat germ extracts, pure spermidine trihydrochloride and spermidine-rich diets.

Forms and Preparations Studied

- Wheat germ extract
- Pure spermidine trihydrochloride
- Spermidine-rich diet
- Fermented foods as a spermidine source (e.g. aged cheese, natto)
- Mixtures with further polyamines (e.g. spermine, putrescine)

Not covered on this page:

- Other polyamines such as spermine and putrescine when they are studied as substances in their own right
- Medicinal substances that influence or inhibit polyamine metabolism (e.g. eflornithine)
- Spermidine as a laboratory reagent in cell-culture experiments
- Foods and preparations in which other ingredients, not the spermidine content, are the subject

2. What Does Spermidine Do? Results by Area

AREA	RESULT IN CONTROLLED STUDIES	STRENGTH OF EVIDENCE	STUDIES	PARTICIPANTS
Biological aging	mixed	low	0 meta-analyses · 2 controlled · 8 other	52
Cognition and memory	mixed	unclear	0 meta-analyses · 1 controlled · 4 other	12
Heart and circulation	mixed	unclear	0 meta-analyses · 1 controlled · 3 other	12
Muscles and physical performance	mixed	unclear	0 meta-analyses · 1 controlled · 0 other	5
Metabolism	mixed	unclear	0 meta-analyses · 1 controlled · 3 other	5
Other investigations	mostly no difference	low	0 meta-analyses · 2 controlled · 7 other	77

How to read the table: counted are human studies whose results concern the area. "High" means at least one meta-analysis and two controlled studies showing improvement, or at least three controlled studies of which three quarters show improvement, with at least 300 participants in total. "Moderate" means at least two controlled studies showing improvement, as a majority, or one meta-analysis alongside controlled studies. "Low" means one controlled study showing improvement. Where an area has no controlled study, the strength of evidence is at most "low" (result "reviews only" or "observational data only"). Everything else is "unclear". A study counts as showing improvement when at least half of its outcomes in this area improved. Reviews of combination products do not count as meta-analyses; results that only describe side effects or shares of users do not count as an effect. The same study is counted only once.

3. What the Studies Show in Detail

Spermidine and Biological Aging: Human Studies

In a placebo-controlled pilot study in older adults, oral spermidine lowered ageing markers in immune cells such as p16 and DNA damage, especially in those with a weak vaccine response ³⁴. A randomised placebo-controlled study with a mixture of AM3, spermidine and hesperidin lowered the biological age measured by immune functions ². A small pilot study without a placebo group compared two amounts of spermidine from rice germ extract; only the higher amount increased autophagy markers compared with baseline ⁶. The strength of evidence is low: the studies are small and short, and some of the findings come from combination preparations with AM3 and hesperidin, so the effect cannot be attributed to spermidine alone ². Observational data on spermidine intake through the diet must be considered separately from these intervention findings and do not allow a statement about effects.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
³ Alsaleh et al. 2026	randomised controlled · 40 participants	oral spermidine, 6 mg daily; 6 mg daily; 13 weeks; vs. placebo, double-blind, randomised
⁶ Bruno et al. 2025	randomised controlled · 12 participants	Miricell™ rice germ extract (Nutraland USA); 1.5 mg or 3.3 mg spermidine daily; 56 days (assessed at week 0 and 8)
¹¹ Kaminsky et al. 2024	cross-sectional study · 432,682 participants	endogenous erythrocyte spermidine (no preparation administered); vs. younger vs. older; deceased vs. living cohorts
²¹ Hofer et al. 2024	study	Fasting/caloric restriction; genetic or pharmacological polyamine blockade; vs. Fasting versus control; intact versus impaired
²² Mackert et al. 2024	case series	spermidine supplementation; three weeks
²³ Mafe et al. 2026	review	Narrative review of dietary and microbiota-derived polyamines
²⁵ Rzeski et al. 2026	review	Spermidine from wheat germ and fermented foods
²⁶ Murillo-Cancho et al. 2025	review	Caloric restriction, intermittent fasting, CR-mimetics incl. spermidine; vs. Comparison of modalities (CR, IF, CR-mimetics)

Further studies in this area: ²⁷ ²⁸

Spermidine, Cognition and Memory: Human Studies

A pilot study in twelve healthy people compared two amounts of spermidine from rice germ extract without a placebo group; with the higher amount, the nerve growth factor BDNF increased compared with baseline ⁶. The strength of evidence is low: it is a single, very small study without independent confirmation, and BDNF is a laboratory value, not a measured memory test. Observational data on a spermidine-rich diet, which also includes spermine and putrescine, point in a more favorable direction, but concern overall intake through the diet and cannot be read as the effect of spermidine alone ¹³. A cross-sectional study with plasma spermidine levels without supplementation even reports less favorable values for hippocampal volume and cortical thickness ¹⁶; such differences in levels are not equivalent to intake through preparations. Whether spermidine intake via rice germ extract, pure spermidine or the diet actually improves memory still needs to be clarified.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
⁶ Bruno et al. 2025	randomised controlled · 12 participants	Miricell™ rice germ extract (Nutraland USA); 1.5 mg or 3.3 mg spermidine daily; 56 days (assessed at week 0 and 8); vs. placebo
¹³ Qian et al. 2024	cohort study · 77,092 participants	dietary polyamines including spermidine; intake in quintiles, no dose given; median follow-up 12 years; vs. highest vs. lowest intake

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
¹⁶ Wortha et al. 2023	cross-sectional study · 659 participants	spermidine plasma levels (no intervention); vs. higher versus lower spermidine plasma levels
¹⁹ Zhao et al. 2026	case-control study	none; measurement of fecal spermidine and microbiome; vs. Alzheimer's patients versus controls
²⁸ Varghese et al. 2020	review	Mediterranean/Okinawan diet containing spermidine and other bioactives

Spermidine, Heart and Circulation: Human Studies

For pure spermidine, there is no placebo-controlled study in this area; the small studies available mainly tested combination preparations. A randomised controlled study with a combination preparation of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide showed an improvement in cholesterol levels in overweight older adults ¹. A pilot study in five young men found, after taking a preparation with the same four substances, lower inflammation and radical formation by phagocytes that were treated with their blood plasma ⁸. A non-randomised controlled study with a mixture of trehalose, spermidine, nicotinamide and polyphenols found no difference in blood pressure, but better vascular function ¹⁰. A pilot study without a placebo group compared two amounts of spermidine from rice germ extract; with the higher amount, hs-CRP, VLDL and triglycerides fell compared with baseline ⁶. The strength of evidence is unclear: the studies are small, some not randomised, and three of four investigated combination preparations, so the findings cannot be attributed to spermidine alone. Observational data on the diet with the dietary polyamines spermidine, spermine and putrescine point to a lower risk of cardiovascular disease, but measure intake differently from intervention studies and do not allow proof of an effect ¹². What remains open is the effect of pure spermidine, the suitable form and amount, and long-term effects.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
⁶ Bruno et al. 2025	randomised controlled · 12 participants	Miricell™ rice germ extract (Nutraland USA); 1.5 mg or 3.3 mg spermidine daily; 56 days (assessed at week 0 and 8); vs. C
¹² Han et al. 2024	cohort study · 184,732 participants	dietary polyamines (spermidine, spermine, putrescine) from diet; quintiles: Q1 ≤17.4 mg/day to Q5 >33.5 mg/day; median f
¹⁷ Luo et al. 2026	cross-sectional study · 193 participants	Serum spermidine level (no preparation administered); vs. patients with vs. without vascular calcification
²¹ Hofer et al. 2024	study	Fasting/caloric restriction; genetic or pharmacological polyamine blockade; vs. Fasting versus control; intact versus pertur

Spermidine, Muscles and Physical Performance: Human Studies

A small crossover study in five endurance athletes found, after taking a mixture of trehalose, spermidine, nicotinamide and polyphenols, lower muscle damage markers compared with baseline ⁹. The strength of evidence is low: it is a single, non-randomized study with a very small number of participants, which moreover investigated a combination product of trehalose, spermidine, nicotinamide and polyphenols ⁹. Whether pure spermidine or a spermidine-rich diet influences muscles and performance and how longer intake acts still needs to be clarified.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON	RESU
⁹ D'Amico et al. 2023	controlled · 5 participants	Experimental mixture of trehalose, spermidine, nicotinamide, polyphenols; 10.5 g daily; 30 days; vs. No treatment (crossover)	Musc

Spermidine and Metabolism: Human Studies

In this area, only small studies on combination preparations are available, in which spermidine was combined with other substances. A randomised controlled study in overweight older adults with elevated HbA1c found an improvement in fasting glucose for a combination preparation of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide ¹. A pilot study in five endurance athletes found, for a mixture of spermidine, trehalose, nicotinamide and polyphenols, less oxidative stress and more favourable autophagy markers compared with baseline ⁹. The strength of evidence is unclear: the participant numbers are very small, two of the three studies were not randomised, and no finding can be attributed to spermidine alone, since all the

preparations investigated were mixtures. Observational data on serum spermidine concentration point to associations with insulin resistance and body weight, but are not evidence of an effect of spermidine administration ¹⁴¹⁵. What remains open is whether pure spermidine or spermidine from rice germ extract influences metabolism in humans.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
⁹ D'Amico et al. 2023	controlled · 5 participants	Experimental mixture of trehalose, spermidine, nicotinamide, polyphenols; 10.5 g daily; 30 days; vs. No treatment (cross-over)
¹⁴ Zhang et al. 2022	cross-sectional study · 4,336 participants	Serum spermidine (endogenous/dietary, not administered); vs. Quintiles of serum SPD levels
¹⁵ Gao et al. 2022	cohort study · 4,230 participants	Serum spermidine measured by HPLC with fluorescence detector; 2-year follow-up; vs. Serum spermidine quartiles; or
²⁶ Murillo-Cancho et al. 2025	review	Caloric restriction, intermittent fasting, CR-mimetics incl. spermidine; vs. Comparison of modalities (CR, IF, CR-mimetic)

Spermidine: Further Outcomes in Studies

In a placebo-controlled pilot study in older adults, oral spermidine strengthened the antibody and memory B cell response after the third SARS-CoV-2 vaccination in people with a weak vaccine response ³⁴. A randomised controlled study with a combination preparation of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide found better appetite and satiety perception as well as less abdominal pain and bloating ¹; another randomised controlled study with a mixture of AM3, spermidine and hesperidin reported better immune function and a more favourable oxidative-inflammatory state ². A non-randomised controlled study with a mixture of trehalose, spermidine, nicotinamide and polyphenols showed a reduction in oxidative stress and an increase in autophagy markers in adults with grade 1 hypertension ¹⁰. High-dose pure spermidine trihydrochloride did not change clinical, blood lipid and blood count values in a randomised placebo-controlled study in older men and was well tolerated ⁵. In a randomised placebo-controlled crossover study, spermidine did not increase the spermidine level in plasma, but the spermine level ⁷. The strength of evidence is low: mainly small groups and some combination preparations, whose findings cannot be attributed to spermidine alone. Pure spermidine and combination preparations with other active substances were investigated; what remains open are effects in larger groups, over longer periods and for a spermidine-rich diet.

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
³ Alsaleh et al. 2026	randomised controlled · 40 participants	oral spermidine, 6 mg daily; 6 mg daily; 13 weeks; vs. placebo, double-blind, randomised
⁵ Keohane et al. 2024	randomised controlled · 37 participants	high-purity spermidine trihydrochloride (hpSPD); 40 mg/day; 7 and 28 days; vs. placebo, double-blind, randomized
¹² Han et al. 2024	cohort study · 184,732 participants	dietary polyamines (spermidine, spermine, putrescine) from diet; quintiles: Q1 ≤17.4 mg/day to Q5 >33.5 mg/day; median
¹⁸ León-Letelier et al. 2025	cross-sectional study · 125 participants	none; measurement of polyamines in cystic fluid and tissue; vs. low-grade IPMN vs high-grade IPMN or IPMN/PDAC; CA
²⁰ Díaz-Osorio et al. 2025	case series	Spermidine, a natural polyamine acting as autophagy inducer; vs. Gender/age-matched controls for fibroblast cultures; r
²¹ Hofer et al. 2024	study	Fasting/caloric restriction; genetic or pharmacological polyamine blockade; vs. Fasting versus control; intact versus pert
²² Mackert et al. 2024	case series	spermidine supplementation; three weeks

STUDY	DESIGN · PARTICIPANTS	PREPARATION · DOSE · DURATION · COMPARISON
²³ Mafe et al. 2026	review	Narrative review of dietary and microbiota-derived polyamines

Further studies in this area: ²⁶

4. How Is Spermidine Dosed? Preparation, Dose and Duration in Studies

Studies investigated pure spermidine as a dietary supplement, spermidine from rice germ extract and combination products with other active substances such as nicotinamide, trehalose or hesperidin. The amount taken differed clearly between the studies; details are shown in the table.

PREPARATION OR FORM	DOSE	DURATION	STUDY
Mimio fasting mimetic capsule (spermidine, nicotinamide, PEA, OEA)	—	8 weeks (daily before first meal)	¹
AM3 150 mg, spermidine 0.6 mg, hesperidin 50 mg	two capsules daily	2 months	²
oral spermidine, 6 mg daily	6 mg daily	13 weeks	³
high-purity spermidine trihydrochloride (hpSPD)	40 mg/day	7 and 28 days	⁵
Miricell™ rice germ extract (Nutralland USA)	1.5 mg or 3.3 mg spermidine daily	56 days (assessed at week 0 and 8)	⁶
oral spermidine supplement	15 mg/d	two 5-day phases, 9-day washout	⁷
Fasting mimetic supplement with spermidine, nicotinamide, PEA, OEA	low, medium or high dose	blood sampling up to 4 hours after intake	⁸
Experimental mixture of trehalose, spermidine, nicotinamide, polyphenols	10.5 g daily	30 days	⁹
Mixture of trehalose, spermidine, nicotinamide, and polyphenols	—	two months	¹⁰

5. Is Spermidine Safe? Side Effects in Studies

Pure spermidine was well tolerated in two small placebo-controlled studies; in the study with high-dose spermidine trihydrochloride, no product-related adverse events occurred ³⁵. A combination product of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide did not differ from placebo in side effects ¹; spermidine from rice germ extract showed unremarkable safety values in a small pilot study ⁶.

STUDY	REPORTED SIDE EFFECTS
¹ Grant et al. 2026	no significant differences in adverse effects
³ Alsaleh et al. 2026	well tolerated
⁵ Keohane et al. 2024	no study product-related adverse events
⁶ Bruno et al. 2025	Good safety profile; clinical chemistry, CBC, vital signs, adverse events unremarkable
²² Mackert et al. 2024	well tolerated
²⁴ Lugart et al. 2026	Deleterious effects of excess exposure discussed
²⁵ Rzeski et al. 2026	Bioavailability, safety and regulatory considerations discussed
²⁶ Murillo-Cancho et al. 2025	Long-term safety in healthy populations incompletely defined

6. What Remains Open: Limits of the Evidence

- A large part of the findings comes from combination products, so the contribution of spermidine alone remains unclear.
- The study duration is predominantly short; long-term studies are still pending.
- There are so far only a few small studies on pure spermidine and on spermidine from rice germ extract.
- Observational data on diet measure intake differently from intervention studies and do not allow proof of an effect.

7. Bottom Line: What Is Established About Spermidine

Spermidine is a polyamine that the body produces itself and takes in through the diet. Human studies mainly investigated pure spermidine, spermidine from rice germ extract and combination preparations. In a placebo-controlled pilot study, pure spermidine lowered ageing markers in immune cells and strengthened the vaccine response in poorly responding older people ³⁴; in another study it did not change routine clinical values ⁵.

The overall strength of evidence is low. Many findings come from combination preparations with other active substances and cannot be attributed to spermidine alone ¹. Observational data on a polyamine-rich diet point to a lower mortality and cardiovascular risk, but do not prove an effect ¹². Pure spermidine was well tolerated in the small placebo-controlled studies ³⁵.

Frequently Asked Questions

How well has Spermidine been studied in humans?

We evaluated 30 human studies on Spermidine, including 7 randomised controlled trials and 0 meta-analyses or systematic reviews; the controlled studies include 234 participants in total. As of 13 October 2026.

Does Spermidine help with biological aging? What the studies show

We evaluated 2 controlled studies and 8 further studies; the controlled studies include 52 participants in total. Result of the controlled studies: mixed. Strength of evidence under our published rules: low. Sources: ³⁶¹¹²¹

Does Spermidine help with cognition and memory? What the studies show

We evaluated one controlled study and 4 further studies; the controlled studies include 12 participants in total. Result of the controlled studies: mixed. Strength of evidence under our published rules: unclear. Sources: ⁶¹³¹⁶¹⁹

Does Spermidine help with heart and circulation? What the studies show

We evaluated one controlled study and 3 further studies; the controlled studies include 12 participants in total. Result of the controlled studies: mixed. Strength of evidence under our published rules: unclear. Sources: ⁶¹²¹⁷²¹

Does Spermidine help with muscles and physical performance? What the studies show

We evaluated one controlled study; the controlled studies include 5 participants in total. Result of the controlled studies: mixed. Strength of evidence under our published rules: unclear. Sources: ⁹

Does Spermidine help with metabolism? What the studies show

We evaluated one controlled study and 3 further studies; the controlled studies include 5 participants in total. Result of the controlled studies: mixed. Strength of evidence under our published rules: unclear. Sources: ⁹¹⁴¹⁵²⁶

What is spermidine and where does it occur?

Spermidine is a polyamine that occurs in the cells of humans, animals and plants. The body produces it itself and also takes it in through the diet. Known sources are wheat germ, aged cheese, soy, mushrooms and legumes.

Which forms of spermidine were investigated in human studies?

Studies investigated pure spermidine as an oral product ³⁴, spermidine from rice germ extract ⁶ and combination products, for example with trehalose, nicotinamide and polyphenols ¹⁰. Observational studies, by contrast, recorded intake through the diet ¹². The form and the amount taken differed between the studies.

Do studies show an effect on aging?

In a small placebo-controlled pilot study in older adults, oral spermidine lowered aging markers in immune cells, especially in people with a weak vaccine response ³⁴.

How safe is taking spermidine?

Pure spermidine was well tolerated in two small placebo-controlled studies; in the study with high-dose spermidine trihydrochloride, no product-related adverse events occurred ³⁵. A combination product of spermidine, nicotinamide, palmitoylethanolamide and oleoylethanolamide did not differ from placebo in side effects ¹; spermidine from rice germ extract showed unremarkable safety values in a small pilot study ⁶. A review points out that data on long-term safety in healthy people are still pending ²⁶.

What should be considered regarding the study results?

Many findings come from combination products in which spermidine was combined with other substances, and cannot be attributed to spermidine alone ¹. The number of participants is mostly small and the study duration short. Observational data on diet measure intake differently from intervention studies and do not allow proof of an effect ¹².

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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.
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