



DOSSIER · SUBSTANCE

Lycopene

Lycopene is one of the most intensively researched carotenoids. However, the literature stems predominantly from animal, basic-research and cell studies. Notably, the most frequently cited controlled studies rarely test lycopene as a pure substance against placebo, but instead compare it with or combine it with other substances.

779

STUDIES IN
TOTAL

141

IN HUMANS

39

OF WHICH
CONTROLLED

284

IN ANIMALS

75

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

Lycopene at a Glance

ORIGIN:

Lycopene is a carotenoid, a fat-soluble plant pigment found in tomatoes and other carotenoid-rich vegetables. Unlike β -carotene, it is not a precursor of vitamin A. It is investigated as a component of the diet, as an isolated supplement, as a fortified food and as an adjunct to an existing therapy.

EVIDENCE BASE:

779 evaluated papers · 39 controlled human studies · 102 observational studies · 57 review articles · 284 animal studies · 52 cell-culture studies

STRONGEST EVIDENCE:

- **Proven:** Oral mucosa — the 2020 review on oral submucous fibrosis pools 1,181 participants; lycopene was tested there predominantly against curcumin.
- **Proven:** Prostate — two reviews on prostate-specific antigen (2021, 2022); one finds no effect of lycopene on PSA in non-metastatic prostate cancer.
- **Showed:** Vascular function — a 2026 review with meta-analysis examines lycopene-containing products and endothelial function in healthy adults.
- **Showed:** Male fertility — randomised, placebo-controlled studies on semen parameters and oxidative stress in seminal plasma of infertile men measure markers, not live birth.
- **Showed:** Mobility — the 2021 Framingham analysis (2,452 participants) links total carotenoid intake with smaller loss of muscle strength and gait speed, not lycopene alone.

LIMITATIONS:

- **Open question:** The most-cited controlled studies rarely test lycopene alone against placebo; a between-group difference can be shown, yet cannot readily be attributed to lycopene.
- **Open question:** Emphasis lies on oxidative status and metabolic markers, not on disease courses; mechanistic and preclinical work predominates in oncology.
- **Open question:** It remains open to what extent the radical-neutralising effect described preclinically becomes measurable in humans.

CLASSIFICATION:

Lycopene is among the most intensively researched carotenoids, yet is seldom tested in humans as a pure substance against placebo.

1. What Lycopene Is

Lycopene is a **carotenoid**, a fat-soluble plant pigment found in tomatoes and other carotenoid-rich vegetables. Within this group it occupies a special position: unlike β -carotene, it is not a precursor of vitamin A. These forms address different questions and are kept separate here. β -carotene, lutein and zeaxanthin are also covered within the same substance group, each with its own endpoints, for example at the eye. Part of the literature originates from agricultural and environmental research and does not concern human application.

For the appraisal of all studies it is decisive how lycopene is absorbed and measured. Intake is estimated via dietary questionnaires or captured as blood levels; both routes record different things. The Framingham analysis refers to total carotenoid intake, not to lycopene alone. Added to this is the diversity of forms: isolated supplements, Lactolycopene, lycopene-enriched ice cream, carotenoid-rich vegetables and lycopene as an add-on to ongoing treatment have all been tested. **Plausible:** That absorption differs according to matrix is already suggested by the fact that bioavailability is pursued as a separate research field. The predominant endpoints are markers in blood or seminal plasma, less often clinical endpoints.

2. How Robust the Research Is

Research is distributed unevenly. Animal studies and basic-research papers form the largest group, followed by cell-culture work and studies on human cells as well as a block of environmental and agricultural investigations. In humans, observational studies predominate; controlled studies exist but are clearly in the minority. Content-wise, antioxidant questions dominate, followed by metabolism, fatigue, safety and oncology. Cardiovascular, inflammation, immune system, bioavailability and skin appear with single studies. The emphasis therefore lies on oxidative status and metabolic markers, not on disease courses.

The methodological spectrum is broad. Randomised, double-blind, placebo-controlled studies stand alongside small pilot studies, observational cohorts and mechanistic reviews. **Proven:** For statements about humans the controlled studies carry the main weight. Several of them test lycopene against another substance rather than against placebo or as an add-on to ongoing treatment; a between-group difference can then be shown, yet cannot readily be attributed to lycopene. Other studies form part of larger cohorts with a broader scope, for example on total carotenoid intake. Mechanistic and preclinical work predominates in oncology. What must be clarified first is the contribution of the single substance in a design that tests it alone.

Distribution of **controlled human studies** by application area — the figures are not additive, as one study may be assigned to several areas:

APPLICATION AREA	CONTROLLED STUDIES
Oxidative stress	19
Metabolism	11
Fatigue and stress	9

APPLICATION AREA	CONTROLLED STUDIES
Safety and tolerability	9
Oncology	8
Heart and circulation	7
Inflammatory processes	4
Immune system	3

Attribution to the single substance is the open flank

The most-cited controlled studies do not usually test lycopene alone. Two widely noted papers on oral submucous fibrosis compare lycopene with curcumin, one Phase-II study combines lycopene with docetaxel, another examines an antioxidant treatment as a whole, and the Framingham analysis refers to total carotenoid intake. Such designs yield a between-group difference, but no statement about lycopene as a single substance. This is the most important point when reading this literature.

The field is cleanest where lycopene is tested against placebo. Studies on the spermogram and oxidative stress in seminal plasma in infertile men as well as a study on healthy men follow this design. However, they measure semen parameters and markers, not the birth of a child.

HYPOTHESIS:

If an effect appears, then first on such markers. Whether it is reflected in the clinical course is not decided by this.

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

STATEMENT	STUDY SITUATION
Prostate cancer	The literature is predominantly mechanistic and preclinical. In humans, lycopene was tested in a phase II study in combination with docetaxel. This says nothing
Male fertility	There are randomised, placebo-controlled studies on spermogram and oxidative stress in seminal plasma. Markers are measured, not pregnancy rates.
Oral mucosal changes	Randomised studies exist on oral submucous fibrosis, lichen planus and xerostomia, partly in comparison with curcumin. Symptoms and serum values are reported
Cardiovascular	A randomised study examines risk factors and markers of endothelial function in ischaemic heart failure. The population-based Framingham study examines the

4. Profile: Molecule and Charge

Lycopene 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; this is exactly what the next section addresses.

5. Charge, Electrons, Radicals

A measurement on charge and cation exchange is still outstanding. Electron transfer is described as radical scavenging: carotenoids such as β -carotene, lycopene, lutein and zeaxanthin can neutralise reactive oxygen species and mitigate oxidative stress ²⁷; radical scavengers act via quenching and neutralisation ²⁵. In a preclinical trial, 20 mg/kg lycopene reduced malondialdehyde and reactive oxygen species while catalase, superoxide dismutase and glutathione peroxidase increased; serum BUN, creatinine and cystatin C decreased ²⁴. In cells, pretreatment with three nutrients lowered ROS by 1.7- to 2.2-fold and intracellular MDA by 33.87 % to 40.10 % ²⁶.

Little has been measured in humans so far. A randomised clinical study examined how lycopene modulates oxidative stress and liver enzyme values in patients with metabolic syndrome ²³. Oral supplementation with carotenoids recorded plasma levels as well as visual and skin attributes ²⁵. Direct measurements of charge, cation exchange or electron transfer in humans are not included. It remains open to what extent the radical neutralisation described preclinically becomes measurable in humans; what would need to be clarified is which redox parameters a human study should capture.

6. Interactions with Other Substances

With which other substances on the platform this substance is **jointly** investigated or discussed in human studies and reviews — combination, comparison or shared mechanism of action. The number indicates studies in which both occur.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Acceptance and Commitment Therapy (ACT)	64	12
Chronic inflammation	50	6
Stress, cortisol and inflammation	49	9
High-intensity interval training (HIIT)	28	7
Vitamin C	21	4
Astaxanthin	19	2
Selenium	18	5
Art therapy	17	4
Turmeric and curcumin	13	6
Green tea and EGCG	13	4

Lycopene tablets achieved a healing rate of 63 % in oral leukoplakia, and 72 % of participants were healed after the combination of curcumin and lycopene ²⁸. Docetaxel with lycopene was investigated in a small sample; the authors consider the combination worthy of further examination ²⁰. Sorafenib with lycopene inhibited the proteins Bcl-2, Ki-67, VEGF, IL-1 β and TNF- α in a human observation ³¹. For SMZ, human observations describe that coadministration of lycopene restored cytochrome P450-1A1 homeostasis, reduced intracellular ROS accumulation and normalised immune and apoptosis markers ^{30, 30}.

Two controlled human studies showed that black pepper with an emulsion based on vegetable oil or canola oil synergistically increased the carotenoid bioavailability of raw vegetables ^{29, 29}. A review article addresses synergism and delivery systems of lycopene ³². It remains to be clarified whether the uptake effects also apply to lycopene itself.

7. Overdosage, Tolerability, Limits

These sentences do not contain quantity information on lycopene.

The contraindication there concerns dexamethasone, not lycopene. Preclinical animal studies and clinical studies are used for the safety of carotenoids ³³. A dose at which adverse effects occur, a tolerable daily dose or a limit for intake cannot be derived from this. A dose-finding study in humans that systematically records adverse events and at the same time measures the plasma levels of the carotenoids would need to be clarified ¹⁸.

8. The Most Robust Studies

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

Controlled Human Studies

- ¹ Efficacy of lycopene in management of Oral Submucous Fibrosis- A systematic review and meta-analysis (2020) — Übersichtsarbeit, 1.181 Teilnehmer
- ² Dietary and Nutraceutical Interventions as an Adjunct to Non-Surgical Periodontal Therapy-A Systematic Review (2023) — Übersichtsarbeit
- ³ Systematic review and meta-analysis of the antioxidant capacity of lycopene in the treatment of periodontal disease (2023) — Übersichtsarbeit
- ⁴ Effectiveness of non-pharmaceutical intervention on sperm quality: a systematic review and network meta-analysis (2023) — Übersichtsarbeit
- ⁵ The effect of lycopene supplement from different sources on prostate specific antigen (PSA): A systematic review and meta-analysis of randomized ... (2022) — Übersichtsarbeit
- ⁶ Lycopene Does Not Affect Prostate-Specific Antigen in Men with Non-Metastatic Prostate Cancer: A Systematic Review and Meta-Analysis of Randomized ... (2021) — Übersichtsarbeit
- ⁷ Effects of Lycopene Supplementation on Bone Tissue: A Systematic Review of Clinical and Preclinical Evidence (2025) — Übersichtsarbeit
- ⁸ Effect of Intake of Lycopene-Containing Products on Vascular Endothelial Function in Healthy Adults: A Systematic Review with Meta-Analysis (2026) — Übersichtsarbeit
- ⁹ Total carotenoid intake is associated with reduced loss of grip strength and gait speed over time in adults: The Framingham Offspring Study (2021) — 2.452 Teilnehmer
- ¹⁰ Association between Circulating Antioxidants and Longevity: Insight from Mendelian Randomization Study (2022) — 1.012.240 Teilnehmer
- Phase II randomised control feasibility trial of a nutrition and physical activity intervention after radical prostatectomy for prostate cancer (2019) — 108 Teilnehmer
- ¹¹ Effect of green tea and lycopene on the insulin-like growth factor system: the ProDiet randomized controlled trial (2019) — 133 Teilnehmer

- ¹² Cardiovascular and Osteoporosis Protection at Menopause with Lycopene: A Placebo-Controlled Double-Blind Randomized Clinical Trial (2022) — 100 Teilnehmer
- ¹³ Comparison of therapeutic response of lycopene and curcumin in oral submucous fibrosis: A randomized controlled trial (2019) — 30 Teilnehmer
- ¹⁴ A comparative study to evaluate the efficacy of lycopene and curcumin in oral submucous fibrosis patients: A randomized clinical trial (2018)
- ¹⁵ Antioxidant therapy in idiopathic oligoasthenoteratozoospermia (2017)
- ¹⁶ The effects of lycopene supplement on the spermatogram and seminal oxidative stress in infertile men: A randomized, double-blind, placebo-controlled ... (2019)
- ¹⁷ A randomized placebo-controlled trial to investigate the effect of lactolycopene on semen quality in healthy males (2020)
- ¹⁸ Dietary Intake of Carotenoid-Rich Vegetables Reduces Visceral Adiposity in Obese Japanese men-A Randomized, Double-Blind Trial (2020)
- ¹⁹ Systemic and skin-targeting beneficial effects of lycopene-enriched ice cream: A pilot study (2019)
- ²⁰ A phase II study of docetaxel plus lycopene in metastatic castrate resistant prostate cancer (2021) — 10 participants
- ²¹ Investigating Causal Associations of Diet-Derived Circulating Antioxidants with the Risk of Digestive System Cancers: A Mendelian Randomization Study (2022)
- Natural products for the management of xerostomia: a randomized, double-blinded, placebo-controlled clinical trial (2017) — 60 participants
- ²² Serum 8-isoprostane levels in patients with resistant oral lichen planus before and after treatment with lycopene: a randomized clinical trial (2021)

9. Summary

They are, however, clearly in the minority; observational studies predominate in humans, while animal and basic research constitute the largest group in the overall literature. Several controlled studies test lycopene against another substance rather than against placebo or as an add-on to ongoing treatment; a difference between the groups can then be demonstrated, but not readily attributed to lycopene. Attribution to the single substance remains the open flank of this literature.

Isolated supplements, lycopene-enriched ice cream, carotenoid-rich vegetables and lycopene as an add-on to ongoing treatment were examined.

Hypothesis: Where an effect appears, it shows first in markers in blood or seminal plasma, because the placebo-controlled studies measure semen parameters and markers, not the birth of a child. Whether such a marker finding is reflected in the clinical course remains open.

The first point to clarify would be the contribution of the single substance in a design that tests it alone: a randomised, placebo-controlled study that compares lycopene as a pure substance against placebo and records a clinical endpoint rather than a marker. It is also open how strongly blood levels after supplements, enriched foods and estimates from dietary questionnaires differ from one another. The Framingham study links total carotenoid intake with muscle strength and gait speed; what share lycopene has in this remains a testable question. For tolerability, a dose-finding study in humans would be required that systematically records adverse events while simultaneously measuring plasma levels of the carotenoids.

10. What Remains Open

- **Pure Substance:** Which randomised, placebo-controlled study tests lycopene alone and records a clinical endpoint rather than a marker?
- **Absorption:** How strongly do blood levels after supplements, enriched foods and estimates from dietary questionnaires differ from one another?
- **Carotenoids Overall:** The Framingham study links total carotenoid intake with muscle strength and gait speed. What share does lycopene have in this?

11. Further Paths

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

- Interaction Network

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

Frequently Asked Questions

Which intake forms have actually been tested?

Isolated lycopene supplements, lactolycopene, lycopene-enriched ice cream and carotenoid-rich vegetables have been tested, as well as lycopene as an adjunct to existing treatments. The forms are not interchangeable: whether a substance is absorbed from a capsule or from a food can alter the measured level. Bioavailability is therefore treated as a separate research field.

Do the antioxidant measurement parameters say anything about disease progression?

Antioxidant questions represent the largest application area of the controlled studies. Markers of oxidative status are measured, for example 8-isoprostane in serum in oral lichen planus. A changed marker is an intermediate result. Whether a different disease progression follows from this is not examined by these studies.

Do the studies test lycopene against placebo?

Some do, some do not. Studies on semen parameters as well as certain safety and metabolic studies are placebo-controlled. Others compare lycopene with a second substance, combine it with an existing therapy or investigate a mixture. For assessing the individual substance, the placebo-controlled designs are particularly informative.

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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/lycopene/ · Last updated 2026-10-15