

DOSSIER · SUBSTANCE

Polyphenols

Polyphenols are a class of compounds, not a single substance, which is why there is no common body of studies, but findings on very different materials. The research is predominantly basic-science oriented; controlled studies focus on metabolism, safety and antioxidant markers. The most cited controlled trial examines a polyphenol-rich complex for cognition and neuroprotective biomarkers.

959

STUDIES IN
TOTAL

133

IN HUMANS

64

OF WHICH
CONTROLLED

75

IN ANIMALS

152

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

Polyphenols at a Glance

ORIGIN:
Polyphenols are a class of secondary plant compounds with multiple phenolic hydroxyl groups; they include, among others, the flavonoids. Plants produce them as defence substances against UV radiation, herbivores and microorganisms; they colour flowers and fruits and shape taste and bitterness. The term does not refer to a single compound — every statement must name the material and preparation.

EVIDENCE BASE:
959 evaluated studies · 64 controlled human studies · 69 observational studies · 246 review articles · 75 animal studies · 116 cell culture studies

- STRONGEST EVIDENCE:**
- **Proven:** Review articles with meta-analysis on COPD and non-alcoholic fatty liver pool several controlled studies; they permit statements about the substance group, not about an individual compound (inflammation, liver).
 - Systematic review of 13 investigations in 640 patients with hyperlipidaemia: significant improvements in blood lipids were shown for 9 foods, eight additionally examined oxidative status (metabolism).
 - **Proven:** Meta-analysis on polyphenol-rich seed foods (Brazil nut, almond, linseed) in coronary heart disease: seven studies with 324 patients, significant reduction in triglycerides (MD = -20.03) (heart and circulation).
 - A 28-day randomised, double-blind, placebo-controlled phase with 98 participants showed lower IL-1β, IL-6 and IL-8 values under combined polyphenols (inflammation).
 - A four-week double-blind study in 50 HIV patients with elevated triglycerides showed a triglyceride reduction of -39.8 mg/dL (95 % CI -67.7 to -11.9) under tamarind fruit juice with 30 % fruit pulp (metabolism).

- LIMITATIONS:**
- A substantial proportion of the controlled studies report markers rather than clinical endpoints, follow-up periods are mostly short, and observational studies show associations, not causes.
 - Foods, teas, extracts and supplements differ in composition and form of intake; no effect of an individual polyphenol can be derived from mixture studies.
 - Small groups and short time periods limit individual studies, for example 24 trained participants over seven days; such findings are indications, not proofs.

CLASSIFICATION:
Polyphenols are a substance class, not a single compound — reliable statements therefore apply only to the respective tested material and its preparation.

1. What Polyphenols Are

Polyphenols are secondary plant compounds with multiple phenolic hydroxyl groups. They include, among others, the flavonoids as well as further subgroups that differ markedly in structure, size and solubility. Decisive for research is that the term denotes an entire substance class and not a single compound. Anyone reading about polyphenols encounters, depending on the study, flavonoids, the totality of phenolic compounds of a plant or the composition of an extract. Individual foods, teas and juices, extracts and preparations manufactured from them are investigated. Every reliable statement must therefore name which material was tested and in which preparation.

One point is decisive for the assessment of all studies: polyphenols are scarcely absorbed unchanged. A large proportion is metabolised in the large intestine by the gut flora and subsequently further modified in the liver; predominantly degradation products are present in the blood, not the original compound. One of the most frequently cited studies in the field deals precisely with how the gut flora co-determines absorption and the observed effects. **Plausible:** It follows for the reading of every study that the administered substance is rarely measured and that the absorbed amount depends on the substance, the food matrix and the individual gut flora. The measurement level also comes into play. Many controlled studies record lipid values, oxidative stress parameters or questionnaire scores; others examine cognitive performance. Markers and disease course are not the same. When comparing results, substance, material, preparation and measured variable must be placed side by side.

2. What the Studies Show in Detail

The supporting human studies and the most important reviews — by field of application, with population, duration, preparation, measured variable and result, as the original studies report them. Numbers appear only where the study states them.

Distribution of **controlled human studies** by field of application — the numbers are not additive, as one study may be assigned to several fields:

FIELD OF APPLICATION	CONTROLLED STUDIES
Metabolism	38
Safety and tolerability	27
Oxidative stress	26
Inflammatory processes	25
Heart and circulation	18

FIELD OF APPLICATION	CONTROLLED STUDIES
Fatigue and stress	17
Gut and microbiome	14
Cognition and psyche	14

Oxidative Stress

A randomised, double-blind, placebo-controlled crossover study tested a capsule concentrate from fruit, vegetable and berry juice powders (Juice Plus+ Premium®) in 92 participants over two periods of 16 weeks each, separated by a four-week wash-out phase ²². Stroop test, Trail Making Test and Reynolds Intellectual Screening Test as well as CREB and BDNF in plasma were measured by ELISA. Under the polyphenol-rich preparation the Stroop and RIST values were higher than under placebo, and CREB and BDNF in plasma were markedly elevated ²². The study interprets the finding as modulation of neurobiological mechanisms; the abstract does not state effect sizes.

24 trained participants received 250 mL jaboticaba berry juice with approximately 1300 mg total polyphenols or a fruit-flavoured placebo for seven days ⁴⁰. On the fourth day, 6 × 10 maximum isokinetic eccentric contractions of the elbow flexors followed. The protocol increased myoglobin (p < 0.001) and muscle soreness (p < 0.001) and lowered reduced glutathione (p < 0.001), maximum isokinetic voluntary contraction (p < 0.001), functional (p < 0.001) and morphological muscle quality (p = 0.028). The juice increased GSH (p = 0.001), lowered muscle soreness (p = 0.041) and accelerated recovery of muscle strength (p = 0.004) ⁴⁰. The small group and the short period limit the statement.

30 participants with borderline diabetes drank a tea made from mulberry leaves and water chestnut shell in a randomised, double-blind, placebo-controlled crossover comparison study ³⁸. The test meal of 3 g contained 10.2 ± 0.8 mg 1-deoxynojirimycin and 61.3 ± 1.4 mg total polyphenols and showed higher antioxidant activity than the placebo. Blood glucose was significantly lower 30 and 60 minutes after the rice meal, insulin at all time points (30, 60, 90 and 120 minutes) ³⁸. A systematic review evaluated 13 studies with 640 patients with hyperlipidaemia; 12 commonly consumed food groups as well as medicinal and food plants were recorded ³. All 13 studies reported on blood lipids, significant improvements were shown for 9 foods, and eight studies additionally examined oxidative status ³.

251 participants with increased waist circumference were randomised in a secondary analysis of the Habitual Diet and Avocado Trial to daily avocado or avoidance for six months, without additional dietary counselling ¹⁹. Memory, processing speed, executive function, simple reaction time and working memory reaction time were recorded at baseline and at the end of the intervention; the abstract does not state the results ¹⁹. The review article on polyphenolic compounds screened approximately 141 works from 1979 to 2025 on sources, extraction, purification and antioxidant mechanisms from radical scavenging to modulation of signalling pathways and names open questions in clinical validation and formulation ⁴⁵. A second review describes catechols that act antioxidatively and simultaneously generate controlled reactive oxygen species, and their application in materials, antimicrobial strategies, cancer therapy and tissue regeneration; pharmacokinetics, biosafety, regulation and manufacturing consistency stand in the way of clinical translation ⁴⁶. What is missing are human studies that jointly measure uptake, metabolism and oxidative status over longer periods.

Inflammatory Processes

A systematic review with meta-analysis on dietary polyphenol preparations in COPD searched PubMed, Cochrane, Medline, CNKI and further databases up to 26 December 2024 for Chinese and English works ¹. In connection with the included studies, a triple-blind, placebo-controlled design in patients at GOLD stages II–III with 8-isoprostane and course parameters of lung function is described; the pathways mentioned are an increase in the GSH/GSSG ratio and attenuation of NF-κB-mediated inflammatory cascades, and as lung function parameter an FEV1 improvement of at least 12 % versus baseline ¹. The abstract ends before the pooled results; heterogeneity between the included randomised studies remains the open point there.

BMI, ALT, AST, triglycerides, total cholesterol, HDL-C, LDL-C and TNF-α were assessed. Naringenin lowered total cholesterol (SUCRA 94.59 %) and triglycerides (99.00 %); catechin lowered BMI (77.74 %), ALT (94.21 %), AST (93.56 %) and total cholesterol (92.26 %) and raised HDL-C (93.72 %) ². The ranking is based on indirect comparisons; the abstract ends before the data on dihydromyricetin.

A systematic review on polyphenol-rich seed foods in coronary heart disease included seven studies with 324 patients and three seeds: Brazil nut, almond and linseed ¹¹. The meta-analysis showed a significant reduction in triglycerides (MD = -20.03) ¹¹; the confidence interval is cut off in the abstract. 50 patients with hyperlipidaemia received in a single-blind, randomised clinical study for four weeks either a higher-dose, lower-polyphenol native olive oil (414 mg/kg phenols, 20 g/day) or a lower-dose, higher-polyphenol one (1021 mg/kg phenols, 8 g/day), so that daily polyphenol intake was approximately 8.3 mg in both groups ³⁴. In addition, 20 healthy persons in two groups received the same oils over the same period. Primary endpoints were total cholesterol, LDL, HDL, triglycerides, lipoprotein(a) as well as apolipoprotein A1 and B, measured at baseline and at the end ³⁴; the abstract does not state the results.

In a two-phase population trial, 151 persons were first examined; the median microplastic concentration in stool was 158.28 µg/g dry weight and correlated with seven inflammation indices, four cytokines and two lipid markers ²⁰. In the subsequent 28-day randomised, double-blind, placebo-controlled phase with 98 participants, composite polyphenols lowered IL-1β (P = 0.045, effect size -0.463), IL-6 (P = 0.023, -0.576) and IL-8 (P = 0.022, -0.529) ²⁰. Between high and low exposure, 507 differentially expressed microbiota and 144 different metabolites were found; after the intervention 108 and 85 respectively ²⁰. 100 healthy women aged 25 to 64 years in rural communities of Puno, Peru, were followed for twelve months; the analysis used data from the Cardiopulmonary Outcomes and Household Air Pollution Study ⁴². Mean age was 49 ± 10 years, mean total polyphenol intake 335 ± 193 mg/day, collected via 24-hour recalls and the Phenol-Explorer database. IL-10, IL-6, IL-1β, C-reactive protein, TNF-α as well as VCAM-1 and ICAM-1 from dried blood spots were measured ⁴²; the abstract ends before the regression results. What is missing are studies that link intake and inflammatory markers in an adequate number of participants with pre-specified endpoints.

Metabolism

In a four-week, parallel, double-blind exploratory study, 50 patients with HIV and elevated triglycerides each received two doses of tamarind fruit juice ³⁹. Eligible persons were aged 30 to 60 years with triglycerides of 150 mg/dL or higher. 600 mL juice was drunk daily, with 10 % or 30 % fruit pulp, corresponding to 1556 mg and 1631 mg analysed polyphenols respectively. The primary endpoint was triglycerides; blood pressure and vascular function were also measured, and participants were asked to maintain their usual diet and lifestyle ³⁹.

The juice with 30 % fruit pulp lowered triglycerides by -39.8 mg/dL (95 % CI: -67.7 to -11.9) ³⁹. Analysis was by intention-to-treat; the study is registered under NCT06058845. Food intake, background polyphenol intake and physical activity were also recorded ³⁹. What is missing is a replication with a larger number of participants and longer duration that examines vascular function as a pre-specified endpoint.

Further Studies

A systematic review examined the association between phytochemicals — polyphenols, carotenoids and phytoestrogens — and outcomes of assisted reproductive technologies ¹². PubMed, Scopus, Web of Science and Clinical Trials were searched from January 1978 to March 2023. Included were observational, randomised controlled and cohort studies; 13 works were admitted, among them five randomised controlled trials, one non-randomised controlled study and six prospective cohort studies ¹².

Live birth rate, clinical pregnancy and ongoing pregnancy were recorded. Quality of the included works was assessed independently by two investigators using the Quality Criteria Checklist for Primary Research ¹². The abstract ends before the summarised results. What is missing is an analysis that reports the three endpoints separately and with participant numbers.

Gut and Microbiome

A review describes that the bioactivity of polyphenols depends strongly on the amount ingested and on the interaction with the gastrointestinal tract and the gut microbiota ⁴³. Only a portion is absorbed in the small intestine, where enzymatic hydrolysis releases aglycones; a considerable proportion reaches the large intestine, where microbes convert them into simpler phenolic metabolites that are often more bioavailable and enter the systemic circulation ⁴³. Even low intake or poor absorption can have an effect because polyphenols in the large intestine alter the composition and function of the microbiota; the review places these interactions along the gut–liver–brain axis.

A review evaluated studies on the question of whether encapsulation improves the bioavailability of polyphenols ³³. Clinical evidence focuses on polyphenols from grape pomace, cocoa and blueberries as well as on individual compounds such as fisetin, hesperidin and curcumin; encapsulation proved effective ³³. The majority of the evidence on bioavailability after digestion comes from in-vitro studies that cannot represent physiological conditions and the microbial ecosystem ³³.

A review on nuts describes their content of unsaturated fatty acids, fibre, minerals, vitamins as well as polyphenols and phytosterols and places the bioaccessibility of nut polyphenols and their interaction with the gut microbiota ⁴¹. Observational cohorts and randomised clinical studies consistently report favourable associations with lower risk of obesity, hypertension, elevated LDL cholesterol, cardiovascular diseases, especially coronary heart disease, and cancer ⁴¹. What is missing are intervention studies that measure the intake of the polyphenols and not only nut intake overall.

Cognition and Psyche

A systematic meta-analysis of randomised controlled studies examined cognitive and further endpoints in neurodegenerative diseases under polyphenol administration ⁴. Various polyphenol types across seven neurodegenerative diseases were evaluated; 13 studies with 849 participants were included. Pre-specified endpoints were global cognition (MMSE), domain-specific cognition (ADCS-Cog), activities of daily living (ADCS-ADL), neuropsychiatric symptoms (NPI) as well as plasma amyloid- β 40 and BDNF ⁴. Reporting followed PRISMA 2020, methods followed the Cochrane Handbook, certainty of evidence was assessed with GRADE.

Polyphenol administration was associated with improved global cognition (pooled MD in MMSE = 2.06; 95 % CI 0.62–3.49) ⁴. In subgroups, flavonoids showed a modest but significant improvement in MMSE values, while stilbenes showed markedly improved ADCS-ADL values, without clear gains in MMSE or ADCS-Cog and without a uniform effect on the NPI. Anthocyanidins, phenolic acids and lignans did not significantly influence the cognitive endpoints ⁴. What is missing are studies that directly compare the individual polyphenol classes against each other and against placebo.

Overall Picture

Across the fields, two types of work contribute: randomised controlled studies with concrete endpoints and reviews that bundle many individual studies. Individual studies show results for polyphenol-rich preparations and whole fruits: higher Stroop and RIST values with elevated CREB and BDNF in 92 participants after intake of polyphenol-rich preparations ²², -39.8 mg/dL lower triglycerides in 50 patients with HIV after intake of tamarind ³⁹, elevated GSH and faster strength recovery in 24 trained persons after consumption of jaboticaba berries ⁴⁰.

Where the evidence is open, it is usually due to the number of participants, the duration or abstracts ending before the results — as in the avocado study with 251 participants ¹⁹, the olive oil study with 50 patients ³⁴ and the COPD review ¹. Bioavailability remains the consistent bottleneck: reviews on encapsulation ³³, on microbiota-mediated conversion ⁴³ and on liposomal systems ⁴⁴ name it as the central hurdle. What is missing are long, independently funded studies that jointly measure intake, metabolites and clinical endpoints.

Methodology of the evidence base

The controlled human studies are predominantly randomised, double-blind, placebo-controlled studies, partly in crossover design, with durations from four weeks to six months and participant numbers between 24 and 251 ^{40 34 19 39}. Endpoints range from cognitive tests via plasma parameters such as CREB, BDNF, glutathione and cytokines to blood lipids and fasting glucose ^{22 20 39}. In addition there are meta-analyses with 13 to 54 included studies ^{4 2} and

narrative reviews ^{45 46}. Systematically missing are long-term studies, measurements of intake and of metabolites in plasma as well as independent replications; many abstracts end before the results, so that effect sizes and confidence intervals are not verifiable there.

A collective term carries no shared statement of effect

Polyphenols are a class of substances, not a single substance. A pooled measure across polyphenol-rich supplements therefore describes the mixture that was tested, not a mechanism of action common to all polyphenols. Anyone comparing two studies is usually comparing different materials: an olive oil with high phenol content, a mulberry-leaf tea, a berry extract. Even if both alter the same marker, that says nothing about whether the same pathway was involved. The field's review articles accordingly work with groups of foods or supplements and frame their statements for the group. The collective term is practical for literature reviews but too coarse for transfer to an individual substance.

The second limitation concerns the measurement level. Controlled studies on polyphenols frequently record antioxidant parameters, lipid profiles, inflammatory markers or questionnaire results. Such quantities are markers; they show that a laboratory value changed under supplementation, not that a disease course changed. Cognitive endpoints and neuroprotective biomarkers are so far examined in individual controlled studies, oncological endpoints predominantly in reviews and preclinical models.

PLAUSIBLE:

Attribution is the most common error when reading this literature, because many studies examine preparations containing multiple plant substances. The open question is therefore not whether polyphenols work, but which substance in which preparation changes which endpoint.

3. How Robust the Research Is

The research is clearly basic-science oriented. The largest block consists of mechanistic and foundational studies, followed by reviews on mechanisms of action; together they far outnumber human studies. Cell-culture and animal studies are also numerous, as are environmental and agricultural studies on production and characterisation. In humans, observational studies stand alongside controlled studies. Within the controlled studies the emphasis lies on metabolism and safety, followed by antioxidant markers and inflammation. Cardiovascular, fatigue, gut and cognition follow at a distance; the rarest are studies on bioavailability and oncology. Foundational studies supply the mechanistic logic; clinical studies test individual sections of it.

PROVEN

For chronic obstructive pulmonary disease and for non-alcoholic fatty liver disease there are reviews with meta-analysis that pool several controlled studies; they permit statements about the group of polyphenols, not about an individual substance. Many individual studies are randomised, double-blind and placebo-controlled, some in crossover design, which increases comparability. The weakness lies in the dispersion of the material: foods, teas, extracts and supplements differ in composition and form of administration, follow-up periods are mostly short, and a substantial proportion of the studies report markers rather than clinical endpoints. Observational studies show associations, not causation. No effect of a single polyphenol can be derived from mixture studies.

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

CLAIM	EVIDENCE BASE
Polyphenols act antioxidant in the body	Controlled studies record antioxidant parameters such as glutathione or oxidative stress markers; thus, a laboratory value is measured, not a disease progressi
A polyphenol-rich diet protects the heart	Controlled studies and systematic reviews are available on lipids and inflammatory markers in coronary heart disease and hyperlipidaemia. Sie betreffen Marke
Supplements replace fruit and vegetables	Polyphenol-rich foods, teas, extracts and supplements with different compositions are being tested. Results from mixtures cannot be transferred to a single sut
Same substance, same effect	There is no single substance, intake form or effect here. Absorption and measured effects depend on the substance, food matrix and gut flora; the studies on a

5. Profile: Molecule and Charge

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

6. Charge, Electrons, Radicals

At the centre stands the catechol/o-quinone-hydroquinone/p-quinone cycle with NQO1 and Keap1/NRF2 thresholds ²³. Polyphenols are thereby understood as modulators of redox signalling, not as mere radical scavengers ²³. The quinone species determines safety: reactive quinone intermediates bind protein thiols, deplete glutathione and raise reactive oxygen species ²⁵; alongside these stand metal-ion chelation and interventions in cytochrome P450 ²⁵. Food processing such as PPO-induced browning shifts the quinone pools ²³. In the ABTS assay hydrogels reached a radical-scavenging rate of 96.51 % ²⁷.

In humans, signalling pathways and safety questions have been examined. Human findings are classified as redox signalling ²³; under cytotoxic chemotherapy the simultaneous administration of antioxidants correlated with increased disease recurrence and mortality ¹⁶. Significant reductions in extracellular DNA, reactive oxygen species or MPO signals do not constitute proof of clinical efficacy in humans ²⁴. In human tissue APEX reached 977.08 ± 15.73 mmol Trolox/100 g in vitro and lowered reactive oxygen species and inflammatory cytokines ²⁶. It remains to be tested whether metabotype-appropriate strategies and control of the quinone species hold in humans ²³.

7. Interactions with Other Substances

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

SUBSTANCE	JOINT STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic inflammation	256	33
Green tea and EGCG	230	22
Acceptance and Commitment Therapy (ACT)	206	22
Gut microbiome	184	20
Anthocyanins (berries)	182	40
Stress, Cortisol and Inflammation	131	15
Turmeric and Curcumin	106	16
Cocoa Flavanols	103	27
Olive Polyphenols (Hydroxytyrosol)	91	21
Resveratrol	61	8

Encapsulation is being examined as a strategy to improve the stability and bioavailability of polyphenols ³³; for individual polyphenols such as hesperidin, fisetin and curcumin it is considered an effective technique ³³. Whether it increases bioavailability in humans remains formulated as a question ³³. Combinations with exercise in overweight adults with prediabetes are investigated in a controlled study ²⁸, synergistic effects with standard lipid-lowering agents are to be examined in large, long-term randomised studies ⁵. Synergies with radiation and chemotherapy are also discussed ²⁹.

One study compared polyphenol-microbiota interactions in stool samples from healthy individuals (n = 3), from patients with ulcerative colitis (n = 3) and with Crohn's disease (n = 3) in an in vitro fermentation model with 16S rRNA sequencing ³². Synergistic effects with non-polyphenolic compounds are described for inflammatory enzymes, pro-inflammatory cytokines and oestrogen receptors as well as signalling pathways such as NF-κB and PI3K/AKT, according to preclinical and clinical studies ³⁰. Antibiotic adjuvant and nanotransport are considered future research ³¹. It remains open whether polyphenols alter CYP enzymes or plasma protein binding.

8. Overdosage, Tolerability, Limits

In a controlled human study, 8–20 g EVOO per day was described as well tolerated ³⁴. A polyphenol-rich extract from *S. ramosissima* showed an acceptable safety profile in patients with lacunar infarction over long-term use; the authors classify the findings as hypothesis-generating, not as evidence of efficacy ³⁵. A VF extract was well tolerated, without adverse clinical events or biochemical changes in liver and kidney function; clinical symptoms, liver and kidney values and urinary KIM-1 were examined ³⁶.

In ulcerative colitis, a meta-analysis of randomised controlled trials found no significant differences in adverse effects (ITT: OR 0.99; 95 % CI 0.56–1.76; P = .973; PP: OR 0.99; 95 % CI 0.54–1.80; P = .971) ⁹. A randomised, double-blind, placebo-controlled crossover trial with 31 participants over two weeks examined safety via hypoglycaemia parameters of glucose measurement and blood values; use of MW tea was considered without safety concerns ³⁷³⁷³⁷.

Data on upper limits, toxicity thresholds and contraindications are still absent from the evaluated evidence. What would need to be examined is which dose of polyphenol-containing preparations should be regarded as the upper limit and how safety presents itself with longer administration.

9. The Most Robust Studies

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

Controlled Studies in Humans

- ¹ Efficacy and safety of dietary polyphenol supplements for COPD: a systematic review and meta-analysis (2025) — Systematic review, 894 participants
- ² Efficacy of dietary polyphenol supplement in patients with non-alcoholic fatty liver disease: a network meta-analysis (2025) — Systematic review, 3,132 participants
- ³ Effects of Polyphenol-Rich Foods on Lipids and Oxidative Stress Status in Patients with Hyperlipidemia: A Systematic Review of Randomized Controlled ... (2024) — Systematic review, 640 participants
- ⁴ Polyphenol consumption and neurodegeneration risk: a systematic meta-analysis of randomized controlled trials bridging nutrition and cognitive health (2026) — Systematic review, 849 participants
- ⁵ An updated systematic review and meta-analysis of pomegranate consumption on lipid profile (2025) — Systematic review, 2,695 participants
- ⁶ Olive oil consumption and risk of breast cancer: Prospective results from the Moli-sani Study, and a systematic review of observational studies and ... (2025) — Systematic review, 11,442 participants
- ⁷ The effect of asparagus stem consumption on health outcomes in adults: a systematic review (2026) — Systematic review, 503 participants
- ⁸ Pomegranate juice consumption and lipid profile: An updated systematic review and meta-analysis (2026) — Systematic review, 663 participants
- ⁹ Efficacy of polyphenols in adjuvant treating ulcerative colitis: A meta-analysis of randomized controlled trials (2025) — Systematic review, 742 participants
- ¹⁰ Efficacy of antioxidants as a therapy for Alzheimer's disease: a meta-analysis (2026) — Systematic review, 10,537 participants
- ¹¹ Effects of polyphenol-rich seed foods on lipid and inflammatory markers in patients with coronary heart disease: a systematic review (2024) — Systematic review, 324 participants
- ¹² How phytochemicals influence reproductive outcomes in women receiving assisted reproductive techniques: a systematic review (2025) — Systematic review
- ¹³ Association between polyphenols and inhalation-induced oxidative stress in chronic lung diseases: A systematic review (2026) — Systematic review
- ¹⁴ The Effect of Polyphenol Supplementation in People with Multiple Sclerosis: A Systematic Review of Clinical Trials (2026) — Systematic review
- ¹⁵ Dietary polyphenol intake in the prevention and management of diabetes mellitus: a systematic review of observational studies (2026) — Systematic review
- ¹⁶ Impact of Nutritional Supplements and Antioxidants in the Treatment of Breast Cancer: A Systematic Review (2026) — Systematic review
- ¹⁷ Effects of carob (*Ceratonia siliqua*) and carob-derived products on glycaemic control and insulin resistance: A systematic review of clinical trials (2026) — Systematic review
- ¹⁸ Exploring the effect of avocado on lipid profile modulation: a systematic review and dose-response and meta-analysis of clinical trials (2026) — Systematic review
- ¹⁹ Effects of one avocado a day for six months on cognitive performance in overweight adults: A randomized controlled trial (2026) — 251 participants
- ²⁰ Composite polyphenols mitigate microplastic exposure-related immune disturbances: a two-phase population trial (2026) — 151 participants
- ²¹ Efficacy of Hibiscus sabdariffa L. extract on metabolic parameters in participants with abdominal obesity and mild metabolic syndrome in Bangkok ... (2025) — 108 participants
- Impact of the gut microbiome on health impacts of Haskap berries: study protocol for a randomized control trial (2026) — 120 participants
- ²² Impact of Polyphenol-Rich Nutraceuticals on Cognitive Function and Neuroprotective Biomarkers: A Randomized, Double-Blind, Placebo-Controlled ... (2025) — 92 participants
- From laboratory to clinic: opportunities and challenges of functional food active ingredients in cancer therapy (2025)

10. Summary

Research is clearly basic-oriented: mechanistic studies and reviews on mechanisms of action outnumber human studies many times over. Within controlled human studies, the focus lies on metabolism (38), safety and tolerability (27), oxidative stress (26) and inflammatory processes (25); cardiovascular system (18), fatigue and stress (17), gut and microbiome (14) as well as cognition and psyche (14) follow at a distance, whereby the numbers are not additive. The review articles with meta-analysis on COPD and non-alcoholic fatty liver as well as the meta-analysis on polyphenol-rich seed foods in coronary heart disease, which significantly lowered triglycerides, are considered robust.

PLAUSIBLE Polyphenols are scarcely absorbed unchanged. Rarely is the administered substance itself measured; the absorbed amount depends on the substance, food matrix and individual gut flora. **Hypothesis:** Because microbial metabolites are often better available and the review places these interactions along the gut-liver-brain axis, part of the observed effects could be attributable to degradation products rather than the parent compound. In

human in-vivo studies, encapsulation proved effective for the bioavailability of polyphenols from grape pomace, cocoa and blueberries as well as of fisetin, hesperidin and curcumin.

What a study would need to clarify is the joint measurement of absorption, metabolism and oxidative status over longer periods in humans. For assisted reproduction, an evaluation reporting live birth rate, clinical and ongoing pregnancy separately and with participant numbers is pending. For nuts, intervention studies that measure polyphenol intake rather than nut intake overall remain open. For tamarind juice, a replication with larger participant numbers and longer duration that examines vascular function as a pre-specified endpoint is pending. For COPD, heterogeneity between the included randomised studies remains the open point that the pooled results would need to resolve.

11. What Remains Open

- **Single substances:** Which randomised study tests a single polyphenol representative against placebo, instead of a mixture or a whole food?
- **Clinical endpoints:** Which controlled study examines not markers but disease course and events over longer follow-up?
- **Absorption:** How can gut flora, absorption and measured effect be captured jointly in one study so that the chain becomes traceable?

12. Further Paths

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

- Interaction network

Frequently Asked Questions

How should the overall state of research on polyphenols be assessed?

There are many studies available, but they deal with different substances. There is a broad foundation on basics and mechanisms of action; in humans, studies predominate on metabolism, safety and antioxidant markers. For individual clinical pictures such as COPD or fatty liver, there are review articles with meta-analysis that pool several controlled studies. For practice, this means: Every statement applies to the tested material and the tested endpoint, not to polyphenols in general.

Why can results on different polyphenols not simply be summarised?

Because the substances differ in structure and absorption and because they are tested in different preparations. An extract usually contains several compounds in varying proportions; the absorbed amount additionally depends on the food matrix and the intestinal flora. A pooled evaluation of several supplements therefore describes the average of the tested mixtures. Statements about a specific substance require a study that tests exactly that substance alone.

What role does the intestinal flora play?

A central one when it comes to absorption. The most cited work in the field classifies the intestinal flora as a factor that co-determines bioavailability and thus the observed effects. Some of the polyphenols are only converted in the large intestine into compounds that enter the blood. The amount supplied and the amount measurable in the blood can therefore diverge. Controlled studies that simultaneously record intestinal flora, absorption and clinical endpoint would be the next step.

Sources

- 1 Efficacy and safety of dietary polyphenol supplements for COPD: a systematic review and meta-analysis
Wu D, Dong Y, Zhang D, Wang T, Ye H, Zhang W · 2025
- 2 Efficacy of dietary polyphenol supplement in patients with non-alcoholic fatty liver disease: a network meta-analysis
Wang XC, Song L, Wang XH · 2025
- 3 Effects of Polyphenol-Rich Foods on Lipids and Oxidative Stress Status in Patients with Hyperlipidemia: A Systematic Review of Randomized Controlled Trials
Jia Y, Zhang Q, Zhang Y, Wang H, Niu Q, Zhu R et al. · 2024
- 4 Polyphenol consumption and neurodegeneration risk: a systematic meta-analysis of randomized controlled trials bridging nutrition and cognitive health
Wang X, Yang J, Zhang J, Yu G, Zhu J, Nie Y · 2026
- 5 An updated systematic review and meta-analysis of pomegranate consumption on lipid profile
Cheng W, Liang K, Huang A · 2025
- 6 Olive oil consumption and risk of breast cancer: Prospective results from the Moli-sani Study, and a systematic review of observational studies and randomized clinical trials
Ruggiero E, Sharma S, Di Castelnuovo A, Costanzo S, Panzera T, Esposito S et al. · 2025
- 7 The effect of asparagus stem consumption on health outcomes in adults: a systematic review
Davies A, Lamport D, Homma K, Takanari J, Hepsomali P · 2026
- 8 Pomegranate juice consumption and lipid profile: An updated systematic review and meta-analysis
Ghaemi F, Emadzadeh M, Almahmeed W, Jamialahmadi T, Karav S, Sahebkar A · 2026
- 9 Efficacy of polyphenols in adjuvant treating ulcerative colitis: A meta-analysis of randomized controlled trials
Wang Q, Li L, Zhuang S, Huang M, Xiang Y · 2025
- 10 Efficacy of antioxidants as a therapy for Alzheimer's disease: a meta-analysis
Li J, Chen B, Jiang J, Feng Y, Zhang R, Li D et al. · 2026
- 11 Effects of polyphenol-rich seed foods on lipid and inflammatory markers in patients with coronary heart disease: a systematic review
Jia Y, Wang H, Fan W, Lv J, Niu Q, Zhu R et al. · 2024
- 12 How phytochemicals influence reproductive outcomes in women receiving assisted reproductive techniques: a systematic review
Kircali-Haznedar N, Mumusoglu S, Bilgic P · 2025
- 13 Association between polyphenols and inhalation-induced oxidative stress in chronic lung diseases: A systematic review
Gulyaev AE, Nurgaziyev M, Ikromov A, Nurgaziyeva A, Baurzhan MB, Tekebayev K et al. · 2026
- 14 The Effect of Polyphenol Supplementation in People with Multiple Sclerosis: A Systematic Review of Clinical Trials
Brooks L, Farid AFBA, Poobalan A, Johnstone A, Myint PK · 2026
- 15 Dietary polyphenol intake in the prevention and management of diabetes mellitus: a systematic review of observational studies
Helm MM, Buccini G, Schilling BK, Lindsay AR, Basu A · 2026
- 16 Impact of Nutritional Supplements and Antioxidants in the Treatment of Breast Cancer: A Systematic Review
Uribe-Ramírez D, Laguna-Maldonado KD, Vázquez-Carrada M, Cortés-Peña LF, Vilchis-Landeros MM, Vázquez-Meza H et al. · 2026
- 17 Effects of carob (*Ceratonia siliqua*) and carob-derived products on glycaemic control and insulin resistance: A systematic review of clinical trials
Victoria-Montesinos D, González-Louza R, Barcina-Pérez P, Mercader-Ros MT, Lucas-Abellán C, Daruich-González IB et al. · 2026
- 18 Exploring the effect of avocado on lipid profile modulation: a systematic review and dose-response and meta-analysis of clinical trials
Mostafazadeh P, Etesamnia S, Nasiraei-Moghadam M, Jahan-Mihan A, Haghighi A, Zendedel A et al. · 2026
- 19 Effects of one avocado a day for six months on cognitive performance in overweight adults: A randomized controlled trial
Lee GJ, Morrell HER, Adams M, Sabaté J, Reboussin DM, Kris-Etherton PM et al. · 2026
- 20 Composite polyphenols mitigate microplastic exposure-related immune disturbances: a two-phase population trial
Zhao L, Zheng J, Shen Y, Xu X, Liu X, Yu J et al. · 2026
- 21 Efficacy of Hibiscus sabdariffa L. extract on metabolic parameters in participants with abdominal obesity and mild metabolic syndrome in Bangkok, Thailand: A double-blind, randomized, placebo-controlled trial
Chaisungnern K, Rattananupong T, Klinhom R, Nanta S, Banchuen K, Itharat A et al. · 2025
- 22 Impact of Polyphenol-Rich Nutraceuticals on Cognitive Function and Neuroprotective Biomarkers: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial
Carrillo JA, Arcusa R, Xandri-Martínez R, Cerdá B, Zafilla P, Marhuenda J · 2025
- 23 This review (2015-2025) integrates chemistry, enzymology, and human data to frame polyphenols as modulators of redox sig...
· 2026
- 24 Therefore, statistically significant reductions in extracellular DNA, reactive oxygen species (ROS), or myeloperoxidase ...
· 2026
- 25 Mechanistic pathways involve mainly metal ion chelation, cytochrome P450 interference, and the formation of reactive qui...
· 2026
- 26 APEx demonstrated high antioxidant capacity (977.08 ± 15.73 mmol Trolox/100 g) and significantly reduced reactive oxygen...
· 2025
- 27 Results showed that the GA-loaded hydrogel exhibited a uniform honeycomb-like porous structure and displayed the optimal...
· 2026
- 28 Synergistic Effects of Microencapsulated Polyphenols and Concurrent Training on Metabolic Health and Fitness in Overweig...
· 2025
- 29 The review further discusses the synergistic effects of these compounds when combined with conventional treatments like ...
· 2025
- 30 It also examines their synergistic effects with other non-polyphenolic compounds in reducing these biomarkers, such as i...
· 2026
- 31 Thus, multi-target mechanisms, combined with antibiotic adjuvant potentials and nanodelivery approaches, envisage future...
· 2026
- 32 Using fecal samples from healthy individuals (n = 3), ulcerative colitis (UC) patients (n = 3), and Crohn's disease (CD)...
· 2026
- 33 Does Encapsulation Improve the Bioavailability of Polyphenols in Humans?...
· 2024
- 34 The volumes used (8-20 g/day) reflect typical daily EVOO intake and were well tolerated by participants....
· 2025
- 35 These findings should be considered hypothesis-generating only and not as evidence of efficacy. Conclusions Long-...
· 2026
- 36 Safety was assessed through clinical symptoms, hepatic and renal biomarkers, and urinary levels of kidney injury molecu...
· 2026
- 37 This study aimed to evaluate the postprandial glycemic response and safety of two-week MW tea consumption using continuo...
· 2025
- 38 Mulberry leaves and water chestnut tea reduces postprandial blood glucose in borderline diabetic Japanese: A randomized, double-blind, placebo-controlled crossover study
Yasuda M, Yasutake K, Yoshinaga I, Nakashima K, Saiki M, Takeyama-Mitsuta A et al. · 2025
- 39 Effect of tamarind (*Tamarindus indica* L.) on the cardiometabolic health of patients living with HIV and elevated triglyceride levels: a dose-response double-blind, randomized exploratory trial
Kiyimba T, Kigozi F, Bamuwanye M, Yiga P, Nakatudde K, Nabbanja W et al. · 2025
- 40 Jaboticaba berry (*Myrciaria jaboticaba*) consumption improves plasma GSH levels and accelerates muscle recovery following exercise-induced muscle damage: a randomized, placebo-controlled trial
Junior OJFR, Veiga NS, Alvares TS · 2025
- 41 Nutrients and bioactive compounds in nuts: implications for human health
Alasalvar C, Salas-Salvado J, Plaza-Diaz J, Ni J, Sala-Vila A, Bolling BW et al. · 2026
- 42 Dietary Polyphenols and Inflammatory Markers in Rural Adult Women in Puno, Peru
Laveriano-Santos EP, Tarazona-Meza C, Malpartida G, Barr DB, Williams KN, Kephart JL et al. · 2025
- 43 Unlocking Polyphenol Efficacy: The Role of Gut Microbiota in Modulating Bioavailability and Health Effects
Mahdi L, Graziani A, Baffy G, Mitten EK, Portincasa P, Khalil M · 2025
- 44 Dietary polyphenols and human health: sources, biological activities, nutritional and immunological aspects, and bioavailability- a comprehensive review
Saad AM, Mohammed DM, Alkafaas SS, Ghosh S, Negm SH, Salem HM et al. · 2025
- 45 Antioxidant Potential of Polyphenolic Compounds, Sources, Extraction, Purification and Characterization Techniques: A Focused Review
Ahmad Z, Rauf A, Orhan IE, Mubarak MS, Akram Z, Islam MR et al. · 2025
- 46 The Redox Properties of Polyphenols and Their Role in ROS Generation for Biomedical Applications
Bolaños-Cardet J, Pepió-Tárrega B, Saiz-Poseu J, López-Moral A, Ullah F, Yuste VJ et al. · 2026

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/polyphenols/ · Last updated 2026-10-15