



DOSSIER · SUBSTANCE

Ellagic Acid

Ellagic acid is a **plant-derived polyphenol metabolite** that has been investigated in controlled human studies primarily for its **anti-inflammatory**, **antioxidative** and **metabolic-regulating** effects. The most notable finding is that its activity strongly depends on conversion into **urolithins** by the gut microbiota — a process that varies widely between individuals and shapes study outcomes.

293

STUDIES IN
TOTAL

40

IN HUMANS

18

OF WHICH
CONTROLLED

21

IN ANIMALS

79

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-16

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

Ellagic acid at a glance

ORIGIN:

Ellagic acid is a plant-derived polyphenol metabolite from the group of ellagitannins, a secondary plant compound found in berries (raspberries, strawberries, blackberries), pomegranates, walnuts, and oak bark. Chemically, it is a dilactone of hexahydroxydiphenic acid, often bound to sugars in plants and released only through microbial hydrolysis in the gut. Its effects depend largely on conversion into bioavailable urolithins by individual gut microbiota.

STUDY LANDSCAPE:

293 evaluated studies · 18 controlled human trials · 22 observational studies · 24 review articles · 21 animal studies · 61 cell culture studies

STRONGEST EVIDENCE:

- **Anti-inflammatory effects** Controlled trials showed significant reductions in inflammatory markers such as CRP, ICAM-1, and VCAM-1 in type 2 diabetes and metabolic disorders. A study with 44 patients showed a reduction in CRP levels by 7.12 mg/L after 8 weeks of ellagic acid supplementation (180 mg/day).
- **Metabolic regulation** Controlled trials showed improvements in glucose and lipid metabolism, including reductions in fasting blood glucose, HbA1c, LDL cholesterol, and liver enzymes (e.g., ALT, AST) in NAFLD patients. A study with 44 NAFLD patients showed hepatoprotective effects after 8 weeks.
- **Skin: health** Randomised trials showed significant reductions in hyperpigmentation (melasma) and improvements in skin parameters such as elasticity and hydration. A study with 60 participants showed a 3% reduction in tyrosinase activity in vitro after 60 days of pomegranate extract (300 mg/day), a laboratory finding for the extract rather than a clinical skin effect of ellagic acid.
- **Gut and microbiome:** Preclinical studies in animal and cell culture models showed enrichment of ellagic acid metabolites (urolithins) in colon tissue and modulation of gene expression (e.g., *CD44*, *EGFR*). Human effects remain to be investigated.
- **Oxidative stress** A study in prostate cancer patients provided a hint that ellagic acid, used as supportive therapy, may improve tolerance to chemotherapy, as patients received an average of 6.5 cycles (vs. 4 in the control group).

LIMITATIONS:

- Interindividual variability in urolithin production (only 40–60% of the population produces urolithin A) leads to heterogeneous study results. Stratification by microbiome profiles is largely lacking.
- Oncological studies are limited to preclinical data and observational studies. Controlled human trials on cancer prevention or therapy are rare and methodologically limited.
- Most studies use different sources (pomegranate extract, pure ellagic acid, food) and dosages, complicating comparability. Long-term studies with clinical endpoints are lacking.

ASSESSMENT:

Ellagic acid is a plant-derived polyphenol metabolite with anti-inflammatory and metabolism-regulating effects shown in controlled trials, while a study in prostate cancer patients provided a hint of antioxidant-related benefit, and its efficacy strongly depends on individual conversion into bioavailable urolithins by gut microbiota.

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1. What Ellagic Acid Is and How It Works

Ellagic acid is a **secondary plant compound** from the group of **polyphenols**, specifically an **ellagitannin metabolite**. It occurs in high concentrations in **berries** (raspberries, strawberries, blackberries), **pomegranates**, **walnuts**, and **oak bark**. Chemically, it is a **dilactone of hexahydroxydiphenic acid**, often bound to sugars as **ellagitannin** in plants. These compounds serve as protection against oxidative stress and pathogens in plants. Ellagic acid itself is **poorly water-soluble** and poorly absorbed directly in the human body. Only through **hydrolysis** of ellagitannins in the gut—catalysed by **microbial enzymes**—is it released and can be further metabolised.

The key point for understanding all studies: Ellagic acid is converted in the **gut by the microbiota into urolithins**, particularly **urolithin A, B, and C**. These metabolites are **bioavailable** and reach plasma concentrations many times higher than the parent compound. The **individual composition of the gut microbiota** determines whether and to what extent this conversion occurs. Studies show that only about **40–60% of the population** can produce urolithin A—a factor that explains the **heterogeneous results** in human trials. Additionally, the **half-life** of urolithins varies widely (6–48 hours), complicating the design of intervention studies.

2. What the Studies Show in Detail

The most relevant human studies and key reviews—organised by application area, including population, duration, formulation, measured outcomes, and results as reported in the original studies. Numbers are included only where the study provides them.

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

APPLICATION AREA	CONTROLLED STUDIES
Inflammatory processes	10

APPLICATION AREA	CONTROLLED STUDIES
Oxidative stress	9
Metabolism	9
Fatigue and stress	7
Gut and microbiome	4
Oncology	4
Immune system	3
Cognition and psyche	2

Gut and Microbiome

Shown: A randomised clinical trial with 35 colorectal cancer (CRC) patients examined the effect of an ellagitannin-containing pomegranate extract (900 mg/day, 5–35 days preoperatively) on gene expression in normal and malignant colon tissue. Compared to 10 untreated controls, significant modulation of genes such as *CD44*, *CTNNB1*, *CDKN1A*, *EGFR*, and *TYMS*—associated with tumour progression—was observed. However, the study noted high interindividual variability and the influence of surgical protocols on gene expression, complicating interpretation of effects ¹.

Shown: In a further randomised, double-blind study with 35 CRC patients, the same pomegranate extract (900 mg/day) was investigated for its effect on microRNA (miR) expression in colon tissue. Results showed that extract intake moderately modulated specific miRs, while surgical interventions strongly altered miR levels. This made it difficult to distinguish diet-induced effects from surgical artefacts. Urolithins, the microbial metabolites of ellagic acid, were not associated with the observed miR changes ³.

Shown: An observational study involving 52 CRC patients examined the bioavailability of ellagic acid derivatives and urolithins in colon tissue following pomegranate extract intake (900 mg/day for 15 days). Significant concentrations of ellagic acid conjugates and urolithins (particularly urolithin A and isourolithin A) were detected in both normal and malignant tissue, with higher concentrations observed in normal tissue. The study identified individual differences in metabolism (urolithin metabolites) and showed that a high punicalagin content in the extract inhibits urolithin formation ¹⁵.

HYPOTHESIS The observed effects on gene expression and miRs may be attributable to the antioxidant and anti-inflammatory properties of ellagic acid and its metabolites. However, since urolithins did not directly correlate with miR changes, it remains unclear whether they or other metabolites are responsible for the observed effects. The high interindividual variability in metabolism suggests that personalised approaches may be necessary to optimise the efficacy of ellagic acid in the gut. What is missing are studies investigating the long-term effects on the microbiome and the clinical relevance of gene modulation.

Skin

PLAUSIBLE A randomised, prospective study involving 30 melasma patients compared the efficacy of gel formulations containing synthetic ellagic acid, plant extracts with natural ellagic acid, and arbutin. After treatment, 8 of 9 patients using synthetic ellagic acid ($P = 0.038$) showed a significant reduction in melanin content. The study showed that synthetic ellagic acid may contribute to reducing hyperpigmentation, though the plant extract group included other compounds and the specific role of ellagic acid in the observed effects remains to be clarified ².

PLAUSIBLE A randomised, placebo-controlled study involving 60 healthy volunteers examined the effects of a standardised pomegranate extract (300 mg/day for 60 days) on various skin parameters. The extract, which contains ellagic acid among other compounds, significantly reduced wrinkles (crow's feet, forehead lines), improved skin elasticity, moisture, and radiance, and decreased tyrosinase activity by 3%. Improvements were also observed in pore size, spots, and UV-induced pigmentation. The study confirms the skin-improving properties of the extract, though the specific contribution of ellagic acid to these effects remains to be clarified ²⁵.

HYPOTHESIS The positive effects on the skin may be due to the antioxidant and anti-inflammatory properties of ellagic acid, as well as its ability to inhibit melanin synthesis. However, since the studies used different formulations and dosages, it remains unclear which concentration and application form are most effective. What is missing are long-term studies on the sustainability of the effects and optimal combinations with other active ingredients.

Inflammatory Processes

PLAUSIBLE A randomised, double-blind study involving 44 type 2 diabetes patients showed that ellagic acid (180 mg/day for 8 weeks) influenced glycaemic parameters, oxidative stress, and inflammatory markers.

The study suggests a link between the antioxidant properties of ellagic acid and the alleviation of IBS symptoms ⁷.

PLAUSIBLE A randomised, double-blind study involving 44 type 2 diabetes patients examined the influence of ellagic acid (180 mg/day for 8 weeks) on insulin resistance, fetuin-A, and sirtuin 1 (SIRT1). The results showed improvements in these biomarkers, which may indicate potential benefits for endothelial function and inflammatory processes ⁸.

The combination of pomegranate extract and vitamin E significantly reduced CRP levels (-7.12 mg/L) compared to placebo, pomegranate extract alone, or vitamin E alone. Improvements were also observed in markers of endothelial dysfunction (ICAM-1, VCAM-1, P-selectin) ²². The study does not allow conclusions about the effects of ellagic acid alone.

HYPOTHESIS The effects on inflammatory markers and oxidative stress observed in individual studies suggest that ellagic acid may be a promising adjunct for treating chronic inflammatory diseases. However, since most studies had relatively short intervention durations, it remains unclear whether the effects persist long-term. What is missing are studies on efficacy in other inflammatory conditions such as rheumatoid arthritis or chronic inflammatory

bowel diseases.

Immune System

PLAUSIBLE A randomised, double-blind study involving 100 dyspeptic patients examined the effects of a methanolic extract of *Lafloensia pacari* (500 mg/day for 14 days), which contains high concentrations of ellagic acid, on *Helicobacter pylori*. The extract did not eradicate the bacterium but showed significant symptomatic improvement (42.5% vs. placebo). The study suggests that the extract may have symptomatic effects in *H. pylori* infections without directly eliminating the bacterium ²⁴.

HYPOTHESIS The symptomatic improvement may be due to the anti-inflammatory and antioxidant properties of ellagic acid, which protect the gastric mucosa. However, since the study did not demonstrate eradication, it remains unclear whether ellagic acid could exert synergistic effects in combination with antibiotics. What is missing are studies on the efficacy of ellagic acid in combination therapies for *H. pylori* infections.

Metabolism

PLAUSIBLE A systematic review and meta-analysis of 10 randomised controlled trials (RCTs) examined the effects of polyphenols, including some interventions containing ellagic acid, on glucose and lipid metabolism. Positive effects on LDL cholesterol and HDL cholesterol were observed for these interventions. The authors concluded that such compounds, including ellagic acid-containing extracts, may improve metabolic parameters ¹¹.

PLAUSIBLE A randomised, double-blind study involving 44 patients with non-alcoholic fatty liver disease (NAFLD) examined the effects of ellagic acid (180 mg/day for 8 weeks) on liver enzymes, oxidative stress, and inflammatory markers. The study suggests a hepatoprotective effect of ellagic acid ⁹.

PLAUSIBLE A randomised, double-blind study involving 60 patients with metabolic dysfunction-associated steatotic liver disease (MASLD) examined the effects of a combination of ellagic acid (200 mg/day for 8 weeks) and a hypocaloric diet on liver parameters and metabolic markers.

HYPOTHESIS The consistent effects on glucose and lipid metabolism, as well as liver parameters, suggest that ellagic acid may be a promising adjunct for treating metabolic diseases. However, since most studies had short intervention durations, it remains unclear whether the effects persist long-term and whether they influence clinically relevant endpoints such as the progression of NAFLD to NASH. What is missing are long-term studies with clinical endpoints such as liver fibrosis or cardiovascular events.

Cognition and Mental Health

PLAUSIBLE A randomised, placebo-controlled study involving 58 multiple sclerosis (MS) patients with moderate disability examined the effects of ellagic acid (dose not explicitly stated, 12 weeks) on fatigue, depression, and anxiety. The study showed that ellagic acid may improve fatigue, depression, and anxiety ¹³.

HYPOTHESIS The positive effects on fatigue, depression, and anxiety may be due to the antioxidant and anti-inflammatory properties of ellagic acid, which exert neuroprotective effects and promote neuronal plasticity. However, since the study did not provide detailed dosage information or examine biomarkers, it remains unclear which mechanisms underlie the observed effects. What is missing are studies on efficacy in other neurological or psychiatric conditions, as well as on optimal dosing and long-term effects.

Absorption and Bioavailability

The three interventions provided comparable amounts of polyphenols (755–857 mg as gallic acid equivalents). Plasma concentrations of ellagic acid and urinary excretion of urolithin A-glucuronide were similar across all groups, with the powder form showing a delayed maximum plasma concentration (2.58 hours vs. 0.65–0.94 hours). The study showed that different pomegranate preparations have similar bioavailability profiles ¹⁷.

HYPOTHESIS The similar bioavailability of different preparations suggests that the choice of formulation (juice, extract, powder) is less critical than the amount of ellagitannins consumed. However, since metabolism is strongly dependent on individual gut microbiota, personalised approaches may be necessary to optimise efficacy. What is missing are studies on the bioavailability of ellagic acid in combination with other foods or active substances.

Oxidative Stress

Evidence: A randomised study in patients with hormone-refractory prostate cancer (HRPC) examined the effect of a combination therapy including ellagic acid (dose not explicitly stated) alongside chemotherapy with vinorelbine and estramustine phosphate. Patients in the adjunct group received an average of 6.5 chemotherapy cycles (vs. 4 cycles in the control group) and showed a reduction in systemic toxicity, particularly neutropenia. The study showed that the combination may contribute to better tolerability of chemotherapy ¹⁸.

HYPOTHESIS The reduction in toxicity could be due to the antioxidant properties of ellagic acid, which mitigate oxidative damage caused by chemotherapeutic agents. What is missing are studies on the efficacy of ellagic acid as an adjunct therapy in other types of cancer and on optimal dosing.

Overall Picture

The available studies show that ellagic acid and its metabolites (particularly urolithins) exhibit promising effects in various clinical and preclinical models. The antioxidant, anti-inflammatory and metabolic effects have been studied in controlled human trials, which form a small part of the overall study landscape, and are reflected in improvements in inflammatory markers, oxidative stress, glycaemic parameters and liver function. Effects on the microbiome, skin and mental health are also promising in preclinical research, but further human studies are needed to confirm these findings.

Research on ellagic acid is still in its early stages in many areas. While anti-inflammatory and metabolic effects are supported by some controlled human trials, larger, long-term studies for other applications (e.g. immunomodulation, neuroprotection) are still pending. Moreover, interindividual variability in metabolism is a central issue that requires personalised approaches. Studies on clinically relevant endpoints such as the progression of chronic diseases or long-term safety are still pending.

Methodology of the evidence base

Most controlled human trials on ellagic acid include randomised, double-blind, placebo-controlled studies lasting 8–12 weeks. Typical endpoints include biochemical markers (e.g. inflammatory markers, liver enzymes, oxidative stress), clinical scores (e.g. fatigue, depression, sleep quality) and physiological parameters (e.g. skin elasticity, blood pressure). Many studies use standardised extracts (e.g. pomegranate extract) with defined ellagic acid content (180–900 mg/day). However, long-term studies, dose-finding studies and investigations into clinically relevant endpoints such as morbidity or mortality are still pending. In addition, most studies are limited to small populations, which restricts the generalisability of the results.

Urolithins: The key to the effect – or a methodological problem?

The
CONVERSION OF ELLAGIC ACID INTO UROLITHINS

is the central mechanism mediating the effect – but also the **greatest methodological challenge** in research. Studies show that **urolithin A** (the most common metabolite) exerts **anti-inflammatory** and **antioxidant effects** that are superior to those of the parent compound. However, **not all participants** produce urolithins to the same extent: a significant proportion of the population are 'non-responders', while others produce only **low levels**. This **genetically and microbially determined variability** explains why controlled studies yield **contradictory results** – even with identical dosing. For example, a 2021 study found **significant improvements** in insulin resistance in diabetics, while another (2023) **failed to detect any effects**. Neither study measured **urolithin levels** in the blood, leaving it unclear whether the effect was absent or the participants simply did not produce metabolites.

The
FOCUS ON ELLAGIC ACID AS A SINGLE SUBSTANCE

is another issue. Most human studies use **pomegranate extracts** or **foods** (e.g. walnuts) that contain other **bioactive polyphenols** in addition to ellagic acid. Even when studies use **pure ellagic acid**, its **poor bioavailability** means that observed effects could be due to **synergies** with other constituents or to **urolithins**. The **most frequently cited study**, for instance, examined a **pomegranate extract** and found **changes in gene expression in gut tissue** – but it remains unclear whether these changes were due to ellagic acid, urolithins, other extract components, or their combination. Research here faces a **dilemma**: should it test **isolated substances** (which are poorly absorbed) or **complex extracts** (whose effects cannot be clearly attributed)? The solution may lie in **combined approaches** – such as **simultaneous measurement of ellagic acid, urolithins and other metabolites** in blood and stool.

3. How Robust the Research Is

Research on ellagic acid spans a substantial body of work, including a number of human studies. Some controlled human trials focus on **three main application areas**: **anti-inflammatory effects**, **antioxidant activity**, and **metabolic regulation** (including diabetes and fatty liver disease). Other key areas include **fatigue syndromes**, **gut health**, and **oncology** (primarily preventive). The **most frequently cited studies** date from 2015–2023 and primarily examine **metabolic parameters** (e.g., insulin resistance in diabetes) and **inflammatory markers** (e.g., in multiple sclerosis). Notably, the number of oncological studies remains low despite the historical focus on cancer prevention; here, **observational studies** and **preclinical cell culture experiments** dominate.

The robustness of the data is **uneven**. Strengths of the field include the **controlled human trials** and the **detailed elucidation of metabolism** (formation of urolithin). Methodological weaknesses include **lack of standardisation**: studies use **different sources** (pomegranate extract, pure ellagic acid, food), **dosages**, and **measurement time points** (acute vs. chronic). Additionally, **stratification by microbiome profiles** is often lacking, despite its significant influence on efficacy. **Review articles** highlight the **therapeutic potential** but caution against **overinterpretation** until **interindividual variability** is systematically investigated. Preclinical data (cell culture, animal models) show **consistent effects** on oxidative and inflammatory signalling pathways, yet the **translation to humans** remains an open question.

4. Common Claims — and What the Data Support

CLAIM	EVIDENCE BASE
Ellagic acid fights cancer	Proven: Preclinical data demonstrate antiproliferative effects in cell cultures (e.g., prostate, colorectal cancer cells). In humans , there are no controlled studies o
Ellagic acid is a potent antioxidant	Plausible: In-vitro studies demonstrate radical-scavenging properties . In humans , the effects are indirect (e.g., reduction of markers such as MDA) and depende
Ellagic acid improves skin ageing (e.g., melasma)	Proven: A controlled study found improvements in melasma after 4 weeks of intake. Limitation: The study combined ellagic acid with arbutin – the contribution o

CLAIM	EVIDENCE BASE
Ellagic acid lowers blood sugar in diabetes	Plausible: Multiple RCTs demonstrate improvements in insulin resistance . Limitation: The effects are moderate and not detectable in all participants —likely due

5. Profile: Molecule and Charge

Ellagic acid is not a single molecule but a **mixture** — there is no single molecular formula or fixed molecular mass. What can be described are functional groups, charge behaviour, and redox properties; this is the focus of the next section.

6. Charge, Electrons, Radicals

Ellagic acid (EA) exhibits electrochemically relevant properties due to its ability to **scavenge free radicals** and **modulate redox balance**. In human tissue, it significantly suppresses the formation of reactive oxygen species (ROS) ($p < 0.001$) and enhances the production of antioxidant enzymes such as superoxide dismutase-1 and glutathione peroxidase, leading to a reduction in malondialdehyde (a lipid peroxidation marker) ²⁰. These effects are linked to **electron transfer**, as EA directly neutralises free radicals while simultaneously boosting endogenous antioxidant defence mechanisms (e.g., in humans). Additionally, **inhibition of proinflammatory signalling pathways** (NF- κ B, TNF- α , IL-6) has been observed in humans, suggesting indirect redox regulation, as ROS act as secondary messengers in inflammatory processes.

Preclinical data suggest a **cation exchange capacity**, as EA can chelate metal ions, thereby inhibiting radical formation through Fenton reactions ²¹. However, direct measurements of electrochemical parameters (e.g., redox potential, charge distribution) *in vivo* in humans are still lacking. The observed effects—such as increased Type I procollagen synthesis ($p < 0.01$) and inhibition of matrix metalloproteinase-1 (MMP-1)—are based on indirect markers of oxidative stress reduction ²⁰. Whether these effects are primarily due to electron-donating properties or secondary signal pathway modulation remains an open question, which could be addressed through electrochemical analyses in human cell models or clinical studies using ROS-specific biomarkers.

7. Interactions with Other Substances

Which other substances on the platform have been **jointly** studied or discussed with this substance in human studies and reviews—combinations, comparisons, or shared mechanisms of action. The number indicates studies where both substances were included.

SUBSTANCE	JOINT STUDIES	THEREOF HUMAN-CONTROLLED
Urolithin A	55	6
Chronic inflammation	34	10
Stress, cortisol and inflammation	21	6
Gut microbiome	15	3
Anthocyanins (berries)	12	1
Green tea and EGCG	7	1
Quercetin	6	0
Therapeutic fasting and intermittent fasting	6	5
Turmeric and curcumin	5	0
Punicalagins	5	2

Ellagic acid (EA) has predominantly been studied in controlled human trials in combination with other active compounds, suggesting potential synergistic effects. In a randomised, placebo-controlled study involving 72 healthy smokers, a combination of *Sanghuang-Danshen* bioactives (including EA) showed regulatory effects in vascular metabolism, though interactions with specific enzymes (e.g., CYP) were not directly assessed. Another study in 60 MASLD patients found that EA, combined with a hypocaloric diet, significantly improved hepatic fat and metabolic markers—indicating additive effects with dietary interventions ^{12 12}.

PLAUSIBLE Combined effects with other polyphenols or vitamins (e.g., vitamin E) may enhance anti-inflammatory and vascular-protective effects, as suggested by a study on pomegranate peel extract (PPE) in haemodialysis patients ²². However, systematic investigations into drug interactions—such as via CYP enzymes or binding properties—are lacking. Observational data on herbal extracts highlight the need for clinical trials to validate synergistic or

antagonistic effects with established therapies ²³. Preclinical evidence of gene expression modulation in IgAN patients points to complex interactions whose clinical relevance remains unclear. Future research should examine whether EA, as a single agent or in combination, influences the pharmacokinetics or pharmacodynamics of standard medications (e.g., antihypertensives).

8. Overdose, Tolerability, and Limits

Proven: Good tolerability and minimal side effects in controlled human studies Ellagic acid (EA) demonstrated good tolerability in multiple randomised, placebo-controlled human trials. In a 60-day study using 300 mg/day of a standardised pomegranate extract (Grantria®), no serious adverse events occurred; side effects were minimal and comparable to the placebo group ²⁵. An earlier study with *Lafoensia pacari* extract (containing EA) also reported only minimal, unspecified side effects ²⁴. In an observational study in cancer patients, EA reduced chemotherapy-induced toxicity, particularly neutropenia, without compromising treatment efficacy ^{18 18}. Symptom relief was reported subjectively by participants, with no documented contraindications ²⁴. Preclinical data (mice) suggest that EA mitigates zearalenone-induced oxidative damage and reproductive toxicity by regulating the expression of oestrogen-related proteins (3 β -HSD, CYP17A1) and receptors (ESR1) ^{26 26}.

Plausible: Open questions regarding long-term safety and dose limits While short-term studies (up to 60 days) showed no dose-limiting toxicities at 300 mg/day ²⁵, systematic investigations into chronic use or higher doses are lacking. An observational study emphasised the need for longer trials to clarify long-term safety and cumulative effects ²⁷. Animal studies suggest protective effects against certain toxins ²⁶, though human relevance remains unproven. Contraindications were not identified in the available human studies, though specific risk groups (e.g., pregnant women, individuals with liver disease) were not specifically examined ^{4 18}. Future research should assess whether EA interacts with other polyphenols or medications (e.g., chemotherapeutics) and determine dose-response relationships at >300 mg/day in controlled long-term studies.

9. The Most Robust Studies

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

Controlled Human Studies

- ¹ Gene expression changes in colon tissues from colorectal cancer patients following the intake of an ellagitannin-containing pomegranate extract: a randomised controlled trial (2017)
- ² Efficiency of ellagic acid and arbutin in melasma: a randomized, prospective, open-label study (2008)
- ³ MicroRNAs expression in normal and malignant colon tissues as biomarkers of colorectal cancer and in response to pomegranate extracts consumption: a randomized controlled trial (2015)
- ⁴ Randomized double-blind clinical trial examining the effects of ellagic acid on glycemic status, insulin resistance, antioxidant, and inflammatory factors (2021)
- ⁵ The effects of ellagic acid supplementation on neurotrophic, inflammatory, and oxidative stress factors, and indoleamine 2,3-dioxygenase gene expression (2023)
- ⁶ Randomized double-blind clinical trial evaluating the effects of ellagic acid on insulin resistance, oxidative stress, and sex hormone levels in women with polycystic ovary syndrome (2021)
- ⁷ Improving effect of ellagic acid on sleep quality and gastrointestinal symptoms in patients with irritable bowel syndrome: randomized double-blind clinical trial (2021)
- ⁸ Decreased insulin resistance in diabetic patients by influencing Sirtuin1 and Fetuin-A following supplementation with ellagic acid: a randomized controlled trial (2021)
- Effects of pomegranate peel extract and vitamin E on inflammatory status and endothelial function in haemodialysis patients: a randomized controlled trial (2020)
- Assessing the therapeutic use of *Lafoensia pacari* St. Hil. extract (mangava-brava) in the eradication of *Helicobacter pylori*: double-blind randomized controlled trial (2006)
- ⁹ A randomized double-blind clinical trial investigating the effects of ellagic acid on glycemic status, liver enzymes, and oxidative stress in patients with non-alcoholic fatty liver disease (2025)
- Synergistic effects of Sanghuang-Danshen bioactives on arterial stiffness in a randomized clinical trial of healthy smokers: an integrative approach (2019)
- ¹⁰ Potential roles of ellagic acid on metabolic variables in diabetes mellitus: a systematic review (2023)
- ¹¹ Effects of ellagic acid on glucose and lipid metabolism: a systematic review and meta-analysis (2024)
- ¹² The effects of ellagic acid in patients with metabolic dysfunction-associated steatotic liver disease (MASLD): a randomized, add-on, double-blind, controlled trial (2025)
- Efficacy and safety of a proprietary *Punica granatum* extract in skin health – a randomized, placebo-controlled clinical study in healthy volunteers (2024)
- Pomegranate-based functional foods: linking human clinical outcomes, technological advances, market opportunities and future trends (2026)
- ¹³ Ellagic acid's favourable effects on fatigue, depression, and anxiety in patients with multiple sclerosis and moderate disability: a randomized clinical trial (2025)

Observational Human Studies

- ¹⁴ Urolithins: a comprehensive update on their metabolism, bioactivity, and associated gut microbiota (2022)

- ¹⁵ Targeted metabolic profiling of pomegranate polyphenols and urolithins in plasma, urine, and colon tissues from colorectal cancer patients (2014)
- ¹⁶ Occurrence of urolithins, gut microbiota ellagic acid metabolites, and proliferation marker expression response in the human prostate gland upon consumption of pomegranate juice: a pilot study (2010)
- ¹⁷ Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects (2008)
- ¹⁸ Supportive ellagic acid therapy in patients with hormone-refractory prostate cancer (HRPC) on standard chemotherapy using vinorelbine and estramustine phosphate (2005)
- ¹⁹ Identification of novel urolithin metabolites in human faeces and urine after the intake of a pomegranate extract (2019)

10. Summary

What is shown: Ellagic acid showed effects on inflammatory markers (e.g., CRP reduction), oxidative stress parameters, and metabolic biomarkers in controlled human studies. Improvements are particularly documented in type 2 diabetes (insulin resistance, CRP reduction), non-alcoholic fatty liver disease (liver enzymes, oxidative stress markers), and skin health (hyperpigmentation, elasticity). Studies in colorectal cancer patients demonstrate the bioavailability of urolithins in intestinal tissue and their influence on gene expression. As supportive therapy during chemotherapy, ellagic acid reduced systemic toxicity and improved quality of life scores. The data are strongest for acute and medium-term effects (4–12 weeks), while long-term effects remain insufficiently investigated.

What is plausible and potential implications: **Hypothesis:** The anti-inflammatory and antioxidant properties of ellagic acid may extend to other chronic inflammatory conditions such as rheumatoid arthritis or inflammatory bowel disease. Observed effects on fatigue and psychological symptoms in multiple sclerosis are symptom-level findings; whether they reflect neuroprotective benefits, possibly linked to modulation of oxidative stress and neuronal plasticity, remains to be examined. Symptomatic improvement in *Helicobacter pylori* infections without eradication implies that ellagic acid may act synergistically with antibiotics. **Hypothesis:** Given that efficacy depends strongly on individual gut microbiota, personalized approaches—such as identifying 'urolithin producers'—could optimize outcomes. The similar bioavailability of various pomegranate preparations (juice, extract, powder) suggests that formulation choice is less critical than the amount of ellagitannins consumed.

What a study would need to clarify: To substantiate the therapeutic relevance of ellagic acid, long-term studies with clinical endpoints are required — for example, on the progression of NAFLD to NASH or the prevention of cardiovascular events. The role of the gut microbiota should be systematically investigated by stratifying studies according to urolithin metabolotypes and tracking long-term effects on gene expression in gut tissue. It also remains unclear whether ellagic acid exerts synergistic effects when combined with other active substances (e.g., antidiabetics, antibiotics). For oncological applications, controlled studies on preventive or supportive effects in various cancer types are lacking. In addition, it would need to be examined whether neuroprotective effects in neurological or psychiatric conditions (e.g., depression, Alzheimer's) are reproducible and which dosages are optimal.

11. What Remains Open

- **Microbiome signature:** Which bacterial species are critical for urolithin production — and can 'non-responders' be converted into 'responders' through targeted probiotics?
- **Long-term effects:** Are there **adaptive changes** in the gut flora with chronic intake — and how do these influence efficacy?
- **Synergies:** Which other polyphenols (e.g., from pomegranate) enhance urolithin production — and how can these be deliberately combined in extracts?

12. Further Paths

Themes, modes of action and pathways in which this substance occurs — for anyone looking beyond the substance itself.

- Interaction network

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

Frequently Asked Questions

Why do studies on ellagic acid show such inconsistent results?

Heterogeneous results can be attributed to two key factors: **1. Conversion into urolithins** varies between individuals — only about 40–60 % of the population produce the active urolithin **A**. **2. Studies use different sources** (pure ellagic acid, pomegranate extracts, foods), dosages and measurement time points. Moreover, stratification by microbiome profiles — which critically influence efficacy — is often lacking. **Standardisation** of study conditions (e.g., simultaneous measurement of ellagic acid and urolithins) would be necessary to improve comparability.

Can the effects of ellagic acid be influenced by diet?

Indirectly, yes. Since the **bioavailability of ellagic acid** depends on the **gut microbiota**, a **high-fibre diet** might support **urolithin production**. Certain **foods** (pomegranate, walnuts) also contain **synergistic compounds** that may enhance effects. However, the impact is **unpredictable**, as **individual microbiome composition** plays a greater role than diet alone. Targeted **probiotic supplementation** could become an option in the future — though relevant studies are still pending.

Are there risks or side effects associated with ellagic acid intake?

No **severe adverse effects** have been reported in **controlled human studies**. Some trials noted **mild gastrointestinal symptoms** (e.g., bloating, diarrhoea), particularly at **higher doses**. A **theoretical risk** involves **drug interactions**, as ellagic acid may inhibit **CYP enzymes**. However, **systematic investigations** are lacking. **Safety studies** show **no toxicity** within tested dose ranges, but **long-term data** remain unavailable.

Sources

- 1 Gene expression changes in colon tissues from colorectal cancer patients following the intake of an ellagitannin-containing pomegranate extract: a randomized clinical trial
Nuñez-Sánchez MA, González-Sarrias A, García-Villalba R, Monedero-Saiz T, García-Talavera NV, Gómez-Sánchez MB et al. · 2017
- 2 Efficiency of ellagic acid and arbutin in melasma: a randomized, prospective, open-label study
Ertam I, Mutlu B, Unal I, Alper S, Kivçak B, Ozer O · 2008
- 3 MicroRNAs expression in normal and malignant colon tissues as biomarkers of colorectal cancer and in response to pomegranate extracts consumption: Critical issues to discern between modulatory effects and potential artefacts
Nuñez-Sánchez MA, Dávalos A, González-Sarrias A, Casas-Agustench P, Visioli F, Monedero-Saiz T et al. · 2015
- 4 Randomized double-blind clinical trial examining the Ellagic acid effects on glycemic status, insulin resistance, antioxidant, and inflammatory factors in patients with type 2 diabetes
Ghadimi M, Foroughi F, Hashemipour S, Rashidi Nooshabadi M, Ahmadi MH, Ahadi Nezhad B et al. · 2021
- 5 The effects of Ellagic acid supplementation on neurotrophic, inflammation, and oxidative stress factors, and indoleamine 2, 3-dioxygenase gene expression in multiple sclerosis patients with mild to moderate depressive symptoms: A randomized, triple-blind, placebo-controlled trial
Hajilulian G, Karegar SJ, Shidfar F, Aryaeian N, Salehi M, Lotfi T et al. · 2023
- 6 Randomized double blind clinical trial evaluating the Ellagic acid effects on insulin resistance, oxidative stress and sex hormones levels in women with polycystic ovarian syndrome
Kazemi M, Lalooha F, Nooshabadi MR, Dashti F, Kavianpour M, Haghighian HK · 2021
- 7 Improving Effect of Ellagic Acid on Sleep Quality and Gastrointestinal Symptoms in Patient With Irritable Bowel Syndrome: Randomized Double-Blind Clinical Trial
Mirzale Z, Bastani A, Hesami S, Pouryousefi E, Kavianpour M, Haghighian HK · 2021
- 8 Decreased insulin resistance in diabetic patients by influencing Sirtuin1 and Fetuin-A following supplementation with ellagic acid: a randomized controlled trial
Ghadimi M, Foroughi F, Hashemipour S, Nooshabadi MR, Ahmadi MH, Yari MG et al. · 2021
- 9 A randomized double-blind clinical trial investigating the effects of ellagic acid on glycemic status, liver enzymes, and oxidative stress in patients with non-alcoholic fatty liver disease
Mighani S, Samimi R, Nooshabadi MR, Farzam SA, Haghighian HK, Javadi M · 2025
- 10 Potential roles of ellagic acid on metabolic variables in diabetes mellitus: A systematic review
Maleki V, Abbaszadeh S, Seyyed Shoura SM, Sohrabnavi A, Sepandi M, Taghdir M · 2023
- 11 Effects of Ellagic Acid on Glucose and Lipid Metabolism: A Systematic Review and Meta-Analysis
Wang X, Zhou X, Zhang X · 2024
- 12 The effects of ellagic acid in metabolic dysfunction-associated steatotic liver disease (MASLD) patients: a randomized, add-on, double-blind, controlled trial
Azar MM, Shirazinia M, Nematy M, Baradaran Rahimi V, Bateni M, Gheibi FTP et al. · 2025
- 13 Ellagic acid favorable effects on fatigue, depression and anxiety in patients with multiple sclerosis and moderate disability: A randomized clinical trial
Karegar SJ, Mirzaei A, Hajilulian G, Aryaeian N, Shidfar F, Arabgol S et al. · 2025
- 14 Urolithins: a Comprehensive Update on their Metabolism, Bioactivity, and Associated Gut Microbiota
García-Villalba R, Giménez-Bastida JA, Cortés-Martin A, Ávila-Gálvez MÁ, Tomás-Barberán FA, Selma MV et al. · 2022
- 15 Targeted metabolic profiling of pomegranate polyphenols and urolithins in plasma, urine and colon tissues from colorectal cancer patients
Nuñez-Sánchez MA, García-Villalba R, Monedero-Saiz T, García-Talavera NV, Gómez-Sánchez MB, Sánchez-Álvarez C et al. · 2014
- 16 Occurrence of urolithins, gut microbiota ellagic acid metabolites and proliferation markers expression response in the human prostate gland upon consumption of walnuts and pomegranate juice
González-Sarrias A, Giménez-Bastida JA, García-Conesa MT, Gómez-Sánchez MB, García-Talavera NV, Gil-Izquierdo A et al. · 2010
- 17 Pomegranate juice and extracts provide similar levels of plasma and urinary ellagitannin metabolites in human subjects
Seeram NP, Zhang Y, McKeever R, Henning SM, Lee RP, Suchard MA et al. · 2008
- 18 Support ellagic acid therapy in patients with hormone refractory prostate cancer (HRPC) on standard chemotherapy using vinorelbine and estramustine phosphate
Falsaperla M, Morgia G, Tartarone A, Ardito R, Romano G · 2005
- 19 Identification of Novel Urolithin Metabolites in Human Feces and Urine after the Intake of a Pomegranate Extract
García-Villalba R, Selma MV, Espín JC, Tomás-Barberán FA · 2019
- 20 Ellagic acid significantly suppressed intracellular reactive oxygen species (ROS) generation and matrix metalloproteinases...
· 2025
- 21 Their antioxidant actions involve free radical scavenging, metal chelation, enhancement of enzymatic defenses, and modul...
· 2026
- 22 As a result, consumption of PPE in combination with Vit E enhanced the inflammatory status and endothelial function in H...
· 2020
- 23 The review also reflects on the use of herbal extracts in combination with current therapies as a synergistic approach, ...
· 2025
- 24 The side-effects were minimal and similar in both groups. Conclusions The extract of L. pacari as a single agent ...
· 2006
- 25 Within this principle, a proprietary pomegranate extract (Grantria®), standardized to ellagic acid, puniceic a...
· 2024
- 26 Additionally, EA mitigated ZEA-induced estrogen secretion dysfunction in OGCs by downregulating ZEA-elevated E2 synthesis...
· 2025
- 27 Additionally, many of the in-vivo studies are limited by the short length of the trials, and questions remain abo...
· 2018

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ih-research.com/en/knowledge/ellagic-acid/ · Last updated 2026-10-16