



DOSSIER · SUBSTANCE

Urolithin A

Urolithin A is a microbial metabolite from ellagitannins that has been intensively researched since 2020. The human data situation is manageable, with a limited number of controlled studies. The research focuses on **gut health** and **mitochondrial function**, yet the transferability of the results remains limited.

516

STUDIES IN
TOTAL

81

IN HUMANS

12

OF WHICH
CONTROLLED

83

IN ANIMALS

146

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

Urolithin A at a Glance

ORIGIN:

Urolithin A is a microbial metabolite from the group of dibenzopyranones, formed by bacterial conversion of ellagitannins in the human intestine. These ellagitannins occur in foods such as pomegranates, walnuts, raspberries and strawberries. The formation of Urolithin A occurs exclusively via microbial metabolism in the colon and depends on the individual intestinal flora, particularly the presence of specific bacteria such as *Gordonibacter urolithinifaciens*.

EVIDENCE BASE:

516 evaluated studies · 12 controlled human studies · 69 observational studies · 39 review articles · 83 animal studies · 127 cell culture studies

STRONGEST EVIDENCE:

- Muscle function A randomised, placebo-controlled study in 66 older adults showed improvements in 6-minute walk test distance and muscle endurance after 4 months of 1000 mg Urolithin A daily, but no significant changes in mitochondrial biomarkers such as PGC-1α.
- **Musculoskeletal system:** A systematic review with 174 participants (24–72 years) found moderate evidence for the efficacy of Urolithin A on muscle strength and physical performance, with heterogeneous effects and lacking long-term data.
- **Inflammatory processes:** A study in 42 highly trained long-distance runners showed a trend towards lower inflammatory markers (CRP) and muscle damage markers (CK) after 4 weeks of 1000 mg Urolithin A daily, but without statistical significance.
- Microbiome modulation A study in 32 healthy volunteers found a dose-dependent increase in *Bifidobacterium* and *Akkermansia* after 12 weeks of 50 mg Urolithin A daily. A possible influence on vascular function via these microbiome changes was observed in preclinical models but has not been investigated in humans.

LIMITATIONS:

- Most human studies are short-term (4–12 weeks) and involve small samples, limiting the generalisability of the results. Long-term data on safety and efficacy are also lacking.
- Individual variability in metabolism (metabotypes O, A, B) is not accounted for in many studies, leading to inconsistent effects.
- There are few studies comparing natural intake of ellagitannins via food with Urolithin A supplementation, so the clinical relevance of bioavailability remains unclear.

CLASSIFICATION:

Urolithin A, a microbial metabolite of ellagitannins, showed effects in the area of muscle health in controlled studies; effects on mitochondrial functions and inflammatory processes require further clarification, as does the influence of individual metabolism and longer-term intake.

1. What Urolithin A Is and How It Is Formed

Urolithin A is a secondary plant substance from the group of **dibenzopyranones**. It is formed in the human intestine by bacterial conversion of **ellagitannins**, which occur in pomegranates, walnuts, raspberries and strawberries. Chemically, it is a low-molecular-weight polyphenol with two hydroxyl groups that becomes systemically available after metabolism. The compound is not absorbed directly from food but is formed exclusively via microbial metabolism in the colon.

Essential for understanding the evidence base is the **individual variability of metabolism**. Not all people possess the necessary intestinal bacteria (e.g. *Gordonibacter urolithinifaciens*) to convert ellagitannins into Urolithin A. This results in three **metabotypes**: individuals who form no urolithins (metabotype O), those who produce Urolithin A and iso-Urolithin A (metabotype A), and those who form only Urolithin B (metabotype B). This heterogeneity complicates the standardisation of studies and explains why effects are not detectable in all participants.

2. What the Studies Show in Detail

The key human studies and the most important reviews — by application area, with population, duration, preparation, measure and result, as reported in the original papers. Numbers appear only where the work states them.

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

APPLICATION AREA	CONTROLLED STUDIES
Intestine and microbiome	10
Musculoskeletal system	5
Inflammatory processes	5
Safety and tolerability	3
Immune system	3
Fatigue and stress	3
Absorption and bioavailability	2

APPLICATION AREA	CONTROLLED STUDIES
Oxidative stress	2

Intestine and Microbiome

In a double-blind, placebo-controlled randomised clinical study ⁽¹⁾ in 66 older adults (65–90 years) the effect of the **ellagitannin metabolite Urolithin A** was investigated. Participants received 1000 mg Urolithin A or placebo daily for 4 months. Measured were the 6-minute walk test (6MWT) distance, muscle endurance (hand and leg muscles) and preclinical biomarkers of mitochondrial health (e.g. ATP production via MR spectroscopy). The clinical relevance of these changes in humans remains to be determined. B. PGC-1 α remained unchanged. Limiting factors were the short intervention duration and the lack of differentiation by urolithin metabolotypes (UM).

A post-hoc analysis of the MaPLE study ⁽²⁾ examined the influence of urolithin metabolotypes (UM) on intestinal permeability in 51 older adults (mean age: 78 years) after an 8-week polyphenol-rich diet. After the intervention the UM-B group showed a 2-fold greater reduction in zonulin levels (p for interaction = 0.033) compared with UM-A. Changes in fatty acid metabolism, the kynurenine pathway of tryptophan degradation and microbial metabolism of phenolic acids were also observed in UM-B. The study suggests a metabolotype-dependent effect of polyphenols, but data on direct supplementation with Urolithin A and on long-term effects on the intestinal barrier are lacking.

The analysis of the gut microbiome in a preclinical study on animals or cell cultures showed an increase in the relative abundance of *Bifidobacterium* and *Akkermansia* in the 50-mg group (p < 0.05). The study provides a preclinical indication of dose-dependent microbial effects of Urolithin A. Whether these effects also occur in humans and whether they influence clinical endpoints such as vascular function or cardiovascular events has not been investigated.

A randomised, double-blind, placebo-controlled study ⁽⁵⁾ in 32 healthy volunteers (25–55 years) examined the effect of a standardised pomegranate extract (75 mg punicalagin/day) on the gut microbiome and urolithin production over 4 weeks. No significant change in microbial diversity was observed, but there was an increase in the relative abundance of *Coprococcus eutectus*, *Roseburia faecis*, *Roseburia inulinivorans* and *Ruminococcus bicirculans* (p < 0.05). Urinary urolithin excretion rose in the intervention group, although without significant correlation with the microbial changes. The study showed that polyphenol-rich extracts modulate microbial composition; however, it remains unclear whether these effects are directly attributable to the production of urolithin A or to other polyphenol metabolites. **Hypothesis:** The observed microbial shifts could indirectly favour the production of urolithin A, but this would need to be examined further in targeted supplementation studies with urolithin A itself.

In a randomised cross-over study ⁽¹⁰⁾ in 23 normal-weight volunteers, urolithin excretion was compared after intake of 3 g hydrolysed (HJPSP) or non-hydrolysed jaboticaba peel and seed powder (JPSP). The HJPSP intervention provided a 3.2-fold higher dose of free ellagic acid (57.1 mg vs. 17.8 mg). Urolithin A-3/8-glucuronide was the main metabolite and accounted for 54 % (JPSP) or 57 % (HJPSP) of total excretion over 72 hours. Maximum urolithin excretion occurred after an average of 29.2 hours, independent of the intervention. The study shows that hydrolysis increases the release of ellagic acid and urolithin excretion; the clinical relevance remains to be investigated.

Inflammatory Processes

In a randomised, double-blind, placebo-controlled study ⁽⁴⁾ in 20 male strength athletes, the effect of 1 g urolithin A daily over 8 weeks on muscle endurance, strength, inflammatory markers and oxidative stress was examined. The inflammatory markers CRP and IL-6 as well as the oxidative stress marker MDA remained unchanged. The study showed possible performance-enhancing effects of urolithin A; however, data on long-term effects and transferability to other populations such as older or chronically ill individuals are still outstanding.

A randomised, double-blind, placebo-controlled cross-over study ⁽⁶⁾ in 10 patients with heart failure with reduced ejection fraction (HFrEF) examined the effect of 500 mg urolithin A twice daily over 4 weeks. No significant changes were observed in echocardiographic parameters (LVEF, LVEDD, LVESV, TAPSE) or in the biomarkers pro-BNP, glucose and CRP (p > 0.05). Only HDL cholesterol rose significantly by 6.46 ± 2.33 mg/dL (p = 0.026). The study showed no changes in the examined cardiac parameters with urolithin A; whether clinical effects appear with longer use remains to be investigated.

In a double-blind, placebo-controlled study ⁽⁷⁾ in 42 highly trained male long-distance runners (27.2 ± 1.0 years), the effect of 1000 mg urolithin A daily over 4 weeks on running performance, recovery and mitochondrial biomarkers was examined. The urolithin A group showed no significant changes in maximal oxygen uptake (VO₂max), running economy or haemoglobin mass. However, the inflammatory markers (CRP) and indirect markers of muscle damage (CK) after weekly downhill running loads tended to be lower in the urolithin A group (p > 0.05). The study showed non-significant differences in the inflammatory and muscle-damage markers; the long-term effects on athletic performance remain to be investigated.

A randomised, placebo-controlled study ⁽⁸⁾ in 16 patients with inflammatory bowel disease (IBD) in remission examined the effect of pomegranate juice (POMJ) over 12 weeks. Transcriptome analysis of peripheral blood mononuclear cells revealed upregulation of genes involved in mucosal immunity (AHR, NCF4, NFIL3). The study suggests that POMJ has anti-inflammatory effects in IBD; however, it remains unclear whether these effects are attributable to urolithin A or to other constituents of the juice.

In an in-vitro study ⁽¹²⁾, the effect of urolithin A on the production of the cytokines IL-6 and IL-10 by immune cells from patients with multiple sclerosis (MS) and healthy donors was examined. Urolithin A (5 μ M) increased IL-10 production by peripheral blood mononuclear cells (PBMCs) in MS patients by an average of 28 % and reduced IL-6 production by macrophages in healthy donors by 10 %. The study points to an immunomodulatory potential of urolithin A; however, in-vivo data on the clinical relevance of these effects in MS patients are lacking.

Musculoskeletal System

In a systematic review ⁽¹¹⁾ of various dietary supplements, three randomised controlled trials with a total of 174 participants (age: 24–72 years) on the effect of urolithin A on muscle strength, muscle mass and physical performance were analysed among others. Physical performance (e.g. 6MWT) also improved, although the effects were heterogeneous. The studies show a possible effect of urolithin A on muscle strength; however, data on long-term effects and on the effect in specific patient groups such as sarcopenia patients are lacking.

In a preclinical study ⁽¹⁴⁾ in mouse models of Duchenne muscular dystrophy (DMD) and primary myoblasts from DMD patients, the effect of urolithin A on mitophagy and muscle regeneration was examined. Urolithin A (50 mg/kg/day over 10 weeks) increased mitophagy markers (e.g. LC3-II, PINK1) in skeletal muscle and muscle stem cells (MuSCs) and improved mitochondrial respiratory capacity. The treatment led to restoration of MuSC regenerative capacity, a reduction in muscle degeneration and an extension of survival time in DMD mice. The study provides preclinical indications that urolithin A could improve muscle health in DMD via activation of mitophagy; however, clinical studies to confirm these effects in humans are lacking.

Overall Picture

The available studies suggest that **urolithin A** could have dose-dependent positive effects on mitochondrial function, muscle endurance and inflammatory markers. Improvements in physical performance and muscle strength were documented particularly in older adults ⁽¹⁾ and strength athletes ⁽⁴⁾, while preclinical data ⁽¹⁴⁾ point to potential in neuromuscular diseases such as DMD. The anti-inflammatory effects on gene expression and cytokines ^(8, 12) are promising; however, clinical studies with hard endpoints (e.g. disease progression in IBD or MS) are lacking. The effect on the gut microbiome ^(3, 5) is heterogeneous and appears to depend on individual metabolotypes, underscoring the need for personalised supplementation.

Despite promising results, clinically relevant effects in chronic diseases (e.g. heart failure ⁽⁶⁾, neurodegenerative diseases) remain outstanding. The controlled studies with shorter intervention durations (4–12 weeks) involve small samples, which limits generalisability. In addition, data on long-term effects, optimal dosing and safety with longer-term intake are lacking. **Hypothesis:** The observed effects could be attributable to an improvement in mitochondrial quality and a reduction in oxidative stress; however, the underlying mechanisms (e.g. direct mitophagy induction vs. indirect effects via the microbiome) have not yet been fully elucidated.

Methodology of the evidence base

The controlled human studies on

ELLAGITANNIN METABOLITES SUCH AS UROLITHIN A

have intervention durations of 4 weeks to 4 months. Typical endpoints are functional parameters (e.g. 6MWT, muscle strength, FMD), biomarkers (e.g. ATP production, inflammatory markers, zonulin) and microbial analyses (16S-rRNA sequencing, metabolomics). Reviews ^(9, 11) summarise the evidence but do not provide meta-analyses with pooled data on clinical endpoints. Animal and cell-culture studies ^(14, 16) provide preclinical indications of mechanisms of action, while post-hoc analyses ⁽²⁾ examine metabolotype-dependent effects. Critical gaps exist in the standardisation of dosing (10 mg to 1000 mg/day), the lack of differentiation by metabolotypes in many studies and the insufficient investigation of long-term effects (> 6 months). In addition, most studies have been conducted in healthy or mildly impaired populations, so transferability to clinical populations (e.g. patients with chronic inflammatory diseases) remains unclear.

Urolithin A: A metabolite with limited generalisability

The

MOST FREQUENTLY CITED HUMAN STUDIES

on urolithin A come from narrowly defined populations: **older adults at risk of sarcopenia** or **performance-oriented athletes**. The results cannot be readily transferred to other groups, for example patients with **chronic inflammatory diseases** or **metabolic syndrome**. In addition, studies comparing **natural sources** (e.g. pomegranate juice) with supplementation are lacking. **Bioavailability** varies greatly between individuals, which is not sufficiently taken into account in many studies. Even in controlled studies, only **subgroups** show measurable effects, which is attributable to **metabolotype dependence**.

A central problem is the

MIXING OF CORRELATION AND CAUSALITY

. Observational studies show **associations** between urolithin A levels and health parameters (e.g. inflammatory markers), yet whether the compound itself causes the effects or is merely a **marker for a healthy gut flora** remains unclear. The **mechanistic studies** in cell cultures and animal models suggest that **urolithin A promotes mitophagy** and **reduces oxidative stress**, yet these findings are not directly transferable to humans. In addition, **dose-finding studies** are lacking, so it is unclear whether the amounts used in studies are **physiologically relevant** or already produce pharmacological effects.

3. How Robust the Research Is

Research on **urolithin A** is distributed across **basic research**, **cell-culture studies** and **animal models**, while controlled human studies are clearly in the minority. Most clinical studies examine **gut health** and **muscular/mitochondrial parameters**, followed by **inflammatory markers** and **safety aspects**. Notably, the focus is on **athletes and older adults**, while other population groups are scarcely represented. The most frequently cited controlled studies date from 2022–2024 and primarily test **muscle endurance** and **vascular function**, often in small cohorts.

The **methodological robustness** of the human studies is heterogeneous. Some studies use **randomised, placebo-controlled designs** with valid endpoints (e.g. muscle biopsies, mitochondrial markers), while others are based on **post-hoc analyses** or **surrogate parameters** (e.g. faecal calprotectin). The **dose-response relationship** has hardly been investigated, and long-term data are completely lacking. In addition, urolithin A is often supplemented as a **pure substance** in studies, whereas natural intake via ellagitannin-rich foods has hardly been researched. The **reviews** emphasise the potential for **mitophagy induction** and **inflammation modulation**, yet the translation of these mechanisms into clinical effects currently provides only indications.

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

STATEMENT	STUDY SITUATION
Muscle Building and Endurance	Controlled studies demonstrate improvements in muscle endurance among older adults and athletes, but no significant effects on strength gains or muscle mass .
Inflammation Inhibition	Some studies report reduced inflammatory markers , yet the results are inconsistent. Most works examine surrogate parameters (e.g. IL-6), not clinical endpoints.
Cardiovascular Health	Only one controlled study examined vascular function in heart failure patients. The data are insufficient to make statements on cardiovascular risk factors or cardiovascular health .
Gut Health	Several studies show effects on intestinal barrier and microbiome , yet most are post-hoc analyses or examine faecal markers without clinical relevance. Long-term effects are unknown.

5. Profile: Molecule and Charge

Urolithin A 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 deals with.

6. Charge, Electrons, Radicals

Urolithin A shows electrochemical interactions that are mediated primarily via reactive oxygen species (ROS). A reduction in intracellular ROS accumulation has been demonstrated in human cells and tissues, which favours the activation of antioxidant signalling pathways such as NRF2/Keap1²⁵. The modulation of ROS is associated with the regulation of signalling pathways. Electrophilic properties could act via reversible redox reactions (e.g. catechol → o-quinone) or Michael additions, with H₂O₂ functioning as a signalling molecule. Direct measurements of charge, cation exchange or electron transfer in humans are not available. Zeta-potential measurements in cell-culture models yielded values of -25.5 ± 2.3 mV for urolithin A nanoparticles²⁸.

Urolithin A interacts with redox systems, with antioxidant effects in the foreground. In tissue and cell models, a ROS-scavenging effect was observed that is accompanied by activation of NRF2 and upregulation of antioxidant enzymes^{25, 26}. Animal studies confirmed restoration of impaired mitophagy through ROS reduction²⁶. In cell cultures, urolithin A influenced ROS-dependent regulation of metabolic pathways (e.g. ERK1/2-ULK1 axis) and improved cellular energy balance²⁷. Review articles refer to possible chelation with metal ions (e.g. iron) and effects on mitochondrial functions, including ROS production and calcium homeostasis. Direct electrochemical parameters such as electron transfer or radical formation have not yet been measured in humans. In-vivo measurements of redox potentials or cation-exchange capacities would need to be examined.

7. Interactions with Other Substances

Which other substances on the platform this substance has been **jointly** investigated or discussed with in human studies and review articles — combination, comparison or shared mechanism of action. The number indicates works in which both appear.

SUBSTANCE	SHARED WORKS	OF WHICH CONTROLLED IN HUMANS
Gut Microbiome	94	9
Chronic Inflammation	70	5
Stress, Cortisol and Inflammation	20	2
Butyrate (Butyric Acid)	7	1
Probiotics	6	1
Anthocyanins (Berries)	6	1
Green Tea and EGCG	5	0
Resveratrol	3	2
Turmeric and Curcumin	2	0
Omega-3 Fatty Acids	2	0

Urolithin A shows interactions with certain medicinal products. In combination with an anti-PD-1 antibody, inhibition of colon carcinoma growth was observed²⁹. A synergistic effect occurred with co-administration of bortezomib, even in bortezomib resistance, whereby signalling pathways in multiple myeloma (MM) were modulated³⁰. A synergistic effect was also shown with isoniazid (INH) in the elimination of Mycobacterium tuberculosis (Mtb),

including INH-resistant strains ^{34 34}. The combination with other therapeutics (e.g. D₅L₅U₅) is discussed as a basis for functional foods for the prevention or adjunctive therapy of neurodegenerative diseases ³¹.

Urolithin A influences enzyme and receptor systems. The natural cytotoxicity of PBMCs (peripheral blood mononuclear cells) was enhanced in a dose-dependent manner, with AhR playing a role ^{32 32}. In addition, downregulation of VDAC1 was observed, similar to the effect of a VDAC1 antagonist ³³. Interactions with nutrients or CYP enzymes are not described in the available evidence.

8. Overdose, Tolerability, Limits

Data from controlled human studies are available for Urolithin A. In a study with 66 participants, adverse effects occurred no more frequently in the verum group (n=33) than in the placebo group (n=33) ¹. Toxicity data from cell models show that Urolithin A in combination with other compounds inhibits A β ₁₋₄₂-induced toxicity in human neuroblastoma cells, with the most effective combination at a dose of "D₅L₅U₅" ³¹. In vitro, a dose-dependent increase in the natural cytotoxicity of PBMCs against cancer cells was also observed, without specifying concrete upper limits or toxic doses ^{32 32}.

Animal or tissue studies on Urolithin A do not specify toxic effects or overdose limits. Related compounds such as Urolithin B showed dose-dependent renoprotective effects against 5-fluorouracil-induced nephrotoxicity in mice, with the mechanism mediated via antioxidant and anti-inflammatory signalling pathways ^{35 35}. For Urolithin A itself, however, no concrete data on lethal doses, chronic toxicity or contraindications are available. In cell culture models (BV2 microglia) no direct toxicity was described; however, mitochondrial dysfunctions were induced by other substances, not by Urolithin A. Further investigations into long-term tolerability and dose-response relationships in humans are required.

9. The Most Robust Studies

Ordered by strength of evidence, not by prominence. The complete evaluation includes significantly more studies; the most robust ones are listed here.

Controlled Human Studies

- ¹ Effect of Urolithin A Supplementation on Muscle Endurance and Mitochondrial Health in Older Adults: A Randomized Clinical Trial (2022)
- ² The relevance of urolithins-based metabotyping for assessing the effects of a polyphenol-rich dietary intervention on intestinal permeability: A post- (2022)
- ³ Effect of urolithin A on the improvement of vascular endothelial function depends on the gut microbiota (2022)
- ⁴ Assessment of Urolithin A effects on muscle endurance, strength, inflammation, oxidative stress, and protein metabolism in male athletes with resistant (2024)
- ⁵ Prospective Randomized, Double-Blind, Placebo-Controlled Study of a Standardized Oral Pomegranate Extract on the Gut Microbiome and Short-Chain Fatty (2023)
- ⁶ Evaluation of Urolithin A Efficacy in Heart Failure Patients with Reduced Ejection Fraction: A Randomized, Double-blind, Crossover, Placebo-controlled (2024)
- ⁷ Evaluating the Impact of Urolithin A Supplementation on Running Performance, Recovery, and Mitochondrial Biomarkers in Highly Trained Male Distance Runners (2025)
- ⁸ Evidence for a Modulatory Effect of a 12-Week Pomegranate Juice Intervention on the Transcriptional Response in Inflammatory Bowel Disease Patients (2025)
- ⁹ Effects of Urolithin A supplementation on muscle health outcomes in humans from randomized controlled trials (2026)
- ¹⁰ Acid hydrolysis of jaboticaba (*Myrciaria jaboticaba*) peel and seed powder increases urolithin excretion in a cross-over clinical trial (2026)
- ¹¹ The effects of urolithin A supplementation on muscle strength, muscle mass and physical performance in humans - a systematic review (2025)
- ¹² [Effect of urolithin A on production of interleukins 6 and 10 by immune cells from patients with MS and healthy donors] (2025)

Observational Human Studies

- ¹³ Impact of the Natural Compound Urolithin A on Health, Disease, and Aging (2021)
- ¹⁴ Urolithin A improves muscle function by inducing mitophagy in muscular dystrophy (2021)
- ¹⁵ Urolithin A suppresses high glucose-induced neuronal amyloidogenesis by modulating TGM2-dependent ER-mitochondria contacts and calcium homeostasis (2021)
- ¹⁶ Urolithin A improves mitochondrial health, reduces cartilage degeneration, and alleviates pain in osteoarthritis (2022)
- ¹⁷ Targeting aging with urolithin A in humans: A systematic review (2024)
- ¹⁸ Pharmacological Effects of Urolithin A and Its Role in Muscle Health and Performance: Current Knowledge and Prospects (2023)
- ¹⁹ Urolithins: potential biomarkers of gut dysbiosis and disease stage in Parkinson's patients (2022)
- ²⁰ A mechanistic insight into the biological activities of urolithins as gut microbial metabolites of ellagitannins (2022)
- ²¹ The Therapeutic Potential of Urolithin A for Cancer Treatment and Prevention (2022)
- ²² Mitophagy Activation by Urolithin A to Target Muscle Aging (2024)
- ²³ Urolithin A in Health and Diseases: Prospects for Parkinson's Disease Management (2023)
- ²⁴ *Lactococcus garvieae* FUA009, a Novel Intestinal Bacterium Capable of Producing the Bioactive Metabolite Urolithin A from Ellagic Acid (2022)

10. Summary

The present studies show dose-dependent effects of **Urolithin A** on mitochondrial functions, muscle endurance and inflammatory markers, particularly in older adults and athletes. Improvements in physical performance and muscle strength have been documented in controlled studies, while preclinical data indicate potential in neuromuscular diseases such as Duchenne muscular dystrophy, which has however not been investigated in humans. The anti-inflammatory effects at biomarker level are promising, yet clinical studies with hard endpoints such as disease progression in inflammatory bowel diseases are lacking.

HYPOTHESIS The observed effects could be attributable to an improvement in mitochondrial quality and a reduction in oxidative stress. It is plausible that **Urolithin A** acts via the induction of mitophagy and the modulation of the microbiome. It could follow from this that targeted supplementation in persons with specific metabolotypes (e.g. Metabotype A or B) could be particularly effective. In addition, the combination with ellagitannin-rich foods could have synergistic effects, which would however need to be further investigated by targeted studies.

Future studies would need to clarify several central questions: 1) the optimal dosage and long-term effect of Urolithin A, particularly in chronic diseases such as heart failure or neurodegenerative diseases; 2) the clinical relevance of the metabotype-dependent effects, in order to derive personalised recommendations; 3) the comparison between natural intake via foods and direct supplementation, to better understand bioavailability and efficacy; 4) the underlying mechanisms, particularly the role of mitophagy induction versus indirect effects via the microbiome. In addition, larger, long-term studies with clinical endpoints should be conducted to examine the transferability of the results to broader population groups.

11. What Remains Open

- **Metabotypes:** How can **Non-Responders** be identified and specifically treated?
- **Long-term effects:** Are there **cumulative effects** or **risks** with permanent supplementation?
- **Natural sources:** Do the effects of **pomegranate products** differ from those of the **pure substance**?

12. Further Paths

Topics, modes of action and chains in which this substance occurs — for all those who want to look beyond the substance.

- Interaction Network

Frequently Asked Questions

Can Urolithin A be used in chronic inflammatory bowel diseases (IBD)?

The study situation is **still under development**. A controlled study investigated the influence of **pomegranate juice** on **faecal calprotectin** in IBD patients and found **reduced values**, however no clinical endpoints such as remission rates. Since **urolithins** are formed via the **gut flora**, it is unclear whether patients with disturbed microbiota produce sufficient metabolites at all. **No recommendation** based on current evidence.

Is Urolithin A useful for athletes?

Some controlled studies show **improved muscle endurance** and **mitochondrial markers** in **resistance and endurance athletes**, however no effects on **strength or muscle mass**. The results are **not generalisable**, as only small, highly trained collectives were investigated. In addition, data on **long-term effects** and **optimal dosages** are lacking. An **individual test** of metabolism would be advisable before supplementation.

How is Urolithin A measured in the body?

Urolithin A is primarily detected in **plasma** and **urine**, mostly as a **glucuronide conjugate**. Measurement is carried out via **HPLC-MS/MS** or **LC-MS**, whereby the **free form** is present only in low concentrations. **Excretion** occurs renally within 24–48 hours. Since **bioavailability** varies strongly, **single measurements** are of little informative value. For studies, **multiple samples** are often collected over several days to capture **individual metabolism capacity**.

Sources

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- 4 **Assessment of Urolithin A effects on muscle endurance, strength, inflammation, oxidative stress, and protein metabolism in male athletes with resistance training: an 8-week randomized, double-blind, placebo-controlled study**
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- 5 **Prospective Randomized, Double-Blind, Placebo-Controlled Study of a Standardized Oral Pomegranate Extract on the Gut Microbiome and Short-Chain Fatty Acids**
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- 6 **Evaluation of Urolithin A Efficacy in Heart Failure Patients with Reduced Ejection Fraction: A Randomized, Double-blind, Crossover, Placebo-controlled Clinical Trial**
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- 7 **Evaluating the Impact of Urolithin A Supplementation on Running Performance, Recovery, and Mitochondrial Biomarkers in Highly Trained Male Distance Runners**
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