



DOSSIER · SUBSTANCE

Gamma-Oryzanol

Gamma-oryzanol is a **plant sterol ester complex** derived from rice bran, which has been studied since the 1980s. Research has primarily focused on metabolic and dermatological applications, though most studies remain foundational. The most intriguing finding: even in controlled human trials, it remains unclear whether observed effects are attributable to gamma-oryzanol itself or to accompanying compounds in rice bran.

46

STUDIES IN
TOTAL

9

IN HUMANS

2

OF WHICH
CONTROLLED

1

IN ANIMALS

9

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

Gamma-Oryzanol at a Glance

ORIGIN:

Gamma-oryzanol is a plant-based sterol ester complex comprising ferulic acid esters of phytosterols and triterpene alcohols, naturally occurring in the bran layer of rice (*Oryza sativa*).

STUDY STATUS:

46 evaluated publications · 2 controlled human studies · 7 observational studies · 1 review · 1 animal study · 6 cell culture studies

STRONGEST EVIDENCE:

- Metabolism** Controlled study (2005) with 30 hypercholesterolaemic men demonstrates that rice bran oil containing gamma-oryzanol (0.05 g or 0.8 g/day) reduces LDL cholesterol by 10.5% after 4 weeks, independent of dosage.
- Musculoskeletal System** Controlled study (2014) with healthy men following resistance training shows effects of gamma-oryzanol on anthropometric measurements and muscle strength, though without long-term data or clear mechanisms.
- Inflammatory Processes** Studies with rice bran oil indicate reductions in inflammatory markers such as IL-1β, TNF-α, and thromboxane B2, as well as antioxidant effects, though these findings cannot be attributed to gamma-oryzanol alone.
- Bone and Joints** Study with 119 perimenopausal women confirms supportive effects of a combination of gamma-oryzanol and hormone therapy on bone density and sleep quality, though without isolated data on gamma-oryzanol.

LIMITATIONS:

- Effects of gamma-oryzanol are rarely studied in isolation; most studies use rice bran oil or extracts containing co-occurring substances such as tocotrienols.
- Lack of replication studies and heterogeneous study designs (dosage, duration, outcome parameters) limit generalisability.
- Long-term effects, dose-response relationships, and safety at high dosages or in vulnerable groups remain unclear.

ASSESSMENT:

Gamma-oryzanol, a sterol ester complex from rice bran, is associated with lipid-lowering, anti-inflammatory, and antioxidant effects in studies using rice bran oil or extracts. It remains unclear whether these effects are attributable to gamma-oryzanol itself or to co-occurring compounds.

1. What Gamma-Oryzanol Is and How It Is Studied

Gamma-oryzanol is a **mixture of ferulic acid esters** of phytosterols and triterpene alcohols, naturally occurring in the **bran layer of rice** (*Oryza sativa*). It is obtained through extraction from rice bran oil, a by-product of rice processing. Chemically, it comprises a heterogeneous group of compounds, with cycloartenyl ferulate, 24-methylenecycloartanyl ferulate, and campesterol ferulate as its main components.

For understanding the study landscape, it is crucial that gamma-oryzanol is **rarely studied in isolation**. Most research uses rice bran oil or extracts containing, alongside gamma-oryzanol, **tocopherols, tocotrienols, phytosterols, and unsaturated fatty acids**. Even in controlled human studies, it often remains unclear whether observed effects are attributable to gamma-oryzanol itself, synergistic actions of co-occurring substances, or the oil as a whole. The **bioavailability** of gamma-oryzanol is also limited: in the intestine, it is partially hydrolysed, and only a fraction of the ingested amount enters the bloodstream unchanged.

2. What the Studies Show in Detail

The key human studies and most important reviews—by application area, with population, duration, preparation, measured parameters, and results, as reported in the original publications. Numbers are included only where the study provides 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
Skin	1
Musculoskeletal System	1
Fatigue and Stress	1
Gut and Microbiome	1
Metabolism	1
Absorption and Bioavailability	1

Gut and Microbiome

PROVEN A controlled, randomised parallel study with 30 mildly hypercholesterolaemic men (baseline cholesterol 4.9–8.4 mmol/l, age 38–64 years) compared two rice bran oils (RBO) with differing gamma-oryzanol content over 4 weeks. Participants received 50 g RBO daily containing either 0.05 g or 0.8 g gamma-oryzanol, following a 2-week run-in phase with 50 g peanut oil. After 4 weeks, both RBO variants reduced total cholesterol by 6.3%, LDL cholesterol by 10.5%, and the LDL/HDL ratio by 18.9%, with no significant differences between dosages. Plasma levels of total, LDL, and HDL cholesterol, as well as triglycerides, were measured at baseline and after 2, 4, and 6 weeks. The study demonstrates that gamma-oryzanol in RBO exerts lipid-lowering effects independent of dosage, though without specific findings on the microbiome or gut health ¹.

HYPOTHESIS The lipid-lowering effect may indirectly result from modulation of the gut microbiota, as plant sterols like gamma-oryzanol can influence the composition of gut bacteria. However, the study lacks direct measurements of microbiome parameters or short-chain fatty acids to support this hypothesis. The observed reduction in LDL cholesterol suggests a possible interaction with cholesterol absorption in the gut, though the precise mechanism remains unresolved.

Inflammatory Processes

A group receiving a combination of gamma-oryzanol and other substances (n=20) showed significant improvements in lipid profiles as well as reductions in inflammatory markers such as interleukin-1 β (IL-1 β), tumour necrosis factor- α (TNF- α), and thromboxane B2 (TXB2). Additionally, reactive oxygen species (ROS) decreased, while total antioxidant capacity (TAC) increased. The study thus confirms anti-inflammatory and antioxidant effects of the combination, but does not allow conclusions about gamma-oryzanol's isolated contribution.

PLAUSIBLE A review summarises preclinical and clinical data on various compounds, including gamma-oryzanol, attributing anti-inflammatory effects to them. Mechanistically, inhibition of the transcription factor NF- κ B as well as activation of PPAR- α and AMPK are discussed, which may contribute to improved glucose and lipid homeostasis. Clinical studies in patients with type 2 diabetes, obesity, or postmenopausal women (aged 30–70) suggest changes in inflammatory markers for these compounds; however, large-scale, placebo-controlled trials investigating gamma-oryzanol in isolation are still lacking ⁵.

Viral Infections

HYPOTHESIS A computational study investigated the binding affinity of gamma-oryzanol to the main protease (Mpro) of SARS-CoV-2 using molecular docking analyses. The binding strength was below that of approved antiviral agents such as remdesivir but stronger than that of other tested molecules. The study suggests a theoretical, preclinical potential for gamma-oryzanol as an antiviral agent, though without experimental or clinical validation ³.

Speculation: The *in silico* interaction with viral protease may indicate an antiviral effect of gamma-oryzanol, particularly against SARS-CoV-2. However, preclinical data on efficacy in cell cultures or animal models, as well as clinical trials confirming antiviral activity in humans, are absent. The study provides only a starting point for further research.

Oxidative Stress

PLAUSIBLE A review discusses the role of antioxidants, including gamma-oryzanol, in regulating oxidative stress during and after physical exertion. While the review summarises meta-analyses indicating a positive effect of antioxidants in physical activity, it does not provide specific data on gamma-oryzanol, as it covers multiple compounds in this context.

Speculation: The antioxidant effect of gamma-oryzanol may stem from its ability to neutralise free radicals and increase total antioxidant capacity (TAC). This could be particularly relevant for patients with cardiovascular diseases, in which oxidative stress plays a central role. However, targeted clinical studies investigating gamma-oryzanol in isolation regarding oxidative stress are lacking.

Bone and Joints

Supported: A clinical study involving 119 perimenopausal women (59 in the control group, 60 in the observation group) examined the effect of a *combination therapy* of gamma-oryzanol and Femoston over an unspecified period. The observation group showed higher overall treatment efficacy, a significant increase in bone density (L1–4 and both femora), and elevated estradiol (E₂) levels alongside reduced LH and FSH levels compared to the control group (Femoston only). Additionally, sleep quality improved (shorter sleep duration, fewer nocturnal awakenings). The study thus provides evidence for the supportive effect of the *combination therapy* on perimenopausal symptoms and bone health but does not allow conclusions about the isolated effect of gamma-oryzanol ⁴.

Speculation: The observed increase in bone density may result from an oestrogen-modulating effect of gamma-oryzanol, which could inhibit bone resorption. However, data on the isolated effect of gamma-oryzanol and long-term studies assessing its impact on fracture rates or bone metabolism parameters such as osteocalcin or CrossLaps are lacking.

Safety and Tolerability

Supported: A systematic review of 23 studies compared organically and conventionally grown rice in terms of health and safety parameters, including gamma-oryzanol among other bioactive compounds. The review found no significant differences between cultivation methods specifically for gamma-oryzanol levels. It suggests good tolerability of rice-derived compounds overall, though the review does not provide specific data on adverse effects or long-term toxicity of gamma-oryzanol alone.

Speculation: Gamma-oryzanol is generally considered safe due to its natural origin and widespread use in foods. However, systematic studies on tolerability at high dosages or during long-term use, particularly in vulnerable populations such as pregnant women or patients with hepatic or renal impairment, are lacking.

Overall Picture

Gamma-oryzanol demonstrates promising effects in clinical and preclinical studies across multiple areas, particularly in modulating lipid profiles. Its lipid-lowering effect is supported by controlled human trials. Anti-inflammatory and antioxidant effects have been observed in preclinical models or in studies where gamma-oryzanol was combined with other substances, primarily through laboratory parameters such as inflammatory markers. These findings do not yet translate to clinical outcomes for gamma-oryzanol alone. Preclinical data suggest potential for bone health and antiviral activity, though these effects have not been investigated in humans and are plausibly supported by mechanistic studies.

Systematic gaps persist, particularly regarding the isolated investigation of gamma-oryzanol in placebo-controlled trials, long-term effects, and the translatability of preclinical data to humans. Studies in specific populations (e.g., children, pregnant women) and on interactions with medications are notably absent. Safety appears to be supported by limited data, though comprehensive toxicity data are lacking.

Methodology of the evidence base

[‘The available studies on gamma-oryzanol include controlled clinical trials. Typical endpoints are lipid parameters (LDL, HDL, triglycerides), inflammatory markers (IL-1β, TNF-α), bone density, oxidative stress parameters (ROS, TAC), and binding affinities in silico. Systematic weaknesses include frequent combination with other active substances (e.g., niacin, vitamin E), short study durations, and the absence of dose-response studies. Additionally, long-term data on safety and efficacy, as well as studies with hard clinical endpoints (e.g., fracture rates, cardiovascular events), are lacking.’]

Gamma-oryzanol or rice bran oil? Attributing the effects

SUPPORTED: Gamma-oryzanol is almost exclusively studied in the context of **rice bran oil or extracts**. Even in controlled human trials (e.g., 2005, 2014), it remains unclear whether observed effects—such as on cholesterol levels or muscle strength—are attributable to gamma-oryzanol itself, synergistic effects of accompanying compounds (e.g., tocotrienols), or the oil as a whole. The **most cited study** (129 citations, 2001) is a cell culture investigation that, while examining gamma-oryzanol in isolation, cannot claim clinical relevance. **Plausible:** The chemical structure of gamma-oryzanol suggests it may act as an **antioxidant and modulator of inflammatory processes**. In vitro studies show it influences the activity of enzymes such as superoxide dismutase and glutathione peroxidase. However, whether these effects are relevant in vivo remains speculative.

RESEARCH GAP The is less a lack of studies than a **lack of precision**: until gamma-oryzanol is systematically investigated in isolation, effects cannot be clearly attributed. The **2022 review** highlights the health benefits of organic rice cultivation but does not address the specific role of gamma-oryzanol. Even the **controlled 2019 study**, which demonstrated improvements in lipid profiles and antioxidant status in hyperlipidaemic participants, used rice bran oil—not isolated gamma-oryzanol. Thus, the question of whether gamma-oryzanol alone is effective remains unanswered.

3. How Robust the Research Is

Of the evaluated studies, only **nine involve humans**, with just two being controlled trials. Research spans **five application areas**: skin (1 study), musculoskeletal system (1), fatigue (1), gut (1), and metabolism (1). The most cited controlled study (90 citations, 2005) examined the cholesterol-lowering effects of rice bran oil with varying gamma-oryzanol content in mildly hypercholesterolaemic men. The second controlled study (2014) assessed effects on anthropometric measurements and muscle strength in healthy men after resistance training. **Basic research dominates** the majority of studies, followed by observational human studies and cell culture investigations.

The methodological strength of the field lies in its **broad mechanistic elucidation**: gamma-oryzanol has been investigated in cell cultures and animal models for antioxidant, anti-inflammatory, and metabolism-modulating effects. However, **weaknesses are significant**: first, **replication studies** are lacking—even the most cited works have not been independently confirmed. Second, **generalizability is limited**, as many studies used rice bran oil rather than isolated gamma-oryzanol. Third, **study designs are heterogeneous**, with varying dosages, durations, and endpoints. The two controlled human trials are also **small and short-term**, leaving long-term effects or dose-response relationships unresolved.

4. What Is Often Claimed—and What the Data Show

STATEMENT	STUDY SITUATION
Gamma-oryzanol lowers cholesterol levels	Plausible: Rice bran oil containing gamma-oryzanol demonstrates cholesterol-lowering effects in controlled studies. Whether gamma-oryzanol alone is responsi

STATEMENT	STUDY SITUATION
Gamma-oryzanol improves muscle strength	Proven: A controlled study (2014) demonstrates effects on anthropometric measurements following resistance training. However, the study is small and short-term.
Gamma-oryzanol has antioxidant effects	Plausible: In vitro studies demonstrate antioxidant effects. Whether these are relevant in vivo remains insufficiently investigated. Most studies use rice bran oil rather than gamma-oryzanol.
Gamma-oryzanol is highly bioavailable	Speculation: Gamma-oryzanol is partially hydrolysed in the gut. Only a fraction enters the bloodstream unchanged. Its actual bioavailability has not been systematically investigated.

5. Profile: Molecule and Charge

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

6. Charge, Electrons, Radicals

−34.9 mV in nanostructured lipid carriers (human tissue), indicating stable colloidal dispersion through electrostatic repulsion ⁶. Particle size is below 150 nm with high homogeneity (PDI = 0.216) ⁶. As an antioxidant, gamma-oryzanol reduces reactive oxygen species (ROS) *in vitro*, as demonstrated by radical scavenging assays ⁷, and influences redox parameters such as glutathione (GSH) in oocytes ⁸. Direct evidence of electron transfer or cation exchange at the molecule itself is lacking; data are limited to indirect effects (ROS reduction, zeta potential).

Measurements in humans and open questions: In a human study, gamma-oryzanol was investigated over four months using markers of oxidative stress (ROS, total antioxidant capacity/TAC) and inflammatory parameters (IL-1β, TNF-α, TXB2). The results show modulation of these parameters, but no direct electrochemical measurements such as charge distribution or radical formation *in vivo*. The observed effects (e.g., ROS reduction) may stem from indirect mechanisms like gene expression or enzyme activity ⁸. The next step is to clarify whether gamma-oryzanol acts as an electron donor/acceptor in the human organism or primarily influences redox-active processes via signalling pathways (e.g., iNOS/NO).

7. Interactions with Other Substances

Which other substances from this platform have been **jointly** investigated or discussed in human studies and reviews—whether in combination, comparison, or shared mechanism. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic Inflammation	4	0
Stress, Cortisol, and Inflammation	3	0

Proven: Interactions with pharmaceuticals and hormone preparations Gamma-oryzanol was studied in combination with the hormone preparation *Femoston* (oestradiol/dydrogesterone) for perimenopausal symptoms. The study describes no direct interactions but reports clinical efficacy of the combination for oestrogen-deficiency-related symptoms ⁴. Whether gamma-oryzanol affects the absorption, metabolism, or action of hormones was not examined. Also unresolved is whether gamma-oryzanol alters the bioavailability of other lipophilic pharmaceuticals, as it was formulated in nanostructured lipid carriers (NLCs) to enhance skin penetration ^{6 6}.

Plausible: Potential influences on nutrient absorption and enzyme activity Gamma-oryzanol is a lipophilic plant compound that has been combined with UV filters like TiO₂ in nanogels to achieve synergistic antioxidant effects in the skin ^{6 6}. Whether it affects the absorption of other fat-soluble substances (e.g., vitamins A, D, E, K) or pharmaceuticals has not been investigated. Since it was combined with resistance training in muscle-strength studies ⁹, an interaction with protein metabolism or mitochondrial energy production is conceivable—but data on enzyme induction or inhibition (e.g., CYP isoenzymes) are lacking. The next step is to determine whether gamma-oryzanol, at therapeutic doses, alters the pharmacokinetics of CYP substrates (e.g., statins, antidepressants) or the absorption of micronutrients.

8. Overdose, Tolerability, and Limits

Proven: Safety and adverse effects in humans Gamma-oryzanol (γ-ORY) demonstrates a favourable safety profile in clinical observations, with minimal adverse effects and no serious safety concerns ⁵. However, long-term studies and large-scale clinical trials to optimise dosage and safety are still pending ⁵. **Dose-dependent effects in cell cultures** *In vitro* experiments on cumulus cells suggest potential overdosing: at concentrations of 20, 50, and 100 μM in maturation media, expansion and survival rates tended to decline ¹¹. Human keratinocytes, however, showed no toxicity when exposed to γ-ORY-containing nanovesicles ¹⁰.

Contraindications and toxicity thresholds Current reviews classify γ-ORY as a molecule with "permissible toxicity" but without substantiated contraindications ³. Systematic comparisons of cultivation methods (e.g., organic vs. conventional rice) found no differences in safety or end-product quality. **Animal and basic research** In a *Drosophila melanogaster* model, γ-ORY protected against manganese-induced toxicity without exhibiting toxic effects itself ^{12 12}. **Open questions** It remains to be clarified whether the dose-dependent effects observed in cell cultures ¹¹ are transferable to humans and at what threshold adverse effects may occur. Additionally, standardised long-term data on safety during chronic intake are lacking ⁵.

9. The Most Robust Studies

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

Controlled Human Studies

- ¹ Similar cholesterol-lowering properties of rice bran oil, with varied gamma-oryzanol, in mildly hypercholesterolemic men (2005)

Observational Human Studies

- Biological Functions and Activities of Rice Bran as a Functional Ingredient: A Review (2021)
- ² Effects of combined dietary supplementation on oxidative and inflammatory status in dyslipidaemic subjects (2006)
- ³ An investigation into the interaction of gamma-oryzanol with the Mpro of SARS-CoV-2 to combat COVID-19: DFT, molecular docking, ADME and molecular dynamics (2023)
- Antioxidant Supplementation During Exercise: Friends or Foes for Cardiovascular Homeostasis? (2023)
- ⁴ Clinical efficacy of gamma-oryzanol combined with Femoston for perimenopausal syndrome (2024)
- ⁵ A Review on Gamma-Oryzanol as a Multi-Target Therapeutic Agent for Metabolic Syndrome: Mechanisms, Preclinical Evidence, and Clinical Prospects (2026)

Investigations in Human Tissue

- ⁶ Nanogel Containing Gamma-Oryzanol-Loaded Nanostructured Lipid Carriers and TiO₂/MBBT: A Synergistic Nanotechnological Approach for Potent Natural Sunscreen Formulations (2023)
- Plant-Derived Nanovesicles from Soaked Rice Water: A Novel and Sustainable Platform for the Delivery of Natural Antioxidant γ-Oryzanol (2025)

10. Summary

Showed: A controlled human study showed lipid-lowering effects of rice bran oil containing gamma-oryzanol, with a reduction in LDL cholesterol by up to 10.5% in hypercholesterolaemic men. A second controlled study provided a hint for positive effects on muscle strength following resistance training with rice bran oil. Observational studies suggest supportive effects on bone density and sleep quality in perimenopausal women, though these always involved combinations with other substances or therapies. Preclinical and observational studies provide hints for anti-inflammatory and antioxidant effects, though these have not yet been confirmed for isolated gamma-oryzanol.

In vitro studies show effects on enzymes such as superoxide dismutase and glutathione peroxidase, while mechanistic research discusses inhibition of NF-κB and activation of PPAR-α. Preclinical evidence suggests the oestrogen-modulating effect *may* inhibit bone resorption in animal models, though this remains to be confirmed in isolated studies in humans. The *in silico* demonstrated antiviral potential against SARS-CoV-2 awaits preclinical and clinical validation.

The central open question is whether the observed effects are attributable to gamma-oryzanol itself or to synergistic actions of accompanying compounds in rice bran oil. A placebo-controlled study with isolated gamma-oryzanol across various dosages and extended durations would be necessary to clarify dose-response relationships and long-term effects. Additionally, studies in specific populations—such as children, pregnant women, or patients with hepatic or renal dysfunction—as well as investigations into drug interactions, are lacking. Systematic research on bioavailability and safety at high dosages would further refine the evidence base.

11. Open Questions

- **Isolated effect:** What effects does gamma-oryzanol exhibit alone—without accompanying compounds from rice bran oil?
- **Long-term safety:** Are there adverse effects or interactions with prolonged use?
- **Dose-response relationship:** Which dosages are optimal for which applications?

12. Further Paths

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

- Interaction network

Topics, mechanisms, and chains in which this compound appears—for those looking beyond the substance itself.

Frequently Asked Questions

Can gamma-oryzanol be used for hypercholesterolaemia?

Plausible: Rice bran oil containing gamma-oryzanol has demonstrated cholesterol-lowering effects in controlled studies. However, it remains unclear whether gamma-oryzanol alone is effective, as co-occurring compounds such as tocotrienols exhibit similar effects. The **most cited study** (2005) compared rice bran oils with varying gamma-oryzanol content and found no significant differences—suggesting a lack of isolated efficacy. **Replication studies** and long-term safety data are needed for further clarification.

Is gamma-oryzanol suitable for supporting muscle growth?

Supported: A controlled study (2014) examined the effects of gamma-oryzanol on anthropometric measurements and muscle strength in healthy men following resistance training. The study demonstrated **short-term effects**, though it was small and has not been replicated. Whether gamma-oryzanol alone or co-occurring rice bran oil compounds are responsible for these effects remains unclear. **Long-term studies** and mechanistic investigations are still pending.

How is gamma-oryzanol dosed in studies?

Dosages vary widely and are often not specific to gamma-oryzanol alone. In controlled human trials, **rice bran oils** with defined gamma-oryzanol content have been used, though actual gamma-oryzanol intake is not always reported. **Foundational studies** frequently employ higher concentrations, which are not directly translatable to humans. **Systematic dose-finding studies** have yet to be conducted.

Sources

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Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
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