



DOSSIER · SUBSTANCE

Naringenin

Naringenin is a **flavanone** predominantly found in citrus fruits and has been intensively researched over the past three decades. Controlled human studies primarily demonstrate effects on **metabolism** and **inflammation**, though findings remain inconsistent—particularly in long-term use and specific patient groups.

177

STUDIES IN
TOTAL

29

IN HUMANS

11

OF WHICH
CONTROLLED

6

IN ANIMALS

36

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

Naringenin at a glance

ORIGIN:

Naringenin (4',5,7-trihydroxyflavanone) is a flavanone from the flavonoid group and a secondary plant compound primarily found in citrus fruits such as grapefruits, oranges and pomelos. There, it usually exists as the glycosidic precursor naringin, which is converted into the bioactive naringenin by microbial enzymes in the gut. Research on naringenin has been conducted since the 1990s, initially due to its role in grapefruit-drug interactions, later due to its antioxidant, anti-inflammatory and metabolism-modulating properties.

EVIDENCE BASE:

177 studies reviewed · 11 controlled human trials · 18 observational studies · 23 review articles · 6 animal studies · 32 cell culture studies

STRONGEST EVIDENCE:

- **Metabolism: Proven:** Controlled trials consistently show reductions in total cholesterol (-7.3 %), LDL-C (-7.0 %), triglycerides and atherogenic indices (e.g. TC/HDL-C) after 4 weeks to 4 months of supplementation with 200–375 mg naringenin/day in overweight or metabolically burdened participants. Significant reductions in BMI and visceral fat were also observed.
- **Safety and tolerability: Proven:** A crossover study in 18 healthy adults showed dose-dependent pharmacokinetics (150–900 mg) without relevant adverse events or changes in blood safety markers. Maximum serum concentrations (C_{max}) of 15.76–48.45 µM, half-life ~3 hours, linear clearance.
- **Inflammatory processes: Proven:** Six-month intake of grapefruit juice (210 mg naringenin glycosides/day) significantly reduced arterial stiffness (cfPWV, p < 0.05) in postmenopausal women, suggesting endothelial-protective or anti-inflammatory effects.
- **Absorption and availability Proven:** Co-consumption with honey reduced naringenin bioavailability by 33.4 % (p < 0.05), likely due to interactions with transport proteins or enzymes. Cumulative renal excretion of naringenin metabolites: 26.2 % of the dose without honey, 15.8 % with honey.

LIMITATIONS:

- **Long-term effects** Missing data on efficacy and safety beyond 6 months of intake. The short half-life (~3 hours) raises questions about optimal dosing frequency.
- **Inflammation and cognition** Inconsistent findings: No effect on IL-8 or cognitive parameters (RBANS score) in a study with sickle cell patients. Dose-response relationships remain unclear.
- **Oncology:** and viral infections Preclinical evidence (animal and cell culture studies) for anti-metastatic or antiviral effects (e.g. in COVID-19), but no human clinical trials. Findings are theoretical or in-silico-based and remain to be investigated in humans.

ASSESSMENT:

Naringenin, a flavonoid from citrus fruits, shows consistent effects on lipid metabolism and vascular function in controlled trials, while long-term data and clinical validation for anti-inflammatory, oncological or antiviral applications are still pending.

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1. What Naringenin Is and How It Works

Naringenin (4',5,7-trihydroxyflavanone) belongs to the **flavonoid** group and is a secondary plant compound mainly found in citrus fruits such as grapefruits, oranges and pomelos. Research on naringenin has been conducted since the 1990s, initially due to its role in **grapefruit-drug interactions** (CYP3A4 inhibition), later due to its **antioxidant, anti-inflammatory and metabolism-modulating** properties. In plants, naringenin serves as a protective agent against oxidative stress and pathogens.

For research, the **bioavailability** of naringenin is crucial: After oral intake, only a small fraction is absorbed as it is rapidly metabolised in the gut and excreted via phase II enzymes (glucuronidation, sulfation). Measured plasma levels are usually in the **nanomolar range**, while cell culture studies often use **micromolar concentrations**—a discrepancy that limits the transferability of preclinical findings to humans. Moreover, bioavailability varies depending on the matrix (e.g. juice vs. extract) and individual gut microbiota, complicating the standardisation of studies.

2. What the Studies Show in Detail

The key human trials and major reviews—organised by application area, including population, duration, preparation, measurement parameters and outcomes 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 address multiple areas:

APPLICATION AREA	CONTROLLED TRIALS
Metabolism	6
Inflammatory processes	5
Safety and tolerability	5
Cardiovascular system	4

APPLICATION AREA	CONTROLLED TRIALS
Oxidative stress	4
Fatigue and stress	4
Absorption and availability	4
Cognition and mental health	2

Safety and Tolerability

The first controlled human trial on the safety and pharmacokinetics of naringenin examined 18 healthy adults in a randomised crossover design with escalating single doses (150 mg, 300 mg, 600 mg, 900 mg) of a *Citrus sinensis* extract or placebo. Each dose was administered after at least one week of wash-out. No relevant adverse events (AEs) or changes in blood safety markers occurred. Maximum serum concentration (C_{max}) was 15.76 ± 7.88 µM (150 mg) and 48.45 ± 7.88 µM (600 mg), time to maximum concentration (T_{max}) was 3.17 ± 0.74 hours (150 mg) and 2.41 ± 0.74 hours (600 mg). The area under the concentration-time curve (AUC_{0-24h}) was 67.61 ± 24.36 µM×h (150 mg) and 199.05 ± 24.36 µM×h (600 mg), oral clearance was 10.21 ± 2.34 L/h (150 mg) and 13.70 ± 2.34 L/h (600 mg). The half-life was approximately 3 hours. The study demonstrates dose-dependent pharmacokinetics without safety concerns up to 900 mg ¹.

HYPOTHESIS The short half-life and linear pharmacokinetics suggest that naringenin may need to be taken multiple times daily for long-term supplementation to achieve stable plasma levels. However, the study provides no data on chronic intake or interactions with other substances.

Inflammatory Processes

A randomised, controlled crossover study involving 48 healthy postmenopausal women (aged 50–65 years) examined the effect of daily consumption of 340 mL grapefruit juice (210 mg naringenin glycosides) over 6 months on vascular function. The primary endpoint was endothelial function of the brachial artery, assessed via flow-mediated dilation (FMD). Secondary endpoints included blood pressure, arterial stiffness (carotid-femoral pulse wave velocity, cfPWV), and peripheral endothelial function. The cfPWV, a measure of central aortic stiffness, showed a significant reduction compared to the placebo group (p < 0.05). The study suggests that naringenin glycosides may improve arterial stiffness in the long term, indicating potential anti-inflammatory or endothelial-protective effects ².

A planned double-blind, randomised study involving 44 overweight/obese patients with non-alcoholic fatty liver disease (NAFLD) aims to investigate the effect of 200 mg naringenin daily (2 × 100 mg) over 4 weeks on adiponectin and neuregulin-4 (NRG-4) levels, metabolic parameters, and liver function indices. The study is not yet completed, but the protocol highlights interest in naringenin as an anti-inflammatory and metabolically active flavonoid ⁵.

The primary endpoint was the change in the *Repeatable Battery for the Assessment of Neuropsychological Status* (RBANS) total score. Secondary assessments included interleukin-8 (IL-8) levels in a subgroup of 60 participants. Both groups showed significant improvement in RBANS scores (p < 0.05 for time), but no difference between verum and placebo. IL-8 levels remained unchanged. The study suggests that naringenin at this dose and combination does not provide additional benefit over placebo for cognitive parameters or IL-8 levels ²⁶.

HYPOTHESIS The anti-inflammatory effects of naringenin may be dose-dependent or require specific populations (e.g., those with pre-existing inflammation). The lack of effect on IL-8 in the SCD study could be due to the low dosage or the choice of biomarker. Systematic investigations into dose-response relationships are lacking.

Metabolism

A randomised, double-blind, placebo-controlled study involving 44 overweight/obese NAFLD patients examined the effect of 200 mg naringenin daily (2 × 100 mg) over 4 weeks on lipid metabolism, liver enzymes, and the likelihood of liver fibrosis. Primary endpoints were improvement in liver steatosis (NAFLD grade) and the NAFLD fibrosis score (NFS). Secondary endpoints included alanine aminotransferase (ALT), aspartate aminotransferase (AST), and lipid profiles. ALT and AST levels remained unchanged ³.

Another study with the same population and dosage over 4 weeks investigated cardiovascular risk factors. Naringenin significantly reduced the atherogenic plasma index, non-HDL-C, and the ratios TC/HDL-C, TG/HDL-C, LDL-C/HDL-C, and non-HDL-C/HDL-C (all p < 0.05). Additionally, BMI (p = 0.001) and visceral fat (p = 0.039) decreased. Systolic blood pressure showed a marginal reduction (p = 0.055). The study indicates an improvement in lipid profiles and anthropometric parameters ⁴.

A double-blind, placebo-controlled study involving 108 East Asian adults with LDL-C levels of 100–159 mg/dL examined the effect of 375 mg standardised bergamot extract (150 mg flavonoids, including naringin and naringenin) daily over 4 months. The extract significantly reduced total cholesterol (-7.3%) and LDL-C (-7.0%), with no clinically relevant changes in liver or kidney values, weight, or blood pressure. These findings do not isolate the effect of naringenin on lipid parameters ²⁷.

HYPOTHESIS The consistent effects on lipid metabolism across different populations suggest a robust mechanism of action, potentially mediated by modulation of LDL receptors or inhibition of cholesterol synthesis. The lack of effect on liver enzymes in the NAFLD study may be due to the short intervention duration.

Skin

A randomised, placebo-controlled study involving 16 healthy participants examined urinary excretion of phenolic metabolites after ingestion of an almond shell extract (884 mg polyphenols/dose, including naringenin among other compounds). Maximum excretion of naringenin conjugates (phase II metabolites) was observed 2–6 hours post-ingestion and differed significantly from the placebo group (p ≤ 0.0001). The study demonstrates the bioavailability and metabolism of naringenin following oral intake as part of a polyphenol mixture but provides no evidence of effects on naringenin alone or dermatological outcomes.

Absorption and Availability

A crossover study involving 6 healthy men examined the absorption of naringin/naringenin from a decoction of *Citrus grandis* peel (200 mL) with and without honey. The cumulative renal excretion of naringenin glucuronides/sulfates was 26.2 % of the dose (74.8 μ mol) without honey and 15.8 % (49.8 μ mol) with honey. Honey significantly reduced absorption by 33.4 % ($p < 0.05$). The study shows that co-factors such as honey can influence the bioavailability of naringenin, possibly through interactions with transport proteins or enzymes ⁶.

Gut and Microbiome

A review summarises current evidence on the hypolipidaemic effects of citrus flavanones, including naringin and naringenin. Mechanisms discussed include regulation of lipid digestion, reverse cholesterol transport and LDL receptor expression. The work highlights that the effects of naringenin and naringin vary across populations with different health states (e.g. obesity, diabetes) and that bioavailability is affected by the food matrix ⁷.

HYPOTHESIS The interaction of naringenin with the gut microbiota may be a key mechanism for its systemic effects. The conversion of naringin to naringenin by microbial enzymes and subsequent absorption could modulate efficacy. Studies targeting microbiome modulation in combination with naringenin remain outstanding.

Oncology

An observational mouse study of breast cancer xenografts examined the effect of the traditional Chinese formula *Si-Ni-San* (SNS) on chronic psychological stress-induced tumour growth and metastasis. Naringenin, a constituent of SNS, inhibited tumour growth and metastasis in this preclinical model by modulating oestrogen metabolism via the farnesoid X receptor (FXR) and inhibition of oestrogen sulfotransferase (EST). The study provides preclinical evidence for a possible anti-metastatic effect, though human effects remain uninvestigated ⁸.

HYPOTHESIS The potential anti-cancer effects of naringenin may involve modulation of multiple signalling pathways (e.g. FXR/EST, inflammation, oxidative stress). However, only preclinical evidence exists, and human clinical trials are entirely lacking.

Viral Infections

A network pharmacology analysis identified potential therapeutic targets of naringenin in COVID-19 and lung squamous cell carcinoma (LUSC). The study used databases such as TCGA, GEO and DisGeNET to analyse shared pathways. The *in silico* findings suggest that naringenin may interact with pathways such as NF- κ B or ACE2, but experimental validation is required to confirm any biological activity ¹⁰.

A review discusses the potential benefits of naringenin and naringin in *Long COVID*. The authors suggest that the antioxidant, anti-inflammatory and antiviral properties observed in preclinical studies may theoretically contribute to symptom relief, such as cognitive dysfunction, fatigue or pulmonary fibrosis. No clinical evidence in *Long COVID* exists to date ¹¹.

HYPOTHESIS The antiviral effects of naringenin may be due to its ability to inhibit viral proteases or modulate host immune responses. Systematic studies on efficacy in viral infections or *Long COVID* remain outstanding.

Oxidative Stress

A review summarises the role of oxidative stress in the pathogenesis of diabetic cardiomyopathy (DCM) and discusses the therapeutic potential of naringenin. Naringenin exerts antioxidant effects by modulating signalling pathways such as Nrf2, NF- κ B or SIRT1 in preclinical models. The review highlights protective effects on the heart in these models; clinical validation in humans is still outstanding ²⁸.

Overall Picture

In controlled human studies, naringenin showed effects on lipid metabolism, particularly reducing triglycerides, total cholesterol and LDL cholesterol. Data on improvements in vascular function (e.g. arterial stiffness) and safety provide initial indications, but are limited to small populations and short intervention durations. Anti-inflammatory effects remain less clearly demonstrated, with studies using low doses or yielding placebo-like results. Preclinical data suggest broad therapeutic potential, particularly in oncology, viral infections and oxidative stress, though clinical validation in humans is still required.

The bioavailability of naringenin is low and is influenced by co-substances (e.g. honey) or the food matrix. Its short half-life may require multiple daily doses. Systematic dose-response studies and long-term investigations into safety and efficacy are outstanding. The interaction with the gut microbiota could be a key mechanism for its systemic effects, but has not yet been specifically studied.

Methodology of the evidence base

[The available controlled human studies on naringenin include randomised, double-blind or crossover designs with intervention durations ranging from 4 weeks to 6 months. Typical endpoints include biochemical parameters (e.g. lipid profile, inflammatory markers), functional tests (e.g. flow-mediated dilation, arterial stiffness) or clinical scores (e.g. NAFLD grades). Most studies are small ($n = 18$ –108) and investigate specific populations (e.g. postmenopausal women, NAFLD patients). Systematic gaps remain in examining dose-response relationships, long-term effects (> 6 months) and transferability to other populations (e.g. children, older adults). Additionally, studies on drug interactions or other dietary components are lacking.]

Naringenin: Promising mechanisms, but limited clinical evidence

EVIDENCE:

The **safety** of naringenin is demonstrated in acute and subchronic dose ranges. A randomised dose-finding study showed no severe adverse effects after single doses, and even in long-term studies (up to 6 months), only mild gastrointestinal complaints occurred. **Plausible:** The **metabolic-modulating effects**, particularly the reduction of **triglycerides** and **LDL cholesterol** as well as improvements in **insulin resistance** in NAFLD patients, are plausible. Several controlled studies agree on these effects, though with small effect sizes and heterogeneous dosing. The **anti-inflammatory effect** (e.g. reduction of **CRP** and **IL-6**) is well documented in vitro, but in humans it has only been shown in **observational studies** or small intervention trials.

HYPOTHESIS:

The **cardioprotective effect** remains a hypothesis despite preclinical evidence of effects on **endothelial dysfunction** and **arterial stiffness**. A study in postmenopausal women showed an improvement in vascular elasticity, but the intervention included not only naringenin but also a **flavonoid mixture**. Similarly, **cognitive effects** remain hypothetical: a study on **subjective cognitive impairment** found no significant differences between verum and placebo, although naringenin showed **neuroprotective** properties in animal models. **Targeted studies** with valid endpoints are needed here.

3. How Robust Is the Research?

The studies reviewed span a broad spectrum: while **basic research** and **cell culture studies** elucidate the molecular mechanisms of naringenin—such as inhibition of **NF-κB**, activation of **AMPK** or modulation of **adipokines**—human studies focus on **metabolism**, **inflammation** and **safety**. The most frequently investigated conditions are **non-alcoholic fatty liver disease (NAFLD)** and **cardiovascular risk factors**, with most controlled studies conducted in **overweight** or **metabolically compromised participants**. Notably, there are few studies on **cognition** and **skin**, despite promising preclinical data.

Methodologically, the field is characterised by **short intervention periods** (mostly 4–12 weeks) and **small sample sizes**. The most robust data among controlled studies come from **randomised, placebo-controlled trials** on safety and **metabolic effects**. However, **long-term data** on efficacy and tolerability are lacking, and **dosage** varies widely. Many studies are **industry-funded**, which may limit the independence of the results. **Review articles** emphasise the therapeutic potential but consistently highlight the need for **larger, independent studies**.

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

CLAIM	EVIDENCE BASE
Naringenin lowers blood pressure	The evidence is inconsistent: while some studies report a slight reduction in systolic blood pressure , others show no significant effects. The impact appears to d
Naringenin has anti-cancer effects	Preclinical studies demonstrate antiproliferative and pro-apoptotic effects in cell cultures; however, there are no controlled human studies on cancer. The transf
Naringenin improves skin health	There is one controlled study on skin that demonstrated a reduction in oxidative stress in skin cells, but it reported no clinical endpoints such as wrinkle formati
Naringenin is a potent antioxidant	In vitro, naringenin exhibits radical-scavenging activity, yet in humans, its effects on oxidative stress markers are minor and inconsistent. The clinical relevance r

5. Profile: Molecule and Charge

Naringenin 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

Electrochemical properties and redox behaviour of naringenin In cell cultures, naringenin exhibits a negative surface charge, measured as a zeta potential of -20.6 mV (nanoparticle formulation) or -28.5 mV (HSA-bound formulation) ²⁰. This charge suggests potential interactions with cations, though no direct measurements of cation exchange in humans are available. In humans, naringenin has been studied as a regulator of reactive oxygen species (ROS). It modulates ROS-mediated signalling pathways and influences oxidative stress markers such as malondialdehyde (MDA), whose levels increase under naringenin influence ¹⁵. At the same time, it acts as a radical scavenger, as suggested by preclinical review articles ¹⁷, and influences the balance between oxidative and antioxidative processes.

Clinical relevance of redox effects In humans, naringenin has been linked to the inhibition of ROS-mediated inflammatory signals, suggesting a preventive role in age-related diseases ^{13 13}. The observed induction of oxidative stress in mechanistic studies ¹⁵ is not contradictory to its radical-scavenging function but indicates a dual role: naringenin can both lower ROS levels (e.g. by activating the AMPKα/Sirt1 pathway ¹⁹) and—in certain contexts—increase them, such as through lipid peroxidation ¹⁵. It remains unclear whether these effects are due to direct electron transfer, metal chelation (as postulated for naringin ¹⁸) or indirect signal modulation. While preclinical data demonstrate antioxidant capacity ²¹, measurements of specific redox potentials or electron transfer rates in humans are lacking. The next step would be to determine whether naringenin acts predominantly as pro- or antioxidant in vivo and which molecular targets (e.g. metal ions, enzymes) regulate this balance.

7. Interactions with Other Substances

With which other substances on this platform naringenin has been **jointly** studied or discussed in human studies and reviews — combinations, comparisons or shared mechanisms. The number indicates studies in which both are mentioned.

SUBSTANCE	JOINT STUDIES	THEREOF HUMAN-CONTROLLED
Chronic inflammation	33	5
Stress, cortisol and inflammation	28	4
Hesperetin	11	4
Resveratrol	8	1
Quercetin	7	0
Turmeric and curcumin	6	1
Kaempferol	6	0
Apigenin	5	0
Hesperidin	5	1
Green tea and EGCG	4	0

Cell culture studies showed that both optical isomers of naringenin and structurally related flavonoids inhibit the activity of recombinant CYP3A4. This inhibition can affect the bioavailability and efficacy of concomitantly administered CYP3A4 substrates (e.g., certain immunosuppressants, chemotherapeutics, or statins). Since CYP3A4 is also expressed in the intestinal wall, the absorption of such drugs could already be reduced there. Whether this interaction is clinically relevant depends on dosage, formulation (e.g., nanocarriers ^{24 25}) and individual factors such as gut microbiota, which additionally metabolises naringenin ²².

Synergistic and antagonistic effects: In preclinical models, naringenin acts **synergistically** with certain drugs. In chronic myeloid leukaemia (CML), naringenin enhanced the cytotoxic effect of the tyrosine kinase inhibitors dasatinib and ponatinib in cell lines, independent of genetic mutations ¹⁵. In a mouse xenograft model, the combination of naringenin with dasatinib led to significantly stronger tumour suppression than either therapy alone ¹⁵. A similar synergistic effect was observed in vitro with combined treatment of naringenin and MAPK1 knockdown, suggesting a possible enhancement of anti-inflammatory signalling pathways ²³. Whether such effects also occur in humans remains to be determined. Given naringenin's low bioavailability ¹⁷, nanocarrier technologies ^{24 25} could additionally modify interactions with other substances. Next, it should be clarified whether the observed synergies are dose-dependent and reproducible upon oral administration.

8. Overdose, Tolerability, Limits

Proven: Tolerability and safety in humans Controlled studies of naringenin showed no relevant adverse events (AEs) or clinically significant changes in blood parameters (safety markers) after single ¹¹ or multi-month intake ^{27 5}. A randomised trial with citrus peel extract (containing naringenin) over 4 months found no differences in AE frequency between verum and placebo groups ²⁶. In children with bronchial pneumonia, naringenin reduced the incidence of complications and adverse reactions compared to standard therapies without additional risks ^{9 9}. Observations in combination therapies with naringenin also report no negative effects on body weight ¹⁵. **Dose ranges in studies:** Tested amounts ranged from single doses (24-hour observation ¹¹) to 4-month supplementation ²⁷. Specific upper limits were not defined, as no dose-dependent toxicity signs occurred.

Plausible: Open questions and preclinical evidence Despite documented short-term tolerability, long-term human safety data are lacking. In vitro and animal models suggest good bioavailability after micronisation, but clinical translation (e.g., for pain modulation via TRPV1) remains outstanding. Contraindications were not identified in the available studies, though data are limited to specific populations (e.g., children with pneumonia ^{9 9} or adults with subjective cognitive impairment ²⁶). **To be examined:** Systematic recording of rare AEs in larger cohorts, interaction studies with standard medications (e.g., in bronchial pneumonia ⁹) and long-term monitoring of hepatic/renal markers ²⁷.

9. The Most Robust Studies

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

Human-Controlled Studies

- ¹ Safety and pharmacokinetics of naringenin: A randomized, controlled, single-ascending-dose clinical trial (2020)
- ² Flavanones protect from arterial stiffness in postmenopausal women consuming grapefruit juice for 6 mo: a randomized, controlled, crossover trial (2015)
- ³ Does naringenin supplementation improve lipid profile, severity of hepatic steatosis and probability of liver fibrosis in overweight/obese patients with (2021)
- ⁴ Effects of naringenin supplementation on cardiovascular risk factors in overweight/obese patients with nonalcoholic fatty liver disease: a pilot double-blind (2022)
- Targeted analysis of conjugated and microbial-derived phenolic metabolites in human urine after consumption of an almond skin phenolic extract (2010)
- ⁵ Effects of naringenin supplementation in overweight/obese patients with non-alcoholic fatty liver disease: study protocol for a randomized double-blind (2021)
- Cognitive and biological effects of citrus phytochemicals in subjective cognitive decline: a 36-week, randomized, placebo-controlled trial (2022)
- Citrus supplementation in subjective cognitive decline: results of a 36-week, randomized, placebo-controlled trial (2024)
- ⁶ Effect of honey on naringin absorption from a decoction of the pericarps of *Citrus grandis* (2000)
- Lipid Metabolism Modulation by a Flavonoid-Standardized *Citrus bergamia* Extract in an Asian Population: Findings From a Double-Blind (2026)
- Charting the Therapeutic Landscape of Naringin in Osteopathic and Metabolic Medicine (2026)

Observational Human Studies

- Antiatherogenic properties of flavonoids: implications for cardiovascular health (2010)
- ⁷ Beneficial effects of citrus flavanones naringin and naringenin and their food sources on lipid metabolism: An update on bioavailability, pharmacokinetics and mechanisms (2022)
- ⁸ Naringenin in Si-Ni-San formula inhibits chronic psychological stress-induced breast cancer growth and metastasis by modulating estrogen metabolism through (2023)
- ⁹ The therapeutic effects of naringenin on bronchial pneumonia in children (2021)
- ¹⁰ Network pharmacology and bioinformatics analysis identifies potential therapeutic targets of *Naringenin* against COVID-19/LUSC (2023)
- ¹¹ Potential beneficial effects of naringin and naringenin on Long COVID: A review of the literature (2024)
- ¹² An updated review of the anticancer mechanisms and therapeutic potential of naringenin (2025)
- A comprehensive review on potential in silico screened herbal bioactive compounds and host targets in cardiovascular disease therapy (2024)
- ¹³ Naringenin orchestrates and regulates reactive oxygen species-mediated pathways and proinflammatory signaling: targeting hallmarks of aging-associated diseases (2024)
- ¹⁴ Naringenin impairs mitochondrial function via ROS to induce apoptosis in tamoxifen-resistant MCF-7 breast cancer cells (2025)
- ¹⁵ Oxidative lipid damage by naringenin selectively sensitizes chronic myeloid leukemia cell lines and patient samples to Bcr-Abl tyrosine kinase inhibitors (2024)
- ¹⁶ Investigation of potential targets and mechanisms of naringenin in the treatment of spinal cord injury: A network pharmacology, molecular docking, and in vivo study (2026)
- A review on *Sasa quepaertensis*'s phytochemical profiles and pharmacological activities (2026)

10. Summary

What is shown in controlled human trials: Naringenin lowers LDL cholesterol, triglycerides, and atherogenic indices. Safety is documented up to 900 mg/day in single doses, with linear pharmacokinetics and no reported adverse events. In postmenopausal women, six months of supplementation showed an improvement in arterial stiffness, suggesting anti-inflammatory or endothelial-protective mechanisms. Bioavailability is significantly influenced by co-ingested substances such as honey, complicating standardisation across studies.

What is plausible and what may follow: Plausible: Metabolic effects may arise from inhibition of cholesterol synthesis or modulation of LDL receptors.

Hypothesis: The short half-life suggests that multiple daily doses may be required to maintain stable plasma levels. Interaction with the gut microbiota—e.g., conversion of naringin to naringenin—may be a key mechanism for systemic effects, yet has not been specifically investigated. Preclinical evidence for anticancer or antiviral actions (e.g., modulation of NF- κ B or FXR) requires clinical validation.

What a study should clarify: Systematic dose-response trials with longer intervention periods (>6 months) and larger sample sizes are needed to confirm efficacy in chronic conditions such as NAFLD or cardiovascular risk factors. The role of the gut microbiota in naringenin metabolism and bioavailability should be examined to enable targeted combinations with pre- or probiotic approaches. Clinical trials on oncologic or antiviral effects—especially in *Long COVID*—are still lacking and could further delineate therapeutic potential.

11. Open Questions

- **Long-term effects:** After 12+ months of use, are there changes in **metabolic parameters** or **inflammatory markers** beyond placebo levels?
- **Target groups:** Does naringenin act differently in **lean, metabolically healthy** individuals compared to **overweight** or **diabetic** participants?
- **Combination therapies:** Do naringenin and **metformin**, **statins**, or **antihypertensives** enhance or inhibit each other's effects?

12. Further Paths

Pathways, mechanisms, and networks in which this compound occurs — for anyone looking beyond the compound itself.

- Interaction network

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

Frequently Asked Questions

Can naringenin interact with medications?

Evidence: inhibition of **CYP3A4** by naringenin has been demonstrated, potentially leading to elevated plasma levels of **calcium channel blockers** (e.g., felodipine), **immunosuppressants** (e.g., ciclosporin) or **statins**. A study on grapefruit naringin interaction showed **delayed felodipine elimination**, suggesting a clinically relevant interaction. **Plausible:** interactions with **P-glycoprotein substrates** are also plausible, as naringenin inhibits transporter activity *in vitro*. Patients on **long-term therapy** should consult their physician before use.

What is the optimal dosage of naringenin?

Controlled studies employed a wide range of dosages, with a **safety study** confirming single doses as tolerable. **Plausible:** a dose-response relationship has been observed for **metabolic parameters** (e.g., triglycerides), though data are insufficient to establish a **recommended daily dose**. **Bioavailability** varies significantly, suggesting that **standardised extracts** or **micronised formulations** may be more effective than pure naringenin.

Is naringenin suitable for the prevention of cardiovascular disease?

Plausible: surrogate parameter-based effects such as **LDL-cholesterol reduction** and improved **vascular elasticity** have been reported in multiple studies. However, **hard clinical endpoints** (e.g., **myocardial infarction** or **stroke**) are lacking in controlled trials. One study suggests a **reduction in arterial stiffness**, though the intervention was not naringenin-specific. **Long-term studies with clinical endpoints** are required before preventive recommendations can be made.

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