



DOSSIER · SUBSTANCE

Xanthohumol

Xanthohumol is a **prenylated flavonoid** derived from hops, which has been investigated in a substantial number of studies since 2007. Research focuses on **anti-inflammatory effects** and **gut health**, though most studies are fundamental in nature. Human trials provide initial indications of safety and bioavailability but remain methodologically limited.

140

STUDIES IN
TOTAL

21

IN HUMANS

10

OF WHICH
CONTROLLED

3

IN ANIMALS

42

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

Xanthohumol at a Glance

ORIGIN:
Xanthohumol is a prenylated flavonoid from the chalcone group, primarily found in hops (*Humulus lupulus*). It is characterised by an isoprenoid side chain that enhances its lipophilicity and cell membrane passage. Naturally, it serves the plant as protection against oxidative stress and pathogens but is also produced synthetically or enriched from hop extracts.

STUDY LANDSCAPE:
140 evaluated studies · 10 controlled human trials · 11 observational studies · 9 review articles · 3 animal studies · 33 cell culture studies

- STRONGEST EVIDENCE:**
- **Anti-inflammatory effects** Controlled trials show that xanthohumol (12 mg/day) reduces oxidative DNA damage in lymphocytes and decreases urinary excretion of 8-oxo-7,8-dihydro-2'-deoxyguanosine. In COVID-19 patients, it demonstrated changes in inflammatory markers such as IL-6 and CRP, alongside a lower 28-day mortality (20% vs. 48%).
 - **Gut and microbiome:** The XMaS study series confirms enterotype-dependent modulation of the gut microbiota by xanthohumol, particularly in *Prevotella* and *Ruminococcus* enterotypes. Changes in bile acid metabolism suggest individual interactions, though their clinical relevance remains unclear.
 - **Bioavailability** Micellar formulations of xanthohumol increase bioavailability ninefold compared to native preparations. Despite improved absorption, no acute effects on resting energy expenditure, blood pressure, or heart rate were observed.
 - **Viral infections** Preclinical data show that xanthohumol inhibits the main protease of SARS-CoV-2 in vitro (IC₅₀ = 1.53 µM). The antiviral effect in humans has not been investigated. A clinical study in COVID-19 patients showed reduced mortality and changes in inflammatory markers.

- LIMITATIONS:**
- The clinical relevance of microbiome modulation by xanthohumol is unclear, as long-term studies are lacking and individual differences in gut flora influence efficacy.
 - Despite improved bioavailability of micellar formulations, there are no clinical data on cardioprotective effects or measurable impacts on cardiovascular risk factors.
 - Preclinical data on anticancer effects are promising, but human studies examining its use as an adjuvant cancer therapy are lacking.

ASSESSMENT:
Xanthohumol, a prenylated flavonoid from hops, provides initial evidence for antioxidant and anti-inflammatory effects in human studies. Its clinical relevance is constrained by poor bioavailability and individual differences in gut microbiota, with further research needed to confirm long-term benefits.

1. What Xanthohumol Is and How It Works

Xanthohumol is a secondary plant compound from the **chalcone** group, primarily found in hops (*Humulus lupulus*). It belongs to the **prenylated flavonoids**, characterised by an additional isoprenoid side chain. This structure gives xanthohumol greater **lipophilicity** and thus better cell membrane passage than many other polyphenols. It occurs naturally in hop cones but is also produced synthetically or enriched from hop extracts. In the plant, it likely serves as protection against oxidative stress and pathogens. Of particular interest to research is its **interaction with signalling pathways**, including NF-κB, Nrf2, and AMPK, which regulate inflammation, cellular protection, and metabolism.

The critical factor for all studies is **bioavailability**. Xanthohumol is only partially absorbed in the gut and undergoes extensive **first-pass metabolism** in the liver, where it is converted into glucuronides and sulphates. **Microbial transformation** in the gut plays a central role: bacteria such as *Eubacterium ramulus* can metabolise xanthohumol into **isoxanthohumol** and other metabolites, some of which exhibit higher bioactivity. **Formulation** (e.g., as an extract or in liposomes) influences absorption, as does the **individual's gut microbiota**. This variability explains why controlled studies often yield differing results—even at identical dosages.

2. What the Studies Show in Detail

The key human studies and most important reviews—by application area, including 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 trials** by application area—the numbers are not additive, as one study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED TRIALS
Inflammatory Processes	7
Gut and Microbiome	5
Safety and Tolerability	4
Immune System	4
Oxidative Stress	3
Metabolism	3

APPLICATION AREA	CONTROLLED TRIALS
Absorption and Bioavailability	2
Heart and Circulation	1

Inflammatory Processes

ESTABLISHED A randomised crossover study with 22 healthy participants investigated the effect of xanthohumol (12 mg/day via a beverage preparation) on oxidative DNA damage in lymphocytes. Post-intervention, a significant reduction in oxidatively damaged purines was observed, along with protection against reactive oxygen species-induced DNA damage. Urinary excretion of 8-oxo-7,8-dihydro-2'-deoxyguanosine and 8-oxoguanosine was reduced. A follow-up study with pure xanthohumol (n=10, parallel design) confirmed these DNA-protective effects. Other biochemical parameters, such as redox status, hormone balance, or lipid and glucose metabolism, remained unchanged ¹.

While the overall composition of the microbiome did not change significantly, an enterotype-dependent modulation of specific taxa was observed, particularly in *Prevotella* and *Ruminococcus* enterotypes. Additionally, changes in bile acid metabolism were noted, indicating individual interactions between xanthohumol and the microbiome. Bioavailability of xanthohumol metabolites varied widely among participants ³.

Evidence-based: A randomised, controlled trial involving 50 critically ill COVID-19 patients (PaO₂/FiO₂ < 150) investigated the effects of a *Humulus lupulus* extract rich in xanthohumol (4.5 mg/kg body weight/day over 7 days) on inflammatory markers. The study showed a significantly lower 28-day mortality rate (20% vs. 48%, p < 0.05) and a shorter clinical course in the extract group compared to placebo. Inflammatory parameters such as IL-6, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), CRP, and D-dimer were reduced. These findings refer to the *Humulus lupulus* extract, not to xanthohumol alone ⁶.

PLAUSIBLE Preclinical and clinical data suggest that xanthohumol possesses anti-inflammatory and antioxidant effects, which have been observed in various populations (healthy adults, COVID-19 patients). The enterotype-dependent modulation of the microbiome ³ indicates potential individual differences in gut flora interactions, though this remains a preclinical finding. Long-term studies are needed to determine the clinical relevance of these effects in chronic inflammatory diseases.

Gut and Microbiome

There were no clinically relevant differences between the xanthohumol and placebo groups in terms of laboratory parameters, body weight, vital signs, or health-related quality of life. Mild adverse events occurred in both groups, with no serious or FDA-defined severe events ².

HYPOTHESIS The observed enterotype-dependent modulation of the microbiome by xanthohumol ³ may suggest a prebiotic effect, though this is highly dependent on individual gut flora. Whether these effects lead to long-term improvements in gut health remains an open question. Studies systematically investigating the functional consequences of these microbiome changes are lacking.

Heart and Circulation

Evidence-based: A randomised crossover study examined the bioavailability of xanthohumol in two dosages (86 mg and 172 mg) in native and micellar forms. The micellar preparation resulted in approximately nine times higher bioavailability (AUC and maximum plasma concentration, p < 0.001) compared to the native form. However, a subsequent bioactivity study with 172 mg micellar xanthohumol showed no acute effects on resting energy expenditure, blood pressure, or heart rate ⁷.

HYPOTHESIS The improved bioavailability of micellar xanthohumol formulations ⁷ could provide a basis for future studies on cardioprotective effects. However, clinical data demonstrating whether this increased bioavailability translates into measurable effects on cardiovascular risk factors are currently lacking.

Viral Infections

Evidence-based: A randomised study involving 50 critically ill COVID-19 patients showed that administration of a *Humulus lupulus* extract (4.5 mg/kg body weight/day over 7 days) significantly reduced 28-day mortality (20% vs. 48%, p < 0.05) and shortened the clinical course. Inflammatory markers such as IL-6, NLR, PLR, CRP, and D-dimer were reduced in the extract group. Whether xanthohumol contributes to these effects remains to be investigated ⁸.

Evidence-based: In vitro studies showed that xanthohumol inhibits the main protease (M^{pro}) of various coronaviruses, including SARS-CoV-2 (IC₅₀ = 1.53 μM) and porcine epidemic diarrhoea virus (PEDV, IC₅₀ = 7.51 μM). Pretreatment with xanthohumol inhibited the replication of SARS-CoV-2 and PEDV in Vero E6 cells, indicating a potential antiviral effect in preclinical models. Human studies remain to be conducted to confirm whether these findings translate to antiviral activity in humans ¹⁴.

However, clinical studies investigating these effects in viral diseases other than COVID-19 are lacking.

Metabolism

PLAUSIBLE Preclinical studies suggest that xanthohumol may exhibit hypoglycaemic, antihyperlipidaemic, and antiobesogenic effects. Related hop compounds, such as iso-α-acids (IAA) and matured hop bitter acids (MHBA), improved lipid metabolism, glucose tolerance, and body weight in animal models. Direct evidence specifically for xanthohumol's effects in these areas remains to be established ¹¹.

HYPOTHESIS The metabolism-modulating effects of xanthohumol and related hop compounds ¹¹ could potentially be utilised in the prevention and treatment of metabolic syndrome. However, controlled human studies systematically investigating these effects are lacking.

Oncology

PLAUSIBLE In vitro studies demonstrate that xanthohumol inhibits the growth and proliferation of cancer cells through modulation of multiple signalling pathways (Akt, AMPK, ERK, NF- κ B, STAT3) and proteins (Notch1, caspases, MMPs, Bcl-2, cyclin D1). These preclinical findings require validation in human studies to determine their relevance.

PLAUSIBLE In preclinical models, xanthohumol inhibited cell growth, induced apoptosis, and caused cell cycle arrest in the G1 phase in oesophageal carcinoma cell lines (KYSE70, 450, 510). In patient-derived xenografts (PDX) with high AKT expression, xanthohumol reduced tumour volume and weight, whereas no effect was observed in those with low AKT expression. These findings have not yet been confirmed in human studies.

HYPOTHESIS Preclinical data suggest a broad anticancer potential of xanthohumol, though this is highly dependent on cellular context. Clinical studies investigating these effects in humans and determining whether xanthohumol can be used as an adjuvant therapy in cancer are lacking.

Oxidative Stress

Evidence-based: A controlled human study (n=22) showed that xanthohumol (12 mg/day) reduced oxidative DNA damage in lymphocytes and decreased urinary excretion of 8-oxo-7,8-dihydro-2'-deoxyguanosine and 8-oxoguanosine as biomarkers of oxidative stress ¹.

PLAUSIBLE Theoretical studies suggest that the benzylic-allylic hydrogen atoms in prenylated chalcones such as xanthohumol play a key role in their antioxidant activity. These positions are thermodynamically favoured sites for free radical attack, which may explain the high radical-scavenging capacity of xanthohumol.

However, studies systematically investigating these effects in clinically relevant models are lacking.

Overall Picture

The enterotype-dependent modulation of the microbiome ³ and the improved bioavailability of micellar formulations ⁷ open new perspectives for targeted applications.

However, the clinical data are still limited, particularly regarding long-term effects and the translatability of preclinical findings to humans. Systematic studies on dose-response relationships, individual differences in bioavailability, and clinical relevance in chronic diseases are still pending.

Methodology of the evidence base

[The foundational studies on xanthohumol include a mix of randomised, placebo-controlled trials (n=10–50 participants), observational investigations, and mechanistic studies, with intervention durations ranging from 7 days to 12 weeks. Typical endpoints are inflammatory markers (IL-6, CRP, NLR), oxidative DNA damage, microbiome composition, bioavailability, and clinical parameters such as mortality or disease progression. Systematically lacking are long-term studies, dose-finding studies, and investigations into interactions with other therapies. Furthermore, most controlled studies have been conducted in healthy adults or specific patient groups (e.g., COVID-19, Crohn's disease), which limits generalisability.]

Is xanthohumol a 'miracle molecule'?

The term 'miracle molecule' (e.g., in a 2024 review) is misleading because it suggests

CLINICALLY PROVEN EFFICACY

, which does not exist. **Basic research** does demonstrate **anti-inflammatory** and **antioxidative effects** in cell cultures and animal models—such as through activation of the **Nrf2/HO-1 signalling pathway** or inhibition of NF- κ B. However, these findings cannot be directly extrapolated to humans. Even the **controlled human studies** on anti-inflammatory effects are **not double-blind placebo-controlled** or have sample sizes too small to yield statistically robust conclusions. The **XMaS studies** (2020–2024) do provide indications of **microbiome modulation**, but whether these changes are clinically relevant remains unclear.

Another issue is the

SELECTIVITY OF RESEARCH

. Most studies examine **isolated effects** (e.g., on inflammatory markers) but ignore **systemic interactions**. For example, xanthohumol inhibits **immune cell activation** in vitro, yet whether this leads to **immunosuppression** in the body has never been systematically investigated. **Safety studies** show no severe adverse effects, but long-term data are lacking. **Bioavailability** is another critical point: even if xanthohumol is effective in vitro, it often fails to reach the necessary concentrations in the body. **Formulation research** (e.g., liposomes) could address this, but these approaches have yet to be validated in human studies.

3. How Robust Is the Research?

The evaluated studies are unevenly distributed between basic research and human trials. **Controlled human studies** focus on **anti-inflammatory effects**, **gut health**, and **safety**. Other key areas include antioxidative effects, immune modulation, and metabolic processes. Notably, the **XMaS study series** ('Xanthohumol Microbiome and Signature'), ongoing since 2020, investigates interactions with the gut microbiota. The most-cited human studies (2016–2024) primarily assessed **DNA stability**, **microbiome modulation**, and **safety**, while applications in **COVID-19** (2023) or **oncological questions** remain in early stages.

The **current evidence base** includes small sample sizes and short durations. Controlled human studies are predominantly **Phase I or pilot studies**, which evaluate safety and tolerability but provide initial signals rather than establish efficacy. The **XMaS studies** demonstrate **enterotype-dependent modulation** of the microbiota, yet the clinical relevance of these changes remains to be clarified. **Bioavailability** remains a central challenge: even with standardised intake, plasma levels vary widely, complicating the interpretation of dose-response relationships. **Mechanistic studies** (e.g., on NF-κB inhibition) provide compelling hypotheses, but translation to humans is still pending. **Review articles** highlight the potential but rely on preliminary data until larger clinical trials are completed.

4. Common Claims—and What the Data Show

CLAIM	EVIDENCE BASE
Xanthohumol has antioxidant effects	Proven: In cell cultures and animal models, xanthohumol inhibits oxidative processes via Nrf2 activation. In humans: Only a few controlled studies exist, which :
Xanthohumol helps with intestinal diseases	Plausible: Some controlled studies demonstrate microbiome modulation, but no clinical improvement (e.g., in Crohn's disease).
Xanthohumol helps prevent cancer	Hypothesis: Cell culture studies demonstrate antiproliferative effects, but no human studies on prevention or therapy exist to date.
Xanthohumol is safe	Proven: Controlled studies show no severe adverse effects, but long-term data are lacking.

5. Fact Sheet: Molecule and Charge

Xanthohumol 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 precisely what the next section addresses.

6. Charge, Electrons, Radicals

Electrochemical properties of xanthohumol – laboratory and tissue level Xanthohumol (XH) acts as a Michael acceptor and induces NAD(P)H:quinone oxidoreductase 1 (NQO1) in human tissue, an enzyme that detoxifies quinones through two-electron reduction, thereby stabilising the redox status ²². The compound influences reactive oxygen species (ROS) ambivalently: in glioblastoma cells (T98G), XH increases ROS formation and induces apoptosis ²³, while in other cell models, it lowers ROS levels. In cell cultures, XH exhibits moderate radical-scavenging activity (25–30% of the Trolox reference) against ABTS and DPPH radicals. Additionally, XH activates the transcription factor Nrf2, which regulates cytoprotective genes and maintains intracellular redox balance ^{24 25}. The next step would be to investigate how the structurally determined radical attack points affect ROS modulation *in vivo* and whether Nrf2 induction is dose-dependently reproducible.

Human measurements – redox and DNA protection In a controlled human study, the consumption of a xanthohumol-containing beverage reduced oxidatively damaged purines and protected against ROS-induced DNA damage. The urinary excretion of the biomarkers 8-oxo-7,8-dihydro-2'-deoxyguanosine and 8-oxoguanosine decreased significantly ¹. These findings suggest a systemic antioxidant effect, though it was not directly attributed to electrochemical mechanisms such as cation exchange or charge distribution. It remains unclear whether the observed effects stem primarily from radical-scavenging properties, enzyme induction (e.g., NQO1), or a combination of both processes. The next question is whether the redox mechanisms identified in the laboratory (e.g., Nrf2 activation) are also detectable *in vivo* and how bioavailability influences electrochemical activity.

7. Interactions with Other Substances

Substances from this platform that have been **jointly** investigated or discussed with this compound in human studies and review articles—whether in combination, comparison, or via a shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	STUDIES INVOLVING BOTH	OF WHICH CONTROLLED HUMAN STUDIES
Chronic inflammation	19	7
Gut microbiome	9	7
Ginger	3	1

SUBSTANCE	STUDIES INVOLVING BOTH	OF WHICH CONTROLLED HUMAN STUDIES
Turmeric and curcumin	3	1
Grape seed extract (OPC)	2	0
Stress, cortisol and inflammation	2	0

Evidence-based: Interactions with enzyme systems and bioavailability Xanthohumol (XN) demonstrates high interindividual variability in metabolic profiles and bioavailability of its metabolites in controlled human studies³. Formulation and dosage significantly influence absorption, as shown in randomised trials⁷. Additionally, cell models revealed inhibition of the fibrotic TGFβ1/Smad3 signalling pathway by XN, which was reversed by the Nrf2 inhibitor 385—indicating an interaction with redox-sensitive enzyme systems²⁵.

Plausible: Synergies and antagonistic effects with pharmaceuticals In combination with antibiotics, xanthohumol exhibits synergistic effects in cell cultures, enhancing activity against Gram-positive and Gram-negative bacteria, including multidrug-resistant strains^{26 26}. Concurrently, XN shows an antagonistic interaction with the ROS scavenger N-acetylcysteine (NAC) in vitro, which attenuates XN-induced upregulation of the Nrf2 signalling pathway²⁵. The inhibition of adenylate cyclase (AC) by XN in tumour cells suggests potential interactions with cAMP-dependent pharmaceuticals (e.g., β-agonists), as AC is a central enzyme in their mechanism of action. Whether these effects also occur in vivo would need to be examined through targeted interaction studies with CYP substrates (e.g., midazolam) and antibiotics, particularly considering variable bioavailability^{3 7}.

8. Overdose, Tolerability, and Limitations

Evidence-based: In controlled Phase I human trials, xanthohumol was investigated at a dose of 24 mg daily over eight weeks. The studies were triple-masked, placebo-controlled, and conducted under FDA supervision (Investigational New Drug Application)^{2 5}. Alongside tolerability, biomarkers for inflammation, gut permeability, and microbiome composition were assessed to explore potential mechanisms of action^{5 5}.

PLAUSIBLE Current data are limited to short-term applications (8 weeks) and a fixed dose of 24 mg/day. No upper limit for xanthohumol has been defined, as long-term studies or dose-finding trials with higher amounts are lacking. Contraindications were not identified in the available studies, though participants were exclusively healthy adults or patients with clinically active ulcerative colitis (UC)⁴. The next step would involve Phase II studies with larger cohorts and varying dosages to clarify toxicity thresholds, cumulative effects, and specific risk groups^{5 4}.

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 Impact of xanthohumol (a prenylated flavonoid from hops) on DNA stability and other health-related biochemical parameters: Results of human interventi (2016)
- ² Xanthohumol Microbiome and Signature in Healthy Adults (the XMaS Trial): Safety and Tolerability Results of a Phase I Triple-Masked, Placebo-Controlle (2021)
- ³ Gut enterotype-dependent modulation of gut microbiota and their metabolism in response to xanthohumol supplementation in healthy adults (2024)
- ⁴ Xanthohumol microbiome and signature in adults with Crohn's disease (the XMaS trial): a protocol for a phase II triple-masked, placebo-controlled clin (2022)
- ⁵ Xanthohumol microbiome and signature in healthy adults (the XMaS trial): a phase I triple-masked, placebo-controlled clinical trial (2020)
- ⁶ Humulus lupulus extract rich in xanthohumol improves the clinical course in critically ill COVID-19 patients (2023)
- Effect of a Nutrition Support Formula in Adults With Inflammatory Bowel Disease: A Pilot Study (2019)
- ⁷ The Bioavailability of Xanthohumol in Humans and the Influence of Formulation and Dose: Randomized Controlled Trial Data (2026)
- ⁸ Humulus lupulus extract rich in Xanthohumol reduces the risk of a fatal clinical course in critically ill patients treated for COVID-19 (2022)
- ⁹ Correction to: Xanthohumol microbiome and signature in healthy adults (the XMaS trial): a phase I triple-masked, placebo-controlled clinical trial (2020)

Observational Human Studies

- ¹⁰ Xanthohumol from Hop: Hope for cancer prevention and treatment (2021)
- ¹¹ Hop Phytochemicals and Their Potential Role in Metabolic Syndrome Prevention and Therapy (2017)
- Targeted therapy of the AKT kinase inhibits oesophageal squamous cell carcinoma growth in vitro and in vivo (2019)
- ¹² The hop constituent xanthohumol exhibits hepatoprotective effects and inhibits the activation of hepatic stellate cells at multiple levels (2015)
- ¹³ Bioavailability and cardiometabolic effects of xanthohumol: evidence from animal and human studies (2022)
- ¹⁴ Xanthohumol is a potent pan-inhibitor of coronaviruses targeting the main protease (2021)
- ¹⁵ Dietary prenylated flavonoid xanthohumol alleviates oxidative damage and accelerates diabetic wound healing via Nrf2 activation (2022)
- ¹⁶ Evaluation of the antitumour and antiproliferative effect of xanthohumol-loaded PLGA nanoparticles on melanoma (2021)

- ¹⁷ Xanthohumol: anti-inflammatory effects in mechanically stimulated periodontal ligament stem cells (2024)
- ¹⁸ Is there a role for natural agents with anti-inflammatory and antioxidative properties in critically ill patients? Potential usefulness of xanthohumol (2025)
- ¹⁹ Unlocking the potential of a prenylated flavonoid: xanthohumol's role in combating inflammatory conditions and rheumatic diseases (2026)

Studies on Human Tissue

- Induction of NAD(P)H:quinone oxidoreductase 1 (NQO1) by Glycyrrhiza species used for women's health: differential effects of the Michael acceptors iso (2015)
- ²⁰ Xanthohumol protects against acetaminophen-induced hepatotoxicity via Nrf2 activation through the AMPK/Akt/GSK3 β pathway (2023)
- ²¹ The modulation of phase II drug-metabolising enzymes in proliferating and differentiated CaCo-2 cells by hop-derived prenylflavonoids (2020)

10. Summary

PROVEN Xanthohumol shows antioxidative and anti-inflammatory effects in controlled human studies, particularly through the reduction of oxidative DNA damage and lowering of inflammatory markers such as IL-6 and CRP. In critically ill COVID-19 patients, a pilot study provided initial evidence of trends toward lower 28-day mortality and shortened clinical courses, though these findings require confirmation in larger trials. Bioavailability can be markedly enhanced through micellar formulations, though human studies have not yet demonstrated acute effects on clinical outcomes. Safety studies confirm good tolerability, though long-term data are lacking.

PLAUSIBLE Preclinical and clinical data suggest enterotype-dependent modulation of the gut microbiota, though its clinical relevance remains unclear. In vitro, xanthohumol exhibits antiproliferative effects on cancer cells and inhibits viral proteases, indicating broad therapeutic potential. **Hypothesis:** The observed microbiome changes may exert prebiotic effects, but whether these improve long-term gut health remains open. Enhanced bioavailability of micellar formulations could enable targeted applications in cardioprotection or metabolic regulation, provided clinical studies confirm this.

Next steps include systematic long-term studies on the clinical relevance of microbiome modulation and anti-inflammatory effects in chronic diseases. Dose-finding studies accounting for individual differences in bioavailability and efficacy are also needed. The translatability of preclinical findings—such as cancer inhibition or antiviral effects—to humans must be tested in controlled human trials. Finally, investigations into interactions with other therapies and potential systemic effects (e.g., immunosuppression) are necessary to fully unlock xanthohumol's potential.

11. Open Questions

- **Bioavailability:** Which formulations (e.g., liposomes) demonstrably enhance intestinal absorption?
- **Microbiome interaction:** Do gut bacteria modulation effects lead to clinically measurable outcomes (e.g., anti-inflammatory action)?
- **Long-term safety:** Are there risks (e.g., immunosuppression or interactions) with prolonged use?

12. Further Paths

Pathways, mechanisms, and networks involving this compound—for those who wish to explore beyond the substance itself.

- Interaction network

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

Frequently Asked Questions

Can xanthohumol be used for inflammatory bowel disease?

Plausible but not demonstrated. The XMaS studies (2020–2024) show that xanthohumol modulates the **gut microbiota**, but none of the controlled trials have demonstrated **clinical improvement** (e.g., in Crohn's disease). The **microbiome changes** are enterotype-dependent, meaning not all patients respond uniformly. A **placebo-controlled trial with clinical endpoints** (e.g., remission rate) is still pending.

How well is xanthohumol absorbed by the body?

Limited and variable. Xanthohumol undergoes significant **first-pass metabolism** in the liver and is metabolised by gut bacteria into compounds such as **isoxanthohumol**. **Bioavailability** depends on the **formulation** (e.g., extract vs. pure substance) and the **individual's microbiota**. A **controlled study** shows that even with standardised intake, plasma levels fluctuate widely. **Liposomal formulations** may improve absorption but have not yet been sufficiently tested.

Are there interactions with medications?

Hypothesis: In vitro, xanthohumol inhibits **CYP enzymes** (e.g., CYP1A2), which are responsible for the metabolism of many drugs. Whether this is **clinically relevant** has never been systematically investigated. Since xanthohumol also **inhibits NF-κB**, it could theoretically potentiate the effects of **immunosuppressants** (e.g., corticosteroids). Intake should be discussed with a physician until data from **drug interaction studies** are available.

Sources

- 1 Impact of xanthohumol (a prenylated flavonoid from hops) on DNA stability and other health-related biochemical parameters: Results of human intervention trials
Ferk F, Mišik M, Nersesyan A, Pichler C, Jäger W, Szekeres T et al. · 2016
- 2 Xanthohumol Microbiome and Signature in Healthy Adults (the XMaS Trial): Safety and Tolerability Results of a Phase I Triple-Masked, Placebo-Controlled Clinical Trial
Langley BO, Ryan JJ, Hanes D, Phipps J, Stack E, Metz TO et al. · 2021
- 3 Gut enterotype-dependent modulation of gut microbiota and their metabolism in response to xanthohumol supplementation in healthy adults
Jamieson PE, Smart EB, Bouranis JA, Choi J, Danczak RE, Wong CP et al. · 2024
- 4 Xanthohumol microbiome and signature in adults with Crohn's disease (the XMaS trial): a protocol for a phase II triple-masked, placebo-controlled clinical trial
Langley BO, Ryan JJ, Phipps J, Buttolph L, Bray B, Aslan JE et al. · 2022
- 5 Xanthohumol microbiome and signature in healthy adults (the XMaS trial): a phase I triple-masked, placebo-controlled clinical trial
Bradley R, Langley BO, Ryan JJ, Phipps J, Hanes DA, Stack E et al. · 2020
- 6 Humulus lupulus extract rich in xanthohumol improves the clinical course in critically ill COVID-19 patients
Dabrowski W, Gagos M, Siwicka-Gieroba D, Piechota M, Siwec J, Bielacz M et al. · 2023
- 7 The Bioavailability of Xanthohumol in Humans and the Influence of Formulation and Dose: Randomized Controlled Trial Data
Brehmer-Henkel S, Diekmann C, Eickeler M, Maris R, Kopp C, Coenen M et al. · 2026
- 8 Humulus lupulus extract rich in Xanthohumol reduces the risk of a fatal clinical course in critically ill patients treated for COVID-19
Dabrowski W, Gagos M, Siwicka-Gieroba D, Piechota M, Siwec J, Bielacz M et al. · 2022
- 9 Correction to: Xanthohumol microbiome and signature in healthy adults (the XMaS trial): a phase I triple-masked, placebo-controlled clinical trial
Bradley R, Langley BO, Ryan JJ, Phipps J, Hanes DA, Stack E et al. · 2020
- 10 Xanthohumol from Hop: Hope for cancer prevention and treatment
Girisa S, Salikia Q, Bordoloi D, Bordoloi D, Banik K, Monisha J et al. · 2021
- 11 Hop Phytochemicals and Their Potential Role in Metabolic Syndrome Prevention and Therapy
Dostálek P, Karabin M, Jelinek L · 2017
- 12 The hop constituent xanthohumol exhibits hepatoprotective effects and inhibits the activation of hepatic stellate cells at different levels
Weiskirchen R, Mahli A, Weiskirchen S, Hellerbrand C · 2015
- 13 Bioavailability and Cardiometabolic Effects of Xanthohumol: Evidence from Animal and Human Studies
Neumann HF, Frank J, Venturelli S, Egert S · 2022
- 14 Xanthohumol Is a Potent Pan-Inhibitor of Coronaviruses Targeting Main Protease
Lin Y, Zang R, Ma Y, Wang Z, Li L, Ding S et al. · 2021
- 15 Dietary prenylated flavonoid xanthohumol alleviates oxidative damage and accelerates diabetic wound healing via Nrf2 activation
Lu X, Liu M, Dong H, Miao J, Stagos D, Liu M · 2022
- 16 Evaluation of the Antitumour and Antiproliferative Effect of Xanthohumol-Loaded PLGA Nanoparticles on Melanoma
Fonseca M, Macedo AS, Lima SAC, Reis S, Soares R, Fonte P · 2021
- 17 Xanthohumol: Anti-Inflammatory Effects in Mechanically Stimulated Periodontal Ligament Stem Cells
Niederer C, Tolba RH, Jankowski J, Marx N, Wolf M, Craveiro RB · 2024
- 18 Is there a place for natural agents with anti-inflammatory and antioxidative properties in critically ill patients? Potential usefulness of Xanthohumol
Dabrowski W, Pfortmueller CA, Kotfis K, Jaroszynski A, Gagos M, Plotek W et al. · 2025
- 19 Unlocking potentials of a prenylated flavonoid: Xanthohumol's role in combating inflammatory conditions and Rheumatic diseases
Altalawy FMA, Zwamel AH, Bishoyi AK, Ballal S, Kalia R, Joshi KK et al. · 2026
- 20 Xanthohumol protect against acetaminophen-induced hepatotoxicity via Nrf2 activation through the AMPK/Akt/GSK3 β pathway
Zhu L, Fan X, Cao C, Li K, Hou W, Ci X · 2023
- 21 The Modulation of Phase II Drug-Metabolizing Enzymes in Proliferating and Differentiated CaCo-2 Cells by Hop-Derived Prenylflavonoids
Lněničková K, Šadibolová M, Matoušková P, Šzotáková B, Skálová L, Boušová I · 2020
- 22 We have previously shown that hops and its Michael acceptor xanthohumol (XH) induced the chemoprevention enzyme, Nad(...)
· 2015
- 23 Recently, we have shown that the potential chemotherapeutic polyphenol xanthohumol (XH), isolated from Humulus Lupulus, ...
· 2013
- 24 The nuclear factor erythroid 2-related factor 2 (Nrf2), a master transcription factor controlling a series of cytoprotec...
· 2019
- 25 In addition, Xn was shown for the first time to upregulate reactive oxygen species (ROS) and nuclear factor erythroid 2-...
· 2024
- 26 In combination with distinct antibiotic compounds the hop ingredients can even exert synergistic effects resulting in en...
· 2022

International Health Research

Research, put in context. Every statement leads to the original paper; the decision in the individual case rests with the treating professional.
ih-research.com/en/knowledge/xanthohumol/ · Last updated 2026-10-15