



DOSSIER · SUBSTANCE

Fisetin

Fisetin is a **flavonoid** with a broad preclinical database, yet the **controlled human studies are still being established**. The clinical research focuses on **inflammatory processes, senescence and cardiovascular markers**, while preclinical models suggest neurodegenerative and oncological effects. The discrepancy between laboratory findings and clinical evidence is the central finding.

511

STUDIES IN
TOTAL

57

IN HUMANS

5

OF WHICH
CONTROLLED

86

IN ANIMALS

134

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

Fisetin at a Glance

ORIGIN:

Fisetin is a flavonol from the flavonoid group and counts among the secondary plant compounds with antioxidant and inflammation-modulating properties. It occurs naturally in plants such as strawberries, apples, onions and persimmons. Chemically it is a polyphenol with a characteristic structure of three hydroxyl groups on the flavonoid backbone that enables interactions with signalling pathways such as NF-κB, Nrf2 and SIRT1.

EVIDENCE BASE:

511 evaluated papers · 5 controlled human studies · 52 observational studies · 33 review articles · 86 animal studies · 113 cell-culture studies

STRONGEST EVIDENCE:

- **Lipid profile** A randomised, double-blind study (2026) examined the combination of interval training and fisetin supplementation (200 mg/day) in obese men over 12 weeks and showed an improvement in the lipid profile as a surrogate parameter. The effects cannot be attributed to fisetin alone.
- **Senescence** A randomised study (2026) compared two fisetin dosing regimens (daily 100 mg vs bolus) and provides an indication of a reduction in senescence-associated gene expression (GLB1, P16, MIF, FUCA1) in peripheral mononuclear blood cells already after 15 days.
- **Safety and tolerability:** Two controlled studies examined the safety and tolerability of fisetin, with no serious adverse effects reported. The data situation remains limited owing to small sample sizes and short intervention periods.
- **Epigenetic age acceleration** A longitudinal study (2024) suggested that the combination of fisetin with dasatinib and quercetin might mitigate epigenetic age acceleration as a surrogate parameter, albeit without significant results and with a small number of participants. The effect of fisetin alone has not been investigated.
- **Heart and circulation:** Preclinical reviews (2025) show that fisetin can exert atheroprotective effects in animal models, for example by reducing plaque formation and improving endothelial function. The findings are preclinical, and whether these effects are transferable to humans remains to be clarified.

LIMITATIONS:

- The bioavailability of fisetin is low because it is rapidly metabolised after oral intake and phase-II conjugates with unclear biological activity are formed. This complicates the transferability of preclinical data.
- Clinical studies on fisetin are heterogeneous, with small samples, short intervention periods and a focus on surrogate parameters rather than clinical endpoints. Oncological or neurodegenerative questions are almost completely absent.
- The preclinical data base is extensive, yet its informative value is restricted by high doses, species differences and the absence of tissue-concentration measurements in human studies.

CLASSIFICATION:

Fisetin is a promising flavonol with antioxidant, anti-inflammatory and senescence-modulating properties demonstrated preclinically. The clinical evidence still requires clarification owing to low bioavailability, heterogeneous study data and short intervention periods. Whether the preclinical effects are transferable to humans remains to be clarified.

1. What Fisetin Is and Why the Study Situation Is Difficult to Compare

Fisetin belongs to the group of **flavonols** and occurs in plants such as strawberries, apples, onions and persimmons. It counts among the **secondary plant compounds** with antioxidant and inflammation-modulating properties that have been demonstrated in cell cultures and animal models. Chemically it is a **polyphenol** with a characteristic structure of three hydroxyl groups on the flavonoid backbone. This structure enables interactions with various signalling pathways, including **NF-κB, Nrf2 and SIRT1**, which have been linked in preclinical studies to cellular senescence, oxidative stress and apoptosis.

The **bioavailability** of fisetin is a central methodological problem for all studies. In-vitro and animal models often use **high concentrations** that are not reached in the human organism. **Oral intake** leads to rapid metabolism, with phase-II conjugates formed whose biological activity is unclear. In addition, the **application forms** (native, liposomal, nanoparticulate) vary greatly, which makes direct comparisons difficult. Most human studies measure **plasma levels or markers in urine**, but not the actual tissue concentration. This limits the informative value regarding **local effects**, for example in the central nervous system or in tumour tissue.

2. What the Studies Show in Detail

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

Distribution of **controlled human studies** by field of application — the numbers are not additive, as one paper may be assigned to several fields:

FIELD OF APPLICATION	CONTROLLED STUDIES
Inflammatory processes	3
Heart and circulation	2
Musculoskeletal system	2
Safety and tolerability	2

FIELD OF APPLICATION	CONTROLLED STUDIES
Oxidative stress	1
Cognition and psyche	1
Metabolism	1
Oncology	1

Oncology

The randomised, double-blind, adaptive phase-2 study *STOP-Sepsis* (2024) investigates the effect of fisetin in older sepsis patients (age > 65 years, planned number of participants: 220). Participants received either a single dose of fisetin (20 mg/kg orally), two doses of 20 mg/kg at one-day intervals, or placebo. The primary endpoint was the change in the *Sequential Organ Failure Assessment (SOFA)* score (cardiovascular, respiratory, renal) after 7 days. Secondary endpoints included quantification of senescent CD3+ cells after 7 days as well as 28-day mortality and organ-failure-free days. The study has not yet been completed; results on the efficacy of fisetin in sepsis-related clinical deterioration are pending. A limiting factor is the lack of differentiation by sepsis severity and comorbidities, which could restrict transferability.

A systematic review (2021) analysed preclinical studies on several flavonols, including fisetin, in prostate carcinoma (21 papers) and bladder carcinoma (15 papers). The studies showed in vitro and in animal models that the flavonols examined inhibit proliferation, induce apoptosis and suppress migration/invasion. Mechanistically, the PI3K/Akt, MAPK and NF-κB signalling pathways were modulated. Dosages varied widely. The effect in humans has not been investigated. The review emphasises the need for controlled human studies, particularly for dose finding and combination therapy with chemotherapeutic agents.⁵

A further review article (2023) summarised the anticarcinogenic effect of fisetin in triple-negative breast cancer (TNBC). In preclinical models, fisetin inhibited the proliferation of TNBC cells, induced cell cycle arrest and apoptosis as well as the suppression of migration/invasion. Synergistic effects with chemotherapeutic agents (e.g. doxorubicin) were observed. The molecular mechanisms included the inhibition of the STAT3 and NF-κB signalling pathways. Clinical studies on fisetin in TNBC are completely lacking, and the preclinical data do not allow any conclusions to be drawn about the effect in humans. The work points to the low bioavailability of fisetin, which could be improved by nanotechnology.

HYPOTHESIS The preclinical data suggest that fisetin *could* exert antitumour effects via multiple signalling pathways (PI3K/Akt, MAPK, NF-κB). However, clinical studies are lacking that confirm these mechanisms in humans. The low bioavailability of fisetin could represent a central obstacle to therapeutic application. Systematic dose-response studies and long-term safety data are still outstanding.

Heart and Circulation

A mechanistic review article (2025) analysed the anti-atherosclerotic properties of fisetin on the basis of preclinical studies. In cell and animal models, fisetin showed protective effects on endothelial cells, macrophages, vascular smooth muscle cells and platelets. In animal models, fisetin reduced plaque formation, improved endothelial function and inhibited the oxidation of LDL cholesterol. The doses in the studies ranged from 5–50 mg/kg body weight, and the effects were dose-dependent. The data derive exclusively from preclinical models; clinical studies on the efficacy of fisetin in atherosclerotic cardiovascular disease (ASCVD) in humans are still outstanding. The review article calls for randomised clinical studies to validate the preclinical results.¹

HYPOTHESIS The preclinical data suggest that fisetin could act atheroprotectively via antioxidant and anti-inflammatory mechanisms. However, it is unclear whether these effects are reproducible in humans. Clinical studies with clearly defined endpoints (e.g. reduction of cardiovascular events) and long-term safety data are still outstanding.

Inflammatory Processes

A double-blind, randomised controlled study (2026) investigated the combined effect of interval resistance and endurance training with fisetin supplementation (200 mg/day) in 60 obese men (BMI ≥ 30 kg/m²) over 12 weeks. The participants were randomised into four groups: placebo, training + placebo, training + fisetin. Primary endpoints were the adipokines asprosin, MCP-1 and adiponectin; secondary endpoints included leptin and the lipid profile. The *training + fisetin* group showed a significant reduction in body weight ($p < 0.001$, $\eta^2 = 0.340$) and an improvement in the lipid profile compared with the other groups. The study does not permit conclusions about the isolated effect of fisetin. Limitations include the short study duration and the lack of differentiation by fat distribution (visceral vs. subcutaneous).²

A randomised, double-blind study (2026) compared two fisetin dosing regimens. The primary endpoint was the expression of senescence-associated genes (GLB1, P16, MIF, FUCA1) in peripheral blood mononuclear cells (PBMCs). The effects were detectable after 15 days and persisted until day 60. Limitations include the absence of a placebo control and the small number of participants per group ($n = 40\text{--}41$).³

A preclinical study in MRL/lpr mice (2022) investigated the effect of fisetin in lupus nephritis. Fisetin reduced the number of senescent tubular epithelial cells (TECs) and proliferating myofibroblasts, resulting in a decrease in renal fibrosis and the expression of the *Senescence-Associated Secretory Phenotype (SASP)*. In vitro, fisetin inhibited TGF-β-induced senescence of TECs and the proliferation of fibroblasts. The dose was 100 mg/kg body weight over 8 weeks. The results are preclinical; transferability to humans has not been investigated.⁸

A preclinical study (2022) showed that fisetin modulates the mTOR/IL-17A signalling pathways and autophagy in psoriasis-like skin inflammation in cell cultures and animal models. In human keratinocytes (HEKa) and CD4+ T cells, fisetin reduced the expression of genes associated with PI3K/Akt/mTOR and psoriasis. The effects were stronger than with rapamycin (an mTOR inhibitor). The study used concentrations of 1–10 μM fisetin in vitro. The results are preclinical; clinical studies for validation in humans are lacking.⁶

HYPOTHESIS The preclinical data suggest that fisetin could eliminate senescent cells and exert anti-inflammatory effects, particularly in chronic inflammatory diseases. Bolus dosing showed stronger effects than daily administration in animal models. Clinical studies with clearly defined endpoints (e.g. reduction of inflammatory markers or improvement of organ function) are still outstanding.

Oxidative Stress

A longitudinal study (2024) investigated the effect of dasatinib + quercetin (DQ) and the combination with fisetin (DQF) on epigenetic ageing in 19 participants. After 6 months of DQ treatment, a significant increase in epigenetic age acceleration (measured with *first-generation epigenetic clocks*) and a shortening of telomere length were observed. The additional administration of fisetin (DQF) over 6 months led to non-significant changes in epigenetic age acceleration, suggesting a potentially mitigating effect of the combination. The study used no placebo control, had a small number of participants and does not permit conclusions about the effect of fisetin alone. ⁷

A review article (2023) summarised the antioxidant mechanisms of fisetin. In preclinical studies, fisetin was shown to reduce reactive oxygen species (ROS), lipid peroxidation and DNA damage. ³³

HYPOTHESIS The preclinical data (animal experiments and cell cultures) suggest that fisetin could reduce cellular stress via antioxidant mechanisms. The combination of fisetin with other senolytics could show synergistic effects in preclinical models.

Viral Infections

A review article (2023) summarised the antiviral effect of flavonols, including fisetin. In preclinical studies (cell cultures), fisetin showed antiviral effects through inhibition of viral entry proteins and reduction of viral replication. The mechanisms included modulation of signalling pathways such as NF- κ B and inhibition of the viral protease. However, the data are based exclusively on in-vitro studies; clinical studies on the antiviral effect of fisetin in humans are still outstanding.

HYPOTHESIS The preclinical data (cell cultures) suggest that fisetin could possess antiviral properties, particularly through inhibition of viral entry mechanisms. There are no data on the efficacy of fisetin in specific viral infections (e.g. influenza, SARS-CoV-2) in humans.

Overall Picture

The studies available show that fisetin exhibits effects in the areas of oncology, inflammatory processes, oxidative stress and cardiovascular diseases in preclinical models (animal experiments and cell cultures). The preclinical data on senescence inhibition and inflammation modulation are particularly consistent, with fisetin dose-dependently reducing the expression of senescence-associated genes (e.g. P16, GLB1) and inhibiting the secretion of pro-inflammatory cytokines. In oncology, preclinical studies show antitumour effects through inhibition of proliferation, induction of apoptosis and modulation of central signalling pathways (PI3K/Akt, MAPK, NF- κ B). However, these results are based almost exclusively on in-vitro and animal models; clinical studies with clearly defined clinical endpoints in humans are still outstanding.

The greatest gaps exist in the translation of preclinical data into clinical practice. Although there are initial phase-2 studies (e.g. *STOP-Sepsis*), their results are still outstanding. Systematic dose-finding studies, long-term safety and efficacy data and studies with clear clinical endpoints (e.g. reduction of mortality, improvement of organ function) are urgently required. In addition, the bioavailability of fisetin is a central obstacle that could be addressed by nanotechnology or structural modifications. The five controlled studies in humans are not yet sufficient to evaluate fisetin as a therapeutic option.

Methodology of the Evidence Base

The studies on fisetin encompass a broad spectrum of designs, from preclinical in-vitro and animal models to initial phase-1/2 studies in humans. Preclinical studies typically use cell cultures (e.g. tumour cell lines, keratinocytes) with fisetin concentrations of 1–100 μ M or animal models (e.g. MRL/lpr mice) with doses of 5–100 mg/kg body weight over 4–12 weeks. The endpoints include molecular markers (e.g. gene expression, signalling pathway activation), histological changes (e.g. tumour size, fibrosis) and biochemical parameters (e.g. adipokines, lipid profile). Controlled clinical studies include 20–220 participants and last from 12 weeks to 6 months. Primary endpoints are frequently surrogate parameters (e.g. SOFA score, gene expression), while clinically relevant endpoints (e.g. mortality, organ function) are investigated less frequently. Long-term studies (> 1 year), dose-finding studies and studies with clear clinical endpoints are systematically lacking. In addition, the transferability of preclinical data to humans is often unclear, as no validated biomarkers for the efficacy of fisetin exist.

Senolytic Effect: From Laboratory to Clinical Application?

FISETIN

is discussed in preclinical models as a **senolytic substance** that is supposed to eliminate **aged cells** (senescence) and thereby influence age-associated diseases. The **mechanistic basis** derives predominantly from **cell cultures and animal models**, in which fisetin reduces **SASP factors** (Senescence-Associated Secretory Phenotype) and induces **apoptosis in senescent cells**. The **most frequently cited work** shows an **inhibition of ferroptosis** in cardiomyocytes, a finding that is nevertheless **not transferable to humans**. Even in animal models, the effects are **dose-dependent and organ-specific**, for example in **cognitive impairment** or **renal fibrosis**.

The

CLINICAL EVIDENCE

is **still under development and preliminary**. One of the five controlled human studies examines **senescence-associated genes in peripheral blood cells**, without however measuring **clinical endpoints** such as functionality or disease progression. The **STOP-Sepsis study**, which is designed as an **adaptive design**, could provide initial indications, yet its results are pending. Even if **biomarkers** such as **p16INK4a** or **SA- β -Gal** are reduced, it remains unclear whether this has **clinically relevant effects**. The **review articles** emphasise the **therapeutic potential**, but at the same time point to **missing long-term data** and **unclear dosing windows**. The **senolytic hypothesis** thus remains a **laboratory observation** whose clinical relevance has not yet been proven.

3. How Reliable the Research Is

The research on fisetin is **strongly characterised by preclinical work**: a considerable part of the studies relates to **basic research, cell cultures and animal models**. The human studies predominantly consist of **observational designs**, while only **five randomised controlled studies** are available. These focus on **inflammatory markers, cardiovascular parameters and senescence-associated genes**, with the areas of application **cardiovascular system, musculoskeletal system and metabolism** dominating. Oncological or neurodegenerative questions, which are frequently investigated in preclinical models, are hardly represented in clinical research.

The **methodological quality** of the human studies is **heterogeneous**. The five controlled studies show **small samples** and **short intervention periods**. Two studies examine **safety and tolerability**, three further investigate **surrogate parameters** such as inflammatory markers or adipokines, but not clinical endpoints. The **most cited controlled study** (STOP-Sepsis) is a **protocol for an adaptive study** whose results are still pending. Observational studies show **associations** between fisetin exposure and biomarkers, but do not permit **causal conclusions**. The preclinical data situation is extensive, yet **transfer problems** (dosage, metabolism, species differences) limit relevance for humans.

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

STATEMENT	STUDY SITUATION
Fisetin has been investigated in preclinical models for neuroprotection in neurodegenerative diseases; the controlled results in humans are inconsistent and lacking for clinical endpoints.	The data derive almost exclusively from cell cultures and animal models . Controlled human studies on neurodegenerative effects are lacking.
Fisetin has been investigated in preclinical models for antitumour properties; controlled studies in humans on oncological applications are not available.	Preclinical models show antiproliferative effects , yet there are no controlled studies in humans on oncological applications.
Fisetin was investigated in a controlled study on cognitive markers, but not on clinical endpoints such as dementia progression or everyday functionality.	A controlled study investigates cognitive markers , but not clinical endpoints such as dementia progression or everyday functionality.
The antioxidant capacity of fisetin was demonstrated in vitro; however, bioavailability and tissue concentration in humans are insufficiently researched.	The antioxidative capacity has been demonstrated in vitro, yet the bioavailability and tissue concentration in humans remain insufficiently researched.

5. Profile: Molecule and Charge

Fisetin is not a single molecule but a **mixture** — there is no molecular formula and no fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; this is exactly what the next section addresses.

6. Charge, Electrons, Radicals

Fisetin exhibits electrochemical properties in the context of redox processes and radical regulation. In human tissue fisetin reduces reactive oxygen species (ROS) and thereby influences oxidative stress responses. This was demonstrated by measurements of ROS levels in skin and intestinal cancer cells, with a decrease in ROS production as well as inhibition of proinflammatory signalling pathways such as MAPK/AP-1 and NADPH oxidase (NOX) observed ^{19 22}. At the same time fisetin promotes the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione (GSH), catalase (CAT) and glutathione peroxidase (GPx) in ischaemic tissue ²¹. These effects indicate involvement in electron transfer processes, for example through modulation of mitochondrial membrane potentials and induction of apoptosis via ROS-mediated mechanisms ²⁰.

In humans fisetin has been investigated in connection with ROS reduction, with a lowering of reactive oxygen species described as part of its activity profile ¹⁴. Direct measurements of electrochemical parameters such as charge state, cation exchange or specific redox potentials are not available for humans. Whether these effects are due to direct electron transfer or indirect modulation of enzyme systems remains to be examined. Animal and cell culture studies confirm the ROS-modulating effect, for example through influence on mitophagy, NLRP3 inflammasome activation or Nrf2 signalling pathways ^{23 24}.

7. Interactions with Other Substances

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

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic Inflammation	52	5
Quercetin	18	0
Stress, Cortisol and Inflammation	15	0
Turmeric and Curcumin	13	1
Resveratrol	11	1
Green Tea and EGCG	6	0
Berberine	6	0
Mariendistel (Silymarin)	3	0
Apigenin	3	0
Kakaoflavanole	2	0

Fisetin shows interactions with various medicinal products, particularly in oncology. In combination with radiotherapy, a radiosensitisation was observed, as fisetin inhibits DNA damage repair (DDR signalling) and simultaneously induces double-strand breaks ⁹. Synergistic effects are described in combination with chemotherapeutics, for example with capecitabine, where an enhanced inhibition of cell proliferation occurred in certain cell lines ²⁶. A possible protective effect against cardiotoxic effects of conventional chemotherapeutics is also discussed, without specific mechanisms being named ²⁵. In addition, there are indications of binding to enzymes such as metalloproteinase-13, ADAMTS5, PKCα and tyrosinase, suggesting a modulation of catabolic or signalling processes ^{27 28}.

The interaction with mast cells (MCs) via the MRGPRX2 receptor was investigated in cell models: fisetin suppressed calcium mobilisation and cytokine release, suggesting a possible inhibition of hypersensitivity reactions ¹⁸. Clinical studies on dose finding and combination with other therapies are recommended ⁵.

8. Overdosage, Tolerability, Limits

Data on the toxicity and adverse effects of fisetin are limited. In vitro, fisetin showed no toxicity up to 60 µM in human melanoma cells and reduced tyrosinase activity ²⁸. In cardiac progenitor cells (CPCs), fisetin was not cytotoxic at doses of 5–100 µM and lowered senescence-associated markers ²⁹. In human periodontal ligament fibroblasts (PDLFs), fisetin mitigated oxidative stress without evidence of cell damage ³⁰. A fisetin derivative (CMS121) was tested in phase-1 studies in healthy adults: single doses up to 1800 mg and repeated doses up to 900 mg/day over 7 days were predominantly well tolerated, with mostly mild adverse events (TEAEs) ³¹. Cytotoxicity was investigated in patient-derived colorectal carcinoma (CRC) organoids, however without specific dose details for fisetin ¹⁷. Apoptosis induction via caspases 3/7 was observed in adenomatous polyp organoids, while normal cells remained unaffected ³².

Contraindications or upper limits for fisetin are not systematically established. In animal or tissue studies, no concrete indications of neurotoxic or cardiotoxic effects are present; instead, a neuroprotective effect was described under arsenic and fluoride exposure ¹⁵. Safety in combination with chemotherapeutics is discussed, without specific risks or dose restrictions being named ²⁵. Long-term data or large-scale clinical studies on toxicity are outstanding; current recommendations emphasise the need for further investigations into pharmacokinetics, optimal dosing and possible limitations ^{1 4}. In prostate cancer and bladder cancer models, a low expected toxicity is assumed, which justifies clinical studies ⁵. For CMS121, a fisetin derivative, safety and pharmacokinetic data were collected in healthy volunteers, however no specific contraindications were identified ^{31 31}.

9. The Most Robust Studies

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

Controlled Studies in Humans

- Senolytics To sIOW Progression of Sepsis (STOP-Sepsis) in elderly patients: Study protocol for a multicenter, randomized, adaptive allocation clinical (2024)
- ¹ The natural polyphenol fisetin in atherosclerosis prevention: a mechanistic review (2025)
- ² The Effects of Interval Resistance-Aerobic Training and Fisetin Supplementation on Asprosin and Selected Adipokines in Obese Men: A Double-Blind Rando (2026)
- ³ Effects of Two Fisetin Dosing Regimens on Reducing Senescence-Related Genes in Peripheral Blood Mononuclear Cells in Aged Humans (2026)

Observational Studies in Humans

- The anticancer mechanism of action of selected polyphenols in triple-negative breast cancer (TNBC) (2023)
- ⁴ Fisetin as a senotherapeutic agent: Evidence and perspectives for age-related diseases (2024)
- ⁵ Kaempferol, Myricetin and Fisetin in Prostate and Bladder Cancer: A Systematic Review of the Literature (2021)
- ⁶ Dual targeting of mTOR/IL-17A and autophagy by fisetin alleviates psoriasis-like skin inflammation (2022)
- ⁷ Exploring the effects of Dasatinib, Quercetin, and Fisetin on DNA methylation clocks: a longitudinal study on senolytic interventions (2024)
- ⁸ Fisetin reduces the senescent tubular epithelial cell burden and also inhibits proliferative fibroblasts in murine lupus nephritis (2022)
- ⁹ Fisetin induces DNA double-strand break and interferes with the repair of radiation-induced damage to radiosensitize triple negative breast cancer cel (2022)
- ¹⁰ Fisetin Attenuates Diabetic Nephropathy-Induced Podocyte Injury by Inhibiting NLRP3 Inflammasome (2022)
- Accumulation of Senescent Neural Cells in Murine Lupus With Depression-Like Behavior (2021)
- ¹¹ The Neuroprotective Role of Fisetin in Different Neurological Diseases: a Systematic Review (2023)
- ¹² Therapeutic Potential and Molecular Mechanisms of the Multitargeted Flavonoid Fisetin (2023)
- Ferroptosis-induced Cardiotoxicity and Antitumor Drugs (2024)
- Supplement and nutraceutical therapy in traumatic brain injury (2025)
- ¹³ Role of Fisetin in Selected Malignant Neoplasms in Women (2023)
- ¹⁴ Fisetin's Promising Antitumor Effects: Uncovering Mechanisms and Targeting for Future Therapies (2023)
- ¹⁵ Fisetin attenuates arsenic and fluoride subacute co-exposure induced neurotoxicity via regulating TNF- α mediated activation of NLRP3 inflammasome (2023)
- Identification of Natural Products as SENP2 Inhibitors for Targeted Therapy in Heart Failure (2022)
- ¹⁶ Nerve Guide Conduits Integrated with Fisetin-Loaded Chitosan Hydrogels for Reducing Oxidative Stress, Inflammation, and Nerve Regeneration (2024)
- ¹⁷ Fisetin induces the upregulation of AKAP12 mRNA and anti-angiogenesis in a patient-derived organoid xenograft model (2023)
- ¹⁸ Fisetin alleviates chronic urticaria by inhibiting mast cell activation via MRGPRX2 (2023)

10. Summary

Fisetin shows consistent effects on cellular senescence, inflammatory processes and oxidative stress in preclinical models, with inhibition of signalling pathways such as NF- κ B, Nrf2 and SIRT1 as well as the reduction of senescence-associated genes (e.g. P16, GLB1) being at the forefront. In humans, initial controlled studies are available that primarily investigate inflammatory markers, cardiovascular parameters and senescence-associated genes. Preclinical models showed changes in the lipid profile and a reduction in senescent cells, albeit with methodological limitations such as small samples and short intervention periods. Oncological or neurodegenerative effects that appear promising in preclinical models have been scarcely investigated clinically and have not been confirmed in humans.

However, systematic dose-response studies, long-term safety data and clinical studies with clearly defined endpoints, for example on the reduction of mortality or improvement of organ function, are lacking. The low bioavailability of Fisetin represents a central obstacle to therapeutic application and could be addressed through structural modifications or nanotechnology. **Hypothesis:** Should the preclinical findings be confirmed in human studies, Fisetin could play a role particularly in combination therapy with other senolytics or chemotherapeutics.

To clarify the therapeutic relevance of Fisetin, randomised, placebo-controlled studies with sufficient power and clear clinical endpoints are required. Priority would be given to studies on dose finding, long-term safety and efficacy in specific indications such as chronic inflammatory diseases, cardiovascular diseases or oncological questions. In addition, biomarkers would need to be identified that enable precise measurement of tissue concentration and local effects of Fisetin, for example in the central nervous system or tumour tissue. The development of improved application forms, for instance through liposomal or nanoparticulate preparations, could increase bioavailability and improve the transferability of preclinical data. Finally, studies on combination therapy with established active substances would be useful to investigate synergistic effects.

11. What Remains Open

- **Dosage:** Which plasma concentrations are required for clinical effects?
- **Long-term effects:** Are there sustainable changes with chronic intake?
- **Specificity:** Do the effects differ in various tissues or age groups?

12. Further Paths

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

- Interaction Network

Frequently Asked Questions

Can Fisetin be used in inflammatory diseases?

Three controlled studies examine **inflammatory markers** such as **CRP** or **cytokines**, but no clinical endpoints such as pain or functionality. The data do not permit **any statement on therapeutic efficacy**. Observational studies show **associations** between Fisetin exposure and inflammatory parameters, yet **causal conclusions** are not possible. The **mechanistic basis** derives predominantly from preclinical models in which Fisetin modulates **NF-κB signalling pathways**.

Is Fisetin safe in use?

Two controlled studies examine **safety and tolerability**, albeit with **small samples and short intervention periods**. **Acute tolerability** appears given, yet **long-term data** are lacking. In preclinical models **no serious toxicities** were reported, yet **dosages and metabolism** differ markedly from humans. **Interactions** with other polyphenols or medications have not been systematically investigated.

Are there differences between Fisetin from foods and supplements?

The **bioavailability** of Fisetin from foods is **low**, as it occurs in **bound form** and is **rapidly metabolised**. Supplements often employ **modified forms** (e.g. liposomal) to improve absorption. Whether this leads to **clinically relevant differences** remains unclear. **No study** directly compares the effects of **native Fisetin** from foods with **supplements**. Plasma levels after supplementation are higher, yet **tissue concentration** remains unknown.

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- 16 Nerve Guide Conduits Integrated with Fisetin-Loaded Chitosan Hydrogels for Reducing Oxidative Stress, Inflammation, and Nerve Regeneration
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- 17 Fisetin induces the upregulation of AKAP12 mRNA and anti-angiogenesis in a patient-derived organoid xenograft model
Kim N, Kwon J, Shin US, Jung J · 2023
- 18 Fisetin alleviates chronic urticaria by inhibiting mast cell activation via MRGPRX2
Zhang Y, Huang Y, Dang B, Hu S, Zhao C, Wang Y et al. · 2023
- 19 In addition, fisetin was rescued, which decreased mRNA levels of pro-inflammatory cytokines, reactive oxygen species pro...
· 2023
- 20 Flow cytometry analysis revealed that Fisetin significantly restricted the progression of skin cancer cells in the G<...
· 2023
- 21 Studies were imported in End- Note X8, and the primary information was recorded in Excel. Results Fisetin reduced...
· 2024
- 22 Fisetin strongly inhibited the production of reactive oxygen species (ROS) and the expression of pro-apoptotic proteins....
· 2021
- 23 The mitophagy, reactive oxygen species (ROS) generation, NLRP3 inflammasome activation, and pro-inflammatory cytokines l...
· 2022
- 24 This article describes correlative profiles of autophagy and apoptotic markers versus nuclear factor erythroid 2-related...
· 2023
- 25 This inconvenience has been tackled by developing less or no cardiotoxic antitumor drugs or by discovering cardioprotect...
· 2024
- 26 The combination of fisetin and capecitabine in cell proliferation caused greater reductions in wild-type HT29 cells than...
· 2024
- 27 Notably, FST-PNP suppressed the expression of metalloproteinase-13 and a disintegrin and metalloproteinase with thrombos...
· 2026
- 28 Computational docking integrated with deep learning-based CNN scoring revealed that fisetin interacts with PKC α , β -caten...
· 2025
- 29 In vitro, pre-treatment of CPCs with increasing doses of fisetin and resveratrol (5 μ M-100 μ M) were non-cytotoxic, decreas...
· 2025
- 30 In vitro experiments showed that fisetin alleviated the cytotoxicity caused by high oxidative stress levels in human per...
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- 31 Safety, Pharmacokinetics, and Cardiodynamics of CMS121, a Novel Small Molecule Fisetin Derivative with Neuroprotective P...
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- 32 All molecules tested induced apoptosis through activation of caspases 3/7. Conclusions QER, EGG, and FIS can be e...
· 2024
- 33 Biological effects and mechanisms of fisetin in cancer: a promising anti-cancer agent
Zhou C, Huang Y, Nie S, Zhou S, Gao X, Chen G · 2023

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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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