



DOSSIER · SUBSTANCE

# Apigenin

Apigenin is a **flavonoid** that occurs in numerous plants. The human evidence base is still developing. The only controlled study investigates the effect on the skin. The predominant research takes place in cell cultures and animal models, which limits transferability.

**464**

STUDIES IN  
TOTAL

**21**

IN HUMANS

**1**

OF WHICH  
CONTROLLED

**55**

IN ANIMALS

**131**

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

## Apigenin at a Glance

### ORIGIN:

Apigenin (4',5,7-Trihydroxyflavon) is a flavonoid from the subgroup of flavones. It occurs in numerous plants, including chamomile, parsley, celery, onions and tea. Particularly in flowers and leaves it serves as a secondary plant substance for protection against oxidative stress and UV radiation. In the plant it is mostly present in glycosidically bound form, e.g. as apigenin-7-glucoside. Bioavailability is limited because it is only poorly absorbed in the intestine and is subject to a pronounced first-pass effect.

### EVIDENCE BASE:

464 evaluated papers · 1 controlled human study · 20 observational studies · 39 review articles · 55 animal studies · 120 cell-culture studies

### STRONGEST INDICATIONS:

Vasomotor symptoms The only controlled human study showed a significant reduction in vasomotor symptoms (mean difference: -0.82; 95 % CI: -1.25 to -0.39;  $p \leq 0.001$ ) after 12 weeks of apigenin intake. No effects on psychological, physical or sexual quality of life. Two participants discontinued due to mild adverse effects (oral mucosal lesions, skin spots).

### LIMITATIONS:

- The only controlled human study (skin) and the observational papers do not permit generalisable statements.
- A large part of the research is based on preclinical models (cell cultures, animal studies) with high, non-physiological doses. Transferability to humans remains to be established.
- Clinical studies on long-term effects, dose-response relationships, pharmacokinetics and safety remain to be conducted. Data on interactions or allergic reactions are not available.

### CLASSIFICATION:

Apigenin shows consistent anti-inflammatory and antioxidant effects in preclinical models (cell cultures, animal studies). The clinical relevance of these findings for humans has not been investigated and requires further research.

## 1. What Apigenin Is

Apigenin (4',5,7-Trihydroxyflavon) belongs to the group of **flavonoids** and counts among the **flavones**. It occurs in many plants, including chamomile (*Matricaria chamomilla*), parsley, celery, onions and tea. It is particularly abundant in flowers and leaves, where it acts as a secondary plant substance offering protection against oxidative stress and UV radiation. Apigenin is colourless to yellowish and in the plant is mostly present in glycosidically bound form, for example as apigenin-7-glucoside.

For research, **bioavailability** and **metabolism** are decisive. Apigenin is only limitedly absorbed in the intestine and is subject to a pronounced first-pass effect. The free form is lipophilic, whereas glycosidic compounds are more water-soluble. In the body it is converted into various metabolites, including glucuronides and sulphates. Measured plasma concentrations are often low, even after oral administration. This limits the interpretability of studies based on high doses in cell cultures.

## 2. What the Studies Show in Detail

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

Allocation of the **controlled human study** by indication — the numbers are not additive, as one paper may be assigned to several areas:

| INDICATION | CONTROLLED STUDIES |
|------------|--------------------|
| Skin       | 1                  |

### Skin

The control group received a placebo. The primary endpoint was quality of life (QOL) measured with the *Menopause-Specific Quality of Life Questionnaire* in the domains vasomotor, psychological, physical and sexual symptoms. After 12 weeks the verum group showed a significant reduction in vasomotor symptoms compared with the placebo group (mean difference: -0.82; 95 % CI: -1.25 to -0.39;  $p \leq 0.001$ ). No significant changes were observed in the psychological, physical, sexual or overall QOL scores. Limitations include the short intervention duration of 12 weeks and the lack of assessment of long-term effects or dose-dependent actions. In addition, the study was conducted exclusively in Iranian women, which restricts transferability to other populations.

### HYPOTHESIS

The selective effect on vasomotor symptoms could indicate a specific interaction of apigenin with thermoregulatory centres in the hypothalamus or a modulation of oestrogen-receptor-mediated signalling pathways. However, this study lacks direct measurements of hormone levels or neuroendocrine markers that could support this hypothesis. Preclinical findings suggest a possible local irritant effect, but its transferability to humans has not been investigated and must therefore be classified as preclinical.

## Inflammatory Processes

In a preclinical study <sup>(4)</sup> the anti-inflammatory effect of a combination of apigenin and melatonin in *nanostructured lipid carriers* (NLC) was investigated. The NLC showed suitable physicochemical parameters, physical stability and delayed release of both substances. In vitro (corneal cell line) and in ovo (chicken-egg chorioallantoic-membrane test) the NLC proved biocompatible. In a rabbit model of ocular inflammation the combination reduced cytokine levels of interleukin-6 (IL-6), IL-8 and *Monocyte Chemoattractant Protein-1* (MCP-1) as well as clinical signs of inflammation. However, the study neither quantifies the applied dose of apigenin nor the exact reduction rates of the cytokines. In addition, a direct comparison with a non-encapsulated formulation is missing, so the contribution of the NLC or the individual substances to the effect remains unclear. Further limitations are the absence of long-term observation or a dose–response analysis.

An animal study <sup>(6)</sup> investigated, preclinically, the effect of apigenin on ovarian dysfunction induced by 4-vinylcyclohexene diepoxide (VCD) in mice. Apigenin normalised the oestrous cycle disrupted by VCD and prevented shrinkage of ovarian tissue. The VCD-induced reduction in anti-Müllerian hormone and the increase in follicle-stimulating hormone (FSH) and luteinising hormone (LH) were dose-dependently reversed. In addition, apigenin increased the number of primordial, primary, secondary and antral follicles compared with the VCD control. Oxidative stress, measured as reactive oxygen species (ROS), was significantly reduced by the high apigenin dose. Apoptosis markers such as Bax, Bcl-2, *cleaved PARP1* and caspase-3 were also dose-dependently regulated. The study also shows activation of the AKT/FOXO3a signalling pathways by apigenin. Limitations include the absence of a placebo control group without VCD and the lack of translation to human models. The preclinical results permit no conclusions about an effect in humans, and the mechanisms remain speculative because no direct receptor interactions were examined.

In a review article <sup>(30)</sup> preclinical studies on the effect of apigenin on atherosclerosis were summarised. Apigenin showed, in animal and cell models, antioxidant and anti-inflammatory effects, a blood-pressure-lowering action and regulation of lipid metabolism. The underlying mechanisms include inhibition of NF-κB, activation of Nrf2 and modulation of inflammatory mediators such as IL-6 and TNF-α. However, the review is based exclusively on animal and *in-vitro* data, with the applied doses and formulations varying considerably. Direct transfer to humans is therefore not possible. In addition, clinical studies investigating the preclinical effects in atherosclerotic diseases in humans are lacking. The work highlights apigenin as a promising candidate for atherosclerosis therapy, but emphasises the need for further research on dose-finding, bioavailability and long-term effects.

## Oncology

In an *in-vitro* study <sup>(3)</sup> the effect of apigenin on acute lymphoblastic leukaemia (ALL) cells (SUP-B15 and Jurkat cell lines) was investigated preclinically. Apigenin reduced cell viability in a dose-dependent manner, measured by MTT assay, and lowered the expression of the proliferation markers Ki67 and *Proliferating Cell Nuclear Antigen* (PCNA). In addition, apigenin induced apoptosis, demonstrated by TUNEL assay, and activated the AMP-activated protein kinase (AMPK) signalling cascade. At the same time ferroptosis was triggered, evident from elevated intracellular Fe<sup>2+</sup> levels and increased lipid peroxidation (measured via TBARS assay). Inhibition of AMPK with Compound C abolished the apigenin-induced effects, indicating a central role of this signalling pathway. The study provides preclinical data that do not allow conclusions about an effect on primary ALL cells or *in-vivo* models. In addition, investigation of systemic toxicity or the pharmacokinetics of apigenin is missing, which would be essential for clinical translation.

An animal study <sup>(5)</sup> investigated, preclinically, the effect of apigenin on vascular remodelling in spontaneously hypertensive rats (SHR). Apigenin reduced media thickness, vessel-wall diameter and wall-to-lumen ratio in aortic cross-sections. In vitro apigenin inhibited angiotensin-II-induced proliferation and migration of vascular smooth-muscle cells (VSMC) and lowered the expression of PCNA, matrix metalloproteinase-9 (MMP9) and MMP2. In addition, apigenin induced cell-cycle arrest in the G0/G1 phase through activation of the tumour-suppressor protein p53 (TP53). Inhibition of TP53 with pifithrin-α (PFT-α) abolished the apigenin effects. Network-pharmacological analyses and molecular docking identified TP53 as a key target of apigenin. Limitations include the absence of a dose–response analysis and the lack of investigation of long-term effects or possible adverse effects of apigenin in this model. The preclinical results permit no conclusions about an effect in humans.

## Oxidative Stress

A systematic review <sup>(29)</sup> summarises the effect of natural products, including apigenin, on the Nrf2-Keap1-ARE signalling pathway and their influence on neurodegenerative diseases. In preclinical models apigenin activates the Nrf2 pathway, leading to expression of antioxidant enzymes such as haem oxygenase-1 (HO-1) and NAD(P)H quinone oxidoreductase 1 (NQO1). This reduces oxidative stress and mitochondrial dysfunction, two central factors in the pathogenesis of neurodegenerative diseases such as Alzheimer's and Parkinson's. The review draws on preclinical studies that demonstrate a neuroprotective effect of apigenin in cell and animal models. However, clinical studies confirming these preclinical effects in humans are lacking. In addition, the apigenin doses used in the studies vary widely. The work emphasises the need for further research on the bioavailability, pharmacokinetics and long-term effects of apigenin in neurodegenerative diseases.

## Safety and Tolerability

An *in-vitro* study <sup>(31)</sup> examined the interactions between tea protein (TP) and three flavonoids, including apigenin. Apigenin formed stable complexes with TP, the binding occurring via hydrogen bonds and van der Waals forces. Fluorescence spectroscopy showed static quenching of TP fluorescence by apigenin, albeit with lower affinity than luteolin. Thermodynamic analyses confirmed the spontaneity of the binding. The study provides structural insights into the interaction of apigenin with proteins, but offers no indications of possible toxicological or allergenic effects in humans. Data on the bioavailability or metabolism of the TP-apigenin complexes are also lacking. The clinical relevance of these interactions therefore remains unclear.

## Overall Picture

The available studies provide preclinical indications that apigenin may exert effects in various therapeutic areas. Preclinical data from cell cultures and animal models consistently show anti-inflammatory and antioxidant effects. One human study <sup>(1)</sup> investigated chamomile in menopausal complaints. Apigenin modulates central signalling pathways such as Nrf2, NF-κB and AMPK, which in preclinical models leads to a reduction in inflammatory mediators (e.g. IL-6, MCP-1) and oxidative stress. In oncology, *in-vitro* studies <sup>(3)</sup> show dose-dependent inhibition of proliferation and induction of apoptosis in

leukaemia cells, while animal data <sup>(5)</sup> indicate a protective effect on vascular remodelling in preclinical settings. Whether these effects are transferable to humans has not been investigated. The clinical study with chamomile for menopausal symptoms <sup>(1)</sup> showed a significant reduction in vasomotor complaints, but no effects on other QOL domains.

Systematic clinical testing of the efficacy and safety of apigenin in humans over longer periods and at different doses remains outstanding. A large proportion of the data originates from preclinical models whose transferability to humans is limited. In addition, the apigenin formulations used (e.g. free substance versus encapsulated NLC) and doses vary widely, which complicates comparison of the studies. In particular, oncological use has hardly been investigated, as no clinical data exist, nor have neurodegenerative diseases, where only preclinical indications of neuroprotective effects are available. The safety of apigenin proved largely unremarkable in the studies conducted; however, systematic investigations into long-term effects, interactions with other medicines or possible allergic reactions are lacking.

### Methodology of the Evidence Base

The studies on apigenin encompass a broad spectrum of designs, with preclinical models (cell cultures, animal experiments) accounting for a large proportion. Typical endpoints in cell studies are measurement of cell viability (MTT assay), apoptosis (TUNEL assay), oxidative stress (ROS, TBARS assay) and inflammatory markers (ELISA, Western blot). Animal studies frequently examine histological changes (e.g. vascular remodelling) or biochemical markers (hormone levels, cytokines); behavioural parameters (e.g. motor function in Parkinson models) remain restricted to preclinical models. The only controlled study with chamomile <sup>(1)</sup> is a randomised, placebo-controlled triple-blind trial with 80 participants and a duration of 12 weeks that recorded quality of life as the primary endpoint. Systematic clinical studies with larger populations, longer intervention periods and standardised doses are nevertheless lacking. There is also a shortage of studies examining the pharmacokinetics, bioavailability and metabolism of apigenin in humans. Most preclinical studies use high, often non-physiological doses whose transferability to humans is questionable. The formulation of apigenin (e.g. free substance versus encapsulated systems) is also rarely varied systematically, which complicates interpretation of the results.

### Apigenin: Laboratory Findings versus Clinical Relevance

The overwhelming majority of studies on apigenin originate from

#### CELL CULTURES

and **animal models**. These works show consistent effects on molecular signalling pathways, for example inhibition of **NF-κB** or activation of **Nrf2**. Such findings are valuable for basic research but do not permit conclusions about effects in humans. Cell cultures operate with concentrations that are scarcely achievable in vivo, and animal models only incompletely reflect human metabolic processes.

The

#### DATA IN HUMANS

are still being assembled. The only controlled study examines the effect on the skin and provides no robust statements on other areas of application. Observational studies show associations between an apigenin-rich diet and health parameters, for example in inflammatory or neurodegenerative diseases. Such studies cannot, however, demonstrate causal effects. Without controlled clinical trials the clinical relevance of apigenin remains speculative.

## 3. How Robust the Research Is

A substantial proportion of the evaluated works falls under **basic research**, followed by **cell cultures** and **animal models**. Only a small number of studies were conducted in humans, most of them observational and one controlled. The controlled study examines the effect of chamomile on menopausal symptoms. Reviews and mechanism studies dominate the non-experimental research. The most frequently cited works originate from cell cultures and animal models, particularly on anti-inflammatory, antiproliferative and neuroprotective effects.

The **data in humans** are still being assembled and are methodologically limited. The only controlled study does not permit generalisable statements. Observational studies provide indications of associations, for example between an apigenin-rich diet and certain health parameters, but do not examine causal effects. Animal and cell studies show consistent effects on signalling pathways such as **NF-κB**, **STAT3** and **Nrf2**, yet transferability to humans remains unclear. Research focuses on laboratory findings, while further clinical application studies are still outstanding.

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

| STATEMENT                                                                                                                        | EVIDENCE BASE                                                                                                                                              |
|----------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Apigenin has been investigated for anti-inflammatory effects in the dose ranges studied; the controlled results are inconsistent | The data come almost exclusively from cell cultures and animal models. The only controlled study in humans examines the skin, not systemic inflammation.   |
| Apigenin has been investigated for neuroprotective effects; the controlled results are inconsistent                              | The research is based on cell cultures and animal models. Observational studies show associations, but no controlled studies examine the effect in humans. |
| Apigenin has been investigated for inhibition of tumour growth; the controlled results are inconsistent                          | The data come from cell cultures and animal models. There are no clinical studies that prove an antitumoural effect in humans.                             |
| Apigenin has been investigated for improvement of cardiovascular health; the controlled results are inconsistent                 | The research is limited to laboratory findings and animal models. Observational studies show associations, but no controlled studies examine the effect.   |

## 5. Profile: Molecule and Charge

Apigenin 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

Apigenin exhibits electrochemical properties that have been investigated in cell cultures. Zeta-potential measurements yielded strongly negative values ( $\sim -27,8$  mV in PBS), which decreased to  $\sim -4,2$  to  $-1,2$  mV in acidic media. In the presence of serum proteins the value was  $\sim -12,1$  to  $-13,5$  mV, indicating charge-dependent interactions. Formulations containing apigenin also displayed negative surface charges, e.g.  $-20$  mV in exosome-like vesicles or  $-24,4$  mV in cubosomes<sup>23</sup>. The charge influences stability and interaction with biological systems, for example through cation exchange or shielding effects. No direct measurements of electrochemical parameters are available in humans. Indirectly, however, participation in redox processes is described: apigenin acts as a radical scavenger, as demonstrated in cell cultures by ABTS assays ( $IC_{50} = 25,58 \pm 0,12 \mu M$ )<sup>22</sup>. It reduces reactive oxygen species (ROS) and modulates oxidative stress responses<sup>6 20</sup>.

The antioxidant effect of apigenin is based on electron transfer processes and radical scavenging properties. In cell cultures it showed higher radical scavenging activity than ascorbic acid ( $IC_{50} = 30,43 \pm 0,14 \mu M$ )<sup>22</sup>. Apigenin-containing complexes, such as Cu(II)-loaded nanoparticles, exhibited a surface charge of  $-25,6$  mV and enhanced the cytotoxic effect<sup>24 24</sup>. ROS-responsive nanoparticles with apigenin were developed for therapeutic applications, with the charge ( $\sim -20$  mV) influencing stability<sup>21</sup>. In humans, the activation of ROS by external factors is documented<sup>6</sup>, however no direct measurement of electrochemical parameters. Review articles describe apigenin as a modulator of redox signalling pathways, for example via Nrf2 activation or inhibition of NF- $\kappa B$ <sup>19 20</sup>. Animal or tissue experiments on charge behaviour or cation exchange are not available.

# 7. Interactions with Other Substances

With which other substances of the platform this substance is **jointly** investigated or discussed in human studies and reviews — combination, comparison or shared mechanism of action. The number names works in which both occur.

| SUBSTANCE                          | JOINT WORKS | OF WHICH CONTROLLED IN HUMANS |
|------------------------------------|-------------|-------------------------------|
| Chronic inflammation               | 35          | 0                             |
| Quercetin                          | 22          | 0                             |
| Turmeric and curcumin              | 16          | 0                             |
| Stress, cortisol and inflammation  | 10          | 0                             |
| Adaptogens                         | 9           | 0                             |
| Ginger                             | 7           | 1                             |
| Black cumin (Nigella sativa)       | 7           | 0                             |
| Resveratrol                        | 7           | 0                             |
| Green tea and EGCG                 | 5           | 0                             |
| Olive polyphenols (hydroxytyrosol) | 5           | 0                             |

In human tissue an improved transcellular uptake and oral bioavailability of apigenin via self-nanoemulsifying drug delivery systems was observed <sup>18</sup>. In cell cultures a strengthened inhibition of colorectal cancer was shown by the joint administration of apigenin, FdUMP and a CD276 antibody <sup>26</sup>. Animal experiments indicate an interaction with potassium channel blockers: the combination of apigenin with charybdotoxin and apamin reduced the vasodilatory effect by 50 %, while the additional administration of L-NAME abolished the effect completely <sup>27</sup>.

In review articles synergistic effects with melatonin in the treatment of ocular inflammation are indicated, whereby nanostructures strengthen the effect <sup>4 4</sup>. In addition a synergistic antibacterial effect with colistin was described <sup>25</sup>. The combination with other bioactive compounds, as in IPP, led to strengthened anti-inflammatory effects in human tissue. Further investigations into interactions with medicinal products or nutrients, in particular into binding mechanisms and enzyme modulation, would be required.

# 8. Overdosage, Tolerability, Limits

Limited data are available on adverse effects of apigenin in humans. In a controlled study with chamomile extract (contains apigenin) two participants experienced mild side effects such as oral mucosal inflammation and skin spots, which led to study discontinuation <sup>1</sup>. Systematic investigations into toxicity or overdosage are lacking. In review articles apigenin is described as a promising active substance with a favourable safety profile, however without concrete dose information <sup>7 14</sup>. Bioavailability is considered limited, which may reduce the risk of systemic side effects <sup>14</sup>. In-vivo data on toxicity profiles of apigenin and related flavones (e.g. luteolin) are discussed, without clear upper limits or contraindications being derived <sup>7 7</sup>.

Indications of possible interactions arise from observations on transport proteins such as BCRP, which occur in the blood-milk barrier of mammals and can influence the distribution of phytochemicals <sup>28</sup>. Apigenin showed anti-inflammatory effects in cell and animal models (e.g. reduction of IL-6, TNF-α, IL-1β) <sup>12</sup>, yet clinical studies on safety during longer-term use or high doses are still outstanding <sup>12</sup>. Nanoformulations could improve tolerability, but have not yet been sufficiently tested <sup>4 14</sup>. Contraindications have not been systematically investigated; caution may be advisable with simultaneous intake of substrates for efflux transporters <sup>28</sup>.

# 9. The Most Robust Works

Ordered by strength of evidence, not by familiarity. The complete evaluation comprises considerably more works; the most resilient ones are listed here.

## Controlled Studies in Humans

- <sup>1</sup> Effect of Matricaria chamomilla on the Quality of Life Among Women with Menopausal Symptoms: A Triple-Blind Randomized Controlled T (2026)

## Observational Studies in Humans

- <sup>2</sup> Apigenin enhances Nrf2-induced chaperone-mediated autophagy and mitigates α-synuclein pathology: Implications for Parkinson's disease therapy (2025)
- <sup>3</sup> Apigenin facilitates apoptosis of acute lymphoblastic leukemia cells via AMP-activated protein kinase-mediated ferroptosis (2025)
- <sup>4</sup> Combination of Apigenin and Melatonin with nanostructured lipid carriers as anti-inflammatory ocular treatment (2025)
- <sup>5</sup> Apigenin prevents hypertensive vascular remodeling by regulating the TP53 pathway (2025)
- <sup>6</sup> Apigenin Improves Ovarian Dysfunction Induced by 4-Vinylcyclohexene Diepoxide via the AKT/FOXO3a Pathway (2024)

- <sup>7</sup> Potential anticancer effects and toxicity of flavones luteolin and apigenin *in vivo* (2025)
- <sup>8</sup> Therapeutic targeting of the tryptophan-kynurenine-aryl hydrocarbon receptor pathway with apigenin in MED12-mutant leiomyoma cells (2025)
- <sup>9</sup> Apigenin Induces Autophagy and Apoptosis in Chemoresistant Glioblastoma Cells and Inhibits Tumorigenicity Associated with Regulation of Immunomodulators (2025)
- Inhibitory potential of phytochemicals on species-specific breast cancer resistance protein transport activity (2025)
- The Roles of Flavonoids and Other Plant-Based Phenolics in Mitigating Diabetes-Induced Macrovascular Complications (2025)
- <sup>10</sup> Anti-inflammatory Potential of Apigenin and Luteolin in Oral Mucositis: An *In Silico* Docking Study Targeting IL-6, NF- $\kappa$ B, and COX-2 (2026)
- <sup>11</sup> Apigenin restores macrophage homeostasis and angiogenesis via Fgr/IL10 axis in recurrent spontaneous abortion (2026)
- <sup>12</sup> The effects of apigenin on immune responses and inflammatory biomarkers in sepsis: a comprehensive systematic review (2026)
- The inhibition of pathological IgE in allergic diseases by natural compounds (2026)
- Neuroprotection Through Nature: The Role of Bioactive Phytocompounds in Alzheimer's and Parkinson's Disease (2026)
- <sup>13</sup> *In silico* prediction, molecular docking and simulation of natural flavonoid apigenin and xanthoangelol E against human metapneumovirus (2026)
- <sup>14</sup> Exploring the therapeutic potential of phytochemicals apigenin and ellagic acid in managing polycystic ovarian syndrome and its comorbidities: a comprehensive review (2025)
- ET-1-induced CTGF expression is mediated by STAT3 activation through casein kinase 2 $\alpha$ ' and p300 but not casein kinase 2 $\alpha$  in human lung fibroblasts (2026)
- The Multifaceted Potential of *Adhatoda vasica*: Traditional Uses, Pharmacological Activities and Biotechnological Applications (2026)
- <sup>15</sup> Natural flavonoid apigenin and xanthoangelol E are potent antivirals against human metapneumovirus: an *in-silico* study (2025)

### Investigations on Human Tissue

- <sup>16</sup> Apigenin, a dietary flavonoid, sensitizes human T cells for activation-induced cell death by inhibiting PKB/Akt and NF- $\kappa$ B activation pathway (2008)
- <sup>17</sup> Apigenin Alleviates Intestinal Ischemia/Reperfusion Injury via Upregulating Nrf2-Mediated Tight Junction Integrity (2025)
- <sup>18</sup> Enhancement of *in vitro* transcellular absorption and *in vivo* oral bioavailability of apigenin by self-nanoemulsifying drug delivery systems (2024)

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## 10. Summary

Apigenin showed consistent anti-inflammatory and antioxidant effects in preclinical models, for example through inhibition of NF- $\kappa$ B or activation of Nrf2. The only controlled human study documented a significant reduction in vasomotor symptoms in menopausal women, however without effects on other quality-of-life domains. The evidence base comprises laboratory findings and a methodologically limited clinical study. Observational studies suggest associations between an apigenin-rich diet and health parameters, but do not allow causal conclusions.

Preclinical studies suggest that apigenin could exert antiproliferative and neuroprotective effects through activation of signalling pathways such as AMPK or TP53. However, direct evidence for these mechanisms in humans is lacking. Without further clinical studies, these assumptions remain speculative.

What a study would need to clarify: Randomised, placebo-controlled studies with larger populations, longer intervention periods and standardised dosages are necessary to examine the efficacy and safety of apigenin in humans. Investigations into pharmacokinetics, bioavailability and metabolism would be particularly relevant to determine physiologically achievable plasma concentrations. In addition, dose-response relationships and long-term effects in various areas of application (e.g. inflammatory processes, oncology, neurodegeneration) should be systematically evaluated. Mechanistic studies would need to validate the signalling pathways identified in preclinical models (e.g. NF- $\kappa$ B, Nrf2, AMPK) in humans. Finally, comparisons of different apigenin formulations (e.g. free substance versus encapsulated systems) would be required to determine the optimal dosage form.

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## 11. What Remains Open

- **Bioavailability:** How can the absorption of apigenin in the human body be improved to make laboratory findings clinically usable?
- **Dosage:** Which plasma concentrations are achievable in humans, and how do they compare to the doses effective in cell cultures?
- **Long-term effects:** Are there controlled studies on chronic apigenin intake, and how do metabolites affect this?

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## 12. Further Paths

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

- Interaction network

## Frequently Asked Questions

### Can Apigenin be recommended as a dietary supplement?

The human evidence base is not yet sufficient to justify a recommendation. The only controlled study investigates the skin, not systemic effects. Observational studies show associations between an apigenin-rich diet and health parameters, but do not prove a causal effect. Without further clinical studies, intake as a dietary supplement remains speculative.

### Are there interactions with medications?

Apigenin interacts in cell cultures and animal models with various **cytochrome P450 enzymes**, particularly **CYP1A2** and **CYP3A4**. This could theoretically influence the metabolism of medications. However, clinical data on interactions in humans are lacking. Concurrent intake with medications metabolised via these enzymes should therefore be approached with caution.

### How is apigenin measured in research?

Apigenin is usually quantified via **HPLC** (high-performance liquid chromatography) or **LC-MS/MS** (liquid chromatography with tandem mass spectrometry). In biological samples (blood, urine), **glucuronides** and **sulfates** are primarily measured as metabolites. The free form is often detectable only in trace amounts due to low bioavailability. Measurement in tissues is methodologically demanding and is rarely performed.

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