



DOSSIER · SUBSTANCE

Luteolin

This page summarises scientific studies on **luteolin**, a significant proportion of which involve human subjects. The current research focuses on neuroinflammatory processes and post-COVID symptoms. Notably, combined applications with palmitoylethanolamide (PEA) dominate, while studies on luteolin in isolation are less common.

248

STUDIES IN
TOTAL

33

IN HUMANS

8

OF WHICH
CONTROLLED

16

IN ANIMALS

74

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

Luteolin at a glance

ORIGIN:

Luteolin is a naturally occurring flavonoid from the polyphenol group found in plants such as parsley, celery, thyme, kale, artichokes, and chamomile. It functions as a secondary plant metabolite to defend against oxidative stress and pathogens and is investigated in research both as a pure substance and in plant extracts, primarily administered orally.

STUDY STATUS:

248 evaluated publications · 8 controlled human studies · 25 observational studies · 27 review articles · 16 animal studies · 59 cell culture studies

STRONGEST EVIDENCE:

- Postviral olfactory disorders (post-COVID-19) Controlled studies demonstrate that the combination of ultramicronised palmitoylethanolamide (PEA) and luteolin (PEA-LUT) with olfactory training achieves significantly better results in the Sniffin' Sticks identification test than placebo or training alone. The effects of luteolin alone remain unclear.
- Neuroinflammation (stroke) A randomised controlled trial in acute ischaemic stroke shows that PEA-LUT in addition to standard therapy achieves significant improvements in NIHSS score, Barthel Index, and cognitive tests (MMSE, MoCA). The contribution of luteolin to these effects is not investigated.
- Periodontitis A herbal tincture containing luteolin-7-O-glucoside as an adjunct to non-surgical periodontal therapy significantly reduced the prevalence of certain periodontal pathogens. The effect of luteolin alone and long-term outcomes have not been investigated.
- Cognition (post-COVID-19) Studies suggest a potential improvement in cognitive symptoms ("mental clouding") with PEA-LUT, but placebo-controlled data on the cognitive domain or luteolin alone are lacking. Modulation of GABA_B-ergic transmission is discussed as a mechanism but remains unconfirmed in human studies.

LIMITATIONS:

- Most controlled studies investigate luteolin exclusively in combination with PEA, so isolated effects of luteolin cannot be distinguished.
- Long-term data on safety and efficacy are lacking, particularly for isolated luteolin. Studies are predominantly short-term and monocentric.
- Objective biomarkers or imaging techniques to confirm postulated mechanisms (e.g., microglia modulation) are not yet available.

CLASSIFICATION:

Luteolin, a plant-derived flavonoid with anti-inflammatory and neuroprotective properties, is primarily investigated in combination with palmitoylethanolamide for postviral olfactory disorders and neuroinflammatory conditions. Data on its isolated effects and long-term safety are lacking.

1. What Luteolin Is

Luteolin is a naturally occurring **flavonoid** from the polyphenol group. It is found in numerous plants, including parsley, celery, thyme, kale, artichokes, and chamomile. As a secondary plant metabolite, it serves to defend against oxidative stress and pathogens. Chemically, it is a tetrahydroxyflavone with a characteristic structure attributed to its antioxidant and inflammation-modulating properties. In research, luteolin is studied both as a pure substance and in plant extracts. It is most commonly administered orally, less frequently topically or in combination with other active compounds.

For understanding the study landscape, it is crucial that **luteolin** is used in various **formulations**: as an isolated active compound, in combination with **palmitoylethanolamide (PEA)**, or as part of complex plant extracts. **Bioavailability** is considered limited, which is why micronised or ultramicronised preparations have been developed to improve absorption. Additionally, **target tissues** vary depending on the mode of administration—systemic effects require sufficient absorption, while local applications (e.g., in the oral cavity) can exert direct effects. Most controlled human studies use standardised combination preparations, which limits the transferability of findings to isolated luteolin.

2. What the Studies Show in Detail

The key human studies and most important reviews—by application area, including population, duration, preparation, outcome measures, and results, as reported in the original publications. Numbers are included only where the study provides them.

Distribution of **controlled human studies** by application area—the numbers are not additive, as one study may be assigned to multiple areas:

APPLICATION AREA	CONTROLLED STUDIES
Inflammatory processes	7
Cognition and mental health	3
Immune system	3
Safety and tolerability	2
Viral infections	2
Gut and microbiome	1

Viral Infections – Postviral Olfactory Disorders

The controlled study by ¹ examined 185 patients (130 intervention, 55 control group) with persistent olfactory dysfunction following COVID-19 (>6 months after negative testing, without pre-existing sinonasal conditions). The intervention group received 770 mg of ultramicrosized palmitoylethanolamide combined with luteolin (PEA-LUT) orally plus olfactory training daily, while the control group received only olfactory training plus placebo. After 90 days, the PEA-LUT group showed a significantly greater improvement in the Sniffin' Sticks identification test ($p < 0.0001$), although the exact point difference is not quantified in the abstract. A limitation is the lack of detailed baseline values or absolute improvement per group, leaving the clinical relevance of the statistical significance unclear for the combination therapy.

Parosmia was investigated. The study confirms the anti-neuroinflammatory effect of the PEA-LUT combination but provides no data on the isolated effect of luteolin or the long-term stability of the effects of the combination.

A multicentre, double-blind, placebo-controlled study (³) with 202 patients compared four groups: (1) olfactory training + placebo, (2) 770 mg um-PEA-LUT once daily, (3) 770 mg um-PEA-LUT twice daily, (4) 770 mg um-PEA-LUT once daily + olfactory training. Groups 2 and 3 showed no significant superiority over placebo. The study underscores the synergistic effect of the PEA-LUT combination with olfactory training but leaves open whether luteolin alone or in a different dosage within the combination would achieve similar effects. **Hypothesis:** The combination therapy may specifically target neuroinflammatory processes in the olfactory bulb, but imaging or histological correlates are lacking for confirmation.

Another study (⁷) with an identical design to ³ (202 patients, 4 groups) confirmed the superiority of combination therapy (um-PEA-LUT + olfactory training) over monotherapies (placebo or um-PEA-LUT alone). Groups 2 and 3 (um-PEA-LUT once or twice daily) showed no significant differences from placebo. The study indicates that the dosage of um-PEA-LUT (once vs. twice daily) has no impact on the outcome, suggesting a possible saturation of the mechanism of action for the combination. A limitation is the lack of subgroup analysis by severity of olfactory dysfunction or duration of symptoms.

Cognition and Psyche – Long-Term Consequences of COVID-19

In a longitudinal study (²) involving 69 patients (43 women, 26 men, mean age 40.6 ± 10.5 years) with post-COVID-19 olfactory disorders and cognitive impairments ("mental clouding"), the effect of PEA-LUT (770 mg daily) alone or in combination with olfactory training was investigated. The study suggests that the combination addresses both olfactory and cognitive symptoms; however, the lack of a placebo control group for the cognitive domain and the presence of PEA precludes conclusions about luteolin's specific contribution to these effects.

A randomised, placebo-controlled study (¹¹) with 39 patients (26 women, mean age 49.9 ± 11.4 years) examined the effect of PEA-LUT (700 mg + 70 mg, twice daily) on GABA_B-ergic activity and cortical plasticity in long COVID with cognitive deficits. The study demonstrates normalisation of GABA_B-ergic transmission by the combination but provides no data on clinical relevance (e.g., cognitive tests) or the isolated effect of luteolin. **Hypothesis:** Modulation of GABA_B activity may be a central mechanism for the cognitive effects of the combination, though direct evidence for luteolin alone from human studies is lacking.

An observational study (⁸) discusses the role of luteolin in "brain fog" within the context of neuroinflammatory disorders (e.g., autism spectrum disorders, chronic fatigue syndrome). The authors postulate that luteolin reduces neuroinflammatory processes through inhibition of mast cell activation and microglia inhibition. A liposomal formulation of luteolin in olive fruit extract showed improvement in attention in case series of children with autism, but these findings are preliminary and lack controlled validation. The study remains speculative, as no quantitative data on luteolin dosage, duration, or outcomes in postviral cognitive deficits are provided.

Inflammatory Processes – Neuroinflammation and Systemic Inflammation

In a prospective randomised controlled trial (⁵) with 60 patients with acute ischaemic stroke (AIS), the effect of PEA-LUT (770 mg, twice daily for 90 days) in addition to standard therapy (thrombolysis) was investigated. The intervention group showed a significantly greater improvement in NIHSS score ($p < 0.0001$), Barthel Index ($p < 0.002$), and modified Rankin Scale ($p < 0.0001$), as well as in cognitive tests (MMSE, MoCA) compared to the control group. The study demonstrates the neuroprotective and anti-inflammatory effects of the combination in AIS but leaves open whether luteolin alone or at a different dosage achieves similar effects. A limitation is the lack of subgroup analysis by stroke severity or localisation.

A randomised study (²⁵) with 60 patients with moderate periodontitis (Stage II, Grade A) investigated the effect of a herbal tincture (Tinctura paradentonica®, containing 358.06 ± 5.64 µg/mL luteolin-7-O-glucoside) as an adjunct to non-surgical periodontal therapy (NSPT). After 3 months, the intervention group showed a significant reduction in the prevalence of *Treponema denticola* and *Tannerella forsythensis* ($p < 0.001$) but no change in *Porphyromonas gingivalis*.

a. post-COVID) compared olfactory training + PEA-LUT with olfactory training alone. The study suggests that while PEA-LUT achieves statistically significant effects, these may not be clinically meaningful. A limitation is the lack of detailed presentation of baseline values or absolute improvements.

Overall Picture

The available studies on the combination of luteolin with palmitoylethanolamide (PEA-LUT)—predominantly in postviral olfactory disorders and neuroinflammatory conditions—suggest anti-inflammatory and neuroprotective effects. The strongest evidence comes from controlled studies on post-COVID-19 olfactory disorders, where PEA-LUT combined with olfactory training achieved significant improvements in olfactory function (Sniffin' Sticks test) and cognitive symptoms ("mental clouding"). However, the effects of luteolin alone on parosmia or isolated cognitive deficits remain unclear. **Hypothesis:** The synergistic effect of luteolin with PEA may be based on dual modulation of neuroinflammation (via mast cell inhibition) and neuronal plasticity (via GABA_B-ergic transmission), though direct evidence for this mechanism in human studies is lacking.

Notably, there is heterogeneity in study designs: while some studies examine luteolin in combination with PEA, controlled studies on the isolated effect of luteolin are lacking for most indications. Furthermore, endpoints are often limited to subjective or semiquantitative tests (e.g., Sniffin' Sticks) without objective biomarkers (e.g., inflammatory cytokines) or imaging. The existing studies on systemic inflammatory processes (e.g., periodontitis, stroke) show promising results but remain limited to short observation periods (≤ 3 months) and small sample sizes. What is missing are long-term studies with clear dose-response relationships and mechanistic insights into the role of luteolin.

Methodology of the evidence base

The key studies on the combination of luteolin with palmitoylethanolamide (PEA-LUT) include randomised, placebo-controlled trials (RCTs) with parallel-group designs. Primary endpoints are typically semiquantitative tests (e.g., Sniffin' Sticks for olfactory disorders, NIHSS for stroke) or clinical scores (e.g., Barthel Index, MoCA). Systematic weaknesses include the absence of dose-finding studies (PEA-LUT vs. placebo), short follow-up periods, and reliance on subjective or indirect measurement methods. Additionally, studies with objective biomarkers (e.g., inflammatory cytokines, imaging) or mechanistic analyses (e.g., GABA_B receptor activity) for luteolin alone are lacking.

Luteolin alone or in combination: What do we really know?

The
MOST-CITED CONTROLLED STUDIES

on luteolin almost exclusively examine the **combination with palmitoylethanolamide (PEA)**. These studies assess the effect on **post-COVID olfactory disorders** and demonstrate, in blinded, randomised designs, the superiority of the combination over olfactory training alone. However, these studies lack **comparison groups with isolated luteolin**, leaving it unclear whether the effect is attributable to luteolin, PEA, or their interaction. **Mechanistic reviews** suggest that luteolin and PEA may act synergistically, but clinical data on luteolin monotherapy are still emerging.

Another methodological issue is the
HETEROGENEITY OF FORMULATIONS

. Controlled studies use **ultramicronised preparations**, which promise better bioavailability, while basic and cell culture studies often use native luteolin. Whether the effects observed in vitro (e.g., inhibition of proinflammatory cytokines) also occur in vivo under physiological conditions remains unresolved. Furthermore, **dose-finding studies** defining the optimal therapeutic range are lacking. Research in this area is still in its early stages, particularly regarding **long-term safety** and **applicability to other indications**.

3. How Robust Is the Research?

Research on **luteolin** spans **basic investigations**, **cell culture studies**, and **human studies**. The latter include observational and controlled studies. Controlled studies focus on **inflammatory processes**, **cognitive functions**, and the **immune system**. Notably, there is a focus on **post-COVID symptoms**, particularly olfactory disorders, which are examined in controlled studies. Other applications include stroke, periodontitis, and antiviral effects. Most studies are from recent years, indicating a young but dynamic field of research.

The **robustness** of the evidence base is shaped by several factors: controlled human studies are **small and often monocentric**, with the exception of multicentre post-COVID studies. The **combination with PEA** dominates clinical research, making the isolated effect of luteolin difficult to discern. Additionally, long-term data on safety and efficacy are lacking. While **review articles** highlight promising *preclinical* mechanisms (e.g., inhibition of NF-κB or modulation of microglia), **translating these findings to humans** remains a key challenge. Methodologically strong are the randomised, blinded post-COVID studies, whereas other applications (e.g., stroke) are supported only by individual pilot studies.

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

STATEMENT	EVIDENCE BASE
Luteolin has been investigated for neuroprotection in Alzheimer's disease and stroke; controlled results are inconsistent.	The body of evidence is primarily based on cell culture and animal models . The controlled human studies on stroke examine the combination with PEA and c
Luteolin has been studied for improving cognitive function in long COVID; results are inconsistent.	Controlled studies examine the combination with PEA in Long COVID, focusing on memory and olfactory function . The results suggest a potential associatio

STATEMENT	EVIDENCE BASE
Luteolin has been examined for antiviral properties; results are inconsistent.	Controlled studies examine antiviral effects, albeit in combination with other substances. In vitro data demonstrate inhibition of viral replication, yet clinical e
The safety of luteolin in long-term use was assessed within the studied timeframes; no long-term data on isolated luteolin exist.	Controlled studies examine the safety of combining it with PEA, but only over short periods. Long-term data on isolated luteolin are still pending.

5. Profile: Molecule and Charge

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

6. Charge, Electrons, and Radicals

Luteolin exhibits electrochemical properties associated with radical scavenging and redox processes. In human tissue, it significantly reduces reactive oxygen species (ROS), such as in HepG2 cells ($p < 0.01$ or $p < 0.001$) ²⁴ or HaCaT cells ²³. Its antioxidant capacity has been quantified in vitro: phosphomolybdenum assay (713.51 mg TE/g), ABTS (140.00 mg TE/g), and DPPH tests (99.20 mg TE/g). The half-maximal inhibitory concentrations for radical scavenging were $18.2 \pm 0.4 \mu\text{g/mL}$ (ABTS), $24.5 \pm 0.7 \mu\text{g/mL}$ (DPPH), and $43.2 \pm 1.2 \mu\text{g/mL}$ (hydroxyl radical). Luteolin acts as an electron donor, which explains its affinity for cells and its antioxidant effects.

Indirect evidence of electrochemical effects has been observed in humans, though no direct measurements of charge, cation exchange, or electron transfer have been recorded. Polyphenols such as luteolin demonstrate antioxidant and radical-scavenging properties that mitigate oxidative stress. In cell models (SUP-B15), luteolin led to increased ROS, reduced mitochondrial membrane potential, and decreased ATP ²², while ROS were quantified in retinal tissue. Whether these effects stem from direct electrochemical interactions remains to be investigated.

7. Interactions with Other Substances

Substances from this platform that have been **jointly** studied or discussed with this compound in human trials and reviews—whether in combination, comparison, or shared mechanisms of action. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED HUMAN TRIALS
Chronic Inflammation	56	8
Stress, Cortisol, and Inflammation	21	0
Apigenin	18	0
Quercetin	12	0
Turmeric and Curcumin	10	3
Adaptogens	8	0
Olive Polyphenols (Hydroxytyrosol)	5	0
Fisetin	5	0
Ginger	3	0
Cocoa Flavanols	3	0

No direct data from controlled human studies are available on the interactions of luteolin with drugs or nutrients. Whether luteolin influences the pharmacokinetics of other substances (e.g., via CYP enzymes) has not been investigated. The analysed evidence does not include animal or laboratory studies on interactions with specific drugs or nutrients.

Luteolin belongs to the flavonoid group and often occurs in plants in glycosidically bound form⁹. Whether this binding affects bioavailability or interactions with other substances is not addressed in the cited human studies. The combination with PEA in um-PEA-LUT aims at synergistic effects in neuroinflammatory processes^{14 18}, though no evidence confirms mutual enhancement or attenuation of the individual components. Data on interactions with specific drugs (e.g., CYP substrates), nutrients, or other substances are lacking. Whether luteolin influences the absorption or metabolism of other compounds would require targeted pharmacokinetic studies.

8. Overdose, Tolerability, and Limits

Data on overdose, toxicity, and upper limits of luteolin are limited. In one controlled human study (dose unspecified), no adverse effects were reported³. In human tissue (HaCaT keratinocytes), no significant cytotoxicity was observed at concentrations $\leq 100 \mu\text{g/mL}$ ²⁷. Reviews highlight that preclinical studies suggest a favourable safety profile in lung tissue²⁹, though clinical studies for validation are lacking²⁶. The analysed evidence does not include animal or laboratory studies with specified toxicity doses. No contraindications are mentioned.

No adverse effects of luteolin are directly documented in the evidence. Compared to established therapies (e.g., one review mentions immunomodulatory effects, such as increased NK cell cytotoxicity, without classifying this as undesirable²⁸). The sensitisation of cancer cells to therapeutically induced cytotoxicity¹² could theoretically imply interactions with chemotherapeutic agents but is not confirmed as a direct side effect. Long-term human data are absent.

9. The Most Robust Studies

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

Controlled Human Studies

- ¹ Ultramicronized Palmitoylethanolamide and Luteolin Supplement Combined with Olfactory Training to Treat Post-COVID-19 Olfactory Impairment: A Multicentre Study (2022)
- ² Effect of Ultra-Micronized Palmitoylethanolamide and Luteolin on Olfaction and Memory in Patients with Long COVID: Results of a Longitudinal Study (2022)
- ³ Treatment of COVID-19 Olfactory Dysfunction with Olfactory Training, Palmitoylethanolamide with Luteolin, or Combined Therapy: A Blinded Controlled Multicentre Study (2023)
- ⁴ Parosmia Related to COVID-19 Treated by a Combination of Olfactory Training and Ultramicronized PEA-LUT: A Prospective Randomised Controlled Trial (2023)
- ⁵ PEA-Lut in the Dietary Management of Patients with Acute Ischaemic Stroke: A Prospective Randomised Controlled Clinical Trial (2024)
- **** Microbiological and Clinical Short-Term Evaluation of the Efficacy of an Herbal Tincture as an Adjunctive Treatment in the Management of Stage II Grade A Periodontitis (2025)
- ⁶ Palmitoylethanolamide and Luteolin for Postinfectious Olfactory Disorders: How Clinically Meaningful Is Its Effect? (2024)
- ⁷ Treatment of Persistent COVID-19 Smell Dysfunction with Olfactory Training, Co-Ultramicronized Palmitoylethanolamide with Luteolin, or Combined Therapy: A Multicentre Study (2022)

Observational Human Studies

- ⁸ Brain "Fog", Inflammation and Obesity: Key Aspects of Neuropsychiatric Disorders Improved by Luteolin (2015)
- ⁹ Exploring Luteolin's Therapeutic Potential and Agro-Food-Pharma Applications: Emphasis on *In Vivo* Pharmacological Effects and Bioavailability Traits (2021)
- ¹⁰ Luteolin: A Promising Natural Agent in the Management of Pain in Chronic Conditions (2023)
- ¹¹ Co-Ultramicronized Palmitoylethanolamide/Luteolin Normalises GABA_B-ergic Activity and Cortical Plasticity in Long COVID-19 Syndrome (2023)
- ¹² Application of Luteolin in Neoplasms and Non-Neoplastic Diseases (2023)
- **** *Melissa officinalis* L. as a Nutritional Strategy for Cardioprotection (2021)
- ¹³ Synaptic Effects of Palmitoylethanolamide in Neurodegenerative Disorders (2022)
- ¹⁴ Efficacy of Palmitoylethanolamide and Luteolin Association on Post-COVID Olfactory Dysfunction: A Systematic Review and Meta-Analysis of Clinical Studies (2023)
- ¹⁵ Luteolin Alleviates Airway Remodelling in Asthma by Inhibiting the Epithelial-Mesenchymal Transition via β -Catenin Regulation (2024)
- ¹⁶ Luteolin: A Natural Product with Multiple Mechanisms for Atherosclerosis (2025)
- ¹⁷ Effect of Luteolin on Oxidative Stress and Inflammation in the Human Osteoblast Cell Line hFOB1.19 in an Inflammatory Microenvironment (2024)
- **** Targeting Neuroinflammation to Alleviate Chronic Olfactory Dysfunction in Long COVID: A Role for Investigating Disease-Modifying Therapy (DMT)? (2023)

- ¹⁸ Co-ultraPEALut in Subjective Cognitive Impairment Following SARS-CoV-2 Infection: An Exploratory Retrospective Study (2024)
- ¹⁹ Therapeutic Potential of Luteolin for Diabetes Mellitus and Its Complications (2025)
- ²⁰ Hyaluronic Acid-Modified Luteolin-Copper Complex Nanodelivery System for Bacterial Prostatitis (2024)
- ²¹ Ultramicrosized Palmitoylethanolamide and Luteolin: Drug Candidates in Post-COVID-19 Critical Illness Neuropathy and Positioning-Related Peripheral Neuropathy (2024)

10. Summary

The available controlled studies on luteolin—almost exclusively in combination with palmitoylethanolamide (PEA-LUT)—provide consistent evidence of anti-inflammatory and neuroprotective effects *within the combination therapy*, particularly in post-viral olfactory disorders following COVID-19. The strongest evidence comes from randomised, blinded trials demonstrating significant improvements in olfactory function (Sniffin' Sticks test) and cognitive symptoms through *combination therapy* with olfactory training. Promising results are also observed in acute ischaemic stroke and periodontitis, though always within the context of combination treatment. The applicability of these findings to luteolin alone remains unclear due to the absence of corresponding comparator groups. Furthermore, study endpoints are often limited to subjective or semi-quantitative tests, while objective parameters such as inflammatory biomarkers or imaging correlates are lacking.

HYPOTHESIS The synergistic effect of luteolin with PEA may stem from dual modulation of neuroinflammatory processes, such as inhibition of mast cell activation and microglia inhibition, combined with promotion of neuronal plasticity via GABA_B-ergic mechanisms. This hypothesis is supported by mechanistic *in vitro* data and indirect evidence from human studies but *has not been directly validated in clinical settings*. Should this mechanism be confirmed, luteolin in combination with PEA could represent a promising approach for treating neuroinflammatory conditions, particularly in post-viral syndromes. However, data on optimal dosing, long-term safety, and efficacy in other indications such as neurodegenerative diseases or chronic inflammatory processes are currently lacking.

To clarify the role of luteolin more precisely, controlled studies with the following designs would be necessary: 1) comparator groups with luteolin alone, PEA alone, and their combination to identify the specific contributions of each substance; 2) dose-finding studies to investigate the optimal application range and bioavailability of different formulations (e.g., ultramicrosized vs. native); 3) long-term studies with objective endpoints such as inflammatory biomarkers, imaging techniques, or histological analyses to validate the postulated mechanisms; 4) studies with clearly defined subgroups (e.g., by severity or duration of symptoms) to better contextualise the clinical relevance of the observed effects. Additionally, systematic collection of long-term safety data would be essential to fully assess the therapeutic potential of luteolin—alone or in combination.

11. Unresolved Questions

- **Isolated effect:** Are there clinically relevant effects of luteolin without PEA or other combination partners?
- **Dose-response relationship:** Which formulation and dosage are optimal for which indication?
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12. Further Paths

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

- Interaction network

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

Frequently Asked Questions

Why is luteolin almost always combined with palmitoylethanolamide?

The combination of **luteolin and PEA** dominates clinical research because both substances may exert **synergistic effects** on neuroinflammatory processes. PEA acts as an endogenous lipid mediator via PPAR- α and TRPV1 receptors, while luteolin activates antioxidant and anti-inflammatory mechanisms. The **most frequently cited studies** (e.g., on post-COVID olfactory dysfunction) use this combination, as it demonstrated additive effects in animal models and cell cultures. However, whether luteolin alone produces comparable effects remains insufficiently investigated.

Can luteolin be used in neurodegenerative diseases such as Alzheimer's?

Preclinical research demonstrates promising effects of luteolin on **oxidative stress, neuroinflammation, and amyloid-beta deposits** in cellular and animal models. **Review articles** summarise these mechanisms. However, **clinical studies in humans are entirely lacking**. The available data are insufficient to support **therapeutic use** in Alzheimer's or other neurodegenerative diseases.

How is luteolin dosed in controlled studies?

Controlled studies use **standardised combination preparations** containing ultramicrosised luteolin and PEA, typically in a fixed ratio. The **exact dosages** are not always disclosed in publications, as they often rely on **patented formulations**. The **bioavailability** of luteolin is considered limited, which is why micronised preparations are preferred. **Dose-finding studies** for luteolin in isolation do not exist.

Sources

- 1 Ultramicrosized Palmitoylethanolamide and Luteolin Supplement Combined with Olfactory Training to Treat Post-COVID-19 Olfactory Impairment: A Multi-Center Double-Blinded Randomized Placebo- Controlled Clinical Trial
Di Stadio A, D'Ascanio L, Vaira LA, Cantone E, De Luca P, Cingolani C et al. · 2022
- 2 Effect of Ultra-Micronized Palmitoylethanolamide and Luteolin on Olfaction and Memory in Patients with Long COVID: Results of a Longitudinal Study
De Luca P, Camaioni A, Marra P, Salzano G, Carriere G, Ricciardi L et al. · 2022
- 3 Treatment of COVID-19 olfactory dysfunction with olfactory training, palmitoylethanolamide with luteolin, or combined therapy: a blinded controlled multicenter randomized trial
Di Stadio A, Gallina S, Cocuzza S, De Luca P, Ingrassia A, Oliva S et al. · 2023
- 4 Parosmia COVID-19 Related Treated by a Combination of Olfactory Training and Ultramicrosized PEA-LUT: A Prospective Randomized Controlled Trial
Di Stadio A, Cantone E, De Luca P, Di Nola C, Massimilla EA, Motta G et al. · 2023
- 5 PEALut in the Dietary Management of Patients with Acute Ischemic Stroke: A Prospective Randomized Controlled Clinical Trial
Bonzanino M, Riolo M, Battaglini I, Perna M, De Mattei M · 2024
- 6 Palmitoylethanolamide and Luteolin for Postinfectious Olfactory Disorders: How Clinically Meaningful Is Its Effect?
Gellrich J, Czaplowski L, Hähner A, Hummel T · 2024
- 7 Treatment of Persistent COVID-19 Smell Dysfunction with Olfactory Training, Co-Ultramicrosized Palmitoylethanolamide with Luteolin, or Combined Therapy: Results of Double-Blinded Multicenter Clinical Trial
Stadio AD, Gallina S, Cocuzza S, Luca PD, Ingrassia A, Oliva S et al. · 2022
- 8 Brain "fog," inflammation and obesity: key aspects of neuropsychiatric disorders improved by luteolin
Theoharides TC, Stewart JM, Hatzigelaki E, Kolaitis G · 2015
- 9 Paving Luteolin Therapeutic Potentialities and Agro-Food-Pharma Applications: Emphasis on In Vivo Pharmacological Effects and Bioavailability Traits
Taheri Y, Sharifi-Rad J, Antika G, Yilmaz YB, Turner TB, Abuhamdan S et al. · 2021
- 10 Luteolin: A promising natural agent in management of pain in chronic conditions
Ntalouka F, Tsirovakou A · 2023
- 11 Co-ultramicrosized palmitoylethanolamide/luteolin normalizes GABAB-ergic activity and cortical plasticity in long COVID-19 syndrome
Versace V, Ortelli P, Dezi S, Ferrazzoli D, Alibardi A, Bonini I et al. · 2023
- 12 Application of Luteolin in Neoplasms and Nonneoplastic Diseases
Rakoczy K, Kaczor J, Sołtyk A, Szymańska N, Stecko J, Słeziak J et al. · 2023
- 13 Synaptic Effects of Palmitoylethanolamide in Neurodegenerative Disorders
Assogna M, Di Lorenzo F, Martorana A, Koch G · 2022
- 14 Efficacy of Palmitoylethanolamide and Luteolin Association on Post-Covid Olfactory Dysfunction: A Systematic Review and Meta-Analysis of Clinical Studies
Capra AP, Ardizzone A, Crupi L, Calapai F, Campolo M, Cuzzocrea S et al. · 2023
- 15 Luteolin alleviates airway remodeling in asthma by inhibiting the epithelial-mesenchymal transition via β -catenin regulation
Quan J, Xie D, Li Z, Yu X, Liang Z, Chen Y et al. · 2024
- 16 Luteolin: a natural product with multiple mechanisms for atherosclerosis
Wan C, Liang Q, Ma Y, Wang Y, Sun L, Lai J et al. · 2025
- 17 Effect of luteolin on oxidative stress and inflammation in the human osteoblast cell line hFOB1.19 in an inflammatory microenvironment
Peng Z, Zhang W, Hong H, Liu L · 2024
- 18 Co-ultraPEALut in Subjective Cognitive Impairment Following SARS-CoV-2 Infection: An Exploratory Retrospective Study
Cenacchi V, Furlanis G, Menichelli A, Lunardelli A, Pesavento V, Manganotti P · 2024
- 19 Therapeutic Potential of Luteolin for Diabetes Mellitus and Its Complications
Chang XQ, Yue RS · 2025
- 20 Hyaluronic Acid-Modified Luteolin-Copper Complex Nanodelivery System for Bacterial Prostatitis
Li R, Zheng Y, Li X, Su R, He J, Xue S et al. · 2024
- 21 Ultramicrosized Palmitoylethanolamide and Luteolin: Drug Candidates in Post-COVID-19 Critical Illness Neuropathy and Positioning-Related Peripheral Nerve Injury of the Upper Extremity
Roncati L, Marra C, Gravina D, Di Massa G, Della Rosa N, Adani R · 2024
- 22 Additionally, luteolin led to an increase in reactive oxygen species (ROS) accumulation, a decrease in mitochondrial mem...
· 2025
- 23 Mechanistically, luteolin inhibited the activation of AP-1 and NF- κ B pathways and decreased reactive oxygen species (ROS...
· 2025
- 24 Similarly, luteolin, marein, NGN or CQA treatment greatly enhanced the anti-oxidant activities ($p < 0.05$ or $p < ...$
· 2025
- 25 The increased incidence of periodontitis, the resistance of periodontal pathogens to antibiotics, and the adverse effect...
· 2025
- 26 In particular, clinical studies are needed to validate efficacy and safety and provide a reliable scientific basis. C...
· 2025
- 27 Cytotoxicity assessed by MTT assay on HaCaT keratinocytes indicated no significant reduction in cell viability at concen...
· 2026
- 28 Luteolin may enhance NK-cell cytotoxicity and DC-mediated antigen presentation while curbing eosinophil and basophil act...
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