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Review Article

The Protective Properties of Luteolin: A Comprehensive Review

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ABSTRACT

Luteolin, a flavone abundant in various plant-based foods, presents a multifaceted pharmacological profile with promising therapeutic implications. This review provides a comprehensive analysis of the pharmacokinetics of luteolin, elucidating its absorption, distribution, metabolism, and excretion properties. Additionally, the protective mechanisms of luteolin are presented, encompassing its anti-inflammatory, antioxidant, and anti-apoptotic properties, which have been demonstrated in various *in vitro* and *in vivo* models. Furthermore, the review explores the impact of luteolin on diverse disorders, including cardiovascular diseases, neurodegenerative disorders, cancer, and liver and kidney diseases. In addition, the synergistic effects of luteolin with conventional chemotherapeutic agents are discussed, shedding light on its potential in cancer therapy. Furthermore, we provide insights into ongoing clinical studies, emphasizing the need for more rigorous investigation to validate the therapeutic benefits of luteolin in human populations. Overall, luteolin emerges as a promising therapeutic candidate, warranting further research to unlock its full therapeutic potential and facilitate its clinical application in various disease contexts.

Keywords: *Luteolin; anti-inflammatory; anti-apoptotic; antioxidant; anticancer.*

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1. Introduction

Food and nutrition science continues to advance in medical research, emphasizing the importance of functional plant foods for disease prevention. Flavonoids, bioactive polyphenolic phytochemicals found in natural foods, have garnered substantial attention for their anti-inflammatory and antioxidant properties **[1]**. Scientific evidence strongly suggests that consuming dietary flavonoids regularly in sufficient quantities can decrease the risk of pathogenesis in human diseases associated with oxidative stress and chronic inflammation. These include cardiovascular diseases, certain cancers, and neurological disorders **[2]**.

The flavonoid structure consists of two benzene rings connected by a heterocyclic ring **[3]**. Despite having a similar skeleton, these substances are classified into subfamilies based on the chemical changes they undergo **[4]**. There are several subgroups of flavonoids; including isoflavone, chalcone, anthocyanidin, flavone, flavanol, and flavanone (**Fig. 1**) **[5]**. In particular, flavones represent a diverse group of bioactive polyphenolic compounds present as secondary metabolites in various commonly consumed fruits, vegetables, and plant-based foods,

including tea, cocoa, coffee, and wine. They exhibit various biological and pharmacological properties; including neuroprotection, anti-inflammatory, antioxidant, antimicrobial, antihyperglycemic as well as potential anti-cancer effects **[6]**.

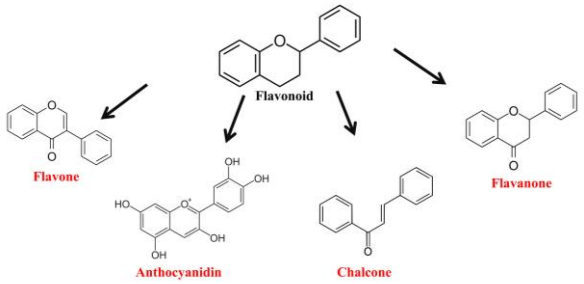

Fig. 1. Subfamilies of flavonoids: A schematic representation illustrating the various subclasses and their structural diversity within the flavonoid family.

Among these flavones is luteolin, a 3',4',5, and 7-tetrahydroxyflavone, which is present in celery pepper, green pepper, and parsley **[7]**. Moreover, luteolin is characterized by hydroxyl groups on the 3',4',5', and 7' carbons. This chemical configuration, along with a double bond between carbons 2 and 3 (**Fig. 2**), has been demonstrated to be responsible for its biochemical and biological properties; including its antioxidant activity **[8]**. Additionally, luteolin exhibits a myriad of pharmacological and biological activities; including anti-inflammatory **[9]**, antioxidant **[10]**, anti-apoptotic **[11]**, anti-cancer **[12]**, hepatoprotective **[13]**, neuroprotective **[14]**, cardioprotective **[15]**, and nephroprotective effects **[16]**. Despite the noteworthy activities associated with luteolin, a commonly faced challenge is their limited bioavailability following oral administration, which restricts their effectiveness. Indeed, luteolin is known for its poor bioavailability **[17]**. Furthermore, there are ongoing studies aimed at enhancing the bioavailability of luteolin either through improving water dispersibility using a microemulsion system **[18]** or using loaded zein nanoparticles **[19]**. Our review will focus on elucidating the protective properties of luteolin and its potential mechanisms in different disorders.

2. Pharmacokinetics of Luteolin.

Several factors influence luteolin *in vivo* absorption; including the formulation of the drug, dosage, route of administration, and gastrointestinal absorption. There are three ways to absorb luteolin: inhalation, intravenous injection, and oral administration. Nonetheless, the bioavailability of luteolin varies depending on the route of administration. For example, luteolin was reported to have an oral bioavailability of approximately 26% after administration, which may have been caused by its poor solubility and high first-pass elimination **[18, 20]**. Remarkably, luteolin demonstrates notable liposolubility, facilitating the absorption through the intestinal mucosa. Its absorption differs depending on the area of the gastrointestinal tract, with the jejunum showing a more prominent role in absorption than the colon. The maximal plasma concentration of luteolin was reached in 30 minutes in pharmacokinetic assays. I*n situ* experiments, the levels of luteolin in jejunum contents were initially 62.3% of the original amount at 5 min., which decreased to 39.7% at 10 min., indicating efficient absorption **[18, 21]**. After oral administration, luteolin is primarily present in the forms of conjugates, with the most prevalent circulating metabolite being luteolin-30-O-β-D-glucuronide. This metabolite is also abundant in most tissues. Besides, luteolin and its metabolites are mainly distributed in the gastrointestinal tract, liver, kidney, and lung following an oral dose **[22]**. Luteolin shows a high affinity for human serum albumin in plasma, which may limit its dispersion **[23, 24]**. The polyphenolic nature of luteolin makes it an ideal substrate for uridine diphosphate glucuronosyltransferases and sulfotransferases. As a result, it primarily undergoes

glucuronidation and sulfation as it traverses the intestinal mucosa or the liver **[25]**. Studies have demonstrated that the primary metabolite of luteolin is luteolin-3′-O-glucuronide. Likewise, other metabolites include luteolin-4'-O-glucuronide, luteolin-3'-O-glucuronide, and luteolin-7,4'-di-O-glucuronide **[22, 26]**. Urine and bile are the principal clearance mechanisms for luteolin and its metabolites, which are removed by the kidney and biliary tract. Additionally, the total cumulative recoveries of luteolin and its metabolites in bile and urine were reported as 54.8% and 5.9%, respectively **[22, 27]**.

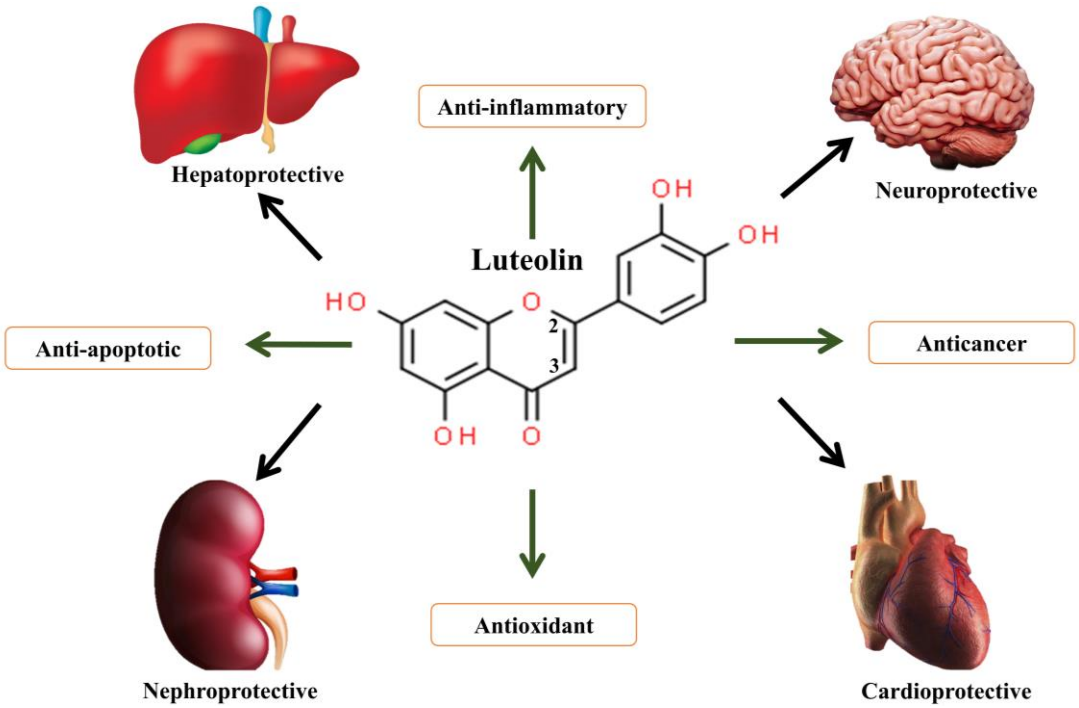

Fig. 2. Overview of the mechanisms of luteolin: A concise summary highlighting its diverse biological activities and therapeutic potential.

3. The underlying mechanisms of the protective effects of luteolin

A summary of the following mechanisms is illustrated in **Fig. 2.**

3.1. Anti-inflammatory properties of Luteolin

Inflammation affects the tissues and organs of the body due to several disorders. Like other flavonoids, luteolin displays a range of pleiotropic characteristics, which makes it challenging to link all its pharmacological actions to a particular metabolic pathway. At micromolar concentrations, luteolin exhibits anti-inflammatory properties that include the inhibition of pro-inflammatory mediators; such as cyclooxygenase-2, nitric oxide, interleukin-6 (IL-6), IL-1β, and tumor necrosis factor-alpha (TNF-α), as well as the control of multiple signaling pathways such as the JAK/STAT, activator protein-1 (AP-1), and nuclear factor kappa β (NFκB) pathways **[28]**.

In an Alzheimer's disease (AD) rat model, luteolin elevated the anti-inflammatory cytokine IL-10 and down-regulated the pro-inflammatory cytokines, inducible nitric oxide synthase (iNOS), TNF-α, IL-6, cyclooxygenase-2, and IL-

1β **[29]**. Luteolin reduces renal damage in rats by inhibiting NFκB transcriptional activity. It also protects human umbilical vein endothelial cells in an *in vitro* study by modulating reactive oxygen species (ROS)/NFκB activation through TNF-α **[11]**. In prior research, luteolin blocked the TAK-1/MAPKs/AP-1 and NFκB signaling pathways in corneal stromal fibroblasts, suppressing the IL-1β-mediated release of inflammatory cytokines, chemokines, and matrix metalloproteases (MMPs) as well as type I collagen degradation in rats with corneal alkali burn **[30]**.

3.2. Antioxidant properties of Luteolin

The various ways that oxidants contribute to cellular damage have been demonstrated by the association between oxidative stress and several illnesses; including cancer, Alzheimer's disease, atherosclerosis, and chronic obstructive pulmonary disease **[31]**. The structure of luteolin, including the quantity of hydroxyl groups (**Fig. 1**), affects its antioxidant capabilities. The nuclear factor erythroid 2–related factor 2/antioxidant responsive element (Nrf2/ARE) signaling pathway, which is linked to the activation of cellular antioxidant enzymes, is another way luteolin reduces oxidative stress **[32]**. A substantial anti-oxidative effect for luteolin was shown in a rat model of polycystic ovarian syndrome, as evidenced by the remarkable restoration of the reduced activities of glutathione peroxidase (GSH-Px), catalase (CAT), and superoxide dismutase (SOD) **[33]**. Luteolin decreases the build-up of oxidative stress in the kidneys of mice via inhibiting NFκB and hypoxia-inducible factor-1α (HIF-1α). Furthermore, HIF-1α downstream genes cyclin-dependent kinase inhibitor (P21), B-cell lymphoma 2 (BCL2), iNOS, and CD18 showed decreased expression after luteolin therapy in a rat model of lupus nephritis **[34]**. Also, it has been demonstrated that luteolin may bind to and target NADPH oxidase 4 (NOX4), suggesting that down-regulating NOX4 levels may have the desired impact of reducing oxidative stress and inflammatory responses in chronic obstructive pulmonary disease *in vivo* and *in vitro* models **[35]**.

3.3. Anti-apoptotic properties of Luteolin

Apoptosis, a process essential for regulating growth and differentiation in multicellular organisms, is conserved throughout evolution. It operates through two main pathways: intrinsic and extrinsic apoptosis. The intrinsic pathway responds to various intracellular signals triggered by conditions like hypoxia, DNA damage, or oncogene activation. Conversely, extrinsic apoptosis, also known as activation-induced apoptosis, involves external agents activating a cascade of intracellular signal transducers, which then prompt morphological alterations through biochemical and gene regulatory signals **[36]**. Flavonoids also have anti-apoptotic qualities that are mediated by raising BCL2 levels, which lowers the ratio of BCL2-associated X protein (BAX)/BCL2, which stops the induction of apoptosis **[37]**. Treatment with luteolin successfully restored the hepato-renal changes caused by methotrexate in the levels of caspase 3, BAX, and BCL2, suggesting that luteolin has anti-apoptotic qualities **[38]**. Also, luteolin, via its anti-apoptotic properties, prevented lead acetate-induced kidney apoptosis by controlling the expression of caspase-3, BCL2 family, p53, and p53 up-regulated modulator of apoptosis (PUMA) protein **[10]**.

4. Exploring the impact of Luteolin across diverse disorders

4.1. Cardioprotective effect of Luteolin

In recent years, there has been a notable surge in scientific inquiry into the consumption of flavonoids for the prevention of cardiovascular diseases and the enhancement of vascular health. Numerous studies have highlighted the beneficial

effects of various classes of flavonoid compounds and plant extracts enriched with flavonoids on cardiovascular health. These compounds have demonstrated the ability to mitigate cellular oxidative stress, alleviate inflammation, and regulate various intracellular signaling pathways, all contributing to improved cardiovascular function **[39]**.

Remarkably, luteolin offered cardioprotective effects during ischemia/reperfusion injury by enhancing myocardial contraction function and suppressing inflammatory responses and cell death. In addition, the activation of the SHP-1/STAT3 signaling pathway appeared to be associated with the beneficial effects of luteolin on heart tissue damaged by myocardial infarction in rats **[40]**. According to Dong, Luo **[41]**, luteolin demonstrated the ability to mitigate cardiac fibrosis, as evidenced by reductions in the expression of fibrotic markers such as transforming growth factor-β (TGF-β), collagen I, collagen III, MMP2, and MMP9. Additionally, luteolin attenuated lipid deposition, as indicated by decreased expression of CD36 and lipoxygenase-1 (LOX-1), thereby alleviating hyperlipidemia-induced cardiac damage in Sprague-Dawley rats. These findings shed light on the potential role of luteolin in protecting against cardiac damage induced by hyperlipidemia **(Fig. 3)**.

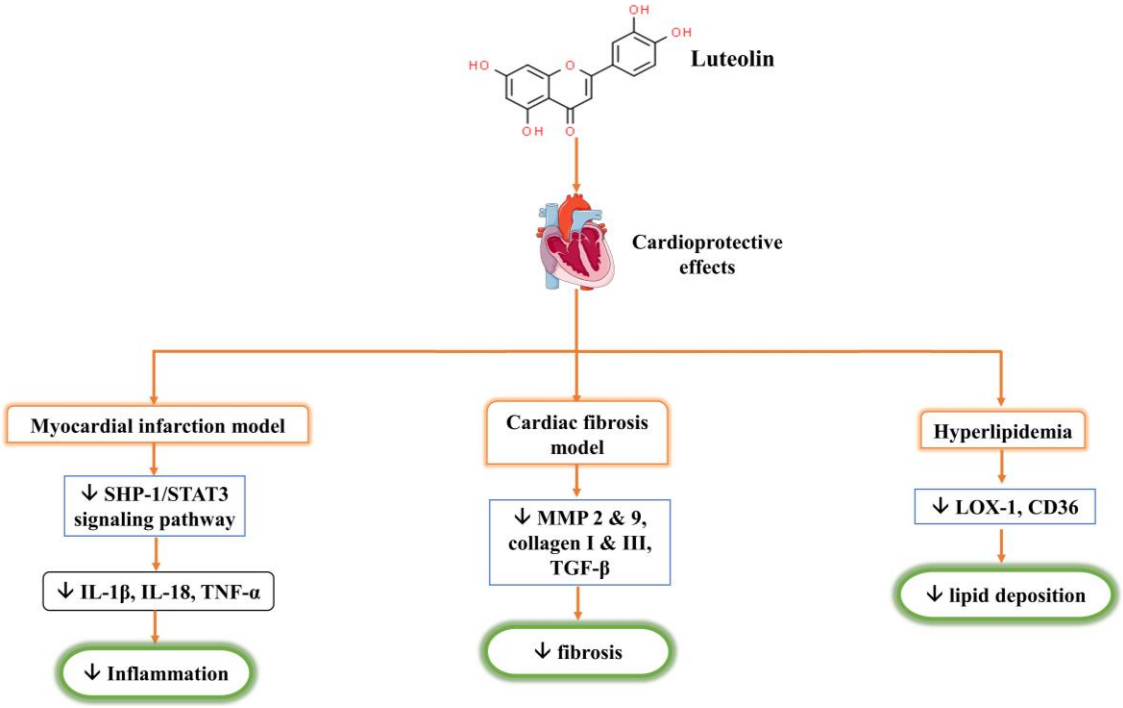

Fig. 3. Possible mechanisms of cardioprotective effects of luteolin, highlighting the therapeutic potential of luteolin in maintaining heart health. CD36, the cluster of differentiation 36; IL, interleukin; LOX-1, lipoxygenase-1; MMP, matrix metalloproteinases; SHP-1, src homology 2–containing protein-1; STAT3, signal transducer and activator of transcription 3; TGF-β, transforming growth factor beta; TNF-α, tumor necrosis factor-alpha.

4.2. Neuroprotective effect of Luteolin.

Several studies have documented the neurogenic potential of phytochemicals, primarily attributed to their antioxidant properties. These compounds have been shown to facilitate the reconstruction of synaptic connections by restoring neuronal processes that may have been compromised. Furthermore, they exhibit promising neuroprotective characteristics by targeting various aspects of neurological dysfunction; including oxidative stress,

accumulation of α-synuclein, neuro-inflammation, and mitochondrial dysfunction **[42, 43]**.

In a recent study, luteolin was found to reverse behavioral alterations by regulating oxidative stress markers, such as Nrf2, CAT, SOD, and MDA, as well as apoptotic factors including BAX and BCL2. Additionally, it reduced inflammatory mediators, such as NFκB, nod-like receptor pyrin domain containing 3 (NLRP3), IL-1β, IL-6, and TNF-α, while increasing the levels of neurotrophic factors, such as brain-derived neurotrophic factor and glial cell-derived neurotrophic factor. Consequently, luteolin exhibited anxiolytic and antidepressant effects in rats with chronic neuropathic pain-induced anxiety and depressive-like behaviors due to chronic constriction of the sciatic nerve. These effects were attributed to its antioxidant, anti-apoptotic, anti-inflammatory, and neuroprotective properties in the hippocampus and prefrontal cortex **[44]**. Notably, luteolin administration demonstrated the capacity to ameliorate cognitive deficits, reduce anxiety levels, and improve exploratory behavior in a triple transgenic AD mouse model. Furthermore, luteolin was found to modulate the activity of beta-secretase-1 (BACE1), thereby reducing the generation of amyloid-beta (Aβ). It also regulated the level of insulin-degrading enzymes to enhance the clearance of Aβ and alleviated mitochondrial impairment, consequently suppressing neuronal apoptosis. In addition, the involvement of peroxisome proliferator-activated receptor γ (PPARγ) was noted in mediating the protective effects of luteolin in AD pathology in mice **(Fig. 4) [45]**.

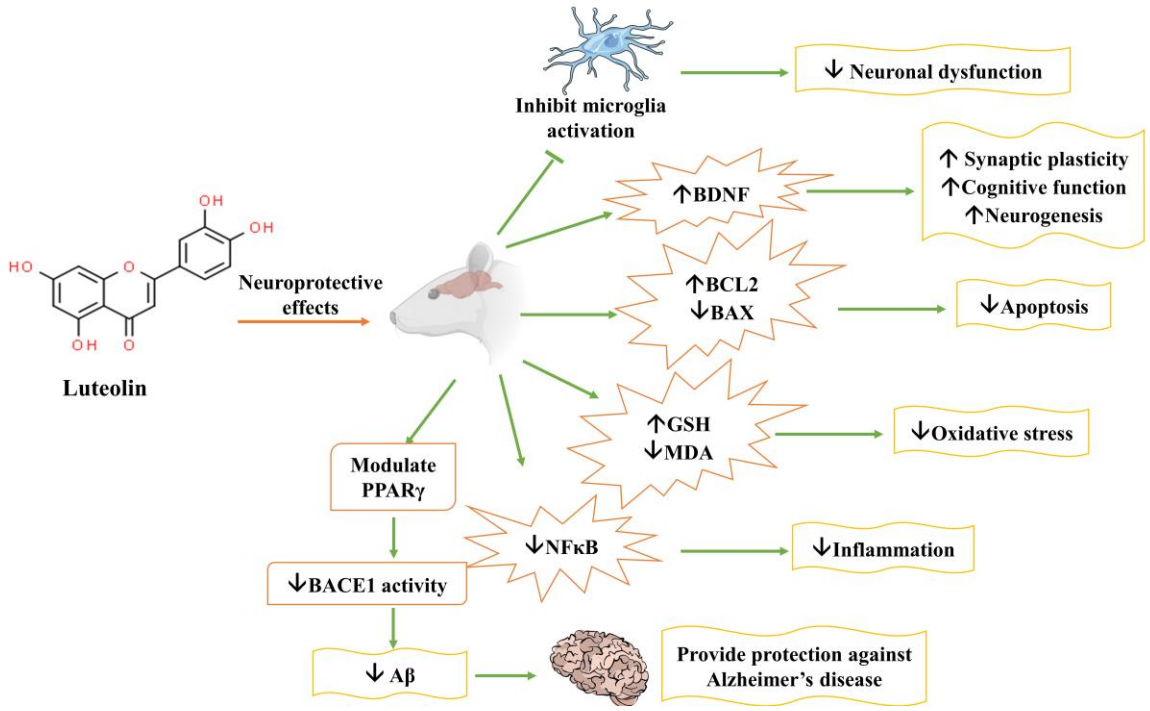

Fig. 4. Possible mechanisms of neuroprotective effects of luteolin. This figure illustrates the potential mechanisms by which luteolin confers neuroprotection, including its anti-inflammatory, antioxidant, and anti-apoptotic properties. These actions may contribute to the prevention or mitigation of neurodegenerative disorders, underscoring the therapeutic potential of luteolin in preserving neurological health. Aβ, amyloid beta; BACE1, beta-secretase-1; BAX, BCL2-associated X protein; BCL2, B-cell lymphoma 2; BDNF, brain-derived neurotrophic factor; GSH, reduced glutathione; MDA, malondialdehyde; NFκB, nuclear factor kappa B; PPARγ, peroxisome proliferator-activated receptor gamma.

4.3. Hepatoprotective effect of Luteolin

There are many different types of liver diseases, and a range of medicinal plants have been shown to have hepatoprotective effects through several different mechanisms. These include lowering lipid peroxidation, enhancing the antioxidant defense (CAT, GSH-Px, and SOD activity), reversing hepatic fibrosis, activating hepatic stellate cells, anti-inflammatory activity, and anti-fibrotic properties **[46]**.

Interestingly, luteolin treatment suppressed oxidative stress induced by aflatoxin (AFB1) as evidenced by decreased ROS and MDA accumulation, strengthened antioxidant defense system (T-SOD, CAT, GSH-Px, and T-AOC), and reduced apoptosis rate in the liver of mice intoxicated by AFB1. It also attenuated growth retardation and alleviated toxic effects on serum biochemical profile and pathological changes **[13]**. Still, luteolin may prevent apoptosis in mouse hepatocytes caused by acetaminophen by lowering activating transcription factor 4 (ATF4) and C/EBP homologous protein (CHOP) levels, which would counteract the endoplasmic stress brought on by acetaminophen through the ATF/CHOP/PUMA pathway **[47]**. Also, luteolin therapy demonstrated its anti-apoptotic action by knowingly reversing the hepato-renal alterations in caspase 3, BAX, and BCL2 levels caused by methotrexate. The antioxidant effect of luteolin may be responsible for the anti-apoptotic activity by reducing oxidative stress, which in turn reduces mitochondrial stress, caspase 3, and BAX levels, and increases the anti-apoptotic BCL2 protein levels **[38]**. Luteolin was observed to alleviate lipopolysaccharide (LPS)-induced acute liver damage by inhibiting the activation of the NLRP3 inflammatory body. This inhibition happened to be dependent on thioredoxin interacting protein (TXNIP), which serves as a mediator of oxidative stress **[48]**.

4.4. Nephroprotective effect of Luteolin

In recent years, there has been extensive research into the protective effects of flavonoids against chemically-induced renal toxicity. Factors; such as arterial hypertension, oxidative stress, inflammatory conditions, and alterations in vascular health pose challenges to renal function **[49]**. Flavonoids have been shown to mitigate these effects and offer promising outcomes in the treatment of both acute and chronic nephropathies, renal fibrosis, and anti-tumor activity. Moreover, flavonoids may directly target the renal parenchyma and modulate signaling pathways, thereby influencing the progression of renal injury and exerting nephroprotective effects in conditions; such as glomerulonephritis, diabetic nephropathy, and chemically-induced kidney insufficiency **[37]**.

Remarkably, luteolin has been shown to protect against the progression of streptozotocin-induced diabetic nephropathy in rats, as evidenced by the restoration of blood glucose levels and serum biochemical parameters, as well as the prevention of early renal dysfunction in hyperglycemic rats. These nephroprotective effects are primarily attributed to its antioxidant, anti-inflammatory, and anti-apoptotic properties. Mechanistic studies have revealed that luteolin inhibits NFκB-mediated production of pro-inflammatory cytokines and caspase 3 involved in apoptosis, while simultaneously enhancing the Nrf2-dependent antioxidant capacity. These findings suggest that luteolin holds promise as a therapeutic option for diabetic kidney disease **[11]**.

4.5. Luteolin as an Anticancer Agent: Exploring Synergistic Effects with Conventional Chemotherapeutic Drugs

4.5.1. Luteolin as anticancer

Natural products have proven to be a valuable and potent reservoir of anticancer agents

over the past few years through structural modifications or utilization of naturally occurring compounds as building blocks. These compounds hold remarkable promise for combating cancer and have contributed substantially to advancements in cancer therapy **[50]**.

In addition, luteolin has been found to inhibit several critical signaling pathways involved in cancer initiation and progression, including mTOR, MAPK, and others. Emerging research suggests that the anticancer effects of luteolin may be attributed to its ability to inhibit certain classical histone deacetylases (HDACs), thereby acting through epigenetic mechanisms. In a colon cancer model, luteolin was shown to suppress the activity and reduce the protein levels of DNA methyltransferases and multiple classical HDACs, leading to the activation of the Nrf2 pathway. These findings highlight the potential of luteolin as a therapeutic agent for cancer treatment, particularly in colon cancer **[12]**. In a previous study, luteolin was found to inhibit tumor incidence and decrease tumor volume while also inhibiting lipid peroxide formation in breast tissues. Notably, luteolin treatment led to increased activities of antioxidant enzymes, such as SOD, CAT, and GSH-Px in breast tissues. Moreover, luteolin was observed to reduce tumor growth by inhibiting tumor cell apoptosis and angiogenesis. These findings collectively suggest that luteolin possesses chemopreventive and anti-angiogenic properties by stimulating the antioxidant defense system in mammary tumors. Yet, luteolin was found to suppress JNK activity in macrophages, while it initiated this kinase in cancer cells. Likewise, luteolin was shown to suppress NFκB activity by repressing IκB kinase (IKK) activation during inflammation in both epithelial cells and macrophages **[51]**.

4.5.2. The synergistic effects of luteolin with chemotherapeutic agents

In a previous study, luteolin and oxaliplatin acted synergistically to inhibit the growth of HCT116 xenograft tumors in mice. This synergistic effect was achieved by promoting apoptosis and inhibiting proliferation, with indications pointing towards a mechanism associated with AMP-activated protein kinase (AMPK) **[52]**. According to Qin, and Zhu **[53]**, subsequent analysis uncovered that the treatment of sensitive MG63 cells with luteolin efficiently packaged miRNA-384 into secreted exosomes. Interestingly, these exosomes could enhance the response to doxorubicin in doxorubicin-resistant MG63/Doxorubicin cells. This suggests that luteolin may hold promise as a therapeutic agent for chemo-resistant osteosarcoma by targeting the pleiotrophin/β-catenin/multi-drug resistance-1 axis.

5. Safety and toxicity studies on luteolin

Although luteolin exhibits a spectrum of pharmacological properties that hint at its promising therapeutic potential, ranging from antioxidant and anti-inflammatory effects to potential anticancer activity, its safety profile remains incompletely characterized. While numerous studies have elucidated its beneficial effects, the comprehensive assessment of its safety and toxicity is paramount for its clinical translation. Understanding the potential adverse effects and toxicological considerations associated with luteolin is crucial for harnessing its therapeutic benefits effectively.

According to Orji, Okpoko **[54]**, a study was conducted to focus on the acute toxicity of luteolin and its effects on various hematological and liver function parameters in animal models. The acute toxicity assessment revealed that the LD50 (lethal dose for 50% of the population) of pure luteolin was above 5000 mg/kg, indicating that it is not acutely toxic. However, caution is advised regarding chronic consumption, particularly at high doses, as it may not be entirely harmless. Hematological analysis

showed considerable increases in red blood cell count, packed cell volume, and hemoglobin concentration at doses of 100 mg/kg and 200 mg/kg after 14 days of treatment, suggesting potential favorable effects on blood indices. There were no substantial changes in white blood cell count, indicating no immune stimulation. However, liver function parameters such as ALT, AST, and ALP showed notable increases with higher doses and longer duration of treatment, suggesting potential liver enzyme elevation. While histopathological examination did not reveal major liver damage, prolonged and high-dose usage might pose a risk of hepatotoxicity. Therefore, careful monitoring of liver function is recommended with prolonged and high-dose luteolin consumption.

In a study that investigated the acute toxicity of *Artemisia afra*, focusing on the safety of its aqueous extract in mice. The findings suggest that *Artemisia afra* demonstrated low toxicity levels when administered orally and intra-peritoneally to mice. Interestingly, luteolin, a flavonoid present in the extract, did not drastically contribute to the toxicity of the plant. Traditional doses of *Artemisia afra* used in self-medication or recommended by herbal practitioners were found to be much lower than doses predicted to be toxic, indicating relative safety in humans. These results suggest that *Artemisia afra*, including its luteolin content, is relatively safe for human consumption in recommended doses **[55]**.

From the results of the study, it can be concluded that chronic doses of luteolin, administered through *Artemisia afra* extract, exhibited a low toxicity profile in rats. Despite an increase in plasma levels of luteolin with escalating doses, no substantial accumulation over time was observed. While minor intermittent adverse effects such as diarrhea, salivation, and hypo-activity were noted at higher doses of *Artemisia afra*, there were no noteworthy alterations in growth, hematological or blood biochemical parameters, or organs. Additionally, although luteolin levels increased with dose escalation, there was no clear correlation between luteolin levels and observed adverse effects. Nevertheless, luteolin was reasonably absorbed, suggesting its potential as a marker for bioavailability.

6. Clinical studies on luteolin

While preclinical studies have shed light on the promising therapeutic properties of luteolin in various disease models, translation of these findings into clinical practice remains a critical endeavor. Clinical studies play a pivotal role in elucidating the efficacy, safety, and therapeutic potential of luteolin in human populations. Despite the wealth of preclinical evidence supporting its anti-inflammatory, antioxidant, and anti-cancer properties, the clinical utility of luteolin necessitates rigorous investigation to validate its therapeutic benefits and establish optimal dosing regimens.

In an open-label investigation, luteolin was observed to offer meaningful advantages to children with autism spectrum disorder in terms of both adaptive functioning and behavioral challenges. These enhancements most likely resulted from reducing inflammation in the brain, perhaps by blocking several inflammatory pathways **[56]**. In another clinical trial exploring the administration of luteolin in patients with COVID-19, it was observed that luteolin was associated with enhanced restoration of olfactory function. This improvement was ascribed to the capacity of luteolin to reduce detrimental microglia activation, limit neuronal cell degeneration, and attenuate motor and sensory deficits. Additionally, luteolin was found to counteract the activation of the Toll-like receptor 4 (TLR4)/TNF receptor-associated factor 6 (TRAF6)/NFκB signaling pathway, consequently

mitigating inflammation **[57]**. In addition, luteolin has been shown to improve sprint performance during exercise, especially in male physical education students who are in good health. Improved brain oxygenation was assumed to be the reason behind this rise, allowing muscles to work efficiently during exercise **[58]**. Altilix®, a product containing luteolin as one of its components, is utilized in treating cardiovascular and liver function in individuals with metabolic syndrome. Findings from a study revealed that the consumption of Altilix® supplementation led to improvements in either liver or cardiovascular functions among patients with metabolic syndrome **[59]**.

Conclusion

In conclusion, luteolin shows promise as a therapeutic agent due to its diverse range of benefits, including anti-inflammatory, antioxidant, and protective properties for the nervous system, heart, liver, and kidneys. It holds the potential for managing various conditions like cardiovascular diseases, neurodegenerative disorders, cancer, and liver and kidney diseases. However, challenges such as poor bioavailability require innovative delivery systems. While current evidence is encouraging, larger trials are necessary for validation, and future research should focus on optimal dosing, synergistic effects with other treatments, and improving bioavailability. Long-term safety and drug interactions also need thorough investigation. Despite obstacles, the diverse pharmacological characteristics of luteolin highlight its importance, urging continued research and clinical exploration to fully realize its therapeutic potential for human health.

Declarations

Consent to publish

All authors have read and agreed to the published version of the manuscript

Ethics approval and consent to participate

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article in the main manuscript.

Conflict of Interest

The authors assert that there are no conflicts of interest.

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Authors Contribution

Rasha D. Abdrabou: Review idea and outline, writing - original draft, manuscript revision. Rania M. Salama: Editing & supervision. Reem N. El-Naga: Editing & supervision. Samar S. Azab: Review & supervision, all authors approved the final manuscript.

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