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An Overview of Pharmacology of Luteolin

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Abstract

Luteolin is a Flavonoids recognized for its potent antioxidant, anti-inflammatory, and gastro protective properties, which collectively contribute to its relevance in promoting gastric health. Luteolin is widely found in various natural sources, particularly in fruits, vegetables, and herbs. An increasing amount of evidence suggests that Flavonoids intake may play an important role in health through regulating metabolism, weight, chronic illness, and cell proliferation.[1] It exhibits gastro protective effects by enhancing the secretion of gastric mucus and bicarbonate, which are crucial for maintaining the mucosal barrier. These combined actions not only safeguard the gastric lining against harmful substances, such as NSAIDs like aspirin, but also facilitate the recovery of the gastric mucosa following injury. Thus, Luteolin emerges as a promising natural compound for the prevention and management of gastric disorders, emphasizing its therapeutic potential in supporting gastrointestinal health.

Keywords – Luteolin, Peptic ulcer, NSAID, Gastro protective, Flavonoids.

Introduction

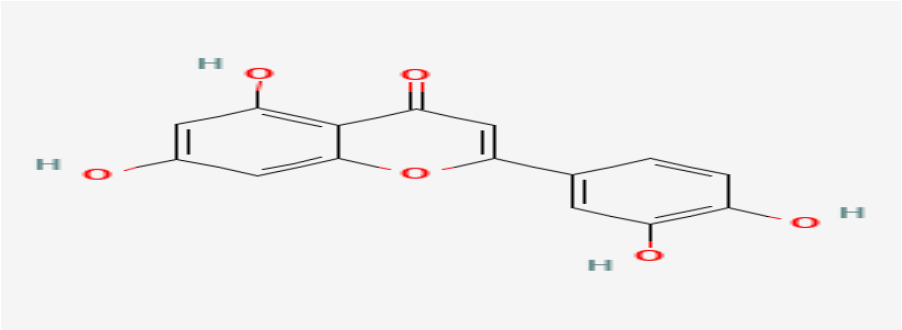
In recent years, there has been a great deal of public and scientific interest in the use of phytochemicals in the control of human illnesses. Herbal drugs are now very popular among these days and having greater importance in the treatment of various disease with desirable therapeutic effect. [1,2] Natural products and their derivatives have been recognized for many years as a source of therapeutic agents. Natural products have a diverse range of multidimensional chemical structure; however, the utility of natural products as a biological function modifier has achieved significant attention. The utilization of phytochemicals as anti-inflammatory, antioxidants, anti-cancer, neuro protective and pivotal role in severe gastrointestinal tract (GIT) diseases with having a different target which overcome and prevents the severity of disease. [3,4]

Flavonoid, chemical substances common in plants, have emerged as a new area of study in nutrition in recent decades. [5] An increasing amount of evidence suggests that flavonoid intake may play an important role in health through regulating metabolism, weight, chronic illness, and cell proliferation. [6] Animal and human epidemiologic studies show that various flavonoid has antioxidant and anti-inflammatory properties that could have preventive and/or therapeutic effects for cardiovascular disease, neurodegenerative disorders, cancer, and obesity.

Long-term intake of flavonoids-rich diets may protect against some malignancies, cardiovascular illnesses, type 2 diabetes, osteoporosis, pancreatitis, gastrointestinal difficulties, lung damage, and neurological disorders. [7]

Luteolin is a flavonoid characterized by its chemical structure, which includes a flavone backbone featuring a 3',4',5'-trihydroxyphenyl group and a 4-keto group. Its molecular formula is $C_{15}H_{10}O_6$, and it has a distinctive arrangement of hydroxyl groups that contribute to its antioxidant and anti-inflammatory properties. Luteolin is widely found in various natural sources, particularly in fruits, vegetables, and herbs. Significant dietary sources include celery, green peppers, parsley, artichokes, and chamomile tea, where it contributes to the overall health benefits of these foods. [8] Other sources include citrus fruits, such as oranges and grapefruits, as well as certain grains and spices. The presence of luteolin in these natural sources highlights its potential role in promoting health and preventing disease through dietary intake.

Luteolin is recognized for its potent antioxidant, anti-inflammatory, and gastroprotective properties, which collectively contribute to its relevance in promoting gastric health. As an antioxidant, luteolin effectively scavenges reactive oxygen species (ROS) and reduces oxidative stress, a key factor in mucosal injury and ulcer formation. [9] This action helps to protect gastric epithelial cells from damage caused by free radicals, thereby maintaining cellular integrity. Its anti-inflammatory properties are equally significant; luteolin inhibits the production of pro-inflammatory cytokines and modulates signaling pathways, such as the NF-κB pathway, which is often activated during gastric injury. [10] By reducing inflammation, luteolin can help alleviate symptoms associated with gastric distress and promote healing. Furthermore, luteolin exhibits gastro protective effects by enhancing the secretion of gastric mucus and bicarbonate, which are crucial for maintaining the mucosal barrier. These combined actions not only safeguard the gastric lining against harmful substances, such as NSAIDs like aspirin, but also facilitate the recovery of the gastric mucosa following injury. Thus, luteolin emerges as a promising natural compound for the prevention and management of gastric disorders, emphasizing its therapeutic potential in supporting gastrointestinal health.



Structure of Luteolin

Molecular Formula – $C_{15}H_{10}O_6$

IUPAC Name - 2-(3,4-dihydroxyphenyl)-5,7-dihydroxychromen-4-one

Molecular Weight - 286.24g/mol

Melting Point – 329.5 °C

Solubility – Aq. Alkaline solution, Ethanol, NaOH, DMSO And Methanol.

Absorption – Luteolin is absorbed by intestinal mucosa.

Distribution – After oral administration, Luteolin and its metabolites are mainly distributed in Liver, Kidney, Lung and GI tract.

Half life – The half life of luteolin is 8.94 hrs for free luteolin and 4.98 hrs for conjugated luteolin.

Plasma Concentrations – Luteolin plasma concentration decreases rapidly at first, then more slowly after 90 minutes. [11]

Luteolin offers several advantages compared to commonly used gastroprotective agents such as sucralfate and proton pump inhibitors (PPIs), making it an interesting alternative or complement in managing gastric health. Sucralfate works by forming a protective barrier over ulcers and damaged gastric mucosa, promoting healing; however, it requires frequent dosing and may not address underlying inflammation. In contrast, luteolin not only enhances mucosal protection but also possesses significant antioxidant and anti-inflammatory properties, targeting the root causes of gastric injury, such as oxidative stress and inflammation. Proton pump inhibitors, while effective at reducing gastric acid secretion and providing quick symptomatic relief, can lead to potential long-term side effects, including alterations in gut microbiota and increased risk of gastrointestinal infections. Luteolin, on the other hand, appears to be well-tolerated with minimal adverse effects, and its incorporation into treatment regimens may enhance gastric mucosal defense without the drawbacks associated with prolonged PPI use. Additionally, luteolin may exhibit synergistic effects when combined with these agents; for instance, it could enhance the mucosal healing effects of sucralfate or provide a protective layer while PPIs reduce acid secretion. [12] This multifaceted approach could lead to improved therapeutic outcomes in patients at risk for NSAID-induced gastric damage, emphasizing the potential role of luteolin in modern gastroenterology.

In preclinical models, luteolin has demonstrated efficacy at varying doses, highlighting its potential in promoting health and preventing disease. However, while the bioactivity of luteolin is well-documented, challenges remain regarding its bioavailability and optimal dosing for therapeutic effects. [13] Further research is needed to explore its mechanisms of action and clinical applicability in human populations.

Luteolin has been the focus of numerous animal experiments to investigate its medicinal potential for a variety of health disorders. In cancer research, mice models have shown that luteolin can reduce tumor development and spread, notably in breast and colon malignancies, by causing apoptosis and altering critical signaling pathways such as PI3K/Akt. [14] Furthermore, in models of neurodegenerative disorders such as Alzheimer's, luteolin has been demonstrated to diminish amyloid-beta plaque accumulation and improve cognitive performance in rats, implying strong neuroprotective effects due to its anti-inflammatory qualities. [15]

According to research on inflammation and allergic responses, luteolin can reduce airway inflammation and hyper responsiveness in asthma models, indicating its potential as a therapeutic agent for allergic disorders. [16] In metabolic tests with diabetic rats, luteolin was found to improve insulin sensitivity and lower blood glucose levels, indicating a role in metabolic control. [17] Furthermore, in hypertensive rats, luteolin treatment has been linked to lower blood pressure and better endothelial function, highlighting its cardiovascular preventive benefits. [18] Finally, in research on gastrointestinal health, luteolin has shown gastroprotective effects against peptic ulcers, most likely due to its capacity to reduce gastric acid output and strengthen mucosal defense mechanisms.

Collectively, these studies illustrate the diverse biological activities of luteolin and its potential applications in preventing and treating a range of diseases, although further research is necessary to fully understand its efficacy and safety in human populations.

Pharmacological Actions

Zamanian MY et al., (2024) stated that the combination of pylorus ligation and aspirin-induced ulcer models serves as a critical tool for understanding the mechanisms of peptic ulcer disease. By elucidating the interplay between increased gastric acid secretion, mucosal injury, and the effects of NSAIDs, these studies highlight the need for protective strategies in patients requiring long-term aspirin therapy, ultimately contributing to the development of safer therapeutic options for managing gastric health. [19]

Mohamed MM et al., (2024) revealed that In vitro studies have demonstrated luteolin's protective effects on gastric epithelial cells exposed to aspirin, showcasing its potential as a therapeutic agent against NSAID-induced gastric damage. One key study found that pre-treatment with luteolin significantly enhanced the viability of gastric epithelial cells subjected to aspirin-induced toxicity. The researchers observed that luteolin treatment effectively reduced cell death and promoted cell survival, indicating its protective role. Furthermore, luteolin was shown to mitigate oxidative stress by decreasing levels of reactive oxygen species (ROS) generated by aspirin exposure. This reduction in oxidative stress correlated with enhanced antioxidant enzyme activity, suggesting that luteolin not only scavenges free radicals but also boosts the cells' intrinsic antioxidant defenses. In terms of inflammation, luteolin significantly decreased the expression of inflammatory markers, including cyclooxygenase-2 (COX-2) and various pro-inflammatory cytokines, which are typically elevated in response to aspirin-induced damage. These findings collectively underscore luteolin's ability to protect gastric epithelial cells by improving cell viability, reducing oxidative damage, and attenuating inflammation, thereby highlighting its potential as a natural protective agent in preventing aspirin-induced gastric injury. [20]

Hussain MS et al., (2023) stated that in preclinical models, luteolin has demonstrated efficacy at varying doses, highlighting its potential in promoting health and preventing disease. However, while the bioactivity of luteolin is well-documented, challenges remain regarding its bioavailability and optimal dosing for therapeutic effects. Further research is needed to explore its mechanisms of action and clinical applicability in human populations. [21]

Gendrisch F et al., (2021) stated that Luteolin has been shown to modulate several biological pathways, including those involved in inflammation, cell proliferation, and apoptosis. This has led to investigations into its therapeutic applications in diseases such as cancer, neurodegenerative disorders, cardiovascular diseases, and metabolic syndromes. Notably, studies have indicated that luteolin can inhibit the growth of various cancer cell lines and reduce neuroinflammation, suggesting its promise as a complementary therapeutic agent. [22]

Summary

Luteolin, being a naturally occurring flavonoid with potent antioxidant and anti-inflammatory properties, presents a promising alternative due to its ability to enhance mucosal defense mechanisms and reduce oxidative stress. Luteolin offers several advantages compared to commonly used gastroprotective making it an interesting alternative or complement in managing gastric health. It also plays a vital role in safeguarding the stomach from damage and enhancing recovery, making it a promising candidate for therapeutic interventions aimed at preventing and treating gastric ulcers and other related disorders. However, while the bioactivity of luteolin is well-documented, challenges remain regarding its bioavailability and optimal dosing for therapeutic effects. Further research is needed to explore its mechanisms of action and clinical applicability in human populations.

References

1. Fan X, Fan Z, Yang Z, Huang T, Tong Y, Yang D, Mao X, Yang M. Flavonoids—Natural gifts to promote health and longevity. International Journal of Molecular Sciences. 2022 Jan;23(4):2176.
2. Moghadam ET, Yazdanian M, Tahmasebi E, Tebyanian H, Ranjbar R, Yazdanian A, Seifalian A, Tafazoli A. Current herbal medicine as an alternative treatment in dentistry: In vitro, in vivo and clinical studies. European journal of pharmacology. 2020 Dec 15;889:173665.
3. Islam F, Mitra S, Emran TB, Khan Z, Nath N, Das R, Sharma R, Awadh AA, Park MN, Kim B. Natural small molecules in gastrointestinal tract and associated cancers: molecular insights and targeted therapies. Molecules. 2022 Sep 3;27(17):5686.
4. Baranwal M, Gupta Y, Dey P, Majaw S. Antiinflammatory phytochemicals against virus-induced hyperinflammatory responses: Scope, rationale, application, and limitat-ions. Phytotherapy Research. 2021 Nov;35 (11):6148-69.
5. Shen N, Wang T, Gan Q, Liu S, Wang L, Jin B. Plant flavonoids: Classification, distribution, biosynthesis, and antioxidant activity. Food chemistry. 2022 Jul 30;383:13 2531.
6. Fan X, Fan Z, Yang Z, Huang T, Tong Y, Yang D, Mao X, Yang M. Flavonoids—Natural gifts to promote health and longevity. International Journal of Molecular Sciences. 2022 Jan;23(4):2176.
7. Singh S, Ahuja A, Sharma H, Maheshwari P. An Overview of Dietary Flavonoids as a Nutraceutical Nanoformulation Approach to Life-threatening Diseases. Current Pharmaceutical Biotechnology. 2023 Nov 1; 24(14):1740-73.
8. Bangar SP, Kajla P, Chaudhary V, Sharma N, Ozogul F. Luteolin: A flavone with myriads of bioactivities and food applications. Food Bioscience. 2023 Apr 1;5 2:102366.
9. Murti Y, Agrawal KK, Semwal BC, Singh S. Lead phytomolecules for gastroprotective drug development. Advances in Traditional Medicine. 2023 Sep;23(3):715-32.
10. Li B, Du P, Du Y, Zhao D, Cai Y, Yang Q, Guo Z. Luteolin alleviates inflammation and modulates gut microbiota in ulcerative colitis rats. Life sciences. 2021 Mar 15;269: 119008.https://pubchem.ncbi.nlm.nih.gov/co mpound/luteolin.
11. Fasoulakis Z, Koutras A, Syllaios A, Schizas D, Garmpis N, Diakosavvas M, Angelou K, Tsatsaris G, Pagkalos A, Ntounis T, Kontomanolis EN. Breast cancer apoptosis and the therapeutic role of luteolin. Chirurgia. 2021 Mar 1;116(170): 10-21614.
12. Serafim C, Araruna ME, Júnior EA, Diniz M, Hiruma-Lima C, Batista L. A review of the role of flavonoids in peptic ulcer (2010–2020). Molecules. 2020 Nov 20;25(22): 54 31.
13. Muruganathan N, Dhanapal AR, Baskar V, Muthuramalingam P, Selvaraj D, Aara H, Shiek Abdullah MZ, Sivanesan I. Recent updates on source, biosynthesis, and therapeutic potential of natural flavonoid luteolin: A review. Metabolites. 2022 Nov 20;12(11):1145.
14. Zughaibi TA, Suhail M, Tarique M, Tabrez S. Targeting PI3K/Akt/mTOR pathway by different flavonoids: a cancer chemopre ventive approach. International Journal of Molecular Sciences. 2021 Nov 18;22(22):12 455.
15. He Z, Li X, Wang Z, Cao Y, Han S, Li N, Cai J, Cheng S, Liu Q. Protective effects of luteolin against amyloid beta-induced oxidative stress and mitochondrial impairments through peroxisome proliferator-activated receptor γ-dependent mechanism in Alzheimer's disease. Redox Biology. 2023 Oct 1;66:102848.
16. Wang S, Wuniqiemu T, Tang W, Teng F, Bian Q, Yi L, Qin J, Zhu X, Wei Y, Dong J. Luteolin inhibits autophagy in allergic asthma by activating PI3K/Akt/mTOR signaling and inhibiting Beclin-1-PI3KC3

complex. International immunopharmaco logy. 2021 May 1;94:107460.
17. Park HS, Lee K, Kim SH, Hong MJ, Jeong NJ, Kim MS. Luteolin improves hypercholesterolemia and glucose intolerance through LXRα-dependent pathway in diet-induced obese mice. Journal of Food Biochemistry. 2020 Sep;44(9):e1 3 358.
18. Rahman MM, Ghoshal UC, Kibria MG, Sultana N, Yusuf MA, Nahar S, Ahmed F, Rowshon AH, Hasan M. Functional dyspepsia, peptic ulcer, and Helicobacter pylori infection in a rural community of South Asia: an endoscopy-assisted household survey. Clinical and translational gastroenterology. 2021 Apr 1;12(4):e00334.
19. Zamanian MY, Jahdari A, Gardanova Z, Hjazi A, Abdulelah FM, Noori SD, Abosaooda M, Khalaj F, Golmohammadi M, Taheri N. The Promising Therapeutic Effects of Pomegranate (Punica granatum) on Gastric Ulcers: A Comprehensive Review on Antioxidant, Anti-inflammatory Properties and Molecular Mechanisms.
20. Mohamed MM, Farid O. Gastro-Protective, Antioxidant, and Anti-Inflammatory Potential of Three Vegetable Oils Against Indomethacin-Induced Gastric Ulceration in Rats: in Vivo and in Vitro Study. Egyptian Journal of Chemistry. 2024 Jul 1;67(7):341-59.
21. Hussain MS, Gupta G, Goyal A, Thapa R, Almalki WH, Kazmi I, Alzarea SI, Fuloria S, Meenakshi DU, Jakhmola V, Pandey M. From nature to therapy: Luteolin's potential as an immune system modulator in inflammatory disorders. Journal of biochemical and molecular toxicology. 2023 Nov;37(11):e23482.
22. Gendrisch F, Esser PR, Schempp CM, Wölfle U. Luteolin as a modulator of skin aging and inflammation. Biofactors. 2021 Mar;47(2):170-80.