Editorial

Luteolin: A potential flavonoid for cancerous diseases

Dr. Santram Lodhi

Department of Pharmacognosy,
Smt. Sharadchandrika Suresh Patil College of Pharmacy, Chopda, Jalgaon 425107, M. S. India.

Cancer is a major worldwide health problem in both developed and developing countries. Several natural anti-cancer agents including taxol, vinblastine, vincristine, topotecan, irinotecan, etoposide etc. are clinically used. Some other major anti-cancer agents are including flavopiridol, roscovitine, betulinic acid and silvestrol. Among the various phytochemicals, particular flavonoids, are one of the most effective chemical classes which possess a wide range of health-promoting activities and pharmacological effects (Batra and Sharma, 2013).

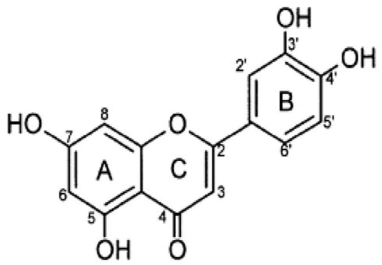

Figure 1. Luteolin (3,4,5,7-tetrahydroxy flavone)

Luteolin (3,4,5,7-tetrahydroxy flavone) is an important flavone, which is naturally found in several plant species. Chemically, it has a C6-C3-C6 structure that contains two benzene rings and one oxygen-containing ring with a C2-C3 carbon double bond (Bravo, 1998). Structure-activity studies have shown that the presence of hydroxyl moieties at carbons 5, 7, 3 and 4 positions of the luteolin structure and the presence of the 2–3 double bond are responsible for its multiple pharmacological effects (Lin et al., 2008). Luteolin, which is naturally found as a glycosylated form, is present in different fruits and vegetables, including broccoli, pepper, thyme, and celery (Nabavi et al., 2015). Luteolin possesses antioxidant, anticancer, anti-inflammatory, and neuroprotective effects.

**Address for Corresponding Author:*
Dr. Santram Lodhi
Department of Pharmacognosy,
Smt. Sharadchandrika Suresh Patil College of Pharmacy, Chopda, Jalgaon 425107, M. S. India.
Email: srlodhi78@gmail.com

The bioavailability of luteolin needs to be sufficiently high and its metabolism sufficiently low; otherwise, many activities of luteolin observed *in vitro* will not be relevant *in vivo*. Since luteolin is a common dietary constituent and since the oral route is the preferred route of administration for most drugs, it is important to know the bioavailability and metabolism of this flavonoid after oral ingestion (López-Lázaro, 2009).

Luteolin and its glycosides are widely distributed in the plant kingdom and have been found in many edible plants. Numerous preclinical studies have shown that luteolin possesses a wide range of biological activities and several possible mechanisms of action have been elucidated. Although the oral bioavailability of luteolin and its glycosides is not too high, animal experiments have shown that luteolin exerts its biological properties *in vivo*. Accumulating evidence suggests that luteolin could be developed as a potential anti-inflammatory agent as well as cancer chemopreventive agent and be useful in cancer therapy to sensitize tumor cells to the cytotoxic effects of some chemotherapeutic drugs. It is suggested that long-term animal toxicity studies should be conducted before people are able to take high doses of luteolin safely over a long period of time.

Luteolin suppresses JNK in macrophages while it activates this kinase in cancer cells. Also, luteolin suppresses NF-κB through inhibiting IKK activation during inflammation in epithelial cells and macrophages. However, in cancer cells suppression of NF-κB by luteolin is apparently a nuclear event. It remains to be determined whether the distinct mechanisms are due to differences in cell contexts. Because luteolin inhibits NF-κB in lung cancer cells and is associated with its pro-oxidant effect, it will be interesting to determine if the distinct mechanisms in NF-κB suppression are dependent on the redox status of the cell or the redox-regulating function of luteolin (Lin et al., 2008). Luteolin significantly reduces VRK1-mediated

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phosphorylation of the cell cycle-related substrates BAF and histone H3, and directly interacts with the catalytic domain of VRK1. In addition, luteolin regulates cell cycle progression by modulating VRK1 activity, leading to the suppression of cancer cell proliferation and the induction of apoptosis (Kim et al., 2014). Luteolin also acts as an antiproliferative by suppressing receptor tyrosine-kinase activity and apoptosis, in breast cancer. Many of these antimetastatic characteristics accredited to luteolin are likely functionally related (Cook, 2018). These findings suggest that luteolin can be used as a potential molecule for treatment of different types of cancer diseases.

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