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Biological Properties of Chrysin: A review

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Abstract

The flavone chrysin (5, 7-dihydroxyflavone), which occurs naturally in many plants, honey, and propolis. A number of *in vitro* and *in vivo* studies have revealed the therapeutic effects of chrysin against various diseases. In general, chrysin exhibits many biological activities and pharmacological effects, including antioxidant, anti-inflammatory, anticancer, and antiviral activities. Moreover, many studies have reported on the bioavailability of chrysin. Because of its compromised bioavailability and enhanced protein stability, chrysin solid lipid nanoparticle (SLN) synthesis avoids proteolytic degradation and sustained release of drug delivery.

Keywords: Chrysin, Chemical compounds, plants, bioactivities.

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1. Introduction

Flavonoids are ubiquitous plant specialized metabolites that contain large groups of low-molecular-weight polyphenolic com-pounds, which present benefits to human health because of their biological properties. To date, approximately 5000 diverse flavonoids have been identified [1]. Chrysin is one of the flavonoids fruits, vegetables, and plant especially found in honey, it has been indicated that its cardiovascular protective effect is due to its antioxidative effects and anti-inflammatory activities. Chrysin exerts an antioxidant effect by enhancing the antioxidant system, suppressing pro-oxidant enzymes, scavenging free radicals and chelating redox active transition-metal ions. Chrysin decreases lipid synthesis and also increases its metabolism, thereby ameliorating blood lipid profile. Chrysin modulates vascular function by increasing the bioavailability of endothelial nitric oxide. Chrysin inhibits the development of atherosclerosis by decreasing vascular inflammation. The anti-inflammatory effects of chrysin may relate to its inhibitory effect on the nuclear transcriptional factor-kB signaling pathway. It also prevents vascular smooth muscle cells proliferation and thrombogenesis. Altogether, chrysin may be effective as a natural agent for the prevention and treatment of cardiovascular diseases. [2-4]

Chrysin has been shown to be a very active flavonoid including many pharmacological properties such as antihypercholesterolemic activity [5], cardioprotective activity by improving post-ischemic functional recovery [6], suppressive effect on Vascular Endothelial Growth Factor (VEGF)-induced angiogenesis [7], anti-inflammatory activity by blocking histamine release and proinflammatory cytokine expression [7]. This present review showed the main biological activities of Chrysin compound.

2. Biological Activities

2.1 Hepatoprotective effect

Chrysin showed promising hepatoprotective and antihyperlipidemic effects, which are evidenced by the decreased levels of triglycerides, free fatty acids, total cholesterol, phospho-lipids, low-density lipoprotein-C, and very low-density lipoprotein-C and increased levels of high-density lipoprotein-C in the plasma and tissues of hepatotoxicity in rats. The hepatoprotective activity of

chrysin is mediated through TNF- as chrysin reduces soluble TNF- generation by blocking TNF- converting enzyme activity [8].

2.2 Antidiabetic effect

The hypoglycemic effects of natural compounds were determined by monitoring the glucose consumption of HepG2 cells treated with chrysin, chrysin derivatives, and a positive reference, rosiglitazone. An O7-nitrooxyalkyl nitric oxide (NO) donor moiety is attached to the chrysin as a parent compound, and its O7-[(nitro-oxyl) alkyloxycarbonyl] methyl analogs were synthesized. Furthermore, a novel class of hybrid ester prodrugs was synthesized. The methyl derivatives of (nitrooxyl) ethoxycarbonyl are the most powerful inhibitors of AR and AGE, and chrysin is a potent inhibitor of AGE. All the hybrid ester prodrugs release NO gradually in the presence of L-cysteine, and the O7-nitrooxyethyl chrysin derivatives O7-[(nitrooxyl) butoxy carbonyl] methyl analog and O7-[(nitrooxyl) hexoxycarbonyl]methyl analog (5c) drastically promote the glucose consumption of HepG2 cells. This hybrid ester NO donor prodrugs offer a potential drug design concept for the development of preventive or therapeutic agents for vascular complications of diabetes [9].

2.3 Antiasthmatic effect

Chrysin reduces allergic airway inflammation by the degranulation of certain types of cells. The antioxidant potential of chrysin may be attributed to altered Th1/Th2 polarization through the suppression of iNOS, NF- B, and activator protein 1 [10].

2.4 Anti-inflammatory effect

The flavone chrysin fascinatingly exhibited anti-inflammatory activities. This evidence was also supported by docking studies suggesting that chrysin's established interactions with the COX-2 binding site are sufficient to justify the anti-inflammatory activity of this flavone. Neuroinflammatory responses are mostly mediated by increased levels of proinflammatory cytokines and decreased levels of antiinflammatory cytokines [11].

2.5 Antihyperammonemic effect

Oral administration of chrysin (100 mg/kg b.w.) significantly restored the levels of LPO by-products, lipid profile, and antioxidant activities. In general, flavonoids exert free radical scavenging properties depending on the OH groups present in the ring structure of the compound. Nevertheless, chrysin's structure has two OH groups in it's A ring at the C-5 and C-7 positions, which play a major role in the free radical scavenging activities. Hence, chrysin' ability to increase the antioxidant levels along with its anti-lipid peroxidative activity suggests that this compound is potentially useful in counteracting free radical-mediated tissue damage caused by ammonia toxicity. Thus, the beneficial action of chrysin repressing ammonium chloride (NH4Cl)-induced ammonia intoxication could be attributed to its free radical scavenging properties [12].

2.6 Antidepressant effect

The chronic unpredictable mild stress (CUMS) animal model was developed to mimic the initiation and progress of clinical depression in humans. Studies suggested that CUMS induces behavioral and physiological changes that resemble symptoms of human depression. CUMS decreases the BDNF and nerve growth factor (NGF) levels and the activity of Naþ/Kþ-ATPase in the prefrontal cortex and hippocampus, respectively. In addition to the defense action against changes in the level of neurotrophin, activity of Naþ/Kþ-ATPase, and CUMS-induced behavioral alteration, chrysin also prevented alterations in the corticosterone levels and antioxidant status. Furthermore, chrysin alters the upregulation of BDNF and NGF levels [13].

2.7 Antiarthritic effect

Chrysin has alleviating actions against testicular impairment that are mediated by enhancing the expression of testicular StAR gene and associated testosterone production. Moreover, chrysin modulates inflammatory cytokines, neutrophil infiltration, and expression of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) besides the oxidative stress. They also inhibited RNA expression of FasL and caspase-3 activity. These data also endorse chrysin as a safe complementary approach for the management of testicular dysfunction in patients with RA [14].

2.8 Nephroprotective effect

Chrysin effectively prevented DNA fragmentation in nephrotoxicity. Reduction of endogenous damage can indicate chrysin's enhanced protection toward DNA against ROS attack and/or increased rates of repair toward DNA damage. It justifies the hypothesis that nephrotoxicity is closely related to increased generation of ROS, leading to the reduction of antioxidant defense mechanism. A previous study illustrated that reduced levels of serum protein, GFR, and protein uria development in diabetic rats clearly indicated the development of diabetic nephropathy [15].

2.9 Anticancer activity

Chrysin administration improved the status of lipid peroxidation and antioxidants, which regulated the homeostasis of oxidant and antioxidant status during carcinogenesis. Chrysin inhibits tumor growth through apoptosis related the activation of Notch1 signaling pathway, both *in vitro* and *vivo* [16]. The primary mechanism of action of chrysin consists of a decrease in cell proliferation, induction of cell death by optosis, and reduction of inflammation [17].

3. Conclusion

Chrysin, a naturally occurring polyphenol, hasmany pharmacological activities such as anticarcinogenic, pro-apoptotic, antiangiogenic, antimetastatic, immunomodulatory and antioxidant properties and this review showed the importance of Chrysin.

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