



KAEMPFEROL-3-O-D-GLUCOSIDE BIOACTIVITIES: A REVIEW

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ABSTRACT

Natural products have bioactive chemical entities, persist as an inexhaustible resource for discovery of drugs. One of the naturally occurring flavonoids, astragalín (kaempferol 3-glucoside), which is a bioactive constituent of various traditional medicinal plants such as *Cuscuta chinensis*. It is well known for its various pharmacological effects such as anti-inflammatory, antioxidant, neuroprotective, cardioprotective, antiobesity, antiosteoporotic, anticancer, antiulcer, and antidiabetic properties. It showed the highest antiproliferation effect on the human hepatoma cell line HepG2, mouse colon cancer cell line CT26 and mouse melanoma cell line B16F1.

Keywords: Kaempferol-3-O-D-glucoside, plants, bioactivities

INTRODUCTION

Medicinal plants have been an infinite source of therapeutic agents since millions of years. Most of the discovered drugs either belong to natural products or derivatives of natural compounds [1,2]. The term “natural products” encompasses chemical entities derived from plants, bread molds, microorganisms, terrestrial vertebrates as well as invertebrates, and marine organisms [3]. these chemical entities are known to have immense chemical diversity with outstanding drug-like properties that contribute towards their multitargeted action [4]. Kaempferol is one of the flavonoids commonly found in some vegetable, fruits, and traditional medicine. In nature, almost all dietary flavonoids exist in their glycoside forms [5]. Kaempferol usually bonds with glucose, rhamnose, galactose, and rutinose to exist in its glycoside form [6]. Some kaempferol glycosides are easily found in nature, e.g. kaempfero-3-O-glucoside, because their biosynthesis progresses in simple ways; i.e. it only requires some type of enzymes that are widespread in nature. However, some other kaempferol glycosides are more restricted because glycosides can only be synthesized by certain plant species that can provide certain enzymes along with genetic information [5]. Astragalín (kaempferol-3-O-D-glucoside), a bioactive natural flavonoid, has been well known for its medicinal importance. It has been reported to exhibit multiple pharmacological properties including antioxidant [7,8], anti-inflammatory [9], anticancer [10], neuroprotective [11], and cardioprotective property [11]. This review gives some information about the properties of a bioactive natural flavonoid Astragalín (kaempferol-3-O-D-glucoside).

BIOLOGICAL ACTIVITIES

Anticancer Activity:

Several studies on astragalín showed its anticancer effect due to its promising competency to inhibit proliferation in different cancer cell lines including leukemia (HL-60), hepatocellular (HepG2, Huh-7, and H22) [12], skin (HaCaT, A375P, and SK-MEL-2), and lung (A549 and H1299) cancerous cells. In another report, astragalín strongly exerted cytotoxic effects in A375P and SK-MEL-2 cancerous cells in a concentration-dependent way through induction of apoptosis. The underlying cell death mechanism involves activation of Bax and caspase-3/-9, cleavage of PARP, and downregulation of cyclin D1 and Mcl-1 along with inhibition of Sry-related HMg-Box Gene 10 (SOX10) signaling cascade [13, 14].

Antiosteoporotic Activity:

Osteoporosis is characterized by structural deterioration of tissues in the bone along with lower bone mass and bone fragility. The main causes of osteoporosis include estrogen deficiency, excess of glucocorticoids, and oxidative stress. Astragalín, an active compound, isolated from crude methanolic extract of the seeds of *C. chinensis* showed estrogenic activity against osteoporosis, and it is responsible for significant osteoblastic cell proliferation in UMR-106 osteoblastic cells [15].

Antioxidant Activity:

Astragalins also inhibit the endotoxin-induced oxidative stress, which can lead to epithelial apoptosis and eosinophilia. It can also act as an antagonizing agent against endotoxin-induced oxidative stress via modulation of LPSTLR signaling network. Astragalins cause the suppression of 6-hydroxydopamine-stimulated neurotoxicity in *Caenorhabditis elegans* via modulation of apoptosis-related pathways and alleviation of oxidative stress [16]. Astragalins have the capability to improve neural function in the ischemia brain injury model of rats via blocking the apoptosis in the hippocampus region [17].

Neuroprotective Activity:

Astragalins have been reported to decrease neurodegeneration in *C. elegans* stimulated by 6-OHDA and increase the lifespan of astragalins-treated nematode. It also reduces ROS levels, inhibits lipid peroxidation, and increases SOD and GPx activities. Furthermore, it is capable of enhancing AChE and reducing the transcript level of proapoptotic gene *egl-1* associated with neuronal cell death [16]. Astragalins also suppress carrageenan-stimulated paw edema in rats. Neural function is also reported to be improved by the use of astragalins in ischemic brain injury rat models [17].

Antiobesity Activity:

Astragalins along with other known flavonoids isolated from *N. nucifera* showed an inhibitory effect on diet-induced obesity and also activated β -adrenergic receptor pathway, but additional experimentation is required to fully elucidate its possible mechanism of action [18].

Antidiabetic Activity:

Diabetic retinopathy (DR) arises due to diabetes mellitus and is one of the most common causes of vision loss. Hyperglycemia leads to overexpression of many biological effectors such as vascular endothelial growth factor (VEGF) which is very crucial for the development of DR. Astragalins derived from *A. membranaceus* have beneficial effects against hyperglycemia. It helps to prevent DR by decreasing the overexpression of VEGF in cultured Muller cells and alleviating the effects caused by high concentration of glucose in the blood [19].

Antifibrotic Activity:

Astragalins isolated from leaves of persimmon and green tea can be effective in allaying ROS-prompted bronchial fibrosis as it has the capability to inhibit auto phagosome formation in the airways. It also alleviates hepatic fibrosis by regulating PAR2 (protease-activated receptor 2) mechanism. Astragalins regulate proinflammatory cytokines namely IL-6, IL-1 β , and TNF- α . It also attenuates the PAR2 signaling expression, and its protective effects are especially prominent in diabetic animal models [20].

Antiulcer Activity:

Flavonoids stimulate mucus secretion, block pepsinogen, prohibit Ca²⁺ influx, and also change GSH metabolism. Astragalins, a pharmacologically active flavonoid isolated from *C. cyparissias*, has been examined

for its antiulcer activity. Results demonstrated that 30 mg/kg dosage of astragalin effectively decreases percentage of lesion area, total area of lesion, and ulcer index in the mice model of gastric secretion [21].

Cardioprotective Activity:

Previous studies have confirmed that flavonoids stimulated cardioprotective effects against myocardial ischemia. Astragalin was proved to be effective against acute I/R injury in Sprague- Dawley rats as its mechanism of action precedes via diminishing intracellular oxidative stress and apoptosis. The associated mechanism involves decreased expression of MDA, TNF- α , IL-6, ROS, and Bax along with the increased ratio of GSH/GSSG, respectively [22].

CONCLUSION

This review showed the pharmacological effects of Astragalin.

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