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Biological Properties of Naringenin: A review

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Abstract

Flavonoids are important secondary metabolites that has a multitude of functions including pigments and antioxidant activity. Naringenin is a naturally occurring flavanone (flavonoid) known to have a bioactive effect on human health and is mainly found in fruits (grapefruit and oranges) and vegetables. Naringenin possesses various biological activities such as antidiabetic, antiatherogenic, antidepressant, immunomodulatory, antitumor, anti-inflammatory, DNA protective, hypolipidaemic, antioxidant, peroxisome proliferator-activated receptors (PPARs) activator, and memory improving. A number of molecular mechanisms underlying its beneficial activities have been elucidated. This review provides naringenin medicinal uses for the treatment of many infectious and degenerative diseases.

Keywords: Naringenin, Chemical compounds, plants, bioactivities.

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1. Introduction

Plants have been used by human being since antiquity for diverse purposes such as food and medicine. Many of the currently available drugs have been derived from natural sources. More than 25% of the drugs prescribed worldwide are derived from plants, and 121 such active phytoconstituents are used for different disorders [1]. Flavonoids are plant-derived phytochemicals responsible for the different colors of plant parts like shades of yellow, orange and red in flowers. More than 4,000 flavonoids, such as flavonols, flavones, flavanols, flavanonols, flavanones, and isoflavones have been reported in the edible plants and are consumed regularly in the human diet [2]. Flavonoids, found in fruits and vegetables, have various health benefits [3]. Naringenin is a flavonoid belonging to flavanones subclass. It is widely distributed in several Citrus fruits, bergamot, tomatoes and other fruits, being also found in its glycosides form (mainly naringin). Naringenin is one of the most important naturally-occurring flavonoid, predominantly found in some edible fruits, like Citrus species and tomatoes, and figs belonging to smyrna-type *Ficus carica*. Chemically named as 2, 3-dihydro-5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-1-benzopyran-4-one [4, 5]. It has been reported for the hypocholesterolemic, antiestrogenic, hypolipidemic, antihypertensive, and antiflammatory activities [6]. This review provides naringenin medicinal uses for the treatment of many infectious and degenerative diseases.

2. Biological Activities

2.1 Anti-inflammatory activity

Naringenin is a naturally occurring flavonoid that can be extracted from citrus fruits, tomatoes, cherries, grapefruit, and cocoa. Like most of the flavonoids, naringenin was experimentally found to have several pharmacological potentials, including anti-inflammatory because of naringenin has properties to produce sufficient hydroxyl (-OH) substitutions, which give it the capability to scavenge ROS. Thus, it has considered that naringenin may diminish and/or improve pathological conditions where oxidation or inflammation is deemed to play a vital role [7].

2.2 Anticarcinogenic Effect

Naringenin is also known to cause cytotoxic and apoptotic effects in several cancer cell lines in a dose-dependent manner as well as inhibits tumor growth in

sarcoma S-180 implanted mice, suggesting that naringenin can potentially be used to inhibit tumor growth . Cytotoxic effects were also induced in human cancer cell lines when high concentrations of naringenin were administered (50% effective concentration: 150-560 μM). However, the use of flavonoids as cancer chemo preventive or chemotherapeutic agents requires the development of novel flavonoids or naringenin derivatives that can induce cytotoxicity at low concentrations in a cell type-dependent manner [8].

2.3 Gastro-intestinal activity

Pre-administration of naringenin significantly reduced the severity of colitis and resulted in down-regulation of proinflammatory mediators (inducible NO synthase (iNOS), intercellular adhesion molecule-1 (ICAM-1), monocyte chemoattractant protein-1 (MCP-1), cyclo-oxygenase-2 (Cox2), TNF-α and IL-6 mRNA) in the colon mucosa [9].

2.4 Hepatoprotective Effect

Naringenin has been found to have a hepatoprotective characteristic similar to silymarin. Animal studies have demonstrated turmeric's hepatoprotective effects from a variety of he-patotoxic insults, including carbon tetrachloride (CCl4), alactosamine, acetaminophen (paracetamol), and Aspergillus aflatoxin. Turmeric's hepatoprotective effect is mainly a result of its antioxidant properties, as well as its ability to decrease the formation of pro-inflammatory cytokines. The protective capacity of naringenin on dimethylnitrosamine (DMN) - induced hepatic damage in rats was investigated. Oral administration of naringenin (20 and 50 mg/kg daily over 4 wk) notably diminished DMN-induced dam-age when the weight of the liver was evaluated, as well as alanine transaminase (ALAT), aspartate transaminase (ASAT), alkaline phosphatase (ALP), and bilirubin levels [10].

2.5 Anti-Obesity effect

It is an important component of metabolic syndrome, is a chronic low-grade inflammatory condition leading to adipocyte differentiation and growth in adipose tissues. In mice fed a high fat diet, naringin decreased visceral adiposity and lowered plasma lipid concentrations, probably by activation of AMP kinase [11].

2.6 Naringenin Enhances Immunity

Various flavonoids were used as stimulants to enhance the expression of NKG2D ligands. NK cell lysis activity against Raji was not changed by pre-treatment of naringenin with luteolin, kaempferol, taxifolin and hesperetin. However, treatment with naringenin showed increased sensitivity to NK cell lysis than untreated control cells. The activity of naringenin was due to enhanced NKG2D ligand expression. These results provide evidence that narigenin's antitumor activity may be due to targeting of NKG2D ligand expression and suggests a possible immunotherapeutic role for cancer treatment [12].

2.7 Anti-oxidant effect

Naringenin exhibited higher antioxidant capacity and hydroxyl and superoxide radical scavenger efficiency. The glycosylation attenuated the efficiency in inhibiting the enzyme xanthine oxidase and the aglycone could act like a more active chelator of metallic ions than the glycoside. Additionally, naringenin showed a greater effectiveness in the protection against oxidative damage to lipids in a dose-dependent manner. The flavanone was effective in reducing DNA damage (13).

2.8 Cardiovascular Effect

Naringin showed a range of properties that help protect the ardiovascular system, including antihypertensive, lipid lowering, insulin-sensitising, anti-oxidative and antiinflammatory properties. Naringin prevented the age-related increase in systolic blood pressure in stroke-prone spontaneously hypertensive rats, increased nitric oxide production, improved endothelial function and decreased cerebral thrombotic tendency. Further, naringin prevented oxidative stress in the hearts of rats with isoprenaline-induced myocardial infarction [14].

2.9 Naringenin as Anti-HCV agent

Naringenin has also been proposed as a novel therapeutic agent for hepatitis C virus (HCV) infection treatment. Indeed, this flavanone has been described to reduce HCV secretion in infected cells by 80%, at a concentration below to the toxic value in primary human hepatocytes and in mice [15].

2.10 Role of Naringenin in Weight Control

A commercial polyphenolic extract from several Citrus fruits (Sinetrol-XPur), containing about 20% of naringenin, was tested in 95 healthy overweight volunteers (BMI ranging from 26 to 29.9 kg/m2) [100]. The main overweight-related endpoints were improved after 12-weeks randomized protocol (including waist and hip circumference, abdominal fat, body weight). Moreover, inflammatory and oxidative stress markers were all decreased [16].

3. Conclusion

This review showed the importance of Naringenin.

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