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ANTITOXIC EFFECTS OF NARINGIN: A FLAVONOID WITH DIVERSE BIOLOGICAL ACTIVITIES

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ABSTRACT

Naringin is a naturally occurring flavonoid in citrus plants. It is a phytochemical commonly found in grapefruit juice with numerous health benefits. Naringin has been reported to show broad spectrum of therapeutic and pharmacological properties including anti-inflammatory, free radical-scavenging, lipid-lowering, antioxidant and anti-fibrosis activity. This paper emphasizes on the antitoxic activities of naringin and presents a short review of the studies done in the field. This summary of the research done in the field of antitoxicty of naringin will be helpful to understand its protective nature against various toxins.

KEYWORDS: Naringin, antitoxic, antioxidant, genotoxicity, grapefruit, phytochemical.

INTRODUCTION

Naringin is a naturally occurring phytochemical commonly found in grapefruit juice with numerous health benefits. Normally, its concentration in grapefruit juice is 400 mg/l. Naringin has been reported to show broad spectrum of therapeutic and pharmacological properties including anti-inflammatory, free radical-scavenging, lipid-lowering and antioxidant, anti-fibrosis, beneficial role of naringin on nickel induced nephrotoxicity, anti-osteoporosis, prokinetic and anti-obesity effects. Recently, its anticarcinogenic, neuroprotective, memory impairment improving, anti-diabetic and antidepressant-like effects are also been reported. Naringin is gaining its importance due to its protective effects against genotoxicity also. Naringin causes bitter taste of grapefruit juice. It is water soluble flavonoid and is most commonly studied for its antioxidant and anticarcinogenic properties. It is also found to affect the enzyme activities in the digestive tract. It is also used in many supplements to enhance the activity of the drugs.

Pure naringin is a yellow powder and is a conjugate product of naringenin and a sugar molecule. The Structure of naringin has 3 rings with 15 carbon atoms and 2 benzene rings. The chemical formula of naringin is $C_{27}H_{32}O_{14}$ with molar mass of 580.54 g/mol. and melting point of 439 K (331° F, 166° C). IUPAC name of naringin is 7-[[2-*O*-(6-Deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-2,3-dihydro-5-hydroxy-2-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one. Other common names for naringin are 4,5,7-Trihydroxyflavanone 7-rhamnoglucoside and naringenin-7-neohesperidoside.

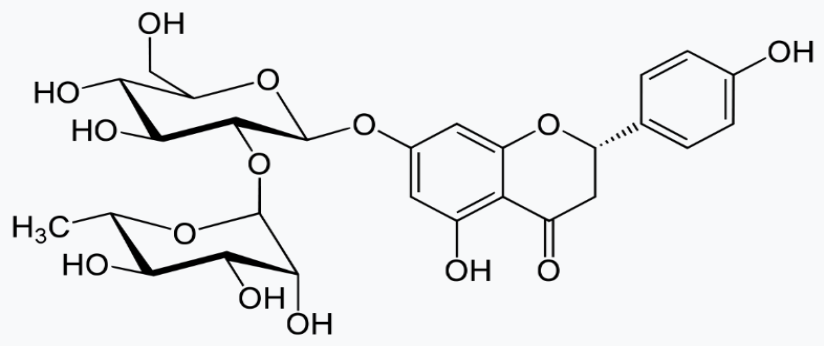

Fig. 1. Structure of Naringin.

Naringinase is found in the liver of humans which metabolizes naringin to naringenin. The conversion is done in 2 steps. Firstly naringin is hydrolysed by α-L-rhamnosidase to rhamnose and prunin then β-d-glucosidase hydrolyses prunin to naringenin and glucose. Naringenin is the absorbable form of the naringin.

Antitoxic Nature

Toxicological studies give an insight into the nature of a particular compound under consideration like arsenic[1,2], pesticides[3], metal particulates[4,5] and lead.[6] Antioxidant status is a key factor in the assessment of human health.[6-8] In recent studies, naringin gained much importance because of its antioxidant, metal chelating, free radical-scavenging and cholesterol lowering effects. Its protective effects against anticancer drugs induced toxicity have also been reported. Heat treatment of naringin has been shown to preserve the activities of native naringin and its inhibitory effect on lipid peroxidation.[9] Naringin also promotes the osteogenesis of the human bone marrow mesenchymal stem cells (hBMSCs) by activating the ERK signalling pathway. Naringin is thought to be a therapeutic agent in osteoporosis and it has been shown to promote the proliferation of hBMSCs.[10] Naringin also shows neuroprotective effect by diminishing hyperammonemia and acts as a potential therapeutic agent.[11] Naringin also reduces oxidative stress and NTRI (nucleoside reverse transcriptase

inhibitors) induced mitochondrial damage and is considered beneficial in managing the toxicities and different ill effects of NTRI use.[12]

Arsenic induced cardiovascular toxicity by contaminated food and water is a serious concern today. Naringin also has properties to reduce cardiovascular toxicity by reducing myocardial apoptosis and modulating TGF-beta-Smad-3 and Nrf-2/HO-1 pathways.[13,14] Naringin also has nephron-protective and hepato-protective effects against Acetaminophen (APAP) which is an analgesic and antipyretic agent causing renal and hepatic toxicity at higher doses.[15] Most commonly used chemotherapeutic agent used to cure various types of cancer is Doxorubicin (Dox) which causes cardiovascular toxicity. Naringin also shows cardio-protective effects against the Dox-induced cardiomyopathy.[16] Naringin has been reported to show protective effects against dose dependent toxicity of Cisplatin.[17] Bleomycin has been shown to cause genotoxicity in the form of chromosomal aberrations. Naringin was found to show protective effects against the genotoxicity induced by bleomycin (20 µg/ml).[18] Naringin also attenuated the cytotoxicity induced by Microcystin-LR.[19] Naringin inhibited the uptake of microcystin (MC-LR) in the freshwater snail *Sinotaia histrica.*[20] Naringin, itself was also checked for its toxicity in rats. It was administered orally for 6 months up to 1250 mg/kg/day to Sprague-Dawley (SD) rats and no adverse effects were seen. Thus, naringin can be used as a therapeutic agent without any ill effects on the body.[21,22] Naringin also showed protective effects against cycloporine-A (CS-A) induced toxicity.[23] Naringin has been reported to have protective effects against nickel toxicity.[24,25] Naringin has also revealed both antioxidative and anti-inflammatory effects.[26] Naringin has also been found to be associated with promoting proliferation and differentiation of MC3TC3-E1 cells.[27] Naringin and vitamin C, in combination, showed antihyperglycemic and antioxidant effects in streptozotocin -induced type II diabetes mellitus in rats.[28] Naringin also showed protective effects on peroxides and antioxidants in isoproterenol induced cardiotoxicity.[29]

CONCLUSION

Naringin is a flavonoid with diverse therapeutic and pharmacological properties. The protective effects include anti-inflammatory, lipid-lowering, free radical-scavenging and antioxidant activities. Its anti-carcinogenic, neuroprotective, anti-diabetic and antidepressant effects have also been reported. Naringin has been widely tested on rats and mice to reveal its protective effects against toxicity of different chemicals including Microcystin-LR, Dox and Cycloporine-A. Naringin should further be explored in future for its protective effects.

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