

Editorial:

RECENT STUDIES ON FLAVONOIDS AND THEIR ANTIOXIDANT ACTIVITIES

Soo Cheon Chae¹, Jai-Heon Lee^{2*}, Sang Un Park^{3*}

¹ Department of Horticultural Science, College of Industrial Sciences, Kongju National University, 1 Daehoe-ri, Yesan-kun, Chungnam, 340-720, Korea

² Department of Genetic Engineering, Dong-A University, Busan 604-714, Korea

³ Department of Crop Science, College of Agriculture and Life Sciences, Chungnam National University, 99 Daehangno, Yuseong-gu, Daejeon, 305-764, Korea

* corresponding author:

Dr. Jai-Heon Lee: Phone: + 82-51-200-7592. E-mail: jhnlee@dau.ac.kr

Dr. Sang Un Park: Phone: +82-42-821-5730. E-mail: supark@cnu.ac.kr

Flavonoids are widely distributed plant secondary metabolites with various metabolic functions. They are ubiquitous in fruits and vegetables that are regularly consumed by humans. These natural compounds are categorized by their chemical structure into 6 major subgroups as follows: chalcones, flavones, flavonols, flavandiols, anthocyanins, and proanthocyanidins or condensed tannins (Winkel-Shirley, 2001; Falcone Ferreyra et al., 2012). More than 6000 different flavonoids have been identified, and this number is certain to increase as more researches are conducted on them (Ferrer et al., 2008).

Flavonoids have attracted considerable interest because of their potentially beneficial effects in humans; they have been reported to have antiviral, antiallergic, antiplatelet, antiinflammatory, antitumor, and antioxidant activities (Izzi et al., 2012; Kay et al., 2012). Many investigations have focused on these health-promoting effects and antioxidant activities of flavonoids, particularly their role in the chemoprevention of cancer (Gonzalez-Paramas et al., 2011; Galleano et al., 2012). We have reviewed the most recent studies on flavonoids and their antioxidant activities (Table 1).

Table 1: Recent studies on flavonoid compounds and their antioxidant activities

Key message	Reference
Flavonoid is a general name of a class of more than 6500 molecules based upon a 15-carbon skeleton. The core structure is a 2-phenylbenzopyranone, in which the three-carbon bridge between the phenyl groups is commonly cyclised with oxygen. Therefore flavonoids have been recognised as one of the largest and most widespread groups of plant secondary metabolites, with marked antioxidant properties.	Corradini et al., 2011
Flavonoids are efficient quenchers of singlet oxygen and could be valuable antioxidants in systems under oxidative stress, particularly if a flavonoid-rich diet was previously consumed.	Morales et al., 2012
It is well known that rutin, an active flavonoid compound, possesses potent antioxidant properties against oxidative stress. Rutin (50 µM) blocked apoptosis in human umbilical vein endothelial cells through decreasing reactive oxygen species, increasing glutathione, restoring DeltaPsim and thus protecting DNA damage.	Gong et al., 2010

Table 1 (cont.): Recent studies on flavonoid compounds and their antioxidant activities

Key message	Reference
Quercetin acts against isoproterenol-induced myocardial oxidative injury and immune function impairment; the mechanism involved in the pharmacological action is related at least in part to the antioxidant activity of quercetin.	Liu et al., 2012a
Luteolin is a flavone which occurs in medicinal plants as well as in some vegetables and spices. Luteolin displayed excellent radical scavenging and cytoprotective properties, when it interact with other antioxidants like vitamins. In vivo, luteolin reduced increased vascular permeability and was effective in animal models of inflammation after parenteral and oral application.	Seelinger et al., 2008
Numerous preclinical studies have shown that kaempferol and some of its glycosides have a wide range of pharmacological properties, including antioxidant effects.	Calderón-Montaño et al., 2011
Myricetin restored the activity and protein expression of cellular antioxidant defense enzymes such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) reduced by hydrogen peroxide (H ₂ O ₂) treatment.	Wang et al., 2010
The antioxidant capacity of the tested quercetin and epigallocatechin gallate is due to their stabilizing effect on the cell membranes; this contributes to cell protection in various pathologies and acting as an adjuvant therapy in highly toxic treatment regimens.	Margina et al., 2012
Baicalein has antioxidant activity and exerts a cytoprotective role in H ₂ O ₂ -induced apoptosis by inhibiting mitochondria-dependent caspase activation and the p38 MAPK pathway.	Liu et al., 2012b
Baicalin is efficient in reducing hyperglycemia-induced oxidative stress through the increased expression of antioxidant enzyme activities.	Waisundara et al., 2011
Both cyclic voltammetry and quantum-chemical analysis, antioxidative properties of naturally occurring flavon-3-ol, fisetin were observed. Through oxidation potential values, used as quantitative parameter in determining its oxidation capability, indicated good antioxidative properties found with this molecule (flavon-3-ol, fisetin).	Marković et al., 2009
Scavenging effect depends on the structural conditions of hydroxyflavone. Hydroxyl groups neighboring to each other showed much higher antioxidative activities than the compound with separated hydroxyl groups. Therefore, ortho position of dihydroxyl groups is one of the structural conditions of hydroxyflavone for the good scavenging effect.	Hyun et al., 2010
Isorhamnetin-3-glucoside can significantly hinder selenite cataracts in vitro by its antioxidant property.	Devi et al., 2010
This study emphasizes the importance of iron binding in polyphenol antioxidant behavior and provides insights into the iron-binding antioxidant activities of flavonols such as quercetin and myricetin.	Verdan et al., 2011
Isoquercitrin (IQ) is one of the most important flavonoids, possesses scavenging abilities for superoxide anion, hydroxyl radical and nitrite. Such scavenging capacities increase with the concentration of IQ.	Li et al., 2011
Hesperetin (Bioflavonoids) metabolites (2.5-20 μM) showed higher antioxidant activity against various oxidative systems, including superoxide anion scavenging, reducing power, and metal chelating effects, than that of hesperidin (aglycon).	Yang et al., 2012

Table 1 (cont.): Recent studies on flavonoid compounds and their antioxidant activities

Key message	Reference
Naringenin exhibits antihyperglycemic and antioxidant effects in experimental diabetic rats.	Annadurai et al., 2012
Eriodictyol acts as an antagonist of the transient potential vanilloid 1 (TRPV1) receptor and as an antioxidant.	Rossato et al., 2011
Genistein significantly decreased the levels of reactive oxygen species and induced the expression of the antioxidant enzymes, manganese superoxide dismutase and catalase.	Park et al., 2010
Flavonols and anthocyanins have greater antioxidant properties and exert greater influence on cholesterol concentration in erythrocyte membranes than simple hydroxycinnamic acids.	Duchnowicz et al., 2012
Kaempferol is a flavonoid found in many edible plants and in plants or botanical products commonly used in traditional medicine. Epidemiological studies have found a positive association between the consumption of foods containing kaempferol and a reduced risk of developing several disorders such as cancer and cardiovascular diseases.	de Pascual-Teresa et al., 2010

ACKNOWLEDGEMENTS

This work was carried out with the support of the "Cooperative Research Program for Agriculture Science & Technology Development (Project No. PJ906938)" Rural Development Administration, Republic of Korea.

REFERENCES

Annadurai T, Muralidharan AR, Joseph T, Hsu MJ, Thomas PA, Geraldine P. Antihyperglycemic and antioxidant effects of a flavanone, naringenin, in streptozotocin-nicotinamide-induced experimental diabetic rats. *J Physiol Biochem* 2012;68:307-18.

Calderón-Montaña JM, Burgos-Morón E, Pérez-Guerrero C, López-Lázaro M. A review on the dietary flavonoid kaempferol *Mini Rev Med Chem* 2011;11:298-344.

Corradini E, Foglia P, Giansanti P, Gubbiotti R, Samperi R, Lagana A. Flavonoids: chemical properties and analytical methodologies of identification and quantitation in foods and plants. *Nat Prod Res* 2011;25:469-95.

de Pascual-Teresa S, Moreno DA, García-Viguera C. Flavanols and anthocyanins in cardiovascular health: a review of current evidence. *Int J Mol Sci* 2010;11:1679-703.

Devi VG, Rooban BN, Sasikala V, Sahasranamam V, Abraham A. Isorhamnetin-3-glucoside alleviates oxidative stress and opacification in selenite cataract in vitro. *Toxicol In Vitro* 2010;24:1662-9.

Duchnowicz P, Broncel M, Podśędek A, Koter-Michalak M. Hypolipidemic and antioxidant effects of hydroxycinnamic acids, quercetin, and cyanidin 3-glucoside in hypercholesterolemic erythrocytes (in vitro study). *Eur J Nutr* 2012;51:435-43.

Falcone Ferreyra ML, Rius SP, Casati P. Flavonoids: biosynthesis, biological functions, and biotechnological applications. *Front Plant Sci* 2012;3:222.

Ferrer J, Austin M, Stewart CJ, Noel J. Structure and function of enzymes involved in the biosynthesis of phenylpropanoids. *Plant Physiol Biochem* 2008;46:356-70.

- Galleano M, Calabro V, Prince PD, Litterio MC, Piotrkowski B, Vazquez-Prieto MA et al. Flavonoids and metabolic syndrome. *Ann N Y Acad Sci* 2012;1259:87-94.
- Gong G, Qin Y, Huang W, Zhou S, Yang X, Li D. Rutin inhibits hydrogen peroxide-induced apoptosis through regulating reactive oxygen species mediated mitochondrial dysfunction pathway in human umbilical vein endothelial cells. *Eur J Pharmacol* 2010;628:27-35.
- Gonzalez-Paramas AM, Santos-Buelga C, Duenas M, Gonzalez-Manzano S. Analysis of flavonoids in foods and biological samples. *Mini Rev Med Chem* 2011;11:1239-55.
- Hyun J, Woo Y, Hwang DS, Jo G, Eom S, Lee Y et al. Relationships between structures of hydroxyflavones and their antioxidative effects. *Bioorg Med Chem Lett* 2010;20:5510-3.
- Izzi V, Masuelli L, Tresoldi I, Sacchetti P, Modesti A, Galvano F et al. The effects of dietary flavonoids on the regulation of redox inflammatory networks. *Front Biosci* 2012;17:2396-418.
- Kay CD, Hooper L, Kroon PA, Rimm EB, Cassidy A. Relative impact of flavonoid composition, dose and structure on vascular function: A systematic review of randomised controlled trials of flavonoid-rich food products. *Mol Nutr Food Res* 2012;56:1605-16.
- Li R, Yuan C, Dong C, Shuang S, Choi MM. In vivo antioxidative effect of isoquercitrin on cadmium-induced oxidative damage to mouse liver and kidney. *Naunyn Schmiedebergs Arch Pharmacol* 2011;383:437-45.
- Liu H, Zhang L, Lu S. Evaluation of antioxidant and immunity activities of quercetin in isoproterenol-treated rats. *Molecules* 2012a;17:4281-91.
- Liu B, Jian Z, Li Q, Li K, Wang Z, Liu L et al. Baicalein protects Human melanocytes from H₂O₂-induced apoptosis via inhibiting mitochondria-dependent caspase activation and the p38 MAPK pathway. *Free Radic Biol Med* 2012b;53:183-93.
- Margina D, Ilie M, Manda G, Neagoe I, Mocanu M, Ionescu D et al. Quercetin and epigallocatechin gallate effects on the cell membranes biophysical properties correlate with their antioxidant potential. *Gen Physiol Biophys* 2012;31:47-55.
- Marković ZS, Mentus SV, Dimitrić Marković JM. Electrochemical and density functional theory study on the reactivity of fisetin and its radicals: implications on in vitro antioxidant activity. *J Phys Chem A* 2009;113:14170-9.
- Morales J, Günther G, Zanocco AL, Lemp E. Singlet oxygen reactions with flavonoids. A theoretical - experimental study. *PLoS One* 2012;7:e40548.
- Park CE, Yun H, Lee EB, Min BI, Bae H, Choe W et al. The antioxidant effects of genistein are associated with AMP-activated protein kinase activation and PTEN induction in prostate cancer cells. *J Med Food* 2010;13:815-20.
- Rossato MF, Trevisan G, Walker CI, Klafke JZ, de Oliveira AP, Villarinho JG et al. Eriodictyol: a flavonoid antagonist of the TRPV1 receptor with antioxidant activity. *Biochem Pharmacol* 2011;81:544-51.
- Seelinger G, Merfort I, Schempp CM. Antioxidant, anti-inflammatory and anti-allergic activities of luteolin. *Planta Med* 2008;74:1667-77.

Verdan AM, Wang HC, García CR, Henry WP, Brumaghim JL. Iron binding of 3-hydroxychromone, 5-hydroxychromone, and sulfonated morin: Implications for the antioxidant activity of flavonols with competing metal binding sites. *J Inorg Biochem* 2011;105:1314-22.

Waisundara VY, Siu SY, Hsu A, Huang D, Tan BK. Baicalin upregulates the genetic expression of antioxidant enzymes in Type-2 diabetic Goto-Kakizaki rats. *Life Sci* 2011;88:1016-25.

Wang ZH, Ah Kang K, Zhang R, Piao MJ, Jo SH, Kim JS et al. Myricetin suppresses oxidative stress-induced cell damage via both direct and indirect antioxidant action. *Environ Toxicol Pharmacol* 2010;29:12-8.

Winkel-Shirley B. Flavonoid biosynthesis. a colorful model for genetics, biochemistry, cell biology, and biotechnology. *Plant Physiol* 2001;126:485–93.

Yang HL, Chen SC, Senthil Kumar KJ, Yu KN, Lee Chao PD, Tsai SY et al. Antioxidant and anti-inflammatory potential of hesperetin metabolites obtained from hesperetin-administered rat serum: an ex vivo approach. *J Agric Food Chem* 2012;60:522-32.