Editorial:

RECENT STUDIES ON FLAVONOIDS AND THEIR ANTIOXIDANT ACTIVITIES

Soo Cheon Chae¹, Jai-Heon Lee²*, Sang Un Park³*

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 DeltaPsi 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 (H₂O₂) 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 H₂O₂-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 ex-      | Annadurai et al., 2012                         |
| perimental diabetic rats.                                                  |                                                 |
| Eriodictyol acts as an antagonist of the transient potential vanilloid 1  | Rossato et al., 2011                           |
| (TRPV1) receptor and as an antioxidant.                                    |                                                 |
| Genistein significantly decreased the levels of reactive oxygen spe-      | Park et al., 2010                              |
| cies and induced the expression of the antioxidant enzymes, manga-      |                                                 |
| nese superoxide dismutase and catalase.                                   |                                                 |
| Flavonols and anthocyanins have greater antioxidant properties and        | Duchnowicz et al., 2012                        |
| exert greater influence on cholesterol concentration in erythrocyte      |                                                 |
| membranes than simple hydroxycinnamic acids.                              |                                                 |
| Kaempferol is a flavonoid found in many edible plants and in plants or   | de Pascual-Teresa et al., 2010                  |
| botanical products commonly used in traditional medicine. Epidemiologic- |                                                 |
| 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.                     |                                                 |

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-Montaño 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, Gubbio 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, Garcia-Viguera C. Flavanols and anthocyanins in cardiovascular health: a review of current evidence. Int J Mol Sci 2010;11:1679-703.

Duchiowicz P, Broncel M, Potscheidok 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, Dueñas 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 antioxidative and immunity activities of quercetin in isoproterenol-treated rats. Molecules 2012a;17:4281-91.
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.