Biological Forum – An International Journal **7**(2): 884-887(2015)

ISSN No. (Print): 0975-1130
ISSN No. (Online): 2249-3239

Effect of Phenolic Compounds as Antioxidant on Cell Oxidation: A Review

Hooshyar Ghafory*, Vahid Yousefinejad**, Kourosh Mohammadi and Muhammad Piri*******

**Liver and Digestive Research Center, Kurdistan University of Medical Sciences, Sanandaj, Iran*
***Assistant Professor, Liver & Digestive Research Center, Kurdistan University of Medical Sciences, Internal Medicine Department, Sanandaj, Iran.*
****Faculty of Veterinary Medicine, Sanandaj Branch, Islamic Azad University, Sanandaj, Iran*
*****Bachelor of Science, Master of Public Health and Medical student at Tehran University of Medical Science, Tehran, Iran*

(Corresponding author: Vahid Yousefinejad)
(Received 28 August, 2015, Accepted 29 November, 2015)
(Published by Research Trend, Website: www.researchtrend.net)

ABSTRACT: Research on the effects of dietary polyphenols on human health has developed considerably in the past decade. It strongly supports a role for polyphenols in the prevention of degenerative diseases, particularly cardiovascular diseases and cancers. The antioxidant properties of polyphenols have been widely studied, but it has become clear that the mechanisms of action of polyphenols go beyond the modulation of oxidative stress. So, this review paper was using the paper from PubMed to investigate the "Polyphenols: antioxidants and beyond". Additionally, in this paper we tried to investigate medical properties of polyphenols against diseases.

Keywords: Phenolic compounds, Antioxidant, Oxidation

INTRODUCTION

For million years, humankind is completely dependent on plants as source of carbohydrates, proteins and fats for food and shelter. In addition, plants are a valuable source of a wide range of secondary metabolites, which are used as pharmaceuticals, agrochemicals, flavours, fragrances, colours, biopesticides and food additives. The number of known chemical structures is estimated to be nearly fourfold greater than that in the microbial kingdom. The United State market sales of medicinal plant have risen up about US$ 3 billion per year (Ramachandra Rao and Ravishankar, 2002). During growth and maturation period in plants some substances can be found in structure of them which they have essential role in plant fortune. These substances called plants secondary metabolites (Hagerman and Buther, 1981; Hassanpour *et al*, 2011). It has been suggested that accumulation of secondary compounds in plants is dependent upon photosynthetic capacity, season, rain and temperature (Mooney *et al*, 1975). One of the most important secondary metabolites is polyphenols (e.g. tannins) (Hagerman and Buther, 1981; ChaichiSemsari *et al*, 2011; Hassanpour *et al*, 2011; Maheri-sis *et al*, 2011). A great deal of research with tannins has followed an approach that looks at biological relationships: taxonomy, phylogeny, biosynthesis, etc. Polyphenols are the most widely distributed class of plant secondary metabolites and several thousand different compounds have been identified. Polyphenols play many different roles in plant biology and human life, including UV protective agents, defensive compounds against herbivores and pathogens, contributors to plant colors, contributors to the taste of food and drink, and pharmaceuticals (Haslam,, 1989; Hassanpour *et al*, 2011).

Polyphenols are the most abundant antioxidants in the diet. Their total dietary intake could be as high as 1 g/d, which is much higher than that of all other classes of phytochemicals and known dietary antioxidants. For perspective, this is 10 times higher than the intake of vitamin C and 100 times higher than the intakes of vitamin E and carotenoids. Their main dietary sources are fruits and plant-derived beverages such as fruit juices, tea, coffee, and red wine. Vegetables, cereals, chocolate, and dry legumes also contain polyphenols. Despite their wide distribution in plants, the health effects of dietary polyphenols have come to the attention of nutritionists only rather recently (Scalbert *et al*. 2005).

Antioxidant activity

Oxidation of DNA, proteins and lipids by reactive oxygen species (ROS) plays an important role in aging and in a wide range of common diseases, including cancer and cardiovascular, inflammatory and neurodegenerative diseases, such as Alzheimer's disease and other age-related degenerative conditions (Borek, 1997). Research studies evidence that plant-based diets, in particular those rich in vegetables and fruits, provide a great amount of antioxidant phytochemicals, such as vitamins C and E, glutathione, phenolic compounds (flavonoids) and vegetable pigments, which offer protection against cellular damage (Dimitrios, 2006).

Polyphenols are strong scavengers against superoxide, hydrogen peroxide, hydroxy radicals, and nitric oxide produced by various chemicals. Chen and Ho (1994) extensively investigated the antioxidant properties of various tea polyphenols. Their study showed that the 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging ability of various tea polyphenols was EGCG > ECG > EGC > EC = TF-2 > TF-1 > TF. The DPPH radical-scavenging activity was proportional to the number of -OH groups in the catechins or theaflavins. The superoxide-scavenging activity of the catechins was EGCG > ECG > EGC > EC. All the theaflavins exhibited the same ability to inhibit the production of superoxide. The lipid oxidation-inhibition activity of the catechins was also EGCG > ECG > EGC > EC, which was the same trend found for the DPPH radical-scavenging activity and the superoxide scavenging activity. Recently, several studies have found that black tea and green tea offered protection against oxidative damage to red blood cells induced by a variety of inducers, e.g., H_2O_2, primaquine, 2,2'-azo-bis(2- amidinopropane) dihydrochloride (AAPH), phenylhydrazine(PHx), Cu^{2+}-ascorbic acid, and the xanthine/xanthine oxidase system (Halder and Bhaduri, 1998). Oral administration of green or black tea leaf powder inhibited the lipid peroxidation of liver induced by tert-butyl hydroperoxide in rats (Sano *et al*., 1995) while in the kidney, the antioxidant effect was observed only for the green tea-fed group.

As antioxidants, polyphenols may improve cell survival; as prooxidants, they may induce apoptosis and prevent tumor growth. However, the biological effects of polyphenols may extend well beyond the modulation of oxidative stress. One of the best-known examples involves the interaction of soy isoflavones with estrogen receptors and the effects of these compounds on endocrine function. These effects could explain the prevention by isoflavones of bone resorption among postmenopausal women. A detailed understanding of the molecular events underlying these various biological effects is essential for evaluation of the overall impact on disease risk and progression (Scalbert *et al*. 2005).

Effect of polyphenols on diabetic hyperglycemia

The diabetic hyperglycemia induces elevation of plasma levels of urea and creatinine which are considered as significant markers of renal dysfunction (Almdal and Vilstrup, 1988). It is showed significant increase in the level of plasma urea and creatinine in the diabetic groups. These results indicated that diabetes could be lead to renal dysfunction. While, after treatment of alloxan-diabetic rats with polyphenols, the level of urea was decreased. Similarly, the elevation of creatinine level caused by diabetes was declined after administration of polyphenols. The increase in the activities of plasma Aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), and alkaline and acid phosphatases (AlP, AcP) indicated that diabetes may be induced hepatic dysfunction.

Supporting our finding it has been found by Larcan *et al*. (1979) that liver was necrotized in diabetic patients. Therefore, the increment of the activities of AST, ALT, LDH, AlP and AcP in plasma may be mainly due to the leakage of these enzymes from the liver cytosol into the blood stream (Navarro *et al*., 1993), which gives an indication on the hepatotoxic effect of alloxan. On the other hand, treatment of the diabetic rats with polyphenols caused reduction in the activity of these enzymes in plasma compared to the mean values of diabetic group. These results are in agreement with those obtained by Ohaeri (2001) in rats. Furthermore, the improvement of the liver damage by oral administration of polyphenols could be confirmed through studying their effect on the level of plasma bilirubin. Rana *et al*. (1996) reported polyphenols increase in plasma bilirubin (hyper-bilirubenimia) may be resulted from the decrease of liver uptake, conjugation or increase bilirubin production from hemolysis and this finding coincided with the decrease in total erythrocyte counts. Also, the elevation in plasma bilirubin indicates liver damage as confirmed by the changes in the activities of plasma and liver enzymes.

Effect of polyphenols on sperm characteristics and testicular oxidative damage

Every day number of medical reports increases about rate of infertility in the world. Infertility is a multi-parametric phenomenon and wide range of factors influence on spermatogenesis and sperm quality which in these clinical manifestations, insufficient nutrition and toxins are the most prominent (Vincent *et al*., 2012). It is reported that spermatozoa has a high levels of polyunsaturated fatty acids (PUAFAs) and makes it vulnerable to ROS (Hsieh *et al*., 2006). Malondialdehyde is end product of lipid peroxidation and elevation in MDA level is sign of lipid peroxidation in testes. So, increase in MDA level results to irreversible effects on sperm fertility characteristics and leads to infertility (Hsieh *et al*., 2006). Several lines of evidence suggested phenolic compounds are high source of antioxidants and scavenging ROS by amplification intercellular antioxidant enzymes include SOD, GPx and CAT (Corzo-Marti´nez *et al*., 2007). It is suggested that a correlation exists between excessive ROS generation in semen and infertility (Hsieh *et al*., 2006). Recently it is suggest that presumably polyphenols juice protects semen oxidation in rat testes (Ghiasi Ghalehkandi *et al*., 2015).

Effect of polyphenols on lipid oxidation in meat

Information is available on the fatty acid composition of the meat (Romanelli *et al*., 2008), oil characteristics (Grompone *et al*., 2005), mineral content of the meat and meat technological parameters (Sales, 2006). However, information concerning the oxidative/antioxidant status of rhea meat is not known.

Oxidative changes are the main non-microbial causes of quality deterioration of meat (Xiong *et al*., 2007). Lipid oxidation in muscle foods is initiated by several components arising from both internal and external sources. For example, during handling, processing and storage of fresh meat, endogenous iron is partially responsible for the catalysis of lipid oxidation, formation of rancid odours and other off-flavours (Descalzo *et al*., 2005). However, endogenous antioxidant factors, such as enzymes, control the oxidation in muscle tissues. Enzymes, such as superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx), can counteract the meat oxidation (Daun & Åkesson, 2004). It is reported phenolic compounds impress their antioxidant role via these enzymes.

Effects of polyphenols on cardiovascular diseases

Polyphenols have been widely recognized as agents for prevention and treatment of cardiovascular diseases. The wealth of scientific literature supports the proposal that polyphenols have significant effects on lowering blood pressure, prevention of atherosclerosis, reduction of serum cholesterol and triglyceride, inhibition of platelet aggregation, and increasing fibrinolytic activity (Chan *et al*., 2013). Both experimental and clinical studies on different polyphenols preparations demonstrate these favorable cardiovascular effects. Garlic, as polyphenol source administration in rats suffering from hypercholesterolemia, induced by a high-cholesterol diet, significantly reduced serum cholesterol, triglyceride, and LDL, but there was no effect on serum HDL (Kamanna and Chandrasekhara, 1982). In in vitro experiments, polyphenol administration suppressed LDL oxidation and increased HDL, which may be one of the protective mechanisms of the beneficial effects of polyphenols in cardiovascular health (Rahman and Lowe, 2006).

Anti-tumor effect of polyphenols

Many in vitro and in vivo studies have suggested possible cancer-preventive effects of phenolic compounds preparations and their respective constituents. Phenolic compounds have been found to contain a large number of potent bioactive compounds with anticancer properties, largely allylsulfide derivatives. Different phenolic derivatives have been reported to modulate an increasing number of molecular mechanisms in carcinogenesis, such as DNA adduct formation, mutagenesis, scavenging of free radicals, cell proliferation and differentiation as well as angiogenesis. The growth rate of cancer cells is reduced by phenolic compounds, with cell cycle blockade that occurs in the G2/M phase (Capasso, 2013). In 1983, Conney *et al*. were first to demonstrate that hydroxylated flavonoids in tea had a potent inhibitory effect on mutagenic activity (Huang *et al*., 1997). Sugimura and his colleagues were first to use a two-stage skin carcinogenesis mouse model to demonstrate that topical application of EGCG inhibited tumor promotion induced by teleocidin in 7,12-dimethylbenz (a)anthracene (DMBA)-initiated mouse skin (Yoshizawa *et al*., 1987). Studies by Mukhtar *et al*. further showed that green tea polyphenols had a potent inhibitory effect on skin tumorigenicity in Sencar mice (Khan *et al*., 1988). In recent years, many studies demonstrated that topical application or oral feeding of a polyphenolic fraction from tea extract, and individual atechin derivatives, had anticarcinogenic effects in animal skin experiments (Katiyar and Mukhtar, 1997).

CONCLUSION

A considerable body of literature supports a role for oxidative stress in the pathogenesis of age-related human diseases and a contribution of dietary polyphenols to their prevention. The complex relationships between antioxidant status and disease are still poorly understood and have been studied intensively. More likely, cells respond to polyphenols mainly through direct interactions with receptors or enzymes involved in signal transduction, which may result in modification of the redox status of the cell and may trigger a series of redox-dependent reactions. Both antioxidant and pro-oxidant effects of polyphenols have been described, with contrasting effects on cell physiologic processes.

REFERENCE

Almdal, T.P., Vilstrup, H., (1988). Strict insulin treatment normalizes the organic nitrogen contents and the capacity of urea-N synthesis in experimental diabetes in rats. *Diabetologica* **31**: 114-118.

California evergreen srub (*Heteroeles erbutifolia*). *Oecologia*., **19**: 293-302.

Capasso A. (2013). Antioxidant action and therapeutic efficacy of *Allium sativum* L. *Molecules,* **18**: 690-700.

Chaichi Semsari M., Maheri Sis, N., Sadaghian, M.., Eshratkhah, B., & Hassanpour S. (2011). Effects of administration of industrial tannins on nutrient excretion parameters during naturally acquired mixed nematode infections in Moghani sheep. *J. Amer. Sci.,* **7**(6): 245-248.

Chan JY, Yuen AC, Chan RY, Chan SW. (2013). A review of the cardiovascular benefits and antioxidant properties of allicin. *Phytother Res*. **27**: 637-646.

Chen, C.W. and Ho, C.T. (1994) Antioxidant properties of polyphenols extracted from green and black teas. *J. Food Lipids*, **2**: 35-46.

Corzo-Marti´nez M, NCorzo, M Villamiel. (2007). Biological properties of onions and garlic. *Trends in Food Science & Technology,* **18**: 609-625.

Daun, C., & Åkesson, B. (2004). Comparison of glutathione peroxidase activity, and of total and soluble selenium content in two muscles from chicken, turkey, duck, ostrich and lamb. *Food Chemistry,* **85**: 295-303.

Descalzo, A. M., Insani, E. M., Biolatto, A., Sancho, A. M., García, P. T., Pensel, N. A., *et al*. (2005). Influence of pasture or grain-based diets supplemented with vitamin E on antioxidant/oxidative balance of Argentine beef. *Meat Science,* **70**: 35-44.

Dimitrios, B. (2006). Sources of natural phenolic antioxidants. *Trends in Food Science & Technology*, **17**(9): 505-512.

Ghiasi Ghalehkandi J., Hassanpour S., Issabeagloo E., Asghari A. (2015). Assessment of the effects of red onion (*Allium cepa* Linn) juice on semen oxidative status compared to Zn sulfate in rats. *Anim. Reprod.,* **12**(2): 298-304.

Grompone, M. A., Irigaray, B., & Gil, M. (2005). Composition and thermal properties of Rhea oil and its fractions. *European Journal of Lipid Science and Technology*, **107**: 762-766.

Hagerman A. E. & Buttler, L. G. (1981). The specificity of proanthocyanidin-proteininteractions. *J. Bio. Chem.,* (**256**): 4494-4497.

Halder, J. and Bhaduri, A.N. (1998). Protective role of black tea against oxidative damage of human red blood cells. *Biochem. Biophys. Res. Commun.,* **244**: 903-907.

Haslam E. (1989). Plant Polyphenols- Vegetable Tannins Revisited. Camb. University_Press, Cambridge, UK.

Hassanpour S., Sadaghian, M., Maheri Sis, N., Eshratkhah, B., & Chaichi Semsari, M. (2011). Effect of condensed tannin on controlling faecal protein excretion in nematode-infected sheep: in vivo study. *J. Amer. Sci.,* **7**(5), 896-900.

Hsieh Y, C Chang, C Lin. (2006). Seminal malondialdehyde concentration but not glutathione peroxidase activity is negatively correlated with seminal concentration and motility. *Int J Biol Sci,* **2**(1): 23-29.

Huang, M.T., Xie, J.G., Wang, Z.Y., Ho, C.T., Lou, Y.R., Wang, C. X., Hard, G.C. and Conney, A.H. (1997). Effects of tea, decaffeinated tea, and caffeine on UVB light-induced complete carcinogenesis in SKH-1 mice: demonstration of caffeine as a biologically important constituent of tea. *Cancer Res.,* **57**: 2623-2629.

Kamanna VS, Chandrasekhara N. (1982). Effect of garlic on serum lipoproteins cholesterol levels in albino rats rendered hypercholesteremic by feeding cholesterol. *Lipids,* **17**: 483-488.

Katiyar, S.K., Mohan, R.R., Agarwal, R. and Mukhtar, H. (1997) Protection against induction of mouse skin papillomas with low and high risk of conversion to malignancy by green tea polyphenols. *Carcinogenesis,* **18**: 497-502.

Khan, W.A., Wang, Z.Y., Athar, M., Bickers, D.R. and Mukhtar, H. (1988) Inhibition of the skin tumorigenicity of (±)-7□, 8□- dihydroxy-9□, 10□-epoxy-7,8,9,10,-tetrahydrobenzo[a] pyrenl by tannic acid, green tea polyphenols and quercetin in Sencar mice. *Cancer lett.,* **42**: 7-12.

Larcan, A., Lambert, H., Laprevote-Heully, M.C., Delorme, N., (1979). Light and electron microscopic study of hepatic lesions in the course of hyperlactatemia in diabetic patients. *Diabetes Metabolism* **5**: 103-112.

Maheri-Sis N., Chaichi Semsari, M., Eshratkhah, B., Sadaghian, M., Gorbani, A., & Hassanpour, S. (2011). Evaluation of the effects of Quebracho condensed tannin on faecal egg counts during naturally acquired mixed nematode infections in Moghani sheep. *Annals Biol. Res.,* **2**(2): 170-174.

Mooney, H. A., Harrison, A. T. & Morrow, P. A. (1975). Environmental limitations of photosynthesis on a

Rahman K, Lowe GM. (2006). Significance of garlic and its constituents in cancer and cardiovascular disease. *J Nutr*, **136**: 736S-740S.

Ramachandra Rao, S., Ravishankar G. A. (2002). Plant cell cultures: Chemical factories of secondary metabolites. *Biotechnol. Adv.,* **20**: 101-153.

Rana, S.V., Rekha, S., Seema, V., (1996). Protective effects of few antioxidants on liver function in rats treated with cadmium and mercury. *Indian Journal of Experimental Biology* **34**: 177-179.

Romanelli, P. F., Trabuco, E., Scriboni, A. B., Visentainer, J. V., & de Souza, N. E. (2008). Chemical composition and fatty acid profile of rhea (*Rhea americana*) meat. *Archivos Latinoamericanos de Nutricion*, **58**: 201-205.

Sales, J. (2006). The rhea, a ratite native to South America. Avian and Poultry Biology Reviews, **17**: 105-124.

Sano, M., Takahashi, Y., Yoshino, K., Shimoi, K., Nakamura, Y., Tomita, I., Oguni, I. and Konomoto, H. (1995) Effect of tea (*Camellia sinensis* L.) on lipid peroxidation in rat liver and kidney: a comparison of green and black tea feeding. *Biol. Pharmaceutical Bull*., **18**: 1006-1008.

Scalbert A, Johnson IT, Saltmarsh M. (2005). Polyphenols: antioxidants and beyond. *Am J Clin Nutr;* **81**(suppl): 215S-7S.

Vincent P, SL Underwood, C Dolbec, N Bouchard, T Kroetsch, P Blondin. (2012). Bovine semen quality control in artificial insemination centers. *Anim Reprod*, **9**(3): 153-165.

Xiong, Y. L., Mullins, O. E., Stika, J. F., Chen, J., Blanchard, S. P., & Moody, W. G. (2007). Tenderness and oxidative stability of post-mortem muscles from mature cows of various ages. *Meat Science,* **77**: 105-113.

Yoshizawa, S., Horiuchi, T., Fujiki, H., Yoshida, T., Okuda, T. and Sugimura, T. (1987) Antitumor promoting activity of (-)-epigallocatechin gallate, the main constituent of "tannin" in green tea. *Phytother. Res.,* **1**: 44-47.