

Antioxidative Properties of Polyphenolic Compounds of Plants

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ABSTRACT

Polyphenols are present in a variety of plants utilized as important components of both human and animal diets. The structure of natural polyphenols varies from simple molecules, such as phenolic acids, to highly polymerized compounds, such as condensed tannins. Structural variations within the rings subdivide the flavonoids into several families: flavonoids, flavones, flavanols, isoflavones, anthocyanidins and others.

This review article summarizes properties of polyphenolic compounds their distribution in plants, catabolism, and the structure-activity relationships. Polyphenols probably protect LDL oxidation in vivo with significant consequences in atherosclerosis and also protect DNA from oxidative damage with important consequences in the age-related development of some cancers. They also inhibit lipid peroxidation, lower blood cholesterol level, and decrease atherosclerosis and cardiovascular diseases. Polyphenolic compounds inhibit cancer, while some polyphenolic compounds have estrogen-like activities. Uptake of dietary antioxidative agents to decrease the risk of cancer, cardiovascular, and other diseases plays an important role in preventive medicine.

Keywords : antioxidant、 Polyphenolic Compounds、 flavonoids

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REFERENCES

- 1.山根一元。1998。綠茶健康法。第40-53頁。主婦之友出版事業有限公司。台北，台灣。
- 2.小國伊太郎著。2007。綠茶與健康。第43-46頁。天佑資訊。台北，台灣。
- 3.中?洋子、蒲原聖可。2005。營養素全書-植物性化學物質篇。第33-40頁。世茂出版。台北，台灣。
- 4.尤新輝。1997。簡介茶多元酚成分之機能性及其應用。食品調配料之加工與應用。食品工業發展研究所卅週年紀念叢書系列。食品工業發展研究所。新竹，台灣。
- 5.王志偉。2004。茶葉兒茶素之生理活性。國立臺灣海洋大學食品科學系碩士論文。基隆，台灣。
- 6.王增興著。2005。葡萄籽萃取物OPC的威力。第44-49頁。青春出版。台北，台灣。
- 7.吳映蓉著。2008。植物素防癌抗老調節免疫力。第25-87頁。臉譜出版。台北，台灣。
- 8.呂鋒洲著。1999。神奇抗氧化劑。第35-42頁。元氣齋。台北，台灣。
- 9.呂麗琴。2003。白藜蘆醇對人類大腸癌細胞株生長抑制作用之訊號傳遞機轉。私立實踐大學食品營養研究所。台北，台灣。
- 10.阮逸明、陳英玲。1998。茶葉中兒茶素萃取及純化之研究。台灣茶葉研究彙報。17:1-8。
- 11.林天送。1994。自由基與健康。科學月刊。25:515-21。
- 12.林天送。1994。人體自由基知多少?。健康世界雜誌。228:20-24。
- 13.肯尼士 庫柏著。2001。如何去除自由基。第35-42頁。世潮出版。台北，台灣。
- 14.施瑞瑄著。2009。自然葡萄酒。第37-42頁。商周出版。台北，台灣。
- 15.胡家碩、蕭千佑。2006。多酚年代。第24-97頁。星盒子出版。台北，台灣。
- 16.原征彥。1998。兒茶素(Catechin)類的生理活性作用(1)。茶多酚在食品保健食品產業之製造及應用研討會。11。食品工業發展研究所。新竹，台灣。
- 17.孫璐西、吳宜亮、林志城。2004。茶與其生理保健作用。元培學報。40週年校慶特輯。83-96。
- 18.徐任生主編。2006。天然產物化學導論。第125-140頁。科學出版。大陸。
- 19.桑野和民。1995。綠茶健康法。第22-84頁。暖流出版社。台北，台灣。
- 20.翁?家編著。2009。白藜蘆醇。第44-51頁。成龍健康禮約。台北，台灣。
- 21.高清玉著。1998。自由基。第25-39頁。活泉出版。台北，台灣。
- 22.敏濤、章巧敏。2006。葡萄健康魔法書。第88-94頁。智慧大學。台北，台灣。
- 23.陳英玲。2005。茶葉的保健功效。科學發展391:66-73。行政院農委會茶葉改良場。
- 24.陳清泉。1999。兒茶素之抗癌及抗腫瘤效應。食品工業月刊31(9):1-15。
- 25.陳清泉。2001。茶葉之兒茶素的機能及應用。食品市場資訊。90(8):16-23。
- 26.郭智宏。1999。兒茶素在生理抗氧化上之作用。食品工業月刊。31(9):27-33。
- 27.曾仁傑。2004。葡萄皮中花青素最佳萃取條件之評估及其經驗模式之建立。屏東科技大學國立屏東科技大學食品科學研究所碩士論文。屏東，台灣。
- 28.曾馨誼、許瑞瑱、盧訓。2007。2007年國內保健食品產業概況分析。中華穀類食品工業技術研究所。台北，台灣。
- 29.萊斯特派克·卡羅科曼。2008。抗氧化物的奇蹟。第35-71。原水出版。台北，台灣。
- 30.楊明玉。2000。以氣相層析質譜儀分析氧化壓力指標-水楊酸鹽產物並評估多酚性化合物清除氫氧自由基之能力。私立台北醫學院藥學研究所。台北，台灣。

。31.楊清木。2000。綠茶多元酚的特點與機能性。茶訊89(09):3-4。32.楊新玲著。2009。五色蔬果養生法。第30-50頁。活泉出版。台北，台灣。33.葉銘溪。2007。綠茶麵條之研發與品質分析。私立大葉大學生物產業科技學系研究所。彰化，台灣。34.劉芳珍著。2008。多了多酚就健康多多。第25-29頁。常春月刊。台北，台灣。35.錢明賚。1999。植物中之多元酚化合物-單寧。食品工業31(6):44-53。36.羅珮文。2001。台灣數種特有水果抗氧化活性及清除自由基能力之評估。私立輔仁大學食品營養研究所碩士論文。台北，台灣。37.蘇瓦茲著。2000。蘇老師辦化學。第100-125頁。天下文化出版。台北，台灣。38.Abe, L. and T. Tanaka. 2001. Ellagitannins and hexahydroxydiphenoyl esters as inhibitor of vertebrate squalene oxidase. *J. Nat. Prod.* 64:1010-1014.39.Abu-Amsha, R., Croft, K. D., Puddey, I. B., Proudfoot, J. M. and Beilin, L. J. 1996. Phenolic content of various beverages determines the extent of inhibition of human serum and low-density lipoprotein oxidation in vitro: identification and mechanism of action of some cinnamic acid derivatives from red wine. *Clin. Sci.* 91: 449-58.40.Afaq, F., Ahmad, V.M. and Ahmad, M. 2003. Prevention of short-term ultraviolet B radiation-mediated damages by resveratrol in SKH-1 hairless mice. *Toxicol Appl Pharmacol*, 186 : 28 – 37.41.Ahmad, N., Denise, K.F., N. Anna-Liisa., and Hasan, M. 1997. Green tea constituent epigallocatechin-3-gallate and induction of apoptosis and cell cycle arrest in human carcinoma cells. *Cancer* 1.89:1881-1885.42.Alexandrakis, M. G., Kyriakou, D. S., Kempuraj, D., Huang, M., Boucher, W., Seretakis, D. and Theoharides, T. C. 2003. The isoflavone genistein inhibits proliferation and increases histamine content in human leukemic mast cells. *Allergy Asthma Proc.* 24: 373-377.43.Amal, Abu-Shakra., Eric, T., McQueen. and Michael, L. 2000. Cunningham: Rapid analysis of base-pair substitution induced by mutagenic drugs through their oxygen radical or epoxide derivatives. *Mutation Research* 470,11-8.44.Anggard, E. 1994. Nitric oxide: Mediator, murderer, and medicine. *Lancet*; 343: 191-306.45.Anderson, J. J., Anthony, M. S., Cline, J. M., Washburn, S. A. and Garner, S. C. 1999. Health potential of soy isoflavones for menopausal women. *Public Health Nutr.* 2: 489-504.46.Arai, Y., Watanabe, S., Kimira, M., Shimo, K., Mochizuki, R. and Kinoshita, N. 2002. Dietary intakes of flavonols, flavones and isoflavones by Japanese women and the inverse correlation between quercetin intake and plasma LDL cholesterol concentration. *J. Nutr.* 130: 2243-2250.47.Arora, A., Byrem, T. M., Nair, M. G. and Strasburg, G. M. 2000. Modulation of liposomal membrane fluidity by flavonoids and isoflavonoids. *Arch Biochem Biophys.* 373: 102-109.48.Aviram M. and Fuhrman, B. 2002. Wine flavonoids protect against LDL oxidation and atherosclerosis. *Ann. N. Y. Acad. Sci.* 957:146-161.49.Aziz, AA., Edwards, CA., Lean MEJ. and Crozier A. 1998. Absorption and excretion of conjugated flavanols, including quercetin-4'-O-b-glucoside and isorhamnetin-4'-O-b-glucoside by human volunteers after the consumption of onions. *Free Rad Res* 29:257-269.50.Balentin, D. A., S. Wiseman, and L. C. Bouwens. 1997. The chemistry of tea flavonoids. *Critical Reviews in Food Science & Nutrition* 37:693-704.51.Belinky, P. A., Aviram, M., Mahmood, S. and Vaya, J. 1998. Structural aspects of the inhibitory effect of glabridin on LDL oxidation. *Free Rad. Biol. Med.* 24(9): 1419-29.52.Bernhard, D., Schwaiger, W., Crazzolara, R., Tinhofer, I., Kofler, R. and Csordas, A. 2003. Enhanced MTT-reducing activity under growth inhibition by resveratrol in CEM-C7H2 lymphocytic leukemia cells. *Cancer Lett.* 195: 193-199.53.Birt, D. F., Hendrich, S. and Wang, W. 2001. Dietary agents in cancer prevention: flavonoids and isoflavonoids. *Pharmacol. Ther.* 90: 157-177.54.Boersma, B. J., Barnes, S., Kirk, M., Wang, C. C., Smith, M., Kim, H., Xu, J., Patel, R. and Darley-Usmar, V. M. 2001. Soy isoflavonoids and cancer metabolism at the target site. *Mutat. Res.* 480-481: 121-127.55.Booth, C., Hargreaves, D. F., Hadfield, J. A., McGown, A. T. and Potten, C. S. 1999. Isoflavones inhibit intestinal epithelial cell proliferation and induce apoptosis in vitro. *Br. J. Cancer* 80: 1550-1557.56.Bot. Bull., Acad. Sin. 1996. Chen and Pan Assay of superoxide dismutase activity Assay of superoxide dismutase activity by combining electrophoresis and densitometry. 37: 107-1157. Bouic, P. J. and Lamprecht, J. H. 1999. Plant sterols and sterolins: a review of their immune-modulating properties. *Altern. Med. Rev.* 4: 170-177.58.Boveris AD., Galatro A, Puntarulo S. 2000. Effect of nitric oxide and plant antioxidants on microsomal content of lipid radicals. *Biol Res* 33: 159-165.59.Brown, BG., Zhao, XQ., Chait, A., Frohlich, J., Cheung, M., Heise, N., Dowdy, A., DeAngelis, D., Fisher, LD. and Albers, J. 1998. Lipid altering or antioxidant vitamins for patients with coronary disease and very low HDL cholesterol?: the HDL-Atherosclerosis Treatment Study Design. *Can J Cardiol.*;14 (suppl A): 6A – 13A.60.Brown, BG., Zhao, XQ., Chait, A., Frohlich, J., Cheung, M., Heise, N., Dowdy, A., DeAngelis, D., Fisher, LD. and Albers, J. Lipid altering or antioxidant vitamins for patients with coronary disease and very low HDL cholesterol: the HDL-Atherosclerosis Treatment Study Design. *Can J Cardiol.* 1998. 14 (suppl A): 6A – 13A.61.Bravo, L. 1998. Polyphenols: Chemistry, dietary sources, metabolism, and nutritional significance. *Nutr Rev* 56:317-333.62.Bronner, YL. 1996. Nutritional status outcomes for children: ethnic, cultural, and environmental contexts. *J Am Diet Assoc* 96:891-903.63.Brownson, D. M., Azios, N. G., Fuqua, B. K., Dharmawardhane, S. F. and Mabry, T. J. 2002. Flavonoid effects relevant to cancer. *J. Nutr.* 132: 3482S-3489S.64.Cao, G., E. Sofic, and R. Prior. 1996. Antioxidant capacity of tea and common vegetables. *J Agric Food Chem.* 44:3426-3431.65.Cao, Y., Cao, R. and Brakenhielm, E. 2002. Antiangiogenic mechanisms of diet-derived polyphenols. *J. Nutr. Biochem.* 13, 380-390.66.Carreras, MC., Schpfer, F., Lisdero, C., Riobo, N. and Poderoso, JJ. 2000. Mitochondrial function and nitric oxide utilization. *Biol Res* 33: 175-181.67.Cheong, H., Ryu, SY., Oak, MH., Cheon, SH., Yoo, GS. and Kim, KM. 1998. Studies of structure activity relationship of flavonoids for the anti-allergic actions. *Arch Pharm Res*; 21(4): 478-80.68.Cheung, MC., Zhao, XQ., Chait, A., Albers, JJ. and Brown, BG. 2001. Antioxidant supplements block the response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL. *Arterioscler Thromb Vasc Biol.* 21: 1320 – 1326.69.Choi, Y. J., Kang, J. S., Park, J. H., Lee, Y. J., Choi, J. S. and Kang, Y. H. 2003. Polyphenolic flavonoids differ in their antiapoptotic efficacy in hydrogen peroxide-treated human vascular endothelial cells. *J. Nutr.* 133: 985-991.70.Chopro, M., Fitzsimons, PE., Strain, JJ., Thurnham, DI. and Howard, AN. 2000. Nonalcoholic wine extract and quercetin inhibit LDL oxidation without affecting plasma antioxidant vitamin and carotenoid concentrations. *Clin Chem*;46:1162-70.71.Clifford, MN. 1999. Chlorogenic acids and other cinnamates: nature, occurrence and dietary burden. *J Sci Food Agric* 79:362-372.72.Cowan, M. M. 1999. Plant products as antimicrobial agents. *Clin Microbiol Rev.* 12: 564-582.73.Cox, BD., Whithelow, MJ. and

Prevost, AT. 2000. Seasonal consumption of salad vegetables and fresh fruit in relation to the development of cardiovascular disease and cancer. *Public Health Nutr* 3:19-29.

74.Crespy, V. and G. Willianson. 2004. A review of the health effect of green tea catechins in vivo animal models. *J.Nutr.*134:3431-3440.

75.Crespy, V. and G. Willianson. 2004. A review of the health effect of green tea catechins in vivo animal models. *J.Nutr.*134:3431-3440.

76.Crozier A, Burns J, Aziz AA, Stewart AJ, Rabiasz HS, Jenkins GI, Edwards CA, Lean MEJ. 2000. Antioxidant flavonols from fruits, vegetables and beverages: measurements and bioavailability. *Biol Res* 33: 79-88.

77.Das, NP. and Griffiths, LA. 1969. Studies on flavonoid metabolism. Metabolism of (+)-[14C] catechin in the rat and guinea pig. *Biochem J* 115:831-836.

78.Das NP, Sothy SP .1971. Studies on flavonoid metabolism. Biliary and urinary excretion of metabolites of (+)-(U-14 C) catechin. *Biochem J* 125:417-423.

79.Dawn, C. Schwenke. 1998. Antioxidants and atherogenesis. *J. Nutr. Biochem.* 9: 424-445.

80.Deak, G., Muzes, G., Lang, I., Nekam, K., Gonzalez-Cabello, R., Gergely P. and Feher, J. 1990. Effects of two bioflavonoids on certain cellular immune reactions in vitro. *Acta. Physiol. Hung.* 76: 113-121.

81.Dreosti, I. E. 2000. Antioxidant polyphenols in tea, cocoa and wine. *Nutri.* (16): 692-694.

82.Eastwood, MA. 1999. Interaction of dietary antioxidants in vivo: how fruit and vegetables prevent disease? *Q J Med* 92:527-530.

83.Ebeler, S.E., Brennehan, C.A., Kim, G. -S., Jewell, W.T., Webb, M.R., Chacon-Rodriguez, L., MacDonald, E.A., Cramer, A.C., Levi, A., Ebeler, J.D., Islas- Trejo, A., Kraus, A., Hinrichs, S.H. and Clifford, A.J. 2002. Dietary catechin delays tumor onset in a transgenic mouse model. *Am. J. Clin. Nutr.* 76, 865-872.

84.Edwards, S. W. 1995. Cell signaling by integrins and immunoglobulin receptors in primed neutrophils. *TIBS.* 20, 362-7.

85.Elattar, T. M. and Virji, A. S. 2000. The inhibitory effect of curcumin, genistein, quercetin and cisplatin on the growth of oral cancer cells in vitro. *Anticancer Res.* 20: 1733-1738.

86.Frankel, EN., Waterhouse, AL. and Teissedre, PL. 1995. Principal phenolic phytochemicals in grapes and wines. *J Agric Food Chem*:43:890-4.87.Frankel, E. N., Bosanek, C. A., Meyer, A. M., Silliman, K. and Kirk, L. L. 1998. Commercial grape juices inhibit the in vitro oxidation of human low density lipoproteins. *Food Chem.* 46, 834-838.

88.Frei, B. and Higdon, J. V. 2003. Antioxidant activity of tea polyphenols in-vivo evidence from animal studies. *J. Nutr.*133:3275s-3284s.

89.Fremont, L. 2000. Biological effects of resveratrol. *Life Sci.* 66, 663-673.

90.Fuhrman, B., Volkova, N., Kaplan, M., Presser, D., Attias, J., Hayek, T. and Aviram, M. 2002. Antiatherosclerotic effects of licorice extract supplementation on hypercholesterolemic patients: increased resistance of LDL to atherogenic modifications, reduced plasma lipid levels, and decreased systolic blood pressure. *Nutrition.* 18: 268-273.

91.Galati, G., Moridani, M. Y. and Chan, T. S. 2001. Quercetin: glutathione oxidation and conjugation. *Free Radic. Biol. Med.* 30: Peroxidative metabolism of apigenin and naringenin versus luteolin and 370-382.

92.Gali-Muhtasib, H.U., Yamout, S. Z. and Sidani, M.M.1999. Plant tannins as inhibitors of hydroperoxide production and tumor promotion induced by Ultraviolet radiation in mouse skin in vivo. *Oncol Rep.* 6:547 – 83.

93.Gaulejac, N., Glories, Y and Vivas, N. 1999. Free radical scavenging effect of anthocyanins in red wines. *Food Res. Inter.* 32: 37-333.

94.Gerritsen, M. E., Carley, WW., Ranges, GE. Shen, C-P., Phan, SA., Ligon, GF. and Perry, CA. 1995. Flavonoids inhibit cytokine-induced endothelial cell adhesion protein gene expression. *Am J Pathol* 147:278-292.

95.Gerritsen, M. E. 1998. Flavonoids: inhibitors of cytokine induced gene expression. *Adv. Exp. Med. Biol.* 439: 183-190.

96.Ginter, E. 2000. Effect of free radicals and antioxidant on the vascular wall. *Vnitr.Lek.*46:354-359.

97.Gillman MW, Cupples LA, Gagnon D, Posner BM, Ellison RC, Casstelli WP, Wolf PA. 1995. Protective effect of fruits and vegetables on development of stroke in men. *J Am Med Assoc* 273:1113-1117.

98.Gomes, A., J. R. Vedasiromone, M. Das, R. M. Sharma, and D. K. Ganguly. 1983. Anti-Hyperglycemic effect of black tea in rat. *Journal of Ethnopharmacol.*46:232-234.

99.Gryglewski, R. J., Korbut, R., Robak, J. and Swies, J. 1987. On the mechanism of anti-thrombotic action of flavonoids. *Biochem. Pharmacol.* 36: 317-322.

100.Guardia, T., Rotelli, A. E., Juarez, A. O. and Pelzer, L. E. 2001. Anti-inflammatory properties of plant flavonoids. Effects of rutin, quercetin and hesperidin on adjuvant arthritis in rat. *Farmacol.* 56: 683-687.

101.Gupta, S., Nihal, A., Rajiv, M. R., Mirza, H. M. and M. Hasan. 1999. Prostate cancer chemoprevention by green tea in vitro and in vivo inhibition of testosterone-mediated induction of ornithine decarboxylase. *Cancer Res.*59:2115-2120.

102.Halliwell, B, and Gutteridge, JMC. 1984. Oxygen toxicity, oxygen radicals, transition metals and disease. *Biochem J*; 219: 1-14.

103.Halliwell, B. and Gutteridge, JMC. 1989. Free radical in biology and medicine. 2nd ed. Oxford: Clarendon Press; pp. 1-81.

104.Halliwell, B. and Kaur, H. Detection of hydroxyl radical by aromatic hydroxylation. *Method Enzym* 1994; 233: 67-82.

105.Halliwell, B. 1994. Free radical and antioxidant: A personal view. *Nutr. Rev.* 52: 253-265.

106.Halliwell, B. 1999. Establishing the significance and optimal intake of dietary antioxidants: The biomarker concept. *Nutr Rev* 57:104-113.

107.Hara, Y. and Honda, M. 1990. The inhibition of amylase by tea polyphenols. *Agric.Biol.Chem.*54:1939-1945.

108.Hara, Y., Matsuzaki, S. and Nakamura, K. 1989. Antitumor activity of tea catechins. *J. Jpn. Soc.Food Sci.*,43:39-45.

109.Harborne, JB. 1980. Plant phenolics. In: BELL EA, CHARLWOOD BV (eds) *Encyclopedia of Plant Physiology*, volume 8 Secondary Plant Products, Springer-Verlag, Berlin Heidelberg New York. Pp:329-395.

110.Hazarika, M. and Mahanta, PK. 1983. Some studies on carotenoids and their degradation in black tea manufacture. *Journal of the Science of Food and Agric* ,34:1390-1396.

111.Heim, K. E., Tagliaferro, A. R. and Bobilya, D. J. 2002. Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships. *J. Nutr. Biochem.* 13: 572-584.

112.Hertog, M.G.L., Feskens, EJM., Hollman, PCH., Katan, MB. and Kromhout, D. 1993. Dietary antioxidant flavonoids and risk of coronary heart disease: the Zutphen elderly study. *Lancet* 342:1007-1011.

113.Hiroyuki, U. K.E.D.A. 2000. Essay of Enzyme Superoxide Dismutase(SOD), *Rev. Dojindo Newsletter Vol.*3.

114.Hodnick, WF. and Pardini, RS .1998. Inhibition of mitochondrial function by flavonoids. In: RICE-EVANS, PACKER L (eds) *Flavonoids in Health and Disease*. New York: Marcel Dekker Inc., New York. pp:179-197.

115.Hollman, PC., Van Trijp JM., Mengelers, MJ., De Vries JH. and Katan, MB .1997. Bioavailability of the dietary antioxidant flavonol quercetin in man. *Cancer Lett* 114:139-140.

116.Horvath, P.M. 1983. Synergistic effect of vitamin E and selenium in the chemoprevention of mammary carcinogenesis in rats. *Cancer Research.*43:5331-5341.

117.Horvathova, K., Novotny, L. and Vachalkova, A. 2003. The free radical scavenging activity of four flavonoids determined by the comet assay. *Neoplasma.* 50: 291-295.

118.Hubbard, G. P., Wolfram, S., Lovegrove, J. A. and Gibbins, J. M. 2003.

The role of polyphenolic compounds in the diet as inhibitors of platelet function. *Proc. Nutr. Soc.* 62: 469-478.119.Jacob, RA and Burri, B. 1996. Oxidative damage and defense. *Am. J. Clin. Nutr.* 63: 985-990.120.Jang, M., Cai, L., Udeani, G.O., Slowing, K.V., Thomas, C.F., Beecher, C.W.W., Fong, H.H.S., Farnsworth, N.R., Kinghorn, A.D., Mehta, R.G., Moon, R.C., and Pezzuto, J.M. 1997. Cancer chemopreventive activity of resveratrol, a natural product derived from grapes. *Science* 275, 218-220.121.Janssen, K., Mensink, R. P., Cox, F. J., Harryvan, J. L., Hovenier, R., Hollman, P. C. and Katan, M. B. 1998. Effects of the flavonoids quercetin and apigenin on hemostasis in healthy volunteers: results from an in vitro and a dietary supplement study. *Am. J. Clin. Nutr.* 67: 255-262.122.Jankun, J., S. H.Selman, and R. Swiercz. 1997. Why drinking green tea could prevent cancer. *Nature*, 387:561.123.Joyeux, M., Lobstein, A., Anton, R. and Mortier, F. 1994. Comparative antilipoperoxidant,antinecrotic and scavenging properties of terpenes and biflavones from ginkgo and some flavonoids. *Planta Med.* 61:126-129.124.Jovanovic, SV., Steenken, S., Slimic, MG. and Hara, Y. 1998. Antioxidant properties of flavonoids: reduction potentials and electron transfer reactions of flavonoid radicals. In: RICE-EVANS, PACKER L (eds) *Flavonoids in Health and Disease*. New York: Marcel Dekker Inc., New York. p:137-161.125.Kaneko, T., Kaji, K. and Matsuo, M. 1994. Protection of linoleic acid hydroperoxide- induced by phenolic antioxidants. *Free Rad. Biol. Med.* 16(3): 405-9.126.Kao, Y. H., A.H.Richard, and S. Liao. 2000. Modulation of endocrine systems and food intake by green tea epigallocatechin gallate.*Endocrinol* 141:980-987.127.Kaul, A. and Khandujk, KL. 1998. Polyphenols inhibit promotional phase of tumorigenesis: relevance of superoxide of superoxide radicals. *Nurt Cancer* 32:81-85.128.Keovil, J. G., Osman, H. E., Reed, J. D. and Folts, J. D. 2000. Grape juice, but not orange juice or grapefruit juice, inhibits human platelet aggregation. *J. Nutr.* 130: 53-56.129.Kimata, M., Inagaki, N. and Nagai, H. 2000. Effects of luteolin and other flavonoids on IgE-mediated allergic reactions. *Planta. Med.* 66: 25-29.130.Knekt, P., Jarvinen, R., Reunanen, A. and Maatela, J. 1996. Flavonoid intake and coronary mortality in Finland: a cohort study. *Brit Med J* 312:478-481.131.Knight, JA. 1999. The aging process. In: *Free Radicals, Antioxidant, Aging and Disease*. AACC Press, Washington, DC, pp. 64.132.Knekt, P. Kumpulainen, J., Jarvinen, R., Rissanen, H., Heliövaara, M., Reunanen, A., Hakulinen, T. and Aromaa, A. 2002. Flavonoid intake and risk of chronic diseases. *Am. J. Clin. Nutr.* 76: 560-568.133.Kobayashi, T., Nakata, T. and Kuzumaki, T. 2002. Effect of flavonoids on cell cycle progression in prostate cancer cells. *Cancer Lett.* 176: 17-23.134.Kunishiro, K., Tai, A. and Yamamoto, I. 2001. Effects of rooibos tea extract on antigen-specific antibody production and cytokine generation in vitro and in vivo. *Biosci. Biotechnol. Biochem.* 65: 2137-2145.135.Kuo, S. M. 1996. Antiproliferative potency of structurally distinct dietary flavonoids on human colon cancer cells. *Cancer Lett.* 110: 41-48.136.Kuo, S. M. 2002. Flavonoids and gene expression in mammalian cells. *Adv. Exp. Med. Biol.* 505: 191-200.137.Lean, ME., Noroozi, M., Kelly, I., Burns, J., Talwar, D., Sattar, N. and Crozier A. 1999. Dietary flavonols protect diabetic human lymphocytes against oxidative damage to DNA. *Diabetes* 48:176-181.138.Leighton, F, Cuevas A, Guasch V, Perez DD, Strobel P, San Martin A, Urzua U, Diez MS, Foncea R, Castillo O, Mizon C, Espinza MA, Urquiaga I, Rozowski J, Maiz A, Germain A .1999. Plasma polyphenols and antioxidants, oxidative DNA damage and endothelial function in a diet and wine intervention study in humans. *Drugs Exp Clin Res* 25:133-141.139.Le Marchand, L., Murphy, S. P., Hankin, J. H., Wilkens, L. R. and Kolonel, L. N. 2000. Intake of flavonoids and lung cancer. *J. Nat. Cancer Inst.* 92: 154-160.140.Leonard, SS., Xia, C., Jiang, BH., Stinefelt, B., Klandorf, H., Harris, GK. and Shi, X. 2003. Resveratrol scavenges reactive oxygen species and effects radical-induced cellular responses. *Biochem. Biophys. Res. Commun.* 309: 1017-1026.141.Lin, A., M., Chyi, B. Y., Wu, L.Y., Hwang, L. S. and Ho, L. T. 1998. The antioxidative property of green tea against iron-induced oxidative stress in rat brain. *Chin. J. Phys.* 41:189-194.142.Lin, J. K. 2002. Cancer chemoprevention by tea polyphenols through modulating signal transduction pathways. *Arch.Pharm. Res.* 25:561-571.143.Lopez-Lazaro, M. 2002. Flavonoids as anticancer agents: structure-activity relationship study. *Curr. Med. Chem. AntiCanc. Agents.* 2: 691-714.144.Lotito, S. B. and Fraga, C. G.1998. (+)-Catechin prevents human plasma oxidation. *Free Radic. Biol. Med.* 24(3):435-441.145.Manach, C., Morand, C., Demigne, C., Texier, O., Regeat, F. and Remesy C. 1997. Bioavailability of rutin and quercetin in rats. *FEBS Lett* 409:12-16 .146.Manach, C., Morand, C., Texier, O., Favier, ML., Agullo, G., Demigne, C., Regeat, F. and Remesy, C. 1995. Quercetin metabolites in plasma of rats fed diets containing rutin or quercetin. *J Nutr* 125:1911-1922.147.Manthey, J. A. 2000. Biological properties of flavonoids pertaining to inflammation. *Microcirculation* 7:S29-S34.148.Mangiapanè, H., Thomson, J., Salter, A., Brown, S., Bell, D. and White, D. A. 1992. The inhibition of low-density lipoprotein by (+) catechin, a naturally occurring flavonoid. *Biochem Pharmacol.* 43:445-450.149.Mcanlis, GT., Mceneny, J., Pearce, J. and Young, IS. 1999. Absorption and antioxidant effects of quercetin from onions, in man. *Eur J Clin Nutr* 53:92-96.150.Middleton, E. Jr. and Kandaswami, C. 1992. Effects of flavonoids on immune and inflammatory cell functions. *Biochem. Pharmacol.* 43: 1167-1179.151.Middleton, E. Jr. 1998. Effect of plant flavonoids on immune and inflammatory cell function. *Adv. Exp. Med. Biol.* 439: 175-182.152.Middleton, E. Jr., Kandaswami, C. and Theoharides, T. C. 2000. The effects of plant flavonoids on mammalian cells: implications for inflammation, heart disease, and cancer. *Pharmacol. Rev.* 52: 673-751.153.Mitscher, L.A., M. Jung, D. Shankel, J. H.Dou, L. Steele, and S.P.Pillai.1997. Chemoprotection a review of the potential therapeutic antioxidant properties of green tea (*Camellia sinensis*) and certain of its constituents. *Med Res Rev* 17:327-365.154.Mitsuaki, S., T., Michiko, S., Masazumi, S., Masakuni, D., Masakuni, M., Toshio., and Mari, M. Y. 2001. Simultaneous determination of twelve tea catechins by high-performance liquid chromatography with electrochemical detection. *Analyst*, 126:816-820.155.Miura, S., Watanabe, J., Tomita, T. Sano, M. and Tomita, I. 1994. Inhibitory effects of tea polyphenols (flavan-3-olderivatives) on Cu2+ mediated oxidative modification of low-density lipoprotein. *Biol Pharm. Bull.* 17:1567-1572.156.Mohamed, Al-Mamary., Ali, Al-Meerri. and Molham, Al-Habori. 2002. Antioxidant activity and total phenolics of different type of honey. *Nutr. Res.* 22: 1041-1047.157.Morand C, Crespy V, Manach C, Besson C, Demigne C, Remesy C .1998. Plasma metabolites of quercetin and their antioxidant properties. *Am J Physiol* 275:R212-R219.158.Morel, I., Cillard, P. and Cillard, J. 1998. Flavonoid-metal interactions in biological systems. In: RICE-EVANS, PACKER L (eds) *Flavonoids in Health and Disease*. New York: Marcel Dekker Inc. pp:163-177.159.Mukhtar, H. and Ahmad, N.

1999. Green tea in chemoprevention of cancer (Review) *Toxicol.Sci.*52 (2 suppl) :111-117.160.Muldoon, MF. and Kritchevsky, SB. 1996. Flavonoids and heart disease. *Brit Med J* 312:458-459.161.Namgoong, S. Y., Son, K. H., Chang, H. W., Kang, S. S. and Kim, H. P. 1994. Effects of naturally occurring flavonoids on mitogen-induced lymphocyte proliferation and mixed lymphocyte culture. *Life Sci.* 54: 313-320.162.Nigdikar SV, Williams NR, Griffin BA, Howard AN .1998.Consumption of red wine polyphenols reduces the susceptibility of low-density lipoproteins to oxidation in vivo. *Am J Clin Nutr* 68:258-265.163.Niki, E. 1992. Active oxygens and free radicals in biology. *J. Jpn. Oil Chem. Soc.* 41(9): 768-773.164.Nomura, M., Kimura, A., Zhiwei, H., Wei-Ya, M., M.Ken-ichi, H., Chung-S, Y. and Zigang, D. 2001. Inhibitory mechanisms of tea Polyphenols on the ultraviolet B-activated phosphatidylinositol 3-kinase-dependent pathway. *J. Biol. Chem.*276:46624-46631.165.Oberley, L.W. 2005. Mechanism of the tumor suppressive effect of MnSOD overexpression. *Biomed Pharmacother.*,59:143-148.166.Oguni, I., Nasu, K., Yamomoto, S. and Nomura, T. 1988. On the antitumor activity of fresh green tea leaf. *Agric. Biol. Chem.* 52:1879-1880.167.Olivero-Verbel, J. and Pacheco-Londono, L. 2002. Structure-activity relationships for the anti-HIV activity of flavonoids. *J. Chem. Inf. Comput. Sci.* 42:1241-1246.168.Pedersen, CB., Kyle, J., Jenkinson, AM., Gardner, PT., McPhoil, OB. and Duthie, GG. 2000. Effects of blueberry and croriberry juice consumption on the plasma antioxidant capacity of healthy female volunteers, *Eur J Clin Nutr*;54:405- 8.169.Peterson, J., Lagiou, P., Samoli, E., Lagiou, A., Katsouyanni, K., La Vecchia, C., Dwyer, J. and Trichopoulos, D. 2003. Flavonoid intake and breast cancer risk: a case--control study in Greece. *Br. J. Cancer* 89: 1255-1259.170.Pier-Giorgio, P. 2000. Flavonoids as antioxidants. *J Nat Prod*: 63: 1035-42.171.Piskula, M. K. and J. Terao. 1998. Accumulation of (-)-epicatechin metabolites in rat plasma after oral administration and distribution of conjugation enzymes in rat tissues. *Jul.*, 128(7):1172-1178.172.Rafat H, S., Josiane, C. and Pierre C. 1987. Hydroxyl radical scavenging activity of flavonoids. *Phytochemistry*; 26: 2489-91.173.Ren, W., Qiao, Z., Wang, H., Zhu, L. and Zhang, L. 2003. Flavonoids: Promising anticancer agents. *Med. Res. Rev.* 23: 519-534.174.Renaud, S., De Lorgeril, M. and Wine. 1992. Alcohol, platelets and the French paradox for coronary heart disease. *Lancet*: 339:1523-6.175.Rice, CA., Miller, NJ. and Paganga, G .1997. Antioxidant properties of phenolic compounds. *Trends in Plant Science* 2:152-159.176.Rice-Evans, C., Miller, N. and Paganga, G. 1996. Structure antioxidants activity relationship of flavonoid and phenolic acids. *Free Rad. Biol.Med.* 20(7): 933-956.177.Rice-Evans, C., Miller, N. and Paganga, G. 1997. Antioxidants properties of phenolic compound. *Trends in Plant Sci.* 2(4): 152-159.178.Rice-Evans, C. 2001. Flavonoid antioxidants. *J. Pharm. Pharmacol.* 53: 653-668.179.Rifici, VA., Stephecin, EM., Schneider. and Khachadurian, AK. 1999. Red wine inhibits the cell-mediated oxidation of LDL and NDL *JAm Coil Nutr*:18:137-43.180.Rochelle, LG., Fischer, BM. and Adler, KB. 1998. Concurrent production of reactive oxygen and nitrogen species by airway epithelial cells in vitro. *Free Radic. Bio.Med.*, 24, 863-8.181.Ross, J.A. and Kasum, C.M. 2002. Dietary flavonoids: bioavailability, metabolic effects, and safety. *Annu. Rev. Nutr.* 22, 19-34.182.Rotelli, A. E., Guardia, T., Juarez, A. O., de la Rocha, N. E. and Pelzer, L. E. 2003. Comparative study of flavonoids in experimental models of inflammation. *Pharmacol. Res.* 48: 601-606.183.Sanchez, I., Gomez-Garibay, F., Taboada, J. and Ruiz, B. H. 2000. Antiviral effect of flavonoids on the dengue virus. *Phytother. Res.* 14: 89-92.184.Sato, T. and G. Miyata. 2000. The nutraceutical benefit, part : green tea. *Nutrition* 16:315-317.185.Satoh, K., Sakamoto, Y., Ogata, A., Nagai, F., Mikuriya, H., Numazawa, M., Yamada, K. and Aoki, N. 2002. Inhibition of aromatase activity by green tea extract catechins and their endocrinological effects of oral administration in rats. *Food Chem.,Toxicol.*40:925-933.186.Sfakianos J, Coward L, Kirk, M. and Barnes, S .1997. Intestinal uptake and biliary excretion of the isoflavone genistein in rats. *J Nutr* 127:1260-1268.187.Shalia, NA., Curtis, CG., Powell, GM. and Roy, AB. 1991. Sulphation of the flavonoids quercetin and catechin by rat liver. *Xenobiotica* 21:881-893.188.Sheehan, E. W., and Zematis, M. A..1983. A Constituent of *Pterocarpus marsupium*(-)-epicatechin, as a potential antidiabetic agent. *Journal of Natrura, Product*,46:2232-2234.189.Sheila, A., Wisemen, D. A. and F. Balz. 1997. Antioxidants in tea. *Crit Rev in Food Sci and Nutri.*,37 (8) :705-718.190.Shih, I.-M., Yu, J., He, T.-C., Vogelstein, B. and Kinzler, K.W. 2000. The β -catenin binding domain of adenomatous polyposis coli is sufficient for tumor suppression. *Cancer Res.* 60, 1671-1676.191.Sies, H. and Stahl, W. 1998. Lycopene: antioxidant and biological effects and its bioavailability in the human, *Experimental Biology & Medicine* . 218, 121-4.192.Siess, M. H., Le Bon, A. M., Canivenc-Lavier, M. C. and Suschetet, M. 2000. Mechanisms involved in the chemoprevention of flavonoids. *Biofactors* 12: 193-199.193.Subbaramaiah, K., Chung, W.J., Michaluart, P., Telang, N., Tanabe, T., Inoue, H., Jang, M., Pezzuto, J.M. and Dannenberg, A.J. 1998. Resveratrol inhibits cyclooxygenase-2 transcription and activity in phorbol ester-treated human mammary epithelial cells. *J. Biol. Chem.* 273, 21875-21882.194.Tikkanen, MJ. and Adlercreutz, H. 2000. Dietary soy-derived isoflavone phytoestrogens. Could they have a role in coronary heart disease prevention? *Biochem Pharmacol.* Jul 1;60(1):1-5. Review.195.Tournaire, C., Croux, S., Maurette, M., Beck, L., Hocquaux, M. A., Braun, M. and Oliveros, E. 1993. Antioxidant activity of flavonoids: efficiency of singlet oxygen quenching. *J. Photochem Photobiol Bi Biol* 19:205-215.196.Valentao, P., Fernandes, E., Carvalho, F., Andrade, P. B., Seabra, R. M. and de Lourdes Basto, M. 2002. Studies on the antioxidant activity of *Lippia citriodora* infusion: scavenging effect on superoxide radical, hydroxyl radical and hypochlorous acid. *Biol. Pharm. Bull.* 25: 1324-1327.197.Van het Hof, K. H., Wiseman, S. A., Yang, C. S. and Tijburg, L. B. 1999. Plasma and lipoprotein levels of tea catechins following repeated tea consumption. *Proc Soci Exp Biol Med* 220:203-209.198.Veraart, J. R., Groot, M. C. E. C., Gooijer, H., Lingeman, N., Velthorst, H. and Brinkman, U. A. 1999. On-line dialysis-SPE-CE of acidic drugs in biological samples. *Analyst*, 124:115-118.199.Vinson, J. A. and Jang, J. 2001. In Vitro and In Vivo Lipoprotein Antioxidant Effect of a Citrus Extract and Ascorbic Acid on Normal and Hypercholesterolemic Human Subjects. *J. Med. Food* 4: 187-192.200.Wadsworth, T. L. and Koop, D. R. 1999. Effects of the wine polyphenolics quercetin and resveratrol on pro-inflammatory cytokine expression in RAW 264.7 macrophages. *Biochem. Pharmacol.* 57: 941-949.201.Wang, J. and Mazza, G. 2002. Effects of anthocyanins and other phenolic compounds on the production of tumor necrosis factor alpha in LPS/IFN gamma-activated RAW 264.7 macrophages. *J. Agric. Food Chem.* 50: 4183-4189.202.Wang, J. and Mazza, G. 2002. Inhibitory

effects of anthocyanins and other phenolic compounds on nitric oxide production in LPS/IFN gamma-activated RAW 264.7 macrophages. *J. Agric. Food Chem.* 50: 850-857.203. Wiseman, S. A., D.A. Balentine, and B. Fire. 1997. Antioxidants in Tea, *Critical Review in Food Science and Nutrition.*, Vol.37:705-718.204. Wu, Jingcun, Xie, W., and P. Janusz. 2000. Automated in-tube solid phase microextraction coupled with HPLC-ES-MS for the determination of catechins and caffeine in tea. *Analyst*, 1252216 - 1252222.205. Yamanish, I.T. 1995. *Spec*