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關鍵字(中)	黑豆；染料木黃酮；黏附分子； α 腫瘤致死因子；主動脈內皮細胞；核因子 κ B 聚丙烯醯胺 分析法 心血管 墨點法 敏感性
關鍵字(英)	Black soybean; Genistein; Adhesion molecules; TNF- α ; Human aortic endothelial cells; NF- κ B
摘要(中)	摘要 氧化壓力與發炎反應是影響致粥狀最重要的因素與促進者，由於影響血管內皮黏附分子的表現，在動脈粥狀硬化形成和慢性發炎中扮演重要角色。許多研究顯示膳食補充大豆食品可降低心血管疾病，尤其是黑豆富含的異黃酮素包括染料木黃酮(genistein)、二羥異黃酮(daidzein)，並且在其種子外皮富含矢車菊色素配質(cyanidin)，而其所具有良好的抗氧化物質是否能在細胞內調控對活性氧敏感性的訊息傳遞路徑之基因表現，進而影響黏附分子的表現與致粥狀的發展。是以本研究主要探討黑豆萃取物及其主成分 genistein、daidzein 和 cyanidin 對前發炎細胞激素腫瘤壞死因子 (TNF- α) 誘導人類主動脈內皮細胞(human aortic endothelial

	<p>cells；HAEC)發炎反應的影響。首先以 MTT 檢測樣品對 HAEC 的影響，結果顯示黑豆萃取物在 200 μg/mL 濃度以下及 genistein、daidzein 和 cyanidin 各分別在 40、40、20 μM 濃度以下對 HAEC 不具細胞毒性；將 HAEC 預先以 100 μg/mL 黑豆萃取物及 10 μM genistein、daidzein、cyanidin 和 aspirin 處理 18 小時，可顯著降低人類單核球細胞株-U937 與 HAEC 間的黏附性，其抑制率依序為 98.2%、97.2%、98.8%、93.1% 和 90.9%；利用細胞酵素連結免疫分析法顯示：genistein 與對照組 aspirin 可明顯降低細胞間黏附分子 (ICAM-1) 表現分別達 17.1% 和 14.5%；黑豆萃取物及 genistein、daidzein、cyanidin、aspirin 亦可顯著降低血管黏附分子 (VCAM-1) 表現依序達 47%、56.8%、59%、38.9% 和 42.7%；而對 E-selectin 的表現則不具影響。經由 10% 聚丙烯醯胺膠體電泳分析和西方墨點法分析，黑豆萃取物，可顯著降低腫瘤壞死因子所引起 NF-κB p65 的表現。綜合研究顯示黑豆萃取物及其主要成分有助於減緩發炎反應及動脈粥狀硬化的進展。</p>
<p>摘要 (英)</p>	<p>Abstract Oxidative stress and inflammation are thought to be an important contributor and promoter of atherogenesis. While altered expression of cell adhesion molecules by the arterial endothelium plays a major role during atherogenesis and chronic inflammation. Several studies have demonstrated that the dietary intakes of soy foods were associated with reduction of cardiovascular risk. Interestingly, black soybeans rich in isoflavones (genistein and daidzein), and its seed coat contains cyanidin. Antioxidants may modulate of oxidative stress which may trigger intracellular signaling pathways influencing gene and adhesion molecules expression and atherogenesis. We determined the potential anti-atherogenic activity of black soybeans extract and its components by examining their effects on monocytes adhesion of human aortic endothelial cells (HAEC), adhesion molecules expression, and NF-κB-p65 expression. The black soybean extract (less than 200 μg/mL) and its components such as genistein, daidzein and cyanidin (less than 40, 40 and 20 μM, respectively) had no toxicity to HAEC. Pre-incubated of HAEC with 100 μg/mL black soybean extract and 10 μM of genistein, daidzein, cyanidin and aspirin for 24h, significantly decreased adhesion of U937 monocytic cells to TNF-α-stimulated HAEC by 98.2%, 97.2%, 98.8%, 93.1% and 90.9%, respectively. Ten micromoles of genistein, daidzein, cyanidin and aspirin significantly suppressed the expression of vascular cell adhesion molecule-1(VCAM-1) by 47%, 56.8%, 59%, 38.9% and 42.7%, respectively. Genistein and aspirin significantly decreased intracellular adhesion molecule-1(ICAM-1) expression by 7.1% and 14.5% while all treatments had no effect on E-selectin. Pretreated black soybean extract could significantly inhibited NF-κB-p65 activity in TNF-α-stimulated HAEC was assayed by SDS-PAGE and western blot. In conclusion, black soybean and its components may have potential on anti-inflammatory and anti-atherogenesis.</p>
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參考
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參考文獻 陳建和、楊忻淵、呂思潔編譯(2000) 實用免疫學。藝軒圖書出版社 pp149-166, pp257-288。 李少君、陳同偉、楊永寧、蕭碧瑩、張淑芬編譯 (2005) 分子細胞生物學。藝軒圖書出版社，pp743-771。 楊志元、林智暉、劉定萍、王聖予、汪蕙蘭 (2002) 免疫生物學。臺北市，藝軒出版社。 趙璧玉(1998) 黑豆對於高膽固醇血症之紐西蘭白兔抗致粥狀性的影響。八十七年度國科會專題研究計畫成果報告。 錢明賽 (1998) 蔬菜中之抗氧化物質。食品工業月刊 30 (8) :21-34。 連大進、游添榮、吳昭慧、吳振碩、王裕權 (1998) 黑豆新品種台南 3 號之育成。台南區農業改良場研究彙報 35 : 14-24。 連大進、游添榮、吳昭慧(1998) 黑豆新品種台南 3 號。雜糧與畜產 299 : 28-31。 連大進 (1994) 台灣黑豆。鄉間小路 20 : 39-42。 連大進 (2000) 黑豆-抗氧化、提高免疫力的保健食品。鄉間小路 26(2): 42-45. 李時珍 (1990) 本草綱目。大台北出版社 p. 862。 肖湘、盧剛、張捷、俞麗君、張爾賢 (2000)。黑色食品色素清除活性氧功效及抗氧化活性。藥物生物技術 7(2): 112-115。 曹祐慈、黃偉春、林少琳 (2003) 心血管疾病之內皮細胞功能失調。臨床醫學 52: 342-350。 詹文雄 (2004) 大豆異黃酮 Genistein 防止過氧化氫所引起的 BALB/c 3T3 細胞凋亡。台灣農業化學與食品科學 42: 404-411。 高彩華 (2002) 異黃酮素分析方法評估暨溫度對豆漿之異黃酮素安定性的影響。輔仁大學食品營養學系碩士論文。 戴文禎 (1997) 黑豆萃取物之抗氧化效用。中國文化大學生活應用科學研究所碩士論文。 郭士榮 (1998) 黑豆豆腐及豆漿加工中抗氧化力與異黃酮之改變。中國文化大學生活應用科學研究所碩士論文。 楊勝智 (1999) 黑豆發芽期間抗氧化效力及異黃酮含量之變化之探討。中國文化大學生活應用科學研究所碩士論文。 陳秀貞 (2004) Leflunomide 之抗發炎及其抗血小板凝集作用。中原大學化學系碩士學位論文。 黃為瑜(2003) 紅色鄉土中類黃酮抗氧化力及其對淋巴球 DNA 氧化損傷的保護作用。中國文化大學生活應用科學碩士論文。 蘇正德 (1992) 果實種子類中藥之抗氧化性及生育醇類之調查研究。食品科學 19: 12-14。 彭德蘭(1999) 烘烤黑豆對血膽固醇正常者低密度脂蛋白氧化敏感性之影響。中國文化大學生活應用科學碩士論文。 Adams J (2001) Proteasome inhibition in cancer: development of PS-341. Semin Oncol 28: 613-619. Adlercreutz H, Bannwart C, W?h?l? K, M?kel? T, Brunow G, Hase T,

Arosemena PJ, Kellis JT Jr and Vickery LE (1993) Inhibition of human aromatase by mammalian lignans and isoflavonoid phytoestrogens. *J Steroid Biochem Mol Biol* 44: 147-153. Akiyama T, Ishida J, Nakagawa S, Ogawara H, Watanabe S, Itoh N, Shibuya M and Fukami Y (1997) Genistein, a specific inhibitor of tyrosine protein kinase. *J Biol Chem* 262: 5592-5595. Albertazzi P, Panzini F, Bonaccorsi G, Zanotti L and Aloissio D (1998) The effect of diet soy supplementation on hot flushes. *Obstet Gynecol* 1: 6-10. Amberger A, Hala M, Saurwein-Teissl M, Metzler B, Grubeck-Loebenstein B, Xu Q and Wick G (1999) Suppressive effects of anti-inflammatory agents on human endothelial cell activation and induction of heat shock proteins. *Mol Med* 5: 117-28. Anderson J and Garner S (1998) Phytoestrogens and bone. *Baillieres Clin Endocrinol Metab* 12: 547-557. Arora A, Nair MG and Strasburg GM (1998) Antioxidant activities of isoflavones and their biological metabolites in a liposomal system. *Arch Biochem Biophys* 356: 133-41. Borradaile NM, de Dreu LE, Wilcox LJ, Edwards JY and Huff MW (2002) Soya phytoestrogens, genistein and daidzein, decrease apolipoprotein B secretion from HepG2 cells through multiple mechanisms. *Biochem J* 366: 531 - 539. Baeuerle PA and Baltimore D (1988) I Kappa B: a specific inhibitor of the NF-kappa B transcription factor. *Science* 242:540-546. Bagchi D, Bagchi M, Stohs SJ, Das DK, Ray SD, Kuszynski CA, Joshi SS and Pruess HG (2000) Free radicals and grape seed proanthocyanidin extract: importance in human health and disease prevention. *Toxicology* 148: 187-197. Baldwin AS (1996) The NF- κ B and I κ B proteins: New discoveries and insights. *Annu Rev Immunol* 14: 649-651. Bannwart C, Fotsis T, Heikkinen R and Aldercreutz H (1984) Identification of the isoflavonic phytoestrogen daidzein in human urine. *Clin Chim Acta* 136: 165-172. Barnes PJ and Karin M (1997) Nuclear factor kappaB: a pivotal transcription factor in chronic inflammatory diseases. *N Engl J Med* 336: 1066-1071. Bevilacqua MP, Pober JS, Mendrick DL, Cotran RS and Gimbrone MA Jr. (1987) Identification of an inducible endothelial-leukocyte adhesion molecule. *Proc Natl Acad Sci U S A* 84: 9238-9242. Beg AA, Finco TS, Nantermet PV and Baldwin AS Jr. (1993) Tumor necrosis factor and interleukin-1 lead to phosphorylation and loss of I κ B- α : a mechanism for NF- κ B activation. *Mol Cell Biol* 13: 3301-3310. Bevilacqua MP and Nelson RM (1993) Selectins. *Clin Invest* 91:379-387. Bito T, Roy S, Sen CK and Packer L (2000) Pine bark extract Pycnogenol downregulates IFN-gamma-induced adhesion of T cells to human keratinocytes by inhibiting inducible ICAM-1 expression. *Free Rad Biol Med* 28: 219-227. Bodetti TJ and Timms P (2000) Detection of Chlamydia pneumoniae DNA and antigen in the circulating mononuclear cell fractions of humans and koalas. *Infect Immun* 68: 2744-2747. Boik J (2001) Natural compounds in cancer therapy natural compounds in cancer therapy. Quality Books, Inc. pp67-72, pp251-267. Boman J, Soderberg S and Forsberg J (1998) High prevalence of Chlamydia pneumoniae DNA in peripheral blood mononuclear cells in patients with cardiovascular disease and in middle-aged blood donors. *J Infect Dis* 178: 274-2747. Brett J, Gerlach H, Nawroth P, Steinberg S, Godman G and Stern D (1989) Tumor necrosis factor/cachectin increases permeability of endothelial cell monolayers by

a mechanism involving regulatory G proteins. *J Exp Med* 169: 1977-1991. Cai Q and Wei H (1996) Effect of dietary genistein on antioxidant enzyme activities in SENCAR mice, *Nutr Cancer* 25: 1-7. Carr AC, Zhu BZ and Frei B (2000) Potential antiatherogenic mechanisms of ascorbate (vitamin C) and α -tocopherol (vitamin E). *Circ Res* 87: 349-352. Cassidy A, De Pascual Teresa S and Rimbach G (2003) Molecular mechanisms by which dietary isoflavones potentially prevent atherosclerosis. *Expert Rev Mol Med* 5: 1-15. Cassidy A and Griffin B (1999) Phyto-oestrogens: a potential role in the prevention of CHD? *Proc Nutr Soc* 58: 193-199. Chen YH, Lin SJ, Ku HH, Shiao MS, Lin FY, Chen JW and Chen YL (2001) Salvianolic acid B attenuates VCAM-1 and ICAM-1 expression in TNF- α -treated human aortic endothelial cells. *Cell Biochem* 82: 512-521. Chen YH, Lin SJ, Chen JW, Ku HH and Chen YL (2001) Magnolol attenuates VCAM-1 expression in vitro in TNF- α -treated human aortic endothelial cells and in vivo in the aorta of cholesterol-fed rabbits. *Bri J Pharm* 135: 37-47. Chen PN, Chu SC, Chiou HL, Kuo WH, Chiang CL and Hsieh YS (2006) Mulberry anthocyanins, cyaniding 3-rutinoside and cyaniding 3-glucoside, exhibited an inhibitory effect on the migration and invasion of a human lung cancer cell line. *Cancer Lett* 235: 248-259. Chin-Dusting JPR, Fisher LJ, Lewis TV, Piekarska A, Nestel PJ and Husband A (2001) The vascular activity of some isoflavone metabolites: implication for a cardioprotective role. *Br J Pharmacol* 133: 595-605. Coward L, Barnes N C, Setchell K D R, Barnes S (1993) Genistein, daidzein and their β -glycoside conjugates: Antitumor isoflavones in soybean foods from American and Asian diets. *J Agri Food Chem* 41: 1961-1967. Collins T and Cybulsky MI (2001) NF- κ B: pivotal mediator innocent bystander in atherogenesis? *J Clin Invest* 107: 255-264. Cybulsky MI, Iiyama K, Li H, Zhu S, Chen M, Iiyama M, Davis V, Gutierrez-Ramos JC, Connelly PW, and Milstone DS (2001) A major role for VCAM-1, but not ICAM-1, in early atherosclerosis. *J Clin Invest* 107: 1255-1262. Cybulsky MI and Gimbrone Jr MA (1991) Endothelial expression of a mononuclear leukocyte adhesion molecule during atherogenesis. *Science* 251: 788-91. Cyrus T, Sung S, Zhao L, Funk CD, Tang Syun and Pratic? D (2002) Effect of low-dose aspirin on vascular inflammation, plaque stability, and atherogenesis in low-density lipoprotein receptor-deficient mice. *Circulation* 106: 1282-1287. David TZ and Gail D (1997) Estrogenic and antiproliferative properties of genistein and other flavonoids in human breast cancer cells in vitro. *Nutr Cancer* 27: 31-40. Davis JN, Kucuk O, Djuric Z and Sarker FH (2001) Soy isoflavones supplementation healthy men prevents NF-kappa B by TNF- α in blood lymphocytes. *Free Radic Biol Med* 30: 1293-1302. Davis JN, Kucuk O and Sarker FH (1999) Genistein inhibits NF-kappa B activation in prostate cancer cells. *Nutr Cancer* 35: 167-74. Dignam JD, Lebovitz RM and Roeder RG (1983) Accurate transcription initiation by RNA polymerase II in a soluble extract from isolated mammalian nuclei. *Nucleic Acids Res* 11: 1475-1489. Dixon RA and Ferreira D (2002) Molecules of Interest genistein. *Phytochemistry* 60: 205-211. Dixon RA and Ferreira D (2002) Genistein. *Phytochemistry* 60: 205-211. Durst RW and R Wrolstad (2001) Separation and characterization of anthocyanins by

HPLC. In: Current Protocols in Food Analytical Chemistry. RE Wrolstad (ed) John Wiley & Sons New York Unit 1.3: 1-13. Densem CG, Hutchinson IV, Yonan N and Brooks NH (2001) Influence of tumor necrosis factor alpha gene-308 polymorphism on the development of coronary vasculopathy after cardiac transplantation. *J Heart Lung Transplant* 20: 1265-1273. Eigler A, Sinha B, Hartmann G and Endres S (1997) Taming TNF: strategies to restrain this proinflammatory cytokine. *Immunol Today* 18: 487-492. Eri W, Weber C, Wardermann C and Weber PC (1997) alpha-Tocopheryl succinate inhibits monocytic cell adhesion to endothelial cells by suppressing NF- κ B mobilization. *Am J Physiol* 273: H634-H640. Feng AN, Chen YL, Chen YT, Ding YZ and Lin SJ (1999) Red wine inhibits MCP-1 expression and reduces neointimal hyperplasia following balloon injury in cholesterol-fed rabbits. *Circulation* 100: 2254-2259. Fleet JC, Clinton SK, Salomon RN, Loppnow H and Libby P (1992) Atherogenic diets enhance endotoxin-stimulated interleukin-1 and tumor necrosis factor gene expression in rabbit aorta. *J Nutr* 122: 294-305. Foti P, Erba D, Riso P, Spadafranca A, Criscuoli F and Testolin G (2005) Comparison between daidzein and genistein antioxidant activity in primary and cancer lymphocyte. *Arch Biochem Biophys* 433: 421 - 427. Fotsis T, Pepper M, Adlercreutz H, Hase T, Montesano R and Schweigerer L (1995) Genistein, a dietary ingested isoflavonoid, inhibits cell proliferation and in vitro angiogenesis. *J Nutr* 125: 790S-797S Fuchs D, Erhard P, Turner R, Rimbach G, Daniel H and Wenzel U (2005) Genistein reverses changes of the proteome induced by oxidized-LDL in EA?hy 926 human endothelial cells. *J Proteome Res* 4: 369-37. Gallin JI and Snyderman R (1999) Inflammation: Basic principles and clinical correlates. Third edition. Lippincott Williams and Wilkins 471-475. Galvano F, La Fauci L, Lazzarino G, Fogliano V, Ritieni A, Ciappellano S, Battistini NC, Tavazzi B and Galvano G (2004) Cyanidins: metabolism and biological properties. *J Nutr Biochem* 15: 2-11. Garg A and Aggarwal BB (2002) Nuclear transcription factor- κ B as a target for cancer drug development. *Leukemia* 16: 1053-1068. Gerard C and Rollins BJ (2001) Chemokines and disease. *Nature Immunol* 2:108-115. Goldsby RA, Kindt TJ and Osborne BA (2002) Kuby immunology 4th edition, W.H. Freeman Co. Gottstein N, Ewins B, Eccleston C, Hubbard G, Kavanagh I, Minihane AM, Weinberg PD and Rimbach G (2003) Effect of genistein and daidzein on platelet aggregation and monocyte and endothelial function. *Br J Nutr* 89: 607- 616. Green LM, Reade JL and Ware CF (1984) Rapid colorimetric assay for cell viability: application to the quantitation of cytotoxic and growth inhibitory lymphokines. *J Immunol Methods* 70: 257-268. Gudbrandsen OA, Wergedahl H, Liaset B, Espe M (2005) Dietary proteins with high isoflavone content or low methionine-glycine and lysine-arginine ratios are hypocholesterolaemic and lower the plasma homocysteine level in male Zucker fa/fa rats. *Br J Nutr* 94: 321-30. Guo Q, Rimbach G, Moini H, Weber S and Packer L (2002) ESR and cell culture studies on free radical-scavenging and antioxidant activities of isoflavonoids. *Toxicology* 179: 171-180. Hajjar DP, Pomerantz KB, Falcone DJ, Weksler BB and Grant AJ (1987) Herpes simplex virus infection in human arterial cells.

Implications in arteriosclerosis. *J Clin Invest* 80: 1317-1321. Halliwell B (1992) Oxygen radicals as key mediators in neurological disease: fact or fiction? *Annals of Neurol* 32: S10-S15. Hansson GK, Holm J and Jonasson L (1989) Detection of activated T lymphocytes in the human atherosclerotic plaque. *Am J Pathol* 135: 169-175. Hansson GK, Jonasson L, Seifert PS and Stemme S (1989) Immune mechanisms in atherosclerosis. *Arteriosclerosis* 9: 567-578. Hayashi T, Ueno Y and Okamoto T (1993) Oxidoreductive regulation of nuclear factor kappa B. Involvement of a cellular reducing catalyst thioredoxin. *J Biol Chem* 268: 11380-11388. Henderson BE, Ross RK, Pike MC and Casgrande JT (1982) Endogenous hormones as a major factor in human cancer. *Cancer Res* 42: 3232-3239. Hendrich S (2002) Bioavailability of isoflavones. *J Chromatog B* 777: 203-210. Henkel T, Machleidt T, Alkalay I, Kronke M, Beneriah Y and Baeuerle PA (1993) Rapid proteolysis of I κ B- α is necessary for activation of transcription factor NF- κ B. *Nature* 365: 182-185. Hecht SS, Huang C, Stoner GD, Li J, Kenney PM, Sturla SJ and Camella SG (2006) Identification of cyanidin glycosides as constituents of freeze-dried black raspberries which inhibit anti-benzo[a]pyrene-7,8-diol-9,10-epoxide induced NF κ B and AP-1 activity. *Carcinogenesis* in press. Hillis GS and Flapan AD (1998) Cell adhesion molecules in cardiovascular disease: a clinical perspective. *Heart* 79: 429-431. Hon KL, Leung CW and Cheng WT (2003) Clinical presentations and outcome of severe acute respiratory syndrome in children. *Lancet* 361: 1701-1703. Hollenbaugh D, Mischel-Petty N, Edwards CP, Simon JC, Denfeld RW and Kiener PA (1995) Aruffo A: Expression of functional CD40 by vascular endothelial cells. *J Exp Med* 182: 33-40. Hynes RO and Lander AD (1992) Contact and adhesive specificities in the associations, migrations, and targeting of cells and axons. *Cell* 68: 303-322. Iiyama K, Hajra L, Iiyama M, Li H, DiChiara M, Medoff BD and Cybulsky M I (1999) Patterns of vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 expression in rabbit and mouse atherosclerotic lesions and at sites predisposed to lesion formation. *Circ Res* 85: 199 - 207. Jenkins DJ, Kendall CW, Jackson CJ, Connelly PW, Parker T, Faulkner D, Vidgen E, Cunnane SC, Leiter LA and Josse RG (2002) Effects of high- and low-isoflavone soyfoods on blood lipids, oxidized LDL, homocysteine, and blood pressure in hyperlipidemic men and women. *Am J Nutr* 76: 365-372. Jha HC, Von Recklinghausen G and Zilliken F (1985) Inhibition of in vitro microsomal lipid peroxidation by isoflavonoids. *Biochem Pharmacol* 34: 1367-1369. Jovinge S, Hultgardh-Nilsson A, Regnstrom J and Nilsson J (1997) Tumor necrosis factor- α activates smooth muscle cell migration in culture and is expressed in the balloon-injured rat aorta. *Arterioscler Thromb Vasc Biol* 17: 490 - 497. Kalin R, Righi A, Del Rosso A, Bagchi D, Generini S, Cerinic MM and Das DK (2002) Activin, a grape seed-derived proanthocyanidin extract, reduces plasma levels of oxidative stress and adhesion molecules (ICAM-1, VCAM-1 and E-selectin) in systemic sclerosis. *Free Radic Res* 36: 819-825. Kang SY, Seeram NP, Nair MG and Bourquin LD (2003) Tart cherry anthocyanins inhibit tumor development in ApcMin mice and reduce proliferation of human colon cancer cells. *Cancer Lett*

194: 13-19. Kao TH, Lu YF, Hsien HC and Chen BH (2004) Stability of isoflavone glucosides during processing of soymilk and tofu. *Food Res Intern* 37: 891-900. Katsube N, Iwashita K, Tsushida T, Yamaki K and Kobori MI (2003) Induction of apoptosis in cancer cells by bilberry (*Vaccinium myrtillus*) and the anthocyanins. *J Agric Food Chem* 51: 68-75. Kerry N and Abbey M (1998) The isoflavone genistein inhibits copper and peroxy radical mediated low density lipoprotein oxidation in vitro. *Atherosclerosis* 140: 341-347. Kempe S, Kestler H, Lasar A and Wirth T (2005) NF- κ B controls the global pro-inflammatory response in endothelial cells: evidence for the regulation of a pro-atherogenic program. *Nucleic Acids Res* 33: 5308-5319. Kharbanda RK, Walton B, Allen M, Klein N, Hingorani AD, MacAllister RJ and Vallance P (2002) Prevention of inflammation-induced endothelial dysfunction: a novel vasculo-protective action of aspirin. *Circulation* 105: 2600-2604. Kim HJ, Tsoy I, Park JM, Chung JI, Shin SC and Chang KC (2006) Anthocyanins from soybean seed coat inhibit the expression of TNF- α -induced genes associated with ischemia/reperfusion in endothelial cell by NF- κ B-dependent pathway and reduce rat myocardial damages incurred by ischemia and reperfusion in vivo. *FEBS Lett* 580: 1391-1397. Kobuchi H, Roy S, Sen CK, Nguyen HG and Packer L (1999) Quercetin inhibits inducible ICAM-1 expression in human endothelial cells through the JNK pathway. *Am J Physiol* 277: C403-C411. Kuijpers TW and Harlan JM (1993) Monocyte-endothelial interactions: insights and questions. *J Lab Clin Med* 122: 641-651. Lakshminarayanan V, Beno DW, Costa RH and Roebuck KA (1997) Differential regulation of interleukin-8 and intercellular adhesion molecule-1 by H₂O₂ and tumor necrosis factor- α in endothelial and epithelial cells. *J Biol Chem* 272: 32910-32918. Larrick JW and Wright SC (1990) Cytotoxic mechanism of tumor necrosis factor- α . *FASEB J* 4: 3215-3223. Lee YB, Lee HJ, T and Sohn HS (2005) Soy isoflavones and cognitive function. *J Nutr Biochem* 16: 641-649. Libby P, Ridker PM and Maseri A (2002) Inflammation and atherosclerosis. *Circulation* 105: 1135-1143. Li H, Cybulsky MI, Gimbrone Jr MA and Libby P (1993) An atherogenic diet rapidly induces VCAM-1, a cytokine-regulatable mononuclear leukocyte adhesion molecule, in rabbit aortic endothelium. *Arterioscler Thromb* 13: 197-204. Lichtenstein AH (1998) Soy protein, isoflavones and cardiovascular disease risk. *J Nutr* 128: 1589-92. Lin JK (2000) Mechanisms of cancer chemoprevention by phytochemicals and phytopolyphenols. *Food Sci and Agri Chem* 2: 189-201. Liu L, Zubik L, Collins FW, Marko M and Meydani M (2004) The antiatherogenic potential of oat phenolic compounds. *Atherosclerosis* 175: 39-49. Loo G (2003) Redox-sensitive mechanisms of phytochemical-mediated inhibition of cancer cell proliferation. *J Nutr Biochem* 14: 64-73. Lum H and Roebuck KA (2001) Oxidant stress and endothelial cell dysfunction. *Am J Physiol - Cell Physiol* 280: C719-C741. Lusis AJ (2000) Atherosclerosis. *Nature* 407: 233-241. Makarov SS (2000) NF kappa B as a therapeutic target in chronic inflammation: recent advances. *Mol Med Today* 6: 441-448. Manach C, Scalbert A, Morand C, Remesy C and Jimenez L (2004) Polyphenols : food sources and bioavailability. *Am J Clin Nutr* 79: 727-747.

Marui N, Offermann MK, Swerlick R, Kunsch C, Rosen CA, Ahmad M, Alexander RW and , Medford RM (1993) Vascular cell adhesion molecule-1 (VCAM-1) gene transcription and expression are regulated through an antioxidant-sensitive mechanism in human vascular endothelial cells. *J Clin Invest.* 92: 1866-1874. Martin AR, Villegas I, Casa CL and Lastra CA (2004) Resveratrol a polyphenol found in grapes suppresses oxidative in rats. *Biochem Pharmacol.* 67: 1399-1410. Masters CJ (1996) Cellular signalling: the role of the peroxisome. *Cellular Signalling* 8: 197-208. Messins MJ, Persky V, Setchell KD and Branes S (1994) Soy intake and cancer risk: a review of the in vitro and in vivo data. *Nutr Cancer* 21: 113-31. Morton MS, Wilcox G, Wahlqvist ML and Griffiths K (1994) Determination of lignans and isoflavonoids in human female plasma following dietary supplementation. *J Endocrinol* 142: 251-259. Mosmann T (1983) Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *J Immuno Methods* 65: 55-63. Moyer RA, Hummer KE, Finn CE, Frei B and Wrolstad RE (2002) Anthocyanins, phenolics, and antioxidant capacity in diverse small fruits: vaccinium, rubus, and ribes. *J Agric Food Chem* 50: 519-525. Mullen W, McGinn J, Lean ME, MacLean MR, Gardner P, Duthie GG, Yokota T and Crozier A (2002) Ellagitannins, flavonoids, and other phenolics in red raspberries and their contribution to antioxidant capacity and vasorelaxation properties. *J Agric Food Chem* 50: 5191-5196. Murphy CT, Kellie S and Westwick J (1993) Tyrosine-kinase activity in rabbit platelets stimulated with platelet-activating factor. The effect of inhibiting tyrosine kinase with genistein on platelet-signal-molecule elevation and functional responses. *Eur J Biochem* 216: 639-51. Mutaugh MP and Foss DL (2002) Inflammatory cytokines and antigen presenting cell activation. *Veterina immunol immunopathol* 87: 109-121. Nawroth PP and Stern DM (1986) Modulation of endothelial cell hemostatic properties by tumor necrosis factor. *J Exp Med* 163: 740-745. Nestel P (2004) Isoflavones: effects on cardiovascular risk and functions. *Int Congr Ser* 1262: 317-319. O' Brien KD, Allen MD, McDonald TO, Chait A, Harlan JM, Fishbein D, Mccarty J, Furgerson M, Hudkins K, Benjamin C D, Lobb R and Alpers C E (1993) Vascular cell adhesion molecule-1 is expressed in human coronary atherosclerotic plaques. *J Clin Invest* 92: 945-951. Okura A, Arakawa H, Oka H, Yoshinari T and Monden Y (1988) Effect of genistein on topoisomerase activity and on the growth of [Val 12]Ha-ras-transformed NIH 3T3 cells. *Biochem Biophys Res Comm* 157: 183-189. Opal SM and Depalo VA (2000) Anti-inflammatory cytokines. *Impact of basic research on tomorrow medicine* 117: 1162-1172. Palinski (2003) Circulation research:conjunct regulation of aortic antioxidant enzymes during atherogenesis. *Circ Res* 8: 262-269. Peterson G and Barnes S (1991) Genistein inhibition of the growth of human breast cancer cells: independence from estrogen receptors and the multi-drug resistance gene. *Am J Clin Nutr* 66: 46-51. Pool-Zobel BL, Bub A, Schr?der N and Rechkemmer G (1999) Anthocyanins are potent antioxidants in model systems but do not reduce endogenous oxidative DNA damage in human colon cells. *Eur J Nutr* 38: 227-234. Poston RN, Haskard DO, Coucher JR, Gall NP and

Johnson-Tidey RR (1992) Expression of intercellular adhesion molecule-1 in atherosclerotic plaques. *Am J Pathol* 140: 665-673. Price DT and Loscalzo J (1999) Cellular adhesion molecules and atherogenesis. *Am J Med* 107: 85-97. Printseva OY, Pecló MM and Grwn A (1992) Various cell types in human atherosclerotic lesions express ICAM-1. *Am J Pathol* 140: 889-896. Read MA, Whitley MZ, Gupta S, Pierce JW, Best J, Davis RJ and Collins T (1997) Tumor necrosis factor alpha-induced E-selectin expression is activated by the nuclear factor-kappaB and c-JUN N-terminal kinase/p38 mitogen-activated protein kinase pathways. *J Biol Chem* 272: 2753-2761. Reape TJ and Groot PH (1999) Chemokines and atherosclerosis. *atherosclerosis* 147: 213-25. Record IR, Dreosti IE and McInerney JK (1995) The antioxidant activity of genistein in vitro. *J Nutr Biochem* 6: 481-485. Reinli K and Block G (1996) Phytoestrogen content of foods--a compendium of literature values. *Nutr Cancer* 26: 123-48. Rimbach G, Weinberg PD, de Pascual-Teresa S, Alonso MG, Ewins BA, Turner R, Miniñane AM, Botting N, Fairley B and Matsugo S (2004) Sulfation of genistein alters its antioxidant properties and its effect on platelet aggregation and monocyte and endothelial function. *Biochim Biophys Acta* 1670: 229-237. Piek JJ, van der Wal AC, Meuwissen M, Koch KT, Chamuleau SA, Teeling P, van der Loos CM and Becker AE (2000) Plaque inflammation in restenotic coronary lesions of patients with stable or unstable angina. *J Am Coll Cardiol* 35: 963-967. Roebuck K and Finnegan A (1999) Regulation of intercellular adhesion molecule-1 (CD54) gene expression. *J Leukoc Biol* 60: 876-888. Roitt I, Brostoff J and Male D (1998) Immunology. 5th Edition. Chapter 3, 5, 16, 17. Ross R (1993) The pathogenesis of atherosclerosis: a perspective for the 1990s. *Nature* 362: 801-809. Ross R (1999a) Mechanisms of disease: Atherosclerosis: An inflammatory disease. *N Engl J Med* 340: 115-126. Ross R (1999b) Atherosclerosis is an inflammatory disease. *Am Heart J* 138: S419-S420. Ross R and Glomsel JA (1976) The pathogenesis of atherosclerosis. *N Engl J Med* 295: 369-371. Roth E (1997) Oxygen free radicals and their clinical implications. *Acta Chirurgica Hungarica* 36: 302-305. Ruiz-Larrea MB, Mohan AR, Paganga G, Millwe NJ and Bolwell GP (1997) Antioxidant activity of phytoestrogenic isoflavones. *Free Radic Res* 26: 63-70. Rus HG, Niculescu F and Vlaicu R (1991) Tumor necrosis factor-alpha in human arterial wall with atherosclerosis. *Atherosclerosis* 89: 247-254. Sarkar FH and Li Y (2004) Soy isoflavones and disease prevention - a mechanistic approach. *Nutrition Abstracts and Reviews Series* 74: 1N-13N. Sato M, Bagchi D, Tosaki A and Das DK (2001) Grape seed proanthocyanidin reduces cardiomyocyte apoptosis by inhibiting ischemia/reperfusion-induced activation of JNK-1 and c-JUN. *Free Radic Bio Med* 31: 729-737. Serafini FM and Rosemary AS (2000) Adhesion molecules Clinical implications. *Surgery* 127: 481-3. Setchell KD (1998) Phytoestrogens: the biochemistry, physiology, and implications for human health of soy isoflavones. *Am J Clin Nutr* 68: 1333-1346. Smith CA, Davis T, Anderson D, Solam L, Beckmann MP, Jerzy R, Dower SK, Cosman D and Goodwin RG (1990) A receptor for tumor necrosis factor defines an unusual family of cellular and viral proteins. *Science* 248: 1019-1023. Springer

TA (1994) Traffic signals for lymphocyte recirculation and leukocyte emigration: the multistep paradigm. *Cell* 76: 301-314. Stary HC, Chandler AB, Glagov S, Insull Jr W, Rosenfeld ME, Schaffer SA, Schwartz CJ, Wagner WD and Wissler RW (1994) A definition of initial, fatty streak, and intermediate lesions of atherosclerotic. A report from the committee on vascular lesions of the council on arteriosclerosis, American Heart Association. *Circulation* 89: 2462-2478. Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull WJ, Rosenfeld ME, Schwartz CJ, Wagner WD and Wissler RW (1995) A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation* 92: 1355-1374. Stocker R and Keaney J F (2003) Role of oxidative modifications in atherosclerosis. *Physiol Rev* 84: 1381-1478. Subarnas A and Wagner H (2000) Analgesic and anti-inflammatory activity of the proanthocyanidin shelleagueain A from *Polypodium feei* METT. *Phytomedicine* 7: 401-405. Takahashi R, Ohmor R, Kiyose C, Momiyama Y, Ohsuzu F and Kondo K (2005) Antioxidant activities of black and yellow soybeans against low density lipoprotein oxidation. *J Agri Food Chem* 53: 4578-4582. Takahata Y, Ohnishi-Kameyama M, Furuta S, Takahashi M and Suda I (2001) High polymerized procyanidins in brown soybean seed coat with a high radical-scavenging activity. *J Agric Food Chem* 49: 5843-5847. Tamura DY, Moore EE, Johnson JL, Zallen G, Aiboshi J and Silliman CC (1998) p38 mitogen-activated protein kinase inhibition attenuates intercellular adhesion molecule-1 up-regulation on human pulmonary microvascular endothelial cells. *Surgery* 124: 403-407. Tikkanen MJ and Adlercreutz H (2000) Dietary soy-derived isoflavone phytoestrogens. Could they have a role in coronary heart disease prevention? *Biochem Pharmacol* 60: 1-5. Tiran A, Gruber HJ, Graier WF, Wagner AH, Van Leeuwen EB and Tiran EB (2002) Aspirin inhibits *Chlamydia pneumoniae* - induced nuclear factor- κ B activation, cytokine expression, and bacterial development in human endothelial cells. *Arterioscler Thromb Vasc Biol* 22: 1075-80. Tsujimoto M, Yokota S, Vilcek J and Weissmann G (1986) Tumor necrosis factor provokes superoxide anion generation from neutrophils. *Biochem Biophys Res Commun* 137: 1094-1100. Tsuda T, Kato Y and Osawa T (2000) Mechanism for the peroxynitrite scavenging activity by anthocyanins. *FEBS Lett* 484: 207-210. Vaddi K, Nocolini FA, Mehta P and Mehta JL (1994) Increased secretion of tumor necrosis factor- α and interferon- γ by mononuclear leukocytes in patients with ischemic heart disease. Relevance in superoxide anion generation. *Circulation* 90: 694-699. van der Schouw YT, de Kleijn MJ, Peeters PH and Grobbee DE (2000) Phyto-oestrogens and cardiovascular disease risk. *Nutr Metab Cardiovasc Dis* 10: 154-167. Verdeal K, Brown RR, Richardson T and Ryan DS (1980) Affinity of phytoestrogens for estradiol binding protein and effect of coumesterol on growth of 7, 12-dimethylbenz (a) anthracene induced rat mammary tumors. *J Natl Cancer Inst* 64: 285-290. Wang AM, Creasey AA, Ladner MB, Lin LS, Strickler JV, Arsdell JN, Yamamoto R and Mark DF (1985) Molecular cloning of the complementary DNA for human tumor necrosis factor.

Science 228: 149-154. 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. Wal AC, van der Das PK, Tigges AJ and Becker AE (1992) Adhesion molecules on the endothelium and mononuclear cells in human atherosclerotic lesions. *Am J Pathol* 141: 1427-1433. Weber C, Erl W, Pietsch A and Weber PC (1995) Aspirin inhibits nuclear factor-kappa B mobilization and monocyte adhesion in stimulated human endothelial cells. *Circulation* 91: 1914-7. Wei H, Bowen R, Cai Q, Barnes S and Wang Y (1995) Antioxidant antipromotion effects of the soybean isoflavone genistein. *Pro Soc Exp Biol Med* 208: 109-115. Wei H, Cai Q and Rahn RO (1996) Inhibition of UV light and fenton reaction-induced oxidative DNA damage by the soybean isoflavone genistein. *Carcinogenesis* 17: 73-77. Wei H, Cai Q, Rahn RO and Zhang X (1997) Singlet oxygen involvement in ultraviolet (254 nm) radiation-induced formation of 8-hydroxy-deoxyguanosine in DNA. *Free Radic Biol Med* 23: 148-154. Weyand CM, Goronzy JJ, Liuzzo G, Kopecky SL, Holmes Jr DR and Frye RL (2001) T-cell immunity in acute coronary syndromes. *Mayo Clinic Proc* 76: 1011-1020. Wolle J, Hill RR, Ferguson E, Devall LJ, Devall BK, Trivedi BK, Newton RS and Saxena U (1996) Selective inhibition of tumor necrosis factor-induced vascular cell adhesion molecule-1 gene expression by a novel flavonoid. Lack of effect on transcription factor NF-kappa B. *Arterioscler Thromb Vasc Biol* 16: 1501-1508. Wong W, Smith E, Stuff J, Hachey D, Heird W and Pownell H (1998) Cholesterol-lowering effect of soy protein in normocholesterolemic and hypercholesterolemic men. *Am J Clin Nutr* 68: 1385S-1389S. Xia P, Gamble JR, Rye KA, Wang L, Hii CS, Cockerill P, Khew-Goodall Y, Bert AG, Barter PJ and Vadas MA (1998) Tumor necrosis factor-alpha induces adhesion molecule expression through the sphingosine kinase pathway. *Proc Nat Acad Sci USA* 95: 14196-14201. Xu X, Wang HJ, Murphy PA, Cook L and Hendrich S (1994) Daidzein is a more bioavailable soymilk isoflavone than is genistein in adult women. *J Nutr* 124: 825-32. Xu X, Harris KS, Wang HJ, Murphy PA and Hendrich S (1995) Bioavailability of soybean isoflavones depends upon gut microflora in women. *J Nutr* 125: 2307-15. Yamakoshi J, Piskula M K, Izumi T, Tobe K, Saito M, Kataoka S, Obata A and Kikuchi M (2000) Isoflavone aglycone - rich extract without soy protein attenuates atherosclerosis development in cholesterol-fed rabbits. *J Nutr* 130: 1887-1893. Yan X, Murphy BT, Hammond GB, Vinson JA and Neto CC (2002) Antioxidant activities and antitumor screening of extracts from cranberry fruit (*Vaccinium macrocarpon*). *J Agric Food Chem* 50: 5844-5849. Yen GC and Lai HH (2003) Inhibition of reactive nitrogen species effects in vitro and in vivo by isoflavones and soy-based food extracts. *J Agric Food Chem* 51: 7892-7900. Youdim KA, McDonald J, Kalt W and Joseph JA (2002) Potential role of dietary flavonoids in reducing microvascular endothelium vulnerability to oxidative and inflammatory insults (small star, filled). *J. Nutr Biochem* 13: 282-288. Zapolska-Downar D, Zapolski-Downar A, Markiewski M, Ciechanowicz A, Kaczmarczyk M, and Naruszewicz M (2001) Selective inhibition by probucol of

	vascular cell adhesion molecule-1 (VCAM-1) expression in human vascular endothelial cells. <i>Atherosclerosis</i> 155: 123-130. Zheng W, Dai Q, Custer LJ, Shu XO, Wen WQ, Jin F and Franke AA (1999) Urinary excretion of isoflavonoids and the risk of breast cancer. <i>Cancer Epidemiol Biomark Prev</i> 8: 35-40. Zibara K, Chignier E, Covacho C, Poston R, Canard G, Hardy P and McGregor J A K (2000) Modulation of expression of endothelial intercellular adhesion molecule-1, platelet-endothelial cell adhesion molecule-1, and vascular cell adhesion molecule-1 in aortic arch lesions of apolipoprotein E-deficient compared with wild-type mice. <i>Arterioscler Thromb Vasc Biol</i> 20: 2288-2296.
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