

萊菔子、白芥子及葶藶子萃取物之抗氧化性及抑制胃腺癌細胞影響之研究

、張基郁

E-mail: 364882@mail.dyu.edu.tw

摘要

萊菔子、白芥子及葶藶子為十字花科屬其中之中藥材之一，許多研究發現這些種子具有很好的改善消化系統、及改善呼吸系統的作用。另外，萊菔子有降血壓及抗菌的作用；白芥子有抗癌及刺激(皮膚)的作用；葶藶子有降低心血管疾病、調節血脂及利尿的作用。然而，目前對於這些種子的抗氧化性、抗癌及免疫調節的作用並無相關完整的研究。經過不同溶劑萃取後，本研究比較萊菔子、白芥子及葶藶子萃取物之抗氧化性，包括測定總酚類化合物含量、類黃酮化合物含量、總抗氧化能力、還原力之測定、*-diphenyl- -picrylhydrazyl* (DPPH) 自由基之清除能力、過氧化氫清除能力、LDL氧化延滯期(LDL oxidation Lag phase)測定等。本研究亦比較各種萃取物之抑制胃腺癌細胞能力，及免疫調節的作用，包括測定Human peripheral blood mononuclear cell (MNC)細胞分泌Tumor necrosis factor-1 (TNF-1)、Interleukin-1 (IL-1)、Interferon-1 (IFN-1)及產生Nitrogen Monoxide (NO)與對Cyclooxygenase-2 (COX-2)蛋白表現的影響等。結果顯示萊菔子、白芥子及葶藶子的熱水、冷水、甲醇、乙酸乙酯及丙酮之不同極性溶劑萃取物，以萊菔子之甲醇萃取物具有最好的抗氧化效果。此外，萊菔子之甲醇萃取物亦顯示最佳的抑制癌細胞生長能力及免疫調節的作用。, 本研究顯示萊菔子之甲醇萃取物具有功能性中草藥開發的潛力。

關鍵詞：萊菔子、白芥子、葶藶子、抗氧化作用、抗癌作用、免疫調節

目錄

封面內頁 簽名頁 中文摘要.....	iii 英文摘要.....
v 誌謝.....	vii 目錄.....
viii 圖目錄.....	x 表目錄.....
xv 名詞縮寫.....	xvi 1. 緒論..... 12.
文獻回顧.....	5.2.1自由基與活性氧..... 5.2.2自由基對細胞或組織的傷害..... 7.2.3多酚化合物的分類..... 9.2.4發炎反應.....
細胞或組織的傷害.....	12.2.5細胞激素..... 13.2.6癌症及免疫系統.....
18.2.7萊菔子介紹.....	20.2.8白芥子介紹.....
24.2.9葶藶子介紹.....	27.2.10胃腺癌介紹..... 30.3. 材料與方法.....
與方法.....	36.3.1材料..... 36.3.2藥品.....
37.3.3重要儀器.....	43.3.4方法.....
45.4. 結果與討論.....	60.4.1萊菔子、白芥子及葶藶子分別經冷水、熱水、甲醇、乙酸乙酯及丙酮萃取後選擇最佳抗氧化的萃取物進行體外生物活性研究.....
60.4.2萊菔子、白芥子及葶藶子之甲醇萃取物在體外之對胃癌細胞之生長抑制能力及免疫調節能力之研究.....	82.4.3萊菔子、白芥子及葶藶子萃取油其體外抗氧化能力及對胃癌細胞(AGS)抑制能力和發炎反應機制之研究..... 106.5. 結論.....
131 參考文獻.....	135

參考文獻

- 1.中國衛生部網站www.moh.gov.cn。2.中國國家中醫藥管理局(中華本草)編委會。1996。中華本草。上海:上海科學技術出版社。729。
- 3.中國藥典。2005。
- 4.中國醫學科學院藥物研究所。1972。中草藥有效成分的研究(第一分冊) [M]1 北京:人民衛生出版社。pp. 1375。
- 5.王自軍，鄧紅。白芥子多糖的提取與含量測定。新疆中醫藥。2005 , 23: 13。
- 6.冉先德。1993。中華藥海(下冊:第二冊)。哈爾濱:哈爾濱出版社。pp. 1396。
- 7.李錦裳。2008。研究ZAK在胃癌細胞發展中的分子調控機轉。中山醫學大學碩士論文。台中。
- 8.李書。1983。白芥子化學成分的研究。,陝西新醫藥。12:57-58。
- 9.李青舊，莊銀清。動物與細胞研究模式在抗生素抗發炎相關研究之應用。感染控制雜誌第14卷。第六期。2004 , 383-389。
- 10.李廣勳。1992。中藥藥理毒理與臨床。天津:天津科技翻譯出版公司。pp. 284。
- 11.江蘇新醫學院編。1986。中藥大辭典(下冊)。上海:上海科學技術出版社。pp. 2320。
- 12.任仁安。1986。中藥鑑定學。上海，上海科學技術出版社。pp. 37。
- 13.何尉旗。2007。沒食子酸(Gallic acid)干擾Small GTPase, Ras/PI3K及Ras/ERK路徑抑制人類胃癌細胞的轉移能力之作用。中山醫學大學碩士論文。台中。
- 14.邢小燕，向瑞華，候冬岩。2005。萊菔子中脂肪酸成分分析。分析試驗室。24 :96。
- 14.余正江

。2005。白芥子化學成分及鎮咳活性研究，沈陽藥科大學碩士論文，中國。15.吳秋燁。2003。蜂膠不同溶劑萃取物消化前後組成及生物活性之評估。中山醫學大學營養科學研究所碩士論文，台中。16.吳政訓。2010。(1).探討EP4調控Ras訊息表現在人類結腸組織癌化之作用，(2).荷葉水萃物改善動物高脂飲食所引發的肥胖與肝脂肪堆積之作用中山醫學大學碩士論文。台中。17.吳國欣，歐敏銳，林躍鑫。2002。白芥子脂肪酸成分的研究。海峽藥學。23:37-39。18.吳明賢，林肇堂，李威傑等。1994。國家衛生研究院癌症研究組。胃癌診治共識。台灣的胃癌。台灣醫誌。93:s77-89。19.南京藥學院藥材學教研室編著。1960。藥材學。上海，上海科學技術出版社。第一版。20.柏正平，鄭兵，葛獻春。2000。複方葶藶子膠囊止咳祛痰作用的實驗研究。湖南中醫藥導報。6(5):41-42。21.孫凱，李銑。2002。葶藶子化學成分和藥理作用的研究進展。中草藥。33:pp.3-5。22.段禮新。2007。中藥復方三子養親湯及其味藥萊菔子物質基礎的研究。沈陽藥科大學。博士論文。中國。23.唐健元，於軍橋，張碩。2001。萊菔子現代研究及臨床應用。時珍國醫國藥。12:36-37。24.袁鵬，陳寶安，劉德龍。2008。異硫氰酸鹽的抗腫瘤機制和研究進展。中國天然藥物。6:325-332。25.凌關庭。2004。抗氧化食品與健康。化學工業出版社。北京，中國 pp. 1-51。26.曹巧吟。2003。樟芝中免疫調節蛋白的純化與其生理活性之探討。國立台灣大學園藝學研究所碩士論文，台北。27.曹仁烈，孫在原等。1957。中藥水浸劑在試管內抗皮膚真菌的觀察。中華皮膚科雜誌。4:286-296。28.張巍峨，梁文波，張學梅，刑福有，王永奇。萊菔子提取物鎮咳祛痰平喘作用研究，大連大學學報，2002，23: 4。29.張學梅，劉凡亮，梁文波，王永奇，邢福有，張巍峨，烏蘭，付子棟，吳麗霞。2003。白芥子提取物的鎮咳、祛痰及平喘作用研究。中草藥。34:635-637。30.陳志瑋。2010。牛初乳蛋白水解物在體外之免疫調節及細胞活性之研究。大葉大學博士論文。彰化縣。31.陳振德，莊志銓，許重遠。2000。白芥子油含量及其脂肪酸測定，廣東藥學院學報。17: 113。32.陳毓群，李榮芷，王雲雯。1981。華東葶藶子中強心?的分離鑑定。藥學學報。16: 62-64。33.常敏毅。1998。抗癌中藥[M]1。長沙，湖南科學技術出版社。34.凌一授。1984。中藥學。上海，上海科學技術出版社。pp. 17。35.趙海譽，王秀坤，陸景珊。2005。北葶藶子中揮發油及脂肪油類成分的研究。36(6): 827-828。36.劉繼林，鍾蒿，張世波。1990。萊菔子降氯化痰的實驗研究。成都中醫學院學報。13:29-31。37.劉忠良。2000。南葶藶子提取物調血脂作用的實驗研究，藥學實踐雜誌。18:15-17。38.劉波，張華。1990。葶藶子炮製前後芥子?的含量比較中成藥。12 (7):191。39.韓志君，魏鐵花，萊菔子的現代藥理及臨床研究。中醫藥資訊。1998。3: 62-64。40.縱偉，馬歌麗，張文葉。2006。芥菜籽中活性成分的研究進展，中國食物與營養。6:14-16。41.Aseno, Y. Okamura, S. Ogo, T. Eto, T. Otsuka, T. and Niho, Y. 1997. Effect of (-)- epigallocatechin gallate on leukemia blast cells from patients with acute myeloblastic leukemia. Life Sci. 60 : 135-142. 42.Arnao, M. B. Casas, J. L. Del R ' io, J. A. Acosta, M. and Carc ' ia-C ' anovas. 1990. An enzymatic colorimetric method for measuring naringin using 2,2 ' -azino-bis-(3-ethylbenzthiaoline-6-sulfonic acid (ABTS) in the presence of peroxidase. Anal. Biochem. 185: 335-338. 43.Arai, T. and Kino, I. 1995. Role of apoptosis in modulation of the growth of human colorectal tubular and villous adenomas. J. Pathol. 176: 37-44. 44.Anwarul, H. G. and Ghayur, M. N. 2004. pharm acological basis for the gut stimulatory activity of Raphanus sativus leaves. J. Ethnopharmacol. 95: 169-173. 45.Afsharypuor, S. L. 1985. GB1 Glucosinolate degradation products, alkane and fatty acids from plants and cell cultures of Descurainia Sophia. Plant Cell Rep. 4: 341-343. 46.Brown, K. and Fridovich, I. 1981. DNA strand scission by enzymatically-generated oxygen radicals. Arch. Biochem. Biophys. 206: 414-419. 47.Bingle, L. Brown, N. J. and Lewis, C. E. 2002. The role of tumor-associated macrophages in tumour progression: implications for new anticancer therapies. J. Pathol. 196: 254-265. 48.Baslas, K. K. 1959. Chemical examination of the seeds of Descurainia Sophia. Indian J. Appl. Chem. 22: 122. 49.Corsò, S. Migliore, C. Ghiso, E. De Rosa, G. Comoglio, P. M. and Giordano, S. 2008. Silencing the MET oncogene leads to regression of experimental tumors and metastases. Oncogene 27: 684-693. 50.Cheng, K. C. and Loeb, L. A. 1993. Genomic instability and tumor progression: mechanistic considerations. Adv Cancer Res. 60: 121-56. 51.Clausen, S. Ole Olseni, O. and Sorensen, H. 1960. 4-hydrobenzoylcholine: a natural product present in Sinalba alba. Phytochem.7ed. 21: 917-922. 52.Clancy, R. M. and Abramson, S. B. 1995. Nitric oxide: a novel mediator of inflammation. Soc. Exp. Biol. Med. 210: 93-101 53.Chen, P. N. Chu, S. C. Chiou, H. L. Kuo, W. H. Chiang, C. L. and Hsieh, Y. S. 2006. Mulberry anthocyanins, cyanidin 3-rutinoside and cyanidin 3-glucoside, exhibited an inhibitory effect on the migration and invasion of a human lung cancer cell line. Cancer Lett. 235: 248-259. 54.Clancy, R. M., Amin, A. R. and Abramson, S. B. 1998. The role of nitric oxide in inflammation and immunity. Arthritis Rheum 41: 1141-1151. 55.Christel, Q. D. Bernard, G. Jacques, V. Thierry, D. Claude, B. Michel, L. Micheline, C. Jean-Claude, C. Francois, B. and Francis, T. 2000. Phenolic compounds and antioxidant activities of buckwheat (*Fagopyrum esculentum* Moench) hulls and flour. J. Ethnopharmacology. 72: 35-42. 56.Denizot, F. and Lang, R. 1986. Rapid colorimetric assay for cell growth and survival. Modifications to the tetrazolium dye procedure giving improved sensitivity and reliability. J. Immuno. Meth. 89: 271 – 277. 57.Fairey, A. S. Courneya, K. S. Field, C. J. and Mackey, J. R. 2002. Physical exercise and immune system function in cancer survivors: a comprehensive review and future directions. Cancer Lett. 94: 539-551. 58.Fridovich, I. 1975.Superoxide dismutases. Annu. Rev. Biochem. 44: 147-159. Fridovich, I. 1978. The biology of oxygen radicals. Sci. 201: 875-880. 59.Francisco, B. M. Alicia, S. Manuel, D. L. and Francisco, R. 1996. Lipid peroxidation products in human subretinal fluid. Free Radic. Biol. Med. 20: 899-903. 60.Fuchs, C. S. and Mayer, R. J. 1995. Gastric carcinoma. N. Engl. J. Med. 333(1): 32-41. 61.Fenwick, G. R. Heaney, R. K. and Mullin, W. J. 1983. Glucosinolates and their breakdown products in food and food plants. CRC Cnt. Rev. Food Sci. Nur. 18: 123-201. 62.Fuchs, C. S. and Mayer, R. J. 1995. Gastric carcinoma N. Engl. J. Med.; 333 (1): 32-41. 63.Floyd, R. A. 1981. Free-radical events in chemical and biochemical reactions involving carcinogenic arylamines. Radiation Res. 86: 243-263. 64.Fiala, E. S. Reddy, B. S. and Weisburger, J. H. 1985. Naturally occurring anticarcinogenic substances in foodstuffs. Annu. Rev. Nutr. 5: 295-321. 65.Groemeveld, P. H. P. Kwappenberg, K. M. C. Langermans, J. A. M. Nibbering, P. H. and Curtis, L. 1997. Relation between pro- and anti-inflammatory cytokines and the production of nitric oxide (NO) in severe sepsis. Cytokine 2: 138-142. 66.Halliwell, B. 1997. Antioxidants and human disease: a general introduction. Nutri. Rev. 55: S44-52. 67.Halliwell, B. and Gutteridge, J. M. C. 1984. Oxygen toxicity, oxygen radicals, transition metals and disease. Biochem. J. 219: 1-14. 68.Harborne, J. B. 1989. Plant phenolics. In Method in Plant Biochemistry. Academic press,

London, UK, 1-28. 69.Hollman, P. C, de Vries, J. H. van Leeuwen, S. D. Mengelers, M. J. and Katan, M. B. 1995. Absorption of dietary quercetin glycosides and quercetin in healthy ileostomy volunteers. *Am. J. Clin. Nutr.* 62:1276-1282. 70.Harbome, J. B. and Williams, C. A. 2000. Advances in flavonoid research since 1992. *Phytochem.* 55: 481-504. 71.Hershman, H. R. 1996. "Prostaglandin synthase 2." *Biochim Biophys Acta*, 1299(1):125-140. 72.Hundahl, S. A. Phillips, J. L. and Menck, H. R. 2000. The National Cancer Data Base Report on poor survival of U.S. gastric carcinoma patients treated with gastrectomy: Fifth Edition American Joint Committee on Cancer staging, proximal disease, and the "different disease" hypothesis. *Cancer.* 88: 921-932. 73.Hendricks, J. C. 1986. Malignant tumors of the stomach. *Surg Clin North Am.* 66: 683-693. 74.Harborne, J. B. and Williams, C. A. 2000. Advances in flavonoid research since 1992. *Phytochmistry* 55: 481-504. 75.Ho, C. T. Chen, Q. Shi, H. Zhang, K. Q. and Rosen, R. T. 1992. Antioxidative effect of polyphenol extract prepared from various Chinese teas. *Prev Med.* 21: 520-525. 76.Huang, M. T. and Ferraro T. 1992. Phenolic compounds in food and cancer prevention. In: Huang, M.T. Ho, C.T. Lee, C.Y. (Eds.), *Phenolic Compounds in Food and Health: II. Antioxidants and Cancer Prevention*. Am. Chem. Soc. Symp. Ser, 507, American Chemic al Society, Washington, D. C. 48 – 52. 77.Ikeda, Y. Mori, M. Adachi, Y. Matsushima, T. Sugimachi, K. and Saku, M. 1993. Carcinoembryonic antigen (CEA) in stage IV gastric cancer as a risk factor for liver metastasis: a univariate and multivariate analysis. *J. Surg. Oncol.* 53: 235-238. 78.Isshiki, K. Tokuoka, K. Mori, R. and Chiba, S. 1992. Preliminary examination of allyl isothiocyanate vapor for food preservation. *Biosci.,Biotechno. Biochem.* 56: 1476-1477. 79.Jabs, T. Dietrich, R. A. and Dang, J. L. 1996. Initiation of runaway cell death in an *Arabidopsis* mutant by extracellular superoxide. *Sci.* 273: 1853-1856. 80.James A. Duke. 1983. *Handbook of Energy Crops.* 81.Jin, D. Q. Lim, C. S. Sung, J. Y. Choi, H. G. Ha, I. and Han, J. S. 2006. *Ulva conglobata*, a marine algae, has neuroprotective and anti-inflammatory effects in murine hippocampal and microglial cells. *Neuroscience letters.* 402: 54-158. 82.Julkunen-Tiitto, R. 1985. Phenolic Constituents in the Leaves of Northern. Willows: Methods for the analysis of Certain Phenolics. *J. Agr. Food Chem.* 33: 213-217. 83.Kleinveld, H. A. Demacker, P. N. De Haan, A. F. and Stalenhoef, A. F. 1993. Decreased in vitro oxidizability of low-density lipoprotein in hypercholesterolaemic patients treated with 3-hydroxy-3-methylglutaryl -CoA reductase inhibitors. *Eur. J. Clin. Invest.* 23: 289-295. 84.Konishi, Y. and Kobayashi, S. 2004. Transepithelial transport of chlorogenic acid, caffeic acid, and their colonic metabolites in intestinal caco-2 cell monolayers. *J. Agric. Food Chem.* 52: 2518-2526. 85.Konishi, Y. Zhao, Z. and Shimizu, M. 2006. Phenolic acids are absorbed from the rat stomach with different absorption rates. *J. Agric. Food Chem.* 54: 7539-7543. 86.Kim, H. P. Mani, L. Iversen, L. and Ziboh, V. A. 1998. Effects of naturally occurring flavonoids and biflavonoids on epidermal cyclooxygenase and liopxygenase from guinea pigs. *Prostaglandins Leukotrienes Essen. Fatty Acids* 58: 17-24. 87.Lockwood, L. 1986. GB1 Comparative study of the volatile aglucons of glucosinolates from in vivo and in vitro grown *Descurainiasophia* and *Alyssum minimum* using gas chromatographymass spectrometry. *J. Chromatogr.* 356(3): 438-441. 88.Lin, H. M. Tseng, H. C. Wang, C. J. Chyau, C. C. Liao, K. K. Peng, P. L. and Chou, F. P. 2007. Induction of autophagy and apoptosis by the extract of *Solanum nigrum* Linn in HepG2 cells. *J. Agric. Food Chem.* 55: 3620-3628. 89.Lockwood, L. 1986. Phenolic constituents of plants and cell cultures of two Iranian cruciferae. *Bull liaison-Groupe Polyphenols.* 13: 598. 90.Lowry, O. H. Rosebrough, N. J. Farr, A. L. and Randell, R. J. 1951. Protein measurement with the Folin phenol reagent. *J. Bio.I Chem.* 193, 265-275. Moncada, S. Palmer, R. M. and Higgs, E. A. 1991. Nitric oxide: physiology, pathophysiology, and pharmacology. *Pharmacol Rev.* 43: 109-142. 91.Manach, C. Scalbert, A. Morand, C. Re'me'sy, C. and Jim'e'nez, L. 2004. Polyphenols: food sources and bioavailability. *Am. J. Clin. Nutri.* 79: 727-747. 92.Marie, C. Fitting, C. Muret, J. Payen, D. and Cavaillon, J. M. 2000. Interleukin 8 production in whole blood assays: Is interleukin 10 responsible for the downregulation observed in sepsis? *Cytokine* 12: 55-61. 93.Moser, C. Lang, S. A. Kainz, S. Gaumann, A. Fichtner-Feigl, S. Koehl, G. E. Schlitt, H. J. Geissler, E. K. and Stoeltzing, O. 2007. Blocking heat shock protein-90 inhibits the invasive properties and hepatic growth of human colon cancer cells and improves the efficacy of oxaliplatin in p53-deficient colon cancer tumors in vivo. *Mol. cancer ther.* 6: 2868-2878. 94.Mosmann, T. 1983. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. *J. Immuno. Meth.* 65: 55-63. 95.Morgera, S. Haase, M. Rocktaschel, J. Bohler, T. Heymann, C. V. Vargas-Hein, O. Krausch, D. Zuckermann-Becker, H. Muller, J. M. Kox, W. J. and Neumayer, H. H. 2003. High permeability haemofiltration improves peripheral blood mononuclear cell proliferation in septic patients with acute renal failure. *Nephrol. Dial. Transplant.* 18: 2570 – 2576. 96.Nishikimi, M. and Yamada, H. Y. 1980. Oxidation by superoxide of Tocopherols dispersed in aqueous media with deoxycholate. *Biochem. Biophys. Acta.* 627: 101-110. 97.Olsson, M. E. Gustavsson, K. E. Andersson, S. Nilsson, A. and Duan, R. D. 2004. Inhibition of cancer cell proliferation in vitro by fruit and berry extracts and correlations with antioxidant levels. *J. Agric. Food Chem.* 52: 7264-7271. 98.Ohshima, H. and Bartsch, H. 1994. Chronic infections and inflammatory processes as cancer risk factors:possible role of nitric oxide in carcinogenesis. *Mutation Res.* 305, 253-264. 99.Riddle, D. L. in *Caenorhabditis elegans* II, Riddle, D. Blumenthal, T. Meyer, B. Priess, J. Ed. (Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1997), pp. 739 – 768; C. Kenyon, ibid., pp. 791-813. 100.Rice-Evans, C. A. Miller, N. J. and Paganga, G. 1996. Structure and antioxidantactivity relationships of flavonoids and phenolic acids. *Free Radical Biol Med* 20,933-956. 101.Regen, D. Henry, R. Shu-Wei, G. Zewdu, G. Timothy, R. O. Gerald, P. H. and Steven, A. A. 1996. Cupric ion/ascorbate/hydrogenperoxide-induced DNA damage: DNA-bound copper ion primarily induces base modifications. *Free Radic. Biol. Med.* 21: 261-273. 102.Raes,M. Michiels, C. and Remacle, J. 1987. Comparative study of the enzymatic defense systems against oxygen-derived free radicals: the key role of glutathione peroxidase. *Free Radic. Biol. Med.* 3: 3-7. 103.Sollmann, T. A. 1957. *Mannual of Pharmacology.* 7ed. pp. 167. 104.Santos-Buelga, C. and Scalbert, A. 2000. Proanthocyanidins and tannin-like compounds: nature, occurrence, dietary intake and effects on nutrition and health. *J. Sci. Food Agric.* 80: 1094-117. 105.Shimonoi, K. Masuda, S. Furogori, M. Esaki S. and Kinae, N. 1994. Radioprotective affect of antioxidative flavonoids in γ -ray irradiated mice. *Carcinogenesis.* 15: 2669-2672. 106.Slater, T. F. Sawyer, B. C. and Striuli, U. 1963. *Biochim. biophys. Acta.* 77: 383. 107.Shimada, K. Fujikawa,

K. Yahara, K. and Nakamura, T. 1992. Antioxidative properties of Xanthan on the autoxidation of soybean oil in cyclodextrin emulsion. *J. of Agri. Food Chem.* 40: 945 – 948. 108.Scandalios, J. G. 1993. Oxygen stress and superoxide dismutase. *Plant Physiol.* 101: 7-12. 109.Schieber, A. Keller, P. and Carle, R. 2001. Determination of phenolic acids and flavonoids of apple and pear by HPLC. *J Chromato* 910: 265-273. 110.Scandalios, J. G. 1992. Molecular biology of free radical scavenging systems. 111.Subbaramaiah, K. and Dannenberg, A. J. 2003. "Cyclooxygenase 2: a molecular target for cancer prevention and treatment " *Trends Pharmacol Sci*, 24: 96-10. 112.Subbaramaiah, K. Zakim, D., Weksler, B. B., and Dannenberg, A. J. 1997. "Inhibition of cyclooxygenase: a novel approach to cancer prevention." *Proc Soc Exp Biol Med*, 216: 201-210. 113.Sipponen, P. Ja"rvi, O. Kekki, M. and Siurala, M. 1987. Decreased incidences of intestinal and diffuse types of gastric carcinoma in Finland during a 20-year period. *Scand. J. Gastroenterol.* 22:865-871. 114.Schieber, A. Keller, P. and Carle, R. 2001. Determination of phenolic acids and flavonoids of apple and pear by HPLC. *J. Chromato.* 910: 265-273. 115.Soledade, M. Pedras, C. Irina L, and Zaharia. 2000. Sinalbins a and b, phytoalexins from Sinapis alba: elicitation, isolation, and synthesis. *Phytochem.* 55: 213-216. 116.Steller, H. 1995. Mechanisms and genes of cellular suicide. *Sci.* 267: 1445-1448. 117.Tanaka, T. Takahashi, R. Kouno, I. and Nonaka, G. 1994. Chemical evidence for the de-astringency (insolubilization of tannins) of persimmon fruit. *J. Chem. Soc.*

[Perkin 1]: 3013 – 3022. 118.Tamir, S. de Rojas-Walker, T. Gal, A. Waller, A. H. Fox, J. G. and Wagan, G. N. 1995. Nitric oxide production in relation to spontaneous B cell lymphoma and myositis in SJL mice. *Cancer Res.* 55: 5391-5397. 119.Parkin, D. M. Bray, F. I. and Devesa, S. S. 2000. Cancer burden in the year. The global picture. *Eur. J. Cancer.* 2001; 37 Suppl 8:S4-66. 120.Palmer, R. M. Ferrige, A. G. and Moncada, S. 1987. Nitric oxide release accounts for the biological activity endothelium-derived relaxing factor. *Nature* 327: 524-526. 121.Nakadai, A. Li, Q. and Kawada, T. 2006. Chlorpyrifos induces apoptosis in human monocyte cell line U937. *Toxicol.* 224: 202-209. 122.Oyaizu, M. 1986. Studies on products of browning reaction: Antioxidative activities of products of browning reaction prepared from glucosamine. *Jpn. J. Nutri.* 44: 307. 123.Rinkus, S. J. and Taylor, R. T. 1990. Analysis of hydrogen peroxide in freshly prepared coffees. *Food Chem.* 1 Toxico. 28: 323-331. 124.Wolff, S. P. Gamer, A. and Dean, R. T. 1986. Free radicals, lipid and protein degradation. *Trends Biochem. Sci.* 11: 27-31. 125.Winston, G. W. 1990. Physiochemical basis for free radical formation in cells: Production and defense, in *Stress Responses in Plants: Adaptation and Acclimation Mechanisms*. Wiley-Liss, Inc., pp. 57-86. ISBN 0-471-56810-56814. 126.Walling, C. 1982. In oxidase and related redox systems. Pergamon Press, Oxford. pp. 85-97. 127.Yamanaka, H. Hagiwara, K. Kirisawa, R. and Iwai, H. 2003. Proinflammatory cytokines in bovine colostrum potentiate the mitogenic response of peripheral blood mononuclear cells from newborn calves through IL-2 and CD25 expression. *Microbiological Immunology.* 47: 461 – 468. 128.Yoshiaki, T. Yoshihito, K. and Tadashi, F. 2003. Antioxidant constituents of radish sprout (Kaiware-daikon), *Raphanus sativus* L. *J. Agric. Food Chem.* 51: 8061-8065. 129.Yonish-Rouach, E. Grunwald, D. Wilder, S. Kimchi, A. May, E. Lawrence, J. J. and May, P. 1993. Oren M. p53-mediated cell death: relationship to cell cycle control. *Mol Cell Biol.* 13: 1415-1423. 130.Zhang, Y. Vareed, S. K. and Nair, M. G. 2005. Human tumor cell growth inhibition by nontoxic anthocyanidins, the pigments in fruits and vegetables. *Life Sci.* 76: 1465-1472. 131.Zhao, C. Giusti, M. M. Malik, M. Moyer, M.P. and Magnuson, B. A. 2004. Effects of commercial anthocyanin-rich extracts on colonic cancer and nontumorigenic colonic cell growth. *J. Agric. Food Chem.* 52: 6122-6128.