

REFERENCES

- Aggarwal, B.B., and Shishidia, S. 2006. Molecular targets of dietary agents for prevention and therapy of cancer. Biochemical Pharmacology 71: 1397-1421.
- Ahn, S.C., Kim, B.Y., Park, Y.M., Kim, H.M., and Ahn, J.S. 2006. Colorimetric heparinase assay for alternative anti-metastatic activity. Life Sciences 79: 1661-1665.
- Andlauer, W., Stumpf, C., and Fürst, P. 2001. Intestinal absorption of rutin in free and conjugated forms. Biochemical Pharmacology 62(3): 369-374.
- Arabshahi-Duloulee, S. and Urooj A. 2007. Antioxidant properties of various solvent extracts of mulberry (*Morus indica* L.) leaves. Food Chemistry 102: 1233-1240.
- Arts, I.C., Sesink, A.L., Faassen-Peters, M., and Hollman, P.C. 2004. The type of sugar moiety is a major determinant of the small intestinal uptake and subsequent biliary excretion of dietary quercetin glycosides. British Journal of Nutrition 91(6): 841-847.
- Aruoma, O.I. 2003. Methodological consideration for characterizing potential antioxidant actions of bioactive components in plant foods. Mutation Research 523-524: 9-20.
- Atoui, A.K., Mansouri, A., Boskou, G., and Kefalas, P. 2005. Tea and herbal infusions: Their antioxidant activity and phenolic profile. Food Chemistry 89: 27-36.
- Bandeke, O.J., and Osheroff, N. 2007. Bioflavonoids as poisons of human topoisomerase II α and II β . Biochemistry 46:6097-6108.

- Beauchamp, C. and Fridovich, I. 1971. Superoxide dismutase improved assays and an assay applicable to acrylamide gels. Analytical Biochemistry. 44: 276-287.
- Bokkenheuser, V.D., Shackleton, C.H.L., and Winter, J. 1987. Hydrolysis of dietary flavonoid glycosides by strains of intestinal Bacterosides from humans. Biochemical Journal 248: 953-956.
- Burda, S. and Oleszek, W. 2001. Antioxidant and antiradical activities of flavonoids. Journal of Agricultural and Food Chemistry 49: 2774-2779.
- Cantero, G., Campanella, C., Cortés, F. 2006. Topoisomerase II inhibition and high yield of endoreduplication induced by the flavonoids luteolin and quercetin. Mutagenesis 21(5): 321-325.
- Carbonaro, M and Grant, G. 2005. Absorption of quercetin and rutin in rat small intestine. Annals of Nutrition and Metabolism 49(3): 1780182.
- Cardador-Martinez, A., Loacea-Pina, G., Oomah, B.D.2002. Antioxidant activity in common bean (*Phaseolus vulgaris* L.). Journal of Agricultural and Food Chemistry 50: 6975-6980.
- Chae, J.Y., Lee, J.Y., Houn, I.N., Whangbo, D., Chao, P.W., Lee, W.C., Kim, J.W., Kim, S.Y., Choi, S.W., and Rhee, S.J. 2003. Analysis of functional components of leaves of different mulberry cultivars. Journal of the Korean Society of Food Science and Nutrition 32(1): 15-21.
- Chetty, R. 2003. p27 protein and cancers of the gastrointestinal tract and liver. Journal of Clinical Gastroenterology 37(1): 23-27.
- Cheyrier, V. 2005. Polyphenols in food are more complex than often thought. American Journal of Clinical Nutrition 81(suppl): 223S-229S.
- Cho, Y., Chan, W.K., Birkhofer, M.J., Wang, S.S., Huang, Y.S., Liu, M., Whang-Peng, J., Chi, K.H., Luis, W.Y., and Lee, S.D. 1998. Phase II and

- pharmacokinetic study of palliative therapy for unresectable hepatocellular carcinoma. British Journal of Cancer 78:34-39.
- Cho, K.H., Peseta, J.M., Bolton, J.L., Steele, V.E., Karloff, G.J., Lee, S.K., and Constantine. 2000. Selection of cancer chemopreventive agents based on inhibition of topoisomerase II activity. European Journal of Cancer 36: 2146-2156.
- Choi, C.W., Kim, S.C., Hwang, S.S., Choi, B.K., Ahn, H.J., Lee, M.Y., Park, S.H., and Kim, S.K. 2002. Antioxidant activity and free radical scavenging capacity between Korean medicinal plants and flavonoids by assay-guided comparison. Plant Science 163: 1161-1168.
- Chu, Q., Lin, M., Tina, X., and Ye, J. 2006. Study on capillary electrophoresis- amperometric detection profiles of different parts of *Morus alba* L. Journal of Chromatography A 1116, 286-290.
- Chun, E. and Lee, K.Y. 2004. Bcl-2 and Bcl-xL are important for the induction of paclitaxel resistance in human hepatocellular carcinoma. Biochemical and Biophysical Research Communications 315(3): 771-719.
- Clarke, D. J.G.-A. 2000. Checkpoints controlling mitosis. Bioassays 22: 351-363.
- Coffman, F.D. and Studzinski, G.P. 1999. Differentiation-related mechanisms which suppress DNA replication. Experimental Cell Research 248: 58-73.
- Cook, N.C. and Samman, S. 1996. Flavonoids: Chemistry, metabolism, cardioprotective effects, and dietary sources. Nutritional Biochemistry 7: 66-76.
- Cortés, F., Pastro, N., Mateos, S., and Domínguez, I. 2003. Roles of DNA topoisomerases in chromosome segregation and mitosis. Mutation Research 543: 59-66.

- Cummings, J., and Smyth, J.F. 1993. DNA topoisomerase I and II as targets for rational design of new anticancer drugs. Annals of Oncology 4: 533-543.
- D'Alessandro, N., Poma, P. and Montalto, G.M. 2007. Multifactorial nature of hepatocellular carcinoma drug resistance: Could plant polyphenols be helpful? World Journal of Gastroenterology 13(14): 2037-2043.
- Downes, C. S., Clarke, D.J., Mullinger, A.M., Glmenez-Ablan, J.F., Crelghton, A.M., Johnson, R.T. 1994. A topoisomeraseII-dependent G2 cycle checkpoint in mammalian cells. Nature 372: 467-470.
- Doi, K., Kojima, T., Makino, M., Kimura, Y., and Fujimoto, Y. 2001. Studies on the constituents of the leaves of *Morus alba* L. Chemical & Pharmaceutical Bulletin (Tokyo) 49(2): 151-153.
- Fischer, P.M., Glover, D.M., and Lane, D.P. 2004. Targeting the cell cycle. Drug Discovery Today 1(4): 417-423.
- Galati, G. and O'Brien, P.J. 2004. Potential toxicity of flavonoids and other dietary phenolics: significance for their chemopreventive and anticancer properties. Free Radical Biology and Medicine 37(1):287-303.
- Ghobrial, I.M., Witzig, T.E., and Adjei, A.A. 2005. Targeting apoptosis pathways in cancer therapy. CA: a Cancer Journal for Clinicians 55: 178-194.
- Granado-Serrano, A.B., Martin, M.A., Bravo, L., and Ramos, S. 2006. Quercetin induces apoptosis via caspase activation, regulation of Bcl-2, and inhibition of PI-3-kinase/Akt and ERK pathways in a human hepatoma cell line (HepG2). The Journal of Nutrition 136: 2715-2721.
- Granado-Serrano, A.B., Martin, M.A., Izquierdo-Pulido, M., Goya, L., Bravo, L., and Ramos, S. 2006. Molecular mechanisms of (-)-epicatechin and chlorogenic acid on the regulation of the apoptotic and survival/proliferation pathways in a

- human hepatoma cell line. Journal of Agricultural and Food Chemistry 55: 2020-2027.
- Greenwald, P. 2002. Cancer prevention. British Medical Journal 324: 714-718.
- Griffiths, L.A. and Barrow, A. 1972. Metabolism of flavonoid compounds in green-free rats. Biochemical Journal 130: 1161-1162.
- Guendez, R., Kallithraka, S., Makris, D.P., Kefalas, P. 2005. Determination of low molecular weight polyphenolic constituents in grape (*Vitis vinifera* sp.) seed extracts: Correlation with antiradical activity. Food Chemistry 89: 1-9.
- Halliwell, B. 2007. Oxidative stress and cancer: Have we moved forward. The Biochemical Journal 401: 1-11.
- Hartwell, L. H. and Kastan, M.B. 1994. Cell cycle control and cancer. Science 266, 1821-1828.
- Hande, K.R. 1998. Clinical applications of anticancer drugs targeted to topoisomerase II. Biochimica et Biophysica Acta 1400(1-3): 173-184.
- Heck, M.M.S., and Earnshaw, W.C. 1986. Topoisomerase II: a specific marker for cell proliferation. The Journal of Cell Biology 103: 2568-2581.
- Heim, K.E., Tagliaferro, A.R., and Bobilya, D.J. 2002. Flavonoids antioxidants: chemistry, metabolism and structure-activity relationships. Journal of Nutritional Biochemistry 13: 572-584.
- Hollman, P.C.H., de Vries, J.H.M., van Leewen, S.D., Mengelers, M.J.B., and Katan, M.B. 1995. Absorption of dietary quercetin glycosides and quercetin in healthy ileostomy volunteers. American Journal of Clinical Nutrition 62: 1276-1282.
- Hong, Ch., Hur, S.K., Oh, O.J., Kim, S.S., Nam, K.E., and Lee, S.K. 2002. Evaluation of natural products on inhibition of inducible cyclooxygenase

- (COX-2) and nitric oxide synthase (iNOS) in cultured mouse macrophage cells. Journal of Ethnopharmacology 83: 153-159.
- Hsieh, W.T. H., K-Y., Lin, H-Y., and Chung, J-G. 2006. *Physalis angulata* induced G2/M phase arrest in human breast cancer cells. Food and Chemical Toxicology 44: 974-983.
- Ivanova, D., Gerova, D., Chervenkov, T., Yankova, T. 2005. Polyphenols and antioxidant capacity of Bulgarian medicinal plants. Journal of Ethnopharmacology 96: 145-150.
- Javanmardi, J., Stushnoff, C., Locke, E., Vivanco, J.M. 2003. Antioxidant activity and total phenolic content of *Iranian Ocium* accessions. Food Chemistry 83: 547-550.
- Jia, X. D., Han, C., Chen, J.S. 2005. Tea pigments induce cell-cycle arrest and apoptosis in HepG2 cells. World Journal of Gastroenterology 11(34): 5273-5276.
- Jo, J.Y., de Mejia, E.G., and Lila, M.A. 2005. Effects of grape cell culture extracts on human topoisomerase II catalytic activity and characterization of active fractions. Journal of Agricultural and Food Chemistry 53: 2489-2498.
- Katiyar, S.K., and Mukhtar, H. 1997. Tea antioxidant in cancer prevention. Journal of Cellular Biochemistry Supplement 27: 59-67.
- Katsube, T., Imawaka, N., Kawano, Y. Yamazaki, Y., Shiwaku, K., Yamane, Y.2006. Antioxidant flavonol glycosides in mulberry (*Morus alba* L.) leaves isolated based on LDL antioxidant activity. Food Chemistry 97: 25-31.
- Kim, S.Y., Gao, J.J., Lee, W-C., Ryu, K.S., Lee, K.R., and Kim, Y.C. 1999. Antioxidative flavonoids from the leaves of *Morus alba*. Archives of Pharmacal Research 22(1):81-85.

- Kim, S.Y., Gao, J.J., and Kang, H.K. 2000. Two flavonoids from the leaves of *Morus alba* induce differentiation of the human promyelocytic leukemia (HL-60) cell line. Biological & Pharmaceutical Bulletin 23(4): 451-455.
- Kris-Etherton, P.M., Hecker, K.D., Bonanome, A., Coval, S.M., Binkoski, A.E., Hilpert, K.F., Griel, A.E., and Etherton, T.D. 2002. Bioactive compounds in foods: their role in the preventive of cardiovascular disease and cancer. The American Journal of Medicine 113 (Suppl. 9B): 71S-88S.
- Larsen, A.K., Escargueil, A.E., and Skladanowski, A. 2003. From DNA damage to G2 arrest: the many roles of topoisomerase II. Progress in Cell Cycle Research 5: 295-300.
- Lavrik, I.N., Golks, A., and Khammer, P.H. 2005. Caspases: pharmacological manipulation of cell death. The Journal of Clinical Investigation 115: 2665-2672.
- Lee, S. H., Choi, S.Y., Kim, H., Hwang, J.S., Lee, B.G., Gao, J.J., and Kim, S.Y. 2002. Mulberroside F isolated from the leaves of *Morus alba* inhibits melanin biosynthesis. Biological & Pharmaceutical Bulletin 25(8): 1045-1048.
- Loo, G. 2003. Redox-sensitive mechanism of phytochemical-mediated inhibition of cancer cell proliferation. Journal of Nutrition Biochemistry 14: 64-73.
- Lorenz, P., Roychowdhury, S., Englemann, M., Wolf, G., and Horn, T.F.W. 2003. Oxyresveratol and resveratol are potent antioxidants and free radical scavengers: effect on nitrosative and oxidative stress derived from microglial cells. Nitric oxide 9: 64-76.
- Loloyd, R.V., Erickson, L.A., Jin, L., Kujig, E., Quian, X., Cheville, J.C., and Scheithauer, B.W. 1999. p27^{Kip1}: A multifunctional cyclin-dependent kinase

- inhibitor with prognostic significance in human cancers. American Journal of Pathology 154: 313-323.
- Matsumoto, M., Chiji, H., and Hara, H. 2005. Intestinal absorption and metabolism of a soluble flavonoid, alpha-rutin, in portal annulated rats. Free Radical Research 39(10): 1139-1146.
- Mersch-Sundermann, V., Knasmüller, S., Wu, X.J., Darroudi, F., and Kassie, F. 2004. Use of a human-derived liver cell line for the detection of cytoprotective, antigenotoxic and cogenotoxic agents. Toxicology 198: 329-340.
- Moure, A., Cruz, J.M., Franco, D., Domínguez, J.M., Sineiro, J., Domínguez, H., Núñez, M.J., and Parajó. 2001. Natural antioxidant from residual sources. Food Chemistry 72: 145-171.
- Mizushina, Y., Xu, X., Asano, N., Kasai, N., Kato, A., Takemura, M., Asahara, H., Linn, S., Sugawara, F., Yoshida, H., and Sakaguchi, K. 2003. The inhibitory action of pyrrolidine alkaloids, 1,4-dideoxy-1,4-imino-D-ribitol, on eukaryotic DNA polymerase. Biochemical and Biophysical Research Communication 304: 78-85.
- Monks, A., Scudiero, D., Skehan, P., Shoemaker, R., Paull, K., Vistica, D., Hose, C., Langley, J., Cronise, P., Vaigro-Wolff, A., Gray-Goodrich, M., Campbell, H., Mayo, J. and Boud, M. 1991. Feasibility of a high-flux anticancer drug screen using a diverse panel of cultured human tumor cell lines. Journal of the National Cancer Institute 83(1): 757-766.
- Morand, C., Manach, C., Crespy, V., and Remesy, C. 2000. Respective bioavailability of quercetin aglycone and its glycosides in a rat model. Biofactors 12(1-4):169-174.

- Mutaro, K and Terao, J. 2003. Antioxidative flavonoid quercetin: implication of its intestinal absorption and metabolism. Archives of Biochemistry and Biophysics 417: 12-17.
- Nam, S-Y., Yi, H-K., Lee, J.C., Kim, J.C., Song, C.H., Park, J.W., Lee, D.Y., Kim, J.S., and Hwang, P.H. 2002. Cortex Mori extract induces cancer cell apoptosis through inhibition of microtubule assembly. Archives of Pharmacal Research 25(2): 191-196.
- Nehir-El, S. and Karakaya, S. 2004. Radical scavenging and iron-chelating activities of some greens used as traditional dishes in Mediterranean diet. International Journal of Food Science and Nutrition 55(1): 67-74.
- Nichenametla, S.N., and Turuscio, T.G. 2006. A review of the effects and mechanisms of polyphenolics in cancer. Clinical Reviews in Food Science and Nutrition 46: 161-183.
- Niculescu, A.B., Chen, X., Smeets, M., Hengst, L., Prives, C., and Reed, S.I. 1998. Effect of p21(Cip1/Waf1) at both the G1/S and the G2/M cell cycle transition: pRb is critical determinant in blocking DNA replication and in preventing endoreduplication. Molecular and Cellular Biology 18: 629-643.
- Nita, M. E., Alves, A.F., Carrillo, F.J., Ono-Nita, S.K., Mello, E.S. and Gama-Rodrigues, J.J. 2002. Molecular aspecto of hepatic carcinogenesis. Revista do Instituto de Medicina Tropical de Sao Paulo 44(1): 39-48.
- Nomura, T. 1999. The chemistry and biosynthesis of isoprenylated flavonoids from moraceous plants. Pure and Applied Chemistry 71(6): 1115-1118.
- Nurmi, K., Ossipov, V., Haukioja, E., Pihlaja, K.1996. Variation of total phenolic content and individual low-molecular-weight phenolics in foliage of mountain

- birch trees (*Betula pubescens* ssp. *torruosa*). The Journal of Chemical Ecology 22: 2023-2040.
- Oh, H., Ko, E.K., Jun, J.Y., Oh, M.H., Park, S.U., Kang, K.H., Lee, H.S., and Kim, Y.C. 2002. Hepatoprotective and free radical scavenging activities of flavonoids, coumarin and stilbene from *Morus alba*. Planta Medica 68: 930-932.
- Parkin, D.M., Bray, F., Ferlay, J., and Pisani, P. 2005. Global cancer statistics, 2002. CA: a Cancer Journal for Clinicians 55: 74-1-8.
- Philipp, J.A., Vo, K., Gurley, K.E., Seidel, K., and Kemp, C.J. 1999. Tumor suppression by p27/Kip1 and p21/Cip1 during chemically induced skin carcinogenesis Oncogene 18: 4689-4698.
- Philipp-Staheli, J., Kim, K.H., Liggitt, D., Gurley, K.E., Longton, G., and Kemp, C.J. 2004. Distinct roles for p53, p27Kip1, p21Cip1 during tumor development. Oncogene 23: 905-913.
- Pietta, P., Simonetti, P., Mauri, P. 1998. Antioxidant activity of selected medicinal plants. Journal of Agricultural and Food Chemistry 46: 4487-4490.
- Ping, Z., Nan, K.N., and Hu, M.L. 2005. Cell proliferation, apoptosis and the related regulators p27, p53 expression in hepatocellular carcinoma. World Journal of Gastroenterology 11(13): 1910-1916.
- Pozarowski, P., Halicka, D.H., and Darzynkiewicz, Z. 2003. NF- κ B inhibitor sesquiterpene parthenolide induces concurrently atypical apoptosis and cell necrosis: difficulties in identification of dead cells in such cultures. Cytometry Part A 54A: 118-121.

- Prior, R.L., Wu, X., and Schach, K. 2005. Standardized methods for the determination of antioxidant capacity and phenolics in foods and dietary supplements. Journal of Agricultural Food Chemistry 53: 4290-4302.
- Qin, L.X. and Tang, Z.Y. 2002. The prognostic molecular markers in hepatocellular carcinoma. World Journal of Gastroenterology 8(3): 385-392.
- Racchi, M., Daglia, M., Lanni, C., Papetti, A., Govoni, S., and Gazzani, G. 2002. Antiradical activity of water soluble component in common diet vegetables. Journal of Agricultural and Food Chemistry. 50: 1272-1277.
- Ramiraz-Mares, M.V., Chandra, S., and de Mejia, E.G. 2004. In vitro chemopreventive activity of *Camellia sinensis*, *Ilex paraguariensis* and *Ardisia compressa* tea extracts and selected polyphenols. Mutation Research. 554: 53-65.
- Ramos, S., Alía, M., Bravo, L., and Goya, L. 2005. Comparative effects of food-derived polyphenols on the viability and apoptosis of human hepatoma cell line (HepG2). Journal of Agricultural and Food Chemistry 53: 1271-1280.
- Rao, K., Vaughan, A., and Moon, R. 1995. Flavonoids as DNA topoisomerase antagonists and poisons: structure-activity relationships. Journal of Natural Products 58(2): 217-225.
- Rivard, N., Boucher, M.J., Asslin, C., L'Allemain, G. 1999. MAP kinase cascade is required for 27 down regulation and S phase entry in fibroblast and endothelial cells. American Journal of Physiology 277: C652-C664.
- Robards, K., Prenzler, P.D., Swatsitang, P., and Glover, W. 1999. Phenolic compounds and their role in oxidative processes in fruits. Food Chemistry 66: 401-436.

- Sánchez-Moreno, C., Larrauri, J.A., and Saura-Calixto, F. 1999. Free radical scavenging capacity and inhibition of lipid oxidation of wines, grape juices and related polyphenolic constituents. Food Research International 32:407-412.
- Seow, T.K., Liang, R.C.M.Y., Leow, C.K., and Chung, M.C.M. 2001. Hepatocellular carcinoma from bedside to proteomics. Proteomics 1: 1249-1263.
- Skladanowski, A., Côme, M.G., Sabisz, M., Escargueil, A.E., and Larsen, A.K. 2005. Down-regulation of DNA topoisomerase II α leads to prolonged cell cycle transit in G2 and early M phases and increased survival to microtubule-interacting agents. Molecular Pharmacology 68(3): 625-634.
- Smolewski, P., Grabarek, J., Halicka, H.D., and Darzynkiewicz, Z. 2002. Assay of caspases activation in situ combined with probing plasma membrane integrity to detect three distinct stages of apoptosis. Journal of Immunological Methods 265: 111-121.
- Srivastava, S., Kapoor, R., Thathola, A., and Srivastava, R.P. 2006. Nutritional quality of leaves of some genotypes of mulberry (*Morus alba*). International Journal of Food Sciences and Nutrition 57(5/6): 305-313.
- Sun, S. Y., Hail, N., Lotan, R. 2004. Apoptosis as a novel target for cancer chemoprevention. Journal of the National Cancer Institute 96: 662-672.
- Takuya, K., Yukikazu, Y. 2002. Apoptosis-inducing activity of ethanol extracts from the tea of mulberry (*Morus alba*) leaves in HL-60 cells. Journal of the Japanese Society for Food Science and Technology 49(3):195-198.
- Tamm, I., Schriever, F., and Dorken, B. 2001. Apoptosis: implications of basic research for clinical oncology. Lancet 2: 33-42.

- Tien, K.M. and Savaraj, N. 2006. Poles of reactive oxygen species in hepatocarcinogenesis and drug resistance gene expression in liver cancers. Molecular Carcinogenesis 45(9): 701-709.
- Tiwari, A.K. 2001. Imbalance in antioxidant defense and human diseases: Multiple approach of natural antioxidant therapy. Current Science 81(9): 1179-187.
- Thorgeirsson, S.S., and Grisham, J.W. 2002. Molecular pathogenesis of human hepatocellular carcinoma. Nature Genetic 31: 339-346.
- Thomas, M.B. and Abbruzzese, J.L. 2005. Opportunities for targeted therapies in hepatocellular carcinoma. Journal of Clinical Oncology 23(31): 8093-8108.
- Tuberoco, C.I.G., Kowalczyk, A., Sarritzu, E. and Cabras, P. 2007. Determination of antioxidant compounds and antioxidant activity in commercial oilseeds for food use. Food Chemistry 103: 1494-1501.
- Tsao, R., and Deng, Z. 2004. Separation procedures for naturally occurring antioxidant phytochemicals. Journal of Chromatography B 812: 85-99.
- Tsuda, H., Ohsima, Y., Nomoto, H., Fujita, K., Matsuda, E., Iigo, M., Takasuka, N., and Moore, M.A. 2004. Cancer prevention by natural compounds. Drug Metabolism and Pharmacokinetics 19(4): 245-63.
- Valero, A., Merino, F., Wolbers, F., Luttge, F., Vermes, I., Andersson, H., and van den Berg, A. 2005. Apoptotic cell death dynamics of HL60 cells studies using a microfluidic cell trap device. Lap Chip 5: 49-55.
- Van, B. R., Haenen, G.R.M.M., Berg, H., Bast, A. 1999. Applicability of an improved Trolox equivalent antioxidant capacity measurement of mixtures. Food Chemistry 66: 511-517.

- Valko, M., Rhodes, C.J., Monocol, J.R., Izakovic, M.M., and Mazur, M. 2006. Free radicals, metal and antioxidants in oxidative stress-induced cancer. Chemico-Biological Interaction 160: 1-40.
- Vatanasapt, V., Sriamporn, S., and Vatanasapt, P. 2002. Cancer control in Thailand. Japanese Journal of Clinical Oncology 32(Supplement 1): S82-S91.
- Wagayama, H., Shiraki, K., Sugimoto, K., Ito, T., Fugikawa, K., Yamanaka, Y., Takase, K., and Nakano, T. 2002. High expression of p21^{WAF1/CIP1} is correlated with human hepatocellular carcinoma in patients with hepatitis C virus-associated chronic liver diseases. Human Pathology. 33(4): 429-434.
- Walker, J.V., and Nitiss, J.L. 2002. DNA topoisomerase II as target for cancer therapy. Cancer Investigation 20(4): 570-589.
- Walle, T., Browning, A.M., Steed, L.L., Reed, S.G., and Walle, U.K. 2005. Flavonoid glucosides are hydrolyzed and thus activated in the oral activity in human. Journal of Nutrition 135: 48-52.
- Watanuki, A., Ohwada, S., Fukusato, T., Makita, F., Yamada, T., Kikuchi, A., and Morishita, Y. 2002. Prognostic significance of DNA topoisomerase II α expression in human hepatocellular carcinoma. Anticancer Research 22(2B): 1113-1119.
- Watson, W.H., Cai, W.J. and Jones, D.P. 2000. Diet and apoptosis. Annual Review of Nutrition 20: 485-505.
- William R.T., Spencer, J.P.E., and Rice-Evans, C. 2004. Flavonoids: antioxidant or signalling molecules? Free Radical Biology & Medicine 36(7): 839-849.
- Wlodkowic, D., Skommer, J., and Pelkonen, J. 2007. Brefeldin A triggers apoptosis associated with mitochondrial breach and enhances HA 14-1- and anti-Fas-

- mediated cell killing in follicular lymphoma cells. Leukemia Research 31; 1687-1700.
- Wong, C.H., Chan, S.K.P., Chan, H.L.K., and Tsui, S.K.W. 2006. The molecular diagnosis of hepatitis B virus-associated hepatocellular carcinoma. Critical Reviews in Clinical Laboratory Sciences 43(1):69-101
- Wong, S.H., Leong, L.P., and Koh, J.H.W. 2006. Antioxidant activities of aqueous extracts of selected plants. Food Chemistry 99: 775-783.
- Xu., J.J., Diaz, D., and O'Brien, P.J. 2004. Application of cytotoxicity assays and pre-lethal mechanistic assays for assessment of human hepatotoxicity potential. Chemico-Biological Interaction 150: 115-128.
- Yamashita, N., and Kawanishi, S. 2000. Distinct mechanisms of DNA damage in apoptosis induced by quercetin and luteolin. Free Radical Research 33: 623-633.
- Yamatake, Y., Shibata, M., and Nagai, M. 1978. Pharmacological studies on root bark of mulberry tree (*Morus alba* L.). The Japanese Journal of Pharmacology 26(4): 461-9.
- Yan, J., Wang, M., and Lu, J. 2004. Determination of rutin, quercetin, and chlorogenic acid in mulberry leaves by capillary zone electrophoresis. Analytical Letters 37(15): 3287-3297.
- Yang, C.S., Landau, J.M., Huang, M.T., and Newark, H.L. 2001. Inhibition of carcinogenesis by dietary polyphenolic compounds. Annual Review of Nutrition 21:381-406.
- Yao, L.H., Jiang, Y.M., Shi, J., Tomás-Barberán, F.A., Datta, N., Singanusong, R., and Chen, S.S. 2004. Flavonoids in food and their health benefits. Plant Food for Human Nutrition 59: 113-122.

- Yeh, M.M., Larson, A.M., Campbell, J.S., Fausto, N., Rulyak, S.J., and Swanson, P.E. 2007. The expression of transforming growth factor- α in cirrhosis, dysplastic nodules, and hepatocellular carcinoma. American Journal of Clinical Pathology 31(5): 681-689.
- Yousef, G. G., Seigler, D.S., Grusak, M.A., Rogers, R.B., Knight, C.T., Kraft, T.F.B., Erdman, J.W., Lila, M.A. 2004. Biosynthesis and characterization of C14-enriched flavonoids fractions from plants cell suspension cultures. Journal of Agricultural and Food Chemistry 52: 1138-1145.
- Yuwen, H., Hsia, C.C., Nakashima, Y., Evangelista, A., and Tabor, E. 1997. Binding of wild-type p53 by topoisomerase II and overexpression of topoisomerase II in human hepatocellular carcinoma. Biochemical and Biophysical Research Communications 234: 194-197.
- Zheng, Q., Hirose, Y., Yoshimi, N., Murakami, A., Koshimizu, K., Ohigashi, H., Sakata, K., Mutsumoto, Y., Sayama, Y., and More, H. 2002. Further investigation of the modifying effect of various chemopreventive agents on apoptosis and cell proliferation in human colon cancer cells. Journal of Cancer Research and Clinical Oncology 128(10): 539-546.
- Zhishen, J., Mengcheng, T., and Jianming, W. 1999. The determination of flavonoids contents in mulberry and their scavenging effects on superoxide radicals. Food Chemistry 64: 555-559.

APPENDICES

APPENDIX

PREPARATION OF REAGENTS

Preparation of DPPH assay

DPPH solution

To make 50 mL of 150 μ M DPPH solution (in 80% v/v aqueous methanol), the solution are containing

DPPH	3	mg
80% Methanol	50	mL

All ingredients were mixed completely and stored at -20°C .

Trolox standard curve

To make 50, 100, 300 and 400 μ M Trolox standard solutions

1. Prepared 1 mM Trolox stock solution

Trolox	0.25	mg
PBS buffer, pH 7.4	1	mL

All ingredients were mixed completely and stored at -20°C .

2. Prepared Trolox working solution

Trolox concentration (μ M)	Trolox stock solution (μ L)	PBS buffer, pH 7.4 (μ L)
50	50	950
100	100	900
300	300	700
400	400	600

All ingredients were mixed completely and stored at -20°C .

Preparation of cell cycle distribution analysis

Propidium iodide staining solution

To make 20 mL propidium iodide staining solution (0.02 mg/mL PI, 0.2 mg/mL RNase), the solution are containing

PBS, pH 7.4	19.576 mL
PI	400 μ L
RNase	4 μ L
Triton X-100	20 μ L

All ingredients were mixed completely and stored at 4 °C.

Preparation of apoptosis analysis

1X Wash buffer

Once prepared, the 1X wash buffer is stable for 14 days at 2-8 °C.

1. Warm 10X wash buffer (supplied in the kit; Vybrant® FAM Caspases Assay Kit, Catalog number V35117) to dissolve any salt crystals.
2. Prepare a 1 in 10 dilution by adding 1 part of 10X wash buffer to 9 parts deionized H₂O.

Note: If using entire bottle of 10X wash buffer add 135 mL of deionized H₂O.

150X FLICA reagent stock solution

1. To make the 150X FLICA stock solution, add 50 μ L of DMSO (supplied in the kit) to lyophilized FLICA reagent.
2. Mix vial by swirling or tilting until completely dissolved.

3. Store unused portion at ≤ -20 °C protected from light.

Note: 150X stock solution may be frozen and thawed up to times. After it has been thawed for a second time, any 150X FLICA reagent stock solutions not used for that day's experiments should be discarded.

30X FLICA reagent working solution

Prepared a 1 in 5 dilution by adding 1 part of FLICA reagent stock solution to 4 parts phosphate-buffered saline (PBS), pH 7.4.

Note: Any 30X FLICA reagent working solution remaining at the end of the day should be discarded.

Preparation of SDS-PAGE and Western Blot Analysis

Running buffer

To make 1 L of running buffer (2.5 mM Tris, 192 mM glycine, 0.1% SDS, pH 8.3), the solution containing

10X Tris-glycine SDS stock solution (Bio-Rad)	100	mL
Deionized H ₂ O	900	mL.

All ingredients were mixed completely and stored at 4 °C.

Sample buffer

To make Laemmli sample buffer (containing 5% the solution containing β -Mercaptoethanol), the solution containing

Laemmli Sample buffer (Bio-Rad)	950	μ L
β -Mercaptoethanol	50	μ L

All ingredients were mixed completely and stored at 4 °C.

SDS-PAGE gel

10% Tris-HCl Bio-Rad Ready Gel, 50 μ L, 10 well combs

Distaining solution

To make 10% acetic acid in deionized H₂O, the solution containing

Acetic acid	10	mL
Deionized H ₂ O	90	mL.

All ingredients were mixed completely and stored at 4 °C.

PVDF membrane

Bio-Rad Immun-Blot PVDF membrane 10x15 cm

Filter paper

Bio-Rad Mini Trans Blot Fiber Pads

Transfer buffer

To make 1X Transfer buffer, the solution containing

Methanol	100	mL
20X NuPAGE Transfer Buffer (Invitrogen)	50	mL
Deionized H ₂ O	90	mL.

All ingredients were mixed completely and stored at 4 °C.

TBST solution

To make 1L of 1X TBST (0.1% Tween 20, 0.05 M Tris, 0.138 M NaCl and 0.0027 M KCl), the solution containing Sigma T-664 tris-buffered saline , pH 8.0 packet was dissolved in 1000 mL deionized H₂O and add 1 mL of Tween 20.

All ingredients were mixed completely and stored at 4 °C.

TBS solution

To make 1L of 1X TBST (0.1% Tween 20, 0.05 M Tris, 0.138 M NaCl and 0.0027 M KCl), the solution containing Sigma T-664 tris-buffered saline , pH 8.0 packet was dissolved in 1000 mL deionized H₂O.

All ingredients were mixed completely and stored at 4 °C

Blocking buffer solution

To make Blocking solution, the solution containing

TBST solution	80	mL
Blocking agent	2.4	g

(Amersham Biosciences, ECL Advance Blocking Reagent)

All ingredients were mixed completely and stored at 4 °C.

Primary antibody

Actin (C-2), P21 (F-5), P27 (F-8) and Topo II α (KF4) antibody purchased from Santa Cruz Biotechnology, CA

Secondary antibody

ECL Plus Western Blotting Reagent Pack RPN2124, Anti-mouse HRP Conjugate (Amersham Biosciences)

Detection Reagent

ECL Advance Western Blotting Detection Kit RPN2135

CURRICUM VITAE

Miss Wanlaya Naowaratwattana was born on March 26, 1975 in Khon Kaen Province. She graduated in Bachelor of Science (Biochemistry) in 1996 from Khon Kaen University and Master's degree of Science (Medical Biochemistry) in 1999 from Khon Kaen University. Since 1996 to present, she has been working as lecturer in Mahasarakham University, Mahasarakham Province, Thailand.