

- Adjei, A.A., 2001. Review: Blocking oncogenic ras signaling for cancer therapy, *J Nat. Canc. Inst.* **93** (14), 1062-1074.
- Agarwal, R. 2000. Cell signaling and regulators of cell cycle as molecular targets for prostate cancer prevention by dietary agents. *Biochem. Pharmacol.* **60**:1051-1059.
- Andersen, T.I., R. Holm and J.M. Nesland. 2000. Prognostic significance of TP53 alterations in breast carcinomas. *Br. J. Canc.*, **68**:540-548.
- Anderson, L. E., Boorman, G. A., Morris, J. E., Sasser, L. B., Mann, P. C., Grumbein, S. L., Hailey, J. R., Mc Nally, A., Sills, R. C. and J.K. Haseman. 1999, Effect of 13 week magnetic fields exposure on DMBA-initiated mammary gland carcinomas in female Sprague-Dawley Rats, *Carcinogenesis*, **8** (20) : 1615-1620.
- Anonim a, 2004. Pharmacogenomics in oncology-potential modulating factor, diambil dari <http://www.eohsi.rutgers.edu>.
- Anonim b, 2004. dna preparation on fresh/frozen tissue. section of cancer genomics, genetics branch, NCI National Institute of Health. <http://www.potocal.online.org>, diakses pada April 2005.
- Anonim. 2007. Antioxidant Response Element Reporter Cell Line (ARE32). CXR Biosciences Scotland. <http://www.crxbiosciences.com>
- Anggraita,H., 1998. Aktivitas biologis fraksi residu ekstrak etanol daun *Gynura procumbens* (luor.) merr. terhadap kultur sel vero dan kultur sel mieloma, *Skripsi*, Fakultas Farmasi Universitas Gadjah Mada, Yogyakarta.
- Appelt, L.C., and M.M. Reicks. 1999. Soy Induces Phase II But Does Not Inhibit Dimethylbenz(a)anthracene-Induced Carcinogenesis in Female Rats. *J Nutr.* **129** : 1820-1826.
- Arianti S., 1998. Aktivitas Biologis Ekstrak Etanol Daun *Gynura Procumbens* (Lour) Merr. Terhadap Sel Vero dan Sel Mieloma, *Skripsi*, Fakultas Farmasi Universitas Gadjah Mada, Yogyakarta.
- Asepgana, Suganda, Iwang Sudiro dan Ganthina. 1988. Skrining fitokimia dan asam fenolat daun dewa (*Gynura procumbens* (Lour) Merr), Simposium Penelitian Tumbuhan Obat III, Universitas Indonesia Jakarta.

- Backer, C.A., and Van Den Brink, R.C.B., 1965. *Flora of Java (Spermatophytes Only)*, Vol II., N.V.D. Noordhoff-Groningen-The Netherlands.
- Bancroft, J.D. and H.C. Cook. 1998. manual of histological techniques and their diagnostic application. 35-38. Logman Singapore Pub. Singapore..
- Bankfalvi, A., G. Giuffre, D. Ofner, R. Diallo, C. Poremba, I.B. Buchwalow, V. Barresi, W. Bocker., and G. Tuccari, 2002. Relationship between HER2 status and proliferation rate in breast cancer assessed by immunohistochemistry, fluorescence *in situ* hybridisation and standardized AgNOR analysis, *Intr. J. Oncol.* 23 : 1285-1292.
- Barbacid, M., S. Sukumar, V. Notario, and D. Martin-Sanca, 1985. Induction of mammary carcinomas in rats by nitroso-methylurea involves malignant activation of H-ras-1 locus by single point mutations. *Nature* 306. 658-661.
- Barl, J., E. Cohen-Noyman, B. Geiger, and M. Oren. 2004. Attenuation of the p53 response to DNA damage by high cell density. *J. Oncog.* : 1-10.
- Barletta, E., G. Gorini, P. Vinels, L. Miligi, L. Davico, G. Mugnai, S. Ciolli, F. Leoni, M. Bertini, G. Matullo, and A.S. Costantini. 2004. *Ras* gene mutations in patients with acute myeloid leukaemia and exposure to chemical agents. *Carcinogenesis*. 5 (25) pp. 749-755.
- Basil, F., El-Rayes, Shadan, A, Lance K., Heilbrun, Samir, L., David, B., David, V., and P.A., Philip. 2003. cytochrome p450 and glutathione transferase expression in human breast cancer. *Clin. Can. Resc.* 9. 1705-1709.
- Bend, R.J. and C.J. Serabjit-Singh, 1994. xenobiotic metabolism by extra hepatic tissue: relationship to target organ and cell toxicity. drug metabolism and drug toxicity. pp. 99-114, Raven Press, New York.
- Berge, G., S. Ovrebo, I.V. Botnen, A. Hewer, D.H. Phillips, A. Haugen, and S. Mollerup. 2004^a. Resveratrol inhibits benzo[a]pyrene-DNA adduct formation in human bronchial epithelial cells. *Br J Canc.*, 91: 333-338.
- Berge, G., S. Ovrebo, E. Eilertsen, A. Haugen, and S. Mollerup. 2004^b. Analysis of resveratrol as a lung cancer chemopreventive agent in A/J mice exposed to benzo[a]pyrene. *Br. J. Canc.*, 91: 1380-1383.

- Bernard, W.I. 2000. Disorders in cell circuitry during multistage carcinogenesis: the role of homeostasis. *Carcinogenesis* 21. 857-64.
- Brauch H., Bruning T., Fischer H., Hamann U., Hart V., Justenhoven C., Ko Y. and Pesch B., 2004. *Breast Cancer Risk and Predictive Factors : Association with Genetic Polymorphisms and Expression of human Drug-Metabolizing Enzymes*, diakses://www.dhgp.de/research/projects/abstracts/9975.html.
- Brem, S., MD., 1999. Angiogenesis and cancer control: from concept to therapeutic trial, moffit cancer center & research institute (diakses://www.medscape.com).
- Cardenas, E.E., Sanfridson, A., Cutler, N.S., and Heitman, J. 1998. signal-transduction cascades as target for therapeutic intervention by natural products, *Tibtech*, 16: 425-428
- Ciolino, HP. and G.C. Yeh. 1999. Inhibition of aryl hydrocarbon-induced cytochrome P-450 1A1 enzyme activity and CYP1A1 expression by resveratrol. *Mol. Pharmacol.* 56: 760-767.
- Ciolino, HP., P.J. Daschner, and G.C. Yeh. 1998^a . Resveratrol inhibits transcription of CYP1A1 in vitro by preventing activation of the aryl hydrocarbon receptor. *Canc. Res.* 58: 5707-5712.
- Ciolino, HP., P.J. Daschner, T.T. Wang, and G.C. Yeh. 1998^b . Effect of curcumin on the aryl hydrocarbon receptor and cytochrome P450 1A1 in MCF-7 human breast carcinoma cells. *Biochem. Pharmacol.* 56: 197-206.
- Costa, Irmgard, Solanas, Montserrat, Escrich, and Eduard. 2002. Histopathologic characterization of mammary neoplastic lesions induced with 7, 12 dimethylbenz(alpha)anthracene in the rat: A comparative analysis with human breast tumors. *Archives of Pathology & Laboratory Medicine*, 126:915-927.
- Cotelle N. 2001. Role of flavonoids in oxidative stress, Current topics in medicinal chemistry. 1 (6): 569-590.
- Craig, WJ. 1999. Health-promoting Properties of Common Herbs, *Am. J. Clin. Nutr.* 70 : 419S-9S.

- Crowell, P.L. 1999. Prevention and Therapy of Cancer by Dietary Monoterpenes, *J. of Nutr.*, **129**: 775-778.
- Davit B.K. Reynolds and Yuan R., 1999. FDA evaluations using in vitro metabolism to predict and interpret in vivo metabolic drug-drug interactions: impact on labeling. *Clin. Pharmacol.* **39**: 899-910.
- Dandekar, S., Sukumar, S., Zaebl, H., Young, L. J. T. and Cardiff, R. D., 1986. Specific activation of the cellular harvey-ras oncogene in dimethylbenzanthracene-induced mouse mammary tumors, *Mol Cell Biol.* **6** (11), 4104-4108.
- Denison, M.S., and S.R. Nagy. 2003. Activation of the aryl hydrocarbon receptor by structurally diverse exogenous and endogenous chemicals. *Annu. Rev. Pharmacol. Toxicol.* **43**: 309-34.
- Dhaygude V., 2006. *The study of canine mammary tumors with special reference to mutations in p53 tumor suppressor gene by pcr-sscp*. masters thesis, college of veterinary science and animal husbandry, Anand Agricultural University, Anand, Gujarat, INDIA.
- Dutra, A.P., G.M. Azevedo Junior, F.C. Schmitt., and G.D. Cassali. 2008. Assesment of cell proliferation and prosnestic factors in canine mammary glands tumors. *Arq. Bras. Med Vet. Zootec.*, **60**(6). p. 1403-1412.
- El-Rayes, B.F., S. Ali, L. K. Heilbrun, S. Lababidi, D. Bouwman, D. Visscher and, P.A. Philip, 2003. Cytochrome P450 and Glutathione Transferase expression in human breast cancer. *Clin. Canc. Res.*, Vol. 9, 1705-1709.
- El-Sohehy A and M.C. Archer, 2000, Inhibition of *N*-methyl-*N*-nitrosourea- and 7,12-dimethylbenz[*a*] anthracene-induced rat mammary tumorigenesis by dietary cholesterol is independent of Ha-*ras* mutations. *Carcinog.*, **21** (4) 827-831.
- Elston, C.W., and I.O. Ellis. 1009. Pathological prognostic factors in breast cancer I. The value histological grade in breast cancer : experience from a large study with long term follow up. *Histopathol.*, **19** : 403-10.
- Elzagheid, A., T. Kuopio, M. Ilmen, and Y. Collan. 2002. Prognostication of invasive ductal breast cancer by quantification of E-cadherin immunostaining: the methodology and clinical relevance. *Histopathol.*, **41**(2):127-33.

- Feng Z., Hu W., Chen, JX., Pao A., and Tang M., 2002. Preferential DNA damage and poor repair determine ras gene mutational hotspot in human cancer, *J Nat. Canc. Inst.*, 94 (20), 1527-1536.
- Finco, T.S., J.K. Westwick, J.L. Norris, A.A. Beg, C.J. Der, and A.S. Baldwin Jr. 1997. Oncogenic Ha-Ras-induced signaling activates nf- κ b transcriptional activity, which is required for cellular transformation. *The Am. Soc. for Biochem. and Mol. Biol.*, 39.(272). pp. 24113-24116.
- Futreal, P.A., Coin, L., Marshall, M., Down, T., Hubbard, T., Wooster, R., Rahman, R., and M. R. Stratton. 2004. Reviews. a census of human cancer genes. *Nat. Rev. Canc.*, Vol 4 177-183.
- Gabriela, I., J.A. Akinsete, and W. E. Hardman. 2010. Maternal consumption of canola oil suppressed mammary gland tumorigenesis in C3(1) TAG mice offspring. *BMC. Canc.*, Vol 10:81. 1471-2407.
- Gabriel, A.A., 2000. phytochemical and hypoglycaemic studies of *Gynura procumbens* (Lour) Merr(Compositae). M Sc ThesisUniversiti Sains Malaysia.
- Gregus, Z., & Klaasen, C.D., 2001. Mechanisms of Toxicity, in Curtis D. Klaasen, Casarett & Doull's : *Toxicology, The Basic Science of Poisons*, 6th Ed., Mc.Graw Hill. Medical Publishing Division, New York, 40-41.
- Gibbs, J.B., 2000. Mechanism-based target identification and drug discovery in cancer research. *Scien.* 287 1969-1973.
- Griffith, E.J.F., Miller, D.T., Suzuki, R.D., Lewontin, W., and M. Gelbart. 1993. An Introduction to Genetic Analysis. 5th Ed. W.H. Freeman and Company. New York. p. 841.
- Gritter, R.J., Bobbit, J.M., & Schwarting A.E., 1991. Terjemahan *Pengantar Kromatografi*, Penerbit ITB, Bandung.
- Guengerich, FP., and T. Shimada. 1998. Activation of procarcinogens by human cytochrome P450 enzymes. *Mutat. Res.* 400: 201-213.
- Guthrie, N. 2000. Effect of cranberry juice and products on human breast cancer cell growth. *J. FASEB* 14: 531.13 Abs.



EFEK EKSTRAK *Gynura procumbens* PADA KARSINOGENESIS KELENJAR MAMAE TIKUS YANG DIINDUKSI

7,12-DIMETHYLBENZ(a)ANTRASEN: KAJIAN ENZIMATIK DAN GENETIK

Iwan Sahrial Hamid, Prof. Sugiyanto, SU., Ph.D., Apt.

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first enzymatic step in mercapturic acid formation, *J. Biol. Chem.*, **249** (22), 7130-7139.

- Hariyadi, 1991. Analisis kualitatif kandungan kimia dan isolasi kandungan kimia utama daun *Gynura procumbens* (Luor) Merr. Dengan Kromatografi Lapis Tipis, Skripsi, Fakultas Farmasi, Universitas Gadjah Mada Yogyakarta.
- Hanahan, D. and Weinberg, R.A., 2000. The Hallmarks of Cancer, *Cell*, **100** :57-70.
- Haghiak, M and Walle, T. 2005. Quercetin induces necrosis and apoptosis in scc-9 oral cancer cells. *Nutr. and Canc.*, **53** (2): 220-231.
- Heidel, SM., P.S. MacWilliams, W.M. Baird, W.M. Dashwood, J.T.M. Buters, F.J. Gonzalez, M.C. Larsen, C.J. Czuprynski, and C.R. Jefcoate. 2000. Cytochrome P4501B1 mediates induction of bone marrow cytotoxicity and preleukemia cells in mice treated with 7,12 Dimethylbenz[a]anthracene. *Canc. Res.*, **60** : 3454-3460.
- Harborne, JB. 1996. The Flavonoids : Advances In Research Since. Chapman and Hall. London.
- Hayes, J.D. and D.J. Pulford. 1995. S-Transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprevention and drug resistance. *Biochem. Mol. Biol.*, **30** (6), 445-600.
- Heyne, K., 1987, *Tanaman Berguna Indonesia*, jilid II, p. 1029. cetakan pertama, diterjemahkan oleh Badan Litbang Departemen Kehutanan, Yayasan Sarana Wana Jaya, Jakarta.
- Hodek, P., P. Trefil, and M. Stiborova. 2002. Flavonoids-potent and versatile biologically active compounds interacting with cytochromes P450. *Chem.- Biol. Interact.*, **139**: 1-21.
- Hollstein, M, Sidransky D, Vogelstein B, Harris CC. 1991. p53 mutation in human cancers. *Scien.*, **253**: 49-53.
- Jansen, D., Romert, L., and L. Zhang, L, 1988, Metabolism mediated mutagenesis in mammalian cells *in vitro*. *Live Sci. Adv.* (in press).
- Juliano, R.L. 2002. Annu Rev. Pharmacol. Toxicol. In Attenuate of the p53 response to DNA damage by high cell density. *Oncogen.*, pp. 283-323.
- Josephy, P. D., 1997, *Molecular Toxicology*, Oxford University Press, New York.

Hanahan, D. and Weinberg, R.A., 2000. The Hallmarks of Cancer, *Cell*, 100 :57-70.

Haghiak, M and Walle, T. 2005. Quercetin induces necrosis and apoptosis in scc-9 oral cancer cells. *Nutr. and Canc.*, **53** (2): 220-231.

Heidel, SM., P.S. MacWilliams, W.M. Baird, W.M. Dashwood, J.T.M. Buters, F.J. Gonzalez, M.C. Larsen, C.J. Czuprynski, and C.R. Jefcoate. 2000. Cytochrome P4501B1 mediates induction of bone marrow cytotoxicity and preleukemia cells in mice treated with 7,12 Dimethylbenz[*a*]anthracene. *Canc. Res.* **60** : 3454-3460.

Harborne, JB. 1996. The Flavonoids : Advances In Research Since. Chapman and Hall, London.

Hayes, J.D. and D.J. Pulford. 1995. S-Transferase supergene family: regulation of GST and the contribution of the isoenzymes to cancer chemoprevention and drug resistance. *Biochem. Mol. Biol.*, **30** (6), 445-600.

Heyne, K.,1987, *Tanaman Berguna Indonesia*, jilid II, p. 1029. cetakan pertama, diterjemahkan oleh Badan Litbang Departemen Kehutanan, Yayasan Sarana Wana Jaya, Jakarta.

Hodek, P., P. Trefil, and M. Stiborova. 2002. Flavonoids-potent and versatile biologically active compounds interacting with cytochromes P450. *Chem.-Biol. Interact.*, **139**: 1-21.

Hollstein, M, Sidransky D, Vogelstein B, Harris CC. 1991. p53 mutation in human cancers. *Scien.*, 253: 49-53.

Jansen, D., Romert, L., and L. Zhang, L., 1988, Metabolism mediated mutagenesis in mammalian cells *in vitro*. *Live Sci. Adv.* (in press).

Juliano, R.L. 2002. Annu Rev. Pharmacol. Toxicol. In Attenuate of the p53 response to DNA damage by high cell density. *Oncogen.*, pp. 283-323.

Josephy, P. D., 1997, *Molecular Toxicology*, Oxford University Press, New York.

- Kerbel, R. and J. Folkman, 2002. Clinical translation of angiogenesis inhibitors. *Nat. Pub. Group.* (2), 727-739.
- Kern SE, Pietenpol JA, Thiagalingam S, Seymour A, Kinzler KW. and Vogelstein B. 1991. Oncogenic forms of p53 inhibit p53-regulated gene expression. *Sci.*, **252**: 1708-11.
- Khan, TH., T. Jahangir, L. Prasad, and S. Sultana. 2006. inhibitory effect of apigenin on benzo(a)pyrene-mediated genotoxicity in swiss albino mice. *J. Pharm. Pharmacol.*, **58**(12): 1655-1660.
- Kim, K., M.J. Lindstrom, and M. N. Gould, 2002. Regions of H- and K-Ras that provide organ specificity/potency in mammary cancer induction 1. *Cancer Res.*, **62**, 1241-1245.
- King, R.J.B., 2000, *Cancer Biology*, 2nd Ed., Pearson Education Limited, London.
- Knudson AG Jr. 2003. Hereditary cancer, oncogenes, and antioncogenes. *Cancer Res.*, **45**,1437-43.
- Kronqvist P, Kuopio T, Collan Y: Morphometric grading of invasive ductal breast cancer. I. Thresholds for nuclear grade. *Br. J. Canc.*, **78**(6):800-5.
- Kubatka, P., Ahlersova, E., Ahlers, I., Bojkova, B., Kalicka, K., Adamekova, E., Markova, M., Chamilova, M., Cermakova, M., 2002, variability of mammary carsinogenesis induction in female Sprague-Dawley and Wistar : Han Rats : The Effect of Season and Age, *Physiol. Res.* **51**: 633-640
- Kubbutat MHG, Jones SN, Vousden KH. 1997. Regulation of p53 stability by Mdm2. *Nat.* **387**: 299-303.
- Kujari, HP, Y.U. Collan, and N.B. Atkin NB. 1994. Use of the mitotic counts for the prognosis and grading of breast cancer. Method evaluation study. *Pathol. Res. Pract.*, **190**(6):593-9.
- Le Blanc., GA., and W.C. Dauterman. 2001. Conjugation and Elimination of Toxicants, in Hodgson, E., dan Smart, RC., *Introductions to biochemical Toxicology*, 3rd ed. A john Wiley & Sons, Inc. New York.
- Lewis, D.F.V., Costas, I., and D.V. Parker. 1998. Cytochromes P450 and spesies different in xenobiotic metabolism and activation of carcinogenesis. *Environ. Health Perspec.*, **106**(10) : 633-641.

2002. cDNA microarray profiling of rat mammary gland carcinomas induced by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine and 7,12-dimethylbenz[a]anthracene. *J. Carcinog.*, **23**(10), 1561-1568.

Liptak, J., 2004. *mammary tumors in cats and dogs*. (diakses://www.acvs.org/AnimalOwners/HealthConditions/SmallAnimalTopics/MammaryTumorsinCatsandDogs/).

Lundgren, B., Meijer, J., and J.W DePierre, 1987. Characterization of the induction of cytosolic and microsomal epoxide hydrolases by 2-ethylhexanoic acid in mouse liver, *Drug. Metab. Dispos.*, **15**, pp. 114-121.

Lowry, O.H, N.J. Rosebrough, A. Lewis Farr, And R. I. Randall. 1951. Protein Measurement With The Folin Phenol Reagent. From the Department of Pharmacology, Washington University School of Medicine, St. Louis, Missouri) (Received for publication, May 28, 1951).

MacDonald, F., and Ford, C.H.J., 1997. *Molecular Biology of Cancer*, Bios Scientific Publishers, Oxford.

Massarelli, G. 2004. New concepts and perspectives in dcis and lcis of the breast. vi congreso virtual hispanoamericano de anatomia patologica. desde cuba.

Matter, A., 2001. Tumor angiogenesis as a therapeutic target, *Drug Disc Today.*, **6**(19): 1005-1020.

Mechanic, L.E., A.G. Marrogi, J.A. Welsh, E.D. Bowman, M.A. Khan, L. Enewold, Yun-Ling Zheng, S. Chanock, P.G. Shields, and C.C. Harris. 2005. Polymorphism in XPD and TP53 and mutation in human lung cancer. *Carcinog.*, **26**(3), pp. 597-604.

Medina, D., and F.S., Kittrell. 2003. p53 Function is required for hormone-mediated protection of mouse mammary tumorigenesis. *Canc. Res.* **63** : 6140-6143.

Meiyanto, E., 1999. Kurkumin sebagai obat antikanker: menelusuri mekanisme aksinya, *Majalah Farmasi Indonesia* **10**(4), 224-236.

Meiyanto, E., Sugiyanto, and R. Murwanti. 2004. Efek anti karsinogenesis ekstrak etanol tanaman daun dewa (*Gynura procumbens* (luor) merr) pada kanker payudara tikus yang diinduksi dengan Dimetilbenz(a)antrazena (DMBA). *Laporan Penelitian Hibah Bersaing*. Hal. 6-12.

Meiyanto, E., S. Susilowati, S. Tasminatun, R. Murwanti dan Sugiyanto. 2007^a. Efek kemopreventif ekstrak etanolik *Gynura procumbens* (Lour), Merr

- Meiyanto, E., S. Susilowati, S. Tasminatun, R. Murwanti dan Sugiyanto. 2007^b. Penghambatan karsinogenesis kanker payudara tikus terinduksi DMBA pada fase post inisiasi oleh ekstrak etanolik daun *Gynura procumbens* (Lour), Merr. *Majalah Farmasi Indonesia* **18**(4), 169 – 175.
- Melendez-Colon, V., Luch, A., Seidel, A. and Baird, W.M., 1999. cancer initiation by polycyclic aromatic hydrocarbon results from formation of stable dna adducts rather than apurinic sites, *Carcinog.*, **20** (10), 1885-1891.
- Miao, Weimin, L. Hu, P.J. Scrivens, and G. Batist. 2005. Transcriptional regulation of Nrf2 expression by the AHR-XRE signaling pathway : direct cross-talk between phase i and ii drug-metabolizing enzymes. *J. Biol. Chem.*, **13**: 1-24.
- Minshu Yu and Snyderwine E.G. 2002. H-ras oncogene mutation during development of 2-amino-1-methyl-6-phenylimidazo(4,5b)pyridine (PhIP)-induced rat mamary gland cancer. *Carcinogenesis*. **23**(12) : 2123-2128.
- Molina, R., M.A. Segui and M.A. Climent. 1998. p53 oncoprotein as a prognostic indicator in patients with breast cancer. *Anticanc. Res.* **18**:507-511.
- Murray, R.K., Granner, D.K., Mayes, P.A., Rodwell, V.W., 1990. Kanker, onkogen, dan faktor-faktor pertumbuhan, dalam *Biokimia Harper*, diterjemahkan oleh: Hartono, A., Edisi II, Penerbit EGC, Jakarta.
- Namba, R., L.J.T. Young, J.E. Maglione, E.T. McGoldrick, S. Liu, G.T. Wurz., DeGregorio M.W., Borowsky A.D, MacLeod C.L., Cardiff R.D, and Gregg J.P. 2005. Selective estrogen receptor modulators inhibit growth and progression of premalignant lesions in a mouse model of ductal carcinoma *insitu*. *J. Breast Canc. Res.*, (7) : 881-889.
- Nash, H. 2007. Mammary cancer in rats and mice. Owned & Operated by Practicing Veterinarians.
- Nebert, D.W., T.P. Dalton, A.B. Okey, and F.J. Gonzalez. 2004. Role of aryl hydrocarbon reseptor-mediated induction of the CYP1B1 enzim in environmental toxicity and cancer. *J. Biol. Chem.*, (279). 23847-23850.
- Nguyen, Sherrat and Pickett. 2003. Transcriptional regulation of the rat GSTA2 and NQO1 genes by bifunctional and monofunctional inducers. *Ann. Rev. of Pharmacol. and Toxicol.*, 233-260.
- Novalina. 2003. Penggunaan tanaman obat sebagai upaya alternatif dalam terapi kanker. Pengantar ke Falsafah Sain. PPS Institut Pertanian Bogor.

- Pan, M. H., Chen, W. J., Shiau, S.Y.L., Ho, C.T., Lin, J.K., 2002, Tangeretin induces cell cycle G1 arrest through inhibiting cyclin dependent kinases 2 and 4 activities as well as elevating Cdk inhibitor p21 and p27 in human colorectal carcinoma cell, *Carcinog.*, **10**. vol 23 : 1677-1684
- Paciucci, R. & Pellicer A., 1991. Dissection of the mouse n-ras gene upstream regulatory sequences and identification of the promoter and a negative regulatory elements, *Mol. Cell. Bio.*, **11**(3), 1334-1343.
- Pethe, V., and P.V.M. Shekhar. 1999. Estrogen inducibility of c-ha-ras transcription in breast cancer cells identification of functional estrogen-responsive transcriptional regulatory elements in exon 1/Intron 1 Of The c-Ha-ras gene. *J. Biol. Chem.*, **43**. (274). 30969-30978.
- Pitot, H.C., 1993. The molekuler biology of carcinogenesis, *Cancer* (72) 962-970.
- Qiu, C., Minshu Yu, Liang Shan, and E.G. Snyderwine. 2003. Allelic imbalance and altered expression of genes in chromosome 2q11-2q16 from rat mammary gland carcinomas induced by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine. *J. oncog.*, (61). 1476-5594.
- Relling, M.V., and, T. Dervieux. 2001. Pharmacogenetics and cancer therapy. *Nat. Rev. Canc.*, **1**, 99 -108.
- Ren, W., Z. Qiao, H. Wang, L. Zhu, and L. Zhang. 2003. Flavonoids: promising anticancer agents, *Med. Res. Rev.*, **23** (4): 519-534.
- Rendic, S., and F.J. Di Carlo. 1997. Human cytochrome P450 enzymes: a status report summarizing their reactions, substrates, inducers, and inhibitors. *Drug Metab Rev.*, **29**: 413-580.
- Roitt, I. 1997. Roitt's essential immunology. 380-385. 9th Edition. Blackwell Science Ltd. London.
- Rouslahti, E., 1996, How cancer spread, *Scien. Am.*, (9) 72-77.
- Rundle, A., D. Tang, P. Brandt-Rauf, J. Zhou, A. Kelly, F. Schnabel, and, F. P. Pererab 2002. Association between the ras p21 oncoprotein in blood samples and breast cancer. *Canc. Lett.*, **185**. 71-78.
- Russo J. Reina D, Frederick J and Russo IH. 1988. Expression of phenotypical changes by human breast epithelial cells treated with carcinogens *in vitro*. *Canc. Res.*, **48**:2837-2857.

- Russo, M., I. Tedesco, G. Iacomino, R. Palumbo, G. Galano, and G.L. Russo. 2005. Dietary Phytochemicals in Chemoprevention of Cancer, *Curr. Med.Chem. -- Immun., Endoc. & Metab. Agents.*, 5: 61-72.
- Santostefano, M., M. Merchant, L. Arellano, V. Morrison, M.S. Denison, and S. Safe. 1993. Naphthoflavone-induced CYP1A1 gene expression and cytosolic aryl hydrocarbon receptor transformation. *Mol. Pharmacol.* 43: 200-206.
- Sarker, S. 2002. Mean nuclear area of fine needle aspirates of primary preoperative palpable breast carcinoma using image cytometry. *Anal Quant. Cytol. Histol.*, 24(2):85-8.
- Schilter, B., I. Perrin, C. Cavin, and A.C. Huggett. 1996. Placental Glutathione S- Transferase (GST-P) Induction as a Potential Mechanism For The Anti- Carcinogenic Effect of The Coffee Specific Components Cafestol and Kahweol. *Carcinog.*, 17 (11): 2377-2384.
- Schneider, K.A., 1997. Cancer genetics, *Encyclopedia of human biology.* pp. 311-320. 2.
- Shankar, J.C., P.K. Reddy, M.T. Cheri, M. Turman, W. Henry, Strobel and, Vijayalakshmi Ravindranath. 2005. Constitutive expression and localization of cytochrome P-450 1A1 in rat and human brain: presence of a splice variant form in human brain1. *J. Neurochem.*, 93, 724-736.
- Shepelt, L.A., Hong Lan, J.D. Hagg, G.M. Brasic, M.E. Ghenn, J.S. Simon, P. Hoff, M.A. Newton, and. Gould,M.N. 1998. Genetic Identification of Control Breast Cancer Susceptibility in The Rat. *Genetic.* 149. 289-299.
- Shih, M. 2002. Ras signaling pathway. (<http://www.biocarta.com//redirect/hras>).
- Singh, SV., P.J. Benson, X. Hu, A. Pal, H. Xia, S.K. Srivastava, S. Awasthi, H.A. Zaren, J.L. Orchard, and Y.C. Awasthi. 1998. Gender-related differences in susceptibility of A/J mouse to benzo[a]pyrene-induced pulmonary and forestomach tumorigenesis. *Cancer. Lett.*, 128: 197-204.
- Singletary,K., Macdonald,C., and Wallig,M., 1997. The Plasticizer Benzyl Butyl Phtalate (BBP) Inhibits 7,12-dimethylbenz(a)anthracene (DMBA)-induced rat Mammary DNA Adduct Formation and Tumorigenesis, *Carsinog.*, 18 (8) 1669-1673.

- Soeripto, 1977. Mekanisme molekuler karsinogenesis, *Bagian Patologi Anatomi Fakultas Kedokteran UGM*, Yogyakarta, 38-42.
- Stahl, E., 1985. analisis obat secara kromatografi dan mikroskopi, Penerbit Institut Teknologi Bandung, Bandung.
- Sturgill, M.G. and G. H. Lambert. 1997. Xenobiotic-induced hepatotoxicity: mechanisms of liver injury and methods of monitoring hepatic function, *J. Clin. Chem.*, **43**, 1512-1526.
- Sudarto, B., dan Pramono, S., 1985. skrining fitokimia daun dewa (*Gynura procumbens*, Luor Merr yang diduga berkhasiat sebagai anti-kanker, PPPT-UGM, Lembaga Penelitian UGM, Yogyakarta.
- Suganda, A.G., Iwang, S. dan Ganthina, 1988. *Skrining fitokimia dan asam fenolat dalam daun dewa, simposium penelitian tumbuhan obat III*, UI, Jakarta.
- Sugiyanto, Sudarto, B., dan Edy Meiyanto, 1993. Efek Penghambatan Karsinogenisitas Benzo(a)piren oleh preparat tradisional tanaman *Gynura* sp. Dan identifikasi awal senyawa yang berkhasiat, *Laporan Penelitian P4M Ditjen DikTi Fak. Farmasi UGM*, Yogyakarta.
- Sugiyanto, Sudarto, B., Meiyanto, E. 1999. Aktivitas anti karsinogenik senyawa yang berasal dari tumbuhan, *Laporan Penelitian Kompresensif*, 74 Lembaga Penelitian Universitas Gadjah Mada, Yogyakarta.
- Sugiyanto, Sudarto, B., Meiyanto, E., Nugroho A.E. dan Umar A. Jenie., 2003. Aktivitas antikarsinogenik senyawa yang berasal dari tumbuhan, *Majalah Farmasi Indonesia*, **14**(4), 216-225.
- Sugiyono. 2010. Metode penelitian kuantitatif, kualitatif dan R&D. Cetakan ke-10. Mei. Penerbit Alfabeta, Bandung. Hal. 72-79.
- Suprati, S., 2000. Isolasi dan identifikasi struktur senyawa flavonoid dalam fraksi etil asetat ekstrak etanol daun *Gynura procumbens* (Lour) Merr., *Skripsi Fakultas Farmasi, Universitas Gadjah Mada Yogyakarta*.
- Susilowati, S. 2004. Efek kemopreventif ekstrak etanolik daun *Gynura procumbens* (Lour) Merr terhadap kanker payudara tikus yang diinduksi 7,12-Dimetilbenz(a)antrasen (DMBA). *Tesis Program Pascasarjana Universitas Gadjah Mada*.

Sutandyo, N. 2008. Docetaxel trial for advanced breast cancer in Dharmais Cancer Center Hospital. *simposium PHTDI* Perhimpunan Hematologi dan Transfusi Darah Indonesia. Des 19 Malang-Jatiin.

Szeliga, J., and A. Dipple. 1998. DNA adduct formation by polycyclic aromatic hydrocarbon dihydrodiol epoxides. *Chem. Res. Toxicol.*, **11**: 1-11.

Tamimi, R.M., Lagiou, P., Adami, H.O., and D. Trichopoulos. 2002. Review. Prospects for chemoprevention of cancer. *J. Intr. Med.*, **251**: 286-300.

Tasminatun, S. 2005. Efek antikarsinogenesis ekstrak etanolik daun *Gynura Procumbens* (Lour.) Merr. setelah inisiasi pada kanker payudara tikus terinduksi 7,12-Dimetil Benz(a)Antrasen (DMBA). *Tesis Program Pascasarjana Universitas Gadjah Mada Yogyakarta*.

Tedjawanata, S. 2010. Surabaya rawan kanker, serang 2.800 Orang/Tahun. *Yayasan Paliatif Surabaya*.

Thomas, A.N.S., 1989. Tanaman obat tradisional hal 120-121, Penerbit Kanisius, Yogyakarta.

Tullo, A., and E. Sbisa. 2002. Molecular characterization of *p53* mutations in primary and secondary liver tumors. Diagnostic and Therapeutic perspectives. *Mol. Biotechnol.*, **21**. Pp. 265-278.

Ulfa E.M., 1999. Pengaruh pemberian ekstrak etanol daun *Gynura procumbens* (Lour) Merr pada fase pre inisiasi sampai fase inisiasi pertumbuhan tumor lambung mencit karena Benz(a)pirena, *Skripsi*, Fakultas Farmasi Universitas Gadjah Mada, Yogyakarta.

Walaszek, Z., Hanausek, M., and Slaga, T.J., 2004. Mechanisms of Chemoprevention, *Suppl. Am. Coll. Phys.*, **125**, 128-133.

Whalle, T. and, X. Wen. 2005. Preferential induction of CYP1B1 by benzo[a]pyrene in human oral epithelial cells: impact on DNA adduct formation and prevention by polyphenols. *Carcinog.*, **10** (26) pp.1774-1781.

Walum, E., Stenberg, K., and D. Jenssen. 1990. Understanding *Cell Toxicology. Principles and Practice*. Ellis Horwood Limited. England. pp.136-140.

Wattenberg, L.W. 1996. Inhibition of tumorigenesis in animals. *IARC Sci. Publ.* **139**: 151-158.

Weinberg, R.A. 1996. How Cancer Arises, *Sci. Am.*, September, 62-69.

- Van der Aar, E.M., Tan, K.T., Commander, J.N.M., and Vermeulen, N.P.E., 1998. Strategies to characterize the mechanisms of action and the active sites of Glutathione S-Transferase : *A Review, Drug. Metab. Rev.*, **30** (3) , 569-643.
- Van Steenis, C.G.G.J, 1975. Flora, hal 128-131, Pradnya Paramitha, Jakarta.
- Veeriah, S., Hofman, T., Glei, M., Dietrich, H., Will, F., Schreier, P., Knaup, B., and Pool-Zobel, B. 2007. Apple polyphenols and products formed in the gut differntly inhibit survival of human cell lines derived from colon adenoma (LT97) and carcinoma (HT29). *J. Agric. and Fd. Chem.*, **18**. 55(8): 2892-2900.
- Velde CJH, 1999. Tumor payudara dalam Velde CJH, Bosman FT, Wagener DJT, Onkologi, Edisi e-5, Panitia Kanker RSUP Dr Sardjito Yogyakarta, hal 467-92.
- Yang, S.K, Mustaq, M., and Chiu, P.L., 1985. Stereoselective metabolism & activation of polycyclic aromatic hydrocarbons in Harvey, R.O., (Editor) : *Polycyclic Hydrocarbons & Carcinogenesis* 19-31 American Society, Washington.
- Ye, B., Aponte, M., Dai, Y., Li, L., Ho, M., Vitonis, A., Edward, D., Huang, T., and Cramer, D. 2007. Ginkgo biloba and ovarian cancer prevention: epidemiological and biological evidence. *Canc. Lett.*, **18**; 251(1): 43-52.
- Yen, Gow-Chin, Duh, Pin-Der, Tsai, Hui-Ling, Huang and Shih-Li. 2003. Pro-oxidative Propeties of Flavonoids in Human Lymphocytes, *Biosci, Biotechnol, Biochem*, **67** (6), 1215-1222.
- Yonish-Rouach, E., D. Resnitzky., J. Lotem. 1991. Wild-type *p53* induces apoptosis of myeloid leukaemic cells that is inhibited by interleukin-6. *Nat.*, **352**: 345-347.
- Zhang, Y. and G.B. Gordon. 2004. A strategy for cancer prevention : stimulation of the Nrf2-ARE Signaling Pathway. *Mol. Canc. Therap.*, **3** (7): 885-893.
- Zhai, S., R. Dai, F. Friedman, and R. Vestal. 1998. Comparative inhibition of human cytochromes P450 1A1 and 1A2 by flavonoids. *Drug Metab. Dispos.*, **26** (10): 989-992.