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DAFTAR PUSTAKA

Abbasalipourkabir, R., Salehzadeh, A. and Abdullah, R., 2010, Antitumor activity of tamoxifen loaded solid lipid nanoparticles on induced mammary tumor gland in *Sprague Dawley* rats, *African Journal of Biotechnology*, 9:7337-7345.

Abid, M.R., Schoots, I.G. Spokes, K.C. Wu, S.Q., Mawhinney, C. dan Aird, W.C., 2004, Vascular endothelial growth factor-mediated induction of manganese superoxide dismutase occurs through redox-dependent regulation of forkhead and InB/NF-nB, *J. Biol. Chem.* 279:44030– 44038.

Abdulkadir, A.R., Jahan M.S. dan Zawawi, D.D., 2015, Effect of chlorophyll content and maturity on total phenolic, total flavonoid contents and antioxidant activity of *Moringa oleifera* leaf (Miracle tree), *J Chem Pharm Res*, 7(5):1147-1152.

Abuja, P.M. dan Albertini, R., 2001, Methods for monitoring oxidative stress, lipid peroxidation and oxidation resistance of lipoproteins, *Clin Chim Acfa*, 306: 1-17.

Abrahamse, S.L., Kloots, W.J., van Amelsvoort, J.M.M., 2005, Absorption,distribution, and secretion of epicatechin and quercetin in the rat, *Nutr. Res*., 25 :305–317.

Adina, A.B., Goenadi, F.A., Handoko, F.F., Nawangsari D.D., Adam Hermawan, A., Jenie, R.I. dan Meiyanto, E., 2014, Combination of ethanolic extract of *Citrus aurantifolia* peels with doxorubicin modulate cell cycle and increase apoptosis induction on MCF-7 cells, *Iran J Pharm Res.*,13(3): 919–926.

Aggarwal, B. B., Shishir S., Santosh K. S., Manoj K. P., Gautam S., 2006, Inflammation and cancer: How hot is the link?, Biochemical Pharmacology, 72:1605–1621.

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Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker Payudara
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Ahmad, N., Fazal, H., Ayaz, M., Abbasi, B.H., Mohammad, I., Fazal, L., 2011, Dengue fever treatment with Carica papaya leaves extracts, *Asian Pac J Trop Biomed*, 1(4): 330-333.

Aliahmat, N.S., Noor, M.R.M., Yusof, W.J.W., Makpol, S., Ngah, W.Z.W. dan Yusof, Y.A.M., 2012, Antioxidant enzyme activity and malondialdehydelevels can be modulated by Piper betle, tocotrienol rich fraction and Chlorella vulgaris in aging C57BL/6 mice, *CLINICS*, 67(12):1447-1454.

Allavena, P., Sica, A., Garlanda, C. dan Mantovani, A.,2008, The Yin-Yang of tumor-associated macrophages in neoplastic progression and immune surveilance, *Immunological Reviews*, 13(1): 23-35.

Alipieva, K., Petreska, J., Gil-Izquierdo, A., Stefova, M., Evstatieva, L. dan Bankova, V., 2010, Influence of the extraction method on the yield of flavonoids and phenolics from *Sideritis spp*. (Pirin Mountain tea), Nat Prod Commun 5 (1)**;** 51-54.

Allred, D.C., Mohsin, S.K. dan Fuqua, S.A., 2001, Histological and biological evolution of human premalignant breast disease. Endocr Relat Cancer 8:47-61.

Althunibat, O.Y., Ridzwan Bin Hashim, Taher, M., Daud, S.M., Ikeda, M.S. dan Zali, B.J., 2009, In vitro antioxidant and antiprolverative activities of three Malaysian sea cucumber species, *European Journal of Scientific Research*, 37:376-387

Akira, S., Uematsu, S. danTakeuchi, O., 2006, Pathogen recognition and innate immunity, *Cell*, 124: 783–801.

Alupului, A., Călinescu, I., Lavric, V., 2012, Microwave extraction of active principles from medical plants, *U.P.B. Sci. Bull*, Series B Vol. 74, Iss. 2

American Cancer Society, 2014, Breast Cancer, www.cancer.org. Atlanta.

Amiot, M.J., Tacchini, M., Aubert, S.Y. dan Oleszek, W., 1995, Influence of cultivar, maturity stage and storage conditions on phenolic composition and browning of pear fruits, *J Agric Food Chem*, 43:1132-37.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Aprilita, K., Astuti, M. dan Marsono, Y., 2014, Pengaruh Campuran Ekstrak Antosianin Beras Hitam (*oryza Sativa L.*) Dan Ekstrak Protein Kedelai Hitam (*glycine Max (l)merr.*) Terhadap Profil Lipid Dan Status Antioksidan Plasma Tikus Dislipidemia, Tesis, S2 Ilmu dan Teknologi Pangan UGM.

Aravind, G., Debjit, B., Duraivel, S. dan Harish, G., 2013, Traditional and medicinal uses of *carica papaya*, *Journal of Medicinal Plants Studies*, 1:7–15.

Argenta, G., Silva, P.R.F., Forsthofer E.L. dan Strieder, M.L., 2001, Relationship of reading of portable chlorophyll meter with contents of extractable chlorophyll and leaf nitrogen in maize, *Rev Bras Fisiol Veg*, 13(2):158-167.

Arts, I.C. dan Hollman, P.C., 2005, Polyphenols and disease risk in epidemiologic studies, *Am J Clin Nutr*., 81; 317S-325S.

Atta, K.B., 1999, "The power of garlic",Cardiovascular disease prevention Association, Buea Cameroon, pp.72

Ayoola, P.B. dan Adeyee, A., 2009, Phytochemical and nutrient evaluation of Carica papaya (Pawpaw) Leaves, *IJRRS*, 5(3); 325-328.

Azizah, D.N., Kumolowati, E. dan Faramayuda, F., 2014, Penetapan Kadar Flavonoid Metode $AlCl_3$ pada Ekstrak Metanol Kulit Buah Kakao (*Theobroma cacao L.*), Kartika Jurnal Ilmiah Farmasi, 2 (2): 45-49

Babior, B. M., 1999, NADPH-oxidase: an Update, *Blood*, 93:1464–1476.

Babior, B.M., R.S. Kipnes, dan J.T. Curnutte, 1973, The Productions By Leukocytes Of Superoxide; A Potential Bactericidal Agent, *J. Clin. Invest.*, 52:741

Bartlett, J.M.S., Mallon, E.A. dam Cooke, T.G., 2003, The clinical evaluation of HER2 status, which test to use?, *J Pathol*, 99:411–417

Barros, A.C., Muranaka, E.N., Mori, L.J., Pelizon, C.H., Iriya, K., Giocondo, G. dan Pinotti, J.A., 2004, Induction of experimental mammary carcinogenesis in rats with 7,12-dimethylbenz(a)anthracene, Rev Hosp Clin Fac Med Sao Paulo 59(5):257-261.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Basu, A. Dan Haldar, S., 2008, Dietary isothiocyanate mediated apoptosis of human cancer cells is associated with Bcl-xL phosphorylation, *International Journal of Oncology*, 33:657–663.

Battacharya, D. dan Yusuf, N., 2012, Expression of Toll-Like Receptors on Breast Tumor Taking a Toll on Tumor Microenvironment. *International Journal of Breast Cancer*, p 1-6.

Benmebarak, A., Zerizer, S., Lakhal, H. dan Kabuche, Z., 2014, Biphasic dose response effect of Stachys ocymastrum on the reticuloendothelial system phagocytic activity. *International Journal Pharmacy and Pharmaceutical Science*, 6(2):534-537.

Betteridge, D.J., 2000, What is oxidative stress?, *Metabolism*, 49 (supp 1): 3-8.

Biber, P.D., 2007, Evaluating a Chlorophyll Content Meter on Three Coastal Wetland Plant Species, *J Agric Food Environ Scie*, 1(2):1-11.

Bimark, M., Rahman, R.A., Taip, F.S., Ganjloo, A., Salleh, L.M., Selamat, J., Hamid, A., Zaidul, I.S.M., 2011, Comparison of different extraction methods for the extraction of major bioactive flavonoid compounds from spearmint (Mentha spicata L.) leaves, *Food and Bioproducts Processing*, 89 ; 67–72.

Black, J.K., 2016, The Anti-inflammation Diet and Recipe Book, Publisher Group West, Barkeley, Canada.

Boland, G.P., Butt, I.S., Prasad, R., Knox, W.F. dan Bundred, N.J., 2004, COX-2 expression is associated with an aggressive phenotype in ductal carcinoma in situ, *Br J Cancer*, 90:423–429

Bombonati, A. dan Sgroi, D.C., 2011, The molecular pathology of breast cancer progression, J Pathol 223:307-317.

Bouayed, J., Rammal, H. dan Soulimani, R.,2009, Oxidative stress and anxiety: Relationship and cellular pathways, *Oxid Med Cell Longev*, 2:63-67.

Bouayed, J., 2010, Polyphenols: a potential new strategy for the prevention and treatment of anxiety and depression, *Curr Nutr Food Sci*., 6:13-8.

Bouayed, J. dan Bohn, T., 2010, Exogenous antioxidants—Double-edged swords in cellular redox state; Health beneficial effects at physiologic doses versus deleterious effects at high doses *Oxid Med Cell Longev*, 3(4); 228-237.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Brown, N.S. dan Bicknell, R., 2001, Hypoxia and oxidative stress in breast cancer. Oxidative stress; its effects on the growth, metastatic potential response to therapy of breast cancer, *Breast Cancer Res*,3; 323-327.

Brown, N.S. dan Bicknell, R., 2001, Hypoxia and oxidative stress in breast cancer. Oxidative stress; its effects on the growth, metastatic potential response to therapy of breast cancer, *Breast Cancer Res*,3; 323-327.

Brown, J.E., Khodr, H., Hider, R.C. dan Rice-Evans, C., 1998, Structural dependence of flavonoid interactions with Cu^{2+} ions: implications for their antioxidant properties, Biochemical Journal, 330 (3):1173–1178.

Bursal, E. dan Gulcin, I., 2011, Polyphenol contents and in vitro antioxidant activities of lyophilised aqueous extract of kiwi fruit (Actinidia deliciosa), *Food Research International*, 44 (5):1482–1489.

Canini, A., Alesiani, D., D'Arcangelo, G. dan Tagliatesta, P., 2007, Gas chromatography–mass spectrometry analysis of phenolic compounds from *Carica papaya L.* Leaf, *Journal of food Composition and Analysis*, 20:584–590.

Castagna, M., Takai, Y., Kaibuci, K., Sana, K., Kikkawa, U. dan Nishizuka, Y., 1982, Direct activation of calcium-activated, phospholipid-dependent protein kinase by tumor-promoting phorbol esters, *Journal of Biological Chemistry*, 257:7847-7851.

Caldwell, J., Gardner, I., Swales, N.,1995, An Introduction to Drug Disposition: The Basic Principles of Absorption, Distribution, Metabolism, and Excretion, *Toxicologic Pathology,* 43(2):102-113.

Cao, G., Sofic, E.dan Prior, R.L., 1997, Antioxidant and prooxidant behavior of flavonoids: Structure-activity relationships, *Free Radical Bio Med*, 22:749-60.

Cerella C., Radogna, F., Dicato, M. dan Diedrich, M., 2013, Natural compounds as regulator of the cancer cell metabolism, *International Journal of Cell Biology*, 1-16.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Chen, J., Zeng, J., Xin, M., Huang, W., Chen, X., 2011, Formononetin induces cell cycle arrest of human breast cancer cells via IGF1=PI3K=Akt pathways in vitro and in vivo, *Horm Metab Res*., 43(10):681–6.

Chen, G.Q., Yao, Z.W., Zheng W.P., Chen, L., Duan, H. dan She, Y., 2010, Combined antitumor effect of ursolic acid and 5-fluorouracil on human eshopageal carcinoma cell eca-190 in vitro, *Chin J Cancer Res*, 22:62-67.

Chen, M.S., Chen, D., Dou, Q.P., 2004, Inhibition of proteasome activity by various fruits and vegetables is associated with cancer cell death In vivo, 18:73–80.

Chen, C., Li, S., Lin, Y., Hsu, C., Shuh, M. dan Liu, J., 2005, Consumption of purple sweet potato leaves modulates human immune response: T-lymphocyte functions, lytic activity of natural killer cell and antibody production, *World Journal of Gastroentrology*, 11(37):5777-5781.

Ching, L.S. dan Mohamed, S., 2001, Alpha-tcopherol content in 62 edible tropical plants, *Journal of Agricultural and Food Chemistry*, 49: 3101-3105.

Cho, Y.A., Kim, J., Park, K.S., Lim, S.Y., Shin, A. *et al.*, 2010, Effect of dietary soy intake on breast cancer risk according to menopause and hormone receptor status, *Eur J Clin Nutr.*, *64*: 924-932.

Chou, C.C., Yang, J.S., Lu, H.F., Ip. S.W., Lo, C., Wu, C.C. *et al.*, 2010, Quercetin-mediated cell cycle arrest and apoptosis involving activation of a caspase cascade through the mitochondrial pathway in human breast cancer MCF-7 cells. *Arch Pharm Res.*, 33(8):1181–91.

Chowa, L.W.C., Yip, A.Y.S., Loo, W.T.Y., Lam, C.K. dan Toi, M., 2008 Celecoxib anti-aromatase neoadjuvant (CAAN) trial for locally advanced breast cancer, *J Steroid Biochem Mol Biol*, 111:13–17.

Clarkson, P.M. dan Thompson, H.S., 2000, Antioxidants what role do they play in physical activity and health?, *Am J Clin Nutr.,* 72 (2 supp);637S-646S.

Claude, B. dan Paule, S., 1979, The manual of natural living. 1st Ed. Biddles Ltd, pp. 98-101.

Cook, N.C. dan Samman, S., 1996, Flavonoids; Chemistry, metabolism, Cardioprotective Effects, and dietary sources, *J Nutr Biochem*, 7:66-76.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Costa, C., Soares, R., Reis-Filho, J.S., Leitão, D., Amendoeira, I. dan Schmitt, F.C., 2002, Cyclo-oxygenase 2 expression is associated with angiogenesis and lymph node metastasis in human breast cancer, *J Clin Pathol*, 55:429–434

Correa, P., 2005, New strategies for the prevention of gastric cancer: *Helicobacter pylori* and genetic susceptibility. *J Surg Oncol*.,90:134–8.

Cox, A.G., Winterbourn, C.C. dan Hampton, M.B., 2010, Mitochondrial peroxiredoxin involvement in antioxidant defence and redox signalling, *Biochem J*, 425(2):313–325.

Cravottoa, G., Boffaa, L., Mantegnaa, S., Peregob, P., Avogadrob, M. dan Pedro Cintasc, P., 2008, Improved extraction of vegetable oils under high-intensity ultrasound and/or microwaves, Ultrasonics Sonochemistry 15: 898–902.

Creagh, E.M. dan O'Neill, L.A., 2006, TLRs, NLRs and RLRs: a trinity of pathogen sensors that co-operate in innate immunity. *Trends Immunol*, 27: 352-357.

Crissman, J. W., Dawn, G. G., Paul, K. H., Robert, R. P., Donald, A. P., Julia, H. R., William, J. S., Daryl, C. T., 2004, Best Practices Guideline: Toxicologic Histopathology, *Toxicologic Pathology*, 32:126–131.

Dabrosin, C. dan Ollinger, K., 1998, Protection by alpha-tocopherol but not ascorbic acid from hydrogen peroxide induced cell death in normal breast epithelial cells in culture, *Free Rad Res* 29, 227–234, 1998.

David, H., 1983, The new holistic herbal. 3rd Ed. Findhorn press, USA, pp ; 241

Depinho, R., 2002, The age of cancer, *Nature*, 408:248–254.

Depkes RI, 2008, Farmakope Herbal Indonesia Edisi 1, Jakarta: Departemen Kesehatan Republik Indonesia, Hal. 8-9, 11-12.

De Boer, V.C., Dihal, A.A., van der Woude, H., Arts, I.C., Wolffram, S., Alink, G.M., Rietjens, I.M., Keijer, J., Hollman, P.C., 2005, Tissue distribution of quercetin in rats and pigs, *J. Nutr*., 135;1718–1725.

De Cesare, M., Calcaterra, C., Pratesi, G., Gatti, L., Zunino, F., Ménard, S. dan Balsari, A., 2008, Eradication of ovarian tumor xenografts by locoregional administration of targeted immunotherapy. *Clin Cancer Res*, 14:5512–5518.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

DeNardo, D.G., Johansson, M., Coussens, L.M., 2000, Immune cells as mediators of solid tumor metastasis, *Cancer and Metastases Reviews*, 7(1); 11-18.

Dharmarathna, S.L., Wickramasinghe, S., Waduge, R.N., Rajapakse, R.P., Kularatne, S.A., Halim, S.Z., 2013, Does Carica papaya leaf-extract increase the platelet count? An experimental study in a murine model, *Asian Pac J Trop Biomed*, 3(9): 720-724.

Direktorat Gizi Depkes R.I., 1981, Daftar Komposisi Bahan Makanan Bhratara Karya Aksara, Jakarta.

Dixon, R.A. dan Paiva, N.L., 1995, Stress-induced phenylpropanoid metabolism. *Plant Cell*,7:1085-97.

Dunn, G.P., Old, L.J., Schreiber, R.D., 2004, The immunobiology of cancer immunosurveilance and immunoediting, *Immunity*, 21(2) ; 137-148.

Duthie, S.J. dan Dobson, V.L., 1999, Dietary Flavonoids protect human colonocyte DNA from oxidative attack in vitro, *Eur J Nutr*., 38: 28-34.

Ebada, E.S., Edrada, R.U., Lin, W. and Proksch, P., 2008, Methods for isolation, Purification and Structural elucidation of bioactive secondary metabolites from marine invertebrates, *Nature Protocols*, 3(12): 1820-1831.

Edewor, T.I., 2016, A review: Immunological potential of bioactive flavonoids and flavonoid containing fractions isolated from medicinal plants, *Cibtech Journal of Bio-Protocols*, 5 (2):7-14Kaput, J., 2004, Diet-Disease Gene Interactions, *Nutrition*, 20; 26-31.

Ellis, I.O., 2010, Intraductal proliferative lesions of the breast: morphology, associated risk and molecular biology, Mod Pathol 23 (Suppl 2) :S1-S7.

Elmore, S., 2007, Apoptosis: a review of programmed cell death, *Toxicology Pathology*, 35:495-516.

European Pharmacopoeia 5.0, 2005. Bitterness value. Council of Europe, Strasbourg, pp. 221–222.

Fauzi, I. A., Amalia F., Sabila, N., Hermawan, A., Ikawati, M. dan Meiyanto, E., 2011, Aktivitas Antiproliferasi Ekstrak Etanolik Herba Ciplukan (*Physalis angulata* L.) Terhadap Sel Hepar Tikus Betina Galur Sprague Dawley

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Terinduksi 7,12 Dimetilbenz[a]antrasena, Majalah Kesehatan PharmaMedika, 3(1); 194-199.

Ferguson, P.J., Kurowska, E., Freeman, D.J., Chambers, A.F., Koropatnick, D.J., 2004, A flavonoid fraction from cranberry extract inhibits proliferation of human tumor cell lines. *J. Nutr*., 134:1529–1535.

Fernandez, S.P., Wasowski, C., Loscalzo, L.M., Granger, R.E., Johnston, G.A.R., Paladini, A.C., Marder, M., 2006, Central nervous system depressant action of flavonoid glycosides, *European Journal of Pharmacology*, 539: 168-176.

Fleischauer, A.T., Simonsen, N., Arab, L., 2003. Antioxidant supplements and risk of breast cancer recurrence and breast cancer-related mortality among postmenopausal women, *Nutr. Cancer*, 46:15–22.

Foss, F.M., 2002, Immunologic mechanisms of antitumor activity, *Semin Oncol*., 29 : 5–11.

Freisleben, H.J.F., 2001, Free radicals and ROS in biological systems, Kursus Penyegar 2001, Radikal bebas dan antioksidan dalam kesehatan, Bagian Biokimia, Jakarta.

Fukui, R., Saitoh, S., Matsumoto, F., Kozuka-Hata, H., Oyama, M., Tabeta, K., B. Beutler, B., dan Miyake. K., 2009, Unc93B1 biases Toll-like receptor responses to nucleic acid in dendritic cells toward DNA- but against RNA-sensing, *J. Exp. Med.*, 206:1339–1350.

Garcia-Salas, P., Morales-Soto, A., Segura-Carretero, A. & Fernández-Gutiérrez, A, 2010, Phenolic-compound extraction systems for fruit and vegetable samples, *Molecules* ,15: 8813-8826.

Gbolahan, D., 2001, Lesson note on medical importance of trace elements, Center for Natural Health Studies, Surulere, Lagos, Nigeria.

Gerdes, J., Schwab, U., Lemke, H. dan Stein, H.,1983, Production of a mouse monoclonal antibody reactive with a human nuclear antigen associated with cell proliferation, *Int J Cancer*, 31(1):13–20.

Giri, U., Sharma, S.D., Abdulla, M. dan Athar, M., 1995, Evidence that in situ generated reactive oxygen species act as a potent stage I tumor promoter in mouse skin, *Biochem Biophys Res Commun*, 209:698–705.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Goli, A.H., Barzegar, M. dan Sahari, M.A., 2004, Antioxidant Activity and Total Phenolic Compounds of Pistachio (Pistachia vera) Hull Extracts, *Food Chem*, 92:521-25.

González-Reyes, S., Marín. L., González, L., González, L.O., del Casar, J.M., Lamelas, M.L., González-Quintana, J.M. dan Vizoso, F.J., 2010, Study of TLR3, TLR4 and TLR9 in breast carcinomas and their association with metastasis. *BMC Cancer,* 10:665.

Gorman, J.S.T., 2006, Transition metal mediated cyclizations and synthesis of Annonaceous Acetogenin Analogs (Repository) University of Texas, Texas.

Gropper, S.S., Smith J.L. dan Groff, J.L., 2009, Advanced nutrition and human metabolism. Cengage Learning, Wadsworth.

Gurcan, M. N., Laura, E. B., Ali, C., Anant, M., Nasir, M. R., Bulent, Y., 2009, Histopathological Image Analysis: A Review, *IEEE Reviews In Biomedical Engineering*, 2: 147-149

Hahn, D.B. dan Payne, W.A., 2003, Focus on Health, New York: Mc-Graww Hill.

Häkkinen, S.H., Kärenlampi, S.O., Mykkänen, H.M. dan Törrönen, A.R., 2000, Influence of domestic processing and storage on flavonol contents in berries, *J Agric Food Chem*, 48:2960-65.

Halliwell, B. dan Gutteridge, J.M.C, 1984, Oxygen toxicity, oxygen radicals, transition metals and disease, *Biochemical Journal*, 219(1):1–14.

Halliwell, B. dan Gutteridge, J.M.C., 1998, Free Radicals in Biology and Medicine, Oxford University Press, Oxford, UK.

Halvorsen,B.L. Holte, K., Myhrstad, M.C.W., Barikmo,I., Hvattum, E., Remberg, S.F., Wold, A.B., Haffner, K., Baugerød, H.,Andersen,L.F., Jan Moskaug, J., Jacobs, D.R.J. dan Blomhoff, J., 2002, A Systematic Screening of Total Antioxidants in Dietary Plants, *J. Nutr.,* 132; 461-471.

Half, E., Tang, X.M., Gwyn, K., Sahin, A., Wathen, K. dan Sinicrope, F.A., 2002 Cyclooxygenase-2 expression in human breast cancers and adjacent ductal carcinoma in situ, *Cancer Res,* 62:1676–1681

Hanahan, D. dan Weinberg, R.A., 2011, Hallmarks of Cancer : The Next Generation, *Cell*, 144 (5); 646-674.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Hanten, J.A., Vasilakos, J.P., Riter, C.L., Neys, L., Lipson, K.E., Alkan, S.S. dan Birmachu, W., 2008, Comparison of human B cell activation by TLR7 and TLR9 agonists, *BMC Immunol*., 9:39

Harman, D., 2000, Aging: Overview, Ann. N. Y. Acad. Sci. 928:1–21.

Harwood, M., Danielewska-Nikiel, B., Borzelleca, J.F., Flamm, G.W., Williams, G.M., Lines, T.C., 2007, A critical review of the data related to thes afety of quercetin and lack of evidence of in vivo toxicity, including lack of genotoxic/ carcinogenic prperties, *Food and Chemical Technology*, 45 : 2179-2205.

Haytowitz, D.B., Bhagwat, S. dan Holden, J.M.,2013, Sources of variability in the flavonoid content of foods, *Procedia Food Science*, 2 ;46 – 51.

Heiss, C., Keen, C.L., Kelm, M., 2010, Flavanols and cardiovascular disease prevention, *Eur Heart J*., 21:2583–92.

Henson, P.M., 2005, Dampening inflammation, *Nat. Immunol*., 6:1179-1181.

Henry, L. dan Narendra, P.S., 2006, Oral artemisinin prevents and delays the development of 7,12-dimethylbenz[a]anthracene (DMBA)-induced breast cancer in the rat, *Cancer Lett*, 231:43–44.

Hernani dan Rahardjo, M., 2005, Tanaman Berkhasiat Antioksidan. Jakarta: Penebar Swadaya.

Herwiyanti, S., Mustofa, Haryana, S.M., Astuti, I., 2015, Potensi senyawa 1,2-Epoksi-3(3-(,4-dimetoksifenil)-4H-1-benzopiran-4-on)propane sebagai anti kanker, Disertasi, FK UGM.

Hondermarck, H., 2003, Breast cancer, *Molecular & Cellular Proteomics*, 2:281–291.

Hoffman, E.J., Webster, N.R., Wiggins, P.A., Chisholm, E.M., Glies, G.R. dan Leveson, S.H., 1985, Free radical detoxifying systems in human colorectal cancer, *Br. J. Cancer*, 51:127-129.

Hollman, P.C.H., 2004, Absorption, Bioavalability and Metabolism of Flavonoids, *Pharmaceutical Biology*, 42:74-83.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Huang, B., Zhao, J., Li, H., *et al*., 2005, Toll-like receptors on tumor cells facilitate evasion of immune surveilance, *Cancer Research*, 65(12) ; 5009-5014.

Hue, S.M., Boyce, A.N. dan Somasundram, C., 2012, Antioxidant activity, phenolic and flavonoid contents in the leaves of different varieties of sweet potato (*Ipomoea batatas*). *Aust J Crop Sci*, 6 (3):375-80.

Hui, C., Qi X, Qianyong Z, Xiaoli P, Jundong Z, Mantian M, 2013, Flavonoids, Flavonoid subclasses and breast cancer risk: A meta analysis of epidemiologic studies, *PLOSone*, 8(1);1-8.

Hu, H., Liu, H., Zhang, H., Zhu, J., Yao, X., Zhang, X. dan Zheng, K., 2010, Assessment of chlorophyll content based on image color analysis, comparison with SPAD-502, DOI: 10.1109/ICIECS.2010.5678413

Hunt, S., Goff, J.L. dan Holbrook, J., 1980, Nutrition principles and chemical practices, Jhon Wiley and Sons, New York, pp; 49-52.

Hussain, S.P., Aguilar, F., Amstad, P., Cerutti, P., 1994, Oxy-radical induced mutagenesis of hotspot codons 248 and 249 of the human p53 gene, *Oncogene.*; 9: 2277-2281.

Hsie, A.W., Recio, L., Katz, D.S., Lee, C.Q., Wagner, M., Schenley, R.L.,1986, Evidence for reactive oxygen species inducing mutations in mammalian cells, *Proc Natl Acad Sci U S A.*;83:9616- 9620.

Iparraguirre, A., Tobias, J.W., Hensley, S.E., Masek, K.S., Cavanagh, L.L., Rendl, M., Hunter, C.A., Ertl, H.C., von Andrian, U.H. dan Weninger, W., 2008, Two distinct activation states of plasmacytoid dendritic cells induced by influenza virus and CpG 1826 oligonucleotide. *J. Leukoc. Biol*, 83:610–620.

Jablonska, E., J Gromadzinska, J., Peplonska, B., Fendler, W., Reszka, R., Krol, M.B., Wieczorek, E., Bukowska, A., Gresner, P., Galicki, M., Quispe, O.Z., Morawie, Z. dan Wasowicz, W., 2015, Lipid peroxidation and glutathione peroxidase activity relationship in breast cancer depends on functional polymorphism of GPX1, *BMC Cancer*,15:657

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Jain, T., Jain, V., Pandey, R., Vyas, A., Shukla,S. S., 2009, Microwave Assisted Extraction for Phytoconstituents – An Overview, *Asian Journal Research Chemistry* , 1 (2);19-25.

Jana, D., Sarkar, D.K., Maji, A., Chikkala, B.R., Hassanujjaman, S., Mukhopadhyay, M. dan Ganguly, S., 2012, Can cyclo-oxygenase-2 be a useful prognostic and risk stratification marker in breast cancer?, *J Indian Med Assoc*, 110:429–433.

Jana, D., Sarkar, D.K., Ganguly, S., Saha, S., Sa G., Manna A.K., Banerjee, A. dan Mandal, S., 2014, Role of Cyclooxygenase 2 (COX-2) in Prognosis of Breast Cancer, *Indian J Surg Oncol*, 5(1):59–65

Jaruga, P., Zastawny, T.H., Skokowski, J., Dizdaroglu, M., Olinski, R., 1994, Oxidative DNA base damage and antioxidant enzyme activities in human lung cancer, *FEBS Lett.*, 341:59-64.

Janeway, C.A.Jr., Travers, P., Walport, M., Shlomchik, J., 2001, Immunobiology, The Immune System in Health and Disease 5th edition, New York: Garland Science.

Jeong, J.H., An, J.Y., Kwon, Y.T., Rhee, S.G. dan Lee, Y.Y., 2009, Effects of low dose quercetin cancer cell-specific inhibition of cell cycle progression, *J Cell Biochem*, 106: 73-82.

Jo, E.H., Hong, H.D., Ahn, N.C., Jung, J.W., Yang, S.R., Park, J.S., Kim, S.H., Lee, Y.S., Kang, K.S., 2004, Modulations of the Bcl-2/Bax family were involved in the chemopreventive effects of licorice root (Glycyrrhiza uralensis Fisch) in MCF-7 human breast cancer cell, *J. Agric. Food Chem.*, 52;1715–1719.

Juárez-Rojop, I.E., Díaz-Zagoya, J.C., Ble-Castillo, J.L., Miranda-Osorio, P.H., Castell-Rodríguez, A.E., Tovilla-Zárate, C.A., Rodríguez-Hernández, A., Aguilar-Mariscal, H.,Ramón-Frías, T., Bermúdez-Ocaña, D.Y., 2012, Hypoglycemic effect of Carica papaya leaves in streptozotocin-induced diabetic rats, *BMC Complement Altern Med*, 12: 236.

Kacharava, N., Chanishvili, S., Badridze, G., Chkhubianishvili, E. dan Janukashvili, N, Effect of seed irradiation on the content of antioxidants in

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

leaves of Kidney bean, Cabbage and Beet cultivars, *Aust J Crop Sci*, 3 (3):137-145.

Kang, D.H., 2002, Oxidative Stress, DNA Damage and Breast Cancer, *AACN Clinical Issues*, Vol. 13, No. 4. Pp. 540-549.

Kanzler, H.; Barrat, F.J.; Hessel, E.M.; Coffman, R.L. Therapeutic targeting of innate immunity with toll-like receptor agonists and antagonists. *Nat. Med.* 2007, *13*, 552–559.

Kaput, J. dan Rodriguez, R., 2003, Nutritional genomics. The next frontier in the postgenomic era. *Physiol Genomics (in press).*

Katsuragi, Y., Mitsui, Y., Umeda, T., Otsuji, K., Yamasawa, S. dan Kurihara, K., 1997, Basic studies for the practical use of bitterness inhibitors: selective inhibition of bitterness by phospholipids, *Pharm Res*, 14: 720–724.

Kelly, E.H., Anthony, R.T. dan Dennis, J.B., 2002, Flavonoid antioxidants: chemistry, metabolism and structure-activity relationships, *Journal of Nutritional Biochemistry*, 13 (10): 572–584

Kennedy, R. dan Celis, E., 2008, Multiple roles for CD4+ T cells in anti-tumor immune responses, *Immunological Reviews*, Vol. 222: 129–144.

Kent, S. dan Faloon, W., 2003, Disease Prevention and Treatment, Life extension Media, US.

Kim, Y.M., Brinkmann, M.M., Paquet, M.E. dan Ploegh, H.L., 2008, UNC93B1 delivers nucleotide-sensing toll-like receptors to endolysosomes. *Nature* 452:234–238.

Klaunig, J.E., Kamendulis, L.M. dan Hocevar, B.A., 2010, Oxidative Stress and Oxidative Damage in Carcinogenesis, *Toxicologic Pathology*, 38: 96-109.

Kochi, T., Masahito S., Tomohiko O., Atsushi B., Takafumi S., Masaya K., Yohei S., Hisashi T., Takuji T., Hisataka M., 2013, Enhanced Development of Azoxymethane-Induced Colonic Preneoplastic Lesions in Hypertensive Rats, *Int. J. Mol. Sci.*, 14 :14700-14711.

Kondo, Y., Takano, F. Dan Hojo, H., 1994, Suppression of chemically and immunologically induced hepatic injuries by gentiopicroside in mice, *Planta Med*, 60:414–416.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Khan, M.M., 2008, Immunopharmacology, New York: Springer, Science Business Media LLC halaman 1-29.

Kresno, S.B., 2012, Ilmu dasar onkologi. Jakarta: Badan Penerbit Fakultas Kedokteran Universitas Indonesia.

Kris-Etherton, P.M., Lefevre, M., Beecher, G.R., Gross, M.D., Keen C.L., Etherton T.D., 2004, Bioactive compounds in nutrition and health-research methodologies for establishing biological function: the antioxidant and anti-inflammatory effects of flavonoids on atherosclerosis. *Annu Rev Nutr.*, 24:511–538.

Krug, A., Rothenfusser, S., Hornung, V., Jahrsdorfer, B., Blackwell, S., Ballas, Z.K., Endres, S., Krieg, A.M. dan Hartmann, G., 2001, Identification of CpG oligonucleotide sequences with high induction of IFN-α/β in plasmacytoid dendritic cells. *Eur. J. Immunol.* 31:2154–2163.

Kumar, S dan Pandey, A.K., 2013, Chemistry and Biological Activities of Flavonoids: An Overview, *The ScientificWorld Journal*, volume 2013;1-16

Kuno, T., Tsukamoto, T., Hara, A. and Tanaka, T. 2012. Cancer chemoprevention through the induction of apoptosis by natural compounds. Journal of Biophysical Chemistry 3:156-73.

Kusar, A., Zupancic, A., Sentjurc, M. dan Baricevicc, D., 2006, Free radical scavenging activities of yellow gentian (Gentiana lutea L.) measured by electron spin resonance, *Hum Exp Toxicol*, 25: 599–604.

Ladas, E.J., Jacobson, J.S., Kennedy, D.D., Teel, K., Fleischauer, A. dan Kelly, K.M., 2004, Antioxidants and cancer therapy: a systematic review. *J Clin Oncol*, 22(3):517–28.

Lapenna, S. dan Giordano, A., 2009, Cell cycle kinases as therapeutic targets for cancer, *Nat Rev Drug Discov*., 8:547-66.

Laranjinha, J.A., Almeida L.M. and Madeira, V.M., 1994, Reactivity of dietary phenolic acids with peroxyl radicals: antioxidant activity upon low density lipoprotein peroxidation, *Biochem Pharmacol*, 48(3):487-94.

Lee, K.W. dan Lee, H. J., 2006, The roles of polyphenols in cancer chemoprevention, *Biofactors*, 26(2):105-121.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Lee, Y.K., Park, S.Y., Kim, Y.M., Lee, W. dan Sand Park, O.J., 2009, AMP kinase/cyclooxygenase-2 pathway regulates proliferation and apoptosis cancer cells treated with quercetin, *Exp Mol Med*, 41(3):201-207.

Lee, B.L., Moon, J.E., Shu, J.H., Yuan, L., Newman, Z.R., Schekman, R. dan Barton, G.M., 2013, UNC93B1 mediates differential trafficking of endosomal TLRs. *Elife*, 2:1-22.

Lewandowska U., Gorlach, S., Owczarek, K., Hrabec, E. dan Szewczyk, K., 2014, Synergistic Interactions Between Anticancer Chemotherapeutics and Phenolic Compounds and Anticancer Synergy Between Polyphenols, *Postepy Hig Med Dosw (online)*, 68: 528-540.

Ley, J.P., 2008. Masking bitter taste by molecules. Chemosen. Percep., 1:58–77.

Li, S., Yan, T., Yang, J.Q., Oberley, T.D. dan Oberley, L.W., 2000, The role of cellular glutathione peroxidase redox regulation in the suppression of tumor cell growth by manganese superoxide dismutase, *Cancer Res.* 60:3927– 3939.

Li, C.I., Moe, R.E. dan Daling, J.R., 2002, Risk of mortality by histologic type of breast cancer among women aged 50 to 79 years, *Arch Intern Med.*, 163:2149-2153

Li, F., Ye, L., Lin, S.M., Leung, L.K., 2011, Dietary flavones and flavonones display differential effects on aromatase (CYP19) transcription in the breast cancer cells MCF-7. *Mol Cell Endocrinol*., 344(1–2):51–8.

Li, Y., Xing, D., Chen, Q., Chen, W.R. 2010. Enhancement of chemotherapeutic agent induced apoptosis by inhibition of NF-kB using ursolic acid. Int J Cancer 127: 462-473.

Liu, C.H., Sung-Hee, C., Kirsi, N., Ovidiu, C.T., Ming-Tao, W., Elizabeth, S., Christian, H., Timothy, F.L. dan Timothy, H., 2001, Overexpression of Cyclooxygenase-2 Is Sufficient to Induce Tumorigenesis in Transgenic Mice, *J. Biol. Chem*., 276(21): 18563–18569.

Liou, G.Y. and Storz, P., 2010, Reactive oxygen species in cancer, *Free Radic Res*, 44(5):1-31

Lindley, C. dan Michaud, L.B., Breast cancer, dalam Dipiro, T.J. *et al*., 2005, Pharmachoterapy 6th edition, Mc Grawhill, New York, p. 2329-2364.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
FATMA ZUHROTUN NISA, Prof. Dr. Ir. Mary Astuti, MS; Prof. dr. Sofia Mubarika Haryana, M.Med.Sc. Ph.D.; Prof. Dr
Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Low, P.S. dan Merida, J.R., 1996, The Oxidative Burst In Plant Defense: Function And Signal Transduction, *Physiol. Plant.*, 96:533–42

Luo, S., Zhou, L., Lu, X. dan Zhong, Z., 2014, Study on effect of total flavonoids of Oldenlendia difflusa on ulcerative colitis and its immunological mechanism. *China Journal of Chinese Material Medica*, 39(5):896-900.

Mahmood, A. A., Sidik, K., Salmah, I., 2005, Wound healing activity of *Carica papaya* L. Aqueous leaf extarct in rats, *International Journal of Molecular Medicine and Advance Sciences*, 1(4): 398-401.

Magalhaes, L.M., Barreiros, L., Reis, S. dan Segundo, M. A., 2014, Kinetic matching approach applied to ABTS assay for high-throughput determination of total antioxidant capacity of food products, *Journal of Food Composition and Analysis*, 33 (2):187–194.

Maisarah, A.M., Nurul, A.B., Asmah, R. dan Fauziah, O., 2013, Antioxidant analysis of different parts of *Carica papaya*, *Int Food Res J*, 20 (3):1043-48.

Mahassni, S.H. dan Al-Reemi, R.M., 2013, Apoptosis and necrosis of human breast cancer cells by an aqueous extract of garden cress (Lepidium sativum) seeds, *Saudi J Biol Sci*, 20(2): 131-139.

Malava, M. P. dan Neitzel, L.T., 2000, Vitamin E succinate promotes breast cancer tumor dormancy, *J Surg Res* 93, 163–170.

Malumbres, M. dan Barbacid, M., 2009, Cell cycle, CDKs and cancer: A changing paradigm, *Nat Rev Cancer*., 9:153-66.

Mandal, V., Mohan, Y. dan Hemalatha, S., 2007, Microwave Assisted Extraction-An innovative and promising extraction tool for medical plant research, *Pharmacognosy Review*, 1(1);7-18.

Manuaba, T.W., 2010, Panduan Penatalaksanan Kanker Solid PERABOI. Edisi ke-2. Jakarta: Sagung Seto, h.17-47.

Manu, K.A. dan Kutan, G., 2008, Ursolic acid induces apoptosis by activating p53 and caspase-3 gene expressions and suppressing NF-kB mediated activation of Bcl-2 in B16F-10 melanoma cells, *Int Immunopharmacol*, 8: 974-981.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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FATMA ZUHROTUN NISA, Prof. Dr. Ir. Mary Astuti, MS; Prof. dr. Sofia Mubarika Haryana, M.Med.Sc. Ph.D.; Prof. Dr
Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Maniyar, Y. dan Bhixavatimath, P., 2012, Antihyperglycemic and hypolipidemic activities of aqueous extract of Carica papaya Linn. leaves in alloxan-induced diabetic rats. *J Ayurveda Integr Med*, 3(2): 70-74.

Mansara, P., Ketkar, M., Deshpande,R., Chaudhary, A.,Shinde, K. dan Kaul-Ghaneka, R., 2015, Improved antioxidant status by omega-3 fatty acid supplementation in breast cancer patients undergoing chemotherapy: a case series, *J Med Case Rep*, 9: 148-153.

Marengo, B., Nitti, M., Furfaro, A.L., Colla, R., De Ciucis, C., Marinari, U.M., Pronzato, M.A., Traverso, N. and Domenicotti, C., 2016, Redox Homeostasis and Cellular Antioxidant Systems: Crucial Players in Cancer Growth and Therapy, Oxid Med Cell Longev. D: 10.1155/2016/6235641

Mariño, G., Niso-Santano, Baehrecke, E.H. dan Kroemer, G., 2014, Self-consumption: the interplay of autophagy and apoptosis, *Nature Reviews Molecular Cell Biology*, 15:81-94.

Martin, S.J. dan Green, D.R., 1995, Protease activation during apoptosis: death by a thousand cuts, *Cell*, 82:349-52.

Martin, K.R., 2006, Targeting apoptosis with dietary bioactive agents, *Experimental Biology and Medicine*, 231: 117-129.

Maruyama, K., Selmani, Z., Ishii, H. dan Yamaguchi, K., 2011, Innante immunity and cancer therapy, 11(3): 350-357

Mashentseva, A. A., Dehaen, T., Seitembetov, T.S., Seitembetova, A.J., 2011, Comparison of the antioxidant activity of the different *Betula pendula Roth*. extract from Northern Kazahstan, *Journal of Phytology* 3(1): 18-25.

Maulid, R. R. dan Laily, A.N., 2015, Kadar total pigmen klorofil dan senyawa antosianin ekstrak katsuba (*Euphorbia phulcherrima*) berdasarkan umur daun, Seminar Nasional Konservasi dan Pemanfaatan Sumber daya Alam. Universitas Sebelas Maret Surakarta.

McDonnell, D.P., Park, S., Goulet, M.T., Jasper, J., Wardell, S.E., Chang, C.Y., Norris, J.D., Guyton, J.R., Nelson, E., 2014, Obesity, Cholesterol Metabolism and Breast Cancer Pathogenesis, *Cancer Res canres*.,1756.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Mello, V.J., Gomes, M.T., Lemos, F.O., Delfino, J.L., Andrade, S.P., Lopes, M.T., Salas,C.E., 2008. The gastric ulcer protective and healing role of cysteine proteinases from Carica candamarcensis, *Phytomedicine*, 15; 237–244.

Meiyanto, E., Susidarti R.A., Handayani, S., Rahmi, F., 2008, Ekstrak etanolik biji buah pinang (*Areca catechu L.*) mampu menghambat proliferasi dan memacu apoptosis sel MCF-7. Majalah Farmasi Indonesia, 19(1), 12-19.

Melisi, D., Frizziero, M., Tamburrino, A., Zanotto, M., Carbone, C., Piro, G., dan Tortora, G., 2014, Toll-Like Receptor 9 Agonists for Cancer Therapy *Biomedicines, 2*:211-228.

Miean, K.H., Mohamed, S., 2001, Flavonoid (myricetin, quercetin, kaempferol, luteolin, and apigenin) content of edible tropical plants, *Journal of Agricultural and Food Chemistry* 49; 3106–3112.

Mishra, A., Kumar, S. dan Pandey, A.K., 2013, Scientific validation of the medicinal efficacy of Tinospora cordifolia, The Scientific World Journal, volume 2013: 1-8.

Moghadasian, M.H., Freeman, H.J. dan Godin, D.V., 1996, Endogenous antioxidant status in neoplastic and adjacent tissues in 1,2-dimethylhydrazine-induced colon cancer in rats: effects of olsalazine, *Carcinogenesis*, 17(5) 983-987.

Monikawati, A., Farida, S., Putri, L.W., Ikhtiarsyah, Y.G. dan Meiyanto, E., 2011, Antiproliferative activity of ethanolic extract of Ciplukan Herbs (*Physalis angulata L.*) on 7,12- Dimethylbenz[a]nthracene-induced rat mammary carcinogenesis *Indonesian Journal of Cancer Chemoprevention*, 2(2):227-232

Moon, Y., Wang X. dan Morris, M., 2006, Dietary flavonoids: effects on xenobiotic and carcinogen metabolism, *Toxicol in Vitro*, 20(2):187–210.

Morel, Y. dan Barouki R., 1999, Repression of gene expression by oxidative stress, Biochem J, 342:481-496.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Murakami, A., Hajme, O., dan Koichi, K., 1996, Anti-tumor promotion with food phitochemicals: A strategy for cancer chemoprevention, *Bioscience, Biotechnology and Biochemistry*, 64(1):9-16.

Muller, M. dan Kersten, S., 2003, Opinion. Nutrigenomics: goals and strategies, *Nat Rev Genet.*, 4:315

Munoz, V., Sauvain, M., Bourdy, G., Callapa, J., Rojas, I., Vargas, L., Tae, A., Deharo,E., 2000, The search for natural bioactive compounds through a multidisciplinary approach in Bolivia. Part II. Antimalarial activity of some plants used by Mosetene indians, *Journal of Ethnopharmacology*, 69;139–155.

Murray, R.K., Bender, D.A., Botham, K.M., Kennelly, P.J., Rodwell, V.W., Weil, P.A., 2003, Harper's Ilustrated Biochemistry 26th ed., McGraw-Hills Companies, New York.

Nantitanon, W., Yotsawimonwat, S., Okonogi, S., 2010, Factors influencing antioxidant activities and total phenolic content of guava leaf extract, *LWT-Food Sci Technol*, 43: 1095- 1103.

Nechuta, S., Lu, W., Chen, Z., Zheng, Y., Gu, K., Cai, H., Zheng, W. dan Shu, X.O., 2011, Vitamin supplement use during breast cancer treatment and survival: a prospective cohort study, *Cancer Epidemiol Biomarkers Prev*, 20(2):262–271.

Neuhouser, M.L., 2004, Dietary flavonoids and cancer risk: evidence from human population studies, *Nutr Cancer*, 50: 1-7.

Nishida, K., Yamaguchi, O. dan Otsu, K., 2008, Crosstalk between autophagy and apoptosis in heart disease, *Circulation Research*, 103:343-351.

Nugraheni, M., Santoso, U., Suparmo, Wuryastuti, M., 2011, Potensi ekstrak kentang (*Coleus tuberosus*) sebagai antioksidan dan anti-proliferasi sel kanker payidara (MCF-7) *in vitro*, Disertasi Ilmu Pangan Universitas Gadjah Mada, Yogyakarta.

Nurrahman, Astuti, M., Suparmo dan Marsetyawan, H.N.E.S., 2012, Peran tempe kedelai hitam dalam meningkatkan aktivitas enzim antioksidan dan daya

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

tahan limfosit tikus terhadap hydrogen peroksida *in vivo*, Seminar Hasil-Hasil Penelitian, LPPM UNIMUS.

Oberley, D.T., 2002, Oxidative damage and cancer, *American Journal of Pathology*, Vol 160 (2) :403-408.

Obinaju, Blessing, E., Martin dan Franchis, L, 2010, Dose-related effects of quercetin in the human breast carcinoma MCF-7 cell line, *Am J Sci Ind Res*, 1: 242-261.

Olinski, R., Zastawny, T.H., Budzbon, J., Sokowski, J., Zegarski, W. dan Dizdarogly, M., 1992, DNA base modifications in chromatin of human cancerous tissues, *FEBS Lett.*, 309:193-198.

Okoko, T. dan Ere, D., 2012, Reduction of hydrogen peroxide-induced erythrocyte damage by Carica papaya leaf extract, *Asian Pac J Trop Biomed*, 2(6): 449-53.

Okwu, D.E. dan Okwu, M.E., 2004, Chemical composition of Spondia mombin plants, *J. Sustain Agric. Environ*., 6;140-147.

Okwu, D.E. dan Ekeke, O., 2003, Phytochemical screening and mineral composition of chewing sticks in South Eastern Nigeria, Global, *J. Pure Appl. Sci.*, 9; 235-238.

O'Leary, K.A., de Pascual-Teresa, S., Needs, P.W., Bao, Y.P., O'Brien, N.M. dan Williamson, G., 2004, Effect of flavonoids and vitamin E on cyclooxygenase-2 (COX-2) transcription, *Mutat Res*, 551(1-2):245-254.

Olivier D.K. dan Wyk, B.E., 2013, Bitterness values for traditional tonic plants of southern Africa, *J Ethnopharm*, 147: 676–679

Oloyede, F.M., Oloyede, F.A. dan Obuotor, E.M., 2013, Effect of Plant Maturity on the Antioxidant Profile of *Amaranthus cruentus L.* and *Celosia Argentea L. Bull Env Pharmacol Life Sci*, 2(2):18- 21.

Otsuki, N., Dang, N.H., Kumagai, E., Kondo, A., Iwata, S., Morimoto, C., 2010. Aqueous Extract of *Carica papaya* leaves exhibits anti-tumor activity and immunomodulatory effect, *Journal of Ethnpharmacology*, 127; 760-767.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
FATMA ZUHROTUN NISA, Prof. Dr. Ir. Mary Astuti, MS; Prof. dr. Sofia Mubarika Haryana, M.Med.Sc. Ph.D.; Prof. Dr
Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Ouyang, L., Shi, Z., Zhao, S., Wang, F.T., Zhou, T.T., Liu, B. dan Bao, J.K., 2012, Programmed cell death pathways in cancer: a review of apoptosis, autophagy and programmed necrosis, *Cell Proliferation*, 45:487-498.

Owoyele, B.V., Adebukola, O.M., Funmilayo, A.A., Soladoye, A.O., 2008, Anti-inflammatory activities of ethanolic extract of Carica papaya leaves, *Inflammopharmacology*, 16(4): 168-173.

Pal, R.S., Ariharasivakumar, G., Girhepunjhe, K., Upadhay, A., 2009, In vitro antioxidative activity of phenolic and flavonoids compounds extracted from seeds of *Abrus precatorius*, *International Journal of Pharmacy and Pharmaceutical Sciences*, 1;136-140.

Pandey, A.K., Mishra, A. K. dan Mishra, A., 2012, Antifungal and antioxidative potential of oil and extracts derived from leaves of Indian spice plant Cinnamomum tamala," Cellular and Molecular Biology, 58 : 142–147.

Panieri, E. dan Santoro, M.M., 2016, ROS homeostasis and metabolism: a dangerous liason in cancer cells, *Cell Death and Disease*, 7(6):1-12

Panis. C., Herrera, A.C., Victorino, V.J., Campos, F.C., Freitas, L.F., De Rossi, T., Colado Simão, A.N., Cecchini, A.L. dan Cecchini, R., 2012, Oxidative stress and hematological profiles of advanced breast cancer patients subjected to paclitaxel or doxorubicin chemotherapy, *Breast Cancer Res Treat*, 133(1):89–97.

Pathak, A.K., Bhutani, M., Nair, A.S., Ahn, K.S., Chakraborty, A., Kandungana, H., Guha, S., Sethil, G. dan Aggarwal, B.B., 2007, Ursolic acid inhibits STAT3 activation Pathway leading to suppression of proliferation and chemosensitization of human multiple myeloma cells, *Mol Cancer Res*, 5: 943-955.

Patil, B.S., Pike, L.M. dan Hamilton, B.K., 1995, Changes in quercetin concentration in onion (Allium cepa L.) owing to location, growth stage and soil type. *New Phytol*,130: 340-55.

Pattanayak, S.P., Mazumder P.M. dan Sunita, P., 2012, Total phenolic content, flavonoid content and in vitro antioxidant activities of *Dendrophthoe falcata* (L.f.) Ettingsh, *Int J Pharm Tech Res*, 3(3):1392-1406

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Pecorino, L., 2008, Molecular Biology of Cancer Mecanism, Target and Therapeutics, Second Edition, Oxford University Press.

Percival, P., 1998, Antioxidant, *CLINICAL NUTRITION INSIGHT, Advance Nutrition Publicationts, Inc., Revised.*

PERMENTAN, 2012, Pedoman penanganan pasca panen tembakau, NOMOR 56/Permentan/OT.140/9/2012.

Peschel, W., Sanchez-Rabaneda, F., Plescher, A., Gartzia, I., Jimenez, D., Lamuela-Raventos, R., Buxaderas, S., Condina, C., 2006, An industrial approach in the search of natural antioxidants from vegetable and fruit wastes, *Food Chemistry*, 97: 137-150.

Pharoah, P.D., 2003, Genetic Susceptibility, predicting risk and preventing cancer, Recent Result Cancer Res., 163;7-18.

Poulsen, H.E., Prieme H. dan Loft, S., 1998, Role of oxidative DNA damage in cancer initiation and promotion, *Eur J Cancer Prev*, 7(1):9-16.

Pirani, M., Sepehri, H., Delphi L.dan Khosrawi, A., 2016, Combination effect of broccoli extract and doxorubicin on cell proliferation and cell cycle arrest in LNCaP prostate cancer cell line, *International Journal of Pharmacognosy and Phytochemical Research*, 8(6); 949-955.

Pitot, H.C. dan Dragon, Y.P., 1991, *Federation of American Societies for Experimental Biology, J.5, 2280-2286.*

Prins, R.M., Craft, N, Bruhn KW, et al. The TLR-7 agonist, imiquimod, enhances dendritic cell survival and promotes tumor antigen-specific T cell priming: relation to central nervous system antitumor immunity. J Immunol. 2006;176(1):157–164.

Prior, R.L. dan Cao, G., 2000, Antioxidant phytochemicals in fruits and vegetables: diet and health implications, *Hortic Sci*, 35(4): 588–92.

Quan, V. V., Hirun, S., Chuen, T.L.K., Goldsmith, C.D., Murchie, S., Bowyer, M.C., Philips, P.A., Scarlett, C.J., 2014, Antioxidant and anticancer of saponin enriched *Carica papaya* leaf extracts, Article first published online: 5 Juli 2014.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Rajeswari, N., Ahuja, Y.R., Malini, U. *et al*., 2000, Risk assessment in first degree female relatives of breast cancer patients using the alkaline comet assay, *Carcinogenesis*, 21: 557-561.

Rao, V.A., Klein, S.R., Bonar, S.J., Zielonka, J., Mizuno, N., Dickey, J.S. Keller, P.W., Joseph, J., Kalyanaraman, B. dan Shacter, E., 2010, The antioxidant transcription factor Nrf2 negatively regulates autophagy and growth arrest induced by the anticancer redox agent mitoquinone. *J Biol Chem*, 285: 34447–34459.

Ranasasmita, R., 2008, Aktivitas anti kanker ekstrak etanol Daun *Aglaia eliptica Blume* pada tikus betina yang diinduksi DMBA, Program Studi Biokimia, Fakultas MIPA IPB, Bogor.

Rather, L.J., 1971, Disturbance of function (functio laesa): the legendary fifth cardinal sign of inflammation, added by Galen to the four cardinal signs of Celsus. *Bull NY Acad Med*.,47: 303-322.

Ratnam, D.V., Ankola, D.D., Bhardwaj, V., Sahana, D.K. dan Kumar, M.N., 2006, Role of antioxidants in prophylaxis and therapy: A pharmaceutical perspective. *J Control Release*, 113:189-207.

Rebecca, S., Matthew, B., Amanda, P., Christopher, W. dan Barbara, B., 2003, Apoptosis, chemoresistance and breast cancer : insights from the MCF-7 cell model system, *Experimental Biology and Medicine (Maywood)*, 228(9): 995-1003.

Rechtseiner, G., Warger, T., Osterioh, P., Schild, H. dan Radsak, M.P., 2005, Cutting edge: priming of CTL by transcutaneous peptide immunization with imiquimod, *J Immunol*, 174(5): 2476-2480

Redha, A., 2010, Flavonoid: struktur, sifat antioksidatif dan peranannya dalam sistem biologis, *Jurnal Belian*, Vol. 9, No. 2 ; 196-202.

Reinberger, S., 2006. Bitter could be better. Scie. Am. Mind, 17: 56–61

Ren, W., Qiao, Z., Wang, H., Zhu, L., Zhang, L., 2003, Flavonoids : Promising anticancer agents, *Medicinal Research Review*, Vol. 23, No. 4, pp. 519-534.

RISKESDAS, 2013, Riset Kesehatan Dasar 2013, http://www.litbang.depkes.go.id.

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Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker Payudara
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Robinson, T., 1985, The organic constituents of higher plants. "Their Chemistry and Interrelationships. 3rd Ed., Corcleus press, North Amherst mass, 6;430-435

Rockenbach, G., Di Pietro, P.F., Ambrosi, C., Boaventura, B.C., Vieira, F.G., Crippa, C.G., Da Silva, E.L. dan Fausto, M.A., 2011, Dietary intake and oxidative stress in breast cancer: before and after treatments, *Nutr Hosp*, 26(4):737–744.

Rogmanolo, D.F. dan Selmin, O.I., 2012, Flavonoids and Cancer Prevention: A Review of the evidence, *Journal of Nutrition in Gerontology and Geriatrics*, 31:206-238.

Rohmatussolihat, 2009, Antioksidan, penyelamat sel-sel tubuh manusia, *BioTrends*, Vol. 4, No. 1.

Ross, E.A., Koo, L.C. dan Moberly, J.B., 1997, Low whole blood and erythrocyte levels of glutathione in hemodialysis and peritoneal dialysis patients, *Am. J. Kidney Dis*. 30:489– 494.

Rosu A., Nistor, N., Miron, N. and Popa, R., 2012, Ultrasound assisted extraction of photosynthetic pigments from dried dill (*Anethum graveolens*), *J Faculty Food Engin*, 11(4): 5-9

Ross, J.A., Kasum, C.M., 2002, Dietary flavonoids: bioavailability, metabolic effects, and safety, *Annu Rev Nutr.*, 22:19–34.

Rukmana, R., 1995, Pepaya; Budidaya Pasca Panen, Kanisius, Yogyakarta.

Rubin, R., Strayer, D., Rubin, E., dan McDonald, J., 2007, Rubin's Pathology: Clinicopathologic Foundations of Medicine. Baltimore, MD: Lippincott Williams & Wilkins

Salih, H.R. dan Nussler, V., 2001, Commentary: immune escape versus tumor tolerance: how do tumors evade immune surveillance?, *Eur J Med Res*. 6:323–332.

Salet, C. dan Moreno, G., 1990, Photosensitization of mitochondria. Molecular and cellular aspects, *J Photochem Photobiol*, 5:133–150.

Sansonetti, P.J., 2006, The innate signaling of dangers and the dangers of innate signaling, *Nat. Immunol. 7*:1237–1242.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
FATMA ZUHROTUN NISA, Prof. Dr. Ir. Mary Astuti, MS; Prof. dr. Sofia Mubarika Haryana, M.Med.Sc. Ph.D.; Prof. Dr
Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Santen, R.J. dan Mansel, R., 2005, Benign breast disorders. N Engl J Med 353:275-285.

Sasai, M., Linehan, M.M. dan Iwasaki, A., 2010, Bifurcation of toll-like receptor 9 signaling by adaptor protein 3. *Science*, 329:1530–1534.

Sasidharan, S., Sumathi, V., Jegathambigai, N.R., Latha, L.Y., 2011, Antihyperglycaemic effects of ethanol extracts of Carica papaya and Pandanus amaryfollius leaf in streptozotocin-induced diabetic mice, *Nat Prod Res.*, 25(20): 1982-7.

Sato, Y., Goto, Y., Narita, N. dan Hoon, D.S., 2009, Cancer Cells Expressing Toll-like Receptors and the Tumor Microenvironment, *Cancer Microenviron*, 2(Suppl 1): 205–214.

Sayed, D.M., EL-Attar, M.M. dan Hussein, A.A.R.M., 2009. "Evaluation of flow cytometric immunophenotyping and DNA analysis for detection of malignant cells in serosal cavity fluids", *Cytopathology*, 37 (7) : 498-504.

Schiavone, J.R. dan Hassan, H.M., 1988, The role of redox in the regulation of manganese-containing superoxide dismutase biosynthesis in Escherichia coli, *J. Biol. Chem*. 263:4269–4273.

Schiavano, G.F., De Santi, M., Brandi, G., Fanelli, M., Bucchini, A., Giamperi, L. dan Giomaro, G., 2015, Inhibition of Breast Cancer Cell Proliferation and *In Vitro* Tumorigenesis by a New Red Apple Cultivar, *PLOS one*, 1-17.

Schinor, E.C., Salvador, M.J. dan Turatti, I.C.C., 2004, Comparison of classical and ultrasound-assisted extractions of steroids and triterpenoids from three Chresta spp., Ultrasonics Sonochemistry 11: 415-421.

Seigler, D.S., Pauli, G.F., Nahrstedt, A., Leen, R., 2002. Cyanogenic allosidesand glucosides from Passiflora edulis and Carica papaya. *Phytochemistry*, 60 :873–882.

Selvakumaran, M., Pisarcik, D.A., Bao, R., Yeung, A.T., Hamilton, T.C., 2003. Enhanced cisplatin cytotoxicity by disturbing the nucleotide excision repair pathway in ovarian cancer cell lines, *Cancer Res.*, 63, 1311–1316.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Sener, D.E., Gönenç, A., Akinci, M. dan Torun, M., Lipid peroxidation and total antioxidant status in patients with breast cancer. *Cell Biochem Funct*, 25(4):377-82.

Setiari, N dan Nurchayati, Y., 2009, Chlorophyll content exploration on some Greens as Alternative Basic Materials Food Supplement, BIOMA, 11(1):6-10.

Shan, J.Z., Xuan, Y.Y., Zheng, S., Dong, Q. dan Zhang, S.Z., 2009, Ursolic acid inhibits proliferation and induces apoptosis of HT-29 colon cancer cells by inhibiting the EGFR/MAPK pathway, *J Zhejiang Univ Sci B*,10: 668-674.

Sheu, S.S., Nauduri D. dan Anders, M.W., 2006, Targeting antioxidants to mitochondria: A new therapeutic direction, *Biochimica et Biophysica Acta*, 1762: 256 – 265.

Shewchuk, L.D., Baracos, V.E., Field, C.J., 1996, Reduced splenocyte metabolism and immune function in rats implanted with the Morris Hepatoma 7777. *Metab* ;45:848–55.

Shukla, Y. dan George, J., 2011, Combinatorial strategies employing nutraceuticals for cancer development, *Annals of the New York Academy of Sciences*, 1229:162-175.

Shyu, M.H., Kao, T.C. dan Yen, G.C., 2010, Oleanolic acid and ursolic acid induce apoptosis in HuH7 human hepatocellular carcinoma cells through a mitochondrial-dependent pathway and down regulation of XIAP, *J. Agr Food Chem*, 58: 610-648.

Siegel, R., Ma, J., Zou, Z. dan Jemal, A., 2014, Cancer Statistics, *CA Cancer J Clin*., 64:9-29.

Sidransky, D., Tokino, T., Helzlsourer, K., Zehnbauer, B., Rausch, G., Shelton, B., Prestigiacomo, L., Vogelstein, B. dan Davidson N, 1992, Inherited p53 gene mutations in breast cancer, *Cancer Res*., 52: 2984–2985.

Simao, A.A., Santos, M.A.I., Fraguas, R.M., Braga, M.A., Marques, T.R., Duarte, M.H., Santos, C.M., Freire, J.M., dan Correa, A.D., 2013, Antioxidants and chlorophyll in cassava leaves at three plant ages, *African J. Agric. Res.*, 8(28): 3724-3730.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
FATMA ZUHROTUN NISA, Prof. Dr. Ir. Mary Astuti, MS; Prof. dr. Sofia Mubarika Haryana, M.Med.Sc. Ph.D.; Prof. Dr
Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Smith, R.A. dan Murphy, M.P., 2010, Animal and human studies with the mitochondria-targeted antioxidant MitoQ, *Ann NY Acad Sci.*, 1201:96–103.

Sreelatha S. dan Padma, P.R., 2009, Antioxidant activity and total phenolic content of *Moringa oleifera* leaves in two stages of maturity, *Plant Food Human Nutr.*, 64(4):303-311

Stary, G., Bangert, C., Tauber, M., Strohal, R., Kopp, T. dan Stingl, G., 2007, Tumoricidal activity of TLR7/8-activated inflammatory dendritic cells, *J Exp Med*, 204(6):1441–1451.

Starley, I.F., Mohammed, P., Schneider, G. dan Bickler, S.W., 1999, The treatment of paediatric burns using topical papaya, *Burns*, 25:636–639.

Stief, T. W., 2000, The Blood Fibrinolysis/Deep-Sea Analogy: A Hypothesis On The Cell Signals Singlet Oxygen/Photons As Natural Atithrombotics, *Thromb Res*., 99:1–20

Storz, P., 2005, Reactive oxygen species in tumor progression, *Front Biosci*, 10:1881–1896.

Stuehr, D. J., Kwon N. S., Nathan C. F., 1990, FAD And GPX Participate In Macrophage Synthesis Of Nitric Oxide. *Biochem Biophys Res Comm.*,168:558–65.

Stray, F., 1998. The natural guide to medicinal herbs and plants. Tiger Books International, London, pp: 12-16.

Soebagio, 2002, Kimia Analitik, Universitas Negeri Makasar, Fakultas MIPA Makasar.

Subbaramaiah, K., Norton, L., Gerald, W. dan Dannenberg, A.J., 2002, Cyclooxygenase- 2 is overexpressed in HER-2 ⁄ neu-positive breast cancer—evidence for involvement of AP-1 and PEA3, *J Biol Chem*, 277:18649–18657

Subenthiran, S., Choon, T.C., Cheong, K.C., Thayan, R., Teck, M.B., Muniandy, P.K., Afzan, A., Abdullah, N.R., Ismail, Z., 2013. Carica papaya Leaves Juice Significantly Accelerates the Rate of Increase in Platelet Count among Patients with Dengue Fever and Dengue Haemorrhagic Fever. *Evid Based Complement Alternat Med*, 616737.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
Payudara
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Sugahara, T., Ueno, M., Goto, Y., Shiraishi, R., Doi, M., Akiyama, K. dan Yamauchi, S., 2006. Immunostimulation effect of jellyfish collagen. *Biosci. Biotechnol. Biochem.*, 70(9):2131-2137.

Suhail, N., Bilal, N., Khan, H.Y., Hasan, S., Sharma, S., Khan, F., Mansoor, T. dan Banu, N., 2012, Effect of vitamins C and E on antioxidant status of breast-cancer patients undergoing chemotherapy, *J Clin Pharm Ther*, 37(1):22–26.

Sullivan, L.B., dan S Chandel, N.S., 2014, Mitochondrial reactive oxygen species and cancer, *Cancer & Metabolism*, 2(17):1-12.

Sumadi dan Marianti, A., 2007, Biologi sel, Graha Ilmu, Yogyakarta.

Surh, Y.J., 2003, Cancer chemoprevention with dietary phytochemicals, *Nat Rev Cancer*, 10 :768–80.

Suryanto, E. dan Wehantouw, F., 2009, Aktivitas Penangkapan Radikal Bebas dari Ekstrak Fenolik Daun Sukun (Artocarpus altilis F.), *Chem. Prog.*, 2 (1): 1-7.

Suriawiria, 2002, Tanaman Berkhasiat sebagai Obat, Papas Sinar Sinanti, Jakarta.

Synder, L.R. dan Kirklan, J., 1979, Introduction to modern liquid chromatography, Jhon Wiley & Son, Canada

Szatrowski, T.P. dan Nathan, C.F., 1991, Production of large amounts of hydrogen peroxide by human tumor cells. *Cancer Res.*, 51:794-798.

Tabeta, K., Hoebe, K., Janssen, E.M., Du, X., Georgel, P., Crozat, K., Mudd, S., Mann, N., Sovath, S., Goode, J., Shamel, L., Herskovits, A.A., Portnoy, D.A., Cooke, M., Tarantino, L.M., Wiltshire, T., Steinberg, B.E., Grinstein, S. dan Beutler, B., 2006, The Unc93b1 mutation 3d disrupts exogenous antigen presentation and signaling via toll-like receptors 3, 7 and 9, *Nat Immunol*, 7:156–164.

Taie, H.A.A., El-Mergawi, R. dan Radwan, S., 2008, Isoflavonoids, Flavonoids, Phenolic Acids Profiles and Antioxidant Activity of Soybean Seeds as Affected by Organic and Bioorganic Fertilization, *American-Eurasian J. Agric. & Environ. Sci*., 4 (2): 207-213.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Takahashi, K., Shibata, T., Akashi-Takamura, S., Kiyokawa, T., Wakabayashi, Y., Tanimura, N., Kobayashi, T., Matsumoto, F., Fukui, R., Kouro, T., Nagai, Y., Takatsu, K., Saitoh, S. dan Miyake, K., 2007, A protein associated with Toll-like receptor (TLR) 4 (PRAT4A) is required for TLR-dependent immune responses, *J Exp Med*, 204:2963–2976.

Takauji, R.; Iho, S.; Takatsuka, H.; Yamamoto, S.; Takahashi, T.; Kitagawa, H.; Iwasaki, H.; Iida, R.; Yokochi, T.; Matsuki, T. CpG-DNA-induced IFN-α production involves p38 MAPK-dependent STAT1 phosphorylation in human plasmacytoid dendritic cell precursors. *J. Leukoc. Biol.* 2002, *72*, 1011–1019.

Tambunan, 2003, Diagnosis dan tata laksana sepuluh jenis kanker di Indonesia, EGC., Jakarta.

Thompson, E. B.,1985, Drug Bioscreening. America: Graceway Publishing Company, Inc. Pp. 40, 118.

Tie Tze, 2002, Terapi Pepaya, PT Prestasi Pustaka Raya, Jakarta.

Timmonsa, M.D., Bradleya, M.A., Lovella,M.A., Lynna B.C., 2011, Procedure for the isolation of mitochondria, cytosolic and nuclear material from a single piece of neurological tissue for high-throughput mass spectral analysis, *Journal of Neuroscience Methods*, 197: 279–282.

Tsujii, M., Kawano, S., Tsuji, S., Sawaoka, H., Hori, M. dan Dubois, R.N., 1998, Cyclooxygenase regulates angiogenesis induced by colon cancer cells. *Cell*, 93:705–716.

Turkmen, N., Sari, F. dan Velioglu, Y.S., 2006, Effects of extraction solvents on concentration and antioxidant activity of black and black mate tea polyphenols determined by ferrous tartrate and Folin–Ciocalteu methods, *Food Chem*, 99:835–41.

Tzagoloff, A., 1982, Mitochondria, Plenum Press, New York.

Ulfah, M., 2010, “Flow cytometry untuk Evaluasi Aktifitas Obat Antiplasmodial pada Gametosit Plasmodium falciparum”, Malaria Journal 9:49.

Uauy, R. dan Solomons, N., 2005. Diet, Nutrition, and The Life Course Approach to Cancer Prevention, *J. Nutr.*, 1355; 2934S-2945S.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Ujianto, A., Darwito, Dharmana, H., 2010, Jumlah limfosit darah tepi dan sebukan limfosit sekitar jaringan tumor pada penderita keganasan payudara yang mendapat injeksi Vitamin C, Tesis, Program Pasca Sarjana Magister Ilmu Biomedik dan Program Pendidikan Dokter Spesialis I Ilmu Bedah UNDIP, Semarang.

Usatiuk S. and Pelekhova, L., 2014, Chlorophyll content and antioxidant activity of sunflower oil with aromatic raw materials, *Food and Environ Safety*, 8(4):317-320

USDA, 2007, USDA Database for the Flavonoid Content of Selected Foods, Release 2.1, Nutrient Data Laboratory Home Page. Accessed at http://www.ars.usda.gov/nutrientdata.

USDA, 2008, USDA Database for the Isoflavone Content of Selected Foods, Release 2.0. Nutrient Data Laboratory Home Page. Accessed at http://www.ars.usda.gov/nutrientdata/isoflav.

USDA, 2011, USDA Database for the Flavonoid Content of Selected Foods, Release 3.0. Nutrient Data Laboratory Home Page. Accessed at http://www.ars.usda.gov/nutrientdata/flav.

Valko, M., Leibfritz, D., Moncol, J., Cronin, M.T., Mazur, M. dan Telser, J., 2007, Free radicals and antioxidants in normal physiological functions and human disease, *Int J Biochem Cell Biol*, 39:44-84.

Van Breemen, R.B. dan Pajkovic, N., 2008, Multitargeted therapy of cancer by lycopene, *Cancer Letters*, 269 : 339–351.

Van der Sluis, A.A., Dekker, M., De Jager, A. dan Jongen, W.M.F., 2001, Activity and concentration of polyphenolic antioxidants in apple: Effect of cultivar, harvest year, and storage conditions, *J Agric Food Chem.*, 49:3606-13.

Vadlamudi, R., Mandal, M., Adam, L., Steibach, G., Mendelsohn, J. dan Kumar, R., 1999, Regulation of cyclooxygenase-2 pathway by HER2 receptor, *Oncogene*,18:305–314

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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Universitas Gadjah Mada, 2017 | Diunduh dari http://etd.repository.ugm.ac.id/

Vichitphan, S., Vichitphan, K. dan Sirikhansaeng, P., 2007, Flavonoid content and antioksidan activity of krachaidum (*Kaemferia parviflora*) Wine, *Journal of Science Technology*, (7): 97- 105.

Victorio, C.P., Lage, C.L.S., Kuster, R.M., 2009, Flavonoid extraction from Alpinia zerumbet (Pers.) Burtt et Smith leaves using different techniques and solvents, *Ecl. Quim., Sao Paulo*, 34 (1) ;19-24.

Villo, P., 2008, Syhthesis of Acetogenin Analogeus, Thesis, University of Tartu, Estonia.

Visavadiya, N.P., Soni, B. dan Dalwadi, N., 2009, Free radical scavenging and antiatherogenic activities of *Sesamum indicum* seed extracts in chemical and biological model systems, *Food Chem Toxicol*, 47:2507-15.

Wang, R.F., Miyahara, Y. dan Wang, H.Y., 2008, Toll-like receptors and immune regulation: implications for cancer therapy. *Oncogene*, 27:181–189.

Wang, X., Li, L., Wang, B. dan Xiang, J., 2009, Effects of ursolic acid on the proliferation and apoptosis of human ovarian cancer cells, *Medicine J Huazhong Univ Sci-Med*, 29: 761-764.

Warner, B.B., Stuart, L., Gebb,S. dan Wispe, J.R., 1996, Redox regulation of manganese superoxide dismutase, *Am. J. Physiol*., 271: L150– L158.

Weinberg, F., Hamanaka, R., Wheaton, W.W., Weinberg, S., Joseph, J., Lopez, M., Kalyanaraman, B., Mutlu, G.M., Budinger, G.R. dan Chandel N.S., 2010, Mitochondrial metabolism and ROS generation are essential for Kras-mediated tumorigenicity, *Proc Natl Acad Sci USA*,107:8788–8793.

Winarno, M.W., Hargono, D. dan Leydia M.S., 2005, Efek antimalarial ekstrak daun pepaya gantung (*Carica papaya* L.) pada tikus terinfeksi *Plasmodium berghei*, *Jurnal Bahan Alam Indonesia*, 4 (1) : 219-222.

Weitzman, S.A. dan Gordon, L.I., 1990, Inflammation and cancer: role of phagocyte-generated oxidants in carcinogenesis, *Blood*, 76:655-663.

Wen, L., Wua, D., Jiangan Y, Prassad, K. N., Lina, S., Jianga, G., Ha, J., Zhaob, M., Luob, W., Yanga, B., 2013, Identification of flavonoids in Litchi (*Litchi chinensis Sonn*.) leaf and evaluation of anticancer activities, *Journal of Functional Food*, 1-9.

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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WHO (World Health Organization), 2008, World Health Statistic, WHO Press, Geneva.

Wietrzyk, J., Grynkiewicz, G. and Opolski, A. 2005. Phytoestrogens in cancer prevention and therapy-mechanisms of their biological activity, *Anticancer Research,* 25:2357-2366.

Williams, C.S., Mann, M. dan Dubois, R.N., 1999, The role of cyclooxygenases in inflammation, cancer, and development. *Oncogene* 18:7908–7916

Winterbourn, C.C. dan Hampton, M.B., 2008, Thiol chemistry and specificity in redox signaling, *Free Radic Biol Med.*, 45(5):549–561.

Winkel-Shirley, B., 2002, Biosynthesis of flavonoids and effect of stress, Curr *Opin Plant Biol.*, 5: 218-23.

Witsch, E., Sela, M. dan Yarden,Y., 2010, Roles for Growth Factors in Cancer Progression, *Physiology (Bethesda)*, 25(2): 85–101.

Witton, C.J., Hawe, S.J.K., Cooke TG, Bartlett, J.M.S., 2004, Cyclooxygenase 2 (COX2) expression is associated with poor outcome in ER-negative, but not ER-positive, breast cancer. *Histopathology*, 45:47–54 7.

World Cancer Research Fund, 2000, American Institute for Cancer Research: *Food, Nutrition and the Prevention of Cancer: A Global Perspective*. Menasha, WI: BANTA Book Group.

Wood, Z.A., Schroder, E., Robin, H.J. dan Poole, L.B., 2003, Structure, mechanism and regulation of peroxiredoxins, *Trends Biochem Sci.*, 28(1):32–40.

Wu, M., Han-Fei D., David E. F., 2001, Apoptosis: Molecular Mechanisms, Encyclopedia Of Life Sciences,1-2.

Wyllie, A. H., Kerr J. F. R., dan Currie A. R., 1980, Cell death: the significance of apoptosis, *International Review of Cytology*, 68: 251–306.

Xiao, X., Shi, D., Liu, L., Wang, J., Xie, X., Kang, T., *et al.*, 2011, Quercetin suppresses cyclooxygenase-2 expression and angiogenesis through inactivation of P300 signaling, *PLoS One*, 6(8):e22934.

Yang, H., Zhou, H., Feng, P., *et al*., 2010, Reduced expression of Toll-like receptor 4 inhibits human breast cancer cells proliferation and inflammatory

Potensi Ekstrak Daun Pepaya (Carica papaya L) Sebagai Antioksidan Dalam Upaya Menghambat Kanker
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cytokines secretion, *Journal of Experimental and Clinical Cancer Research*, 29 (1) article 92.

Yao, L.H., Jiang, Y.M., Shi, J., Toma´s-Barbera´n, F.A., Datta, N., Singanusong, R., Chen, S.S., 2004, Flavonoids in food and their health benefits. *Plant Foods Hum Nutr*., 59 (3):113–22.

You, H., Yu, W., Sanders, B.G., Kline, K., 2001, Rrr-alpha-tocopheryl succinate induces MDA-MB-435 and MCF-7 human breast cancer cells to undergo differentiation, *Cell Growth Differ.*, 12: 471–480.

Yuan, C., Huang, X., Cheng, L., Bu, Y., Liu, G., Yi, F., Yang, Z. and Song, F. 2009. Evalution of antioxidant and immune activity of Phellinus ribis glucan in mice. *Food Chemistry,* 115: 581-584

Yu, W., Simmons-Menchaca, M., Gapor, A., Sanders, B.G., dan Kline, K., 1999, Induction of apoptosis in human breast cancer cells by tocopherols and tocotrienols, *Nutr Cancer,* 33: 26–32.

Yu, H., Kortylewski, M. dan Pardoll, D., 2007, Crosstalk between cancer and immune cells: role of STAT3 in the tumor microenvironment, *Nat Rev Immunol*, 7: 41–51.

Yusuf, N., 2014, Toll like receptors and breast cancer, *Front Immunol,* 5:84-89.

Zelko, I.N., Mariani, TJ dan Folz, R.J., 2002, Superoxide dismutase multigene family: a comparison of the CuZn-SOD (SOD1), Mn-SOD (SOD2), and EC-SOD (SOD3) gene structures, evolution and expression, *Free Radical Biology & Medicine*, Vol. 33, No. 3, pp. 337–349.

Zhang, H.J., Drake, V.J., Xu, L., Hu, J., Domann, F.E., Oberley, L.W. dan Kregel, K.C., 2002, Redox regulation of adenovirus-induced AP-1 activation by overexpression of manganese-containing superoxide dismutase, *J. Virol.* 76:355– 363.

Zowczak-Drabarczyk,M.M., Murawa, D., Kaczmarek, L., Połom, K. dan Litwiniuk, M., 2013, Total antioxidant status in plasma of breast cancer patients in relation to ERβ expression, *Contemp Oncol (Pozn),* 17(6): 499–503.

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Zunjar, V., Mammen, D., Trivedi, B.M. and Daniel, M. 2011. Pharmacognostic, physicochemical and phytochemical studies on *Carica papaya Linn*. leaves. *Pharmacognosy Journal*, 3:5–8.