

## Daftar Pustaka

- '4T1 ATCC ® CRL-2539™ Mus musculus mammary gland This tumor i', n.d.  
URL: <https://www.atcc.org/Products/All/CRL-2539.aspx#generalinformation> (diakses tanggal 15/5/2018).
- Aksoy, O., Chicas, A., Zeng, T., Zhao, Z., McCurrach, M., Wang, X., dkk., 2012. The atypical E2F family member E2F7 couples the p53 and RB pathways during cellular senescence. *Genes & Development*, **26**: 1546–1557.
- Altieri, D.C., 2003. Validating survivin as a cancer therapeutic target. *Nature Reviews Cancer*, **3**: 46–54.
- Anonim 'Cellular Reactive Oxygen Species Detection Assay Kit (Red Fluorescence) (ab186027)', 2016. URL: <http://www.abcam.com/cellular-reactive-oxygen-species-detection-assay-kit-red-fluorescence-ab186027.html> (diakses tanggal 7/6/2018).
- Antoniou, A., Pharoah, P.D.P., Narod, S., Risch, H.A., Eyfjord, J.E., Hopper, J.L., dkk., 2003. Average Risks of Breast and Ovarian Cancer Associated with BRCA1 or BRCA2 Mutations Detected in Case Series Unselected for Family History: A Combined Analysis of 22 Studies. *The American Journal of Human Genetics*, **72**: 1117–1130.
- Bae, I.-K., Min, H.-Y., Han, A.-R., Seo, E.-K., dan Lee, S.K., 2005. Suppression of lipopolysaccharide-induced expression of inducible nitric oxide synthase by brazilin in RAW 264.7 macrophage cells. *European Journal of Pharmacology*, **513**: 237–242.
- Bannister, J., B.H.P.O., 2007. Free Radicals in Biology and Medicine 10, 250–266.
- Bao, H., Zhang, L.-L., Liu, Q.-Y., Feng, L., Ye, Y., Lu, J.-J., dkk., 2016. Cytotoxic and Pro-Apoptotic Effects of Cassane Diterpenoids from the Seeds of *Caesalpinia sappan* in Cancer Cells. *Molecules*, **21**: 791.
- Bao, H., Zhang, Q., Ye, Y., dan Lin, L., 2017. Naturally occurring furanoditerpenoids: distribution, chemistry and their pharmacological activities. *Phytochemistry Reviews*, **16**: 235–270.
- Bassaneze, V., Miyakawa, A.A., dan Krieger, J.E., 2008. A quantitative chemiluminescent method for studying replicative and stress-induced

- premature senescence in cell cultures. *Analytical Biochemistry*, **372**: 198–203.
- Behrend, L., Henderson, G., dan Zwacka, R.M., 2003. Reactive oxygen species in oncogenic transformation. *Biochemical Society Transactions*, **31**: 1441–1444.
- Block, K.I., Koch, A.C., Mead, M.N., Tothy, P.K., Newman, R.A., dan Gyllenhaal, C., 2007. Impact of antioxidant supplementation on chemotherapeutic efficacy: A systematic review of the evidence from randomized controlled trials. *Cancer Treatment Reviews*, **33**: 407–418.
- Boonstra, J. dan Post, J.A., 2004. Molecular events associated with reactive oxygen species and cell cycle progression in mammalian cells. *Gene*, **337**: 1–13.
- Borrelli, A., Schiattarella, A., Mancini, R., Morelli, F., Capasso, C., Luca, V.D., dkk., n.d. The leader peptide of a human rec. MnSOD as molecular carrier which delivers high amounts of Cisplatin into tumor cells inducing a fast apoptosis in vitro. *International Journal of Cancer*, **128**: 453–459.
- Brandon, M., Baldi, P., dan Wallace, D.C., 2006. Mitochondrial mutations in cancer. *Oncogene*, **25**: 4647–4662.
- Brown, J.P., Wei, W., dan Sedivy, J.M., 1997. Bypass of Senescence After Disruption of p21CIP1/WAF1 Gene in Normal Diploid Human Fibroblasts. *Science*, **277**: 831–834.
- Chien, Y., Scuoppo, C., Wang, X., Fang, X., Balgley, B., Bolden, J.E., dkk., 2011. Control of the senescence-associated secretory phenotype by NF- $\kappa$ B promotes senescence and enhances chemosensitivity. *Genes & Development*, **25**: 2125–2136.
- Chua, M.-T., Tung, Y.-T., dan Chang, S.-T., 2008. Antioxidant activities of ethanolic extracts from the twigs of *Cinnamomum osmophloeum*. *Bioresource Technology*, **99**: 1918–1925.
- Church, S.L., Grant, J.W., Ridnour, L.A., Oberley, L.W., Swanson, P.E., Meltzer, P.S., dkk., 1993. Increased manganese superoxide dismutase expression suppresses the malignant phenotype of human melanoma cells. *Proceedings of the National Academy of Sciences of the United States of America*, **90**: 3113–3117.

- Clement, S.P. and M.-V., 2004. 'Tumor Intracellular Redox Status and Drug Resistance-Serendipity or a Causal Relationship?', *Current Pharmaceutical Design*. URL: <http://www.eurekaselect.com/61904/article> (diakses tanggal 21/6/2018).
- Clerkin, J.S., Naughton, R., Quiney, C., dan Cotter, T.G., 2008. Mechanisms of ROS modulated cell survival during carcinogenesis. *Cancer Letters*, , Oxidative Stress and Carcinogenesis Special Issue **266**: 30–36.
- Costa, A., Scholer-Dahirel, A., dan Mechta-Grigoriou, F., 2014. The role of reactive oxygen species and metabolism on cancer cells and their microenvironment. *Seminars in Cancer Biology*, **25**: 23–32.
- Čunderlíková, B., Vasovič, V., Sieber, F., Furre, T., Borgen, E., Nesland, J.M., dkk., 2011. Hexaminolevulinate-mediated photodynamic purging of marrow grafts with murine breast carcinoma. *Bone Marrow Transplantation*, **46**: 1118–1127.
- De Flora, S. dan Ferguson, L.R., 2005. Overview of mechanisms of cancer chemopreventive agents. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, **591**: 8–15.
- Departemen Kesehatan RI. 2010. *Suplemen I Farmakope Herbal Indonesia*. Departemen Kesehatan RI. Jakarta
- de Stanchina, E., Querido, E., Narita, M., Davuluri, R.V., Pandolfi, P.P., Ferbeyre, G., dkk., 2004. PML Is a Direct p53 Target that Modulates p53 Effector Functions. *Molecular Cell*, **13**: 523–535.
- Dexter, D.L., Kowalski, H.M., Blazar, B.A., Fligiel, Z., Vogel, R., dan Heppner, G.H., 1978. Heterogeneity of Tumor Cells from a Single Mouse Mammary Tumor. *Cancer Research*, **38**: 3174–3181.
- Dhar, S.K., Tangpong, J., Chaiswing, L., Oberley, T.D., dan St Clair, D.K., 2011. Manganese superoxide dismutase is a p53-regulated gene that switches cancers between early and advanced stages. *Cancer research*, **71**: 6684–6695.
- Ditjen POM. 2000. Parameter Standar Umum Ekstrak Tumbuhan Obat. Cetakan Pertama. Departemen Kesehatan RI. Jakarta.
- Eccles, M. dan Li, C., 2012. Senescence Associated  $\beta$ -galactosidase Staining. *BIO-PROTOCOL*, **2**: .

- Elmore, S., 2007. Apoptosis: a review of programmed cell death. *Toxicologic Pathology*, **35**: 495–516.
- Ferbeyre, G., Stanchina, E. de, Querido, E., Baptiste, N., Prives, C., dan Lowe, S.W., 2000. PML is induced by oncogenic ras and promotes premature senescence. *Genes & Development*, **14**: 2015–2027.
- Finkel, T. dan Holbrook, N.J., 2000. Oxidants, oxidative stress and the biology of ageing. *Nature*, **408**: 239–247.
- Fortugno, P., Wall, N.R., Giodini, A., O'Connor, D.S., Plescia, J., Padgett, K.M., dkk., 2002. Survivin exists in immunochemically distinct subcellular pools and is involved in spindle microtubule function. *Journal of Cell Science*, **115**: 575–585.
- Graham, R.S. and C.H., 2008. 'Chemosensitization of Cancer by Nitric Oxide', *Current Pharmaceutical Design*. URL: <http://www.eurekaselect.com/66868/article> (diakses tanggal 21/6/2018).
- Guijarro, M.V., Leal, J.F.M., Blanco-Aparicio, C., Alonso, S., Fominaya, J., Leonart, M., dkk., 2007. MAP17 enhances the malignant behavior of tumor cells through ROS increase. *Carcinogenesis*, **28**: 2096–2104.
- Halliwell, B., 2001. Role of Free Radicals in the Neurodegenerative Diseases: Therapeutic Implications for Antioxidant Treatment. *Drugs & Aging*, **18**: 685–716.
- Hanahan, D. dan Weinberg, R.A., 2000. The Hallmarks of Cancer. *Cell*, **100**: 57–70.
- Hanahan, D. dan Weinberg, R.A., 2011. Hallmarks of Cancer: The Next Generation. *Cell*, **144**: 646–674.
- Haryanti, S. 2017. Potensi Antikanker Kombinasi Ekstrak Tanaman Dengan Doxorubicin Melalui Penghambatan Proliferasi dan Metastasis pada Sel Kanker Payudara Secara *In Vitro*. *Disertasi*. Fakultas Farmasi Universitas Gadjah Mada.
- Haryanti, S., Murwanti, R., Putri, H., Ilmawati, G.P.N., Pramono, S., dan Meiyanto, E., 2017. Different 4T1 Cells Migration under *Caesalpinia sappan* L. and *Ficus septica* Burm.f Ethanolic Extracts. *Indonesian Journal of Cancer Chemoprevention*, **8**: 21.

- Henne, A., 1979. Singlet Oxygen, Reactions with Organic Compounds & Polymers. Herausgegeben von B. Rånby und J. F. Rabek. John Wiley & Sons, New York 1978. 1. Aufl., 331 S., geb. £ 15.00. *Angewandte Chemie*, **91**: 359–360.
- Heppler, G., R Miller, F., dan Malathy Shekhar, P., 2000. Nontransgenic models of breast cancer. *Breast Cancer Research : BCR*, **2**: 331–334.
- Heppler, G.H., Dexter, D.L., DeNucci, T., Miller, F.R., dan Calabresi, P., 1978. Heterogeneity in Drug Sensitivity among Tumor Cell Subpopulations of a Single Mammary Tumor. *Cancer Research*, **38**: 3758–3763.
- Hodgkin, J., 2001. Caenorhabditis Elegans, dalam: Brenner, S. dan Miller, J.H. (Editor), *Encyclopedia of Genetics*. Academic Press, New York, hal. 251–256.
- Horn, H.F. dan Vousden, K.H., 2007. Coping with stress: multiple ways to activate p53. *Oncogene*, **26**: 1306–1316.
- Hsieh, C.-Y., Tsai, P.-C., Chu, C.-L., Chang, F.-R., Chang, L.-S., Wu, Y.-C., dkk., 2013. Brazilein suppresses migration and invasion of MDA-MB-231 breast cancer cells. *Chemico-Biological Interactions*, **204**: 105–115.
- Hu, C.M., Kang, J.J., Lee, C.C., Li, C.H., Liao, J.W., dan Cheng, Y.W., 2003. Induction of vasorelaxation through activation of nitric oxide synthase in endothelial cells by brazilin. *European Journal of Pharmacology*, **468**: 37–45.
- Hu, Y., Rosen, D.G., Zhou, Y., Feng, L., Yang, G., Liu, J., dkk., 2005. Mitochondrial Manganese-Superoxide Dismutase Expression in Ovarian Cancer ROLE IN CELL PROLIFERATION AND RESPONSE TO OXIDATIVE STRESS. *Journal of Biological Chemistry*, **280**: 39485–39492.
- Hung, T.M., Dang, N.H., dan Dat, N.T., 2014. Methanol extract from Vietnamese Caesalpinia sappan induces apoptosis in HeLa cells. *Biological Research*, **47**: .
- Hwang, H.S. dan Shim, J.H., 2018. Brazilin and Caesalpinia sappan L. extract protect epidermal keratinocytes from oxidative stress by inducing the expression of GPX7. *Chinese Journal of Natural Medicines*, **16**: 203–209.

- Irani, K., Xia, Y., Zweier, J.L., Sollott, S.J., Der, C.J., Fearon, E.R., dkk., 1997. Mitogenic Signaling Mediated by Oxidants in Ras-Transformed Fibroblasts. *Science*, **275**: 1649–1652.
- Jacinto, P.K. and J.D., 2001. 'Mechanisms of Carcinogenesis Focus on Oxidative Stress and Electron Transfer', *Current Medicinal Chemistry*. URL: <http://www.eurekaselect.com/65362/article> (diakses tanggal 8/6/2018).
- Jackson, J.G. dan Pereira-Smith, O.M., 2006. p53 Is Preferentially Recruited to the Promoters of Growth Arrest Genes p21 and GADD45 during Replicative Senescence of Normal Human Fibroblasts. *Cancer Research*, **66**: 8356–8360.
- Jayakumar, T., Chang, C.-C., Lin, S.-L., Huang, Y.-K., Hu, C.-M., Elizebeth, A.R., dkk., 2014. Brazilin Ameliorates High Glucose-Induced Vascular Inflammation via Inhibiting ROS and CAMs Production in Human Umbilical Vein Endothelial Cells. *BioMed Research International*, **2014**: .
- Kalliokoski, T., Kramer, C., Vulpetti, A., dan Gedeck, P., 2013. Comparability of Mixed IC50 Data – A Statistical Analysis. *PLoS ONE*, **8**: .
- Kamiguti, A.S., Serrander, L., Lin, K., Harris, R.J., Cawley, J.C., Allsup, D.J., dkk., 2005. Expression and Activity of NOX5 in the Circulating Malignant B Cells of Hairy Cell Leukemia. *The Journal of Immunology*, **175**: 8424–8430.
- Kawanishi, S., Hiraku, Y., Pinlaor, S., dan Ma, N., 2006. Oxidative and nitrative DNA damage in animals and patients with inflammatory diseases in relation to inflammation-related carcinogenesis. *Biological Chemistry*, **387**: 365–372.
- Kim, B., Kim, Sun-Hee, Jeong, S.-J., Sohn, E.J., Jung, J.H., Lee, M.H., dkk., 2012. Brazilin Induces Apoptosis and G2/M Arrest via Inactivation of Histone Deacetylase in Multiple Myeloma U266 Cells. *Journal of Agricultural and Food Chemistry*, **60**: 9882–9889.
- Kim, E.-C., Hwang, Y.-S., Lee, H.-J., Lee, Sun-Kyung, Park, M.-H., Jeon, B.-H., dkk., 2005. *Caesalpinia sappan* Induces Cell Death by Increasing the Expression of p53 and p21WAF1/CIP1 in Head and Neck Cancer Cells. *The American Journal of Chinese Medicine*, **33**: 405–414.

- Komatsu, D., Kato, M., Nakayama, J., Miyagawa, S., dan Kamata, T., 2008. NADPH oxidase 1 plays a critical mediating role in oncogenic Ras-induced vascular endothelial growth factor expression. *Oncogene*, **27**: 4724–4732.
- Kong, H. dan Chandel, N.S., 2017. Regulation of redox balance in cancer and T cells. *Journal of Biological Chemistry*, jbc.TM117.000257.
- Kortlever, R.M., Higgins, P.J., dan Bernards, R., 2006. Plasminogen activator inhibitor-1 is a critical downstream target of p53 in the induction of replicative senescence. *Nature cell biology*, **8**: 877–884.
- Kristiani, N. 2013. Peningkatan Efek Sitotoksik Doxorubicin Oleh Fraksi Etil Asetat Kayu Secang (*Caesalpinia sappan* L.) pada Sel T47D melalui Induksi Apoptosis. *Skripsi*. Fakultas Farmasi Universitas Gadjah Mada.
- Kuilman, T., Michaloglou, C., Mooi, W.J., dan Peeper, D.S., 2010. The essence of senescence. *Genes & Development*, **24**: 2463–2479.
- Kumar, B., Koul, S., Khandrika, L., Meacham, R.B., dan Koul, H.K., 2008. Oxidative Stress Is Inherent in Prostate Cancer Cells and Is Required for Aggressive Phenotype. *Cancer Research*, **68**: 1777–1785.
- Kurz, D.J., Decary, S., Hong, Y., dan Erusalimsky, J.D., 2000. Senescence-associated (beta)-galactosidase reflects an increase in lysosomal mass during replicative ageing of human endothelial cells. *Journal of Cell Science*, **113** ( Pt 20): 3613–3622.
- Lee, A.C., Fenster, B.E., Ito, H., Takeda, K., Bae, N.S., Hirai, T., dkk., 1999. Ras Proteins Induce Senescence by Altering the Intracellular Levels of Reactive Oxygen Species. *Journal of Biological Chemistry*, **274**: 7936–7940.
- Lee, E.B., Xing, M.M., dan Kim, D.K., 2017. Lifespan-extending and stress resistance properties of brazilin from *Caesalpinia sappan* in *Caenorhabditis elegans*. *Archives of Pharmacal Research*, **40**: 825–835.
- Liang, C.-H., Chan, L.-P., Chou, T.-H., Chiang, F.-Y., Yen, C.-M., Chen, P.-J., dkk., 2013. 'Brazilin from *Caesalpinia sappan* L. Antioxidant Inhibits Adipocyte Differentiation and Induces Apoptosis through Caspase-3 Activity and Anthelmintic Activities against *Hymenolepis nana* and *Anisakis simplex*', , *Research article, Evidence-Based Complementary and Alternative Medicine*. URL:

<https://www.hindawi.com/journals/ecam/2013/864892/> (diakses tanggal 20/6/2018).

- Lim, D.-K., Choi, U., dan Shin, D.-H., 1996. Antioxidative Activity of Some Solvent Extract from *Caesalpinia sappan* L. *Korean Journal of Food Science and Technology*, **28**: 77–82.
- Liu, J., Gu, X., Robbins, D., Li, G., Shi, R., McCord, J.M., dkk., 2009. Protandim, a Fundamentally New Antioxidant Approach in Chemoprevention Using Mouse Two-Stage Skin Carcinogenesis as a Model. *PLoS ONE*, **4**: .
- Lugasi, A., 1997. Natural Antioxidants Chemistry, Health Effects, and Applications. Edited by F. Shahidi. VIII and 432 pages, numerous figures and tables. AOCS Press, Champaign, Illinois, 1997. Price: 105.00 US\$. *Food / Nahrung*, **41**: 321–321.
- Mani, S.A., Guo, W., Liao, M.-J., Eaton, E.N., Ayyanan, A., Zhou, A.Y., dkk., 2008. The Epithelial-Mesenchymal Transition Generates Cells with Properties of Stem Cells. *Cell*, **133**: 704–715.
- McConnell, B.B., Starborg, M., Brookes, S., dan Peters, G., 1998. Inhibitors of cyclin-dependent kinases induce features of replicative senescence in early passage human diploid fibroblasts. *Current Biology*, **8**: 351–354.
- Miller, J.H., 1972. *Experiments in Molecular Genetics*. Cold Spring Harbor Laboratory, [Cold Spring Harbor, N.Y.].
- Miyashita, T., Krajewski, S., Krajewska, M., Wang, H.G., Lin, H.K., Liebermann, D.A., dkk., 1994. Tumor suppressor p53 is a regulator of bcl-2 and bax gene expression in vitro and in vivo. *Oncogene*, **9**: 1799–1805.
- Morecki, S., Yacovlev, L., dan Slavin, S., 1998. Effect of indomethacin on tumorigenicity and immunity induction in a murine model of mammary carcinoma. *International Journal of Cancer*, **75**: 894–899.
- Mosmann, T., 1983. Rapid colorimetric assay for cellular growth and survival: Application to proliferation and cytotoxicity assays. *Journal of Immunological Methods*, **65**: 55–63.
- Nirmal, N.P., Rajput, M.S., Prasad, R.G.S.V., dan Ahmad, M., 2015. Brazilin from *Caesalpinia sappan* heartwood and its pharmacological activities: A review. *Asian Pacific Journal of Tropical Medicine*, **8**: 421–430.

- Nishikawa, M., 2008. Reactive oxygen species in tumor metastasis. *Cancer Letters*, , Oxidative Stress and Carcinogenesis Special Issue **266**: 53–59.
- Norbury, C.J. dan Hickson, I.D., 2001. Cellular Responses to DNA Damage. *Annual Review of Pharmacology and Toxicology*, **41**: 367–401.
- Novarina, A., 2014. Peningkatan Sensitivitas Sel Kanker Kolon WiDr terhadap 5-Fluorourasil Oleh Fraksi Etil Asetat Kayu Secang (*Caesalpinia sappan* L.) melalui Induksi Apoptosis. *Skripsi*. Fakultas Farmasi Universitas Gadjah Mada.
- Nurulita, N. A., & Muflih, Y. A. 2006. Efek Sitotoksik Ekstrak Metanol Kayu Secang (*Caesalpinia sappan* L.) pada Sel Kanker Payudara T47D melalui Induksi Apoptosis. *PHARMACY*, 4(1).
- Oh, J.Y., Giles, N., Landar, A., dan Darley-USmar, V., 2008. Accumulation of 15-deoxy- $\Delta$ 12,14-prostaglandin J2 adduct formation with Keap1 over time: effects on potency for intracellular antioxidant defense induction. *The Biochemical journal*, **411**: 297–306.
- Ohanna, M., Giuliano, S., Bonet, C., Imbert, V., Hofman, V., Zangari, J., dkk., 2011. Senescent cells develop a PARP-1 and nuclear factor- $\kappa$ B-associated secretome (PNAS). *Genes & Development*, **25**: 1245–1261.
- Oliveira, I., Coelho, V., Baltasar, R., Pereira, J.A., dan Baptista, P., 2009. Scavenging capacity of strawberry tree (*Arbutus unedo* L.) leaves on free radicals. *Food and Chemical Toxicology*, **47**: 1507–1511.
- Packer, L. dan Fuehr, K., 1977. Low oxygen concentration extends the lifespan of cultured human diploid cells. *Nature*, **267**: 423.
- Patel, B.P., Rawal, U.M., Dave, T.K., Rawal, R.M., Shukla, S.N., Shah, P.M., dkk., 2007. Lipid Peroxidation, Total Antioxidant Status, and Total Thiol Levels Predict Overall Survival in Patients With Oral Squamous Cell Carcinoma Lipid Peroxidation, Total Antioxidant Status, and Total Thiol Levels Predict Overall Survival in Patients With Oral Squamous Cell Carcinoma. *Integrative Cancer Therapies*, **6**: 365–372.
- Pelicano, H., Carney, D., dan Huang, P., 2004. ROS stress in cancer cells and therapeutic implications. *Drug Resistance Updates*, **7**: 97–110.

- Perry, G., Raina, A.K., Nunomura, A., Wataya, T., Sayre, L.M., dan Smith, M.A., 2000. How important is oxidative damage? Lessons from Alzheimer's disease. *Free Radical Biology and Medicine*, **28**: 831–834.
- Piegari, E., Angelis, A., Cappetta, D., Russo, R., Esposito, G., Costantino, S., dkk., 2013. Doxorubicin induces senescence and impairs function of human cardiac progenitor cells. *Basic Research in Cardiology*, **108**: .
- Piskounova, E., Agathocleous, M., Murphy, M.M., Hu, Z., Huddlestun, S.E., Zhao, Z., dkk., 2015. Oxidative stress inhibits distant metastasis by human melanoma cells. *Nature*, **527**: 186–191.
- Pulaski, B.A., Clements, V.K., Pipeling, M.R., dan Ostrand-Rosenberg, S., 2000. Immunotherapy with vaccines combining MHC class II/CD80+ tumor cells with interleukin-12 reduces established metastatic disease and stimulates immune effectors and monokine induced by interferon gamma. *Cancer immunology, immunotherapy: CII*, **49**: 34–45.
- Putri, A.M. 2016. Aktivitas Ekstrak Etanolik Kayu Secang (*Caesalpinia sappan* L.) dalam Menghambat Penuaan Sel Melalui *Senescence-Associated  $\beta$ -Galactosidase Assay*. Skripsi. Fakultas Farmasi Universitas Gadjah Mada.
- Rachmady, R. 2015. Aktivitas Sitotoksik Ekstrak Etanolik Kayu Secang (*Caesalpinia sappan* L.) terhadap Sel Kanker Payudara Bertarget Molekuler pada Reseptor HER-2. Skripsi. Fakultas Farmasi Universitas Gadjah Mada.
- Rachmady, R., Muntafiah, L., Rosyadi, F., Sholihah, I., Handayani, S., dan Jenie, R.I., 2017. Antiproliferative Effect of Secang Heartwood Ethanolic Extract (*Caesalpinia sappan* L.) on HER2-Positive Breast Cancer Cells. *Indonesian Journal of Cancer Chemoprevention*, **7**: 1.
- Radisky, D.C., Levy, D.D., Littlepage, L.E., Liu, H., Nelson, C.M., Fata, J.E., dkk., 2005. Rac1b and reactive oxygen species mediate MMP-3-induced EMT and genomic instability. *Nature*, **436**: 123–127.
- Ramsey, M.R. dan Sharpless, N.E., 2006. ROS as a tumour suppressor? *Nature Cell Biology*, **8**: 1213–1215.
- Redza-Dutordoir, M. dan Averill-Bates, D.A., 2016. Activation of apoptosis signalling pathways by reactive oxygen species. *Biochimica et Biophysica Acta (BBA) - Molecular Cell Research*, **1863**: 2977–2992.

- Ren, L., Yang, X., Wang, G., Zhang, H., Zhao, L., dan Mi, Z., 2011. Inhibition Effect of Brazilin to Human Bladder Cancer Cell Line T24 **5**: 5.
- Rhyu, D.Y., Yang, Y., Ha, H., Lee, G.T., Song, J.S., Uh, S., dkk., 2005. Role of Reactive Oxygen Species in TGF- $\beta$ 1-Induced Mitogen-Activated Protein Kinase Activation and Epithelial-Mesenchymal Transition in Renal Tubular Epithelial Cells. *Journal of the American Society of Nephrology*, **16**: 667–675.
- Ristow, M. dan Schmeisser, S., 2011. Extending life span by increasing oxidative stress. *Free Radical Biology and Medicine*, **51**: 327–336.
- Rivanti, E., Shabrina, B.A., Nurzilah, I., Ayu, C., dan Hermawan, A., 2017. Heartwood of Secang (*CAESALPINIA SAPPAN* L.) Ethanolic Extract Show Selective Cytotoxic Activities on T47D and Widr Cells But Not on Hela Cells. *Indonesian Journal of Cancer Chemoprevention*, **7**: 60.
- Robards, K., Prenzler, P.D., Tucker, G., Swatsitang, P., dan Glover, W., 1999. Phenolic compounds and their role in oxidative processes in fruits. *Food Chemistry*, **66**: 401–436.
- Rodrigues, M.S., Reddy, M.M., dan Sattler, M., 2008. Cell Cycle Regulation by Oncogenic Tyrosine Kinases in Myeloid Neoplasias: From Molecular Redox Mechanisms to Health Implications. *Antioxidants & Redox Signaling*, **10**: 1813–1848.
- Salama, R., Sadaie, M., Hoare, M., dan Narita, M., 2014. Cellular senescence and its effector programs. *Genes & Development*, **28**: 99–114.
- Saravanan, B.C., Sreekumar, C., Bansal, G.C., Ray, D., Rao, J.R., dan Mishra, A.K., 2003. A rapid MTT colorimetric assay to assess the proliferative index of two Indian strains of *Theileria annulata*. *Veterinary Parasitology*, **113**: 211–216.
- Schafer, F.Q. dan Buettner, G.R., 2001. Redox environment of the cell as viewed through the redox state of the glutathione disulfide/glutathione couple. *Free Radical Biology and Medicine*, **30**: 1191–1212.
- Serrano, M., Lin, A.W., McCurrach, M.E., Beach, D., dan Lowe, S.W., 1997. Oncogenic ras Provokes Premature Cell Senescence Associated with Accumulation of p53 and p16INK4a. *Cell*, **88**: 593–602.

- Shelton, D.N., Chang, E., Whittier, P.S., Choi, D., dan Funk, W.D., 1999. Microarray analysis of replicative senescence. *Current Biology*, **9**: 939–945.
- Sherr, C.J. dan DePinho, R.A., 2000. Cellular Senescence: Minireview Mitotic Clock or Culture Shock? *Cell*, **102**: 407–410.
- Shlush, L.I., Itzkovitz, S., Cohen, A., Rutenberg, A., Berkovitz, R., Yehezkel, S., dkk., 2011. Quantitative digital in situ senescence-associated  $\beta$ -galactosidase assay 10.
- Silva, J.P. dan Coutinho, O.P., 2010. Free radicals in the regulation of damage and cell death - basic mechanisms and prevention. *Drug Discoveries & Therapeutics*, **4**: 144–167.
- Sohal, R.S. dan Weindruch, R., 1996. Oxidative Stress, Caloric Restriction, and Aging. *Science*, **273**: 59–63.
- Sosa, V., Moliné, T., Somoza, R., Paciucci, R., Kondoh, H., dan LLeonart, M.E., 2013. Oxidative stress and cancer: An overview. *Ageing Research Reviews*, **12**: 376–390.
- Stuckey, A., 2011. Breast cancer: epidemiology and risk factors. *Clinical Obstetrics and Gynecology*, **54**: 96–102.
- Sugiyanto, R.N. 2014. Menakar Potensi Antigenotoksik Kayu Secang (*Caesalpinia sappan* L.) dalam Prevensi Kerusakan DNA Melalui MNPCE Assay *In Vivo*. *Skripsi*. Fakultas Farmasi Universitas Gadjah Mada.
- Szatrowski, T.P. dan Nathan, C.F., 1991. Production of Large Amounts of Hydrogen Peroxide by Human Tumor Cells. *Cancer Research*, **51**: 794–798.
- Takahashi, A., Ohtani, N., Yamakoshi, K., Iida, S., Tahara, H., Nakayama, K., dkk., 2006. Mitogenic signalling and the p16<sup>INK4a</sup>-Rb pathway cooperate to enforce irreversible cellular senescence. *Nature Cell Biology*, **8**: 1291–1297.
- Tao, L., Li, J., dan Zhang, J., 2013. Brazilein, a compound isolated from *Caesalpinia sappan* Linn., induced growth inhibition in breast cancer cells via involvement of GSK-3 $\beta$ / $\beta$ -Catenin/cyclin D1 pathway. *Chemico-Biological Interactions*, **206**: 1–5.
- Tirtanirmala, P., Novarina, A., Utomo, R.Y., Sugiyanto, R.N., Jenie, R.I., dan Meiyanto, E., 2017. Cytotoxic and Apoptotic-inducing Effect of Fraction

Containing Brazilein from *Caesalpinia sappan* L. and Cisplatin on T47D Cell Lines. *Indonesian Journal of Cancer Chemoprevention*, **6**: 89.

Trachootham, D., Alexandre, J., dan Huang, P., 2009. Targeting cancer cells by ROS-mediated mechanisms: a radical therapeutic approach? *Nature Reviews Drug Discovery*, **8**: 579–591.

Trachootham, D., Lu, W., Ogasawara, M.A., Valle, N.R.-D., dan Huang, P., 2008. Redox Regulation of Cell Survival. *Antioxidants & Redox Signaling*, **10**: 1343–1374.

Ueda, J., Tezuka, Y., Banskota, A.H., Tran, Q.L., Tran, Q.K., Harimaya, Y., dkk., 2002. Antiproliferative Activity of Vietnamese Medicinal Plants. *Biological and Pharmaceutical Bulletin*, **25**: 753–760.

Ushio-Fukai, M. dan Nakamura, Y., 2008. Reactive oxygen species and angiogenesis: NADPH oxidase as target for cancer therapy. *Cancer Letters*, , Oxidative Stress and Carcinogenesis Special Issue **266**: 37–52.

Utomo, R.Y., 2014. Penguatan Sitotoksitas Agen Kemoterapi Doxorubicin Oleh Fraksi Brazilein Secang (*Caesalpinia sappan* L.) melalui Induksi Apoptosis pada Sel Kanker Payudara T47D. *Skripsi*. Fakultas Farmasi Universitas Gadjah Mada.

Utomo, R.Y., Novarina, A., Tirtanirmala, P., Kastian, R.F., dan Jenie, R.I., 2018. Enhancement of Cytotoxicity and Apoptosis Induction of Doxorubicin by Brazilein Containing Fraction of Secang (*Caesalpinia sappan* L.) on T47D Cells. *Indonesian Journal of Cancer Chemoprevention*, **9**: 32–40.

Vafa, O., Wade, M., Kern, S., Beeche, M., Pandita, T.K., Hampton, G.M., dkk., 2002. c-Myc Can Induce DNA Damage, Increase Reactive Oxygen Species, and Mitigate p53 Function: A Mechanism for Oncogene-Induced Genetic Instability. *Molecular Cell*, **9**: 1031–1044.

von Zglinicki, T., Saretzki, G., Döcke, W., dan Lotze, C., 1995. Mild Hyperoxia Shortens Telomeres and Inhibits Proliferation of Fibroblasts: A Model for Senescence? *Experimental Cell Research*, **220**: 186–193.

Wu, W.-S., 2006. The signaling mechanism of ROS in tumor progression. *Cancer and Metastasis Reviews*, **25**: 695–705.

Yen, C.-T., Nakagawa-Goto, K., Hwang, T.-L., Wu, P.-C., Morris-Natschke, S.L., Lai, W.-C., dkk., 2010. Antitumor Agents. 271. Total Synthesis and

Evaluation of Brazilein and Analogs as Anti-inflammatory and Cytotoxic Agents. *Bioorganic & medicinal chemistry letters*, **20**: 1037–1039.

Zanin, J.L.B., de Carvalho, B.A., Salles Martineli, P., dos Santos, M.H., Lago, J.H.G., Sartorelli, P., dkk., 2012. The Genus *Caesalpinia* L. (Caesalpinaceae): Phytochemical and Pharmacological Characteristics. *Molecules*, **17**: 7887–7902.

Zhang, H., Pan, K.-H., dan Cohen, S.N., 2003. Senescence-specific gene expression fingerprints reveal cell-type-dependent physical clustering of up-regulated chromosomal loci. *Proceedings of the National Academy of Sciences of the United States of America*, **100**: 3251–3256.

Zhang, J., Wang, X., Vikash, V., Ye, Q., Wu, D., Liu, Y., dkk., 2016. ROS and ROS-Mediated Cellular Signaling. *Oxidative Medicine and Cellular Longevity*, **2016**: .

Zhao, H., Bai, H., Wang, Y., Li, W., dan Koike, K., 2008. A new homoisoflavan from *Caesalpinia sappan*. *Journal of Natural Medicines*, **62**: 325–327.

Zhong, X., Wu, B., Pan, Y., dan Zheng, S., 2009. Brazilein inhibits survivin protein and mRNA expression and induces apoptosis in hepatocellular carcinoma HepG2 cells. *Neoplasma*, **56**: 387–392.