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DAFTAR PUSTAKA

Abobatta, W.F., 2019. Nutritional Benefits of Citrus Fruits. *American Journal of Biomedical Science & Research*, **3**: 303–306.

Abotaleb, M., Samuel, S., Varghese, E., Varghese, S., Kubatka, P., Liskova, A., dkk., 2018. Flavonoids in Cancer and Apoptosis. *Cancers*, **11**: 28.

Adina, A.B., Goenadi, F.A., Handoko, F.F., Nawangsari, D.A., Hermawan, A., Jenie, R.I., dkk., 2014. Combination of Ethanolic Extract of Citrus aurantifolia Peels with Doxorubicin Modulate Cell Cycle and Increase Apoptosis Induction on MCF-7 Cells. *Shaheed Beheshti University of Medical Sciences and Health Services Iranian Journal of Pharmaceutical Research*, **13**: 919–926.

Aggarwal, V., Tuli, H., Varol, A., Thakral, F., Yerer, M., Sak, K., dkk., 2019. Role of Reactive Oxygen Species in Cancer Progression: Molecular Mechanisms and Recent Advancements. *Biomolecules*, **9**: 735.

Ahamad, M.S., Siddiqui, S., Jafri, A., Ahmad, S., Afzal, M., dan Arshad, M., 2014. Induction of Apoptosis and Antiproliferative Activity of Naringenin in Human Epidermoid Carcinoma Cell through ROS Generation and Cell Cycle Arrest. *PLoS ONE*, **9**: e110003.

Ahmadi, A. dan Shadboorestan, A., 2016. Oxidative stress and cancer; the role of hesperidin, a citrus natural bioflavonoid, as a cancer chemoprotective agent. *Nutrition and Cancer*, **68**: 29–39.

Alenzi, F.Q.B., 2004. Links between apoptosis, proliferation and the cell cycle. *British Journal of Biomedical Science*, **61**: 99–102.

Alshatwi, A.A., Ramesh, E., Periasamy, V.S., dan Subash-Babu, P., 2013. The apoptotic effect of hesperetin on human cervical cancer cells is mediated through cell cycle arrest, death receptor, and mitochondrial pathways. *Fundamental & Clinical Pharmacology*, **27**: 581–592.

Amadori, D., Nanni, O., Marangolo, M., Pacini, P., Ravaioli, A., Rossi, A., dkk., 2000. Disease-Free Survival Advantage of Adjuvant Cyclophosphamide, Methotrexate, and Fluorouracil in Patients With Node-Negative, Rapidly Proliferating Breast Cancer: A Randomized Multicenter Study. *Journal of Clinical Oncology*, **18**: 3125–3134.

Ames, B.N. dan Gold, L.S., 2000. Paracelsus to parascience: the environmental cancer distraction. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, **447**: 3–13.

Arul, D. dan Subramanian, P., 2013. Naringenin (Citrus Flavonone) Induces Growth Inhibition, Cell Cycle Arrest and Apoptosis in Human Hepatocellular Carcinoma Cells. *Pathology & Oncology Research*, **19**: 763–770.

Aveyard, H., 2014. *Doing a Literature Review in Health and Social Care: A Practical Guide*, 3rd ed. McGraw Hill Education, United Kingdom.

Azab, A.E., Adwas, A.A., Elsayed, A.S.I., dan Quwaydir, F.A., 2019. Oxidative stress and antioxidant mechanisms in human body. *Journal of Applied*

Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
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Biotechnology & Bioengineering, **6**: 43–47.

Aziz, M.A., Diab, A.S., dan Mohammed, A.A., 2019. Antioxidant Categories and Mode of Action, dalam: Shalaby, E. (Editor), *Antioxidants*. IntechOpen, London.

Baba, A.I. dan Câtoi, C., 2007. Carcinogenesis and Its Mechanism, dalam: *Comparative Oncology*. The Publishing House of the Romanian Academy, Bucharest.

Babukumar, S., Vinothkumar, V., Velu, P., Ramachandhiran, D., dan Ramados Nirmal, M., 2017. Molecular effects of hesperetin, a citrus flavanone on 7,12-dimethylbenz(a)anthracene induced buccal pouch squamous cell carcinoma in golden Syrian hamsters. *Archives of Physiology and Biochemistry*, **123**: 265–278.

Bailon-Moscoso, N., Cevallos-Solorzano, G., Romero-Benavides, J., dan Ramirez Orellana, M., 2017. Natural Compounds as Modulators of Cell Cycle Arrest: Application for Anticancer Chemotherapies. *Current Genomics*, **18**: 106–131.

Baluk, P., Hashizume, H., dan McDonald, D.M., 2005. Cellular abnormalities of blood vessels as targets in cancer. *Current Opinion in Genetics and Development*, **15**: 102–111.

Banjerdpongchai, R., Wudtiwai, B., Khaw-on, P., Rachakhom, W., Duangnil, N., dan Kongtawelert, P., 2016. Hesperidin from Citrus seed induces human hepatocellular carcinoma HepG2 cell apoptosis via both mitochondrial and death receptor pathways. *Tumor Biology*, **37**: 227–237.

Bao, L., Liu, F., Guo, H. bin, Li, Y., Tan, B. bo, Zhang, W. xing, dkk., 2016. Naringenin inhibits proliferation, migration, and invasion as well as induces apoptosis of gastric cancer SGC7901 cell line by downregulation of AKT pathway. *Tumor Biology*, **37**: 11365–11374.

Batra, P. dan Sharma, A.K., 2013. Anti-cancer potential of flavonoids: recent trends and future perspectives. *3 Biotech*, **3**: 439–459.

Belizário, J., Vieira-Cordeiro, L., dan Enns, S., 2015. Necroptotic Cell Death Signaling and Execution Pathway: Lessons from Knockout Mice. *Mediators of Inflammation*, **2015**: 1–15.

Bellavite, P. dan Donzelli, A., 2020. Hesperidin and SARS-CoV-2: New Light on the Healthy Function of Citrus Fruits. *Antioxidants*, **9**: 742.

Bhavsar, S.K., Joshi, P., Shah, M.B., dan Santani, D.D., 2007. Investigation into Hepatoprotective Activity of Citrus limon. *Pharmaceutical Biology*, **45**: 303–311.

Bhowmick, N.A., Neilson, E.G., dan Moses, H.L., 2004. Stromal fibroblasts in cancer initiation and progression. *Nature*, **432**: 332–337.

Blasco, M.A., 2005. Telomeres and human disease: Ageing, cancer and beyond. *Nature Reviews Genetics*, **6**: 611–622.

Bodduluru, L.N., Kasala, E.R., Madhana, R.M., Barua, C.C., Hussain, M.I., Haloi, P., dkk., 2016. Naringenin ameliorates inflammation and cell proliferation in benzo(a)pyrene induced pulmonary carcinogenesis by modulating CYP1A1,

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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

NFκB and PCNA expression. *International Immunopharmacology*, **30**: 102–110.

Brewer, M.S., 2011. Natural Antioxidants: Sources, Compounds, Mechanisms of Action, and Potential Applications. *Comprehensive Reviews in Food Science and Food Safety*, **10**: 221–247.

Cairns, R.A., Harris, I.S., dan Mak, T.W., 2011. Regulation of cancer cell metabolism. *Nature Reviews Cancer*, **11**: 85–95.

Campêlo, L.M.L., de Almeida, A.A.C., de Freitas, R.L.M., Cerqueira, G.S., de Sousa, G.F., Saldanha, G.B., dkk., 2011. Antioxidant and Antinociceptive Effects of Citrus limon Essential Oil in Mice. *Journal of Biomedicine and Biotechnology*, **2011**: 1–8.

Carneiro, B.A. dan El-Deiry, W.S., 2020. Targeting apoptosis in cancer therapy. *Nature Reviews Clinical Oncology*, **17**: 395–417.

Cavallo, F., De Giovanni, C., Nanni, P., Forni, G., dan Lollini, P.-L., 2011. 2011: the immune hallmarks of cancer. *Cancer Immunology, Immunotherapy*, **60**: 319–326.

Celano, M., Maggisano, V., De Rose, R.F., Bulotta, S., Maiuolo, J., Navarra, M., dkk., 2015. Flavonoid Fraction of Citrus Reticulata Juice Reduces Proliferation and Migration of Anaplastic Thyroid Carcinoma Cells. *Nutrition and Cancer*, **67**: 1183–1190.

Cheng, N., Chytil, A., Shyr, Y., Joly, A., dan Moses, H.L., 2008. Transforming growth factor-β signaling-deficient fibroblasts enhance hepatocyte growth factor signaling in mammary carcinoma cells to promote scattering and invasion. *Molecular Cancer Research*, **6**: 1521–1533.

Chial, H., 2008. 'Tumor Suppressor (TS) Genes and the Two-Hit Hypothesis | Learn Science at Scitable', *Nature Education*. URL: https://www.nature.com/scitable/topicpage/tumor-suppressor-ts-genes-and-the-two-887/ (diakses tanggal 8/3/2021).

Chipuk, J.E., Bouchier-Hayes, L., dan Green, D.R., 2006. Mitochondrial outer membrane permeabilization during apoptosis: The innocent bystander scenario. *Cell Death and Differentiation*, **13**: 1396–1402.

Choi, E.J., 2007. Hesperetin Induced G1-Phase Cell Cycle Arrest in Human Breast Cancer MCF-7 Cells: Involvement of CDK4 and p21. *Nutrition and Cancer*, **59**: 115–119.

Chu, E. dan DeVita Jr, V.T., 2019. *Physicians' Cancer Chemotherapy Drug Manual 2020*. Jones & Bartlett Learning, Burlington.

Cincin, Z.B., Kiran, B., Baran, Y., dan Cakmakoglu, B., 2018. Hesperidin promotes programmed cell death by downregulation of nongenomic estrogen receptor signalling pathway in endometrial cancer cells. *Biomedicine and Pharmacotherapy*, **103**: 336–345.

Cincin, Z.B., Unlu, M., Kiran, B., Sinem Bireller, E., Baran, Y., Cakmakoglu, B., dkk., 2015. Anti-proliferative, apoptotic and signal transduction effects of hesperidin in non-small cell lung cancer cells. *Cellular Oncology*, **38**: 195–

Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
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204.

Cirmi, S., Ferlazzo, N., Lombardo, G., Maugeri, A., Calapai, G., Gangemi, S., dkk., 2016. Chemopreventive Agents and Inhibitors of Cancer Hallmarks: May Citrus Offer New Perspectives? *Nutrients*, **8**: 698.

Clevers, H. dan Nusse, R., 2012. Wnt/β-catenin signaling and disease. *Cell*, .

Cooper, G.M., 2000. Tumor Suppressor Genes, dalam: Cooper, G. (Editor), *The Cell: A Molecular Approach. 2nd Edition.* Sinauer Associates, Sunderland (MA).

de Carvalho, J.T. de G., Baldivia, D.S., Leite, D.F., de Araújo, L.C.A., de Toledo Espindola, P.P., Antunes, K.A., dkk., 2019. Medicinal Plants from Brazilian Cerrado: Antioxidant and Anticancer Potential and Protection against Chemotherapy Toxicity. *Oxidative Medicine and Cellular Longevity*, **2019**: 1–16.

DeBerardinis, R.J., Lum, J.J., Hatzivassiliou, G., dan Thompson, C.B., 2008. The Biology of Cancer: Metabolic Reprogramming Fuels Cell Growth and Proliferation. *Cell Metabolism*, **7**: 11–20.

DeNardo, D.G., Andreu, P., dan Coussens, L.M., 2010. Interactions between lymphocytes and myeloid cells regulate pro-versus anti-tumor immunity. *Cancer and Metastasis Reviews*, **29**: 309–316.

Denaro, M., Smeriglio, A., Xiao, J., Cornara, L., Burlando, B., dan Trombetta, D., 2020. New insights into Citrus genus: From ancient fruits to new hybrids. *Food Frontiers*, **1**: 305–328.

Doonan, F. dan Cotter, T.G., 2008. Morphological assessment of apoptosis. *Methods*, **44**: 200–204.

Ekambaram, G., Rajendran, P., Magesh, V., dan Sakthisekaran, D., 2008. Naringenin reduces tumor size and weight lost in N-methyl-N′-nitro-N-nitrosoguanidine–induced gastric carcinogenesis in rats. *Nutrition Research*, **28**: 106–112.

Elmore, S., 2007. Apoptosis: A Review of Programmed Cell Death. *Toxicologic Pathology*, **35**: 495–516.

Entezari, M., Majd, A., Falahian, F., Mehrabian, S., Hashemi, M., dan Lajimi, A.A., 2009. Antimutagenicity and anticancer effects of Citrus medica fruit juice. *Acta Medica Iranica*, **47**: 373–377.

Fayed, S.A., 2009. Antioxidant and Anticancer Activities of Citrus reticulate (Petitgrain Mandarin) and Pelargonium graveolens (Geranium) Essential Oils. *Research Journal of Agriculture and Biological Sciences*, **5**: 740–747.

Feitelson, M.A., Arzumanyan, A., Kulathinal, R.J., Blain, S.W., Holcombe, R.F., Mahajna, J., dkk., 2015. Sustained proliferation in cancer: Mechanisms and novel therapeutic targets. *Seminars in Cancer Biology*, **35**: S25–S54.

Ferreira, S.S., Silva, A.M., dan Nunes, F.M., 2018. Citrus reticulata Blanco peels as a source of antioxidant and anti-proliferative phenolic compounds. *Industrial Crops and Products*, **111**: 141–148.

Fink, A., 2019. *Conducting Research Literature Reviews: From the Internet to*

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GADJAH MADA
**Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
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Paper, 5th ed. SAGE Publications, New York.

Foley, J.F., Dietrich, D.R., Swenberg, J.A., dan Maronpot, R.R., 1991. Detection and Evaluation of Proliferating Cell Nuclear Antigen (PCNA) in Rat Tissue by an Improved Immunohistochemical Procedure. *Journal of Histotechnology*, **14**: 237–241.

Galadari, S., Rahman, A., Pallichankandy, S., dan Thayyullathil, F., 2017. Reactive oxygen species and cancer paradox: To promote or to suppress? *Free Radical Biology and Medicine*, **104**: 144–164.

Gartel, A.L. dan Radhakrishnan, S.K., 2005. Lost in Transcription: p21 Repression, Mechanisms, and Consequences: Figure 1. *Cancer Research*, **65**: 3980–3985.

Gattuso, G., Barreca, D., Gargiulli, C., Leuzzi, U., dan Caristi, C., 2007. Flavonoid Composition of Citrus Juices. *Molecules*, **12**: 1641–1673.

Gattuso, G., Caristi, C., Gargiulli, C., Bellocco, E., Toscano, G., dan Leuzzi, U., 2006. Flavonoid Glycosides in Bergamot Juice (Citrus bergamia Risso). *Journal of Agricultural and Food Chemistry*, **54**: 3929–3935.

Ghorbani, A., Nazari, M., Jeddi-Tehrani, M., dan Zand, H., 2012. The citrus flavonoid hesperidin induces p53 and inhibits NF-κB activation in order to trigger apoptosis in NALM-6 cells: Involvement of PPARγ-dependent mechanism. *European Journal of Nutrition*, **51**: 39–46.

Grivennikov, S.I., Greten, F.R., dan Karin, M., 2010. Immunity, Inflammation, and Cancer. *Cell*, **140**: 883–899.

Hanahan, D. dan Weinberg, R.A., 2011. Hallmarks of Cancer: The Next Generation. *Cell*, **144**: 646–674.

Harmon, A.W. dan Patel, Y.M., 2004. Naringenin inhibits glucose uptake in MCF-7 breast cancer cells: A mechanism for impaired cellular proliferation. *Breast Cancer Research and Treatment*, **85**: 103–110.

Hipfner, D.R. dan Cohen, S.M., 2004. Connecting proliferation and apoptosis in development and disease. *Nature Reviews Molecular Cell Biology*, **5**: 805–815.

Hornberger, B. dan Rangu, S., 2020. 'Designing Inclusion and Exclusion Criteria', *University of Pennsylvania*. URL: https://repository.upenn.edu/crphttps://repository.upenn.edu/crp/1 (diakses tanggal 6/12/2020).

Inglese, P. dan Sortino, G., 2019. Citrus History, Taxonomy, Breeding, and Fruit Quality, dalam: *Oxford Research Encyclopedia of Environmental Science*. Oxford University Press, United States of America.

Ivanova, D., Zhelev, Z., Aoki, I., Bakalova, R., dan Higashi, T., 2016. Overproduction of reactive oxygen species – obligatory or not for induction of apoptosis by anticancer drugs. *Chinese Journal of Cancer Research*, **28**: 383–396.

Jin, C.Y., Park, C., Lee, J.H., Chung, K.T., Kwon, T.K., Kim, G.Y., dkk., 2009. Naringenin-induced apoptosis is attenuated by Bcl-2 but restored by the

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Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat Proliferasi pada Sel Kanker
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small molecule Bcl-2 inhibitor, HA 14-1, in human leukemia U937 cells. *Toxicology in Vitro*, **23**: 259–265.

Jingwen, B., Yaochen, L., dan Guojun, Z., 2017. Cell cycle regulation and anticancer drug discovery. *Cancer Biology & Medicine*, **14**: 348.

Kamaraj, S., Ramakrishnan, G., Anandakumar, P., Jagan, S., dan Devaki, T., 2009. Antioxidant and anticancer efficacy of hesperidin in benzo(a)pyrene induced lung carcinogenesis in mice. *Investigational New Drugs*, **27**: 214–222.

Kanaze, F.I., Bounartzi, M.I., Georgarakis, M., dan Niopas, I., 2007. Pharmacokinetics of the citrus flavanone aglycones hesperetin and naringenin after single oral administration in human subjects. *European Journal of Clinical Nutrition*, **61**: 472–477.

Khan, K.H., Blanco-Codesido, M., dan Molife, L.R., 2014. Cancer therapeutics: Targeting the apoptotic pathway. *Critical Reviews in Oncology/Hematology*, **90**: 200–219.

Khan, K.H., Yap, T.A., Yan, L., dan Cunningham, D., 2013. Targeting the PI3K-AKT-mTOR singnaling network in cancer. *Chinese Journal of Cancer*, .

Khan, M.K., Zill-E-Huma, dan Dangles, O.O., 2014. A comprehensive review on flavanones, the major citrus polyphenols. *Journal of Food Composition and Analysis*, **33**: 85–104.

Kim, E.K. dan Choi, E.-J., 2010. Pathological roles of MAPK signaling pathways in human diseases. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, **1802**: 396–405.

Kim, D. Il, Lee, S.J., Lee, S.B., Park, K., Kim, W.J., dan Moon, S.K., 2008. Requirement for Ras/Raf/ERK pathway in naringin-induced G1 -cell-cycle arrest via p21WAF1 expression. *Carcinogenesis*, **29**: 1701–1709.

Kim, S.J., Kim, H.S., dan Seo, Y.R., 2019. Understanding of ROS-Inducing Strategy in Anticancer Therapy. *Oxidative Medicine and Cellular Longevity*, **2019**: 1–12.

King, K.L. dan Cidlowski, J.A., 1998. Cell cycle regulation and apoptosis. *Annual Review of Physiology*, **60**: 601–617.

King, R.J.B. dan Robins, M.W., 2006. *Cancer Biology*, 3rd ed. ed. Pearson Prentice Hall, Harlow.

Kiraz, Y., Adan, A., Kartal Yandim, M., dan Baran, Y., 2016. Major apoptotic mechanisms and genes involved in apoptosis. *Tumor Biology*, **37**: 8471–8486.

Knottenbelt, D.C., Patterson-Kane, J.C., dan Snalune, K.L., 2015. Biology of tumour growth, dalam: *Clinical Equine Oncology*. Elsevier, hal. 23–61.

Kopustinskiene, D.M., Jakstas, V., Savickas, A., dan Bernatoniene, J., 2020. Flavonoids as Anticancer Agents. *Nutrients*, **12**: 457.

Kumari, S., Badana, A.K., Murali Mohan, G., Shailender, G., dan Malla, R.R., 2018. Reactive Oxygen Species: A Key Constituent in Cancer Survival. *Biomarker Insights*, **13**: .

Langgut, D., 2017. The Citrus Route Revealed: From Southeast Asia into the Mediterranean. *HortScience*, **52**: 814–822.

Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
Proliferasi pada Sel Kanker
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Lee, E.Y.H.P. dan Muller, W.J., 2010. Oncogenes and tumor suppressor genes. *Cold Spring Harbor perspectives in biology*, .

Lee, K.A., Lee, S.H., Lee, Y.J., Baeg, S.M., dan Shim, J.H., 2012. Hesperidin induces apoptosis by inhibiting Sp1 and its regulatory protein in MSTO-211H cells. *Biomolecules and Therapeutics*, **20**: 273–279.

Lee, Y.K., Bae, K., Yoo, H.-S., dan Cho, S.-H., 2018. Benefit of Adjuvant Traditional Herbal Medicine With Chemotherapy for Resectable Gastric Cancer. *Integrative Cancer Therapies*, **17**: 619–627.

Li, Hongzhong, Yang, B., Huang, J., Xiang, T., Yin, X., Wan, J., dkk., 2013. Naringin inhibits growth potential of human triple-negative breast cancer cells by targeting β-catenin signaling pathway. *Toxicology Letters*, **220**: 219–228.

Li, R.F., Feng, Y.Q., Chen, J.H., Ge, L.T., Xiao, S.Y., dan Zuo, X.L., 2015. Naringenin suppresses K562 human leukemia cell proliferation and ameliorates Adriamycin-induced oxidative damage in polymorphonuclear leukocytes. *Experimental and Therapeutic Medicine*, **9**: 697–706.

Lim, H.K., Moon, J.Y., Kim, H., Cho, M., dan Cho, S.K., 2009. Induction of apoptosis in U937 human leukaemia cells by the hexane fraction of an extract of immature Citrus grandis Osbeck fruits. *Food Chemistry*, **114**: 1245–1250.

Lim, W., Park, S., Bazer, F.W., dan Song, G., 2017. Naringenin-Induced Apoptotic Cell Death in Prostate Cancer Cells Is Mediated via the PI3K/AKT and MAPK Signaling Pathways. *Journal of Cellular Biochemistry*, **118**: 1118–1131.

Lin, R., Hu, X., Chen, S., Shi, Q., dan Chen, H., 2020. Naringin induces endoplasmic reticulum stress-mediated apoptosis, inhibits β-catenin pathway and arrests cell cycle in cervical cancer cells. *Acta biochimica Polonica*, **67**: 181–188.

Liu, R., Chen, Y., Liu, G., Li, C., Song, Y., Cao, Z., dkk., 2020. PI3K/AKT pathway as a key link modulates the multidrug resistance of cancers. *Cell Death & Disease*, **11**: 797.

Liu, Y., Yin, T., Feng, Y., Cona, M.M., Huang, G., Liu, J., dkk., 2015. Mammalian models of chemically induced primary malignancies exploitable for imaging-based preclinical theragnostic research. *Quantitative Imaging in Medicine and Surgery*, **5**: 708–729.

Lotha, R. dan Sivasubramanian, A., 2018. Flavonoids nutraceuticals in prevention and treatment of cancer: A review. *Asian Journal of Pharmaceutical and Clinical Research*, **11**: 42–47.

Lü, J.-M., Lin, P.H., Yao, Q., dan Chen, C., 2010. Chemical and molecular mechanisms of antioxidants: experimental approaches and model systems. *Journal of Cellular and Molecular Medicine*, **14**: 840–860.

Lu, W.L., Yu, C.T.R., Lien, H.M., Sheu, G.T., dan Cherng, S.H., 2020. Cytotoxicity of naringenin induces Bax-mediated mitochondrial apoptosis in human lung adenocarcinoma A549 cells. *Environmental Toxicology*, **35**:

UNIVERSITAS
GADJAH MADA
**Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
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1386–1394.

Lv, X., Zhao, S., Ning, Z., Zeng, H., Shu, Y., Tao, O., dkk., 2015. Citrus fruits as a treasure trove of active natural metabolites that potentially provide benefits for human health. *Chemistry Central Journal*, **9**: 68.

Ly, J.D., Grubb, D.R., dan Lawen, A., 2003. The mitochondrial membrane potential (δψm) in apoptosis; an update. *Apoptosis*, **8**: 115–128.

Macdonald, J.B., Macdonald, B., Golitz, L.E., LoRusso, P., dan Sekulic, A., 2015. Cutaneous adverse effects of targeted therapies. *Journal of the American Academy of Dermatology*, **72**: 203–218.

Macmillan, D., 2012. 'Mendeley: Teaching Scholarly Communication and Collaboration Mendeley: Teaching Scholarly Communication and Collaboration through Social Networking through Social Networking', , dalam: *IATUL Proceedings*. Purdue University, Canada, hal. 37.

Madrigal-Bujaidar, E., Roaro, L.M., García-Aguirre, K., Garcia-Medina, S., dan Alvarez-Gonzalez, I., 2013. Grapefruit juice suppresses azoxymethane-induced colon aberrant crypt formation and induces antioxidant capacity in mice. *Asian Pacific Journal of Cancer Prevention*, **14**: 6851–6856.

Majo, D. Di, Giammanco, M., Guardia, M. La, Tripoli, E., Giammanco, S., dan Finotti, E., 2005. Flavanones in Citrus fruit: Structure–antioxidant activity relationships. *Food Research International*, **38**: 1161–1166.

Malarkey, D.E., Hoenerhoff, M., dan Maronpot, R.R., 2013. Carcinogenesis: Mechanisms and Manifestations, dalam: *Haschek and Rousseaux's Handbook of Toxicologic Pathology*. Elsevier Inc., hal. 107–146.

Marais, J.P.J., Deavours, B., Dixon, R.A., dan Ferreira, D., 2006. The Stereochemistry of Flavonoids, dalam: *The Science of Flavonoids*. Springer New York, New York, NY, hal. 1–46.

Martens, S. dan Mithöfer, A., 2005. Flavones and flavone synthases. *Phytochemistry*, **66**: 2399–2407.

Martin, V., Herrera, F., Garciasantos, G., Antolin, I., Rodriguezblanco, J., dan Rodriguez, C., 2007. Signaling pathways involved in antioxidant control of glioma cell proliferation. *Free Radical Biology and Medicine*, **42**: 1715–1722.

Maru, G., 2014. An update on cancer prevention approaches. *Biomedical Research Journal*, **1**: 146.

Meline, T., 2006. 'Selecting Studies for Systematic Review: Inclusion and Exclusion Criteria', , Contemporary Issues in Communication Science and Disorders.

Mierke, C.T., 2020. *Biological and Medical Physics, Biomedical Engineering. Cellular Mechanics and Biophysics: Structure and Function of Basic Cellular Components Regulating Cell Mechanics*.

Ming, H., Chuang, Q., Jiashi, W., Bin, L., Guangbin, W., dan Xianglu, J., 2018. Naringin targets Zeb1 to suppress osteosarcoma cell proliferation and metastasis. *Aging*, **10**: 4141–4151.

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Muhammad, T., Ikram, M., Ullah, R., Rehman, S., dan Kim, M., 2019. Hesperetin, a Citrus Flavonoid, Attenuates LPS-Induced Neuroinflammation, Apoptosis and Memory Impairments by Modulating TLR4/NF-κB Signaling. *Nutrients*, **11**: 648.

Müller, J.M., Rupec, R.A., dan Baeuerle, P.A., 1997. Study of Gene Regulation by NF-κB and AP-1 in Response to Reactive Oxygen Intermediates. *Methods*, **11**: 301–312.

Nagy, J.A., Chang, S.H., Shih, S.C., Dvorak, A.M., dan Dvorak, H.F., 2010. Heterogeneity of the tumor vasculature. *Seminars in Thrombosis and Hemostasis*, **36**: 321–331.

Nambiar, S. dan Hegde, V., 2016. Apoptosis in cancer therapy. *Journal of Medicine, Radiology, Pathology and Surgery*, **3**: 10–14.

Natarajan, N., Thamaraiselvan, R., Lingaiah, H., Srinivasan, P., dan Maruthaiveeran Periyasamy, B., 2011. Effect of flavonone hesperidin on the apoptosis of human mammary carcinoma cell line MCF-7. *Biomedicine & Preventive Nutrition*, **1**: 207–215.

National Cancer Institute, 2019. 'Definition of Cancer - NCI Dictionary of Cancer Terms', *www.cancer.gov*. URL: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cancer (diakses tanggal 11/12/2020).

Naz, H., Tarique, M., Ahamad, S., Alajmi, M.F., Hussain, A., Rehman, M.T., dkk., 2019. Hesperidin-CAMKIV interaction and its impact on cell proliferation and apoptosis in the human hepatic carcinoma and neuroblastoma cells. *Journal of Cellular Biochemistry*, **120**: 15119–15130.

Nazari, M., Ghorbani, A., Hekmat-Doost, A., Jeddi-Tehrani, M., dan Zand, H., 2011. Inactivation of Nuclear Factor-κB by citrus flavanone hesperidin contributes to apoptosis and chemo-sensitizing effect in Ramos cells. *European Journal of Pharmacology*, **650**: 526–533.

Nogata, Y., Sakamoto, K., Shiratsuchi, H., Ishii, T., Yano, M., dan Ohta, H., 2006. Flavonoid composition of fruit tissues of citrus species. *Bioscience, Biotechnology and Biochemistry*, **70**: 178–192.

Noori, S., Tavirani, M.R., Deravi, N., Rabbani, M.I.M., dan Zarghi, A., 2020. Naringenin enhances the anti-cancer effect of cyclophosphamide against mda-mb-231 breast cancer cells via targeting the stat3 signaling pathway. *Iranian Journal of Pharmaceutical Research*, **19**: 122–133.

Norouzi, S., Norouzi, M., Amini, M., Amanzadeh, A., Nabiuni, M., Irian, S., dkk., 2016. Two COX-2 inhibitors induce apoptosis in human erythroleukemia K562cells by modulating NF-κB and FHC pathways. *DARU Journal of Pharmaceutical Sciences*, **24**: 1.

Obeng, E., 2021. Apoptosis (Programmed cell death) and its signals-a review. *Brazilian Journal of Biology*, **81**: 1133–1143.

Ollitrault, P., Curk, F., dan Krueger, R., 2020. Citrus taxonomy, dalam: Manuel Talon, Marco Caruso, F.G.G. (Editor), *The Genus Citrus*. Woodhead Publishing, hal. 57–81.

UNIVERSITAS
GADJAH MADA
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

Onal, M., Ovet, G., dan Onal, O., 2016. Review of Apoptosis. *MOJ Immunology*, **3**: 1–4.

Palit, S., Kar, S., Sharma, G., dan Das, P.K., 2015. Hesperetin Induces Apoptosis in Breast Carcinoma by Triggering Accumulation of ROS and Activation of ASK1/JNK Pathway. *Journal of Cellular Physiology*, **230**: 1729–1739.

Panche, A.N., Diwan, A.D., dan Chandra, S.R., 2016. Flavonoids: an overview. *Journal of Nutritional Science*, **5**: e47.

Pandey, P., Sayyed, U., Tiwari, R.K., Siddiqui, M.H., Pathak, N., dan Bajpai, P., 2019. Hesperidin Induces ROS-Mediated Apoptosis along with Cell Cycle Arrest at G2/M Phase in Human Gall Bladder Carcinoma. *Nutrition and Cancer*, **71**: 676–687.

Papaliagkas, V., Anogianaki, A., Anogianakis, G., dan Ilonidis, G., 2007. The proteins and the mechanisms of apoptosis: A mini-review of the fundamentals. *Hippokratia*, .

Park, H.J., Choi, Y.J., Lee, J.H., dan Nam, M.J., 2017. Naringenin causes ASK1-induced apoptosis via reactive oxygen species in human pancreatic cancer cells. *Food and Chemical Toxicology*, **99**: 1–8.

Park, H.J., Kim, M.J., Ha, E., dan Chung, J.H., 2008. Apoptotic effect of hesperidin through caspase3 activation in human colon cancer cells, SNU-C4. *Phytomedicine*, **15**: 147–151.

Park, J.H., Jin, C.Y., Lee, B.K., Kim, G.Y., Choi, Y.H., dan Jeong, Y.K., 2008. Naringenin induces apoptosis through downregulation of Akt and caspase-3 activation in human leukemia THP-1 cells. *Food and Chemical Toxicology*, **46**: 3684–3690.

Park, S., Lim, W., Bazer, F.W., dan Song, G., 2018. Naringenin suppresses growth of human placental choriocarcinoma via reactive oxygen species-mediated P38 and JNK MAPK pathways. *Phytomedicine*, **50**: 238–246.

Patel, K., Singh, G.K., dan Patel, D.K., 2018. A Review on Pharmacological and Analytical Aspects of Naringenin. *Chinese Journal of Integrative Medicine*, **24**: 551–560.

Perillo, B., Di Donato, M., Pezone, A., Di Zazzo, E., Giovannelli, P., Galasso, G., dkk., 2020. ROS in cancer therapy: the bright side of the moon. *Experimental & Molecular Medicine*, **52**: 192–203.

Peterson, J. dan Dwyer, J., 1998. Flavonoids: Dietary occurrence and biochemical activity. *Nutrition Research*, **18**: 1995–2018.

Peterson, J.J., Beecher, G.R., Bhagwat, S.A., Dwyer, J.T., Gebhardt, S.E., Haytowitz, D.B., dkk., 2006. Flavanones in grapefruit, lemons, and limes: A compilation and review of the data from the analytical literature. *Journal of Food Composition and Analysis*, **19**: S74–S80.

Pfeffer, C.M. dan Singh, A.T.K., 2018. Apoptosis: A Target for Anticancer Therapy. *International Journal of Molecular Sciences*, **19**: 448.

Pingili, R., Vemulapalli, S., Mullapudi, S.S., Nuthakki, S., Pendyala, S., dan Kilaru, N., 2016. Pharmacokinetic interaction study between flavanones

UNIVERSITAS
GADJAH MADA
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

(hesperetin, naringenin) and rasagiline mesylate in wistar rats. *Drug Development and Industrial Pharmacy*, **42**: 1110–1117.

Porta, C., Paglino, C., dan Mosca, A., 2014. Targeting PI3K/Akt/mTOR Signaling in Cancer. *Frontiers in Oncology*, **4**: 64.

Pucci, B., Kasten, M., dan Giordano, A., 2000. Cell Cycle and Apoptosis. *Neoplasia*, **2**: 291–299.

Qi, F., Zhao, L., Zhou, A., Zhang, B., Li, A., Wang, Z., dkk., 2015. The advantages of using traditional Chinese medicine as an adjunctive therapy in the whole course of cancer treatment instead of only terminal stage of cancer. *BioScience Trends*, **9**: 16–34.

Qian, B.-Z. dan Pollard, J.W., 2010. Macrophage Diversity Enhances Tumor Progression and Metastasis. *Cell*, **141**: 39–51.

Rahmawaty, F., Allenidekania, A., dan Waluyanti, F.T., 2014. Sleep Disturbances and Fatigue in Adolescents with Cancer Receiving Chemotherapy. *Makara Journal of Health Research*, **18**: .

Ramesh, E. dan Alshatwi, A.A., 2013. Naringin induces death receptor and mitochondria-mediated apoptosis in human cervical cancer (SiHa) cells. *Food and Chemical Toxicology*, **51**: 97–105.

Rastogi, P., Anderson, S.J., Bear, H.D., Geyer, C.E., Kahlenberg, M.S., Robidoux, A., dkk., 2008. Preoperative Chemotherapy: Updates of National Surgical Adjuvant Breast and Bowel Project Protocols B-18 and B-27. *Journal of Clinical Oncology*, **26**: 778–785.

Rasul, M.G., 2018. Extraction, Isolation and Characterization of Natural Products from Medicinal Plants. *International Journal of Basic Sciences and Applied Computing (IJBSAC)*, 2394–367.

Rather, R.A. dan Bhagat, M., 2020. Quercetin as an innovative therapeutic tool for cancer chemoprevention: Molecular mechanisms and implications in human health. *Cancer Medicine*, **9**: 9181–9192.

Reczek, C.R. dan Chandel, N.S., 2017. The Two Faces of Reactive Oxygen Species in Cancer. *Annual Review of Cancer Biology*, **1**: 79–98.

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.

Reed, J.C., 2003. Apoptosis-targeted therapies for cancer. *Cancer Cell*, **3**: 17–22.

Riset Kesehatan Dasar, 2018. Hasil Utama Riset Kesehata Dasar (RISKESDAS). *Journal of Physics A: Mathematical and Theoretical*, **44**: 1–200.

Roberts, P.J. dan Der, C.J., 2007. Targeting the Raf-MEK-ERK mitogen-activated protein kinase cascade for the treatment of cancer. *Oncogene*, **26**: 3291–3310.

Ryan, C., Hesselgreaves, H., Wu, O., Paul, J., Dixon-Hughes, J., dan Moss, J.G., 2018. Protocol for a systematic review and thematic synthesis of patient experiences of central venous access devices in anti-cancer treatment. *Systematic Reviews*, **7**: 61.

Sabarinathan, D., Mahalakshmi, P., dan Vanisree, A.J., 2010. Naringenin promote

UNIVERSITAS
GADJAH MADA
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

apoptosis in cerebrally implanted C6 glioma cells. *Molecular and Cellular Biochemistry*, **345**: 215–222.

Sabarinathan, D., Mahalakshmi, P., dan Vanisree, A.J., 2011. Naringenin, a flavanone inhibits the proliferation of cerebrally implanted C6 glioma cells in rats. *Chemico-Biological Interactions*, **189**: 26–36.

Sabarinathan, D. dan Vanisree, A.J., 2013. Plausible role of naringenin against cerebrally implanted C6 glioma cells in rats. *Molecular and Cellular Biochemistry*, **375**: 171–178.

Saiprasad, G., Chitra, P., Manikandan, R., dan Sudhandiran, G., 2013. Hesperidin alleviates oxidative stress and downregulates the expressions of proliferative and inflammatory markers in azoxymethane-induced experimental colon carcinogenesis in mice. *Inflammation Research*, **62**: 425–440.

Salehi, B., Fokou, P., Sharifi-Rad, M., Zucca, P., Pezzani, R., Martins, N., dkk., 2019. The Therapeutic Potential of Naringenin: A Review of Clinical Trials. *Pharmaceuticals*, **12**: 11.

Samadzadeh, G.R., Rigi, T., dan Ganjali, A.R., 2013. Comparison of Four Search Engines and their efficacy With Emphasis on Literature Research in Addiction (Prevention and Treatment). *International Journal of High Risk Behaviors and Addiction*, **1**: .

Sambantham, S., Radha, M., Paramasivam, A., Anandan, B., Malathi, R., Chandra, S.R., dkk., 2013. Molecular Mechanism Underlying Hesperetin-induced Apoptosis by in silico Analysis and in Prostate Cancer PC-3 Cells. *Asian Pacific Journal of Cancer Prevention*, **14**: 4347–4352.

Santos-Sánchez, N.F., Salas-Coronado, R., Villanueva-Cañongo, C., dan Hernández-Carlos, B., 2019. Antioxidant Compounds and Their Antioxidant Mechanism, dalam: Shalaby, E. (Editor), *Antioxidants*. IntechOpen, London.

Saraste, A. dan Pulkki, K., 2000. Morphologic and biochemical hallmarks of apoptosis. *Cardiovascular Research*, **45**: 528–537.

Sayers, T.J., 2011. Targeting the extrinsic apoptosis signaling pathway for cancer therapy. *Cancer Immunology, Immunotherapy*, **60**: 1173–1180.

Sena, L.A. dan Chandel, N.S., 2012. Physiological Roles of Mitochondrial Reactive Oxygen Species. *Molecular Cell*, **48**: 158–167.

Sharma, K., Mahato, N., dan Lee, Y.R., 2019. Extraction, characterization and biological activity of citrus flavonoids. *Reviews in Chemical Engineering*, **35**: 265–284.

Shay, J.W. dan Wright, W.E., 2000. Hayflick, his limit, and cellular ageing. *Nature Reviews Molecular Cell Biology*, **1**: 72–76.

Shi, D., Xu, Y., Du, X., Chen, X., Zhang, X., Lou, J., dkk., 2015. Co-treatment of THP-1 cells with naringenin and curcumin induces cell cycle arrest and apoptosis via numerous pathways. *Molecular Medicine Reports*, **12**: 8223–8228.

Shi, G., Li, Dong, Fu, J., Sun, Y., Li, Y., Qu, R., dkk., 2015. Upregulation of cyclsooxygenase-2 is associated with activation of the alternative nuclear

Potensi Senyawa Flavanon pada Genus Citrus Sebagai Agen Penginduksi Apoptosis dan Penghambat
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

factor kappa B signaling pathway in colonic adenocarcinoma. *American Journal of Translational Research*, **7**: 1612–1620.

Shukla, R., Pandey, V., Vadnere, G.P., dan Lodhi, S., 2019. Role of Flavonoids in Management of Inflammatory Disorders, dalam: *Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases*. Elsevier, hal. 293–322.

Sood, S., Bansal, S., Muthuraman, A., Gill, N.S., dan Bali, M., 2009. Therapeutic Potential of Citrus medica L. Peel Extract in Carrageenan Induced Inflammatory Pain in Rat. *Research Journal of Medicinal Plant*, **3**: 123–133.

Stefova, M., Stafilov, T., dan Kulevanova, S., 2003. HPLC Analysis of Flavonoids, dalam: Cazes, J. (Editor), *Encyclopedia of Chromatography*. Marcel Dekker, Inc., New York, hal. 194–206.

Steward, B., 2004. Literature reviews in general. *British Journal of Occupational Therapy*, **67**: 495–500.

Stohs, S.J., Preuss, H.G., dan Shara, M., 2011. The Safety of Citrus aurantium (Bitter Orange) and its Primary Protoalkaloid p -Synephrine. *Phytotherapy Research*, **25**: 1421–1428.

Sukardja, I.D.G., 2000. *Onkologi Klinik Edisi 2*, Second. ed. Airlangga University Press, Surabaya.

Talmadge, J.E. dan Fidler, I.J., 2010. AACR centennial series: The biology of cancer metastasis: Historical perspective. *Cancer Research*, **70**: 5649–5669.

Testai, L. dan Calderone, V., 2017. Nutraceutical Value of Citrus Flavanones and Their Implications in Cardiovascular Disease. *Nutrients*, **9**: 502.

Tian, X., Li, Y., Shen, Y., Li, Q., Wang, Q., dan Feng, L., 2015. Apoptosis and inhibition of proliferation of cancer cells induced by cordycepin. *Oncology Letters*, **10**: 595–599.

Tober, M., 2011. PubMed, ScienceDirect, Scopus or Google Scholar - Which is the best search engine for an effective literature research in laser medicine? *Medical Laser Application*, **26**: 139–144.

Tsuchiya, K., Nakajima, S., Hosojima, S., Thi Nguyen, D., Hattori, T., Manh Le, T., dkk., 2019. Caspase-1 initiates apoptosis in the absence of gasdermin D. *Nature Communications*, **10**: 2091.

Valdespino-Gómez, V.M., Valdespino-Castillo, P.M., dan Valdespino-Castillo, V.E., 2015. Interacción de las vías de señalización intracelulares participantes en la proliferación celular: potencial blanco de intervencionismo terapéutico. *Cirugia y Cirujanos (English Edition)*, **83**: 165–174.

Vermeulen, K., Van Bockstaele, D.R., dan Berneman, Z.N., 2003. The cell cycle: A review of regulation, deregulation and therapeutic targets in cancer. *Cell Proliferation*, .

Veronesi, G., Pelosi, G., Sonzogni, A., Leon, M.E., D'Aiuto, M., Gasparri, R., dkk., 2005. Tumour CEA as predictor of better outcome in squamous cell carcinoma of the lung. *Lung Cancer*, **48**: 233–240.

UNIVERSITAS
GADJAH MADA
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

Wang, J. dan Yi, J., 2008. Cancer cell killing via ROS: To increase or decrease, that is a question. *Cancer Biology and Therapy*, **7**: 1875–1884.

Wang, L.-H., Wu, C.-F., Rajasekaran, N., dan Shin, Y.K., 2018. Loss of Tumor Suppressor Gene Function in Human Cancer: An Overview. *Cellular Physiology and Biochemistry*, **51**: 2647–2693.

Wang, R., Wang, J., Dong, T., Shen, J., Gao, X., dan Zhou, J., 2019. Naringenin has a chemoprotective effect in MDA-MB-231 breast cancer cells via inhibition of caspase-3 and -9 activities. *Oncology Letters*, **17**: 1217–1222.

Wang, Y., Yu, H., Zhang, J., Gao, J., Ge, X., dan Lou, G., 2015. Hesperidin inhibits HeLa cell proliferation through apoptosis mediated by endoplasmic reticulum stress pathways and cell cycle arrest. *BMC Cancer*, **15**: 682.

Wong, R.S.Y., 2011. Apoptosis in cancer: From pathogenesis to treatment. *Journal of Experimental and Clinical Cancer Research*, .

World Health Organization, 2018. 'Cancer', *http://www.who.int/*. URL: https://www.who.int/en/news-room/fact-sheets/detail/cancer (diakses tanggal 3/11/2020).

Xu, Z., Huang, B., Liu, J., Wu, X., Luo, N., Wang, X., dkk., 2018. Combinatorial anti-proliferative effects of tamoxifen and naringenin: The role of four estrogen receptor subtypes. *Toxicology*, **410**: 231–246.

Yang, N., Ray, S.D., dan Krafts, K., 2014. Cell Proliferation, dalam: *Encyclopedia of Toxicology*. Elsevier, hal. 761–765.

Yang, Y., Zhao, X.J., Pan, Y., dan Zhou, Z., 2016. Identification of the chemical compositions of Ponkan peel by ultra performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. *Analytical Methods*, **8**: 893–903.

Yi, L., Ma, S., dan Ren, D., 2017. Phytochemistry and bioactivity of Citrus flavonoids: a focus on antioxidant, anti-inflammatory, anticancer and cardiovascular protection activities. *Phytochemistry Reviews*, **16**: 479–511.

Yoshinaga, A., Kajiya, N., Oishi, K., Kamada, Y., Ikeda, A., Chigwechokha, P.K., dkk., 2016. NEU3 inhibitory effect of naringin suppresses cancer cell growth by attenuation of EGFR signaling through GM3 ganglioside accumulation. *European Journal of Pharmacology*, **782**: 21–29.

Zaugg, H., West, R.E., Tateishi, I., dan Randall, D.L., 2011. Mendeley: Creating communities of scholarly inquiry through research collaboration. *TechTrends*, **55**: 32–36.

Zeng, L., Zhen, Y., Chen, Y., Zou, L., Zhang, Y., Hu, F., dkk., 2014. Naringin inhibits growth and induces apoptosis by a mechanism dependent on reduced activation of NF-κB/COX-2-caspase-1 pathway in HeLa cervical cancer cells. *International Journal of Oncology*, **45**: 1929–1936.

Zhang, J., Song, J., Wu, D., Wang, J., dan Dong, W., 2015a. Hesperetin induces the apoptosis of hepatocellular carcinoma cells via mitochondrial pathway mediated by the increased intracellular reactive oxygen species, ATP and calcium. *Medical Oncology*, **32**: .

UNIVERSITAS
GADJAH MADA
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Universitas Gadjah Mada, 2021 | Diunduh dari http://etd.repository.ugm.ac.id/

Zhang, J., Wu, D., Vikash, Song, J., Wang, J., Yi, J., dkk., 2015b. Hesperetin Induces the Apoptosis of Gastric Cancer Cells via Activating Mitochondrial Pathway by Increasing Reactive Oxygen Species. *Digestive Diseases and Sciences*, **60**: 2985–2995.

Zhang, M.-F., Zhang, Z.-Y., Fu, J., Yang, Y.-F., dan Yun, J.-P., 2009. Correlation between expression of p53, p21/WAF1, and MDM2 proteins and their prognostic significance in primary hepatocellular carcinoma. *Journal of Translational Medicine*, **7**: 110.

Zhang, Q.W., Lin, L.G., dan Ye, W.C., 2018. Techniques for extraction and isolation of natural products: A comprehensive review. *Chinese Medicine (United Kingdom)*, **13**: 20.

Zhang, W. dan Liu, H.T., 2002. MAPK signal pathways in the regulation of cell proliferation in mammalian cells. *Cell Research*, **12**: 9–18.

Zhang, Y. dan Wang, X., 2020. Targeting the Wnt/β-catenin signaling pathway in cancer. *Journal of Hematology and Oncology*, .

Zou, Z., Xi, W., Hu, Y., Nie, C., dan Zhou, Z., 2016. Antioxidant activity of Citrus fruits. *Food Chemistry*, **196**: 885–896.