

DAFTAR PUSTAKA

- Abdel-Moneim, A., El-Twab, S. M. A., Yousef, A. I., Ashour, M. B., Reheim, E. S. A. dan Hamed, M. A. A., 2020, "New insights into the in vitro, in situ and in vivo antihyperglycemic mechanisms of gallic acid and p-coumaric acid", *Arch. Physiol. Biochem.*, 13, 1-7.
- Abdullah M., Virgus, Y., dan Khairurrijal, 2008, "Review: Sintesis Nanomaterial", *J. Nano Saintek.* 1(2), 33-57.
- Aboonabi, A., Rahmat, A., dan Othman, F., 2014, "Antioxidant effect of pomegranate against streptozotocin-nicotinamide generated oxidative stress induced diabetic rats", *Toxicol Rep.*, 1, 915-922.
- Abubakar A. R., Haque, M., "Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes". *J Pharm Bioallied Sci.*, 2020, 12(1), 1-10. doi: 10.4103/jpbs.JPBS_175_19
- Akbari-Alavijeh, S., Shaddel, R., dan Jafari, S. M., 2020, "Encapsulation of food bioactives and nutraceuticals by various chitosan-based nanocarriers", *Food Hydrocoll.*, 105(2020), 105774.
- Alfarabi, M., 2010, Kajian Antidiabetogenik Ekstrak Daun Sirih Merah (*Piper crocatum*) *In Vitro*, Thesis: Institut Pertanian Bogor.
- Amalan, V., Vijayakumar, N., Indumathi, D., dan Ramakrishnan, A., 2016 "Antidiabetic and antihyperlipidemic activity of p -coumaric acid in diabetic rats, role of pancreatic GLUT 2: In vivo approach", *Biomed Pharmacother.*, 84, 230-236.
- American Diabetes Association, 2020, "2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020", *Diabetes care*, 43, S14-S31.
- Andrews, G. P., Laverty, T. P., dan Jones, D. S., 2009, "Mucoadhesive polymeric platforms for controlled drug delivery", *Eur. J. Pharm. Biopharm.*, 71(3), 505-518.
- Asmat, U., Abad, K., dan Ismail, K., 2016, "Diabetes mellitus and oxidative stress—A concise review", *Saudi Pharm. J.*, 24(5), 547-553.
- Astuti, I. P. dan Esti, M., 2011, "Karakteristik morfologi daun sirih merah: *Piper crocatum* Ruitz & Pav dan *Piper porphyrophyllum* N.E.Br. koleksi Kebun Raya Bogor". *Berk. Penel. Hayati*, 7(A), 83-85.
- Astuti, I.P., Munawaroh, E., Rahayu, E. M. D., Aprilianti, P., dan Sumanto., 2011, "Heteroblastic Development in Six Species of Wild Piper: *Piper baccatum* Blume, *Piper firmum* Blume, *Piper majusculum* C.DC, *Piper miniatum* Blume, *Piper crocatum* Ruiz & Pav. and *Piper retrofractum* Vahl.1", *Ber. Biol.*, 10(5), 621-625.
- Azmir, J., Zaidul, I. S. M., Rahman, M. M., Sharif, K. M., Mohamed, A., Sahena, F., Jahurul, M. H. A., Ghafoor, K., Norulaini, N. A. N., dan Omar, A. K. M., 2013, "Techniques for extraction of bioactive compounds from plant materials: A review", *J. Food Eng.*, 117(4), 426-436.
- Azwanida, N. N., 2015, "A Review on the Extraction Methods Use in Medicinal

- Plants, Principle, Strength and Limitation”, *Medicinal Aromat. Plants*, 04 (03), 196.
- Bacha, W.J. dan Bacha, L.M., 2012, *Color Atlas of Veterinary Histology 3rd ed.*, West Sussex: John Wiley & Sons, Ltd.
- Baynest, H. W., 2015, “Classification, Pathophysiology, Diagnosis and Management of Diabetes Mellitus”, *J. Diabetes Metab.*, 06, 541.
- Boland, B. B., Rhodes, C. J., dan Grimsby, J. S., 2017, “The dynamic plasticity of insulin production in β -cells. *Mol. Metab.*, 6(9), 958–973.
- BPOM, 2005, Peraturan Kepala Badan Pengawas Obat dan Makanan Tentang Pedoman Uji Bioekivalensi, Jakarta: BPOM, Nomor: HK .00.05.3.1818.
- Brahmachari, G., 2011, *Bio-flavonoids with promising anti-diabetic potentials: A critical survey*, dalam Opportunity, Challenge and Scope of Natural Products in Medicinal Chemistry, diedit oleh Tiwari, V. K. dan Mishra, B. B., Kerala: Research Signpost, 187–212.
- Burgos-Morón, E., Z. Abad-Jiménez, A. Martínez de Marañón, F. Iannantuoni, I. Escribano-López, López-Domènech, S., Salom, C., Jover, A., Mora, V., Roldan, I., Solá, E., Rocha, M., dan Víctor, V. M., 2019, “Relationship between Oxidative Stress, ER Stress, and Inflammation in Type 2 Diabetes: The Battle Continues”. *J. Clin. Med.* 8(9) 1385.
- Butkowski, E., 2020, “Oxidative stress markers in diabetes”, dalam *Diabetes: Oxidative Stress and Dietary Antioxidants 2nd ed.*, Diedit oleh Preedy, V. R., London: Academic press, 3-11.
- Cerf, M. E., 2013, “Beta cell dysfunction and insulin resistance”, *Front. Endocrinol. (Lausanne)*, 4, 1–12.
- Chatterjee, S., Khunti, K., dan Davies, MJ., 2017, “Type 2 diabetes”, *Lancet.* 389, 2239–2251.
- Chen, G., Roy, I., Yang, C., dan Prasad, P. N., 2016, “Nanochemistry and Nanomedicine for Nanoparticle-based Diagnostics and Therapy,” *Chem. Rev.*, 116(5), 2826–2885.
- Coskun, O., Kanter, M., Korkmaz, A., dan Oter, S., 2005, “Quercetin, a flavonoid antioxidant, prevents and protects streptozotocin-induced oxidative stress and β -cell damage in rat pancreas”, *Pharmacol. Res.*, 51(2), 117–123.
- Dahlan, M. S., 2008, Statistik untuk kedokteran dan kesehatan: deskriptif, bivariat dan multivariat, dilengkapi dengan menggunakan SPSS, Jakarta: Salemba Medika.
- Dai, J. dan Mumper, R. J., 2010, “Plant Phenolics: Extraction, Analysis and Their Antioxidant and Anticancer Properties”, *Molecules*, 15(10), 7313-7352
- Dang, Y., Lin, G., Xie, Y., Duan, J., Ma, P., Li, G., dan Ji, G, 2014, “Quantitative Determination of Myricetin in Rat Plasma by Ultra Performance Liquid Chromatography Tandem Mass Spectrometry and its Absolute Bioavailability”, *Drug Res.*, 64(10), 516–522. doi:10.1055/s-0033-1363220
- De Jong, W. H., dan Borm, P. J. A., 2008, “Drug delivery and nanoparticles: Applications and hazards”, *Int. J. Nanomedicine.*, 3(2), 133–149.
- Del Prado-Audelo, M. L., Caballero-Florán, I. H., Sharifi-Rad, J., Mendoza-Muñoz, N., González-Torres, M., Urbán-Morlán, Z., Florán, B., Cortes, H., dan Leyva-Gómez, G., 2020, “Chitosan-decorated nanoparticles for drug delivery” *J.*

- Drug. Deliv. Sci. Technol.*, 59, 101896.
- Dewandari, K. T., 2013, Sintesis Nanopartikel Ekstrak Sirih Merah (*Piper crocatum*) dan Kajian Sistem Pengantarannya, Thesis: Institut Pertanian Bogor.
- Dewandari, K. T., Yuliani, S., dan Yasni, S., 2013, “Ekstarksi dan Karakterisasi Nanopartikel Ekstrak Sirih Merah (*Piper crocatum*)”, *J Pascapenen*, 10(2), 58–65.
- Dewi, S. R., Nugroho, W. A., Hendrawan, Y., dan Nisa, G. K., 2015, “Karakterisasi ekstrak etanol daun sirih merah (*piper crocatum*)”, *Prosiding Seminar Nasional PERTETA*, 338–347.
- Dizaj, S. M., Vazifehasl Zh., Salatin S., Adibkia Kh., dan Javadzadeh Y., 2015, “Nanosizing of drugs: Effect on dissolution rate”, *Res. Pharm. Sci.*, 10(2):95-108.
- Do, Q. D., Angkawijaya, A. E., Tran-Nguyen, P. L., Huynh, L. H., Soetaredjo, F. E., Ismadji, S., dan Ju, Y.-H., 2014, “Effect of extraction solvent on total phenol content, total flavonoid content, and antioxidant activity of *Limnophila aromatic*”, *J. Food Drug Anal.*, 22(3), 296–302.
- Drews, G., Krippeit-Drews, P., dan Duifer, M., 2010, “Oxidative stress and beta-cell dysfunction”, *Pflugers. Arch.*, 460(4), 703–718.
- Duncan, R., dan Gaspar, R. 2011, “Nanomedicine(s) under the microscope” *Mol. Pharm.*, 8(6), 2101–2141.
- Dzoyem, J. P., Kuete, V., dan Eloff, J. N., 2014, *Biochemical Parameters in Toxicological Studies in Africa: Significance, Principle of Methods, Data Interpretation, and Use in Plant Screenings*, dalam *Toxicological Survey of African Medicinal Plants*, diedit oleh Kuete, V., London: Elsevier Inc., 659-715.
- Emrizal, Fernando. A, Yuliandari, R., Rullaha, K., Indrayani, N. R., Susanty, A., Yerti, R., Ahmad, F., Sirat, H.M., dan Arbain, D., D., 2014, “Cytotoxic Activities of Fractions and Two Isolated Compounds from Sirih Merah (Indonesian red betel), *Piper Crocatum Ruiz & Pav.*”, *Procedia. Chem.*, 13, 79–84.
- Fadeel, B. dan Alexiou, C., 2020, “Brave new world revisited: Focus on nanomedicine” *Biochem Biophys. Res. Commun.*, 533(1), 36-49.
- Fatmawaty, Anggreni, N. G. M., Fadhil, N., dan Prasasty, V. D., 2019, “Potential in Vitro and in Vivo Antioxidant Activities from *Piper crocatum* and *Persea americana* Leaf Extracts”, *Biomed. Pharmacol. J.*, 12(2), 661–667. Doi: FDA, 2019, Bioavailability Studies Submitted in NDAs or INDs — General Considerations Guidance for Industry. <https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>
- Flohé, L., Toppo, S., Cozza, G., & Ursini, F., 2011, “A Comparison of Thiyl Peroxidase Mechanisms”, *Antioxid. Redox Signal.*, 15(3), 763–780. doi:10.1089/ars.2010.3397
- Gage, G. J., Kipke, D. R., dan Shain, W., 2012, “Whole Animal Perfusion Fixation for Rodents”, *J. Vis. Exp.*, (65), e3564.
- Gandhi, G. R., Jothi, G., Antony, P. J., Balakrishna, K., Paulraj, M. G., Ignacimuthu, S., Stalin, A., Al-Dhabi, N. A., 2014, “Gallic acid attenuates

- high-fat diet fed-streptozotocin-induced insulin resistance via partial agonism of PPAR γ in experimental type 2 diabetic rats and enhances glucose uptake through translocation and activation of GLUT4 in PI3K/p-Akt signaling pathway”, *Eur. J. Pharmacol.*, 745, 201–216.
- Ghasemi, A., Khalifi, S., dan Jedi S., 2014, “Streptozotocin-nicotinamide-induced rat model of type 2 diabetes”, *Acta. Physiol. Hung.*, 101(4), 408–420.
- Ghorbani, A., Rashidi, R. dan Shafiee-Nick, R., 2019, “Flavonoids for preserving pancreatic beta cell survival and function: A mechanistic review”, *Biomed. Pharmacother.*, 111, 947–957.
- Giri, T. K., 2016, *Nanoarchitected Polysaccharide-Based Drug Carrier for Ocular Therapeutics*, dalam *Nanoarchitectonics for Smart Delivery and Drug Targeting*, diedit Holban, A. M. dan Grumezescu, A. M., Oxford: Elsevier Inc., 119-141.
- Gonzalez, L. L., Garrie, K., dan Turner, M. D., 2018, “Type 2 diabetes – An autoinflammatory disease driven by metabolic stress”, *Biochim Biophys Acta Mol Basis Dis BBA*, 1864(11), 3805-3823.
- Grotto, D., Santa Maria, L., Valentini, J., Paniz, C., Schmitt, G., Garcia, S. C., Pomblum, V.J., Rocha, J. B. T., Farina, M., 2009, “Importance of the lipid peroxidation biomarkers and methodological aspects for malondialdehyde quantification”, *Quím. nova*, 32(1), 169–174.
- Guillausseau, P.-J., Meas, T., Virallya, M., M, L.-M., Médeau, V., dan Kevorkian, J.-P., 2008, “Abnormalities in insulin secretion in type 2 diabetes mellitus”, *Diabetes Metab.*, 34, S43–S48.
- Handayani, W., Rudijanto, A., dan Indra, M. R., 2009, “Soybean Milk Reduces Insulin Resistant in *Rattus norvegicus* of Type 2 Model Diabetes Mellitus”, *Jurnal Kedokteran Brawijaya*, XXV(2), 60–66.
- Honka, M.-J., Latva-Rasku, A., Bucci, M., Virtanen, K. A., Hannukainen, J. C., Kalliokoski, K. K., dan Nuutila, P., 2018, “Insulin-stimulated glucose uptake in skeletal muscle, adipose tissue and liver: a positron emission tomography study”, *Eur. J. Endocrinol.*, 178(5), 523–531. Doi: doi:10.1530/eje-17-0882
- Hsu, L. W., Lee, P. L., Chen, C. T., Mi, F. L., Juang, J. H., Hwang, S. M., dan Ho, Y.C., “Sung HW. Elucidating the signaling mechanism of an epithelial tight-junction opening induced by chitosan”, *Biomaterials*, 33(26), 6254-6263.
- Husna, F., Suyatna, F. D., Arozal, W., dan Purwaningsih, E. H., 2019, “Model Hewan Coba pada Penelitian Diabetes” *Pharmaceutical Sciences and Research*, 6(3), 131–141.
- International Diabetes Federation, 2019, *IDF Diabetes Atlas*, 9th ed (internet), Diambil dari <https://www.diabetesatlas.org/data/en/country/94/id.html>
- Ito, F., Sono, Y., dan Ito, T., 2019, “Measurement and Clinical Significance of Lipid Peroxidation as a Biomarker of Oxidative Stress: Oxidative Stress in Diabetes, Atherosclerosis, and Chronic Inflammation”, *Antioxidants*, 8(3), 72. Doi: doi:10.3390/antiox8030072
- Jewell, J. L., Oh, E., dan Thurmond, D. C., 2010, “Exocytosis mechanisms underlying insulin release and glucose uptake: conserved roles for Munc18c and syntaxin 4”, *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 298(3), R517–R531.

- Jusup, S. A., 2016, "Antidiabetic and Antioxidant Activities of 70% Ethanol-Diluted Extract of Piper Crocatum Leaves in Streptozotocin Induced Diabetic Rats", *Jurnal Kedokteran Brawijaya*, 29(1), 1–4.
- Kade, I. J., Ogunbolude, Y., Kamdem, J. P., Rocha, J. B. T., 2014, "Influence of gallic acid on oxidative stress-linked streptozotocin-induced pancreatic dysfunction in diabetic rats", *J. Basic Clin. Physiol. Pharmacol.*, 25(1), 35–45.
- Kaku, K., 2010, "Pathophysiology of Type 2 Diabetes and Its Treatment Policy", *JMAJ*, 53(1), 41–46.
- Kamaruzaman, S. R. S., Kasim, K. F. and Jaafar, M. N., 2020, "The Effect of Harvesting Time on the Antioxidant and Antidiabetic Activity of *Piper Crocatum* (Sirih Merah) Extract", *IOP Conf. Ser.: Mater. Sci. Eng.* 864. Doi: doi:10.1088/1757-899X/864/1/01221
- Karunakaran, U., Park, S. J., Jun, D. Y., Sim, T., Park, K. G., Kim, M. O., dan Lee, I. K., 2015, "Non-receptor tyrosine kinase inhibitors enhances β -cell survival by suppressing the PKC δ signal transduction pathway in streptozotocin-induced β -cell apoptosis," *Cell. Signal.*, 27(6), 1066–1074.
- Kaur, N., Fernandez, R., dan Sim, J., 2017, "Effect of Aloe vera on glycemic outcomes in patients with diabetes mellitus: a systematic review protocol", *JBI Database System Rev. Implement. Rep.*, 15(9), 2300–2306.
- Kelly, S. D., dan Neary, S. L., 2020, "Ominous Octet and Other Scary Diabetes Stories: The Overview of Pathophysiology of Type 2 Diabetes Mellitus", *Physician. Assist. Clin.*, 5(2020), 121–133.
- Kementerian Kesehatan RI., 2019, *Hari Diabetes Sedunia Tahun 2018*, dalam Pusat Data dan Informasi Kementerian Kesehatan RI. Jakarta: Kementerian Kesehatan RI.
- Khalil, N. M., Nascimento, T. C. F. do, Casa, D. M., Dalmolin, L. F., Mattos, A. C. de, Hoss, I., Romano, M. A., Mainardes, R. M., 2013, "Pharmacokinetics of curcumin-loaded PLGA and PLGA-PEG blend nanoparticles after oral administration in rats", *Colloids Surf. B*, 101, 353–360.
- Kishore, L., Anu K, Navpreet K., 2017, "Role of Nicotinamide in Streptozotocin Induced Diabetes in Animal Models", *J. Endocrinol. Thyroid. Res.* 2(1): 555577.
- Lalitha, N., Sadashivaiah B., Ramaprasad T. R., Singh S.A., 2020, "Anti-hyperglycemic activity of myricetin, through inhibition of DPP-4 and enhanced GLP-1 levels, is attenuated by co-ingestion with lectin-rich protein", *PLoS One*, 15(4): e0231543.
- Lawlor, N., Khetan, S., Ucar, D., dan Stitzel, M. L., 2017, "Genomics of Islet (Dys)function and Type 2 Diabetes", *Trends. Genet.*, 33(4), 244–255. Doi:
- Lee, J. S., Kim, Y. R., Song, I. G., Ha, S.-J., Kim, Y. E., Baek, N.-I., dan Hong, E. K., 2014, "Cyanidin-3-glucoside isolated from mulberry fruit protects pancreatic β -cells against oxidative stress-induced apoptosis", *Int. J. Mol. Med.*, 35(2), 405–412.
- Li, Y., Zheng, X., Yi, X., Liu, C., Kong, D., Zhang, J., dan Gong, M., 2017, "Myricetin: a potent approach for the treatment of type 2 diabetes as a natural class B GPCR agonist", *FASEB J.*, 31(6), 2603–2611.
- Liang, J., Yan, H., Puligundla, P., Gao, X., Zhou, Y., and Wan, X., 2017,

- “Applications of chitosan nanoparticles to enhance absorption and bioavailability of tea polyphenols: A review”, *Food Hydrocoll.*, 69, 286-292.
- Liguori, I., G Russo, F Curcio, G Bulli, L Aran, D Della-Morte, G Gargiulo, G Testa, F Cacciatore, D Bonaduce, and P Abete, “2018, “Oxidative stress, aging, and diseases”, *Clin. Interv. Aging*, 13: 757-772. doi: 10.2147/CIA.S158513
- Lister, I. N. E., Ginting, C. N., Girsang, E., Armansyah, A., Marpaung, H. H., Sinaga, A. P. F., Handayani, Rr. A. S., dan Rizal, R., 2019, “Antioxidant properties of red betel (*Piper crocatum*) leaf extract and its compounds”, *J. Nat. Remedies*, 19(4), 198–205.
- Lubos, E., Loscalzo, J., dan Handy, D. E., 2011, “Glutathione peroxidase-1 in health and disease: from molecular mechanisms to therapeutic opportunities”, *Antioxid. Redox Signal.*, 15(7), 1957-1997.
- Manohar, S. M., Vaikasuvu, S. R., Deepthi, K., Sachan, A., dan Narasimha, S. R. P. V. L., 2013, “An association of hyperglycemia with plasma malondialdehyde and atherogenic lipid risk factors in newly diagnosed Type 2 diabetic patients”, *Res. J. Med. Sci.*, 18(2), 89–93.
- Marchetti, P., Suleiman, M., De Luca, C., Baronti, W., Bosi, E., dan Marselli, L., 2020, “A direct look at the dysfunction and pathology of the β cells in human type 2 diabetes”, *Semin. Cell Dev. Biol.*, 103, 83-93.
- Martien, R., K Irianto, I. D., Farida, V., dan Purwita Sari, D., 2012, “Perkembangan Teknologi Nanopartikel Sebagai Sistem Penghantaran Obat”, *Majalah Farmaseutik*, 8(1), 133–144.
- McClements, D. J., 2020, “Advances in nanoparticle and microparticle delivery systems for increasing the dispersibility, stability, and bioactivity of phytochemicals”, *Biotechnol. Adv.*, 38(July 2018), 107287.
- Mi, F. L., Wu, Y. Y., Lin, Y. H., Sonaje, K., Ho, Y. C., Chen, C. T., Juang, J. H., Sung, H. W., 2008, “Oral delivery of peptide drugs using nanoparticles self-assembled by poly (γ -glutamic acid) and a chitosan derivative functionalized by trimethylation”, *Bioconjug Chem.*, 19(6), 1248–1255.
- Missaoui, S., Ben Rhouma, K., Yacoubi, M.-T., Sakly, M., dan Tebourbi, O., 2014, “Vanadyl Sulfate Treatment Stimulates Proliferation and Regeneration of Beta Cells in Pancreatic Islets”, *J. Diabetes Res.*, Article ID 540242, 7 pages. doi:10.1155/2014/540242
- Mohanraj, V. J. dan Chen, Y., 2006, “Nanoparticles - A review”, *Trop. J. Pharm. Res.*, 5(1), 561–573.
- Mulianto, N., 2020, “Malondialdehid sebagai Penanda Stres Oksidatif pada Berbagai Penyakit Kulit”, *Cdk-28*, 47(1), 39-44.
- Müller, T.D., Finan, B., Bloom, S.R., D'Alessio, D., Drucker, D.J., Flatt, P.R., Fritsche, A., Gribble, F., Grill, H.J., Habener, J.F., Holst, J.J., Langhans, W., Meier, J.J., Nauck, M.A., Perez-Tilve, D., Pocai, A., Reimann, F., Sandoval, D.A., Schwartz, T.W., Seeley, R.J., Stemmer, K., Tang-Christensen, M., Woods, S.C., DiMarchi, R.D., Tschöp, M.H., 2019, “Glucagon-like peptide 1 (GLP-1)”, *Mol. Metab.*, 30: 72-130.
- Ormazabal, V., Nair, S., Elfeky, O., Aguayo, C., Salomon, C., dan Zuñiga, F. A., 2018, “Association between insulin resistance and the development of

- cardiovascular disease”, *Cardiovasc. Diabetol.* 17, 122.
- Oroojan, A. A., (2020)., “Eugenol Improves Insulin Secretion and Content of Pancreatic Islets from Male Mouse”, *Int. J. Endocrinol.*, 2020, 1–5.
- Oroojan, A. A., Chenani, N., dan An’aam, M., 2020, “Antioxidant Effects of Eugenol on Oxidative Stress Induced by Hydrogen Peroxide in Islets of *Langerhans* Isolated from Male Mouse”, *Int. J. Hepatol.*, 20, 1-5.
- Paget, G. E., dan Barnes, J. M. 1964. *Toxicity Test*, dalam *Evaluation of Drug Activities: Pharmacometrics*, volume 1, diedit oleh Laurence D. dan Bacharach A., London and New York: Academic Press, 135–166.
- Panwar, R., Raghuwanshi, N., Srivastava, A. K., Sharma, A. K., dan Pruthi, V., 2018, “In-vivo sustained release of nanoencapsulated ferulic acid and its impact in induced diabetes” *Mater. Sci. Eng. C*, 92, 381-392.
- Parfati, N., dan Windono, T., 2016, “Sirih Merah (*Piper crocatum* Ruiz & Pav.) Kajian Pustaka Aspek Botani, Kandungan Kimia, dan Aktivitas Farmakologi”, *Media Pharmaceutica Indonesiana*, 1(2), 106–115.
- Pedroso-Santana, S. dan Fleitas-Salazar, N., 2020, “Ionotropic gelation method in the synthesis of nanoparticles/microparticles for biomedical purposes”, *Polym. Int.*, 69(5), 443–447.
- Poitout, V., dan Robertson, R. P., 2008, “Glucolipotoxicity: Fuel excess and β -cell dysfunction”, *Endocr. Rev.*, 29(3), 351–366.
- Prayitno, S. A., Kusnadi, J., dan Murtini, E. S., 2016, “Antioxidant Activity of Red Betel Leaves Extract (*Piper crocatum* Ruiz & Pav.) By Difference Concentration of Solvents”, *RJPBCS*, 7(5), 1836-1843.
- Putra, R.J.S., Achmad, A., dan P Rachma., H., 2017, “Kejadian Efek Samping Potensial Terapi Obat Anti Diabetes Pada Pasien Diabetes Mellitus Berdasarkan Algoritme Naranjo” *PJI*, 2(2), 45-50.
- Rahier, J., Guiot, Y., R. M. Goebbels, R. M., Sempoux1, C., dan Henquin, J. C., 2008, “Pancreatic b-cell mass in European subjects with type 2 diabetes”, *Diabetes Obes. Metab.*, 10 (Suppl. 4), 32-42s.
- Rains, J. L. dan Jain, S. K. 2011. Oxidative stress, insulin signaling, and diabetes. *Free Radic. Biol. Med.*, 50(5), 567–575.
- Ramadhan, S., Iswari, R. S., dan Marianti, A., 2019, “Pengaruh Ekstrak Daun Sirih Merah (*Piper crocatum* Ruiz & Pav.) terhadap Kadar Glukosa Darah dan Kadar Glutation Peroksidase Tikus Jantan Hiperglikemik”, *Biotropika: Journal of Tropical Biology*, 7(1), 1–10.
- Rangkuti, S. N., Lubis, L. S., dan Karsono, 2018, “Uji Efektivitas Nanopartikel Daun Sirih Merah (*Piper crocatum* Ruiz & Pav.) Sebagai Penurun Kadar Kolesterol Serum Darah marmot (*Cavia cobaya*)”, *Farmagazine*, 10(1), 31-39.
- Raza H., dan John A., 2012, “Streptozotocin-Induced Cytotoxicity, Oxidative Stress and Mitochondrial Dysfunction in Human Hepatoma HepG2 Cells”, *Int. J. Mol. Sci.*, 13(5), 5751-5767.
- Rehman, K., dan Akash, M. S. H., 2017, “Mechanism of Generation of Oxidative Stress and Pathophysiology of Type 2 Diabetes Mellitus: How Are They Interlinked?”, *J. Cell. Biochem.*, 118(11), 3577–3585.
- Riami, R., Sudiana, I. K., dan Purwanto, B., 2019, “The effect of red betel leaves (*Piper crocatum* Ruiz and Pav.) on blood sugar and insulin expression levels

- in rat (*Rattus norvegicus domesticus*) models of diabetes mellitus”, *Drug Invent. Today*, 11(3), 553–557.
- Rostami, E., 2020, “Progresses in targeted drug delivery systems using chitosan nanoparticles in cancer therapy: A mini-review”, *J Drug Deliv Sci Technol*, 58(2020), 101813.
- Safithri, M. dan Fahma, F., 2008, “Potency of Piper crocatum Decoction as an Antihyperglycemia in Rat Strain Sprague dawley” *Hayati*, 15(1), 45–48.
- Sameermahmood, Z., Raji, L., Saravanan, T., Vaidya, A., Mohan, V., dan Balasubramanyam, M., 2009, “Gallic acid protects RINm5F β -cells from glucolipotoxicity by its antiapoptotic and insulin-secretagogue actions”, *Phytother. Res.*, 24(S1), S83–S94.
- Saputra, N. T., Suartha, I. N., dan Dharmayudha, A. A. G. O., 2018, “Agen Diabetagonik Streptozotocin untuk Membuat Tikus Putih Jantan Diabetes Mellitus”, *Bul. Vet. Udayana (Online)*, 10(2), 116-121.
- Schmeltz, L. dan Metzger, B., 2007, *Diabetes/syndrome X*, dalam *Comprehensive Medicinal Chemistry II*, Vol. 6, diedit oleh Taylor, J. B. dan Triggler, D. J., London: Elsevier Ltd., 417–458.
- Sena, C. M., Leandro, A., Azul, L., Seica, R., dan Perry, P., 2018, “Vascular Oxidative Stress: Impact and Therapeutic Approaches” *Front. Physiol.*, 9, 1668.
- Shariatnia, Z., 2019, “Pharmaceutical applications of chitosan”, *Adv. Colloid Interface Sci.*, 263, 131–194.
- Sharkawy, A., Barreiro, M. F., dan Rodrigues, A. E., 2020, “Chitosan-based Pickering emulsions and their applications: A review”, *Carbohydr. Polym.*, 250, 116885.
- Shrestha, J.T.M., Shrestha, H., Prajapati, M., Karkee, A., dan Maharjan, A., “2017. Adverse Effects of Oral Hypoglycemic Agents and Adherence to them among Patients with Type 2 Diabetes Mellitus in Nepal”, *J. Lumbini. Med. Coll.*, 5(1), 34-40.
- Singh, Z., Karthigesu, I. P. P. S., dan Kaur, R., 2015, “Use of malondialdehyde as a biomarker for assessing oxidative stress in different disease pathologies: A review”, *Iran. J. Public Health*, 44(5), 714–715.
- Subandrate, 2016, “Hubungan Kadar Glukosa Darah dengan Peroksidasi Lipid pada Pasien Diabetes Melitus tipe 2”, *CDK-242*, 43(7), 487–489.
- Sundari, Zuprizal, Yuwanta, T., Martien, R., 2014, “Effect of Nanocapsule Level on Broiler Performance and Fat Deposition”, *Int. J. Poult. Sci.* 13(1), 31-35.
- Sung, H. W., Sonaje, K., Liao Z. X., Hsu, L. W., dan Chuang, E. Y., 2012, “pH-Responsive Nanoparticles Shelled with Chitosan for Oral Delivery of Insulin: From Mechanism to Therapeutic Applications”, *Acc. Chem. Res.* 45(4), 619-629.
- Suri, M. A., Azizah, Z., Asra, R., 2021, “A Review: Traditional Use, Phytochemical and Pharmacological Review of Red Betel Leaves (*Piper Crocatum Ruiz & Pav*)”, *AJPRD*, 9(1), 159-163.
- Szkudelski, T., 2012, “Streptozotocin-nicotinamide-induced diabetes in the rat. Characteristics of the experimental model”, *Exp. Biol. Med.*, 237(5), 481–490.

- Tan, J., Li, Y., Hou, D.-X., dan Wu, S., 2019, "The Effects and Mechanisms of Cyanidin-3-Glucoside and Its Phenolic Metabolites in Maintaining Intestinal Integrity", *Antioxidants*, 8(10), 479.
- Tangvarasittichai, S., 2015, "Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus", *World J. Diabetes.*, 6(3), 456.
- Thilakarathna, S. dan Rupasinghe, H., 2013, "Flavonoid Bioavailability and Attempts for Bioavailability Enhancement" *Nutrients*, 5(9), 3367-3387. doi:10.3390/nu5093367
- Tian, Y., Sun, Y., Wang, X., Kasparis, G., dan Mao, S., 2016, *Chitosan and its derivatives-based nano-formulations in drug delivery*, dalam *Nanobiomaterials in Drug Delivery: Applications of Nanobiomaterials*, diedit oleh Grumezescu, A. M., Oxford: William Andrew, 515-572.
- Tiwari, P., Kumar, B., Kaur G., Kaur, H., and Kaur, M., 2011, "Phytochemical Screening and Extraction: A review", *J. Int. Pharm. Sci.*, 1, 98-106.
- Tonahi, J.M.M., S. Nuryanti, dan Suherman., 2014, "Antioksidan Dari Daun Sirih Merah (*Piper crocatum*)", *J. Akademika Kim.* 3(3): 383-389,
- Tsikas, D., 2017, "Assessment of lipid peroxidation by measuring malondialdehyde (MDA) and relatives in biological samples: Analytical and biological challenges", *Anal. Biochem.*, 524, 13-30.
- Velavan, P., Karuppusamy, C., dan Venkatesan, P., 2015, "Nanoparticles as Drug Delivery Vehicles" *J. Pharm. Sci. & Res.*, 7(12), 1118-1122.
- Venkatakrisnan, K., Chiu, H. F., dan Wang, C. K., 2019, "Popular functional foods and herbs for the management of type-2-diabetes mellitus: A comprehensive review with special reference to clinical trials and its proposed mechanism" *J. Funct. Foods*, 57, 425-438.
- Vllasaliu, D., Exposito-Harris, R., Heras, A., Casettari, L., Garnett, M., Illum, L., dan Stolnik, S., 2010, "Tight junction modulation by chitosan nanoparticles: Comparison with chitosan solution", *Int. J. Pharm.*, 400(1-2), 183-193.
- Volpe, C. M. O., Villar-Delfino, P. H., Anjos, P. M. F. dos, dan Nogueira-machado, J. A., 2018, "Cellular death, reactive oxygen species (ROS) and diabetic complications" *Cell. Death. Dis.*, 9, 119.
- Wahjuningsih, S. B., Haslina H., Putranto A. T., dan Azkia M. N., 2020, "Effect of Sago Analogue Rice and Red Bean Diet to the Improvement of β -cell Pancreas in Streptozotocin-Nicotinamide (STZ-NA) Induced Diabetic Rats" *Curr. Res. Nutr. Food. Sci.* 8(2), 667-673.
- Wang, J. dan Wang H., 2017, "Oxidative Stress in Pancreatic Beta Cell Regeneration", *Oxid. Med. Cell Longev.*, Article ID 1930261, 1-9.
- Weiser, A., Feige, J.N., De Marchi, U., 2021, "Mitochondrial Calcium Signaling in Pancreatic β -Cell" *Int. J. Mol. Sci.*, 22 (5), 2515. Doi:
- Weiss, M., Steiner, D. F., dan Philipson, L. H., 2014, *Insulin Biosynthesis, Secretion, Structure, and Structure-Activity Relationships*, dalam *Endotext* (internet), diedit oleh Feingold K. R., South Dartmouth (MA).
- Weni, M., 2014, *Aktivitas Penghambatan Ekstrak Sirih Merah (*Piper crocatum*) terhadap Pembentukan Malondialdehida (MDA) dan Enzim Tirosinase*, Skripsi: Institut Pertanian Bogor.
- Weni, M., Safithri, M., dan Seno, D. S. H., 2020, "Molecular Docking of Active

- Compounds Piper crocatum on The Alpha-Glucosidase Enzyme as Antidiabetic”, *IJPST*, 7(2), 64-72.
- Widiyastuti, Y., Haryanti, S., dan Subositi, D., 2013, “Karakterisasi Morfologi dan Kandungan Minyak Atsiri Beberapa Jenis Sirih (*Piper* sp.) Morphological characterization and volatile oil contain of various (*Piper* sp.)”, *Jurnal Tumbuhan Obat Indonesia*, 6(2), 86–93.
- Wilcox, G., 2005, “Insulin and insulin resistance”, *Clin Biochem Rev*, 26, 19–39.
- Wuryastuti, H., Raharjo S., dan Warsito, R., 1996, *Peroxidation index: 17. methods of analysis and diagnostic value. research report*. Jakarta: Directorate Generale of Higher Education of Indonesia.
- Wysham, C. dan Shubrook J., 2020, “Beta-cell failure in type 2 diabetes: mechanisms, markers, and clinical implications”, *Postgrad., Med.*, 132(8), 676-686. Doi: 10.1080/00325481.2020.1771047
- Yahya, N. A., Attan, N., dan Wahab, R. A., 2018, “An overview of cosmeceutically relevant plant extracts and strategies for extraction of plant-based bioactive compounds”, *Food Bioprod. Process.*, 112, 69-85.
- Yeh, T. H., Hsu, L. W., Tseng, M. T., Lee, P. L., Sonjae K, Ho Y C, Sung H W., 2011, “Mechanism and consequence of chitosan-mediated reversible epithelial tight junction opening”, *Biomaterials*. 32(26), 6164-6173.
- Zeb, A., 2020, “Concept, mechanism, and applications of phenolic antioxidants in foods”, *J. Food Biochem.*, e13394.
- Zhao, J., Yang, J., dan Xie, Y. 2019., “Improvement strategies for the oral bioavailability of poorly water-soluble flavonoids: An overview” *Int. J. Pharm.*, 570, 118642.
- Zhou, Q. dan Melton, D. A., 2018., “Pancreas regeneration”, *Nature*, 557(7705), 351–358.