

DAFTAR PUSTAKA

- Afendi, F. M., Okada T., Yamazaki M., Morita A.H., Nakamura, Y., Nakamura, K., Ikeda, S., Takahashi, H., Altaf-UI-Amin, M., Darusman, L.K., Saito, K., dan Kanaya, S. 2012. KNApSACk Family Database: Integrated Metabolite-Plant Species Database for Multifaceted Plant Research. *Plant and Cell Physiol* 53(2): 1-12.
- Al Disi, S. S., Anwar M.A., dan Eid A.H. 2016. Anti-hypertensive herbs and their mechanisms of action: Part I. *Frontiers in Pharmacology* 6: 1–24.
- Anggraini, N., Prabowo, W.C., dan Kuncoro, H. 2020. Terapi Kombinasi Air Perasan Daging Buah Mengkudu (*Morinda citrifolia* L.) dan Mentimun (*Cucumis sativus* L.) untuk Menurunkan Tekanan Darah Pada Pasien Hipertensi. *Proceeding of Mulawarman Pharmaceuticals Conferences*. 11-12 Desember 2020. *Universitas Mulawarman*: 41-53.
- Atia, A., Abdullah, A., dan Alrawaiq, N. 2014. Overview of The Role of B2-Adrenergic Receptor Variants in Human Hypertension. *International Journal of PharmTech Research* 6(5): 1611-1615.
- Ayunda, M. N., Zulharmita, Azizah, Z., dan Rivai, H. 2020. Review of Phytochemical and Pharmacological Activities of Noni (*Morinda citrifolia* L.). *Scholars Academic Journal of Pharmacy* 9(12): 340–346.
- Azizah, A. R., Raharjo, A.M., Kusumastuti, I., Abrori, C., dan Wulandari, P. 2021. Analisis Faktor Risiko Kejadian Hipertensi di Puskesmas Karangtengah Kabupaten Wonogiri. *Journal of Agromedicine and Medical Sciences* 7(3): 142-146.
- Beck, T. C., Springs, K., Morningstar, J.E., Mills, C., Stoddard, A., Guo, L., Moore, K., Gensemer, C., Biggs, R., Petrucci, T., Kwon, J., Stayer, K., Koren, N., Dunne, J., Fulmer, D., Vohra, A., Mai, L., Dooley, S., Weninger, J., Peterson, Y., Woster, P., Dix, T.A., dan Norris, R.A. 2022. Application of Pharmacokinetic Prediction Platforms in the Design of Optimized Anti-Cancer Drugs. *Molecules* 27: 3678.
- Bouvard, C., Arcangelis, A.D., Dizier, B., Galy-Fauroux, I., Fischer, A.M., George-Labouesse, E., dan Helley, D. 2012. Tie2-dependent knockout of $\alpha 6$ integrin subunit in mice reduces post-ischaemic angiogenesis *Cardiovascular Research* 95: 39–47.

- Cao, Y. L., Lin, J. H., Hammes, H. P., dan Zhang, C. 2022. Flavonoids in Treatment of Chronic Kidney Disease. *Molecules* 27:2365.
- Chen, B., McConnell, K.J., Wale, N., Wild, D.J., dan Gifford, E.M. 2011. Comparing bioassay response and similarity ensemble approaches to probing protein pharmacology. *Bioinformatics* 27(21): 3044–3049.
- Chen, L., Zhu, T., Qi, J., Zhang, Y., dan Liu, H. 2021. Pharmacological mechanism of JiaWeiSiWu granule in the treatment of hypertension based on network pharmacology. *Annals of Palliative Medicine* 10(7): 7486-7513.
- Chirumbolo, S. 2012. Role of quercetin in vascular physiology. *Can. J. Physiol. Pharmacol.* 90: 1652–1657.
- Ciumarneau, L., Milaciu, M. V., Runcan, O., Vesaa, S. C., Rachisan, A. L., Negrean, V., Perne, M. G., Donca, V. I., Alexescu, T. G., Para, I., dan Dogaru, G. 2020. The Effects of Flavonoids in Cardiovascular Diseases. *Molecules* 25(18): 4320.
- Daina, A., Michielin, O., dan Zoete, V. 2019. SwissTargetPrediction: updated data and new features for efficient prediction of protein targets of small molecules. *Nucleic Acids Research* 47: W357–W364.
- De Hert, E., Bracke, A., Pintelon, I., Janssens, E., Lambeir, A.M., Van Der Veken, P., dan De Messter, I. 2021. Prolyl Carboxypeptidase Mediates the C-Terminal Cleavage of (Pyr)-Apelin-13 in Human Umbilical Vein and Aortic Endothelial Cells. *International Journal of Molecular Sciences* 22(13): 6698.
- Delacroix, S., Chokka, R.G., dan Worthley, S.G. 2014. Hypertension: Pathophysiology and Treatment. *Journal of Neurology & Neurophysiology* 5(6): 1-8.
- Diansyah, M. R., Kusuma, W.A., dan Annisa, A. 2021. Identifikasi protein signifikan pada interaksi protein-protein penyakit Alzheimer menggunakan algoritme top-k representative skyline query. *Jurnal Teknologi Dan Sistem Komputer* 9(3): 126–132.
- Dunkel, M., Gunther, S., Ahmed, J., Wittig, B., dan Preissner, R. 2008. SuperPred: drug classification and target prediction. *Nucleic Acids Research* 36: W55–W59.
- Fadhilla, S. N. dan Permana, D. 2020. The use of antihypertensive drugs in the treatment of essential hypertension at outpatient

- installations, Puskesmas Karang Rejo, Tarakan. *Yarsi Journal of Pharmacology* 1(1): 7-14.
- Feng, L., Chen, Y., Xu, K., Li, Y., Riaz, F., Lu, K., Chen, Q., Du, X., Wu, L., Cao, D., Li, C., Lu, S., dan Li, D. 2022. Cholesterol-induced leucine aminopeptidase 3 (LAP3) upregulation inhibits cell autophagy in pathogenesis of NAFLD. *Aging* 14(7): 3259-3275.
- Ferlito, M., Fulton, W.B., Zauher, A. M., Marban, E., Steenbergen, C., dan Lowenstein, C.J. 2010. VAMP-1, VAMP-2 and Syntaxin-4 Regulate ANP Release from Cardiac Myocytes. *J Mol Cell Cardiol* 49(5): 791–800.
- Flamant, M., Placier, S., Dubroca, C., Esposito, B., Lopes, I., Chatziantoniou, C., Tedgui, A., Dussaula, J.C., dan Lehoux, S. 2007. Role of Matrix Metalloproteinases in Early Hypertensive Vascular Remodeling. *Hypertension* 50(1): 212-218.
- Florensia, A. 2016. Evaluasi Penggunaan Obat Antihipertensi di Instalasi Rawat Inap RSUD Kota Tangerang dengan Metode Anatomical Therapeutic Chemical/Defined Daily Dose Pada Tahun 2015. *Skripsi*. Program Studi Farmasi UIN Syarif Hidayatullah Jakarta. Tangerang Selatan.
- Forrester, S. J., Elliott, K.J., Kawai, T., Obama, T., Boyer, M.J., Preston, K.J., Yan, Z., Eguchi, S., dan Rizzo, V. 2017. Caveolin-1 Deletion Prevents H Induced by Angiotensin II. *HHS Public Access* 69(1): 79-86.
- Fu, G., Batchelor, C., Dumontier, M., Hastings, J., Willighagen, E., dan Bolton, E. 2015. PubChemRDF: towards the semantic annotation of PubChem compound and substance databases. *Journal of Cheminformatics* 34(7): 1-15.
- Gao, S., Zhu, H., Zuo, X., dan Luo, H. 2018. Cathepsin G and its role in inflammation and autoimmune diseases. *Arch Rheumatol* 33(4):498-504.
- Gasser, S., Ablasser, K., Scherr, E., Rocssl, U., Lewinski, D.v., Mangge, H., Dellacher, A., Machler, H., TrantinaYates, A., Tschelicsnigg, K.H., dan Gasser, R. 2007. Quantification of GLUT4 Gene Expression in Human Atrial Myocardium of Hypertensive Patients and the Effect of Experimental Ischaemia Thereupon. *J Clin Basic Cardiol* 10.
- Ge, W., Hou, C., Zhang, W., Guo, X., Gao, P., Song, X., Gao, R., Liu, Y., Guo, W., Li, B., Zhao, H., dan Wang, J. 2021. Mep1a contributes to Ang II-induced cardiac remodeling by

- promoting cardiac hypertrophy, fibrosis and inflammation. *Journal of Molecular and Cellular Cardiology*. 152: 52-68.
- Gfeller, D., Grosdidier, A., Wirth, M., Daina, A., Michielin, O., dan Zoete, V. 2014. SwissTargetPrediction: a web server for target prediction of bioactive small molecules. *Nucleic Acids Research* 42: W32-W38.
- Ghatage, T., Goyal, S.G., Dhar, A., dan Bhat, A. 2021. Novel therapeutics for the treatment of hypertension and its associated complications: peptide- and nonpeptide-based strategies. *Hypertension Research* 44: 740–755).
- Graham, T. H. 2017. Prolylcarboxypeptidase (PrCP) inhibitors and the therapeutic uses thereof: a patent review. *Expert Opinion on Therapeutic Patents* 27(10): 1077-1088.
- Ha, J.M., Kim, Y.W., Lee, D.H., Yun, S.J., Kim, E.K., Jin, I.H., Kim, C.D., Shin, H.K., dan B, S.S. 2011. Regulation of arterial blood pressure by Akt1-dependent vascular relaxation. *J Mol Med* 89:1253–1260.
- Hariati, H., dan Ginting, D.S. 2021. Decrease Hypertension Through Giving Noni Fruit Juice. *Jurnal Penelitian Keperawatan Medik* 3(2): 53–58.
- Has, H. F., Azizah, N., dan Juliani. 2021. Formulasi Sediaan Serbuk Effervescent Ekstrak Buah Mengkudu Sebagai Antihipertensi. *Jurnal Herbal dan Farmakologis* 3(2): 102-109.
- Hasanah, A. 2018. Analisis Interaksi Senyawa Aktif Jahe (*Zingiber officinale*) yang Berpotensi Sebagai Antioksidan pada Stress Oksidasi yang Diinduksi Oleh Timbal (Pb^{2+}). *Skripsi*. Jurusan Biologi Fakultas Sains dan Teknologi Universitas Islam Negeri Maulana Malik Ibrahim. Malang.
- Hauke, M., Eckenstaler, R., Ripperger, A., Ender, A., Braun, H., dan Benndorf, R.A. 2022. Active RhoA Exerts an Inhibitory Effect on the Homeostasis and Angiogenic Capacity of Human Endothelial Cells. *Journal of the American Heart Association* 11(12): 1-20.
- Hidayat, R., Agnesia, Y., dan Safitri, Y. 2021. Faktor Risiko Hipertensi Pada Masyarakat di Desa Pulau Jambu UPTD Blud Kecamatan Kuok Kabupaten Kampar. *Jurnal Ners Universitas Pahlawan* 5(1): 8 – 19.
- Hoepfner, L.H., Sinha, S., Wang, Y., Bhattacharya, R., Dutta, S., Gong, X., Bedell, V.M., Suresh, S., Chun, C., Ramchandran, R., Ekker, S.C., dan Mukhoadhyay, D. 2015. RhoC maintains

- vascular homeostasis by regulating VEGF-induced signaling in endothelial cells. *Journal of Cell Science* 128(19): 3556-3568.
- Holidah, D. 2011. Aliskiren, Obat Antihipertensi Baru dengan Mekanisme Penghambat Renin. *J. Trop. Pharm. Chem.* 2011 1(3): 235–246.
- Inada, A. C., Figueiredo, P.S., Santos-Eichler, R.A.D., Freitas, K.C.de, Hiane, P.A., Castro, A.P.de., dan Guimaraes, R.C.A.de. 2017. *Morinda citrifolia* Linn. (Noni) and Its Potential in Obesity-Related Metabolic Dysfunction. *Nutrients* 9: 1-29.
- Istiningrum, R., Amin, M., dan Lestari, U. 2016. Prediksi Kandidat Protein Target Senyawa Alami Anti-Aging Scopoletin dari *Morinda Citrifolia* Secara in Silico. *Seminar Nasional Pendidikan dan Saintek 2016*: 193-196.
- Jackson, R.E., dan Bellamy, M.C. 2015. Antihypertensive drugs. *BJA Education* 15(6): 280–285.
- Janaszak-Jasiecka, A., Siekierzycka, A., Ploska, A., Dobrucki, I.T., dan Kalinowski, L. 2021. Endothelial Dysfunction Driven by Hypoxia—The Influence of Oxygen Deficiency on NO Bioavailability. *Biomolecules* 11(7): 982.
- Jensen, L.J., Kuhn, M., Stark, M., Chaffron, S., Creevey, C., Muller, J., Doerks, T., Julien, P., Roth, A., Simonovic, M., Bork, P., dan Mering, C.von. 2009. STRING 8—a global view on proteins and their functional interactions in 630 organisms. *Nucleic Acids Research* 37: D412–D416.
- Jiang, J., Qi, Y. X., Zhang, P., Gu, W. T., Yan, Z. Q., S, B. R., Yao, Q. P., Kong, H., Chien, S., dan Jiang, Z. L. 2013. Involvement of Rab28 in NF- κ B Nuclear Transport in Endothelial Cells. *Plos One* 8(2): e56076.
- Juhanson, P., Kepp, K., Org, E., Veldre, G., Kelgo, P., Rosenberg, M., Viigimaa, M., dan Laan, M. 2008. N-acetyltransferase 8, a positional candidate for blood pressure and renal regulation: resequencing, association and in silico study. *BMC Medical Genetics* 9: 25.
- Kanehisa, M., Furumichi, M., Tanabe, M., Sato, Y., dan Morishima, K. 2017. KEGG: new perspectives on genomes, pathways, diseases and drugs. *Nucleic Acids Research* 45: D353–D361.
- Karakurt, O., Cagirci, G., dan Eryasar, N.E. 2011. Gamma-glutamyl transferase activity increases in prehypertensive patients. *Turk J Med Sci* 41 (6): 975-980.

- Kawase, H., Bando, Y. K., Nishimura, K., Aoyama, M., Monji, A., dan Murohara, T. 2016. A dipeptidyl peptidase-4 inhibitor ameliorates hypertensive cardiac remodeling via angiotensin-II/sodium-proton pump exchanger-1 axis. *J Mol Cell Cardiol* 98: 37-47.
- Kelly-Robinson, G.A., Reihill, J.A., Lundy, F.T., McGarvey. L.P., Lockhart, J.C., Litherland, G.J., Thornbury, K.D., dan Martin, S.L. 2021. The Serpin Superfamily and Their Role in the Regulation and Dysfunction of Serine Protease Activity in COPD and Other Chronic Lung Diseases. *Int. J. Mol. Sci* 22(12): 6351.
- Khan, F. F. 2013. Role of Gata-4 Transcription Factor Associated with B-Type Natriuretic Peptides in Heart Failure. *Journal of Asian Scientific Research* 3(2): 204-213.
- Khotimah, H., dan Masnina, R. 2020. Hubungan Dukungan Keluarga dengan Tekanan Darah pada Lansia Penderita Hipertensi di Wilayah Kerja Puskesmas Air Putih Samarinda. *Borneo Student Research* 1(3): 1693-1704.
- Kim, S., Cheng, T., He, S., Thiessen, P.A., Li, Q., Gindulyte, A., dan Bolton, E.E. 2022. PubChem Protein, Gene, Pathway, and Taxonomy Data Collections: Bridging Biology and Chemistry through Target-Centric Views of PubChem Data. *Journal of Molecular Biology* 434(11): 167514.
- Klinke, A., Berghausen, E., Friedrichs, K., Molz, S., Lau, D., Remane, L., Berlin, M., Kaltwasser, C., Adam, M., Mehrkens, D., Mollenhauer, M., Manchanda, K., Ravekes, T., Heresi, G.A., Aytekin, M., Dweik, R.A., Hennigs, J.K., Kubala, L., Michaelsson, E., Rosenkranz, S., Rudolph, T. K., Hazen, S.L., Klose, H., Schermuly, R.T., Rudolph, V., dan Baldus, S. 2018. Myeloperoxidase aggravates pulmonary arterial hypertension by activation of vascular Rho-kinase. *JCI Insight* 3(11): e97530.
- Kostov, K. 2021. The Causal Relationship between Endothelin-1 and Hypertension: Focusing on Endothelial Dysfunction, Arterial Stiffness, Vascular Remodeling, and Blood Pressure Regulation. *Life* 11(9): 986.
- Krushkal, J., Xiong, M., Ferrell, R., Sing, C.F., Tumer, S.T., dan Boerwinkle, E. 1998. Linkage and association of adrenergic and dopamine receptor genes in the distal portion of the long arm of chromosome 5 with systolic blood pressure variation. *Human Molecular Genetics* 7(9): 1379–1383.

- Krzeminska, J., Wronka, M., Mlynarska, E., Franczyk, B., dan Rysz, J. 2022. Arterial Hypertension—Oxidative Stress and Inflammation. *Antioxidants* 11(1): 172.
- Lei, W., C, P., Yue, Y., He, Y., Shui, X., Li, G., Zhang, L., Huang, S., dan Chen, C. 2014. Subcellular distribution patterns and elevated expression of GNA11 and GNA14 proteins in the lungs of humans with pulmonary arterial hypertension. *Cell Biol Int* 38: 1041–1049.
- Lewicki, L., Siebert, J., Kolinski, T., Piekarska, K., Reiwer-Gostomska, M., Targonski, R., Trzonkowski, P., dan Marek-Trzonkowska, N. 2019. Mast cell derived carboxypeptidase A3 is decreased among patients with advanced coronary artery disease. *Cardiology Journal* 26(6): 680-686.
- Li, S., Wang, Y., Zeng, X., Zhang, Y., Wang, S., Liu Y., Xu, D., Lan, J., dan Hu, D. 2022. Common Variants in Neuraminidase Genes Contribute to Predisposition to and Progression of Chronic Heart Failure. *Hum Hered.*
- Li, W., Cui, N., Mazzuca, M.Q., Mata, K.M., dan Khalil, R.A. 2017. Increased vascular and uteroplacental matrix metalloproteinase-1 and -7 levels and collagen type I deposition in hypertension in pregnancy: role of TNF- α . *Am J Physiol Heart Circ Physiol* 313: H491–H507.
- Li, X.C., Shull, G.E., Miguel-Qin, E., dan Zhuo, J.L. 2015. Role of the Na/H exchanger 3 in angiotensin II-induced hypertension. *Physiol Genomics* 47: 479–487.
- Li, Y., Li, N., Yao, X., Heizati, M., Zhang, D., Zhu, Q., Chang, G., dan Zhang, X. 2016. Association Between Polymorphisms of ADRBK1 Gene and Plasma Renin Activity in Hypertensive Patients: A Case-Control Study. *Med Sci Monit* 22: 2981-2988.
- Liang, T., Gao, F., dan Chen, J. 2021. Role of PTEN-less in cardiac injury, hypertrophy and regeneration. *Cell Regeneration* 10: 25.
- Liu, Y., Sigman, J.A., Bruce, L.A., dan Wolfson, A.J. 2021. Thimet Oligopeptidase-A Classical Enzyme with New Function and New Form. *Immuno* 1: 332-346.
- Lu, H., Zhou, Q., He, J., Jiang, Z., Peng, C., Tong, R., dan Shi, J. 2020. Recent advances in the development of protein–protein interactions modulators: mechanisms and clinical trials. *Signal Transduction and Targeted Therapy* 5: 1–23.

- Luthfi, A. F. 2014. Farmakologi Balik dan Jejaring Untuk Pencarian Senyawa Aktif Dari Jamu Antihiperkolesterolemia. *Skripsi*. Departemen Kimia Fakultas Matematika dan Ilmu Pengetahuan Alam Institut Pertanian Bogor. Bogor.
- Maier, C., Schadock, I., Haber, P. K., Wysocki, J., Ye, M., Kanwar, Y., Flask, C. A., Yu, X., Hoit, B. D., Adams, G. N., Schmaier, A. H., Bader, M., dan Batle, D. 2017. Prolylcarboxypeptidase deficiency is associated with increased blood pressure, glomerular lesions, and cardiac dysfunction independent of altered circulating and cardiac angiotensin II. *J Mol Med* 95(5):473-486.
- Majumder, K., dan Wu, J. 2014. Molecular Targets of Antihypertensive Peptides: Understanding the Mechanisms of Action Based on the Pathophysiology of Hypertension. *International Journal of Molecular Sciences* 16(1): 256–283.
- Martinez, E., Calvier, L., Fernandez-Celis, A., Rousseau, E., Jurado-Lopez, R., Rossoni, L. V., Jaisse, F., Zannad, F., Rossignol, P., Cachofeiro, V., dan Lopez-Andres, N. 2015. Galectin-3 Blockade Inhibits Cardiac Inflammation and Fibrosis in Experimental Hyperaldosteronism and Hypertension. *American Heart Association* 66(4): 767 – 775.
- Mayr, F., Moller, G., Garscha, U., Fischer, J., Castano, P.R., Inderbinen, S.G., Temml, V., Waltenberger, B., Schwaiger, S., Hartmann, R.W., Gege, C., Martens, S., Odermatt, A., Pandey, A.V., Werz, O., Adamski, J., Stuppner, H., dan Schuster, D. 2020. Finding New Molecular Targets of Familiar Natural Products Using In Silico Target Prediction. *International Journal of Molecular Sciences* 21(19): 7102.
- Mendez, M., Gross, K. W., Glenn, S. T., Garvin, J. L., dan Carretero O. A. 2011. Vesicle-associated Membrane Protein-2 (VAMP2) Mediates cAMP-stimulated Renin Release in Mouse Juxtaglomerular Cells. *The Journal of Biological Chemistry* 286(32): 28608–28618.
- Meng, X., Ma, J., Kang, A.N., Kang, S.Y., Jung, H.W., dan Park, Y.K. 2020. A Novel Approach Based on Metabolomics Coupled with Intestinal Flora Analysis and Network Pharmacology to Explain the Mechanisms of Action of Bekhogainsam Decoction in the Improvement of Symptoms of Streptozotocin-Induced Diabetic Nephropathy in Mice. *Frontiers in Pharmacology* 11: 1-19.

- Miskiyah, R., dan Realita, F. 2021. Literatur Review: Efektivitas Buah Mengkudu (*Morinda Citrifolia* L.) Terhadap Penurunan Hipertensi. *Jurnal Kebidanan* 13(2): 128–242.
- Molla, M.D., Akalu, Y., Geto, Z., Dagnew, B., Ayelign, B., Shibabaw, T. 2020. Role of Caspase-1 in the Pathogenesis of Inflammatory-Associated Chronic Noncommunicable Diseases. *Journal of Inflammation Research* 13: 749–764.
- Ndrepepa, G., dan Kastrati. 2016. Gamma-glutamyl transferase and cardiovascular disease. *Ann Transl Med* 4(24):481.
- Nickel J. Gohlke B.O., Erehman, J., Banerjee, P., Rong, W.W., Goede, A., Dunkel, M., dan Preissner, R. 2014. SuperPred: update on drug classification and target prediction. *Nucleic Acids Research*, 12: 26–31.
- Nikitopoulou, I., Orfanos, S. E., Kotanidou, A., Maltabe, V., Manitsopoulos, N., Karras, P., Kouklis, P., Armaganidis, A., dan Maniatis, N. A. 2016. Vascular endothelial-cadherin downregulation as a feature of endothelial transdifferentiation in monocrotaline-induced pulmonary hypertension. *Am J Physiol Lung Cell Mol Physiol* 311: L352–L363.
- Niwano, K., Arai, M., Koitabashi, N., Hara, S., Watanabe, A., Sekiguchi, K., Tanaka, T., Iso, T., dan Kurabayashi, M. 2006. Competitive Binding of CREB and ATF2 to cAMP/ATF Responsive Element Regulates eNOS Gene Expression in Endothelial Cells. *American Heart Association* 26(5): 1036–1042.
- Nuraini, B. 2015. Risk Factors of Hypertension. *J Majority* 4(5): 10–19.
- Patil, P., Madkaikar, H., dan Shah, N. 2022. *Morinda citrifolia* L. (Noni) - Its Ethnobotanical Knowledge, Phytochemical Studies, Pharmacological Aspects, And Future Prospects. *International Journal of Novel Research and Development (IJNRD)* 7(3): 331–352.
- Putri, R.A., Muhammad, H.N., dan Sukandar, E.Y. 2021. Kajian Pustaka 27 Tanaman Indonesia dengan Aktivitas Antihipertensi. *Acta Pharmaceutica Indonesia*, 46(2): 23–32.
- Rachmania, S., Dewi, R., Helianti, D., dan Munawaroh, A. 2022. Ekstrak Etanol Kulit Bawang Merah (*Allium Cepa* L.) Menurunkan Kadar Advanced Oxidation Protein Product (AOPP) Plasma Pada Tikus Wistar Terpapar Diazinon. *Syntax Literate: Jurnal Ilmiah Indonesia* 7(10): 15608–15619.

- Raghavan, S., Brishti, M. A., dan Leo, M. D. 2022. Rab GTPases as Modulators of Vascular Function. *Cell* 11(19): 3061.
- Rahmi, A.S. 2018. Implementasi Hybrid Sampling Technique untuk Prediksi Interaksi Senyawa Aktif dan Protein pada Data yang Tidak Seimbang. *Skripsi*. Fakultas Matematika dan Ilmu Pengetahuan Alam Institut Pertanian Bogor. Bogor.
- Raina, R., Chauvin, A., Chakraborty, R., Nair, N., Shah, H., Krishna, V., dan Kusumi, K. 2020. The Role of Endothelin and Endothelin Antagonists in Chronic Kidney Disease. *Kidney Dis* 6:22–34.
- Rakib, A., Eva, T.A., Sami, S.A., Mitra, S., Nafiz, I.H., Das, A., Tareq, A.M., Nainu, F., Dhama, K., Emran, T.B., dan Simal-Gandara, J. 2021. Beta-Arrestins in the Treatment of Heart Failure Related to Hypertension: A Comprehensive Review. *Pharmaceutics* 13: 838.
- Ran, J., Li, H., Fu, J., Liu, L., Xing, Y., Li, X., Shen, H., Chen, Y., Jiang, X., Li, Y., dan Li, H. 2013. Construction and analysis of the protein-protein interaction network related to essential hypertension. *BMC Systems Biology* 2013, 7:32.
- Razali, K., Hamid, A.A.A., Zin, N.H.M., Bunnori, N.M., Yusof, H.A., Kamarudin, K.R., dan Rehan, A.M. 2020. In Silico Structural and Functional Annotation of Nine Essential Hypothetical Proteins from *Streptococcus pneumoniae*. *Indonesian Journal of Chemistry* 20(2): 336 – 347.
- Ren, M., Ng, F.L., Warren, H.R., Witkowska, K., Baron, M., Jia, Z., Cabrera, C., Zhang, R., Mifsud, B., Munroe, P.B., Xiao, Q., Townsend-Nicholson, A., Hobbs, A.J., Ye, S., dan Caulfield, M.J. 2018. The biological impact of blood pressure-associated genetic variants in the natriuretic peptide receptor C gene on human vascular smooth muscle. *Human Molecular Genetics* 27(1):199-210.
- Rifai, N.A.K., Afendi, F.M., dan Sumertajaya, I.M. 2017. Simultaneous clustering analysis with molecular docking in network pharmacology for type 2 antidiabetic compounds. *Indonesian Journal of Biotechnology* 22(1): 43-48.
- Roszkowska-Chojacka, M.M., Baranowska, I., Gawrys, O., Sadowski, J., Walkowska, A., Kalisz, M., Litwiniuk, A., dan Kompanowska-Jeziarska, E. 2021. Role of chymase in blood pressure control, plasma and tissue angiotensin II, renal Haemodynamics, and excretion in spontaneously hypertensive rats. *Clinical and Experimental Hypertension*.

- Sa'idah, D. 2018. Evaluasi Rasionalitas Penggunaan Obat Antihipertensi di Instalasi Rawat Jalan RSUD Dr. Soegiri Lamongan Periode Tahun 2017. *Skripsi*. Fakultas Kedokteran dan Ilmu Kesehatan Universitas Islam Negeri Maulana Malik Ibrahim. Malang.
- Safitri, A.R., dan Ismawati, R. 2018. Efektifitas Teh Buah Mengkudu dalam Menurunkan Tekanan Darah Lansia dengan Hipertensi (Studi di UPTD. Griya Werdha Kota Surabaya Tahun 2018). *Amerta Nutr*: 163-171.
- Saharani, S.M., Yuniastuti, A., Susanti, R., Nugrahaningsih, W.H. 2021. Identifikasi Senyawa Bioaktif Tanaman *Syzygium aromaticum* Sebagai Imunostimulan Melalui Toll-Like Receptor Signaling Pathway Berdasarkan Interaksi Senyawa-Protein Secara In Silico. *Prosiding Semnas Biologi ke-9 Tahun 2021* 310-316.
- Saminathan M., Rai, R.B., Dhama, K., Tiwari, R., Chakraborty, S., Amarpal, Ranganath, G.J., dan Kannan, K. 2013. Systematic Review on Anticancer Potential and other Health Beneficial Pharmacological Activities of Novel Medicinal Plant *Morinda citrifolia* (Noni). *International Journal of Pharmacology* 9(8): 462-492.
- Sari, C.Y. 2015. Penggunaan Buah Mengkudu (*Morinda citrifolia* L.) untuk Menurunkan Tekanan Darah Tinggi. *J Majority* 4(3): 34-40.
- Sari, I.K., Arisandi, M., Morika, H.D., dan Novrika, B. 2018. Pengaruh Pemberian Air Perasan Buah Mengkudu (*Morinda citrifolia*) Terhadap Penurunan Tekanan Darah Pada Penderita Hipertensi. *Scientia Journal* 7(2): 117–123.
- Schierwagen, R., Dietrich, P., Heinzen, J., Klein, S., Uschner, F.E., Ortiz, C., Tyc, O., Torres, S., Hieber, C., Kraus, N., Premont, R.T., Grunewald, L.D., Poisson, J., Rautou, P.E., Kristiansen, G., Gracia-Sancho, J., Poglitsch, M., Ludwig-Portugall, I., Walther, T., Trautwein, C., Abdullah, Z., Munch, C., Welsch, C., Fernandez, M., Zeuzem, S., Moreau, R., Hellerbrand, C., Rombouts, K., Kastenmuller, W., Diehl, A.M., dan Trebicka, J. 2021. Intercellular crosstalk regulating ARRB2/RARRES1 is involved in transition from fibrosis to cancer. *bioRxiv*.
- Schreier, B., Dohler, M., Rabe, S., Schneider, B., Schwerdt, G., Ruhs, S., Sibilia, M., Gotthardt, M., Gekle, M., dan Grossmann, C. 2011. Consequences of epidermal growth factor receptor (ErbB1) loss for vascular smooth muscle cells from mice with

- targeted deletion of ErbB1. *Arteriosclerosis, Thrombosis, and Vascular Biology* 31(7): 1643-1652.
- Serfozo, P., Wyasocki, J., Gulua, G., Schulze, A., Ye, M., Liu, P., Jin, J., Bader, M., Myohanen, T., Garcia-Horsman, A., dan Batle, D. 2021. Prolyl Oligopeptidase-Dependent Angiotensin II Conversion to Angiotensin-(1-7) in the circulation. *Hypertension* 75(1): 173–182.
- Shu, Z., Wan, J., Read, R.J., Carrell, R.W., dan Zhou, A. 2021. Angiotensinogen and the Modulation of Blood Pressure. *Frontiers in Cardiovascular Medicine* 8.
- Silva, R.A.P., Chu, Y., Miller, J.D., Mitchell, I.J., Penninger, J.M., Faraci, F.M., dan Heistad, D.D. 2012. Impact of Ace2 Deficiency and Oxidative Stress on Cerebrovascular Function with Aging. *NIH Public Access* 43(12): 3358–3363.
- Sina, H., Dramane, G., Tchekounou, P., Assogba, M.F., Chabi-Sika, K., Boya, B., Socohou, A., Adjanohoun, A., dan Baba-Moussa, L. 2021. Phytochemical composition and in vitro biological activities of *Morinda citrifolia* fruit juice. *Saudi Journal of Biological Sciences* 28(2021): 1331-1335.
- Staruschenko, A., Palygin, O., Ilatovskaya, D.V., dan Pavlov, T.S. 2013. Epidermal growth factors in the kidney and relationship to hypertension. *Am J Physiol Renal Physiol* 305: F12–F20.
- Suhatri., Oktavia, S., Nopiyanti, E. 2019. Efek Proteksi Ekstrak Etanol Buah Mengkudu Terhadap Disfungsi Sel Endotel Yang di Induksi Dengan NaCl Pada Mencit Putih Jantan. *Jurnal Farmasi Higea* 11(1): 11-16.
- Sun, Z., Xu, Y., An, W., Bi, S., Xu, S., Zhang, R., Cong, M., dan Chen, S. 2022. Mining Important Herb Combinations of Traditional Chinese Medicine against Hypertension Based on the Symptom-Herb Network Combined with Network Pharmacology. *Evidence-Based Complementary and Alternative Medicine*. 2022: 1-20.
- Sutton, G., D. Pugh, dan N. Dhaun. 2019. Developments in the Role of Endothelin-1 in Atherosclerosis: A Potential Therapeutic Target? *American Journal of Hypertension* 32(9): 813-815.
- Szklarczyk, D., Gable, A.L., Lyon, D., Junge, A., Wyder, S., Huerta-Cepas, J., Simonovic, M., Doncheva, N.T., Morris, J.H., Bork, P., Jensen, L.J., dan Mering, C.von. 2019. STRING v11: protein–protein association networks with increased coverage,

- supporting functional discovery in genome-wide experimental datasets. *Nucleic Acids Research* 47: D607-D613.
- Szklarczyk, D., Gable, A.L., Nastou, K.C., Lyon, D., Kirsch, R., Pysalo, S., Doncheva, N.T., Legeay, M., Fang, T., Bork, P., Jensen, L.J., dan Mering, C.von. 2021. The STRING database in 2021: customizable protein–protein networks, and functional characterization of user-uploaded gene/measurement sets. *Nucleic Acids Research* 49: D605–D612.
- Tan, C., Zhang H., Yu, D., Hu, Y., Wang, P., Wang, D., Fa, J., Ran, H., Zhang, X., Chen, Y., Xin, W., Fang, C., Ke, T., Dong, N., Cai, J., He, Q., Huo, S., Wang, J., Ren, X., Tu, X., Lin, X., Q. Wang, Q., dan Xu, C. 2021. A genome-wide association study identifies novel association between genetic variants in GGT7 and LINC00944 and hypertension. *Clinical and Translational Medicine* 11(5): e388.
- Tanaka Y., Murata, M., Tanegashima, K., Oda, Y., dan Ito, T. 2022. Nectin cell adhesion molecule 4 regulates angiogenesis through Src signaling and serves as a novel therapeutic target in angiosarcoma. *Scientific Reports* 12: 4031.
- The UniProt Consortium. 2017. UniProt: the universal protein knowledgebase. *Nucleic Acids Research* 45: D158–D169.
- Ulfa, I. dan Kautsar, A.P. 2019. Drug Utilization Research Obat Antihipertensi pada Pasien Rawat Jalan Tahun 2018 di Rumah Sakit Paru Dr H A Rotinsulu dengan Metode ATC/DDD: Cross-Sectional Study. *Farmaka* 17(2): 71-78.
- Ursu, O., Holmes, J., Knockel, J., Bologa, C.G., Yang, J.J., Mathias, S.L., Nelson, S.J., dan Oprea, T.I. 2017. DrugCentral: online drug compendium. *Nucleic Acids Research* 45: D932-D939.
- Wallace, K., Cornelius, D.C., Scott, J., Heath, J., Moseley, J., Chatman, K., dan LaMarca, B. 2014. CD4+ T Cells Are Important Mediators of Oxidative Stress That Cause Hypertension in Response to Placental Ischemia. *Hypertension* 64(4): 1151-1158.
- Wang, X., Wu, M., Lai, X., Zheng, J., Hu, M., Li, Y., dan Li, S. 2020. Network Pharmacology to Uncover the Biological Basis of Spleen Qi Deficiency Syndrome and Herbal Treatment. *Oxidative Medicine and Cellular Longevity* 2020: 1-20.
- Wang, Y., Chen, S., dan Du, J. 2019. Bosentan for Treatment of Pediatric Idiopathic Pulmonary Arterial Hypertension: State-of-the-Art. *Frontiers in Pediatrics* 7: 302.

- Wadhawan, M., Chhabra, V., Katiyar, A., Sharma, V., Khuntia, B.K., Rathore, S., Kaur, P., dan Sharma, G. 2021. A Network Pharmacology-Based Approach to Explore Therapeutic Mechanism of Indian Herbal Formulation Nisha Amalaki in Treating Type 2 Diabetes Mellitus. *Research Square*: 1–30.
- Weiß, E., Berger, H.M., Brandl, W.T., Strutz, J., Hirschmugl, B., Simovic, V., Tam-Ammersdorfer, C., Cvitic, S., dan Hiden, U. 2020. Maternal Overweight Downregulates MME (Neprilysin) in Feto-Placental Endothelial Cells and in Cord Blood. *International Journal of Molecular Sciences* 21: 834.
- Wijaya, S. H., Afendi, F.M., Batubara, I., Huang, M., Ono, N., Kanaya, S., dan Altaf-UI-Amin, M. 2021. Identification of Targeted Proteins by Jamu Formulas for Different Efficacies Using Machine Learning Approach. *Life* 11: 1-12.
- Wiliyanarti, P. F., dan Silaturrohmi. 2020. Pengaruh Ekstrak Mengkudu (*Morinda citrifolia*) Terhadap Penurunan Tekanan Darah Pada Tikus Putih Wistar Jantan dengan Hipertensi. *The Journal of Muhammadiyah Medical Laboratory Technologist* 3(1): 1-12.
- Williams, B., Mancia, G., Spiering, W., Rosei, E.A., Azizi, M., Burnier, M., Clement, D.L., Coca, A., Simone, G.D., Dominiczak, A., Kahan, T., Mahfoud, F., Redon, J., Ruilope, L., Zanchetti, A., Kerins, M., Kjeldsen, S.E., Kreutz, R., Laurent, S., Lip, G.Y.H., McManus, R., Narkiewicz, K., Ruschitzka, F., Schmieder, R.E., Shlyakhto, E., Tsioufis, C., Aboyans, V., dan Desormais, I. 2018. ESC/ESH Guidelines for the management of arterial hypertension. *European Heart Journal* 39: 3021–3104.
- Wu, C.H., Mohammadmoradi, S., Chen, J.Z., Sawada, H., Daugherty, A., dan Lu, H.S. 2018. Renin-Angiotensin System and Cardiovascular Functions. *American Heart Association* 38(7): e108-e116.
- Yart, L., Bahmanyar, E. R., Cohen, M., dan Tejada, B. M. 2021. Role of the Uteroplacental Renin–Angiotensin System in Placental Development and Function, and Its Implication in the Preeclampsia Pathogenesis. *Biomedicine* 9:1332.
- Yosida, I. 2016. Efektivitas Penggunaan Obat Antihipertensi di Instalasi Rawat Inap Bangsal Bakung RSUD Panembahan Senopati Bantul Periode Agustus 2015. *Skripsi*. Fakultas Farmasi Universitas Sanata Dharma. Yogyakarta.

- Zhang, J.Y., Hong, C.L., Chen, H.S., Zhou, X.J., Zhang, Y.J., Efferth, T., Yang, Y.X., dan Li, C.Y. 2019. Target Identification of Active Constituents of Shen Qi Wan to Treat Kidney Yang Deficiency Using Computational Target Fishing and Network Pharmacology. *Frontiers in Pharmacology* 10: 252-270.
- Zhang, R., Zhu, X., Bai, H., dan Ning, K. 2019. Network Pharmacology Databases for Traditional Chinese Medicine: Review and Assessment. *Frontiers in Pharmacology* 10: 1-14.
- Zhai, Z., Tao, X., Alami, M.M., Shu, S., dan Wang, X. 2021. Network Pharmacology and Molecular Docking Combined to Analyze the Molecular and Pharmacological Mechanism of Pinellia ternata in the Treatment of Hypertension. *Current issues in molecular biology* 43: 65-78.
- Zhao, Y., Wang, C., Wang, C., Hong, X., Miao, J., Liao, Y., Zhou, L., dan Liu, Y. 2018. An essential role for Wnt/ β -catenin signaling in mediating hypertensive heart disease. *Scientific reports* 8:8996.
- Zheng, T., Chen, T., Gao, Y, dan Tian, H. 2014. Increased plasma DPP4 activity predicts new-onset hypertension in Chinese over a 4-year period: possible associations with inflammation and oxidative stress. *Journal of Human Hypertension* 1–6.
- Zogovic, B., dan Pilowsky, P.M. 2011. Intrathecal neurotensin is hypotensive, sympathoinhibitory and enhances the baroreflex in anaesthetized rat. *British Journal of Pharmacology* 166: 378–389.