

## DAFTAR PUSTAKA

- Abdel Fattah, M. E., Sobhy, H. M., Reda, A., & Abdelrazek, H. M. A. (2020). Hepatoprotective effect of *Moringa oleifera* leaves aquatic extract against lead acetate-induced liver injury in male Wistar rats. *Environmental Science and Pollution Research*, 27(34). <https://doi.org/10.1007/s11356-020-10161-z>
- Abd-Elsalam, K. A. (2003). Bioinformatic tools and guideline for PCR primer design. *African Journal of Biotechnology*, 2(5). <https://doi.org/10.5897/ajb2003.000-1019>
- Adams, G. (2020). A beginner's guide to RT-PCR, qPCR and RT-qPCR. *Biochemist*, 42(3). <https://doi.org/10.1042/bio20200034>
- Aden, D. P., Fogel, A., Plotkin, S., Damjanov, I., & Knowles, B. B. (1979). Controlled synthesis of HBsAg in a differentiated human liver carcinoma-derived cell line. *Nature*, 282(5739). <https://doi.org/10.1038/282615a0>
- Alchin, J., Dhar, A., Siddiqui, K., & Christo, P. J. (2022). Why paracetamol (acetaminophen) is a suitable first choice for treating mild to moderate acute pain in adults with liver, kidney or cardiovascular disease, gastrointestinal disorders, asthma, or who are older. *Current Medical Research and Opinion*, 38(5). <https://doi.org/10.1080/03007995.2022.2049551>
- Al-Helaly, L. A., & Al-Kado, O. A. (2019). Partial purification and some kinetic studies of glutathione peroxidase (GPx) in normal human plasma and comparing with primary infertility female. In *Tikrit Journal of Pure Science* (Vol. 18, Issue 3). <https://www.researchgate.net/publication/337144541>
- Arzumanian, V. A., Kiseleva, O. I., & Poverennaya, E. V. (2021). The curious case of the HepG2 cell line: 40 years of expertise. *International Journal of Molecular Sciences*, 22(23). <https://doi.org/10.3390/ijms222313135>
- Ayoub, S. S. (2021). Paracetamol (acetaminophen): A familiar drug with an unexplained mechanism of action. *Temperature*, 8(4). <https://doi.org/10.1080/23328940.2021.1886392>
- Barinda, A. J., Arozal, W., Hardi, H., Dewi, Y. R., Safutra, M. S., & Lee, H. J. (2024). Water extracts of *Moringa oleifera* leaves alter oxidative stress-induced neurotoxicity in human neuroblastoma SH-SY5Y cells. *Scientific World Journal*, 2024(1). <https://doi.org/10.1155/2024/7652217>
- Berry, S., & Pelkmans, L. (2022). Mechanisms of cellular mRNA transcript homeostasis. In *Trends in Cell Biology* (Vol. 32, Issue 8). <https://doi.org/10.1016/j.tcb.2022.05.003>

- Boga, I., Prasad, S. V., Deka, D., Das, A., Bisgin, A., Mittal, P., & Banerjee, A. (2022). A study on total RNA including microRNA isolation from cell lines by different cost effective methods. *International Journal of Experimental Research and Review*, 29. <https://doi.org/10.52756/ijerr.2022.v29.011>
- Brigelius-Flohé, R., & Maiorino, M. (2013). Glutathione peroxidases. *Biochimica et Biophysica Acta - General Subjects*, 1830(5), 3289–3303. <https://doi.org/10.1016/j.bbagen.2012.11.020>
- Buranasudja, V., Sanookpan, K., Vimolmangkang, S., Binalee, A., Mika, K., Krobthong, S., Kerdsomboon, K., Kumkate, S., Poolpak, T., Kidhakarn, S., Yang, K. M., Limcharoensuk, T., & Auesukaree, C. (2024). Pretreatment with aqueous *Moringa oleifera* Lam. leaf extract prevents cadmium-induced hepatotoxicity by improving cellular antioxidant machinery and reducing cadmium accumulation. *Heliyon*, 10(18). <https://doi.org/10.1016/j.heliyon.2024.e37424>
- Burdejova, L., Tobolkova, B., Polovka, M., & Neugebauerova, J. (2023). Differentiation of medicinal plants according to solvents, processing, origin, and season by means of multivariate analysis of spectroscopic and liquid chromatography data. *Molecules*, 28(10). <https://doi.org/10.3390/molecules28104075>
- Bustin, S. A., & Mueller, R. (2005). Real-time reverse transcription PCR (qRT-PCR) and its potential use in clinical diagnosis. *Clinical Science*, 109(4). <https://doi.org/10.1042/CS20050086>
- Calabrese, E. J. (2013). Biphasic dose responses in biology, toxicology and medicine: Accounting for their generalizability and quantitative features. In *Environmental Pollution* (Vol. 182). <https://doi.org/10.1016/j.envpol.2013.07.046>
- Chen, F., Xiao, M., Hu, S., & Wang, M. (2024). Keap1-Nrf2 pathway: A key mechanism in the occurrence and development of cancer. *Frontiers in Oncology*, 14. <https://doi.org/10.3389/fonc.2024.1381467>
- Chidiac, A. S., Buckley, N. A., Noghrehchi, F., & Cairns, R. (2023). Paracetamol (acetaminophen) overdose and hepatotoxicity: Mechanism, treatment, prevention measures, and estimates of burden of disease. *Expert Opinion on Drug Metabolism and Toxicology*, 19(5). <https://doi.org/10.1080/17425255.2023.2223959>
- Copple, I. M., Goldring, C. E., Jenkins, R. E., Chia, A. J. L., Randle, L. E., Hayes, J. D., Kitteringham, N. R., & Park, B. K. (2008). The hepatotoxic metabolite of acetaminophen directly activates the Keap1-Nrf2 cell defense system. *Hepatology*, 48(4). <https://doi.org/10.1002/hep.22472>

- Da Silva Parente, T. S. J., Sarandy, M. M., de Araújo, E. R. D., Gonçalves, R. V., & Zucolotto, S. M. (2025). Effect of *Moringa oleifera* on inflammatory diseases: An umbrella review of 26 systematic reviews. *Frontiers in Pharmacology*, 16. <https://doi.org/10.3389/fphar.2025.1572337>
- Đermić, D., Ljubić, S., Matulić, M., Procino, A., Feliciello, M. C., Ugarković, Đ., & Feliciello, I. (2023). Reverse transcription-quantitative PCR (RT-qPCR) without the need for prior removal of DNA. *Scientific Reports*, 13(1). <https://doi.org/10.1038/s41598-023-38383-4>
- Farmasita, R., & Veronica, A. (2024). Hubungan usia, jenis kelamin dan tingkat pendidikan orang tua terhadap pengetahuan swamedika pemberian paracetamol pada anak. *Jurnal Insan Farmasi Indonesia*, 7(1).
- Franceschi, C., Garagnani, P., Parini, P., Giuliani, C., & Santoro, A. (2018). Inflammaging: A new immune–metabolic viewpoint for age-related diseases. *Nature Reviews Endocrinology*, 14(10). <https://doi.org/10.1038/s41574-018-0059-4>
- Gao, X., Yu, X., Zhang, C., Wang, Y., Sun, Y., Sun, H., Zhang, H., Shi, Y., & He, X. (2022). Telomeres and mitochondrial metabolism: Implications for cellular senescence and age-related diseases. *Stem Cell Reviews and Reports*, 18(7). <https://doi.org/10.1007/s12015-022-10370-8>
- Gum, S. Il, & Cho, M. K. (2013). Recent updates on acetaminophen hepatotoxicity: The role of Nrf2 in hepatoprotection. *Toxicological Research*, 29(3). <https://doi.org/10.5487/TR.2013.29.3.165>
- Hammad, M., Raftari, M., Cesário, R., Salma, R., Godoy, P., Emami, S. N., & Haghdoost, S. (2023). Roles of oxidative stress and Nrf2 signaling in pathogenic and non-pathogenic cells: A possible general mechanism of resistance to therapy. *Antioxidants*, 12(7). <https://doi.org/10.3390/antiox12071371>
- Handy, D. E., & Loscalzo, J. (2022). The role of glutathione peroxidase-1 in health and disease. *Free Radical Biology and Medicine*, 188. <https://doi.org/10.1016/j.freeradbiomed.2022.06.004>
- Herndon, C. M., & Dankenbring, D. M. (2014). Patient perception and knowledge of acetaminophen in a large family medicine service. *Journal of Pain and Palliative Care Pharmacotherapy*, 28(2). <https://doi.org/10.3109/15360288.2014.908993>
- Hicks, D. G., & Lester, S. C. (2016). Expression profiling, oncotype DX assay. *Diagnostic Pathology: Breast*, 478–481. <https://doi.org/10.1016/B978-0-323-37712-6.50074-0>

- Hionides-Gutierrez, A., Goikoetxea-Usandizaga, N., Sanz-García, C., Martínez-Chantar, M. L., & Cubero, F. J. (2024). Novel emerging mechanisms in acetaminophen (APAP) hepatotoxicity. *Liver International*. <https://doi.org/10.1111/liv.16167>
- Kadri, K. (2019). Polymerase chain reaction (PCR): principle and applications. *IntechOpen*, 19(5).
- Karthivashan, G., Arulselvan, P., Tan, S. W., & Fakurazi, S. (2015). The molecular mechanism underlying the hepatoprotective potential of *Moringa oleifera* leaves extract against acetaminophen induced hepatotoxicity in mice. *Journal of Functional Foods*, 17. <https://doi.org/10.1016/j.jff.2015.05.007>
- Keum, Y. S., Yu, S., Chang, P. P. J., Yuan, X., Kim, J. H., Xu, C., Han, J., Agarwal, A., & Kong, A. N. T. (2006). Mechanism of action of sulforaphane: inhibition of p38 mitogen-activated protein kinase isoforms contributing to the induction of antioxidant response element-mediated heme oxygenase-1 in human hepatoma HepG2 cells. *Cancer Research*, 66(17). <https://doi.org/10.1158/0008-5472.CAN-05-3513>
- Kim, C. G., Chang, S. N., Park, S. M., Hwang, B. S., Kang, S. A., Kim, K. S., & Park, J. G. (2022). *Moringa oleifera* mitigates ethanol-induced oxidative stress, fatty degeneration and hepatic steatosis by promoting Nrf2 in mice. *Phytomedicine*, 100. <https://doi.org/10.1016/j.phymed.2022.154037>
- Kwong, A. J., Kim, W. R., Lake, J. R., Smith, J. M., Schladt, D. P., Skeans, M. A., Noreen, S. M., Foutz, J., Booker, S. E., Cafarella, M., Snyder, J. J., Israni, A. K., & Kasiske, B. L. (2021). OPTN/SRTR 2019 annual data report: Liver. *American Journal of Transplantation*, 21(S2). <https://doi.org/10.1111/ajt.16494>
- Lee, S. S. T., Buters, J. T. M., Pineau, T., Fernandez-Salguero, P., & Gonzalez, F. J. (1996). Role of CYP2E1 in the hepatotoxicity of acetaminophen. *Journal of Biological Chemistry*, 271(20). <https://doi.org/10.1074/jbc.271.20.12063>
- Libardo, M. D. J., Wang, T. Y., Pellois, J. P., & Angeles-Boza, A. M. (2017). How does membrane oxidation affect cell delivery and cell killing? *Trends in Biotechnology*, 35(8). <https://doi.org/10.1016/j.tibtech.2017.03.015>
- López-Terrada, D., Cheung, S. W., Finegold, M. J., & Knowles, B. B. (2009). Hep G2 is a hepatoblastoma-derived cell line. *Human Pathology*, 40(10). <https://doi.org/10.1016/j.humpath.2009.07.003>
- Lubos, E., Loscalzo, J., & Handy, D. E. (2011). Glutathione peroxidase-1 in health and disease: From molecular mechanisms to therapeutic opportunities.

- Antioxidants and Redox Signaling*, 15(7).  
<https://doi.org/10.1089/ars.2010.3586>
- Luo, G., Huang, L., & Zhang, Z. (2023). The molecular mechanisms of acetaminophen-induced hepatotoxicity and its potential therapeutic targets. *Experimental Biology and Medicine*, 248(5). <https://doi.org/10.1177/15353702221147563>
- Ma, H., Bell, K. N., & Loker, R. N. (2021). qPCR and qRT-PCR analysis: Regulatory points to consider when conducting biodistribution and vector shedding studies. *Molecular Therapy - Methods & Clinical Development*, 20, 152–168. <https://doi.org/10.1016/J.OMTM.2020.11.007>
- Ma, M., Jiang, W., & Zhou, R. (2024). DAMPs and DAMP-sensing receptors in inflammation and diseases. *Immunity*, 57(4), 752–771. <https://doi.org/10.1016/j.immuni.2024.03.002>
- Mahmood, K. T., Mugal, T., & Haq, I. U. (2010). *Moringa oleifera: A natural gift-a review*. *Journal of Pharmaceutical Sciences and Research*, 2(11).
- Mallet, C., Desmeules, J., Pegahi, R., & Eschalier, A. (2023). An updated review on the metabolite (AM404)-mediated central mechanism of action of paracetamol (acetaminophen): Experimental evidence and potential clinical impact. *Journal of Pain Research*, 16. <https://doi.org/10.2147/JPR.S393809>
- Marjan, L. (2018). Hubungan tingkat pendidikan terhadap tingkat pengetahuan orangtua dalam swamedikasi demam pada anak menggunakan obat parasetamol: Studi di kalangan masyarakat Kecamatan Talango Kabupaten Sumenep Jawa Timur. *Fakultas Kedokteran Dan Ilmu Kesehatan Universitas Islam Negeri Maulana Malik Ibrahim Malang*.
- Mazaleuskaya, L. L., Sangkuhl, K., Thorn, C. F., Fitzgerald, G. A., Altman, R. B., & Klein, T. E. (2015). PharmGKB summary: Pathways of acetaminophen metabolism at the therapeutic versus toxic doses. *Pharmacogenetics and Genomics*, 25(8). <https://doi.org/10.1097/FPC.0000000000000150>
- Milla, P. G., Peñalver, R., & Nieto, G. (2021). Health benefits of uses and applications of *Moringa oleifera* in bakery products. *Plants*, 10(2). <https://doi.org/10.3390/plants10020318>
- Morita, C., Tokunaga, Y., Ueda, Y., Ono, M., Kinoshita, H., Kurogi, K., Sakakibara, Y., Suiko, M., Liu, M. C., & Yasuda, S. (2022). Investigation of radical scavenging effects of acetaminophen, p-aminophenol and their O-sulfated conjugates. *Journal of Toxicological Sciences*, 47(10). <https://doi.org/10.2131/jts.47.421>

- Moyo, B., Masika, P. J., Hugo, A., & Muchenje, V. (2011). Nutritional characterization of Moringa (*Moringa oleifera* Lam.) leaves. *African Journal of Biotechnology*, 10(60). <https://doi.org/10.5897/ajb10.1599>
- National Center for Biotechnology Information (NCBI). (2025a). *CYP2E1 (NM\_000773.4)*. National Library of Medicine. <https://www.ncbi.nlm.nih.gov/gene/1571#genomic-regions-transcripts-products>
- National Center for Biotechnology Information (NCBI). (2025b). *GPX1 (NM\_000581.4)*. National Library of Medicine. <https://www.ncbi.nlm.nih.gov/gene/2876>
- Ozougwu, J. C. (2017). Physiology of the liver. In *International Journal of Research in Pharmacy and Biosciences* (Vol. 4).
- Parija, S. C. (2012). Microbiology and Immunology Textbook. In *Elsevier India* (Vol. 148).
- Pei, J., Pan, X., Wei, G., & Hua, Y. (2023). Research progress of glutathione peroxidase family (GPX) in redoxidation. *Frontiers in Pharmacology*, 14. <https://doi.org/10.3389/fphar.2023.1147414>
- Peñalver, R., Martínez-zamora, L., Lorenzo, J. M., Ros, G., & Nieto, G. (2022). Nutritional and antioxidant properties of Moringa oleifera leaves in functional foods. *Foods*, 11(8). <https://doi.org/10.3390/foods11081107>
- Phuong, N. T. D., Dat, T. T., Hue, T. H., Thuy, L. H. A., & Thuan, L. D. (2023). Establishment of protocol to investigate the expression of sucrose phosphate synthase 2 (SPS2) in Vietnamese Golden Melon (*Cucumis melo* L.). *Ho Chi Minh City Open University Journal of Science - Engineering and Technology*, 13(2). <https://doi.org/10.46223/hcmcoujs.tech.en.13.2.2786.2023>
- Porubsky, P. R., Meneely, K. M., & Scott, E. E. (2008). Structures of human cytochrome P-450 2E1. *Journal of Biological Chemistry*, 283(48). <https://doi.org/10.1074/jbc.m805999200>
- POWO. (2025). *Moringa oleifera Lam.* Facilitated by the Royal Botanic Gardens, Kew. <https://powo.science.kew.org/taxon/urn:lsid:ipni.org:names:584736-1/general-information#source-UPFC>
- PubChem. (2025). *PubChem Compound Summary for CID 1983, Acetaminophen*. National Library of Medicine - National Center for Biotechnology Information. <https://pubchem.ncbi.nlm.nih.gov/compound/1983>
- Rahman, A. H. M. M., & Sarker, A. K. (2015). Investigation of medicinal plants at Katakhali Pouroshova of Rajshahi District, Bangladesh and their conservation

- management. *Applied Ecology and Environmental Sciences*, Vol. 3, 2015, Pages 184-192, 3(6).
- Rajappa, R. P. M., Nallupillai, P., Krishna, K. L., Ramesh, M. M., & Venkatappa, A. H. (2024). Exploring the mechanisms and dosages of herbal hepatoprotective agents. *Pharmacognosy Research*, 16(4), 706–717. <https://doi.org/10.5530/pres.16.4.82>
- Razis, A. F. A., Ibrahim, M. D., & Kntayya, S. B. (2014). Health benefits of *Moringa oleifera*. In *Asian Pacific Journal of Cancer Prevention* (Vol. 15, Issue 20). <https://doi.org/10.7314/APJCP.2014.15.20.8571>
- Rocha, A. J., Monteiro-Júnior, J. E., Freire, J. E. C., Sousa, A. J. S., & Fonteles, C. S. R. (2015). Real Time PCR: the Use of Reference Genes and Essential Rules Required to Obtain Normalisation Data Reliable to Quantitative Gene Expression. *Journal of Molecular Biology Research*, 5(1). <https://doi.org/10.5539/jmbr.v5n1p45>
- Rodríguez-Antona, C., Donato, M. T., Boobis, A., Edwards, R. J., Watts, P. S., Castell, J. V., & Gómez-Lechón, M. J. (2002). Cytochrome P450 expression in human hepatocytes and hepatoma cell lines: Molecular mechanisms that determine lower expression in cultured cells. *Xenobiotica*, 32(6). <https://doi.org/10.1080/00498250210128675>
- Sailaja, B. S., Aita, R., Maledatu, S., Ribnicky, D., Verzi, M. P., & Raskin, I. (2021). Moringa isothiocyanate-1 regulates Nrf2 and NF-κB pathway in response to LPS-driven sepsis and inflammation. *PLoS ONE*, 16(4 April). <https://doi.org/10.1371/journal.pone.0248691>
- Sarcinelli, C., Dragic, H., Piecyk, M., Barbet, V., Duret, C., Barthelaix, A., Ferraro-Peyret, C., Fauvre, J., Renno, T., Chaveroux, C., & Manié, S. N. (2020). ATF4-dependent NRF2 transcriptional regulation promotes antioxidant protection during endoplasmic reticulum stress. *Cancers*, 12(3). <https://doi.org/10.3390/cancers12030569>
- Schmittgen, T. D., & Livak, K. J. (2001). Analysis of relative gene expression data using real-time quantitative PCR and the 2(-Delta Delta C(T)) Method. *Methods*, 25(4).
- Singh, D., Arya, P. V., Aggarwal, V. P., & Gupta, R. S. (2014). Evaluation of antioxidant and hepatoprotective activities of *Moringa oleifera* Lam. leaves in carbon tetrachloride-intoxicated rats. *Antioxidants*, 3(3). <https://doi.org/10.3390/antiox3030569>

- Singh, K. P., Miaskowski, C., Dhruva, A. A., Flowers, E., & Kober, K. M. (2018). Mechanisms and Measurement of Changes in Gene Expression. *Biological Research for Nursing*, 20(4). <https://doi.org/10.1177/1099800418772161>
- Steinbrecht, S., Kammerer, S., & Küpper, J. H. (2019). HepG2 cells with recombinant cytochrome P450 enzyme overexpression: their use and limitation as in vitro liver model. *Journal of Cellular Biotechnology*, 5(1). <https://doi.org/10.3233/JCB-189013>
- Stohs, S. J., & Hartman, M. J. (2015). Review of the safety and efficacy of *Moringa oleifera*. *Phytotherapy Research*, 29(6). <https://doi.org/10.1002/ptr.5325>
- Suyono, T., Lieno, L., Ginting, C. N., Lister, I. N. E., Girsang, E., Widowati, W., Zahiroh, F. H., Kusuma, H. S. W., & Rizal, R. (2024). Eugenol protects human liver HepG2 cells from H<sub>2</sub>O<sub>2</sub>-induced oxidative hepatotoxicity by maintaining ROS homeostasis, increasing IL-10 Level, and upregulating CYP1B1 gene expression. *Pharmaceutical Sciences Asia*, 51(1). <https://doi.org/10.29090/psa.2024.01.23.909>
- Tabernilla, A., Rodrigues, B. D. S., Pieters, A., Caufriez, A., Leroy, K., Campenhout, R. Van, Cooreman, A., Gomes, A. R., Arnesdotter, E., Gijbels, E., & Vinken, M. (2021). In vitro liver toxicity testing of chemicals: A pragmatic approach. *International Journal of Molecular Sciences*, 22(9). <https://doi.org/10.3390/ijms22095038>
- Tan, W. S., Arulselvan, P., Karthivashan, G., & Fakurazi, S. (2015). *Moringa oleifera* flower extract of inflammatory mediators in lipopolysaccharide-stimulated RAW 264.7 macrophages via NF- κB pathway. *Mediators of Inflammation*, 2015. <https://doi.org/10.1155/2015/720171>
- Templeton, N. S. (1992). The polymerase chain reaction. history, methods, and applications. *Diagnostic Molecular Pathology : The American Journal of Surgical Pathology, Part B*, 1(1). <https://doi.org/10.1097/00019606-199203000-00008>
- Wagner, E. M. (2013). Monitoring gene expression: Quantitative real-time RT-PCR. *Methods in Molecular Biology*, 1027. [https://doi.org/10.1007/978-1-60327-369-5\\_2](https://doi.org/10.1007/978-1-60327-369-5_2)
- Widowati, W., Priyandoko, D., Lenny, L., Revika, R., Novianti, S., Kusuma, H. S. W., & Rizal, R. (2024). *Camellia sinensis* L. extract suppresses inflammation on acute respiratory distress syndrome cells models via decreasing IL-1β, IL-6 and COX-2 expressions. *Trends in Sciences*, 21(1). <https://doi.org/10.48048/tis.2024.7010>

- Wu, G., Fang, Y. Z., Yang, S., Lupton, J. R., & Turner, N. D. (2004). Glutathione metabolism and its implications for health. *Journal of Nutrition*, 134(3). <https://doi.org/10.1093/jn/134.3.489>
- Xu, J., Zhao, L., Zhang, X., Ying, K., Zhou, R., Cai, W., Wu, X., Jiang, H., Xu, Q., Miao, D., Zeng, Y., & Yu, F. (2023). Salidroside ameliorates acetaminophen-induced acute liver injury through the inhibition of endoplasmic reticulum stress-mediated ferroptosis by activating the AMPK/SIRT1 pathway. *Ecotoxicology and Environmental Safety*, 262. <https://doi.org/10.1016/j.ecoenv.2023.115331>
- Yu, C., & Xiao, J. H. (2021). The Keap1-Nrf2 system: A mediator between oxidative stress and aging. *Oxidative Medicine and Cellular Longevity*, 2021. <https://doi.org/10.1155/2021/6635460>
- Zhu, H., Wang, X., Meng, X., Kong, Y., Li, Y., Yang, C., Guo, Y., Wang, X., Yang, H., Liu, Z., & Wang, F. (2022). Selenium supplementation improved cardiac functions by suppressing DNMT2-mediated GPX1 promoter DNA methylation in AGE-induced heart failure. *Oxidative Medicine and Cellular Longevity*, 2022. <https://doi.org/10.1155/2022/5402997>
- Zordoky, B., & El-Kadi, A. (2009). Role of NF-κB in the regulation of cytochrome P450 enzymes. *Current Drug Metabolism*, 10(2). <https://doi.org/10.2174/138920009787522151>