

BAB 5

KESIMPULAN

5.1 Kesimpulan

1. Pemberian Asam 2-(4-(klorometil)benzoiloksi)benzoat dapat menurunkan jumlah sel splenosit yang mengekspresikan COX-2 pada mencit putih (*Mus musculus*) galur *Swiss Webster* yang diinduksi LPS dibandingkan dengan mencit yang hanya diinduksi inflamasi menggunakan LPS.
2. Pemberian Asam 2-(4-(klorometil)benzoiloksi)benzoat dapat menurunkan kekuatan ekspresi COX-2 pada sel splenosit pada mencit putih (*Mus musculus*) galur *Swiss Webster* yang diinduksi LPS dibandingkan dengan mencit yang hanya diinduksi inflamasi menggunakan LPS.

5.2 Saran

Berdasarkan penelitian yang dilakukan, disarankan untuk melakukan penelitian lebih lanjut terhadap pemberian senyawa asam 2-(4-(klorometil)benzoiloksi)benzoat dosis 60 mg/KgBB dalam kemampuan yang serupa dengan AAS sebagai anti-inflamasi yang dapat menurunkan jumlah ekspresi sel splenosit yang mengekspresikan COX-2 dan kekuatan ekspresi COX-2 pada sel splenosit dengan menggunakan parameter baru yaitu prostaglandin yang diekspresikan oleh aktivasi COX-2 selama inflamasi dan perlu adanya penelitian lebih lanjut mengenai kaskade persinyalan aktivasi ekspresi COX-2 melalui jalur aktivasi NFkB.

DAFTAR PUSTAKA

- Barton, G.M. 2008, A calculated response: control of inflammation by the innate immune system, *The Journal of Clinical Investigation*, **118(2)**: 413-420.
- Britt, S. L., Grable, J.E., Cumbie, J., Cupples, S., Henegar, J., Schindler, K., and Archuleta, K.L. 2011, Student financial counseling: an analysis of a clinical and non-clinical sample. *Journal of Personal Finance*, **10(2)**: 95-121.
- Bronte, V., and Pittet, M. 2013, The spleen in local and systemic regulation of immunity, *Journal Immunity*, **39(5)**: 806-818.
- Caroff, M. and Novikov, A. 2020, Lipopolysaccharides: structure, function, and bacterial identifications, **27(31)**: 1-10.
- Cesta, M.F. 2006, Normal structure, function, and histology of the spleen, *Toxicologic Pathology*, **34(5)**: 455-465.
- Chattopadhyay, P.K., Hogerkorp, C.M., and Roederer, M. 2008, A chromatic explosion; the development and future of multiparameter flow cytometry, *Journal Immunology*, **125(4)**: 441-449.
- Chen, L., Deng, H., Cui, H., Fang, J., Zou, Z., Deng, J., Li, Y., Wang, X., and Zhao, L. 2017, Inflammatory responses and inflammation-associated diseases in organs, *Journals Oncotarget*, **9(6)**: 7204-7218.
- Dewi, 2020, 'Uji toksisitas akut senyawa asam 2-(4-(klorometil)benzoioksi)benzoat pada tikus putih jantan', Skripsi, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.
- Doyle, D. 2014, Thomas MacLagan's 1876 demonstration of the dramatic effects of salicin in rheumatic fever, *Journal of the Royal Society of Medicine*, **107(7)**: 287-289.
- Elmore, S.A. 2006, Hispathology of the lymph nodes, *Toxicologi Pathology*, **34(5)**: 425-454.
- Duan, Y., Chen, F., Zhang, A., Zhu, B., Sun, J., Xie, Q., and Chen, Z. 2014, Aspirin inhibits lipopolysaccharide-induced COX-2

expression and PGE-2 production in porcine alveolar macrophage by modulating protein kinase c and protein tyrosine phosphatase activity, *BMB Reports*, **47(1)**: 45-50.

- Fadele, M.L.M., Aiello, I., Caldart, C.S., Golombek, D.A., Marpegan, L., and Paladino, N. 2020, Differential thermoregulatory and inflammatory patterns in the circadian response to lps-induced septic shock, *Frontiers in Cellular and Infection Microbiology*, **10(100)**: 1-18.
- Frelinger, J., Kepler, T. B., and Chan, C. 2008, Flow: statistics, visualization and informatics for flow cytometry, *Source Code for Biology and Medicine*, **3(1)**: 1-12.
- Gandhi, J., Khera, L., Gaur, N., Paul, C., and Kaul, R. 2017, Role of modulator of inflammation cyclooxygenase-2 in gammaherpesvirus mediated tumorigenesis, *Frontiers in Microbiology*, **8(538)**: 1-12.
- Hamesch, K., Borkham-Kamphorst, E., Strnad, P. and Weiskirchen, R. 2015, Lipopolysaccharide-induced inflammatory liver injury in mice, *Laboratory Animals*, **49**: 37-46.
- Holmes, K. L., Otten, G., and Yokoyama, W. M. 2001, Flow cytometry analysis using the becton dickinson FACS Calibur, *Current Protocols in Immunology*, 5.4.1-5.4.22.
- IACUC. 2020, IACUC guideline 01-01: animal acclimation and quarantine, Laramie: University of Wyoming.
- Javeed, A., Zhang, B., Qu, Y., Zhang, A., Sun, C., Zhang, L., Liu, J., Zeng, C., and Zhao, Y. 2008, The significantly enhanced frequency of functional cd4poscd25 posfop3pos t regulatory cells in therapeutic dose aspirin-treated mice, *Transplant Immunology*, **20(2008)**: 253-260.
- Kaltschmidt, B., Linker, R.A., Deng, J., and Kaltschmidt, C. 2002, Cyclooxygenase-2 is a neuronal target gene of NF- κ B, *BMC Molecular Biology*, **3(16)**: 1-12.
- Kawasaki, T., and Kawai, T. 2014, Toll-like receptor signaling pathways, *Frontiers In Immunology*, **5(461)**: 1-8.
- Kudo, I., and Mukarami, M. 2002, Phospholipase a2 enzymes, *Prostaglandin and Other Lipid Mediator*, **68-69**:3-58.

- Kirkby, N.S., Chan, M.V., Zaiss, A.K., Vaz, E.G., Jiao, J., Berglund, L.M., Verdu, E.F., Shala, B.A., Wallace, J.L., Herschman, H.R., Gomez, M.F., and Mitchell, J.A. 2016, Systemic study of constitutive cyclooxygenase-2 expression: role of nfkb and nfat transcriptional pathways, *Proceedings of the National Academy of Sciences*, **113(2)**: 434-439.
- Kurt, J.S and Jabbour, H.N. 2003, Cyclooxygenase enzymes and prostaglandins in pathology of the endometrium, *Journal Reproduction*, **126**: 559 – 567.
- Lee, S., Shin, S., Kim, H., Han, S., Kim, K., Kwon, J., Kwak, J.H., Lee, C.K., Ha, N.J., Yim, D., and Kim, K. 2011, Anti-inflammatory function of arctiin by inhibiting COX-2 expression via NF- κ B Pathway, *Journal of Inflammation*, **8(16)**: 1-9.
- Lim, J.W., Kim, H., and Kim, K.H. 2001, Nuclear factor- κ B regulates Cyclooxygenase-2 expression and cell proliferation in human gastric cancer cells, *Laboratory Investigation*, **81(3)**: 349-360.
- Liu, G., Xia, X. P., Gong, S.L., and Zhao, Y. 2006, The macrophage heterogeneity: difference between mouse peritoneal exudate and splenic F4/80+ macrophages, *Journal Of Cellular Physiology*, **209(2)**: 341-352.
- Mahdi, J.G. 2010, Medical potential of willow: A chemical perspective of aspirin discovery, *Journal of Saudi Chemical Society*, **14**: 317-322.
- MacIver, N.J., Michalek, R.D., and Rathmell, J.C. 2013. Metabolic regulation of T-lymphocytes, *Annual Review of Immunology*, **31(1)**: 259-283.
- Medhitov, R. 2008, Origin and physiological roles of inflammation, *Nature*, **454(7203)**: 428-435.
- Mebius, R.E. and Kraal, G, Structure and function of the spleen, *Nature Review*, **5**: 606-616.
- Medhizov, R. 2008, Origin and physiological roles of inflammation, *Nature*, **454**: 428-435.
- Minghetti, L. 2004, Cyclooxygenase-2 (COX-2) in inflammatory and degenerative brain diseases, *Journal of Neuropathology and Experimental Neurology*, **63(9)**: 901-910.

- Natalia, O., Caroline, C., and Soekardjo, B. 2015, Pemodelan interaksi turunan potensial Asam Benzoilsalisilat dengan reseptor enzim Siklooksigenase-2, *Journal of Pharmaceutical Science and Pharmacy Practice*, **1(1)**: 19-24.
- Naeem, A., James, N., Tanvir, M., Marriam, M., and Nathaniel, A. 2017, Fluorescence activated cell sorting (FACS): An advanced cell sorting technique, *Pakistan Science Missin Biological Research*, **2(2)**: 83-88.
- Oka, T., Oka, K., Kobayashi, T., Sugimotot, Y., Ichikawat, A., Ushikubi, F., Narumiya, S., and Saper, C.B. 2003, Characterixstics of thermoregulatory and febrile responses in mice deficient prostaglandin EP1 and EP3 reseptors, *Journal Physiol*, **551(3)**: 945-954.
- Parkin, J. and Cohen, B. 2001, An overview of the immune system, *Journal Immunology*, **357(2)**: 1777-1789.
- Pham, P.V. 2015, Flow cytometry data analysis, *Medical Engineering*, 5466-5467.
- Pratiwi, V.D., 2009, 'Sintesis Asam 4-klorometilbenzoil dan Uji aktivitas analgesik pada mencit (*Mus musculus*)', Skripsi, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.
- Raetz, C.R.H., and Whitfield, C. 2002, Lipopolysaccharide endotoxins, *Annual Review of Biochemistry*, **71(1)**: 635-700.
- Radjelović, P., Veljković, S., Stojilković, N., Sokolović, D., Ilic, I., Laketić, D., Randjelović, D., and Randjelović, N. 2015, The Benefit Biological Properties of Salicylic Acid, *Acta Facultatis Medicine Naisensis*, **32(4)**: 259-265.
- Rao, P.P.N., Kabir, S.N., and Mohamed, T. 2010, Nonsteroidal Anti-inflammatory Drug (NSAID): Progress in Small Molecule Drug Development, *Journal Pharmaceuticals*, **3**: 1530-1549.
- Raouzer, C.A. and Marnett, L.J. 2008, Cyclooxygenase: Structural and functional insights, *Journal of Lipid Research*, **50**: S29-S34.
- Sobolewski, Carella, C., Dicato, M., Ghibelli, L., and Diederich, M. 2010, The role of cyclooxygenase-2 in cell proliferation and cell death in human malignancies, *International Journal of Cell Biology*, 1-21.

- Soekardjo B., Caroline, Widharna R.M., 2011. Uji Toksisitas Akut penentuan LD50 senyawa turunan asam benzoilsalisilat pada mencit, LPPM Research Project, Unika Widya Mandala, Surabaya.
- Silverstein, F.E., Faich, G., Goldstein, J.L., Simon, L.S., Pincus, T., Whelton, A., Makuch, R., Eisen, G., Agrawal, N.M., Stenson, W.F., Burr, A.M., Zhao, W.W., Kent, J.D., Lefkowitz, J.B., Verburg, K.M., and Geis, G.S. 2000, Gastrointestinal toxicity with celecoxib vs nonsteroidal anti-inflammatory drugs for osteoarthritis and rheumatoid arthritis, *Journal American Medical Association*, **248(1)**: 1247-1255.
- Skapenko, A., Leipe, J., Lipsky, P.E., and Schulze-Koops, H. 2005, The review of the cell in autoimmune inflammation, *Arthritis Research and Therapy*, **7(2)**: S4-S14.
- Sweetman, S.C., 2009, Martindale: The Complete Drug Reference, Pharmaceutical Press, Thirty-sixth edition.
- Tamayanti, W.D., Wildharna, R.M., Caroline., Soekarjo, B. 2016, Uji aktivitas analgesik asam 2-(3-(klorometil)benzoiloksi)benzoat dan asam 2-(4-(klorometil)benzoiloksi)benzoat pada tikus wistar jantan dengan metode plantar test, *Jurnal Farmasi Sains dan Komunitas*, **13(1)**: 15-22.
- Vallejo, J.A.L., Sarkissian, H.D., Cazes, L., Bacchetti, S., and Reddel, R.R. 2004, Alternative lengthening of telomeres is characterized by high of telomeric exchange, *Cancer Research*, **64(7)**: 2324-2327.
- Wilkerson, M. J. 2012, Principles and applications of flow cytometry and cell sorting in companion animal medicine. *Veterinary Clinics North America Small Animal Practice*, **42**: 53-71.
- Xu, X., Garcia, L., Chen, X., Aleksic, N., Du, M., and Wu, K.K. 1999, Suppression of inducible cyclooxygenase-2 gene transcription by aspirin and sodium salicylate, *Journal Pharmacology*, **96**: 5292-5297.
- Yücel. G., Zhao, Z., El-Batrawy, I., Lan, H., Lang, S., Li, X., Buljubasic, F., Zimmermann, W., Cyganek, L., Utikal, J., Ravens, U., Wieland, T., Borggreffe, M., Zhou, X., and Akin, A. 2017, Lipopoly-saccharides induced inflammatory responses and electrophysiology

ical dysfunctions in human-induced pluripotent stem cell derived cardiomyocytes, *Scientific Reports*, **7(1)**: 1-13.

Zidar, N., Odar, K., Glavac, D., Jerse, M., Zupanc, T., and Stajer, D. 2008, Cyclooxygenase in normal human tissues is COX-1 really a constitutive isoform, and COX-2 an inducible isoform, *Journal of Cellular and Molecular Medicine*, **13(9b)**: 3753-3763.