BAB 5
KESIMPULAN DAN SARAN

5.1 Kesimpulan

1. Pemberian senyawa asam 2-(3-(klorometil)benzoiloksi))benzoat dosis 1,3mg/20gBB (7,21 x 10^{-3} M) memberikan pengaruh signifikan terhadap uji waktu perdarahan dan kuantifiksi jumlah darah mencit jantan (*Mus musculus*), sehingga berpotensi sebagai senyawa anti aggregasi trombosit yang ditunjukkan dengan semakin lama waktu perdarahan dan jumlah darah yang keluar.
2. Pemberian senyawa asam 2-(3-(klorometil)benzoiloksi))benzoat dosis 1,3mg/20gBB (7,21 x 10^{-3} M) memberikan pengaruh terhadap aggregasi trombosit dengan metode *flow cytometry* pada mencit jantan (*Mus musculus*) yang ditunjukkan dengan jumlah rata-rata % aggregasi trombosit yang rendah, sehingga berpotensi sebagai senyawa anti aggregasi trombosit.

5.2 Saran

Meningkatkan jumlah mencit sebagai subjek penelitian dan menggunakan metode *Fluorescence Activated Cell Sorting* (FACS). Metode FACS akan mampu mensortir jenis sel yang lebih spesifik, sehingga hasilnya akan lebih aku

DAFTAR PUSTAKA

Ballenger. L. 1999. Mus musculus. Animal Diversity Web. Museum of Zoology.University of Michigan. http://animaldiversity.ummz.umich.edu.musmusculus.com. [diakses 18 Januari 2013].

Bayat. B.. Tjahjono. Y.. Berghofer. H.. Werth. S.. Deckmyn. H.. De Meyer. S.F.. Sachs. U.J. and Santoso. S. 2016. Choline Transporter-Like Protein-2: New von Willebrand Factor-Binding Partner Involved in Antibody-Mediated Neutrophil Activation and Transfusion-Related Acute Lung Injury. *Arteriosclerosis. Thrombosis. and Vascular Biology*. **35**:1616-1622.

Bandari P. Bateman AC. Metha RL. Patel P. 2005. Mucosal Expression of Cyclooxygenase Isoforms 1 and 2 is Increased with Worsening damage to the Gastric Mucosa. *Histopatology*;**46/3**:280-286.

Biorbyt. 2010. Tools for Science: Rabbit Anti-PECAM-1. Catalog Number orb10315.

Born GVR. 1962. Aggregation of blood trombosits by adenosine diphosphate and its reversal. *Nature* **194**: 927–9.

Brunner and Suddarth. 2002. Buku Ajar *Keperawatan Medikal Bedah*. edisi **8** volume **2**. Jakarta : EGC.

Carlo Patrono. MD; Colin Baigent. MD; Jack Hirsh. MD. FCCP; and Gerald Ruth. MD. 2008. Anti trombosit Drugs. *CHEST*; **133**:1998-233.

Christofidou-Solomidou M. Nakada MT. Williams J. Muller WA. DeLisser HM. 1997. Neutrophil trombosit endothelial cell adhesion molecule-1 participates in neutrophil recruitment at inflammatory sites and is down-regulated after leukocyte extravasation. *J Immunol*;**158**:4872–4878.

Christopoulos C. Mattock C. Trombosit satellitism and alpha granule proteins. *Journal of Clinical pathology*. **44(9).** 1991: 788-9.

Clarke. E. G. C. 1969. *Isolation and Identification of Drugs: In Pharmaceuticals. Body Fluids. and Post-Modern Material*. The Pharmaceutical Press. London. 201. 539.

Climent Casals-Pascual. Steven Allen. Angela Allen. Oscar Kai. Brett Lowe. Arnab Pain. AndDavid J. Roberts. 2001. Short Report: Codon 125 Polymorphism Of Cd31 And SusceptibilityTo Malaria. *Am. J. Trop. Med. Hyg*.. **65(6)**. Pp. 736–737

Coller BS. Trombosit and thrombolytic therapy. *The New England Journal of Medicine*. **322 (1)**. 1990: 33-42.

Colman RW. Hirsh J. Marder VJ. Salzman EW. *Hemostasis and thrombosis. Basic principles and clinical practice*. 1 st ed. JB Lippincott company. Philadelphia 1982:381-2.

Darzynkiewicz. Z.. Roederer. M.. dan Tanke. H. J. 2004. *Methods in Cell Biology*. *Cytometry*. **75**.

Despopoulos. A. And Silbernagl. S. 2003. *Color Atlas of Physiology*. **5th** Ed. Thieme. Stuttgart. New York.

Elisabetta Dejana. Antonella Callioni. Antonio Quintana and Giovanni De Gaetano. 1979. *Bleeding Time in Laboratory Animals*. II-A Comparison of Different Assay Conditions in Rats. Thrombosis Research. **15**:191-197.

Elvers. M.. Herrmann. A.. Seizer. P.. Munzer. P.. Beck. S.. Schonberger. T.. Gawaz. M. 2012. Intracellular Cyclophilin A is an Important Ca2+ Regulator in Trombosits and Critically Involved in Arterial Thrombus Formation. *Blood*. **120(6)**. 1317-1326.

Emanuela Ricciotti. Garret A. FitzGerald. 2011. Prostaglandins and Inflammation. *Arterioscler Thromb Vasc* Biol;**31**:986-1000.

Flower R. 2003. What are all the things that aspirin does? This fascinating but simple and cheap drug has an assured future. BMJ;327;572-3.

Forsythe. N. *Fundamentals of Chemistry: General.Organic and Biological*. 2nd ed. A Division of Simon danSchuster. Inc. United Satates of America.1991.p: 415.

Gretzer B. Maricic N. respondek M. Schuligoi R. Peskar BM. 2001. Effects of Spesific Inhibition of Cyclo-Oxygenase-1 and Cyclo-Oxygenase-

2 in the Rat Stomach with Normal Mucosa and After Acid Challenge. *Br J Pharmacol* 132:1565-1573.

Hitesh M. Soni. A. M. V.. Akshyaya C. Rath.Sateesh Belemkar.dan Mukul R. Jain. 2014."Use of Aspirin in normalization of recombinant human erythropoietin-mediated hyper-reactivity of trombosits in rats." *Indian J Pharmacol* **46**:5.

Hoffbrand. AV. Pettit JE. *Trombosit. pembekuan darah dan hemostasis*. Dalam : Hoffbrand. AV. Pettit JE ed. Essential Haemtology. Terjemahan : darmawan L Ed **2**. EGC penerbit buku kedokteran. Jakarta 1987: 201-18.

Iris M. De Cuyper. Marjolein Meinders. Edith van de Vijver. Dirk de Korte. Leendert Porcelijn. Masja de Haas.Johannes A. Eble. Karl Seeger. Sergio Rutella. Daria Pagliara. Taco W. Kuijpers. Arthur J. Verhoeven. Timo K. van den Berg. and Laura Guti´errez. 2013. A novel flow cytometry–based trombosit aggregation assay. *Blood*. **121**: e70-e80.

Jagroop IA. Matsagas MI. Geroulakos G. Mikhailidis DP. 2007. The effect of clopidogrel. aspirin and both anti trombosit drugs on trombosit function in patients with peripheral arterial disease. *Trombosits.* **15(2):** 117-125.

JHU Joint Heath Safety and Environment. 2006. Use of Ether for Animal Anesthesia. Animal Care and Use Committee. John Hopkins Medicine.

Kiernan JA. 1990. Histological and histochemical methods: Theory and practice. 2nd ed. Pergamon.

Kimberly RP. Plotz PH. *Salicylates including aspirin and sulfasalazine*. In: Kelley WN. Harris ED. Ruddy S. Sledge CB. eds. Philadelphia. Pa: WB Saunders; 1989. pp:739-764.

Kunal Kanani . Sergio C. Gatoulis.and Michael Voelker. 2015.Influence of Differing Analgesic Formulations of Aspirin onPharmacokinetic Parameters. *Pharmaceutics **7***. 188-198.

Laine. Takeuchi K. Tarnawski A. 2008. Gastric Mucosal Defense and Cytoprotection *Gastroenterology*: Bench to Bedside.;135:41-60.

Lehman. J. W.. 2004. *Microscale Operational Organic Chemistry A Problem-Solving Approach to the Laboratory Course*. *Pearson Education. Inc.. NewJersey*. pp:698-699. 703-704.

Leonard A. Herzenberg. David Parks. Bita Sahaf.Omar Perez. Mario Roederer3and Leonore A. Herzenberg. 2002. The History and Future of the FluorescenceActivated Cell Sorter and Flow Cytometry:A View from Stanford. *Clinical Chemistry* 48:101819–1827.

Liebman H. M Chinowsky. J Valdin. G Kenoyer. D Feinstein. 1983. Increased fibrinolysis and amyloidosis. *Arch Intern Med* 143:678-682.

Martak R.. Bambang S.. Siti S.. Caroline dan Irwan S.. 2009. Synthesis of 4-Chloromethylbenzoyl Salicylic Acid and Its Analgesic Activity on Mice (Mus musculus). Poster Presentation in Bandung International Conference on Medical Chemistry. School of pharmacy: Bandung.

Martindale. 2005. *The Complete Drug Reference*. **34**th ed.. Pharmaceutical Press. London. 1157.

Miller RL. Insel PA. Melmon KL. *Inflammatory disorders*. In: Melmon KL. Morrelli HF. eds. *Clinical Pharmacology: Basic Principles in Therapeutics*. New York: Macmillan; 1978.pp: 657-708.

Nagelschmitz. J.. Blunck. M.. Kraetzschmar. J.. Ludwig. M.. Wensing. G. and Hohlfeld. T. 2014. Pharmacokinetics and Pharmacodynamics of acetylsalicylic acid after intravenous and oral administration to healthy volunteers. *Clinical Pharmacology*. **4(6)**: 51-59.

Neal. M. J. 2005. *Medical Pharmacology at a Glance*. **5th** Edition. Wiley-Blackwell.

*Newman PJ. Berndt MC. Gorski J. White GC. Lyman S. Paddock C. Muller WA. 1990. "PECAM-1 (CD31) cloning and relation to adhesion molecules of the immunoglobulin gene superfamily". Science. **247 (4947**): 1219–22.*

Neumüller. J.. Ellinger. A. and Wagner. T. 2015. Transmission Electron Microscopy of Trombosits from Apheresis and Buffy-Coat-Derived Trombosit Concentrates. *In Tech*. **11**: 255-284.

Novitasari A.. 2007. Sintesis Asam 3-klorobenzoil salisilat dan Penentuan ED_{50} Analgesik terhadap Mencit (Mus musculus). Skripsi Sarjana Farmasi. Unika Widya Mandala: Surabaya.

OECD. 2006. Repated dose orao toxicity test method. In: OECD *Guidelines for testing of chemicals*. No.**425**. Organization for Economic Cooperation and Development. Paris. France.

Parise. L. V. 2016. Introduction to a review series: megakaryocytes to trombosits in health and disease. *Blood*. **127**.

Penz. S. M.. Bernlochner. I.. Toth. O.. Lorenz. R.. Calatzis. A.. Siess. W. (2010). Selective and Rapid Monitoring of Dual Trombosit Inhibition by Aspirin and P2Y12 antagonists by Using Multiple Electrode Aggregometry. *Thrombosis Journal*. **8(9)**. 1-8.

Pradipta. I Putu Wahyu. *Efek senyawa asam 2-(3-(klorometil)benzoiloksi) benzoat terhadap aktivitas dan indeks organ tikus wistar jantan sebagai pelengkap uji toksisitas subkronis.* Skripsi Sarjana Farmasi Universitas Katolik Widya Mandala:Surabaya.2016. p: 70.

Praga. C.. Cortellaro. M.. and Pogliani. E. 1972. *Standardized bleeding time in the study of drugs interfering with trombosit function*. *Advances in Experimental Medicine and Biology*. 34:149.

Pratiwi V.D.. 2009. Sintesis Asam 3-klorobenzoil Salisilat dan Uji Aktivitas Analgesik pada Mencit (Mus musculus). Skripsi Sarjana Farmasi. Unika Widya Mandala Surabaya: Surabaya.

Price SA and Wilson LM. 2006. Pathophysiology: Clinical Concepts of Disease Processes. **6th**. New York: Mcgraw Hill. Pp. 417-26.

Rafael Consolin Chelucci. Luiz Antônio Dutra. Maria Elisa Lopes Pires. Thais Regina Ferreira de Melo. Priscila Longhin Bosquesi. Man Chin Chung and Jean Leandro dos Santos. 2014. Anti trombosit and Antithrombotic Activities of Non-Steroidal Anti-Inflammatory Drugs Containing an *N*-Acyl Hydrazone Subunit. *Molecules **19***. 2089-2099.

Rahajuningsih DS. Agregasi Trombosit. Patologi Klinik FKUI. Jakarta 1997: 1-11.

Reis RM. Reis-Filho JS. Filho AL. Tomarev S. Silva P. Lopes JM. 2005. Differential Prox-1 and CD-31 expression in mucousae. cutaneus and soft tissue vascular lesions and tumors. Pathology-Research and Practice 201: 771-776.

Ridwan Ahmad. 2012. Influence of Photoperiod on Stress Response and Reproduction Parameter of Male Mice (Mus musculus L.) of Swiss Webster Strain. Bandung. Vol **17** Nomor 1.

Robbins dan Kumar. 2007. *Buku Ajar Patologi Anatomi II*. Edisi VII. Alih Bahasa: Staf Pengajar Laboratorium Patologi Anatomi Fakultas Kedokteran Universitas Airlangga. Jakarta: Penerbit Buku Kedokteran EGC. **I(15).** p: 609-63.

Robinson. J.P.. 2004. Flow Cytometry. Encyclopedia of Biomaterials andBiomedical Engineering. 630-640.

Robinson. J.P.. 2006. Introduction to Flow Cytometry: Flow cytometry talks.Purdue University Cytometry Laboratories. http://www.cyto.purdue.edu/flowcyt/educated/pptslide.htm(diakses pada 23Mei 2014).

Romer LH. McLean NV. Yan HC. Daise M. Sun J. DeLisser HM. 1995. IFN-gamma and TNF-alpha induce redistribution of PECAM-1 (CD31) on human endothelial cells. *J Immunol*;**154**:6582–6592.

Shaun P. Jackson. 2007. The growing complexity of trombosit aggregation. *Blood* 109: 5087-5095

Sherma. Joseph 1991. *Basic Techniques. Materials and Apparatus*. *In Handbook of Thin-Layer Chromatography.*New York: Marcel Dekker. Inced.Vol. **55**. pp: 3-41.

Sibuea WH. Pangabean MM. Gultom SP. 2005. Ilmu Penyakit Dalam Edisi Ke-2. Jakarta: PT Rineka Cipta**. 1**:169-80.

Szu-Hao Kung. J. Nathan Hagstrom. Darrell Cass. Shing Jen Tai. Hui-Feng Lin. Darrel W. Stafford. dan Katherine A. High. 1998. *Human Factor IX Corrects the Bleeding Diathesis of Mice With Hemophilia B. Blood* **91(3)**;784-790.

Timothy D. Warner. Sven Nylander & Carl Whatling. 2011. Anti-trombosit therapy:cyclo- oxygenase inhibitionand the use of aspirin

withparticular regard to dualanti-trombosit therapy. *British Journal of Clinical Pharmacology* **72**:4/619–633.

Vane J.R. R. M. B. 2003. "The mechanism of action of aspirin." *Thrombosis Research* **110**:3.

Varga-Szabo. D.. Pleines. I.. Nieswandt. B. 2008. Cell Adhesion Mechanisms in Trombosits. *Arteriosclerosis. Thrombosis. and Vascular Biology*. **28(3)**. 403-412.

Véronique Latger-Cannard. O. F.. Sylvain Salignac. Thomas Pierre Lecompte . dan Nicole Schlegel. 2013. Trombosit Morphology Analysis. *Methods* in *molecular biology*. **992**: 18.

Wallace JL 2008. Prostaglandin. OAINS/Aspirin. and gastric Mucosal Protection: Why Doesn't the Stomach Digest it Self? *Physiol Rev*;**88**:1547-1565.