DAFTAR PUSTAKA

Ahmed, S., Zimba, O., & Gasparyan, A. Y. (2020). Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. *Clinical Rheumatology*, *39*(9), 2529–2543. https://doi.org/10.1007/s10067-020-05275-1

Aisyah, A. N., Permana, A. D., Wahyudin, E., Elim, D., Mujahid, M., Ikbal, I., Payung Datu, N. N., & Aswad, M. (2024). Formulation and evaluation of dissolving microneedle for transdermal delivery of piperine: the effect of polymers concentration. *Journal of Biomaterials Science, Polymer Edition*. https://doi.org/10.1080/09205063.2024.2320948

Albadr, A. A., Tekko, I. A., Vora, L. K., Ali, A. A., Laverty, G., Donnelly, R. F., & Thakur, R. R. S. (2022). Rapidly dissolving microneedle patch of amphotericin B for intracorneal fungal infections. *Drug Delivery and Translational Research*, *12*(4), 931–943. https://doi.org/10.1007/s13346-021-01032-2

Aliyah, Aswad, M., Hajrah, & Permana, A. D. (2021). Development and validation of spectrophotometric methods for quantitative determination of total phenolic and total flavonoid content of lyophilizate of the leaf of sweet potato leaf. *IOP Conference Series: Earth and Environmental Science*, *807*(2). https://doi.org/10.1088/1755-1315/807/2/022067

Almeida, M. J., Guillaumon, A. T., Miquelin, D., Joviliano, E. E., Hafner, L., Sobreira, M. L., Geiger, M. A., Moura, R., Raymundo, S., & Yoshida, W. B. (2019). Guidelines for superficial venous thrombosis. *Jornal Vascular Brasileiro*, *18*. https://doi.org/10.1590/1677-5449.180105

Amarnani, R., & Shende, P. (2022). Microneedles in diagnostic, treatment and theranostics: An advancement in minimally-invasive delivery system. *Biomedical Microdevices*, *24*(1). https://doi.org/10.1007/s10544-021-00604-w

Ananda, P. W. R., Elim, D., Zaman, H. S., Muslimin, W., Tunggeng, M. G. R., & Permana, A. D. (2021). Combination of transdermal patches and solid microneedles for improved transdermal delivery of primaquine. *International Journal of Pharmaceutics*, *609*. https://doi.org/10.1016/j.ijpharm.2021.121204

Andrade, G. P. V., Lima, M. A., De Souza, A. A., Fareed, J., Hoppensteadt, D. A., Santos, E. A., Chavante, S. F., Oliveira, F. W., Rocha, H. A. O., & Nader, H. B. (2013). A heparin-like compound isolated from a marine crab rich in glucuronic acid 2-O-sulfate presents low anticoagulant activity. *Carbohydrate Polymers*, *94*(1), 647–654. https://doi.org/10.1016/j.carbpol.2013.01.069

Anjani, Q. K., Permana, A. D., Cárcamo-Martínez, Á., Domínguez-Robles, J., Tekko, I. A., Larrañeta, E., Vora, L. K., Ramadon, D., & Donnelly, R. F. (2021). Versatility of hydrogel-forming microneedles in in vitro transdermal delivery of tuberculosis drugs. *European Journal of Pharmaceutics and Biopharmaceutics*, *158*, 294–312. https://doi.org/10.1016/j.ejpb.2020.12.003

Anjani, Q. K., Sabri, A. H. Bin, Utomo, E., Domínguez-Robles, J., & Donnelly, R. F. (2022). Elucidating the Impact of Surfactants on the Performance of Dissolving Microneedle Array Patches. *Molecular Pharmaceutics*, *19*(4), 1191–1208. https://doi.org/10.1021/acs.molpharmaceut.1c00988

A.R.Abubakar, & Mainul Haque. (2020). Preparation of Medicinal Plants: Basic Extraction and Fractionation Procedures for Experimental Purposes. *Journal of Pharmacy & Bioallied Sciences*, *12*(1), 1–10.

Arista Indraswari. (2008). *Optimasi Pembuatan Ekstrak Daun Dewandaru (Eugenia uniflora L.) Menggunakan Metode Maserasi dengan Parameter Kadar Total Senyawa Fenolik dan Flavonoid*.

Arshad, M. S., Zafar, S., Zahra, A. T., Zaman, M. H., Akhtar, A., Kucuk, I., Farhan, M., Chang, M. W., & Ahmad, Z. (2021). Fabrication and characterisation of self-applicating heparin sodium microneedle patches. *Journal of Drug Targeting*, *29*(1), 60–68. https://doi.org/10.1080/1061186X.2020.1795180

Ascenso, A., Pinho, S., Eleutério, C., Praça, F. G., Bentley, M. V. L. B., Oliveira, H., Santos, C., Silva, O., & Simões, S. (2013). Lycopene from tomatoes: Vesicular nanocarrier formulations for dermal delivery. *Journal of Agricultural and Food Chemistry*, *61*(30), 7284–7293. https://doi.org/10.1021/jf401368w

Aung, N. N., Ngawhirunpat, T., Rojanarata, T., Patrojanasophon, P., Opanasopit, P., & Pamornpathomkul, B. (2021). Enhancement of transdermal delivery of resveratrol using Eudragit and polyvinyl pyrrolidone-based dissolving microneedle patches. *Journal of Drug Delivery Science and Technology*, *61*. https://doi.org/10.1016/j.jddst.2020.102284

Balestrin, L. A., Kreutz, T., Fachel, F. N. S., Bidone, J., Gelsleichter, N. E., Koester, L. S., Bassani, V. L., Braganhol, E., Dora, C. L., & Teixeira, H. F. (2021). Achyrocline satureioides (Lam.) dc (asteraceae) extract-loaded nanoemulsions as a promising topical wound healing delivery system: In vitro assessments in human keratinocytes (hacat) and het-cam irritant potential. *Pharmaceutics*, *13*(8). https://doi.org/10.3390/pharmaceutics13081241

Barile, F. A. (2010). Validating and troubleshooting ocular in vitro toxicology tests. *Journal of Pharmacological and Toxicological Methods*, *61*(2), 136–145. https://doi.org/10.1016/j.vascn.2010.01.001

Barung, E. N., Kalonio, D. E., Banne, Y., & Kambuno, N. T. (2021). Anticancer activities of sesewanua leaf extracts (Clerodendrum fragrans (vent.) willd) against a549 lung cancer cell. *Open Access Macedonian Journal of Medical Sciences*, *9*, 1226–1230. https://doi.org/10.3889/oamjms.2021.7484

Batista-Duharte, A., Jorge Murillo, G., Pérez, U. M., Tur, E. N., Portuondo, D. F., Martínez, B. T., Téllez-Martínez, D., Betancourt, J. E., & Pérez, O. (2016). The Hen's Egg Test on Chorioallantoic Membrane: An Alternative Assay for the Assessment of the Irritating Effect of Vaccine Adjuvants. *International Journal of Toxicology*, *35*(6), 627–633. https://doi.org/10.1177/1091581816672187

Bauersachs, R., Zeymer, U., Brière, J. B., Marre, C., Bowrin, K., & Huelsebeck, M. (2019). Burden of Coronary Artery Disease and Peripheral Artery Disease: A Literature Review. *Cardiovascular Therapeutics*, *2019*. https://doi.org/10.1155/2019/8295054

Bergfeld, F. A. C. P. ;, Donald, V., Belsito, D. E., Cohen, C. D., Klaassen, A. E., Rettie, D., Ross, T. J., Slaga, P. W., Snyder, D. V. M., & Tilton, S. C. (2024). *Safety*

Assessment of Fatty Amphocarboxylates as Used in Cosmetics. www.cir-safety.org

Brodsky, S., Eikelboom, J., & Hebert, L. A. (2018). *Anticoagulant-Related Nephropathy*. 1–7. https://doi.org/10.1681/ASN.2018070741

Bunaciu, A. A., Udriştioiu, E. gabriela, & Aboul-Enein, H. Y. (2015). X-Ray Diffraction: Instrumentation and Applications. In *Critical Reviews in Analytical Chemistry* (Vol. 45, Issue 4, pp. 289–299). Taylor and Francis Ltd. https://doi.org/10.1080/10408347.2014.949616

Butarbutar, R. S. (2013). Pengaruh Aktivitas Wisatawan Terhadap Keanekaragaman Tumbuhan Di Sulawesi. *Journal of Indonesian Tourism and Development Studies*, *1*(2), 87–96. https://dokumen.tips/download/link/jitode-vol-1-no-2-2013pdf

Camire, R. M. (2021). Blood coagulation factor X: molecular biology, inherited disease, and engineered therapeutics. *Journal of Thrombosis and Thrombolysis*, *52*(2), 383–390. https://doi.org/10.1007/s11239-021-02456-w

Chee, Y. L. (2014). Coagulation. *Journal of the Royal College of Physicians of Edinburgh*, *44*(1), 42–45. https://doi.org/10.4997/JRCPE.2014.110

Chekalina, N., Burmak, Y., Petrov, Y., Borisova, Z., Manusha, Y., Kazakov, Y., & Kaidashev, I. (2018). Quercetin reduces the transcriptional activity of NF-kB in stable coronary artery disease. *Indian Heart Journal*, *70*(5), 593–597. https://doi.org/10.1016/j.ihj.2018.04.006

Cheng, A., Sun, W., Xing, M., Zhang, S., & Gao, Y. (2022). The hygroscopicity of polymer microneedles on the performance of dissolving behavior for transdermal delivery. *International Journal of Polymeric Materials and Polymeric Biomaterials*, *71*(1), 72–78. https://doi.org/10.1080/00914037.2020.1798442

Chi, J., Sun, L., Cai, L., Fan, L., Shao, C., Shang, L., & Zhao, Y. (2021). Chinese herb microneedle patch for wound healing. *Bioactive Materials*, *6*(10), 3507–3514. https://doi.org/10.1016/j.bioactmat.2021.03.023

Choi, J. H., Kim, D. W., Park, S. E., Lee, H. J., Kim, K. M., Kim, K. J., Kim, M. K., Kim, S. J., & Kim, S. (2015). Anti-thrombotic effect of rutin isolated from Dendropanax morbifera Leveille. *Journal of Bioscience and Bioengineering*, *120*(2), 181–186. https://doi.org/10.1016/j.jbiosc.2014.12.012

Choxi, R., Kapoor, K., MacKman, N., & Jovin, I. S. (2022). Direct Oral Anticoagulants and Coronary Artery Disease. *Arteriosclerosis, Thrombosis, and Vascular Biology*, *42*(5), 553–564. https://doi.org/10.1161/ATVBAHA.121.317171

Cong, J., Zheng, Z., Fu, Y., Chang, Z., Chen, C., Wu, C., Pan, X., Huang, Z., & Quan, G. (2024). Spatiotemporal fate of nanocarriers-embedded dissolving microneedles: the impact of needle dissolving rate. *Expert Opinion on Drug Delivery*, *21*(6), 965–974. https://doi.org/10.1080/17425247.2024.2375385

De Pablo-Moreno, J. A., Liras, A., & Revuelta, L. (2022). Standardization of Coagulation Factor V Reference Intervals, Prothrombin Time, and Activated Partial Thromboplastin Time in Mice for Use in Factor V Deficiency Pathological

Models. *Frontiers in Veterinary Science*, *9*. https://doi.org/10.3389/fvets.2022.846216

Dehghani, F., Vafa, M., Ebrahimkhani, A., Găman, M. A., & Sezavar Seyedi Jandaghi, S. H. (2023). Effects of quercetin supplementation on endothelial dysfunction biomarkers and depression in post-myocardial infarction patients: A double-blind, placebo-controlled, randomized clinical trial. *Clinical Nutrition ESPEN*, *56*, 73–80. https://doi.org/10.1016/j.clnesp.2023.04.019

Departemen Kesehatan Republik Indonesia. (2017). *Herb Pharmacopheia of Indonesia* (II). Health Department of Indonesia.

Ding, W., Shao, X., Ding, S., Du, Y., Hong, W., Yang, Q., Song, Y., & Yang, G. (2024). Natural herb wormwood-based microneedle array for wound healing. *Drug Delivery and Translational Research*. https://doi.org/10.1007/s13346-024-01520-1

Dobrovolskaia, M. A., & McNeil, S. E. (2013). Understanding the correlation between in vitro and in vivo immunotoxicity tests for nanomedicines. *Journal of Controlled Release*, *172*(2), 456–466. https://doi.org/10.1016/j.jconrel.2013.05.025

Donnelly, R. F., T.R. Singh, D.I.J Morrow, & A.D. Woolfson. (2012). *Microneedle-mediated and Intradermal*. Wiley-Blackwell.

Elim, D., Fitri, A. M. N., Mahfud, M. A. S. ban, Afika, N., Sultan, N. A. F., Hijrah, Asri, R. M., & Permana, A. D. (2023). Hydrogel forming microneedle-mediated transdermal delivery of sildenafil citrate from polyethylene glycol reservoir: An ex vivo proof of concept study. *Colloids and Surfaces B: Biointerfaces*, *222*. https://doi.org/10.1016/j.colsurfb.2022.113018

Enggi, C. K., Satria, M. T., Nirmayanti, N., Usman, J. T., Nur, J. F., Asri, R. M., Djide, N. J. N., & Permana, A. D. (2023). Improved transdermal delivery of valsartan using combinatorial approach of polymeric transdermal hydrogels and solid microneedles: an ex vivo proof of concept investigation. *Journal of Biomaterials Science, Polymer Edition*, *34*(3), 334–350. https://doi.org/10.1080/09205063.2022.2121590

Fikriyah, Y. U., & Nasution, R. S. (2021). Analisis Kadar Air dan Kadar Abu pada Teh Hitam yang Dijual di Pasaran dengan Menggunakan Metode Gravimetri. *Amina*, *3*(2), 50–54.

Frydman, G. H., Olaleye, D., Annamalai, D., Layne, K., Yang, I., Kaafarani, H. M. A., & Fox, J. G. (2020). Manuka honey microneedles for enhanced wound healing and the prevention and/or treatment of Methicillin-resistant Staphylococcus aureus (MRSA) surgical site infection. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-70186-9

Greco, I., Molchanova, N., Holmedal, E., Jenssen, H., Hummel, B. D., Watts, J. L., Håkansson, J., Hansen, P. R., & Svenson, J. (2020). Correlation between hemolytic activity, cytotoxicity and systemic in vivo toxicity of synthetic antimicrobial peptides. *Scientific Reports*, *10*(1). https://doi.org/10.1038/s41598-020-69995-9

Gryglewski, R. J., Korbut, R., Robak, J., & Swies, J. (1987). On the Mechanism of Antithrombotic Action of Flavonoids. *Biochemical Pharmacology*, *36*(3), 317–322.

Gustari, R. A. (2021). *Uji Daya Hambat Fraksi n-Heksan, Etil Asetat, dan Air dari Ekstrak Etanol Bunga Cengkeh (Syzygium aromaticum (L.) Merrill & Perry) terhadap Bakteri Staphylococcus epidermidis*. Universitas Jenderal Achmad Yani.

Haghniaz, R., Kim, H. J., Montazerian, H., Baidya, A., Tavafoghi, M., Chen, Y., Zhu, Y., Karamikamkar, S., Sheikhi, A., & Khademhosseini, A. (2023). Tissue adhesive hemostatic microneedle arrays for rapid hemorrhage treatment. *Bioactive Materials*, *23*, 314–327. https://doi.org/10.1016/j.bioactmat.2022.08.017

Hanny Ferry Fernanda, M., Suryandari, M., Puji Lestari Sudarwati Program Studi Diploma Tiga Farmasi, T., & Farmasi Surabaya, A. (2021). Fraksinasi dan Identifikasi Ektrak Daun Mitragyna Speciosa Menggunakan Metode Kromatografi. *FARMASIS: Jurnal Sains Farmasi*, *2*(2).

Hanumegowda, S. M., Srinivasa, C., Shivaiah, A., M.Venkatappa, M., Santhosh, S., R, R., Gonchigar, S. J., & Sannaningaiah, D. (2023). Antioxidant and Antithrombotic Activities of Kenaf Seed (Hibiscus cannabinus) Coat Ethanol Extract in Sprague Dawley Rats. *Applied Biochemistry and Biotechnology*, *195*(2), 772–800. https://doi.org/10.1007/s12010-022-04144-8

Hasan, N., Nur Fatimah, S., Raihan, M., Zaenal Mustopa, A., Irawan, H., & Rahmat Haedar, J. (2023). Isolasi dan Identifikasi Ethyl p-Methoxycinnamate (EPMC) dari Rimpang Kencur (Kaempheria galanga) sebagai Kandidat Senyawa Antikanker. *Majalah Farmasi Dan Farmakologi*, *27*(3), 140–146. https://doi.org/10.20956/mff.v27i3.28335

He, C., Fang, Z., Wu, H., Li, X., Cheng, L., Wen, Y., & Lin, J. (2024). A flexible and dissolving traditional Chinese medicine microneedle patch for sleep-aid intervention. *Heliyon*, *10*(12). https://doi.org/10.1016/j.heliyon.2024.e33025

Hidayatullah, T., Nasir, F., Khattak, M. A., Pervez, S., Almalki, W. H., Alasmari, F., Maryam, G. e., Rahman, A. ur, & Ali, A. T. (2023). Hybrid Dissolving Microneedle-Mediated Delivery of Ibuprofen: Solubilization, Fabrication, and Characterization. *Pharmaceuticals*, *16*(5). https://doi.org/10.3390/ph16050677

Himawan, A., Anjani, Q. K., Detamornrat, U., Vora, L. K., Permana, A. D., Ghanma, R., Naser, Y., Rahmawanty, D., Scott, C. J., & Donnelly, R. F. (2023). Multifunctional low temperature-cured PVA/PVP/citric acid-based hydrogel forming microarray patches: Physicochemical characteristics and hydrophilic drug interaction. *European Polymer Journal*, *186*. https://doi.org/10.1016/j.eurpolymj.2023.111836

Huliselan, Y. M., Runtuwene, M. R. J., & Wewengkang, D. S. (2015). Aktivitas Antioksidan Ekstrak Etanol, Etil Asetat, dan n-Hexan dari Daun Sesewanua (Clerodendron squamatum Vahl.). *PHARMACON Jurnal Ilmiah Farmasi-UNSRAT*, *4*(3).

Irawati, D; Kinho, J. (2015). Keragaman Tumbuhan Berkhasiat Obat di hutan Pantai Cagar Alam Tangkoko. *Jurnal Wasian*, *2*(1), 01–08.

Jumiarni, W. O., & Komalasari, O. (2017). Inventory of Medicines Plant As Utilized By Muna Tribe in Kota Wuna Settlement. *Majalah Obat Tradisional*, *22*(1), 45. https://doi.org/10.22146/tradmedj.24314

Kabashneh, S., Singh, V., & Alkassis, S. (2020). A Comprehensive Literature Review on the Management of Distal Deep Vein Thrombosis. *Cureus*, *12*(5), 10–13. https://doi.org/10.7759/cureus.8048

Kaharudin, C. L., Afkauni, A. A., Pramudyansyah, A. Y., & Prasetyo, N. (2022). Penambatan Molekul dan Simulasi Dinamika Molekular Kandungan Minyak Kayu Manis dan Minyak Serai Dapur Sebagai Antibakteri Methicillin Resistant Staphylococcus aureus. *ALCHEMY Jurnal Penelitian Kimia*, *18*(2), 140. https://doi.org/10.20961/alchemy.18.2.54997.140-147

Kalaitzopoulos, D. R., Panagopoulos, A., Samant, S., Ghalib, N., Kadillari, J., Daniilidis, A., Samartzis, N., Makadia, J., Palaiodimos, L., Kokkinidis, D. G., & Spyrou, N. (2022). Management of venous thromboembolism in pregnancy. In *Thrombosis Research* (Vol. 211, pp. 106–113). Elsevier Ltd. https://doi.org/10.1016/j.thromres.2022.02.002

Kaneider, N. C., Mosheimer, B., Günther, A., Feistritzer, C., & Wiedermann, C. J. (2010a). *Enhancement of fibrinogen-triggered pro-coagulant activation of monocytes in vitro by matrix metalloproteinase-9*. http://www.thrombosisjournal.com/content/8/1/2

Kaneider, N. C., Mosheimer, B., Günther, A., Feistritzer, C., & Wiedermann, C. J. (2010b). *Enhancement of fibrinogen-triggered pro-coagulant activation of monocytes in vitro by matrix metalloproteinase-9*. http://www.thrombosisjournal.com/content/8/1/2

Kathuria, H., Lim, D., Cai, J., Chung, B. G., & Kang, L. (2020). Microneedles with Tunable Dissolution Rate. *ACS Biomaterials Science and Engineering*, *6*(9), 5061–5068. https://doi.org/10.1021/acsbiomaterials.0c00759

Kementerian Kesehatan RI. (2017). *Farmakope Herbal*.

Kenne, E., Nickel, K. F., Long, A. T., Fuchs, T. A., Stavrou, E. X., Stahl, F. R., & Renné, T. (2015). Factor XII: A novel target for safe prevention of thrombosis and inflammation. *Journal of Internal Medicine*, *278*(6), 571–585. https://doi.org/10.1111/joim.12430

Khandker, S. S., Alam, M., Uddin, F., Shapla, U. M., Lubna, N., Mazumder, T. A., Marzan, M., Mondal, M., Khalil, M. I., Karim, N., Shakil, M. S., & Hossen, M. S. (2022). Subchronic Toxicity Study of Alternanthera philoxeroides in Swiss Albino Mice Having Antioxidant and Anticoagulant Activities. *Journal of Toxicology*, *2022*. https://doi.org/10.1155/2022/8152820

Khouya, T., Ramchoun, M., Amrani, S., Harnafi, H., Rouis, M., Couchie, D., Simmet, T., & Alem, C. (2020). Anti-inflammatory and anticoagulant effects of

polyphenol-rich extracts from Thymus atlanticus: An in vitro and in vivo study. *Journal of Ethnopharmacology*, *252*. https://doi.org/10.1016/j.jep.2019.112475

Kim, Y., Lee, H., Park, H. J., Kim, M. K., Kim, Y. Il, Kim, H. J., Bae, S. K., Kim, Y. J., & Bae, M. K. (2023). Hispidulin Inhibits the Vascular Inflammation Triggered by Porphyromonas gingivalis Lipopolysaccharide. *Molecules*, *28*(18). https://doi.org/10.3390/molecules28186717

Ko, E. Y., Nile, S. H., Jung, Y. S., & Keum, Y. S. (2018). Antioxidant and antiplatelet potential of different methanol fractions and flavonols extracted from onion (Allium cepa L.). *3 Biotech*, *8*(3). https://doi.org/10.1007/s13205-018-1184-4

Konstantinides, S. V., Meyer, G., Bueno, H., Galié, N., Gibbs, J. S. R., Ageno, W., Agewall, S., Almeida, A. G., Andreotti, F., Barbato, E., Baumbach, A., Beygui, F., Carlsen, J., De Carlo, M., Delcroix, M., Subias, P. E., Gaine, S., Goldhaber, S. Z., Gopalan, D., … Pepke-Zaba, J. (2020). 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European respiratory society (ERS). In *European Heart Journal* (Vol. 41, Issue 4, pp. 543–603). Oxford University Press. https://doi.org/10.1093/eurheartj/ehz405

Kopec, A. K., Spada, A. P., Contreras, P. C., Mackman, N., & Luyendyk, J. P. (2018a). Caspase inhibition reduces hepatic tissue factor-driven coagulation in vitro and in vivo. *Toxicological Sciences*, *162*(2), 396–405. https://doi.org/10.1093/toxsci/kfx268

Kopec, A. K., Spada, A. P., Contreras, P. C., Mackman, N., & Luyendyk, J. P. (2018b). Caspase inhibition reduces hepatic tissue factor-driven coagulation in vitro and in vivo. *Toxicological Sciences*, *162*(2), 396–405. https://doi.org/10.1093/toxsci/kfx268

Kristina Enggi, C., Sulistiawati, S., Stephanie, S., Tangdilintin, F., Anas Achmad, A., Adelia Putri, R., Burhanuddin, H., Arjuna, A., Manggau, M. A., & Dian Permana, A. (2023). Development of probiotic loaded multilayer microcapsules incorporated into dissolving microneedles for potential improvement treatment of vulvovaginal candidiasis: A proof of concept study. *Journal of Colloid and Interface Science*, *648*, 203–219. https://doi.org/10.1016/j.jcis.2023.05.165

Kwame Adosraku, R., Kyekyeku, J. O., & Attah, I. Y. (2013). Characterization and HPLC Quantification of Piperine Isolataed from Piper Guineense (Fam.Piperaceae). *International Journal of Pharmacy and Pharmaceuticae Sciences*, *5*(1).

Lamm, M. E., Song, L., Wang, Z., Rahman, M. A., Lamm, B., Fu, L., & Tang, C. (2019). Tuning Mechanical Properties of Biobased Polymers by Supramolecular Chain Entanglement. *Macromolecules*, *52*(22), 8967–8975. https://doi.org/10.1021/acs.macromol.9b01828

Lee, I. C., He, J. S., Tsai, M. T., & Lin, K. C. (2015). Fabrication of a novel partially dissolving polymer microneedle patch for transdermal drug delivery. *Journal of Materials Chemistry B*, *3*(2), 276–285. https://doi.org/10.1039/c4tb01555j

Lelita, R., Gunawan, R., & Astuti, W. (2017). Studi Docking Molekular Senyawa Kuersetin, kalkon dan Turunannya sebagai inhibitor Sel Kanker Payudara MC-7 (Michigan Cancer Foundation-7). *Jurnal Atomik*, *1*(2). www.pdb.org.

Lip, G. Y. H., Collet, J. P., Haude, M., Byrne, R., Chung, E. H., Fauchier, L., Halvorsen, S., Lau, D., Lopez-Cabanillas, N., Lettino, M., Marin, F., Obel, I., Rubboli, A., Storey, R. F., Valgimigli, M., Huber, K., Potpara, T., Lundqvist, C. B., Crijns, H., … Jardine, R. (2019). 2018 Joint European consensus document on the management of antithrombotic therapy in atrial fibrillation patients presenting with acute coronary syndrome and/or undergoing percutaneous cardiovascular interventions: A joint consensus document of the Europ. *Europace*, *21*(2), 192–193. https://doi.org/10.1093/europace/euy174

Liu, H., Beck, T. N., Golemis, E. A., & Serebriiskii, I. G. (2014). Integrating in silico resources to map a signaling network. *Methods in Molecular Biology*, *1101*, 197–245. https://doi.org/10.1007/978-1-62703-721-1_11

Liu, K., Zhao, F., Yan, J., Xia, Z., Jiang, D., & Ma, P. (2020). Hispidulin: A promising flavonoid with diverse anti-cancer properties. In *Life Sciences* (Vol. 259). Elsevier Inc. https://doi.org/10.1016/j.lfs.2020.118395

Lopez, M., Kopec, A. K., Joshi, N., Geddings, J. E., Cline, H., Towery, K. L., Rockwell, C. E., Mackman, N., & Luyendyk, J. P. (2014a). Fas-induced apoptosis increases hepatocyte tissue factor procoagulant activity in vitro and in vivo. *Toxicological Sciences*, *141*(2), 453–464. https://doi.org/10.1093/toxsci/kfu139

Lopez, M., Kopec, A. K., Joshi, N., Geddings, J. E., Cline, H., Towery, K. L., Rockwell, C. E., Mackman, N., & Luyendyk, J. P. (2014b). Fas-induced apoptosis increases hepatocyte tissue factor procoagulant activity in vitro and in vivo. *Toxicological Sciences*, *141*(2), 453–464. https://doi.org/10.1093/toxsci/kfu139

Lutsey, P. L., & Zakai, N. A. (2023). Epidemiology and prevention of venous thromboembolism. In *Nature Reviews Cardiology* (Vol. 20, Issue 4, pp. 248–262). Nature Research. https://doi.org/10.1038/s41569-022-00787-6

Mahfufah, U., Fitri Sultan, N. A., Nurul Fitri, A. M., Elim, D., Sya'ban Mahfud, M. A., Wafiah, N., Ardita Friandini, R., Chabib, L., Aliyah, & Permana, A. D. (2023). Application of multipolymers system in the development of hydrogel-forming microneedle integrated with polyethylene glycol reservoir for transdermal delivery of albendazole. *European Polymer Journal*, *183*. https://doi.org/10.1016/j.eurpolymj.2022.111762

Mentari, I. A., Wirnawati, W., & Putri, M. R. (2020). Karakterisasi Simplisia dan Ekstrak Daun bandotan (Ageratum conyzoides L) sebagai Kandidat Obat Karies Gigi. *Jurnal Ilmiah Ibnu Sina (JIIS): Ilmu Farmasi Dan Kesehatan*, *5*(1), 1–9. https://doi.org/10.36387/jiis.v5i1.346

Migues, V. H., David, J. M., & David, J. P. (2020). Determination of polyphenols in: Schinus terebinthifolius Raddi bark extracts and chemometric analysis. *Analytical Methods*, *12*(11), 1478–1485. https://doi.org/10.1039/d0ay00197j

Milling, T. J., & Ziebell, C. M. (2020). Trends in Cardiovascular Medicine A review of oral anticoagulants , old and new , in major bleeding and the need for urgent

surgery R. *Trends in Cardiovascular Medicine*, *30*(2), 86–90. https://doi.org/10.1016/j.tcm.2019.03.004

Młynarska, E., Hajdys, J., Czarnik, W., Fularski, P., Leszto, K., Majchrowicz, G., Lisińska, W., Rysz, J., & Franczyk, B. (2024). The Role of Antioxidants in the Therapy of Cardiovascular Diseases—A Literature Review. In *Nutrients* (Vol. 16, Issue 16). Multidisciplinary Digital Publishing Institute (MDPI). https://doi.org/10.3390/nu16162587

Mondong, F. R., Sangi, M. S., & Kumaunang, M. (2015). Skrining Fitokimia dan Uji Aktivitas Antioksidan Ekstrak Etanol Daun Patikan Emas (Euprorbia prunifolia Jacq.) dan Bawang Laut (Proiphys amboinensis (L.) Herb). *JURNAL MIPA UNSRAT ONLINE*, *4*(1), 81–87.

Mudjahid, M., Nainu, F., Utami, R. N., Sam, A., Marzaman, A. N. F., Roska, T. P., Asri, R. M., Himawan, A., Donnelly, R. F., & Permana, A. D. (2022). Enhancement in Site-Specific Delivery of Chloramphenicol Using Bacterially Sensitive Microparticle Loaded into Dissolving Microneedle: Potential for Enhanced Effectiveness Treatment of Cellulitis. *ACS Applied Materials and Interfaces*. https://doi.org/10.1021/acsami.2c16857

Mudjahid, M., Sulistiawati, Meidianto Asri, R., Nainu, F., & Dian Permana, A. (2023). Validation of spectrophotometric method to quantify chloramphenicol in fluid and rat skin tissue mimicking infection environment: Application to in vitro release and ex vivo dermatokinetic studies from dissolving microneedle loaded microparticle sensitive bacteria. *Spectrochimica Acta - Part A: Molecular and Biomolecular Spectroscopy*, *291*. https://doi.org/10.1016/j.saa.2023.122374

Murakami, Y., Tripathi, L. P., Prathipati, P., & Mizuguchi, K. (2017). Network analysis and in silico prediction of protein–protein interactions with applications in drug discovery. In *Current Opinion in Structural Biology* (Vol. 44, pp. 134–142). Elsevier Ltd. https://doi.org/10.1016/j.sbi.2017.02.005

Murciano, J. C., Muro, S., Koniaris, L., Christofidou-Solomidou, M., Harshaw, D. W., Albelda, S. M., Granger, D. N., Cines, D. B., & Muzykantov, V. R. (2003). ICAM-directed vascular immunotargeting of antithrombotic agents to the endothelial luminal surface. *Blood*, *101*(10), 3977–3984. https://doi.org/10.1182/blood-2002-09-2853

Muro, S., & Muzykantov, V. R. (2005). Targeting of Antioxidant and Anti-Thrombotic Drugs to Endothelial Cell Adhesion Molecules. In *Current Pharmaceutical Design* (Vol. 11).

Murphy, S. L., Kockanek, K. D., Arias, E., & Xu, J. (2020). Mortality in the United States, 2018. *NCHS Data Brief*, *355*, 1–8.

Muthukumarasamy, R., Kamaruddin, A. F., & Radhakrishnan, S. (2018). Comparative evaluation of different extraction methods for antioxidant activity from Citrus hystrix peels. *Drug Invention Today*, *10*(8), 1458–1462.

Mutmainnah, P. A., Hakim, A., Rudyat, L., & Savalas, T. (2017). Identifikasi Senyawa Turunan Hasil Fraksinasi Kayu Akar Artocarpus odoratissimus. *Jurnal Penelitian Pendidikan IPA (JPPIPA)*, *3*(2), 26–32.

Nandiyanto, A. B. D., Oktiani, R., & Ragadhita, R. (2019). How to read and interpret ftir spectroscope of organic material. *Indonesian Journal of Science and Technology*, *4*(1), 97–118. https://doi.org/10.17509/ijost.v4i1.15806

Ning, X., Wiraja, C., Chew, W. T. S., Fan, C., & Xu, C. (2021). Transdermal delivery of Chinese herbal medicine extract using dissolvable microneedles for hypertrophic scar treatment. *Acta Pharmaceutica Sinica B*, *11*(9), 2937–2944. https://doi.org/10.1016/j.apsb.2021.03.016

Nonke, E., Kaunang, S., & Semuel, M. Y. (2017). Botanical and phytochemical constituents of several medicinal plants from mount Klabat north Minahasa. *Journal of Medicinal Plants Studies*, *5*(2), 29–35. http://www.plantsjournal.com/archives/2017/vol5issue2/PartA/5-1-68-348.pdf

Nur, S., Sami, F. J., Awaluddin, A., & Afsari, M. I. A. (2019). Korelasi Antara Kadar Total Flavonoid dan Fenolik dari Ekstrak dan Fraksi Daun Jati Putih (Gmelina Arborea Roxb.) Terhadap Aktivitas Antioksidan. *Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)*, *5*(1), 33–42. https://doi.org/10.22487/j24428744.2019.v5.i1.12034

Nurhayati, E., Sukma, A. U., & Wahdaniah. (2018). JURNAL LABORATORIUM KHATULISTIWA Pengaruh Ekstrak Kulit Jeruk Bali (Cirus maxime Merr.) Sebagai Antikoagulan Dengan Metode Clotting Time (Lee and White). *Jurnal Laboratorium Kesehatan*, *2*(1).

Nurul Fitri, A. M., Elim, D., Sya'ban Mahfud, M. A., Fitri Sultan, N. A., Saputra, M. D., Afika, N., Friandini, R. A., Natsir Djide, N. J., & Permana, A. D. (2023). Polymeric hydrogel forming microneedle-mediated transdermal delivery of sildenafil citrate from direct-compressed tablet reservoir for potential improvement of pulmonary hypertension therapy. *International Journal of Pharmaceutics*, *631*. https://doi.org/10.1016/j.ijpharm.2022.122549

O'Brien, K. A., Stojanovic-Terpo, A., Hay, N., & Du, X. (2011a). An important role for Akt3 in platelet activation and thrombosis. *Blood*, *118*(15), 4215–4223. https://doi.org/10.1182/blood-2010-12-323204

O'Brien, K. A., Stojanovic-Terpo, A., Hay, N., & Du, X. (2011b). An important role for Akt3 in platelet activation and thrombosis. *Blood*, *118*(15), 4215–4223. https://doi.org/10.1182/blood-2010-12-323204

Ohkura, N., Taniguchi, M., Oishi, K., Inoue, K., & Ohta, M. (2022). Angelica keiskei (Ashitaba) has potential as an antithrombotic health food. *Food Research*, *6*(2), 18–24. https://doi.org/10.26656/fr.2017.6(2).121

Paar, M., Rossmann, C., Nusshold, C., Wagner, T., Schlagenhauf, A., Leschnik, B., Oettl, K., Koestenberger, M., Cvirn, G., & Hallström, S. (2017a). Anticoagulant action of low, physiologic, and high albumin levels in whole blood. *PLoS ONE*, *12*(8). https://doi.org/10.1371/journal.pone.0182997

Paar, M., Rossmann, C., Nusshold, C., Wagner, T., Schlagenhauf, A., Leschnik, B., Oettl, K., Koestenberger, M., Cvirn, G., & Hallström, S. (2017b). Anticoagulant action of low, physiologic, and high albumin levels in whole blood. *PLoS ONE*, *12*(8). https://doi.org/10.1371/journal.pone.0182997

Pangalo, P., Sapiun, Z., Imran, A. K., Muindar, Sabaruddin, Wicita, P. S., Ysrafil, & Mohamad, F. (2022). Optimation of Dimethyl Sulfoxide as an Enhancer on Ex Vivo Penetration of Sesewanua (Clerodendrum fragrans WILD.) Leaf Extracts Emulgel (In Press). *International Journal of Applied Pharmaceutics*, *May*.

Parrilla, M., Vanhooydonck, A., Johns, M., Watts, R., & De Wael, K. (2023). 3D-printed microneedle-based potentiometric sensor for pH monitoring in skin interstitial fluid. *Sensors and Actuators B: Chemical*, *378*. https://doi.org/10.1016/j.snb.2022.133159

Permana, A. D. (n.d.). *Dissolving Microneedle Formulation of Ceftriaxone: Effect of Polymer Concentrations on Characterisation and Ex Vivo Permeation Study*.

Permana, A. D., Anjani, Q. K., Sartini, Utomo, E., Volpe-Zanutto, F., Paredes, A. J., Evary, Y. M., Mardikasari, S. A., Pratama, M. R., Tuany, I. N., & Donnelly, R. F. (2021). Selective delivery of silver nanoparticles for improved treatment of biofilm skin infection using bacteria-responsive microparticles loaded into dissolving microneedles. *Materials Science and Engineering C*, *120*. https://doi.org/10.1016/j.msec.2020.111786

Permana, A. D., McCrudden, M. T. C., & Donnelly, R. F. (2019). Enhanced intradermal delivery of nanosuspensions of antifilariasis drugs using dissolving microneedles: A proof of concept study. *Pharmaceutics*, *11*(7). https://doi.org/10.3390/pharmaceutics11070346

Permana, A. D., Mir, M., Utomo, E., & Donnelly, R. F. (2020). Bacterially sensitive nanoparticle-based dissolving microneedles of doxycycline for enhanced treatment of bacterial biofilm skin infection: A proof of concept study. *International Journal of Pharmaceutics: X*, *2*(April), 100047. https://doi.org/10.1016/j.ijpx.2020.100047

Permana, A. D., Paredes, A. J., Volpe-Zanutto, F., Anjani, Q. K., Utomo, E., & Donnelly, R. F. (2020). Dissolving microneedle-mediated dermal delivery of itraconazole nanocrystals for improved treatment of cutaneous candidiasis. *European Journal of Pharmaceutics and Biopharmaceutics*, *154*, 50–61. https://doi.org/10.1016/j.ejpb.2020.06.025

Permana, A. D., Tekko, I. A., McCrudden, M. T. C., Anjani, Q. K., Ramadon, D., McCarthy, H. O., & Donnelly, R. F. (2019). Solid lipid nanoparticle-based dissolving microneedles: A promising intradermal lymph targeting drug delivery system with potential for enhanced treatment of lymphatic filariasis. *Journal of Controlled Release*, *316*, 34–52. https://doi.org/10.1016/j.jconrel.2019.10.004

Perumal, R. K., Perumal, S., Thangam, R., Gopinath, A., Ramadass, S. K., Madhan, B., & Sivasubramanian, S. (2018). Collagen-fucoidan blend film with the potential to induce fibroblast proliferation for regenerative applications. *International Journal of Biological Macromolecules*, *106*, 1032–1040. https://doi.org/10.1016/j.ijbiomac.2017.08.111

Putri, A. P. D., Ilyas, N. R. A., Abdullah, D. A. P., Pratama, F. A., Azzahra, K. S., & Permana, A. D. (2024). Development and validation of UV–Vis spectrophotometric method for determination of rivastigmine in PBS and biological matrices: Application to ex vivo permeation profiles and in vivo studies

from trilayer dissolving microneedle. *Chemical Data Collections*, *49*. https://doi.org/10.1016/j.cdc.2023.101106

Putri, H. E., Utami, R. N., Aliyah, Wahyudin, E., Oktaviani, W. W., Mudjahid, M., & Permana, A. D. (2022). Dissolving Microneedle Formulation of Ceftriaxone: Effect of Polymer Concentrations on Characterisation and Ex Vivo Permeation Study. *Journal of Pharmaceutical Innovation*, *17*(4), 1176–1188. https://doi.org/10.1007/s12247-021-09593-y

Rababa'h, A. M., Al Yacoub, O. N., El-Elimat, T., Rabab'ah, M., Altarabsheh, S., Deo, S., Al-Azayzih, A., Zayed, A., Alazzam, S., & Alzoubi, K. H. (2020). The effect of hawthorn flower and leaf extract (Crataegus Spp.) on cardiac hemostasis and oxidative parameters in Sprague Dawley rats. *Heliyon*, *6*(8). https://doi.org/10.1016/j.heliyon.2020.e04617

Rahmadani, S., Sa'diah, S., & Wardatun, S. (2018). *Optimasi Ekstraksi Jahe Merah (Zingiber officinale Roscoe) dengan Metode Maserasi*.

Rahman, L., Lembang, R. S., Lallo, S., Handayani, S. R., Usmanengsi, U., & Permana, A. D. (2021). Bioadhesive dermal patch as promising approach for improved antibacterial activity of bioactive compound of Zingiber cassumunar Roxb in ex vivo Staphylococcus aureus skin infection model. *Journal of Drug Delivery Science and Technology*, *63*. https://doi.org/10.1016/j.jddst.2021.102522

Rahmawati, R. (2018). Potensi Antikoagulan Sari Bawang Putih (Allium sativum) Menggunakan Metode Lee-White dan Apusan darah. *Majalah Farmaseutik*, *14*(1).

Rahmawati Rahmawati, Muammar Fawwas, Rais Razak, & Utami Ismlamiati. (2018). Potensi Antikoagulan Sari Bawang Putih (Allium sativum) Menggunakan Metode Lee-White dan Apusan Darah. *Majalah Farmaseutik*, *14*(1), 42–48.

Requena, M. B., Permana, A. D., Vollet-Filho, J. D., González-Vázquez, P., Garcia, M. R., De Faria, C. M. G., Pratavieira, S., Donnelly, R. F., & Bagnato, V. S. (2021). Dissolving microneedles containing aminolevulinic acid improves protoporphyrin IX distribution. *Journal of Biophotonics*, *14*(1). https://doi.org/10.1002/jbio.202000128

Runtuwene, K. N., Yamlean, P. V. Y., & Yudistira, A. (2019). Formulation, Stability Test and Antioxidant Effectiveness Test of Gel Preparations from Ethanol Extract of Sesewanua Leaves (Clerodendron squamatum Vahl) Using the DPPH Method. *Pharmacon*.

Sa'adah, H., & Nurhasnawati, H. (2015). Comparison of Ethanol and Water Solvents in the Preparation of Tiwai Onion (Eleutherine americana Merr) Extract Using the Maceration Method. *Jurnal Ilmiah Manuntung*.

Sabar, J., Fatimah, F., & Rorong, J. A. (2015). Karakterisasi Minyak Ikan dari Pemurnian Limbah Ikan Tuna dengan Zeolit secara Kromatografi Kolom. *Jurnal Mipa Unsrat*, *4*(2), 161–164. https://doi.org/10.1007/bf01707008

Saha, K. C., Seal, H. P., & Noor, M. A. (2013). Isolation and characterization of piperine from the fruits of black pepper (Piper nigrum). *J. Bangladesh Agril. Univ*, *11*(1), 11–16. http://ageconsearch.umn.edu

Salehi, B., Machin, L., Monzote, L., Sharifi-Rad, J., Ezzat, S. M., Salem, M. A., Merghany, R. M., El Mahdy, N. M., Kllç, C. S., Sytar, O., Sharifi-Rad, M., Sharopov, F., Martins, N., Martorell, M., & Cho, W. C. (2020). Therapeutic Potential of Quercetin: New Insights and Perspectives for Human Health. *ACS Omega*, *5*(20), 11849–11872. https://doi.org/10.1021/acsomega.0c01818

Sapiun, Z., Imran, A. K., Teresia, S., Dewi, R., Masita, D. F., Ibrahim, W., Tungadi, R., Abdulkadir, W. S., Banne, Y. O. S., Sartini, S., Permana, A. D., Rifai, Y., Ysrafil, Y., & Sulastri, N. (2023). Formulation and Characterization of Self Nano-Emulsifying Drug Delivery System (SNEEDS) Fraction of n-Hexane:Ethyl Acetate from Sesewanua (Clerodendrum fragrans Wild.). *International Journal of Applied Pharmaceutics*, *15*(2). https://doi.org/10.22159/ijap.2023v15i2.46365

Sapiun, Z., Lasori, S. R., Imran, A. K., Rifai, Y., Subehan, Permana, A. D., & Nainu, F. (2022). Thin Layer Chromatography Profile and Antioxidant Activity of n-Hexan:Ethyl Acetate Fraction of Ethanol Extract of Sesewanua Leaves (Clerodendrum fragrans Wild.). *ICOS*, *May*, 75.

Sapiun, Z., Pangalo, P., Endarti, D., Banne, Y., Wicita, P. S., Imran, A. K., & Mohama, F. (2020). Cytotoxic Activity of Sesewanua (Clerodendrum fragrans Wild) Leaf Ethanol Extract on Breast Cancer Cell. In M. Kes. Drs. Edy Haryanto, M. Kes. Pestariati, S.Pd, M. K. Evy DiahWulansari, S.Si., M. Kes. Suhariyadi, S.Pd., MT. Ferry Kriswandana, S.ST, M. Si. Marlik, & M. K. Narwati (Eds.), *Proceeding 1 st International Conference on Clinical Laboratory and Environmental Health (ICOCLEH)* (p. 24). Health Polytechnic of the Ministry of Health, Surabaya.

Sapiun, Z., Pangalo, P., Imran, A. K., Wicita, P. S., & Daud, R. P. A. (2020). Determination of total flavonoid levels of ethanol extract Sesewanua leaf (Clerodendrum fragrans Wild) with maceration method using UV-vis spectrofotometry. *Pharmacognosy Journal*, *12*(2), 356–360. https://doi.org/10.5530/pj.2020.12.56

Sari, A. P., Amanah, N. L., Wardatullathifa, A., & Nugroho, A. (2022). Comparison of Maseration and Sonication Method on Flavonoid Extraction from Mango Leaves: Effect of Solvent Ratio. *ASEAN Journal of Chemical Engineering*, *22*(2), 274–283. https://doi.org/10.22146/ajche.74204

Senduk, T. W., Montolalu, L. A. D. Y., & Dotulong, V. (2020). Rendemen Ekstrak Air Rebusan Daun Tua Mangrove Sonneratia alba. *Jurnal Perikanan Dan Kelautan Tropis*, *11*. https://ejournal.unsrat.ac.id/index.php/JPKT/index

Seo, J. E., Kim, S., & Kim, B. H. (2017). In vitro skin absorption tests of three types of parabens using a Franz diffusion cell. *Journal of Exposure Science and Environmental Epidemiology*, *27*(3), 320–325. https://doi.org/10.1038/jes.2016.33

Setiawan, F., Yunita, O., & Kurniawan, A. (2018). Antioxidant Activity Test of Secang Wood (Caesalpinia sappan) Ethanol Extract Using DPPH, ABTS, and. *Media Pharmaceutica Indonesiana*, *2*(2), 82–89.

Shim, W. S., Hwang, Y. M., Park, S. G., Lee, C. K., & Kang, N. G. (2018). Role of Polyvinylpyrrolidone in Dissolving Microneedle for Efficient Transdermal Drug Delivery: In vitro and Clinical Studies. *Bulletin of the Korean Chemical Society*, *39*(6), 789–793. https://doi.org/10.1002/bkcs.11476

Simbala, H. (2007). *Floristic Diversity and Its Use as Medicinal Plants in Conservation Area II Bogani Nani Wartabone National Park (Bolaang Mongondow Regency, North Sulawesi)*.

Sławińska, N., Kluska, M., Moniuszko-Szajwaj, B., Stochmal, A., Woźniak, K., & Olas, B. (2023). New Aspect of Composition and Biological Properties of Glechoma hederacea L. Herb: Detailed Phytochemical Analysis and Evaluation of Antioxidant, Anticoagulant Activity and Toxicity in Selected Human Cells and Plasma In Vitro. *Nutrients*, *15*(7). https://doi.org/10.3390/nu15071671

Srivastava, N., Mishra, S., Iqbal, H., Chanda, D., & Shanker, K. (2021). Standardization of Kaempferia galanga L. rhizome and vasorelaxation effect of its key metabolite ethyl p-methoxycinnamate. *Journal of Ethnopharmacology*, *271*. https://doi.org/10.1016/j.jep.2021.113911

Stephanie, S., Enggi, C. K., Sulistiawati, S., Tangdilintin, F., Achmad, A. A., Litaay, M., Kleuser, B., Manggau, M. A., & Permana, A. D. (2024). Fucoidan-incorporated dissolving microneedles: A novel approach to anticoagulant transdermal delivery. *Journal of Drug Delivery Science and Technology*, 105587. https://doi.org/10.1016/j.jddst.2024.105587

Sulastri, L., Oktavia, I., & Simanjuntak, P. (2020). Aktivitas Antioksidan Kecibeling, Bakau Merah, dan Katuk pada Maserasi Ekstraksi dan Rasio Ekstrak yang Berbeda. *Buletin Penelitian Tanaman Rempah Dan Obat*, *31*(1), 1. https://doi.org/10.21082/bullittro.v31n1.2020.1-7

Sulistiawati, Saka Dwipayanti, K., Azhar, M., Rahman, L., Pakki, E., Himawan, A., & Permana, A. D. (2022). Enhanced skin localization of metronidazole using solid lipid microparticles incorporated into polymeric hydrogels for potential improved of rosacea treatment: An ex vivo proof of concept investigation. *International Journal of Pharmaceutics*, *628*. https://doi.org/10.1016/j.ijpharm.2022.122327

Syafika, N., Azis, S. B. A., Enggi, C. K., Qonita, H. A., Mahmud, T. R. A., Abizart, A., Asri, R. M., & Permana, A. D. (2023). Glucose-Responsive Microparticle-Loaded Dissolving Microneedles for Selective Delivery of Metformin: A Proof-of-Concept Study. *Molecular Pharmaceutics*, *20*(2), 1269–1284. https://doi.org/10.1021/acs.molpharmaceut.2c00936

Tentu, N., Ijaz, A., Batool, S., Khan, R. S., Mohammed, F., Khan, M. H., Sandhu, Q. I., & Ali, N. (2022). Comparison of Efficacy and Safety of Anticoagulant Monotherapy and Combined Therapy of Anticoagulant and Antiplatelets in Patients With Stable Coronary Artery Disease and Atrial Fibrillation: A Meta-Analysis. *Cureus*, *14*(9). https://doi.org/10.7759/cureus.29772

Teodorescu, M., Bercea, M., & Morariu, S. (2019). Biomaterials of PVA and PVP in medical and pharmaceutical applications: Perspectives and challenges. In *Biotechnology Advances* (Vol. 37, Issue 1, pp. 109–131). Elsevier Inc. https://doi.org/10.1016/j.biotechadv.2018.11.008

Urrutia, T. C., Guzmán, L., Hirschmann, G. S., Carrasco, R., Alarcón, M., Astudillo, L., Gutierrez, M., Carrasco, G., Yuri, J. A., Aranda, E., & Palomo, I. (2011). Antiplatelet, anticoagulant, and fibrinolytic activity in vitro of extracts from selected fruits and vegetables. *Blood Coagulation and Fibrinolysis*, *22*(3), 197–205. https://doi.org/10.1097/MBC.0b013e328343f7da

Vazquez, P. G., Larrañeta, E., McCrudden, M. T. C., Jarrahian, C., Rein-Weston, A., Quintanar-Solares, M., Zehrung, D., McCarthy, H., Courtenay, A. J., & Donnelly, R. F. (2017). Transdermal delivery of gentamicin using dissolving microneedle arrays for potential treatment of neonatal sepsis. *Journal of Controlled Release*, *265*, 30–40. https://doi.org/10.1016/j.jconrel.2017.07.032

Wahba, H. M., Abouzid, S. F., Sleem, A. A., Apers, S., Pieters, L., & Shahat, A. A. (2011). Chemical and biological investigation of some Clerodendrum species cultivated in Egypt. *Pharmaceutical Biology*, *49*(1), 66–72. https://doi.org/10.3109/13880209.2010.494674

Wahyu, A., & Ningrat, S. (2022). Docking Molekuler Senyawa Brazilein Herba Caesalpina Sappanis Lignum Pada Mycobacterium Tuberculosis Inha Sebagai Antituberkulosis. *Indonesian Helath Journal (Inhealth)*, *1*. www.pdb.org

Wang, Q. L., Ren, J. W., Chen, B. Z., Jin, X., Zhang, C. Y., & Guo, X. D. (2018). Effect of humidity on mechanical properties of dissolving microneedles for transdermal drug delivery. *Journal of Industrial and Engineering Chemistry*, *59*, 251–258. https://doi.org/10.1016/j.jiec.2017.10.030

Wilson, T. D., & Steck, W. F. (2000). A modifed HET-CAM assay approach to the assessment of anti-irritant properties of plant extracts. *Food and Chemical Toxicology*, *38*, 867–872. www.elsevier.com/locate/foodchemtox

World Health Organization. (2024). *Cardiovascular Disease (CVDs)*. who.int/news-room/fact-sheets/detailcardiovascular-diseases-(cvds)

Yamada, K., Naemura, A., Sawashita, N., Noguchi, Y., & Yamamoto, J. (2004). An onion variety has natural antithrombotic effect as assessed by thrombosis/thrombolysis models in rodents. *Thrombosis Research*, *114*(3), 213–220. https://doi.org/10.1016/j.thromres.2004.06.007

Yang, J., Wang, X., Wu, D., Yi, K., & Zhao, Y. (2023). Yunnan Baiyao-loaded multifunctional microneedle patches for rapid hemostasis and cutaneous wound healing. *Journal of Nanobiotechnology*, *21*(1). https://doi.org/10.1186/s12951-023-01936-w

Ysrafil, Y., Sapiun, Z., Slamet, N. S., Mohamad, F., Hartati, H., Damiti, S. A., Alexandra, F. D., Rahman, S., Masyeni, S., Harapan, H., Mamada, S. S., Bin Emran, T., Nainu, F., Kesehatan, K. K., & Raya, P. (2023). Anti-inflammatory activities of flavonoid derivates. *ADMET & DMPK*, *11*(3). https://doi.org/10.5599/adme

Zhang, Y., Ying, D., Liu, H., Yu, Z., Han, L., Xie, J., & Xie, Y. (2017). Serum pharmacokinetics and coagulation aberration induced by sodium dehydroacetate in male and female Wistar rats. *Scientific Reports*, *7*. https://doi.org/10.1038/srep46210

Zhao, W., Zheng, L., Yang, J., Ma, Z., Tao, X., & Wang, Q. (2023). Dissolving microneedle patch-assisted transdermal delivery of methotrexate improve the therapeutic efficacy of rheumatoid arthritis. *Drug Delivery*, *30*(1), 121–132. https://doi.org/10.1080/10717544.2022.2157518

Zhao, X., Dong, S., Wang, J., Li, F., Chen, A., & Li, B. (2012). A comparative study of antithrombotic and antiplatelet activities of different fucoidans from Laminaria japonica. *Thrombosis Research*, *129*(6), 771–778. https://doi.org/10.1016/j.thromres.2011.07.041

Zheng, J., & Zhou, W. (2018). In vitro toxicity test of nano-sized magnesium oxide synthesized via solid-phase transformation. *AIP Conference Proceedings*, *1955*. https://doi.org/10.1063/1.5033589

Zhou, H. Y., Zhang, Y. P., Zhang, W. F., & Chen, X. G. (2011). Biocompatibility and characteristics of injectable chitosan-based thermosensitive hydrogel for drug delivery. *Carbohydrate Polymers*, *83*(4), 1643–1651. https://doi.org/10.1016/j.carbpol.2010.10.022

Zubair, M. S., Maulana, S., & Mukaddas, A. (2020). Penambatan Molekuler dan Simulasi Dinamika Molekuler Senyawa Dari Genus Nigella Terhadap Penghambatan Aktivitas Enzim Protease HIV-1. *Jurnal Farmasi Galenika (Galenika Journal of Pharmacy) (e-Journal)*, *6*(1), 132–140. https://doi.org/10.22487/j24428744.2020.v6.i1.14982

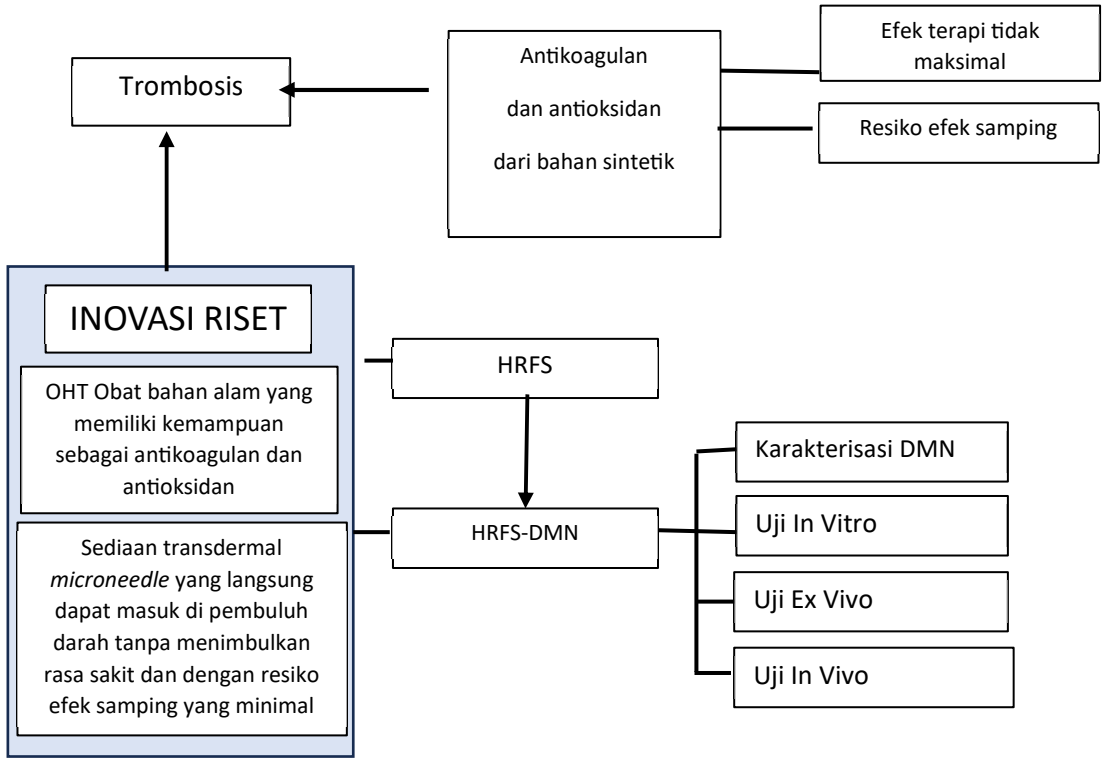
BAB V
KESIMPULAN UMUM

Penelitian ini menyimpulkan bahwa:

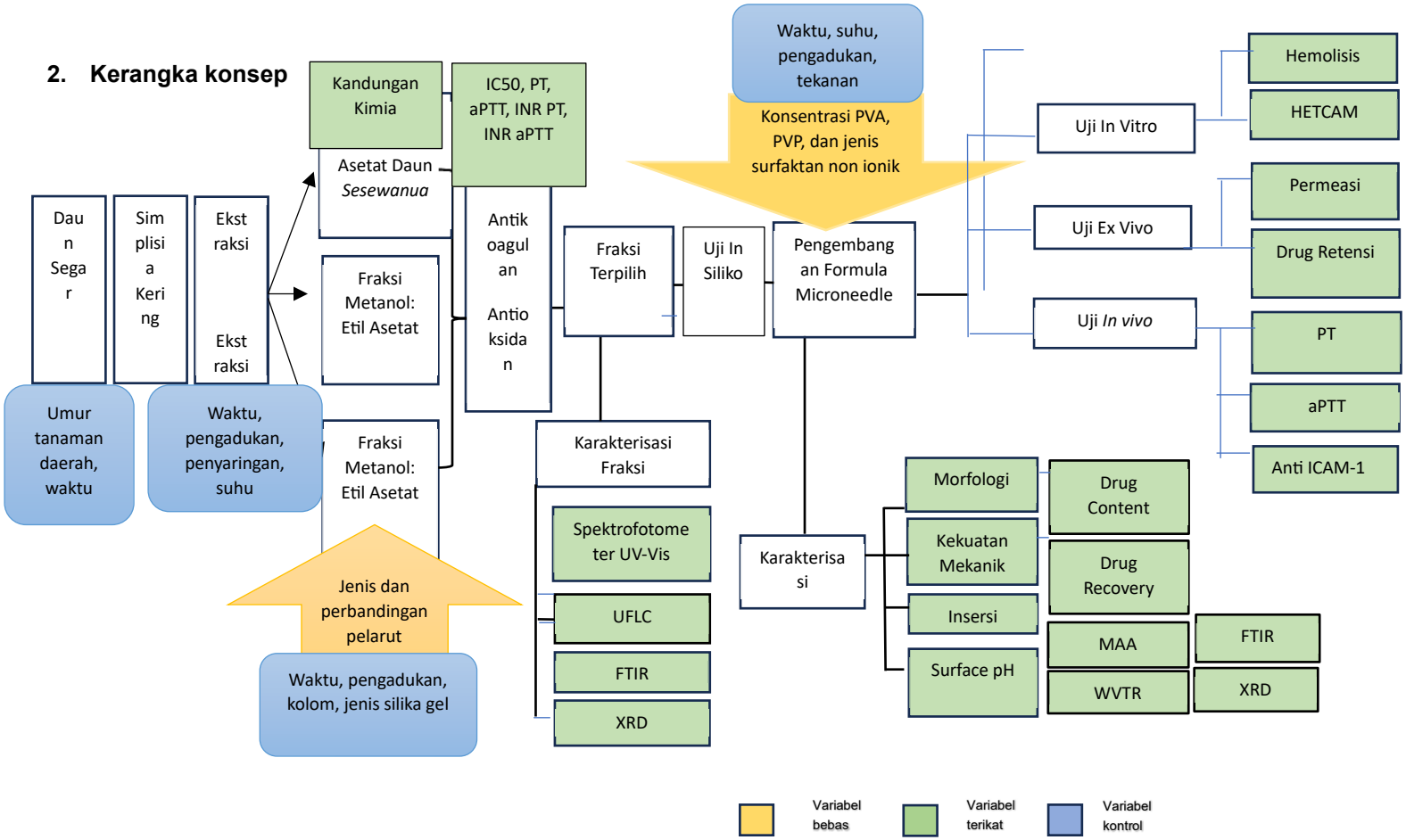
1. Fraksi Toluen-Etil Asetat *Sesewanua* (*Clerodendrum fragrans* Willd.) dengan perbandingan pelarut 10:0 dan 9:1 yang memiliki kadar hispidulin yang tinggi menunjukkan aktivitas antioksidan yang sangat kuat dan antikoagulan.
2. Sediaan *Dissolving Microneedle* dari Fraksi Toluen-Etil Asetat *Sesewanua* merupakan kandidat antitrombosis yang bekerja melalui 2 mekanisme, yaitu: antikoagulan dan antioksidan

LAMPIRAN

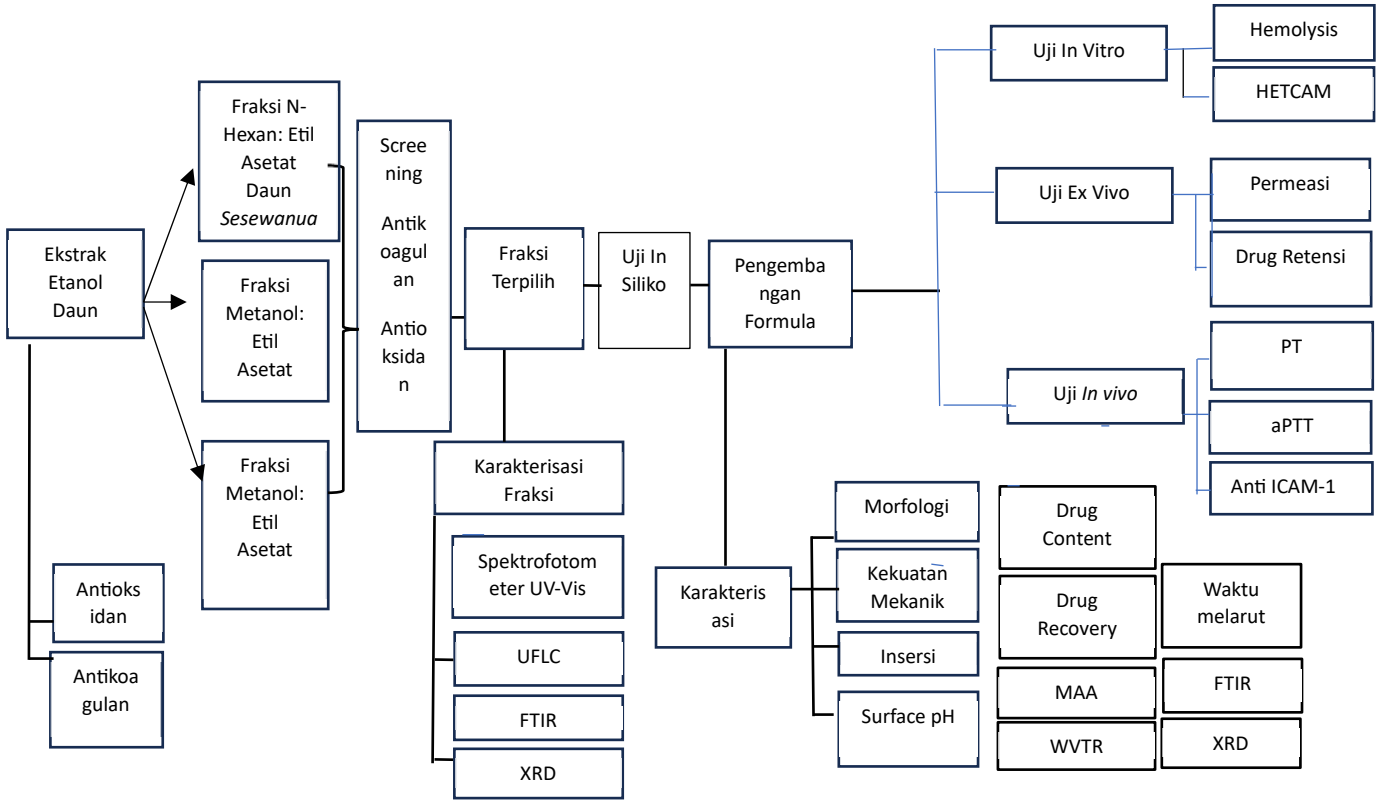
Lampiran 1. Kerangka teori



2. Kerangka konsep



3. Skema Kerja



Lampiran 2. Panjang gelombang maksimum dan kurva baku

1. Panjang gelombang maksimum dan Kurva baku Hispidulin dalam PBS 7,4

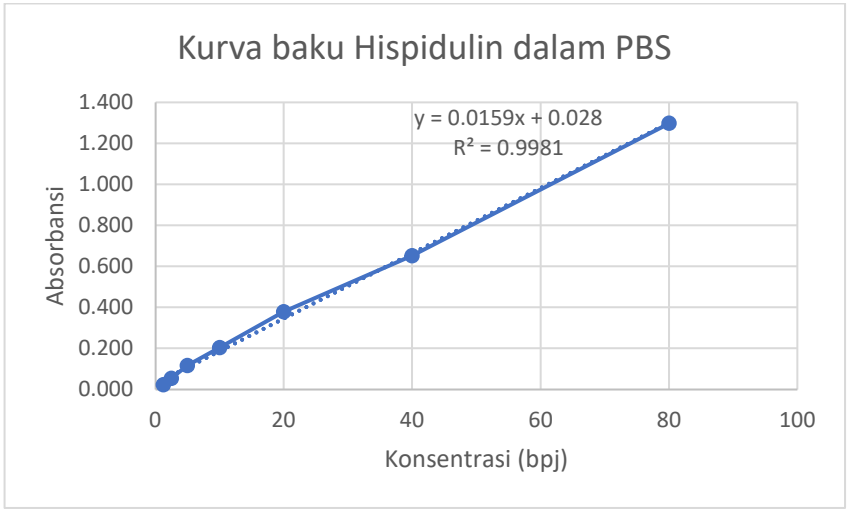
Konsentrasi Baku Hispidulin 1.000 bpj selanjutnya diencerkan menjadi 500 bpj dengan cara, mengambil 80 µl diencerkan dengan PBS hingga 2 ml. Selanjutnya Baku Hispidulin Konsentrasi 500 bpj diencerkan dengan memipet 120 µl larutan 500 bpj dan diencerkan hingga 750 µl sehingga diperoleh larutan dengan kosnentrasi 80 µl dan dimasukkan kedalam Spektro UV VIS dan dilakukan penetapan karakterisitik profil scan lamda senyawa baku hispidulin menggunakan spektrofotometri UV VIS pada panjang gelombang yang telah disetting dari 200 nm sampai dengan 800 nm.

Konsentrasi (bpj)	Rata-rata
80	1.298
40	0,651
20	0,378
10	0,203
5	0,116
2.5	0,054
1,25	0,022

Persamaan garis kurva baku *Hispidulin* dalam PBS pH 7,4

Y=0,0159x+0,028

R2 = 0,9981


Kurva baku Hispidulin dalam PBS
y = 0.0159x + 0.028
R² = 0.9981
Absorbansi
1.400
1.200
1.000
0.800
0.600
0.400
0.200
0.000
0
20
40
60
80
100
Konsentrasi (bpj)

Lampiran 3. Dokumentasi penelitian

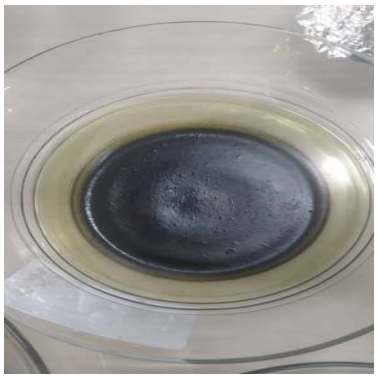
Sesewanua (*Clerodendrum fragrans* Willd.)

Simplisia

Proses maserasi 3x24 jam

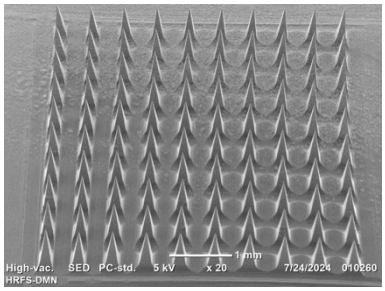
Ekstrak etanol *Sesewanua*

Kromatografi Kolom

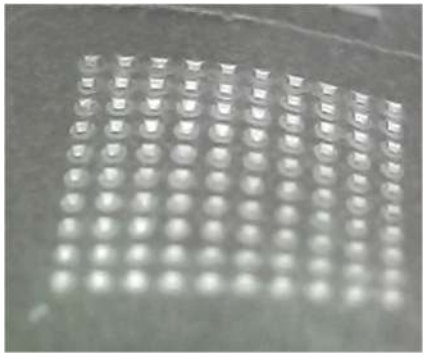


Fraksi *Sesewanua*

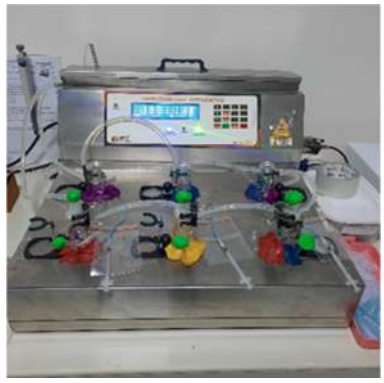
Skrining fitokimia



HFRS-DMN



Parafilm setelah insersi



Uji permeasi

Preparasi Kulit Tikus

Proses penempelan HRFS-DMN

Tikus yang telah ditempelkan 4 buah HFRS-DMN

Pengukuran kekentalan darah HRFS-DMN menggunakan alat *coagulometer*

Alat *coagulometer*

Reagen ICAM-1

Proses pengerjaan pengukuran ICAM-1

Alat ELISA

Lampiran 4. Perhitungan
Perhitungan

a. Perhitungan IC 50

	IC50				
Fraksi	U1	U2	U3	Rata-Rata	SD
TEFS1	9,02180	10,08125	11,70587	10,26964	1,351913
TEFS2	9,11468	10,06671	10,60240	9,92793	0,753504
TEFS3	1,70920	2,21647	4,54435	2,82334	1,511867
TEFS4	6,83376	7,61380	10,06504	8,17086	1,686131
HEFS1	9,29987	9,49732	7,42264	8,73994	1,145082
HEFS2	12,02175	10,24212	8,46746	10,24378	1,777145
HEFS3	8,94570	8,63641	6,63758	8,07323	1,252891
MEFS1	7,81905	9,03636	9,95679	8,93740	1,072298
MEFS2	1,54595	3,26294	4,28784	3,03225	1,385427
MEFS3	9,92323	11,51832	12,83589	11,42581	1,458531
EES	24,66915	17,15466	6,9100595	16,24462	8,914452

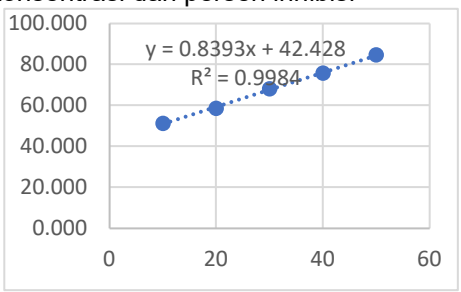
Data inhibisi TEFS1

Konsentrasi	Inhibition			Persen Inhibisi		
	U1	U2	U3	U1	U2	U3
10	0,422	0,419	0,427	51,214	50,822	47,990
20	0,359	0,365	0,344	58,497	57,160	58,100
30	0,276	0,278	0,278	68,092	67,371	66,139
40	0,211	0,205	0,201	75,607	75,939	75,518
50	0,133	0,132	0,132	84,624	84,507	83,922
Kontrol DPPH	0,865	0,852	0,821	0,000	0,000	0,000

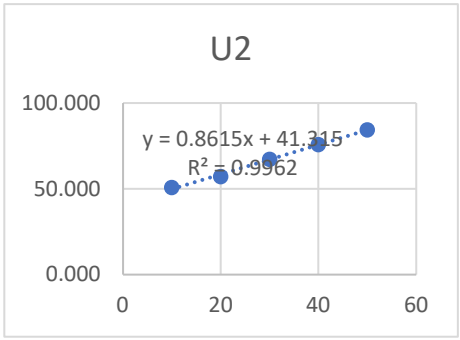
Dibuat kurva baku perbandingan konsentrasi dan persen inhibisi

U1

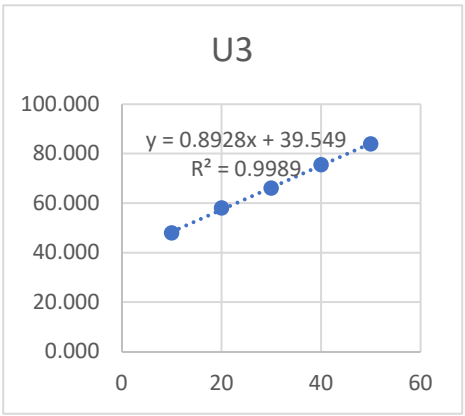
y=0,8393x+42,428
50 = 0,8393x+42,428
X = (50-42,428)/0,8393
= 9,022



U2
Y=0,8615x+41,315
50=0,8615x+41,315)
X = (50-41,315)/0,8615
= 10,081



Y = 0,8928x+39,549
50 = 0,8928x + 39,549
X = (50-39,549)/0,8928
= 11,706



Jadi, IC50 TEFS1 = 10,27±1,35

b. **Perhitungan bahan HRFS-DMN**

Formula :

Formula	HRFS (%)	PVP (%)	PVA (%)	Tween 80 0,5% (%)	Pluronic F-127 0,5% (%)	Akuades
F5	10	35	5	40	-	10
F8	10	25	10	-	40	15
F9	10	30	5	-	40	15
F11	10	40	5	40	-	5
F12	10	40	5	-	40	5

Perhitungan Bahan (5 g):

Formula	HRFS (mg)	PVP 60% (g)	PVA 30% (g)	Tween 80 8% (g)	Pluronic F-127 8% (g))	Akuades (g)
F5	0,500	2,917	0,833	0,125	-	0,625
F8	0,500	2,083	1,667	-	0,125	0,625
F9	0,500	2,500	0,833	-	0,125	1,042

F11	0,500	3,333	0,833	0,125	-	0,208
F12	0,500	3,333	0,833	-	0,125	0,208

Pembuatan stok 50 g:

- PVP 60% : $\frac{60}{100}$x50 g = 30 g, akuades ad 50 g
- PVA 30% : $\frac{30}{100}$x50 g = 15 g, akuades ad 50 g
- Tween 80 8% : $\frac{8}{100}$x50 g = 4 g, akuades ad 50 g
- Pluronic-127 : $\frac{8}{100}$x50 g = 4 g, akuades ad 50 g

Untuk pembuatan 5 g, berikut perhitungan untuk mengetahui jumlah bahan menggunakan stok, contoh F9:

- HRFS 10% : $\frac{10}{100}$x5g = 0,500 g
- PVP 30% : $\frac{30}{60}$x5g = 2,500 g
- PVA 5% : $\frac{5}{30}$x5g = 0,833 g
- Pluronic F-127 0,5% : $\frac{0,5}{8}$x40%x5g = 0,125g
- Akuades ad : 5 - (0,500+2,500+0,833+0,125) = 1,042 g

c. Hasil penentuan volume dan densitas balok HFRS-DMN

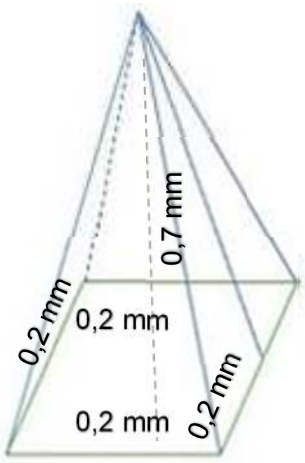
Formula	Berat (mg)	Panjang (mm)	Lebar (mm)	Tinggi (mm)	Densitas (mg/mm3)	Rata-rata	SD
F5	57,3	4,8	4,6	2,0	1,298	1,224	0,076
	48,5	4,6	4,6	2,0	1,146		
	54,2	4,8	4,6	2,0	1,227		
F8	43,1	4,7	4,6	1,7	1,173	1,073	0,223
	43,2	4,5	4,8	1,7	1,228		
	33,2	4,7	4,8	1,8	0,818		
F9	57,7	4,7	4,7	1,7	1,535	1,451	0,118
	51,9	4,7	4,6	1,6	1,500		
	46,3	4,5	4,6	1,7	1,316		
F11	41,5	4,69	4,67	1,77	1,070	1,207	0,118
	50,0	4,58	4,85	1,79	1,270		
	52,8	4,53	4,74	1,92	1,281		
F12	65,8	4,76	4,81	2,04	1,409	1,190	0,191
	49,4	4,61	4,88	1,99	1,103		
	49,3	4,63	4,73	2,13	1,057		

$$\rho = \frac{massa}{volume}$$

$$= \frac{57,3\ mg}{(4,8X4,6X2,0)mm3}$$

$$= 1,298\ mg/mm3$$

d. Data Dimensi dan Volume HRFS-DMN



Panjang (mm)	Lebar (mm)	Tinggi (mm)	Volume (mm^3)	Volume 100 jarum (mm^3)
0,2	0,2	0,7	0,00933	0,933

Volume = 1/3 x Luas alas x tinggi
Volume DMN = 1/3 x 0,2 x 0,2 x 0,7
= 0,00933 mm3

Bobot 100 jarum :
$Bobot = Densitas\ x\ Volume$

Formula	Densitas (mg/mm3)	Volume (mm3)	Bobot 100 jarum (mm)	Rata-rata	SD
F5	1,298	0,993	1,211	1.142	0,071
	1,146	0,993	1,070		
	1,227	0,993	1,145		
F8	1,173	0,993	1,095	1,001	0,208
	1,228	0,993	1,146		
	0,818	0,993	0,763		
F9	1,535	0,993	1,434	1,345	0,110
	1,500	0,993	1,400		
	1,316	0,993	1,228		
F11	1,070	0,993	0,999	1,126	0,111
	1,270	0,993	0,185		
	1,281	0,993	1,196		
F12	1,409	0,993	1,315	1,110	0,179
	1,103	0,993	1,029		
	1,057	0,993	0,986		

e. Perhitungan LOD (*Loss on Drying*) HRFS-DMN

Formula	Bobot basah (g)	Bobot kering (g))	LOD (%)	Rata-rata	SD
F5	0,537	0,217	59,590	55,439	4,709
	0,465	0,231	50,323		
	0,523	0,228	56,405		
F8	0,952	0,342	64,076	60,783	4,278
	0,929	0,350	62,325		
	0,765	0,337	55,948		
F9	0,666	0,241	63,814	60,736	2,958
	0,706	0,279	60,482		
	0,556	0,234	57,914		
F11	0,375	0,175	53,333	55,359	1,776
	0,369	0,162	56,098		
	0,150	0,150	56,647		
F12	0,497	0,210	57,746	57,946	1,655
	0,539	0,235	56,401		
	0,454	0,183	59,692		

$\% \, LOD = \frac{bobot \; basah - bobot \; kering}{bobot \; basah}$ x 100%

$= \frac{0{,}537 - 0{,}217}{0{,}537}$ x 100%

$= 59{,}590\%$

f. Perhitungan persentasi HRFS dalam massa kering

Formula	HRFS (%)	Rata-rata	SD
F5	24,75	22,61	2,33
	20,13		
	22,94		
F8	27,84	25,69	2,67
	26,54		
	22,70		
F9	27,63	25,57	1,95
	25,30		
	23,76		
F11	21,43	22,42	0,87
	22,78		
	23,07		
F12	23,67	23,80	0,94
	22,94		
	24,81		

Diketahui berat HRFS awal dalam formula adalah 10% b/b dan LOD 59,590%.

g. Penentuan bobot teoritis HFRS dan HIS dalam DMN

Formula	HRFS dalam massa kering (mg)	Bobot 100 jarum (mg)	Bobot teoritis HRFS dlm sediaan (mg)	Bobot teoritis HIS dlm sediaan (mg)	Rata-rata	SD
F5	0,247	1,211	0,300	0,147	0,127	0,021
	0,201	1,070	0,215	0,106		
	0,229	1,145	0,263	0,129		
F8	0,278	1,095	0,305	0,150	0,128	0,037
	0,265	1,146	0,304	0,149		
	0,227	0,763	0,173	0,085		
F9	0,276	1,434	0,396	0,195	0,171	0,026
	0,253	1,400	0,354	0,174		
	0,238	1,228	0,292	0,143		
F11	0,214	0,999	0,214	0,105	0,124	0,017
	0,228	0,185	0,270	0,133		
	0,231	1,196	0,276	0,135		
F12	0,237	1,315	0,311	0,153	0,130	0,020
	0,229	1,029	0,236	0,116		
	0,248	0,986	0,245	0,120		

Diketahui HRFS mengandung 49,1% HIS
Berat hispidulin dalam sediaan = bobot HRFS dalam massa kering x bobot 100 jarumx %bobot HIS dalam HRFS
= 0,274 x 1,211 x 0,491
= 0,147 mg

h. Penentuan % drug recovery

Formula	Absorbansi	Konsentrasi (bpj)	Konsentrasi awal (bpj)	Drug recovery (%)	Rata-rata	SD
F5	0,068	2,516	2,546	98,81	97,99	1,426
	0,068	2,516	2,546	98,81		
	0,067	2,453	2,561	96,34		
F8	0,068	2,516	2,561	98,23	96,59	1,418
	0,067	2,453	2,561	95,78		
	0,067	2,453	2,561	98,23		
F9	0,082	3,396	3,412	99,57	98.95	1,064
	0,081	3,333	3,412	97,72		
	0,082	3,396	3,412	99,57		
F11	0,067	2,453	2,487	98,63	97,78	1,460
	0,066	2,390	2,487	96,10		
	0,067	2,453	2,487	98,63		
F12	0,069	2,579	2,593	99,45	98,64	1,400
	0,068	2,516	2,593	97,02		
	0,069	2,579	2,593	99,45		

Diketahui bobot teoritis HIS dalam F5, F8, F9, F11, dan F12 adalah 0,127, 0,128, 0,171, 0,125 dan 0,126
Persamaan kurva baku = 0,0159x + 0,028
Berat teoritis dari HRFS-DMN (F5= 0,127) dilarutkan dalam 5 ml PBS sehingga konsentrasi larutan stok menjadi 25,46 kemudian dicuplik 100 µl dan dicukupkan hingga 1000 µL.

$$\text{Konsentrasi akhir larutan} = \frac{100 \text{ mikroliter}}{1000 \text{ mikroliter}} \text{ x } 25{,}46 \text{ bpj}$$
$$= 2{,}546$$

$$\text{Konsentrasi HIS dalam sampel} = \frac{0{,}068 - 0{,}028}{0{,}0159}$$
$$= 2{,}516 \text{ bpj}$$
$$\%\text{ drug recovery} = \frac{\text{konsentrasi sampel}}{\text{konsentrasi larutan}} \text{ x } 100\%$$
$$= \frac{2{,}516}{2{,}546} \text{ x } 100\%$$
$$= 98{,}81\%$$

i. Permeasi

Contoh perhitungan permeasi obat secara *ex vivo*

Diketahui persamaan garis linear *hispidulin* dalam PBS pH 7,4 adalah y = 0,0159x + 0,028
Ket:
y = serapan / absorbansi
x = konsentrasi
F5 – Replikasi 1, jam ke-60 diperoleh serapan 0,115.
Sehingga perhitungan konsentrasi adalah sebagai berikut:

$x = \frac{y-b}{a}$

$x = \frac{0{,}115-0{,}028}{0{,}0159} =$ 5,472 µg/ml

Konsentrasi dalam 1 ml = 5,472 µg/ml × 1 ml
= 5,472 µg
Faktor pengenceran 4x
Konsentrasi dalam 13 ml = 71,226 µg/ml × 13 × 1 ml x 4
= 284,528 µg
Faktor koreksi = Konsentrasi jam sebelumnya + faktor koreksi jam sebelumnya
= 5,472 µg + 25,660 µg
= 31,132 µg

Jumlah permeasi obat (mg) = Konsentrasi dalam 13 ml + faktor koreksi

$$= \frac{(284{,}528 \text{ µgl} + 31{,}132 \text{ µg})}{1000}$$
= 0,316 mg

Jumlah permeasi obat perluas area kulit = $\frac{0{,}316}{1{,}9856}$ = 0,159 mg/cm^2
= 159 µg /cm^2

j. Perhitungan dosis untuk tikus

Heparin Injeksi

Faktor konversi manusa dengan berat 70 kg ke tikus dengan berat 200 g adalah 0,018.

Diketahui :

Dosis heparin untuk manusia adalah 200 IU/kg BB.

Untuk manusia dengan bobot 70 kg = 200 IU x 70 kg = 14000 IU

Untuk tikus dengan bobot 200 g = 1400 IU x 0,018 = 250 IU

Volume yang akan diebrikan pada tikus dengan bobot 200 g adalah 0,5 ml

Larutan stok yang akan dibuat 5 ml

Bobot etiket heparin injeksi = 5000 IU/ml

Perhitungan :

Jumlah heparin yang dibutuhkan untuk membuat larutan stok 5 ml

250 IU untuk 0,5 ml dan untuk 5 ml =2500 IU

Jumlah heparin yang dicuplik untuk membuat larutan stok 5 ml

$= \frac{(2500)}{5000}$

= 0,5 ml

Pemberian menyesuaikan dengan berat tikus.

Tikus I = $\frac{290\ g}{200\ g}$ x 0,5 ml = 0,73 ml

Tikus II = $\frac{310\ g}{200\ g}$ x 0,5 ml = 0,78 ml

Tikus III = $\frac{290\ g}{200\ g}$ x 0,5 ml = 0,73 ml

Quersetin oral

Dosis manusia = 120 mg/hari, terbagi dalam 3 kali pemberian (Chekalina et al., 2018)

Konversi dosis untuk tikus 200 g = 120 mg x 0,018 = 2,16 mg (dalam 2 ml)

Dibuat suspensi CMC 0,5% sebanyak 10 ml sebagai pembawa, disuspensikan 10,8 mg. Pemberian menyesuaikan dengan berat tikus.

Tikus I = $\frac{290\ g}{200\ g}$ x 2 ml = 2,9 ml

Tikus II = $\frac{310\ g}{200\ g}$ x 2 ml = 3,1 ml

Tikus III = $\frac{290\ g}{200\ g}$ x 2 ml = 2,9 ml

HRFS-O1

Dosis tikus oral 1 diberikan setara dengan drug content 1 HRFS-DMN, yaitu 0,347 mg HRFS yang didispersikan dalam suspensi NaCMC 0,5% sebanyak 2 ml. Dibuat suspensi CMC 0,5% sebanyak 10 ml sebagai pembawa, disuspensikan 1,735 mg. Pemberian menyesuaikan dengan berat tikus.

Tikus I = $\frac{253\ g}{200\ g}$ x 2 ml = 2,5 ml

Tikus II = $\frac{245\ g}{200\ g}$ x 2 ml = 2,5 ml

Tikus III = $\frac{290\ g}{200\ g}$ x 2 ml = 2,9 ml

HRFS-O2

Dosis tikus oral 1 diberikan setara dengan drug content 2 HRFS-DMN, yaitu 0,694 mg HRFS yang didispersikan dalam suspensi NaCMC 0,5% sebanyak 2 ml. Dibuat suspensi CMC 0,5% sebanyak 10 ml sebagai pembawa, disuspensikan 3,47 mg. Pemberian menyesuaikan dengan berat tikus.

Tikus I = $\frac{283\ g}{200\ g}$ x 2 ml = 2,83 ml

Tikus II = $\frac{343\ g}{200\ g}$ x 2 ml = 3,43 ml

Tikus III = $\frac{344\ g}{200\ g}$ x 2 ml = 3,44 ml

HRFS-O4

Dosis tikus oral 1 diberikan setaradengan drug content 4 HRFS-DMN, yaitu 1,388 mg HRFS yang didispersikan dalam suspensi NaCMC 0,5% sebanyak 2 ml. Dibuat suspensi CMC 0,5% sebanyak 10 ml sebagai pembawa, disuspensikan 6,94 mg. Pemberian menyesuaikan dengan berat tikus.

Tikus I = $\frac{231\ g}{200\ g}$ x 2 ml = 2,3 ml

Tikus II = $\frac{235\ g}{200\ g}$ x 2 ml = 2,4 ml

Tikus III = $\frac{225\ g}{200\ g}$ x 2 ml = 2,3 ml

Lampiran 5. Data *In vivo*

A. Data *In vivo* PT

Sediaan	AE	KB	KD	Rata-rata	SD
HEP	17,3	17,1	17,2	17,2	0,1
QUE	13,1	14,0	11,8	13,0	1,1
HRFSFree-DMN	9,5	8,0	7,1	8,2	1,2
HRFS-DMN1	14,3	13,8	13,4	13,8	0,5
HRFS-DMN2	17,1	17,0	16,8	17,0	0,1
HRFS-DMN4	17,2	17,0	17,1	17,1	0,1
HRFS-O1	9,9	6,5	11,0	9,1	2,3
HRFS-O2	11,5	12,4	10,0	11,3	1,2
HRFS-O4	12,7	13,2	14,7	13,5	1,0

B. Data *in vivo* aPTT

Sediaan	AE	KB	KD	Rata-rata	SD
HEP	1,3	33,0	32,2	22,2	18,1
QUE	23,2	23,8	17,1	21,4	3,7
HRFSFree-DMN	12,1	12,0	15,8	13,3	2,2
HRFS-DMN1	23,5	23,8	22,7	23,3	0,6
HRFS-DMN2	29,8	28,8	29,3	29,3	0,5
HRFS-DMN4	32,0	32,6	31,6	32,1	0,5
HRFS-O1	16,6	16,8	16,3	16,6	0,3
HRFS-O2	21,4	19,7	18,4	19,8	1,5
HRFS-O4	22,8	25,5	26,0	24,8	1,7

C. Data *in vivo* ICAM

Sediaan	AE	KB	KD	Rata-rata	SD
HEP	2,9070	3,7053	3,6798	3,4307	0,4537
QUE	3,6334	3,3885	3,848	3,6233	0,2299
HRFSFree-DMN	3,1496	3,1063	3,2043	3,1534	0,0491
HRFS-DMN1	3,0312	3,4469	3,1423	3,2068	0,2152
HRFS-DMN2	2,3751	2,3610	2,3481	2,3614	0,0135
HRFS-DMN4	1,861	2,4383	2,1362	2,1452	0,2888
HRFS-O1	3,1473	4,0559	3,3678	3,5237	0,4739
HRFS-O2	3,468	2,7148	2,5095	2,8974	0,5047
HRFS-O4	2,2216	2,7757	2,9188	2,6387	0,3682

Lampiran 6. Etik Penelitian

KEMENTERIAN PENDIDIKAN, KEBUDAYAAN, RISET DAN TEKNOLOGI
KOMITE ETIK PENELITIAN FARMASI DAN KESEHATAN
FAKULTAS FARMASI
UNIVERSITAS HASANUDDIN
Sekretariat : Lantai 3 Fakultas Farmasi
JL.PERINTIS KEMERDEKAAN KAMPUS UNHAS TAMALANREA KM.10 MAKASSAR 90245.
CP: Nurhasni Hasan, PhD., Apt; No. Hp Sekretariat: 085179788835; email: kep.fekfarmasi@unhas.ac.id

LEMBAR KEPUTUSAN ETIK

Nomor : **265/UN4.17.8/KP.06.07/2024**

Judul Penelitian : Pengembangan Formula *Microneedle* Fraksi Daun *Sesewanua* (*Clerodendrum fragrans* Wild.) sebagai Kandidat Antithrombosis

Nama Peneliti : Zulfiayu

Nomor Registrasi | U | H | 0 | 1 | 2 | 4 | 0 | 2 | 0 | 3 | 9 |

A	Rangkuman penilaian oleh *reviewers*	
B	Perlu *full board*: ☐ Ya ☑ Tidak a. Ya (terus ke C) b. Tidak (terus ke D)	
C	Catatan Rapat Etik (*Full Board*) —	
	Tgl/bulan/tahun	
	Tindak lanjut/catatan rapat etik Dikirimkan kembali ke yang bersangkutan dengan tembusan kepimpinan instansi	
D	Hasil Penilaian	
	☐	a. Disetujui
	☑	b. Disetujui dengan revisi minor (lihat lembaran pertimbangan/saran /petunjuk)
	☐	c. Disetujui dengan revisi mayor (lihat lembaran pertimbangan/saran/petunjuk)
	☐	d. Ditunda untuk beberapa alasan (lihat lembaran pertimbangan/saran/petunjuk)
	☐	e. Ditolak/tidak dapat disetujui (lihat lembaran pertimbangan/saran/petunjuk)
E	Penugasan pengawasan jalannya penelitian di lapangan untuk yang berisiko sedang – berat, mengobservasi apakah ada penyimpangan etik (tulis nama anggota komisi etik yang ditunjuk oleh rapat): —	

Makassar, 4 Maret 2024

Ketua

Prof. Dr. Elly Wahyudin, DEA., Apt
NIP. 19560114 198601 2 001

Sekretaris

Nurhasni Hasan, M.Si., M.Pharm.Sc., Ph.D.,Apt
NIP. 19860116 201012 2 009

CURRICULUM VITAE

A. Data Pribadi

1.	Nama	:	Zulfiayu
2.	Tempat, Tanggal Lahir	:	Selong Lombok, 08-08-1975
3.	Alamat	:	Jalan Brigjen Piola Isa Blok Tatudi No 14 Griya Fitrah Mandiri, Gorontalo
4.	Kewarganegaraan	:	Indonesia

B. Riwayat Pendidikan

1. Tamat SMA tahun 1994 di SMAN 1 Mataram
2. Sarjana Farmasi tahun 2000 di Universitas Hasanuddin, Makassar
3. Profesi Apoteker tahun 2002 di Universitas Hasanuddin, Makassar
4. Magister Farmasi tahun 2006 di Universitas Gadjah Mada, Yogyakarta

C. Pekerjaan dan Riwayat Pekerjaan

1.	Jenis Pekerjaan	:	Dosen
2.	NIDN	:	4008087501
3.	Pangkat/Golongan	:	Pembina/IVA
4.	Jabatan	:	Lektor

D. Karya Ilmiah yang Telah Dipublikasikan

1. Determination of total flavonoid levels of ethanol extract *Sesewanua* leaf (*Clerodendrum fragrans* Willd.) with maceration method using UV-vis spectrofotometry. *Pharmacognosy Journal*, *12*(2), 356–360. https://doi.org/10.5530/pj.2020.12.56
2. *Hispidulin-rich fraction of Clerodendrum fragrans* Willd. *(Sesewanua) dissolving microneedle as antithrombosis candidate: A proof of concept study, International Journal of Pharmaceutics, Vol Volume 666 pp 1-17, 5 December 2024, https://doi.org/10.1016/j.ijpharm.2024.124766.*
3. *Anti-inflammatory activities of flavonoid derivates, ADMET & DMPK, 11(3), 2023, 331-359,* https://doi.org/10.5599/admet.1918.

E. Makalah pada Seminar/Konferensi Ilmiah Nasional dan Internasional

1. *Fractionation of Ethanol Extract of Sesewanua Leaves (Clerodendrum fragrans* Willd*.) in n-Hexan: Ethyl Acetate and Their Antioxidant Activity*, International Conference on Science, FMIPA Unhas, 2022
2. Cytotoxic Activity of *Sesewanua* (*Clerodendrum fragrans* Willd) Leaf Ethanol Extract on Breast Cancer Cell. *Proceeding 1 st International Conference on Clinical Laboratory and Environmental Health (ICOCLEH)* (p. 24). Health Polytechnic of the Ministry of Health, Surabaya