

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

1. Pemberian senyawa triptofan mampu menekan durasi imobilitas pada tikus, sehingga disimpulkan bahwa senyawa triptofan mempunyai aktivitas antidepresan pada tikus putih (*Rattus norvegicus*) dengan metode *Forced Swim Test*.
2. Pemberian senyawa 5-Hidroksitriptofan mampu menekan durasi imobilitas pada tikus, sehingga disimpulkan bahwa senyawa 5-HTP mempunyai aktivitas antidepresan pada tikus putih (*Rattus norvegicus*) dengan metode *Forced Swim Test*.

5.2 Saran

Berdasarkan hasil penelitian yang dilakukan, disarankan untuk melakukan penelitian lebih lanjut terkait dengan depresi kronis yang diberikan perlakuan stress yang lebih lama dengan menggunakan metode *Unpredictable Chronic Mild Stress* (UCMS), kemudian dilanjutkan dengan menganalisis kadar serotonin pada tikus.

DAFTAR PUSTAKA

- Ahyar, H., Maret, U. S., Andriani, H., Sukmana, D. J., Mada, U. G., Hardani, S.Pd., M. S., Nur Hikmatul Auliya, G. C. B., Helmina Andriani, M. S., Fardani, R. A., Ustiawaty, J., Utami, E. F., Sukmana, D. J., & Istiqomah, R. R. 2020. Buku Metode Penelitian Kualitatif & Kuantitatif (Issue March), Jakarta.
- Alvarez-Mon, M. A., Ortega, M. A., García-Montero, C., Fraile-Martinez, O., Monserrat, J., Lahera, G., Mora, F., Rodriguez-Quiroga, A., Fernandez-Rojo, S., Quintero, J., & Alvarez-Mon, M. 2021. Exploring the role of nutraceuticals in major depressive disorder (MDD): Rationale, state of the art and future prospects. *Pharmaceuticals*, **14(8)**, 1–32.
- American Psychiatric Association. 2013. Major Depressive Episode. Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, USA.
- American Psychiatric Association. 2019. The Treatment of Depression Across Three Age Cohorts. APA Clinical Practice Guideline.
- Arifin, W. N., & Zahiruddin, W. M., 2017. Sample size calculation in animal studies using resource equation approach. *Malaysian Journal of Medical Sciences*, **24(5)**, 101–105.
- Attenburrow, M. J., Williams, C., Odontiadis, J., Powell, J., Van De Ouderaa, F., Williams, M., & Cowen, P. J. 2003. The effect of a nutritional source of tryptophan on dieting-induced changes in brain 5-HT function. *Psychological Medicine*, **33(8)**, 1381–1386.
- Azis, A., & Rinding Lawan, G. 2020. Pengaruh Ekstrak Kentos Kelapa (*Cocos nucifera* L.) Terhadap penurunan Immobility Time Sebagai Antidepresan Pada mencit (*Mus musculus*). *Journal.Yamasi.Ac.Id*, **4(1)**, 1–8.
- Badawy, A. A. B. 2019. Hypothesis: Metabolic targeting of 5-aminolevulinat synthase by tryptophan and inhibitors of heme utilize&ation by tryptophan 2,3-dioxygenase as potential therapies of acute hepatic porphyrias. *Medical Hypotheses*, **131(7)**,109-314.
- Baxter, K. 2008. Stockley's Drug Interactions 8th edition. *Pharmaceutical Press*, London UK, pp. 1151–1226.

- British National Formulary 76th Edition. 2018. BMJ Group, London.
- British National Formulary, 2009. BNF Children: The essential resource for clinical use of medicines in children, BMJ Group, Germany
- Burstein, O., & Doron, R. 2018. The Unpredictable Chronic Mild Stress Protocol for Inducing Anhedonia in Mice. *Journal of Visualized Experiments : JoVE*, **140**, 1–9.
- Cengotitabengoa, M., & González-Pinto, A. 2017, Nutritional supplements in depressive disorders, *Actas Espanolas de Psiquiatria*, **45**, 8–15.
- Cleare, A., Pariante, C. M., Young, A. H., Anderson, I. M., Christmas, D., Cowen, P. J., Dickens, C., Ferrier, I. N., Geddes, J., Gilbody, S., Haddad, P. M., Katona, C., Lewis, G., Malizia, A., McAllister-Williams, R. H., Ramchandani, P., Scott, J., Taylor, D., & Uher, R. 2015. Evidence-based guidelines for treating depressive disorders with antidepressants: A revision of the 2008 British Association for Psychopharmacology guidelines. *Journal of Psychopharmacology* (Vol. **29**, Issue 5).
- Contreras, C. M., Rodríguez-Landa, J. F., Gutiérrez-García, A. G., & Bernal-Morales, B. 2001). The lowest effective dose of fluoxetine in the forced swim test significantly affects the firing rate of lateral septal nucleus neurones in the rat. *Journal of Psychopharmacology*, **15(4)**, 231–236.
- Debattista, C., Antidepressant agent . In : Katzung, B.G., Masters, S.B., Trevor, A.J. (Eds). 2018, *Basic & Clinical Pharmacology*.14th Ed., United State: The McGraw Hill Companies Inc, pp. 532 - 552.
- Departemen Kesehatan RI, 2007, Pharmaceutical Care untuk Penderita Gangguan Depresif, Jakarta, Direktorat Bina Farmasi Komunitas Dan Klinik Ditjen Bina Kefarmasian Dan Alat Kesehatan, 81.
- Fernstrom, J. D. 2012, Effects and side effects associated with the non-nutritional use of tryptophan by humans. *Journal of Nutrition*, **142(12)**,1–9.
- Ganiswara, G. S. 2009, *Farmakologi dan Terapi* Edisi V, Fakultas Kedokteran Universitas Indonesia, Jakarta. Hal. 268
- Gebretsadik, M., & Grossberg, G. T. 2007. Nutrition and depression. *Geriatric Nutrition*, 373–396.

- Guan, X. T., Shao, F., Xie, X., Chen, L., & Wang, W. 2014. Effects of aspirin on immobile behavior and endocrine and immune changes in the forced swimming test: Comparison to fluoxetine and imipramine. *Pharmacology Biochemistry and Behavior*, **124**, 361–366.
- Hakkarainen, R., Partonen, T., Haukka, J., Virtamo, J., Albanes, D., & Lönnqvist, J. 2003, Association of dietary amino acids with low mood, *Depression and Anxiety*, **18(2)**, 89–94.
- Hansen, F., de Oliveira, D. L., Amaral, F. U. Í., Guedes, F. S., Schneider, T. J., Tumelero, A. C., Hansel, G., Schmidt, K. H., Giacomini, A. C. V. V., & Torres, F. V. 2011. Effects of chronic administration of tryptophan with or without concomitant fluoxetine in depression-related and anxiety-like behaviors on adult rat. *Neuroscience Letters*, **499(2)**, 59–63.
- Hedrich, H. J. 2019, Taxonomy and stocks and strains, In *The Laboratory Rat*, Elsevier Inc.
- Hilakivi-Clarke, L. A., Durcan, M. J., Lister, R. G., & Linnoila, M. 1990. Effect of tryptophan on the behavior of nonstressed and stressed mice in Porsolt's swim test. *Pharmacology, Biochemistry and Behavior*, **37(2)**, 273–276.
- Jacobsen, J. P. R., Krystal, A. D., Krishnan, K. R. R., & Caron, M. G. 2016, Adjunctive 5-Hydroxytryptophan Slow-Release for Treatment-Resistant Depression: Clinical and Preclinical Rationale, *Trends in Pharmacological Sciences*, **37(11)**, 933–944.
- Javelle, F., Lampit, A., Bloch, W., Haussermann, P., Johnson, S. L., & Zimmer, P. 2020, Effects of 5-hydroxytryptophan on distinct types of depression: A systematic review and meta-analysis, *Nutrition Reviews*, **78(1)**, 77–88.
- Kamran, M., Bibi, F., Rehman, A. U., & Morris, D. W. 2022, Major Depressive Disorder: Existing Hypotheses about Pathophysiological Mechanisms and New Genetic Findings. *Genes*, **13(4)**, 1-19
- Kementrian Kesehatan RI. Keputusan Menteri Kesehatan RI. Tentang Pedoman Nasional Pelayanan Kedokteran Jiwa. Jakarta; 2015.
- Kim, J., & Shin, W. 2014, How to do random allocation (randomization), *Clinics in Orthopedic Surgery*, **6(1)**, 103–109.

- Klepser, B. T., & Nisly, N. 2000, 5-Hydroxytryptophan (5-HTP) for Treatment of Depression, **3(11)**, 121–132.
- Kulikov, A. V., Gainetdinov, R. R., Ponimaskin, E., Kalueff, A. V., Naumenko, V. S., & Popova, N. K. 2018, Interplay between the key proteins of serotonin system in SSRI antidepressants efficacy. *Expert Opinion on Therapeutic Targets*, **22(4)**, 319–330.
- Kumar, K. P. S., Srivastava, S., Paswan, S., & Dutta, A. S. 2012, Depression - Symptoms , Causes , Medications and Therapies. **1(3)**.
- Lindseth, G., Helland, B., & Caspers, J. 2015. The effects of dietary tryptophan on affective disorders. *Archives of Psychiatric Nursing*, **29(2)**, 102–107.
- Meloni, M., Puligheddu, M., Carta, M., Cannas, A., Figorilli, M., & Defazio, G. 2020, Efficacy and safety of 5-hydroxytryptophan on depression and apathy in Parkinson's disease: a preliminary finding, *European Journal of Neurology*, **27(5)**, 779–786.
- Menkes. 2019, *Kementerian Kesehatan Republik Indonesia*, **1(1)**, 1.
- Moncrieff, J. 2010, Challenging conventional models of psychiatric drug therapy: An alternative patient-centered approach, *Future Neurology*, **5(2)**, 213–225.
- Nolen, W. A., Putte, J. J. van de, Dijken, W. A., Kamp, J. S., Blansjaar, B. A., Kramer, H. J., & Haffmans, J. 1988, Treatment strategy in depression. *Acta Psychiatrica Scandinavica*, **78(6)**, 668–675.
- Ong, P. T. W. Y. P. 2001. Acute Antidepressant-Like and Antianxiety-Like Effects of Tryptophan in Mice. **62**, 151–156.
- Papakostas, G. I., Shelton, R. C., Zajecka, J. M., Etemad, B., Rickels, K., Clain, A., Baer, L., Dalton, E. D., Sacco, G. R., Schoenfeld, D., Pencina, M., Meisner, A., Bottiglieri, T., Nelson, E., Mischoulon, D., Alpert, J. E., Barbee, J. G., Zisook, S., & Fava, M. 2012. L-methylfolate as adjunctive therapy for SSRI-resistant major depression: Results of two randomized, double-blind, parallel-sequential trials. *American Journal of Psychiatry*, **169(12)**, 1267–1274.
- Park, L.T. and Carlos A.Z. 2019. Depression in the Primary Care Setting. Clinical Practice, *The New England Journal of Medicine*.**7(2)**, 559-568

- Pedoman Penggolongan dan Diagnosis Gangguan Jiwa di Indonesia III (PPDGJ-III). 1993. Jakarta: *Departemen Kesehatan Republik Indonesia*, 1–408.
- Perhimpunan Dokter Spesialis Kedokteran Jiwa (PP PDSKJI). 2015. Pedoman Nasional Pelayanan Kedokteran (PNPK) Jiwa/Psikiatri. Jakarta: PPPDSKJI, hal.36-44.
- Pujiatiningsih, A. S. 2014. Pemberian ekstrak daun putri malu (*Mimosa pudica* linn) secara oral menurunkan kadar gula darah post prandial pada tikus (*Rattus norvegicus*) jantan galur wistar prediabetes, Skripsi, Program Pasca Sarjana Universitas Udayana, Denpasar.
- Rashighi, M., & Harris, J. E. 2017. HHS Public Access. *Physiology & Behavior*, **176(3)**, 139–148.
- Richard, D. M., Dawes, M. A., Mathias, C. W., Acheson, A., Hill-Kapturczak, N., & Dougherty, D. M. 2009, L-tryptophan: Basic metabolic functions, behavioral research and therapeutic indications, *International Journal of Tryptophan Research*, **2(1)**, 45–60.
- Ridwan, E. 2013, Etika Pemanfaatan Hewan Percobaan dalam Penelitian Kesehatan. *Journal Indonesian Medical Assosiation*, **63(3)**, 112–116.
- Riskesdas. 2018. Hasil Utama Riset Kesehatan Dasar. Kementerian Kesehatan Republik Indonesia.
- Sarris, J. 2017, Clinical use of nutraceuticals in the adjunctive treatment of depression in mood disorders, *Australasian Psychiatry*, **25(4)**, 369–372.
- Setyawan, D. A. 2021, Petunjuk Praktikum Uji Normalitas & Uji Homogenitas Data dengan SPSS. Tahta Media Group.
- Shaw, K., Turner, J., & Del Mar, C. 2002. Are tryptophan and 5-hydroxytryptophan effective treatments for depression? A meta-analysis. *Australian and New Zealand Journal of Psychiatry*, **36(4)**, 488–491.
- Talbot, S. R., Biernot, S., Bleich, A., van Dijk, R. M., Ernst, L., Häger, C., et al. 2020. Defining body-weight reduction as a humane endpoint: a critical appraisal. *Laboratory Animals*, **54(1)**, 99–110.

- Teter, C. S., Kando, J. C., Wells, B. G., & Hayes, P. E. 2008. Depressive Disorder ,dalam Dipiro, J. T., Talbert, R. L., Yee, G. C., Matzke, G. R., Wells, B. G.,& Posey Micheal, L.,(eds). *Pharmacotherapy A Pathophysiologic Approach*,7th Edition, Appleton and lange, New York, 1123-1139.
- Tjay T.H. and Rahardja K. 2015. Obat-Obat Penting Khasiat, Penggunaan dan Efek - Efek Sampingnya. PT Elex Media Komputindo, Jakarta, pp. 464-478.
- Trunnell, E. R., & Carvalho, C. 2021, The forced swim test has poor accuracy for identifying novel antidepressants, *Drug Discovery Today*, **26(12)**, 2898–2904.
- Widiartini, W., Siswati, E., Setiyawati, A., Rohmah, I. M., & Prastyo, E. 2015, Pengembangan Usaha Produksi Tikus Putih (*Rattus norvegicus*) terseretifikasi dalam memenuhi kebutuhan dan mengembangkan berbagai macam bidang ilmu dalam skala penelitian atau pengamatan laboratoris Malole dan kewirausahaan. S-1 Peternakan, Fakultas Peternakan Dan Pertanian, Universitas Diponegoro, 1–8.
- World Health Organization. 2017. Depression and Other Common Mental Disorders, *Global Health Estimates*, 8-13.
- World Health Organization. Depression. 13 September 2021. Available from:<https://www.who.int/news-room/fact-sheets/detail/depression>
- Yankelevitch-Yahav, R., Franko, M., Huly, A., & Doron, R. 2015, The forced swim test as a model of depressive-like behavior, *Journal of Visualized Experiments*, **(97)**, 1–7.