

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

Berdasarkan hasil penelitian dapat disimpulkan beberapa hal yaitu:

1. Kombinasi ekstrak salam dan sambiloto dapat membantu proses penyembuhan luka diabetes melitus ditandai dengan pengecilan diameter luka.
2. Adanya aktivitas inhibisi DPP-IV oleh kombinasi ekstrak salam dan sambiloto dilihat dari hasil % inhibisi yaitu 68,79 %.
3. Adanya korelasi antara inhibisi kombinasi ekstrak salam sambiloto dengan pengecilan diameter luka.

5.2 Saran

Perlu dilakukan penelitian lebih lanjut mengenai penggunaan sediaan topikal yang menggunakan bahan alam dengan konsentrasi tertentu sehubungan dengan mekanisme penghambatan enzim DPP-IV.

DAFTAR PUSTAKA

- Ahren, B. 2005, What mediates the benefits associated with dipeptidyl peptidase-IV inhibition?, *Diabetologia*, **48**: 605–607.
- Armstrong, 1995, *Buku Ajar Biokimia*, Diterjemahkan R.F. Maulany Ed. 3, EGC, Jakarta.
- Banda, M., Nyirenda, J., Muzandu, K., Sijumbila, G. and Mudenda, S. 2018, Antihyperglycemic and antihyperlipidemic effect of aqueous extract of Lannea edulis in alloxan-induced diabetic rats, *Frontiers in Pharmacology*, **9**: 1099
- Bharti, S., Sharma, N., Kumar, A., Jaiswal, S., Krishna, S., Gupta, A., Ghosh, A. and Prakash, O. 2012, Dipeptidyl Peptidase IV inhibitory activity of seedextract of Castanospermum Australe and Molecular docking of their Alkaloids, *Topclass Journal of Herbal Medicine*, **1(1)**: 1-7.
- Breitinger, H. 2012, ‘Drug Synergy-Mechanism and Method of Analysis’, in: Acree, B., *Toxicity and Drug Testing*, Intechopen, London, pp 143-166.
- Brem, H. and Tomic-Canic, M. 2007, Cellular and molecular basis of wound healing in diabetes, *Journal of Clinical Investigation*, **117(5)**: 1219–1222.
- Cooper, G. M., 2000, *The Cell A Molecular Approach Second Edition*, Sinauer Associates, Sunderland.
- Croxtal, J.D. and Keam, S.J. 2008, Vildagliptin: A review of its use in the management of type 2 diabetes mellitus, *Drugs*, **68**: 2387–2409.
- Dahlan, M.S. 2014, *Statistik untuk Kedokteran and Kesehatan: Deskriptif, Bivariat, dan Multivariat*, Epidemiologi Indonesia, Jakarta.
- Deacon, C.F., 2010, Dipeptidyl Peptidase-4 inhibitors in the treatment of type 2 diabetes: a Comparative review, *Diabetes, Obesity and Metabolism*, **13(1)**: 7–18.
- Departemen Kesehatan RI, 2005, *Pharmaceutical care untuk penyakit diabetes mellitus*, Jakarta: Departemen Kesehatan Republik Indonesia.
- Departemen Kesehatan RI, 1979, *Materia Medika Indonesia* Jilid III, Jakarta: Departemen Kesehatan Republik Indonesia.

- Departemen Kesehatan RI, 1980, *Materia Medika Indonesia* Jilid IV, Jakarta: Departemen Kesehatan Republik Indonesia.
- Ditjen POM, 2000, *Parameter Standart Umum Ekstrak Tumbuhan Obat*, Jakarta: Departemen Kesehatan Republik Indonesia.
- Duez, H., Cariou, B. and Staels, B. 2012, DPP-4 inhibitors in the treatment of type 2 diabetes, *Biochemical Pharmacology*, **83**(7): 823-32.
- Farnsworth, N. R., 1966, Biological and Phytochemical Screening of Plants, *J.Pharm. Sci.*, **55**(3): 225-276.
- Federer, W. T. 1966, Randomization and Sample Size in Experimentation. *Lecture Presented at The Food and Drug Administration Statistic Seminar*, Cornell University, Washington D.C, pp 2-5.
- Griya Sehat Aska. 2013, *Manfaat dan khasiat Sambiloto* [online], diakses pada 10 november 2019, (http://www.cafesehat.com/wp-content/uploads/2013/11/manfaat_daun_sambiloto.jpg, 2013).
- Ghosh, P. K. and Gaba, A. 2013, Phyto-Extracts in Wound Healing, *Journal of Pharmacy and Pharmaceutical Sciences*, **16**(5): 760-820.
- Gorrel, M.D., 2005, Dipeptidyl Peptidase IV and Related Enzymes in Cell Biology and Liver Disorders, *Clinical Science*, **108**(4): 277–292.
- Harborne, J.B. 1987, *Metode Fitokimia*, Diterjemahkan dari Bahasa Inggris oleh Padmawinata, K dan Soediro, I, Institut Teknologi Bandung, Bandung.
- He, Y.L. 2012, Clinical pharmacokinetics and pharmacodynamics of vildagliptin, *Clinical Pharmacokinetics*, **51**(3): 147 – 62.
- Henness, S., Keam, S.J. 2006, Vildagliptin, *Drugs*, **66**:1989–2001.
- Hopsu-Havu V.K. and Glenner G.G., 1966, A new dipeptide naphthylamidase hydrolyzing glycyl prolyl-beta-naphthylamide, *Histochemie*, **7**(3):197–201.
- IDF, 2017, *Diabetes Atlas Eighth Edition*, Brussels: International Diabetes Federation.
- Inzucchi, S.E., Bergenstal, R.M., Buse, J.B., Diamant, M., Ferraninni, E., Nauck, M., Peters, A.L., Tsapas,A.,Wender,R. and Matthews, D.R. 2012, Management of Hyperglycemia in Type 2 Diabetes: A Patient Centered Approach, *American Diabetes Association*, **35**: 1367-1368.

- Katzung, B.G. 2013, *Farmakologi Dasar dan Klinik*, Edisi 12, Diterjemahkan dari Bahasa Inggris oleh Soeharsono, R., et al., EGC, Jakarta.
- Katzung, B.G. 2007, *Farmakologi Dasar dan Klinik*, Edisi 7, Diterjemahkan dari Bahasa Inggris oleh Soeharsono, R., et al., EGC, Jakarta.
- Kementerian Kesehatan RI, 2014, Pusat Data dan Informasi Kementerian Kesehatan RI: Situasi dan Analisis Diabetes, Jakarta: Departemen Kesehatan Republik Indonesia.
- Konsue A, Picheansoonthon C. and Talubmook C. 2017, Fasting Blood Glucose Levels and Hematological Values in Normal and Streptozotocin-Induced Diabetic Rats of *Mimosa pudica* L. Extracts, *Pharmacogn J.*, **9(3)**: 315-22.
- Kristanti, A.N., Aminah, N.S., Tanjung, M., Kurniadi, B., 2008, *Buku Ajar Fitokimia*, Airlangga University Press, Surabaya, hal 54.
- Kuherbal, 2013, *Khasiat dan Manfaat Kandungan Daun Salam Bagi Kesehatan*, [online], diakses pada 25 november 2019 https://pemkomedan.go.id/artikel-11226-manfaat-dan-khasiat-daun-salam-untuk-kesehatan.html_2013)
- Lau, T. W., Lam, F. F. Y., Lau, K. M., Chan, Y. W., Lee, K. M., Sahota, D. S., Ho, Y. T., Fung, K.P., Leung, P.C. and Lau, C.B.S. 2009, Pharmacological investigation on the wound healing effects of *Radix Rehmanniae* in an animal model of diabetic foot ulcer, *Journal of Ethnopharmacology*, **123(1)**: 155-162.
- Lehnigner AL. 1990. *Dasar-Dasar Biokimia*, diterjemahkan dari Bahasa inggris oleh Thenawidjaja, Erlangga, Jakarta.
- Lenzen S. 2008, The mechanisms of alloxan- and treptozotocin-induced diabetes, *Diabetologia*, **51**:216–226.
- Lim, N. S. J., Sham, A., Chee, S. M. L., Chan, C. and Raghunath, M. 2016, Combination of ciclopirox olamine and sphingosine-1-phosphate as granulation enhancer in diabetic wounds, *Wound Repair and Regeneration*, **24(5)**: 795–809.
- Lipsky, B. A., Berendt, A. R., Cornia, P. B., Pile, J. C., Peters, E. J. G., Armstrong, D. G., Deery, H.G., Embil, J.M., Joseph, W.S., Karchmer, A.W., Pinzur, M.S. and Senneville, E. 2012, Infectious Diseases Society of America Clinical Practice Guideline for the

Diagnosis and Treatment of Diabetic Foot Infections, *Clinical Infectious Diseases*, **54(12)**: 132–173.

- Lloyd, G., Friedman, G., Jafri, S., Schultz, G., Fridman, A. and Harding, K. 2010, Gas Plasma: Medical Uses and Developments in Wound Care. *Plasma Processes and Polymers*, **7(3-4)**: 194–211.
- Long, M., Cai, L., Li, W., Zhang, L., Guo, S., Zhang, R., Zheng, Y., Liu, X., Wang, M., Zhou, X., Wang, H., Li, X., Li, L., Zhu, Z., Yang, G. and Zheng, H. 2017, DPP-4 Inhibitors Improve Diabetic Wound Healing via Direct and Indirect Promotion of Epithelial-Mesenchymal Transition and Reduction of Scarring, *Diabetes*, **67(3)**: 518–531.
- Malole, M. M. B., dan C. S. U. Pramono, 1989, *Penggunaan Hewan hewan Percobaan Laboratorium*, IPB, Bogor.
- Mohanty A, Pradhan DK, Mishra MR., Sahoo JK, Mishra A, Nandy BC, Meena K. and Mokade L. 2010, Preliminary Pytochemical Screening and Wound Healing Activity of *Andrographis paniculata*, *J Chem Pharm Res*, **2**: 649-654.
- Nagori, B.D. and Solanki, R. 2011, Role of Medicinal Plants in Wound Healing, *Research Journal of Medicinal Plant*, **5(4)**: 392-405.
- Notoatmodjo, S. 2012, *Metodologi Penelitian Kesehatan*, Rineka Cipta, Jakarta.
- Nuratmi, B., Winarno, M.W. dan Sundari, S. 1998, ‘Khasiat Daun Salam (*Eugenia polyantha* Wight) Sebagai Antidiare pada Tikus Putih’, Badan Litbangkes Depkes RI, *Obat Asli Indonesia*, Jakarta, Indonesia, hal 14-17.
- Patel, S., Srivastava, S., Singh, M. R. and Singh, D. 2019, Mechanistic insight into diabetic wounds: Pathogenesis, molecular targets and treatment strategies to pace wound healing, *Biomedicine and Pharmacotherapy*, **112**: 108615.
- Priambodo, S., 1995, *Pengendalian Hama Tikus Terpadu*, Penebar Swadaya, Jakarta.
- Pucar, L.B., Pugel, E.P., Detel, D. and Varljen, J. 2017, Involvement of DPP IV/CD26 in cutaneous wound healing process in mice, *Wound Repair and Regeneration*, **25(1)**: 25-40.
- Rahayu, N.L.P. 2014, ‘Aktivitas inhibisi dipeptidyl peptidase IV dari kombinasi ekstrak Etanol *Syzygium polyanthum* Dan Ekstrak

- Etanol *Andrographis paniculata*', Skripsi, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.
- Robinson, P. K. 2015, Enzymes: principles and biotechnological applications, *Essays in Biochemistry*, **59(0)**: 1–41.
- Rosyid, F.N. 2017, Etiology, pathophysiology, diagnosis and management of diabetes's foot ulcer, *International Journal of Research in Medical Sciences*, **5(10)**: 4206-4213.
- Roy, S., Sehgal, R., Padhy, B.M. and Kumar, V.L. 2005, Antioxidant and protective effect of latex of Calotropis procera against alloxan-induced diabetes in rats. *Journal of Ethnopharmacology*, **102**: 470–473.
- Salazar, J. J., Ennis, W. J. and Koh, T. J. 2016, Diabetes medications: Impact on inflammation and wound healing, *Journal of Diabetes and Its Complications*, **30(4)**: 746–752.
- Scanbur, 2019, Research Models diakses pada 25 November 2019, (<http://www.scanburresearch.com/research-models.html>, 2019)
- Sigma-Aldrich. 2019, Dipeptidyl peptidase IV, diakses pada 25 November 2019, <https://www.sigmaaldrich.com/life-science/metabolomics/enzyme-explorer/cellsignaling-enzymes/dipeptidyl-peptidase-iv.html>.
- Sigma-Aldrich. 2019, Gly-Pro *p*-nitroanilidehydrochloride, diakses pada 25 November 2019, <http://www.sigmaaldrich.com/catalog/product/sigma/g0513?lang=en®ion=ID>.
- Sigma-Aldrich. 2019, Ile-Pro-Ile diakses pada 25 November 2019, [<http://www.sigmaaldrich.com/catalog/product/sigma/i9759?lang=en®ion=ID>].
- Sigma-Aldrich. 2019, 96 well plate diakses pada 25 November 2019, (<https://www.sigmaaldrich.com/technical-documents/articles/biology/96-well-plate-template.html>).
- Siregar, S. 2013, *Metode Penelitian Kuantitatif dilengkapi dengan perbandingan perhitungan manual dan SPSS*, Kencana Prenada Media Group, Jakarta.
- Smith, J.B dan Mangkoewidjojo, S. 1988, *Pemeliharaan Pembibitan dan Penggunaan Hewan Percobaan di Daerah Tropis*, Universitas Indonesia Press, Jakarta.

- Studiawan, H. Santosa, M. H. 2005, Uji Aktivitas Penurunan Kadar Gula Darah Ekstrak Daun *Eugenia polyantha* pada Mencit yand Diinduksi Aloksan, Universitas Erlanga, *Media Kedokteran Hewan*, Surabaya, Indonesia, hal 62-65.
- Sudewo, B., 2007, *Basmi Penyakit dengan Sirih Merah*, PT Agromedia Pusat, Jakarta.
- Suharmiati. 2003, Pengujian Bioaktivitas Anti Diabetes Mellitus Tumbuhan Obat, *Cermin Dunia Kedokteran*, **14**: 140-146.
- Sukarti, E., Hartanti, L. dan Setiawan, H. K. 2013, ‘Pengujian Potensi kombinasi ekstrak air sambiloto (*andrographis paniculata*) dan ekstrak air daun salam (*Syzygium polianthum*) sebagai inhibitor dipeptidyl peptidase IV dan α -Glukosidase pada Penatalaksanaan terapi diabetes mellitus tipe 2’, Direktorat Jenderal Pendidikan Tinggi, *Laporan Penelitian Unggulan Perguruan Tinggi*, Jakarta, Indonesia, hal 39-42.
- Ulumbu, F. 2013, ‘Aktivitas Inhibisi dari Ekstrak Etanol Daun *Syzygium Polyanthum* terhadap Enzim Dipeptidyl Peptidase 4’, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya.
- Van Steenis. 2008. *Flora* Cetakan ke-12, PT Pradnya Paramita, Jakarta.
- Voigt, R. 1995. *Buku Pelajaran Teknologi Farmasi* Edisi V, Gadjah Mada University Press, Yogyakarta.
- Yulinah, E., Sukrasno, dan Fitri, A. 2001, Aktivitas Antidiabetika Ekstrak Etanol Sambiloto (*Andrographis paniculata* Nees (Acanthaceae)), *Jurnal Manajemen Sinergi*, **6(1)**: 13-20
- Zhang, X. 1999, *WHO monographs on selected medicinal plants* Vol 2, World Health Organization, Geneva.