

BAB 5

KESIMPULAN DAN SARAN

5.1. Kesimpulan

Dari penelitian yang telah dilakukan maka dapat disimpulkan,

1. Semua senyawa uji diprediksi dapat memberikan aktivitas antidiabetes seperti pioglitazon, dengan urutan isolikuiritigenin, pterofuran, (-)-epikatekin, pterokarpin, pterostilben, homopterokarpin, formononetin, santalin, flavon, isoflavon. Namun demikian senyawa-senyawa ini tidak lebih poten dalam interaksinya dengan reseptor PPAR γ dibandingkan pioglitazon.
2. Asam amino yang paling banyak terlibat pada interaksi antara senyawa-senyawa dalam tanaman anggasa dengan reseptor 2XKW melalui ikatan hidrogen adalah Ser289, Sis285 dan Glu295. (-)-Epikatekin mempunyai kelebihan dibandingkan senyawa yang lain yaitu mampu mengikat asam amino yang paling banyak melalui ikatan hidrogen.

5.2. Saran

1. Dari hasil *docking* terlihat bahwa senyawa-senyawa yang terkandung dalam daun anggasa dapat membentuk kompleks yang stabil dengan PPAR γ selain itu jika dilihat dari nilai *rerank score*-nya, terdapat senyawa yang memiliki nilai *rerank score* yang mendekati nilai *rerank score* pioglitazon sehingga dapat dimungkinkan bahwa senyawa-senyawa yang terkandung dalam daun anggasa dapat bekerja pada reseptor ini. Untuk membuktikan prediksi tersebut, maka dapat dilakukan pengujian lebih lanjut mengenai aktivitas antidiabetes dari senyawa yang terkandung dalam daun anggasa terhadap PPAR γ secara *in vitro*.

2. Perlu dilakukan studi *insilico* lebih lanjut mengenai senyawa dalam tanaman anggusta terhadap reseptor yang berkaitan dengan efek antidiabetes yang lain seperti DPP-4 (*dipeptidyl peptidase-4*), GLP-1 (*Glucagon-like peptide-1*), atau reseptor insulin.

DAFTAR PUSTAKA

Ahmad F, Khan MM, Rastogi AK, Chaubey M, Kidwai JR, 1991, **Effect of (-) Epicatechin on cAMP Content, Insulin Release and Conversion of Proinsulin to Insulin in Immature and Mature Rat Islets in Vitro**, volume 6, pp.516-20.

Antonius, 2011, **Efek Hipoglikemik Sediaan Transdermal Ekstrak Pterocarpus Indicus Willd Dengan Enhancer Mentol Pada Tikus Diabetes Yang Diinduksi Aloksan**, Skripsi: Unika Widya Mandala, Surabaya.

Backer, C.A. & Van Den Brink, R.C.B., 1963, **Flora of Java**, volume I, Groningen: N.V.P. Noordhoff, p.615.

Bailey, L. H., 1953, **The Standard Cyclopedia of Horticulture**, volume I & III, New York: The Macmillan Company, pp. 2-3, 41-42 (I), 2853 (III).

Behrman R.E., R.M. Kliegman, A.M. Arvin, 1996, **Ilmu Kesehatan Anak**, 15th ed., volume 3, Ed: A.S. Wahab, Jakarta : EGC.

Berger J., Moller DE, 2002, **The Mechanisms of Action of PPARs**, Annu Rev Med, volume 53, pp.409-435.

Block JH, 2011, Drug Design Strategies, in Beale JM ad Block JH (Eds), **Wilson and Gisvold's Textbook of Organic Medicinal and Pharmaceutical Chemistry**, 12th Ed, Philadelphia: Lippincott Williams & Wilkins, pp.38-39.

Chan, S.L., and Labute P, 2010, **Training a Scoring Function for the Alignment of Small Molecules**, *J.Chem.Inf.Model.*, volume 50, pp.1724-1735.

Cronet, P., Petersen, J.F., Folmer, R., Blomberg, N., Sjöblom, K., Karlsson, U., Lindstedt, E.L., Bamberg, K., 2001, **Structure of the PPAR-alpha and -gamma Ligand Binding Domain in Complex with AZ 242; ligand Selectivity and Agonist Activation in the PPAR Family**, *Structure*, volume 9, pp.699-701.

Davis S.N., 2006, **Insulin, Oral Hypoglycemic Agents, and the Pharmacology of the Endocrine Pancreas**, In: Goodman & Gilman's The Pharmacological Basis of Therapeutics, 11th ed., New York: McGraw-Hill.

Departemen Kesehatan RI, 2005, **Pharmaceutical Care untuk Penyakit Infeksi Diabetes Mellitus**, Jakarta: Departemen Kesehatan.

Diabeticbar, 2009, Epiicatechin, [Online]. <http://www.diabeticbar.com/epicathecin.htm>, [2012, Agustus 28].

Dias, R., W.F. de Azevedo Jr, 2008, **Molecular Docking Algorithms, Current Drug Targets**, volume 9, pp.1040-1047.

Drucker DJ, Nauck MA, 2006, **The Incretin System: Glucagon-Like Peptide-1 Receptor Agonists and Dipeptidyl Peptidase-4 Inhibitors in Type 2 Diabetes**, Lancet 368 (9548), pp.1696–705.

Duke, J.A., 1983, *Pterocarpus indicus Willd.*, [Online]. <http://www.hort.purdue.edu/>, [2012, Agustus 28].

Ebadi,M., 2007, **Pharmacodynamic Basis of Herbal Medicine** 2nd ed., London: Taylor&Francis.

Ekins, S., J. Mestres' B. Testa, 2007, *In Silico Pharmacology for Drug Discovery: Methods for Virtual Ligand Screening and Profiling*, British Journal of Pharmacology, volume 152, pp. 9-20.

Evans,W., 2004, **Trease and Evans Pharmacognosy** 15th ed, Philadelphia : Elsevier

Gampe Jr., R.T., Montana, V.G., Lambert, M.H., Miller, A.B., Bledsoe, R.K., Milburn, M.V., Kliewer, S.A., Willson, T.M., Xu, H.E., 2000, **Asymmetry in the PPARgamma/Rxralpha Crystal Structure Reveals the Molecular Basis of Heterodimerization Among Nuclear Receptors**, Mol.Cell, volume 5, pp.545-555

Gampe Jr., R.T., Montana, V.G., Lambert, M.H., Miller, A.B., Bledsoe, R.K., Milburn, M.V., Kliewer, S.A., Willson, T.M., Xu, H.E., 2000, **Asymmetry in the PPARgamma/Rxralpha Crystal Structure Reveals the Molecular Basis of Heterodimerization among Nuclear Receptors**, Mol.Cell, volume 5, pp.545-555 .

Hartanti,L., H.K. Setiawan, A. Kresnamurti, 2011, **Molecular Docking of Several Compound of Bungur (*Lagerstroemia speciosa* [L.] Pers) Leaves to (IGF-1R) Receptor Tyrosine Kinase with Molegro Virtual Docker**, Proceeding of the 2nd International Conference on Pharmacy and Advanced Pharmaceutical Sciences, Book I : Pharmaceutical Science, 1st ed., Universitas Gadjah Madah: Yogyakarta, pp.159-166.

Heyne, K., 1987, **Tumbuhan Berguna Indonesia jilid 2**, Jakarta: Yayasan Sarana Wana Jaya, pp.998-1003.

Holtje, H.D., W. Sippl, D. Rognan, G. Folkers, 2008, **Molecular Modelling**, Weinheim: Wiley-VCH Verlag GmbH & Co. KGaA.

<http://cambridgesoft-chemdraw-ultra.software.informer.com/11.0/> [2012, Agustus 28]

<http://chembionews.cambridgesoft.com/Articles>. [2012, Agustus 28]

<http://en.wikipedia.org/wiki/Pioglitazone> [2012, November 15].

<http://en.wikipedia.org/wiki/Pterostilbene>. [2012, Juni 26].

<http://en.wikipedia.org/wiki/Rosiglitazone> [2012, November 15].

<http://id.wikipedia.org/wiki/Berkas:Flavon.svg>. [2012, Juni 26].

<http://scholarworks.umass.edu>. [2012, Juni 26].

<http://www.chemicalbook.com>. [2012, Juni 26].

<http://www.crcnetbase.com>. [2012, Juni 26].

<http://www.scielo.br/scielo.php>. [2012, Juni 26].

Kapetanovic, I.M., 2008, **Computer-Aided Drug Discovery and Development: In-Silico-Chemico-Biological Approach**, Chem Biol Interact., volume 171(2), pp.165-176.

Katzung, B.G., 2007, **Basic & Clinical Pharmacology** 10th ed., Boston: The McGraw-Hill Companies, Inc., pp.684-701.

Krovat, E.M., Steindl T., Langer T., 2005, **Recent Advances in Docking and Scoring, Current Computer-Aided Drug Design**, volume 1, pp.93-102.

Kumari, A., M. Ratnam, A.K. Kuna, Srinivasulu, 2010, **Computer-Aided Design and Screening of Chalcones as Novel PPAR Gamma Agonists**, IJPT, volume 2, pp.38-65

Li, Y., Wang, Z., Furukawa, N., Escaron, P., Weiszmann, J., Lee, G., Lindstrom, M., Liu, J., Liu, X., Xu, H., Plotnikova, O., Prasad, V., Walker, N., Learned, R.M., Chen, J.L., 2008, **T2384, a Novel Antidiabetic Agent with Unique Peroxisome Proliferator-Activated Receptor Gamma Binding Properties**, J.Biol.Chem, volume 283, pp.9168-9176.

Mahindroo, N., Peng, Y.H., Lin, C.H., Tan, U.K., Prakash, E., Lien, T.W., Lu, I.L., Lee, H.J., Hsu, J.T.A., Chen, X., Liao, C.C., Lyu, P.C., Chao, Y.S., Wu, S.Y., Hsieh, H.P, 2006, **Structural Basis for the Structure-Activity Relationships of Peroxisome Proliferator-Activated Receptor Agonists**, J.Med.Chem., volume 49, pp.6421-6424

Manual Molegro Virtual Docker, 2010

Mueller, J., Schupp, M., Unger, T., Kintscher, U., Heinemann, U. 2011, **Binding Diversity of Pioglitazone by Peroxisome Proliferator-Activated Receptor-Gamma**, <http://www.pdb.org/pdb/explore/explore.do?structureId=2xkw>. [2012, Desember 18].

Muppalaneni,N.B., A.A Rao, 2011, **Computational Analysis on Cuminum Cyminum Compounds Against Aldose Reductase as Anti-Diabetic Agents**, Delivered in: *International Conference on Bioinformatics and Computational Biology*.

O'Donoghue S.I., Russel R.B., Schafferhans A., Three-Dimensional Structure in Target Discovery and Validation, in Leon D., and Markel S. (Eds.), **In Silico Technologies in Drug Target Identification and Validation**, Boca Raton: CRC Press, Taylor and Francis Group, LLC, pp. 290-296.

Ostberg, T., Svensson, S., Selen, G., Uppenberg, J., Thor, M., Sundbom, M., Sydow-Backman, M., Gustavsson, A.L., Jendeberg, L., 2004, **A New Class of Peroxisome Proliferator-Activated Receptor Agonists with a Novel Binding Epitope Shows Antidiabetic Effects**, *J.Biol.Chem.*, volume 279, pp.41124-41130.

Parker, S., 2007, **Ensiklopedia Tubuh Manusia, Penerjemah: Winardini**, Ed: D. Nugraha dan R. Nuraeni, London: Dorling Kindersley Limited.

Prasetia, T., 2011, **Simulasi Dinamika Molekul Kompleks Histone Deacetylase (HDAC) Kelas II Homo Sapiens dengan Suberoylanilidine Hydroxamic Acid (SAHA) dan Turunannya sebagai Inhibitory Kanker Serviks**, *Skripsi Sarjana*, Fakultas Matematika dan Ilmu Pengetahuan Alam Universitas Indonesia.

Puspaningtyas, A.R., 2012, **Docking Studies of ethanol extract *Physalis peruviana* Linn using Molegro Virtual Docker on Insulin Tyrosine Kinase Receptor as Antidiabetic Agent**, Delivered in: International of the Indonesian Chemical Society 2012, HKI: Jawa Timur, p.90.

Rao, B. K., Giri, R., Kesavulu, M. M., Apparao, Ch., 2001, **Effect of Oral Administration of Bark Extracts of *Pterocarpus santalinus* L. On Blood Glucose Level in Experimental Animal**, *Journal of Ethnopharmacology*, volume 70, pp.69-74.

Rognan, D., 2011, **Docking Methods for Virtual Screening: Principles and Recent Advances**, In: *Virtual Screening*, Ed: R. Mannhold, H. Kubinyi, G. Folkers, Weinheim: Wiley-VCH Verlag GmbH & Co. KGaA.

Sauerberg, P., Pettersson, I., Jeppesen, L., Bury, P.S., Mogensen, J.P., Wassermann, K., Brand, C.L., Sturis, J., Woldike, H.F., Fleckner, J., Andersen, A.-S.T., Mortensen, S.B., Svensson, L.A., Rasmussen, H.B., Lehmann, S.V., Polivka, Z., Sindelar, K., Panajotova, V., Ynddal, L., Wulff, E.M., 2002, **Novel Tricyclic-Alpha-Alkyloxyphenylpropionic Acids: Dual Pparalpha/Gamma Agonists with Hypolipidemic and Antidiabetic Activity**, *J.MED.CHEM.*, volume 45, pp.789-804

Siddiqui NI, Januari 2009, **Incretin mimetics and DPP-4 inhibitors: new approach to treatment of type 2 diabetes mellitus**, Mymensingh Med J., 18, volume 1, pp.113-24.

Siswandono, 2011, **Studi Pemodelan Molekul Interaksi Beberapa Turunan Penisilin dengan Reseptor DD-Transpeptidase dari Streptomyces R61(PWC)**, Majalah Farmasi Airlangga, volume 9, no. 2, pp.33-41.

Soedibyo, B., 1998. **Alam Sumber Kesehatan Manfaat Dan Kegunaan**, Jakarta: Balai Pustaka.

Steenis, C.G.G.J.V., Hoed, D.D., Bloembergen, S., Eyma, P.J., 1975, **Flora untuk Sekolah di Indonesia**, penerjemah: M. Surjowinoto, S. Hardjosuwarno, S.S. Adisewojo, Wibisono, M. Partodidjojo, S. Wirjahardja, Cetakan VII Jakarta: PT. Pradnya Paramita, pp.232-233.

Suherman, S.K., 2007, **Insulin dan Diabetik Oral**, In: Farmakologi dan Terapi 5th, Ed: Gunawan,S.G., Jakarta: Departemen Farmakologi dan Terapeutik Fakultas Kedokteran Universitas Indonesia, pp.481-495.

Takeuchi, S., Kono, Y., Nambata, T., Terada, N., Hadiman,Watanabe, R., Suzuki, Y., Kawarada, A. & Adisewojo, S.S., 1986, **A Bioactive Polyphenolic Constituent in the Bark of *Pterocarpus indicus* Willd and Its Effect**, Agricultural and Biological Chemistry, volume 50, pp.1117-1122.

Thomsen, R., M.H. Christensen, 2006, **MolDock: A New Technique for High-Accuracy Molecular Docking**, *J. Med. Chem.*, volume 49, pp. 3315-3321.

Thomson, Lex A. J., [2006, April 26]. **Species Profiles for Pacific Island Pterocarpus indicus**, [Online]. <http://www.traditionaltree.org>. [2012, Agustus 2012].

Thorell A., 1999. **Exercise and Insulin Cause GLUT 4 Translocation in Human Skeletal Muscle**, *Am J. Physiol*, volume 277, pp.733-741.

Weidner, C., De Groot, J.C., Prasad, A., Freiwald, A., Quedenau, C., Kliem, M., Witzke, A., Kodelja, V., Han, C.-T., Giegold, S., Baumann, M., Klebl, B., Siems, K., Mueller-Kuhrt, L., Schuermann, A., Schueller, R., Pfeiffer, A.F.H., Schroeder, F.C., Buessow, K., Sauer, S., 2012, **Amorfrutins are Potent Antidiabetic Dietary Natural Products**, Proc.Natl.Acad.Sci.USA, volume 109, p.7257.

WHO, 2011, Diabetes, [Online]. <http://www.who.int/mediacentre/factsheets/fs312/en/>. [2012, April 12].

www.rcsb.org/pdb/static.do. [2012, Agustus 28].

Xu, H.E., Lambert, M.H., Montana, V.G., Plunket, K.D., Moore, L.B., Collins, J.L., Oplinger, J.A., Kliewer, S.A., Gampe Jr., R.T., McKee, D.D., Moore, J.T., Willson, T.M., 2001, **Structural Determinants of ligand Binding Selectivity Between the Peroxisome Proliferator-Activated Receptors**, Proc.Natl.Acad.Sci.USA, volume 98, pp.3919-13924.

Yuratni, F., 2011, **Efek Hipoglikemik Sediaan Transdermal Ekstrak *Pterocarpus Indicus* Willd Dengan Enhancer Tween 80 Pada Tikus Diabetes Aloksan**, Skripsi: Unika Widya Mandala, Surabaya.