BAB 5
KESIMPULAN DAN SARAN

5.1. Kesimpulan

Berdasarkan hasil penelitian *docking* terhadap 14 senyawa Cinnamomi Cortex dengan reseptor *linked amidobenzimidazole STING agonist* (6DXL) (Ramanjulu *et al*., 2018) memberikan hasil:

1. Terdapat 4 senyawa ligan dari Cinnamomi Cortex yang berpotensi sebagai imunomodulator yang memiliki afinitas ikatan (ΔG) lebih rendah yaitu pada senyawa (-)-katekin (-5,84 kkal/mol), (+)-katekin (-5,81 kkal/mol), beta kariofilen (-5,69 kkal/mol) dan proantosianidin tipe A (-5,61 kkal/mol) dibandingkan dengan ligan asli HG4 (-5,6 kkal/mol).
2. Terdapat 4 senyawa ligan dari Cinnamomi Cortex yang berpotensi sebagai imunomodulator yang memiliki konstanta inhibisi (Ki) lebih rendah yaitu pada senyawa (-)-katekin (52,17 μM), (+)-katekin (55,31 μM), beta kariofilen (67,51 μM) dan proantosianidin tipe A (77,8 μM) dibandingkan dengan ligan asli HG4 (78,72 Mm).
3. Residu-residu asam amino yang berperan penting dalam membentuk interaksi antara makromolekul dengan ligan seperti ikatan hidrogen dan ikatan hidrofobik adalah SER241, SER162, TYR167 dan TYR240.

5.2. Saran

Selanjutnya penelitian ini perlu dilakukan uji simulasi dinamika, uji *in vitro* dan uji *in vivo* untuk mengetahui aktivitas senyawa hasil analisis *docking* yang berpotensi sebagai imunomodulator.

DAFTAR PUSTAKA

Alberti, T.B., Rodrigo, M., Maira, A.B., Nadia, R.B.R., Joao, B.C. and Rafael, C.D. 2014, Essential Oil From *Pterodon emarginatus* Seeds Ameliorates Experimental Autoimmune Enchephalomyelitis By Modulating Th1/Treg Cell Balance, *Journal of Ethnopharmacology*, **155(1)**: 485-494.

Al-Dhubiab, B.E. 2012, Pharmaceutical Applications and Phytochemical Profile of *Cinnamomum burmannii*, *Pharmacognosy Reviews*, **6(12)**: 125-131.

Arwansyah, Laksmi, A., Tony, I.S. 2014, Simulasi *Docking* Senyawa Kurkumin dan Analognya Sebagai Inhibitor Reseptor Androgen pada Kanker Prostat, *Current Biochemistry*, **1(1)**: 11-19.

Balekar, N., Subhash, B., Mohan, V. and Prasad, A.T. 2014, Modulatory Activity of a Polyphenolic Fraction of *Cinnamomum zeylanicum* L. Bark on Multiple Arms of Immunity in Normal and Immunocompromised Mice, *Journal of Applied Pharmaceutical Science*, **4(7)**: 114-122.

Balijepalli, M.K., Ayuba, S.B., Raghavendra, S. and Mallikarjuna, R.P. 2017, *Cinnamomum* Genus: A Review on Its Biological Activities, *International Journal of Pharmacy and Pharmaceutical Sciences*, **9(2)**: 1-11.

Bara, Y., Apriani, H.R., Sri, S.N.N.D.T., Yoga, T.R., Fitra, A.D.N. dan Dewi, R.T.S. 2019, Prediction Potential Chlorogenic Acid as Inhibitor ACE (*In Silico* Study), *Bioscience*, **3(2)**: 197-203.

Behl, T., Keshav, K., Ciprian, B., Marius, R., Delia, C.N., Cristiana, B., Raluca, A.C.A., Carmen, P., Gokhan, Z., Aayush, S., Rajwinder, K., Arun, K., Sandeep, A., Dhruv, S., Deepak, C. and Simona, B. 2021, Exploring the Multifocal Role of Phytochemicals as Immunomodulators, *Biomedicine & Pharmacotherapy*, **133(2021)**: 1-18.

BIOVIA, Dassault Systèmes, 2021, (Discovery Studio Client), (v21.1.0.20298), San Diego: Dassault Systèmes.

Burley, S.K., Helen, M.B., Gerard, J.K., John, L.M., Haruki, N. and Sameer, V. 2018, Protein Data Bank (PDB): The Single Global

Macromolecular Stucture Archive, *Methods in Molecular Biology*, **1607**: 627-641.

Damayanti, S., Khonsa, K. dan Tasia, A. 2021, Antiviral Activity and Toxicity Prediction of Compounds Contained in Figs (*Ficus carica* L.) by *In Silico* Method, Indonesian *Journal of Pharmaceutical Science and Technology*, **8(1)**: 21-23.

Dashti, H., Jonathan, R.W., William, M.W., John, L.M. and Hamid, R.E. 2019, Analysis: Automated Evaluation of Consistency Within the PubChem Compound Database, *Scientific Data*, **6(190023)**: 1-10.

Dias, R. and Walter, F.A.Jr. 2008, Molecular Docking Algorithms, *Current Drug Targets*, **9(12)**: 1040-1047.

Fakhruri, M., Yuni, R. dan Isfanda, 2021, Potensi Fitokimia *Citrus aurantium* (Hesperetin, Naringenin) Dalam Menghambat Xantin Oksidase Pada Hiperurisemia Secara *In Silico*, *Jurnal Health Sains*, **2(1)**: 79-89.

Fariza, A., Entin, M.K. dan Elok, W. 2012, Aplikasi Flash Lite Untuk Pembelajaran Kimia (Materi: Ikatan Kimia & Struktur Atom), Surabaya: Institut Teknologi Sepuluh Nopember.

Ferencz, L. and Daniela, L.M. 2015, Identification of New Superwarfarin-Type Rodenticides by Structural Similarity. The Docking of Ligands on the Vitamin K Epoxide Reductase Enzyme's Active Site, *Acta Universitatis Sapientiae: Agriculture and Environment*, **7**: 108-122.

Gaillard, T. 2018, Evaluation of Autodock and Autodock Vina on the CASF-2013 Benchmark, *Journal of Chemical Information and Modeling*, **58(8)**: 1697-1706.

Ganeshpurkar, A. and Ajay, S. 2018, *In Silico* Interaction of Catechin With Some Immunomodulatory Targets: A Docking Analysis, *Indian Journal of Biotechnology*, **17**: 626-631.

Ganeshpurkar, A. and Ajay, S. 2020, Immunomodulatory Effect of Rutin, Catechin, and Hesperidin on Macrophage Funcion, *Indian Journal of Biochemistry & Biophysics*, **57(1)**: 58-63.

Geldenhuys, W.J., Kevin, E.G., Mark, W., David, D.A. and Cornelis, J.V.S. 2006, Optimizing the Use of Open-Source Software Applications in Drug Discovery, *DDT*, **11(3/4)**: 127-132.

Goodsell, D.S., Christine, Z., Luigi, D.C., Jose, M.D., Brian, P.H., Irina, P., Joan, S., Chenghua, S., Maria, V., John,D.W., Jasmine, Y.Y. and Stephen, K.B. 2020, RCSB Protein Data Bank: Enabling Biomedical Research and Drug Discovery, *Protein Science*, **29(1)**: 52-65.

Hardjono, S. 2013, Sintesis dan Uji Aktivitas Antikanker Senyawa 1-(2-klorobenzoiloksi) urea dan 1-(4-klorobenzoiloksi)urea, *Berkala Ilmiah Kimia Farmasi*, **2(1)**:16-21.

Humphrey, W., Dalken, A. and Schulten, K. 1996, VMD - Visual Molecular Dynamics, *Journal of Molecular Graphic and Modelling*, **14(1)**: 33-38.

Inna, M., Novi, A., Septika, P., 2010, Potential Use of *Cinnamomum burmannii* Essential Oil-based Chewing Gum as Oral Antibiofilm Agent, *Journal of Dentistry Indonesia*, **17(3)**: 80-86.

Keluntur, F.J., Resmi, M. dan Abd. Kakhar, U. 2020, Virtual Screening Kandungan Senyawa Kipas Laut (*Goronia mariae*) Sebagai Antiasma, *ALCHEMY Jurnal Penelitian Kimia*, **16(2**): 199-210.

Kim, S., Jie, C., Tiejun, C., Asta, G., Jia, H., Siqian, H., Qingliang, L., Benjamin, A.S., Paul, A.T., Bo, Y., Leonid, Z., Jian, Z. and Evan, E.B. 2018, PubChem 2019 Update: Improved Access to Chemical Data, *Nucleic Acids Research*, **47(1)**: 1102-1109.

Kim, S., Jie, C., Tiejun, C., Asta, G., Jia, H., Siqian, H., Qingliang, L., Benjamin, A.S., Paul, A.T., Bo, Y., Leonid, Z., Jian, Z. and Evan, E.B. 2021, PubChem in 2021: New Data Content and Improved Web Interfaces, *Nucleic Acids Research*, **49(1)**: 1388-1395.

Kumar, S., Reshma, K. and Shailja, M. 2019, Pharmacological Properties and Their Medicinal Uses of *Cinnamomum*: a review, *Journal of Pharmacy and Pharmacology*, **71(12)**: 1735-1761.

Lalo, H., Satyano, M., Patricia, A. 2021, Studi Efek Permukaan Substrat ITO Pada Proses Deposisi Film DR-19 Dengan Metode E-PVD, *Jurnal Fista: Fisika dan Terapannya*, **2(1)**: 25-30.

Liu, Y.Z., Yong, G.C., Jun, Q.Y., Wei, G.W., Ke, J.S., Xiao, L.W., Chun, H.W., Rong, T.L. and Xu. M.D. 2010, Immunomodulatory Effects of Proanthocyanidin A-1 Derived *In Vitro* From *Rhododendron spiciferum*, *Fitoterapia*, **81(2)**: 108-114.

Mardianingrum, R., Tati, H. dan Unang, S. 2015, Isolasi dan *Molecular Docking* Senyawa 6,7-dihidro-17-hidroksierisotrin Dari Daun Dadap Belendung (*Erythrina poeppigiana*) Terhadap Aktivitas Sitotoksik Antikanker Payudara MCF-7, *Chimica et Natura Acta*, **3(3)**: 90-93.

Martinus, Triana, A., Aida, S.D. dan Evita, H.E. 2019, Penggunaan Imunostimulan dalam Bidang Dermatovenereologi, **46**, Jakarta: Departemen Ilmu Kesehatan Kulit dan Kelamin.

Morris, G.M. and Marguerita, L.W. 2008, 'Molecular Docking', in Andreas, K., Molecular Modeling of Proteins, 443, Humana Press, Hertfordshire, UK, pp 365-382.

Muttaqin, F.Z., Halim, I. dan Hubbi, N. 2019, Studi *Molecular Docking*, *Molecular Dynamic*, dan Prediksi Toksisitas Senyawa Turunan Alkaloid Naftridin Sebagai Inhibitor Protein Kasein Kinase 2-α Pada Kanker Leukimia, *Pharmacoscript*, **2(1)**: 49-64.

Nakhaei, P., John, H. and Rongtuan, L. 2010, STING-ing the Antiviral Pathway, *Journal of Molecular Cell Biology*, **2(3)**: 110-112.

Niphade, S.R., Mohammed, A., Gowda, K.C., Emmanuel, T. and Pradeep, D. 2009, Immunomodulatory Activity of *Cinnamomum zeylanicum* Bark, *Pharmaceutical Biology*, **47(12)**: 1168-1173.

Noori, H.R. and Rainer, S. 2013, *In Silico* Pharmacology: Drug Design and Discovery's Gate to the Future, *In Silico Pharmacologyl*, **1**:1-2.

Parikesit, A.A. dan Dito, A. 2018, Kajian Prediksi 3-Dimensi Biomarker Kanker Payudaradari Jalur Ekspresi Lincrna-ROR/MIR-145/ARF6, *Jurnal Sains dan Teknologi*, **2(1)**: 10-19.

Parkin, J. and Bryony, c. 2001, An Overview of The Immune System, *The Lancet*, **357(9270)**: 1777–89.

Ramanjulu, J.M., Pesiridis, G.S., Jingsong, Y., Nestor, C., Robert, S., Shu-Yun, Z., Jean-Luc, T., Patrick, M., Stephanie, L., Eberl, H.C., Marcel, M., Jessica, L.S., Jim, C., Michael, A., John, M., Joseph, R., Angel, M., James, K., Lara, L., Todd, L.G., Adam, K.C., Guosen, Y., Neysa, N., Kamelia, B., Amaya, I.W., Viera, K., Kelvin, N., Liping, W., Ana, C.P., Yue, L., Michael, K., Christopher, B.H., Jeffrey, G., Marcus, B., Giovanna, B., Michael, A.R., Yiqian, L., Kevin, J.D., Jerry, A., Kevin, P.F., Peter, J.G., Robert, W.M., James, S., Axel, H. and John, B. 2018, Design of Amidobenzimidazole

STING Receptor Agonists with Systemic Activity, *Nature*, **564(7736)**: 439-443.

Rosnizar, R., Siti, M., Kartini, E. dan Suwarno, 2017, Potensi Ekstrak Daun Flamboyan [*Delonix Regia* (Boj. Ex Hook.) Raf.] Terhadap Peningkatan Aktivitas dan Kapasitas Makrofag, *Jurnal Bioleuser*, **1(3)**: 104-115.

Ruslin, Nindy, R.A.Y. dan Mesi, L. 2020, Desain Turunan Senyawa Leonurine Sebagai Kandidat Obat Antiinflamasi, *Jurnal Farmasi Galenika*, **6(1)**: 181-191.

Sabilah, L., Wahyudin, D., Safarinda, N. dan Tamami, 2021, Takhrij and Syarah Hadith of Agrotechnology Study of Black Seed Content in Increasing Body Resistance During the Covid-19 Pandemic, 1, Bandung: Department of Agrotechnology, Faculty of Science and Technology.

Shan, B.E., Yoshida, Y., Sugiura, T. and Yamashita., 1999, Stimulating activity of Chinese Medicinal Herbs on Human Lymphocytes In Vitro, *International Journal of Immunopharmacology*, **21(3)**: 149-159.

Siswandono, 2016, *Kimia Medisinal 1: Edisi Kedua*, Airlangga University Press, Surabaya.

Song, Z., Xiyuan, W., Yan, Z., Wangting, G., Ancheng, S., Chunyong, D., Han, L., Ruoxuan, X., Meiyu, G., Zuoquan, X. and Ao, Zhang, A. 2021, Structure−Activity Relationship Study of Amidobenzimidazole Analogues Leading to Potent and Systemically Administrable Stimulator of Interferon Gene (STING) Agonists, *Journal of Medicinal Chemistry*, **64(3)**: 1649-1669.

Suhud, F. 2015, Uji Aktivitas *In-Silico* Senyawa Baru 1-Benxil-3-benzoilurea Induk dan Tersubstitusi sebagai Agen Antiproliperatif, *Jurnal Farmasi Indonesia*, **7(4)**: 242-251.

Susanti, N.M.P., Wardini, N.K., Juwianti, C., Wisesa, I.N.T. 2017, Potensi Toksisitas Andrografolid dari Sambiloto (*Andrographis paniculata* (Burm.f) Nees) Pada Kulit dan Mata Secara *In Silico*, *Jurnal Farmasi Udayana*, **6(1)**: 47-49.

Trali, G.A., Ambreen, J. and Alia, S. 2018, An *In Silico* Primary and Secondary Structure Prediction of Human Interferon Alpha Receptor 2 Protein, *Pakistan Journal of Physiology*, **14(1)**: 40-43.

Wahyuniati, N. 2017, Peran Interferon Gamma pada Infeksi, *Jurnal Kedokteran Syiah Kuala*, **17(2)**: 126-132.

Widiandani, T., Siswandono, Suko, H., Robby, S., Istifada, Risma, Z. 2013, Docking dan Modifikasi Struktur Senyawa Baru Turunan Parasetamol, *Berkala Ilmiah Kimia Farmasi*, **2(1)**: 41-45.

Widiastuti, N.L.G.K. 2019, Pendidikan Sains Terintegrasi Keterkaitan Konsep Ikatan Kimia Dengan Berbagai Bidang Ilmu, *Jurnal Kajian Pendidikan Widya Accarya FKIP Universitas Dwijendra*, pp 1-16.

Xi, Q., Mingjin, W., Wenqiang, J., Mingjian, Y., Jinping, H., Jing, J., Xiaoguang, C., Dali, Y. and Xiaojian, W. 2020, Design, Synthesis, and Biological Evaluation of Amidobenzimidazole Derivates as Stimulator of Interferon Genes (STING) Receptor Agonists, *Journal of Medicinal Chemistry*, **63(1)**: 260-282.

Yang, L., Qing-Hua, X., Lei, S., Yi-Ping, Z. and Wen-Jun, L. 2007, Cloning and Characterization of a Novel Feline IFN-ω, *Journal of Interferon & Cytokine Research*, **27(2)**: 119-127.

Zadeh, S.F., Zahra, K. and Hamid, G. 2012, VMD DisRg: New User-Friendly Implement for Calculation Distance and Radius of Gyration in VMD Program, *Bioinformation*, **8(7)**: 341-343.