

BAB 5

KESIMPULAN DAN SARAN

5.1. Kesimpulan

Berdasarkan penelitian perhitungan energi bebas menggunakan metode *Umbrella Sampling* dari protein FKBP12-*Rapamycin* kesimpulan sebagai berikut:

1. Perubahan energi bebas dengan empat variasi selisih dan jarak awal memiliki hasil perhitungan ΔG masing-masing pada jarak awal dan selisihnya:
(A) Jarak awal 1,151(0) selisih 0,058 nm dan hasil ΔG -59,259 kJ/mol, (B) jarak awal 1,151(0) selisih 0,114 nm dan hasil ΔG -68,268 kJ/mol, (C) jarak awal 1,15(0) selisih 0,166 nm dan hasil ΔG -74,27 kJ/mol, dan (D) jarak awal 1,189(1) selisih 0,114 nm dan hasil ΔG -55,354 kJ/mol.
2. Celah pada grafik energi bebas terhadap jarak COM bertambah menjadi dua ketika selisih jaraknya meningkat menjadi tiga kali lipat, pertambahan celah ini menyebabkan penurunan perubahan energi bebas. Perbedaan juga terdapat pada penurunan ΔG yang diakibatkan perbedaan selisih COM dan kenaikan ΔG akibat perbedaan jarak awal COM, perbedaan ini menunjukkan adanya pemutusan interaksi antara protein FKBP12-*Rapamycin* yang terjadi secara bersamaan.

5.2. Saran

Penelitian ini dapat dilanjutkan lebih lanjut lagi untuk mengetahui jenis interaksi apa yang terlibat dalam pemutusan interaksi protein FKBP12-*Rapamycin*.

DAFTAR PUSTAKA

- Aliev, A. E., Kulke, M., Khaneja, H. S., Chudasama, V., Sheppard, T. D., & Lanigan, R. M. 2014, Motional timescale predictions by molecular dynamics simulations: Case study using proline and hydroxyproline sidechain dynamics. *Proteins: Structure, Function and Bioinformatics*, **82(2)**: 195–215.
- Berendsen, H. J. C., Postma, J. P. M., van Gunsteren, W. F., Dinola, A., & Haak, J. R. 1984, Molecular dynamics with coupling to an external bath. *The Journal of Chemical Physics*, **81(8)**: 3684– 3690.
- Ceymann, A., Horstmann, M., Ehse, P., Schweimer, K., Paschke, A. K., Steinert, M., & Faber, C. 2008, Solution structure of the Legionella pneumophila Mip-rapamycin complex. *BMC Structural Biology*, **8**: 1-12
- Gattuso, G., Rizzo, R., Lavoro, A., Spoto, V., Porciello, G., Montagnese, C., Cina, D., Cosentio, A., Lombardo, C., Mezzatesa, M.L., and Salmeri, M. 2022, Overview of the clinical and molecular features of Legionella pneumophila: focus on novel surveillance and diagnostic strategies. *Antibiotics*, **11(370)**: 1-18.
- Hollingsworth, S. A., & Dror, R. O. 2018, Molecular Dynamics Simulation for All. In *Neuron* **99(6)**: 1129–1143.
- Holtje, H. D., Sippl, W., Rognan, D. and Folkers, G. 2008, *Molecular Modeling: Basic Principle and Applications*, ed. 3rd, WILEY- VCH Verlag GmbH & Co. KGaA, Germany, **2**: 16-18.
- Iliadi, V., Staykova, J., Iliadis, S., Konstantinidou, I., Sivykh, P., Romanidou, G., Vardikov, D. E., Cassimos, D., Konstantinidis, T.G. 2022, Legionella pneumophila: The Journey from the Environment to the blood. *Clinical Medicine*, **11(6126)**: 1-18.
- Joshi, D. C., Gosse, C., Huang, S. Y., & Lin, J. H. 2022, A Curvilinear-Path Umbrella Sampling Approach to Characterizing the Interactions Between Rapamycin and Three FKBP12 Variants. *Frontiers in Molecular Biosciences*, **9**: 1-12
- Jorgensen, W. L., Chandrasekhar, J., Madura, J. D., Impey, R. W., & Klein, M. L. 1983, Comparison of simple potential functions for simulating liquid water. *The Journal of Chemical Physics*, **79(2)**: 926–935.

- Kang, C. B., Hong, Y., Dhe-Paganon, S., & Yoon, H. S. 2008, FKBP family proteins: Immunophilins with versatile biological functions. *In NeuroSignals*, **16(4)**: 318–325.
- Kästner, J. 2011, Umbrella sampling. In Wiley Interdisciplinary Reviews: *Computational Molecular Science*, **1(6)**: 932–942.
- Kumari, R., Kumar, R., and Lynn, A. 2014, g_mmpbsa-A GROMACS Tool for High-Throughput MM-PBSA Calculation, *Journal of Chemical Information and modeling*, **54(7)**: 1951.
- Kolos, J. M., Voll, A. M., Bauder, M. Hausch, F. 2018, FKBP Ligands—Where We Are and Where to go. *Frontiers in Pharmacology*, **9**: 1-25.
- Lan, N. T., Vu, K. B., Dao Ngoc, M. K., Tran, P. T., Hiep, D. M., Tung, N. T., & Ngo, S. T. 2019, Prediction of AChE-ligand affinity using the umbrella sampling simulation. *Journal of Molecular Graphics and Modelling*, **93**: 1-8
- Liu, Y., Yang, F., Zou, S., & Qu, L. 2019, *Rapamycin*: A Bacteria-Derived Immunosuppressant That Has Anti - atherosclerotic Effects and Its Clinical Application. *Frontiers in Pharmacology*, **9**: 1-15
- Lokken, I. Q., Rusch, C. A., Kastnes, M. H., Kolos, J. M., Jatzlau, J., Hella, H., Holien, T. 2023, FKBP12 is a major regulator of ALK2 activity in multiple myeloma cells. *Cell Communication and Signaling*, **21**: 1-16.
- Tan, L. T., Tee, W. Y., Kan, T. M., Ming, L. C., & Letchumanan, V.. 2021, *Legionella pneumophila* — The causative agent of Legionnaires' disease. *Microbes and Molecular Biology*, **4**: 1-12.
- Van-Duyne, G. D., Standaert, R. F., Schreiber, S. L., dan Clardy, J. 1991, Atomic structure of *rapamycin* human immunophilin FKBP-12 complex. *Journal of the American Chemical Society*, **113**: 7433-743.
- Wang, J., Wolf, R. M., Caldwell, J. W., Kollman, P. A., & Case, D. A. 2004, Development and Testing of a General Amber Force Field. *In J Comput Chem*, **25**: 1-18
- Wang, C., Greene, D., Xiao, L., Qi, R., and Luo, R. 2018, Recent developments and applications of the MMPBSA method, *Frontiers in Molecular Biosciences*, **4(87)**:1-18.