DAFTAR PUSTAKA

Abotaleb, M., Samuel, S., Varghese, E., Varghese, S., Kubatka, P., Liskova, A., and Büsselberg, D., 2018, Flavonoids in Cancer and Apoptosis, *Cancers.*, 11(1), 28.

Ahmad, A., Kaleem, M., Ahmed, Z., and Shafiq, H., 2015, Therapeutic potential of flavonoids and their mechanism of action against microbial and viral infections—A review. *Food Res. Int*, 77, 221–235.

Ahn, S., Jung, H., Jung, Y., Lee, J., Shin, S. Y., Lim, Y., and Lee, Y.H., 2019, Identification of the active components inhibiting the expression of matrix metallopeptidase-9 by TNFα in ethyl acetate extract of Euphorbia humifusa willd. *J. Appl. Biol. Chem.*, 62(4), 367–374.

Alanagreh, L., Alzoughool, F., and Atoum, M., 2020, The Human Coronavirus Disease COVID-19: Its Origin, Characteristics, and Insights into Potential Drugs and Its Mechanisms. *Pathogens*, *9*(5), 331.

Alex, A.A., 2007, 4.16 – Quantum Mechanical Calculations in Medicinal Chemistry: Relevant Method or a Quantum Leap Too Far?, *Comprehensive Medicinal Chemistry II.*, 4, 379-420.

Al-Karmalawy, A.A., Dahab, M.A., Metwaly, A.M., Elhady, S.S., Elkaeed, E.B., Eissa, I.H., and Darwish, K.M., 2021, Molecular Docking and Dynamics Simulation Revealed the Potential Inhibitory Activity of ACEIs Against SARS-CoV-2 Targeting the hACE2 Receptor, *Front. Chem.*, 9, 661230.

Allen, M. P., and Tildesley, D. J., 2017, *Computer Simulation of Liquids* (Vol. 1), Oxford University Press, Oxford.

Al, Q.A., Aga, K., Nassir, K.F., Batineh, Y., Dahman, A.T., Shaban, D., Al, L.A., Aga, K., Agha, M.Y.R., and Traqchi, M., 2021, Safety of COVID-19 Vaccines, *J. Med. Viology*., 2021, 1-7.

Armunanto, R., Schwenk, C.F., Tran, H.T., and Rode, B.M., 2004, Structure and Dynamics of Au+ Ion in Aqueous Solution: Ab Initio QM/MM MD Simulations. *J. Am. Chem. Soc.*, 126(8), 2582–2587.

Babu, T. M.C, Rajesh, S.S., Bhaskar, B. V., Devi, S., Rammohan, A., Sivaraman, T., and Rajendra, W., 2017, Molecular docking, molecular dynamics simulation, biological evaluation and 2D QSAR analysis of flavonoids from Syzygium alternifolium as potent anti-Helicobacter pylori agents, *RSC Adv.*, 7(30), 18277–18292.

Badshah, S.L., Faisal, S., Muhammad, A., Poulson, B.G., Emwas, A.H., and Jaremko, M., 2021, Antiviral activities of flavonoids, *Biomed. Pharmacoter.*, 140, 111596.

Baig, M.H., Sudhakar, D.R., Kalaiarasan, P., Subbarao, N., Wadhawa, G., Lohani, M., Khan, M.K.A., and Khan, A.U., 2014, Insight into the Effect of Inhibitor

Resistant S130G Mutant on Physico-Chemical Properties of SHV Type Beta-Lactamase: A Molecular Dynamics Study., *PLoS ONE*, 9(12), e112456.

Barone, G., Gomez-Paloma, L., Duca, D., Silvestri, A., Riccio, R., and Bifulco, G., 2002, Structure Validation of Natural Products by Quantum-Mechanical GIAO Calculations of 13C NMR Chemical Shifts GIAO gauge including atomic orbitals, *Chem. Eur. J.*, 8(14), 3233.

Becke, A. D., 1993, Density-functional thermochemistry. III. The role of exact exchange, *J. Chem. Phys.*, 98 (7), 5648–5652.

Benhander, G. M., and Abdusalam, A.A.A., 2022, Identification of Potential Inhibitors of SARS-CoV-2 Main Protease from Allium roseum L. Molecular Docking Study, *Chemistry Africa*, 5 (1), 57–67.

Bhati, S., 2020, Structure-based drug designing of naphthalene-based SARS-CoV PLpro inhibitors for the treatment of COVID-19. *Heliyon*, 6(11), e05558.

Bharadwaj, S., El-Kafrawy, S.A., Alandijany, T.A., Bajrai, L.H., Shah, A.A., Dubey, A., Sahoo, A. K., Yadava, U., Kamal, M.A., Azhar, E.I., Kang, S.G., and Dwivedi, V.D., 2021, Structure-Based Identification of Natural Products as SARS-CoV-2 Mpro Antagonist from Echinacea angustifolia Using Computational Approaches, *Viruses*, 13 (2), 305.

Brylinski, M., 2018, Aromatic interactions at the ligand-protein interface: Implications for the development of docking scoring functions, *Chem. Biol. Drug. Des.*, 91 (2), 380–390.

Bulatov, V., Rhee, M., and Cai, W., 2002, Periodic Boundary Conditions for Dislocation Dynamics Simulations in Three Dimensions. *Materials Research Society Symposium Proceedings Volume 653*, 27 November – 1 December 2000, Boston, Massachusetts.

Chen, Y.C., 2015, Beware of docking!, *Trends Pharmacol. Sci.*, 36(2), 78–95.

Cosconati, S., Forli, S., Perryman, A.L., Harris, R., Goodsell, D.S., and Olson, A.J., 2010, Virtual screening with AutoDock: theory and practice, *Expert Opin. Drug Discov.*, 5(6), 597–607.

Cremer, D., and Gräfenstein, J., 2007, Calculation and analysis of NMR spin–spin coupling constants, *Phys. Chem. Chem. Phys.*, 9(22), 2791–2816.

Cucinotta, D., & Vanelli, M, 2020, WHO Declares COVID-19 a Pandemic, *Acta Biomed. Ataneo Parm.*, 91(1), 157–160.

de Vivo, M., Masetti, M., Bottegoni, G., and Cavalli, A., 2016, Role of Molecular Dynamics and Related Methods in Drug Discovery, *J. Med. Chem.*, 59(9), 4035–4061.

Dhaouadi, Z., Nsangou, M., Garrab, N., Anouar, E.H., Marakchi, K., and Lahmar, S., 2009, DFT study of the reaction of quercetin with · O2- and · OH radicals. *THEOCHEM* (*J. Mol. Struct)*, 904(1–3), 35–42.

Durrant, J. D., and McCammon, J. A., 2011, Molecular dynamics simulations and drug discovery, *BMC Biol*, 9 (1), 71.

Fadaka, A.O., Sibuyi, N.R.S., Martin, D.R., Klein, A., Madiehe, A., and Meyer, M., 2021, Development of Effective Therapeutic Molecule from Natural Sources against Coronavirus Protease, *Int. J. Mol. Sci.*, 22(17), 9431.

Ferreira, J.C., Fadl, S., Villanueva, A.J., and Rabeh, W.M., 2021, Catalytic Dyad Residues His41 and Cys145 Impact the Catalytic Activity and Overall Conformational Fold of the Main SARS-CoV-2 Protease 3-Chymotrypsin-Like Protease, *Front. Chem.*, 9, 692168.

Ferreira, L., dos Santos, R., Oliva, G., & Andricopulo, A., 2015, Molecular Docking and Structure-Based Drug Design Strategies, *Molecules*, 20(7), 13384–13421.

Frenkel, D., and Smit, B., 2002, Understanding Molecular Simulation, *Underst. Mol. Simul.*, 638.

Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Scalmani, G., Barone, V., Mennucci B., Petersson, G.A., Nakatsuji, H., Caricato, M., Li, X., Hratchian, H.P., Izmaylov, A.F., Bloino, J., Zheng G., Sonneberg, J.L., Hada, M., Ehara, M., Toyota, K., Fukuda, R., Hasegawa, J., Ishida, M., Nakajima, T., Honda, Y., Kitao, O., Nakai, H., Vreven, T., Montgomery Jr., J.A., Peralta, J.E., Ogliaro, F., Bearpark M., Heyd, J.J., Brothers E., Kudin, K.N., Staroverov, V.N., Kobayashi, R., Normand, J., Raghavachari, K., Rendell, A., Burant, J.C., Iyengar, S.S., Tomasi, J., Cossi, M., Rega N., Millam, J.M., Klene, M., Knox, J.E., Cross, J.B., Bakken, V., Adamo, C., Jaramillo, J., Gomperts, R., Sratmann, R.E., Yazyev, O., Austin, A.J., Cammi, R., Pomelli, C., Ochteriski, J.W., 58 Salvador, P., Danneberg, J.J., Dapprich, S., Daniels, A.D., Farkas, Ö., Foresman, J.B., Ortiz, J.V., Cioslowski, J., and Fox, D.J., 2009, Gaussian 09 Revision D.01.

Gimeno, A., Mestres-Truyol, J., Ojeda-Montes, M.J., Macip, G., Saldivar-Espinoza, B., Cereto-Massagué, A., Pujadas, G., & Garcia-Vallvé, S., 2020, Prediction of Novel Inhibitors of the Main Protease (M-pro) of SARS-CoV-2 through Consensus Docking and Drug Reposition. *Int. J. Mol. Sci*,, 21(11), 3793.

Goerigk, L., and Mehta, N., 2019, A Trip to the Density Functional Theory Zoo: Warnings and Recommendations for the User, *Aust. J. Chem.*, 72(8), 563.

Gupta, S., Singh, A.K., Kushwaha, P.P., Prajapati, K.S., Shuaib, M., Senapati, S., and Kumar, S., 2021, Identification of potential natural inhibitors of SARS-CoV2 main protease by molecular docking and simulation studies, *J. Biomol. Struct. Dyn.*, 39(12), 4334–4345.

Hanna, M.W., 1969, *Quantum Mechanics in Chemistry*, 2nd edition., W.A. Benjamin, New York.

Hellewell, J., Abbott, S., Gimma, A., Bosse, N.I., Jarvis, C.I., Russell, T.W., Munday, J.D., Kucharski, A.J., Edmunds, W.J., Sun, F., Flasche, S., Quilty, B.J., Davies, N., Liu, Y., Clifford, S., Klepac, P., Jit, M., Diamond, C., Gibbs, H., Eggo, R.M., 2020, Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. *Lancet Glob. Health.*, 8(4), e488–e496.

Hiremath, S., Kumar, H.D.V., Nandan, M., Mantesh, M., Shankarappa, K.S., Venkataravanappa, V., Basha, C.R.J., and Reddy, C.N.L., 2021, In silico docking analysis revealed the potential of phytochemicals present in Phyllanthus amarus and Andrographis paniculata, used in Ayurveda medicine in inhibiting SARS-CoV-2, *3 Biotech*, 11(2), 44.

Hohenberg, P., and Kohn, W., 1964, Inhomogeneous Electron Gas, *Phys. Rev.*, 136(3B), B864–B871.

Horvath, Marcou, and Varnek, 2019, Generative Topographic Mapping of the Docking Conformational Space, *Molecules.*, 24(12), 2269.

Hosteny, R.P., Gilman, R.R., Dunning, T.H., Pipano, A., and Shavitt, I., 1970, Comparison of slater and contracted gaussian basis sets in SCF and CI calculations on H2O, *Chem. Phys. Lett.*, 7, 325–328.

Huang, C., Wang, Y., Li, X., Ren, L., Zhao, J., Hu, Y., Zhang, L., Fan, G., Xu, J., Gu, X., Cheng, Z., Yu, T., Xia, J., Wei, Y., Wu, W., Xie, X., Yin, W., Li, H., Liu, M., Cao, B., 2020, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *The Lancet.*, 395(10223), 497–506.

Huey, R., Morris, G.M., Olson, A.J., and Goodsell, D.S., 2007, A semiempirical free energy force field with charge-based desolvation, *J. Comput. Chem.*, 28(6), 1145–1152.

Humprey, W., Dalke, A., Schulten, K., 1996, "VMD – Visual Molecular Dynamics", *J. Molec. Graphics.*, 14, 33-38.

Jaimes, J.A., André, N.M., Chappie, J.S., Millet, J.K., and Whittaker, G.R., 2020, Phylogenetic Analysis and Structural Modeling of SARS-CoV-2 Spike Protein Reveals an Evolutionary Distinct and Proteolytically Sensitive Activation Loop, *J. Mol. Biol.*, 432(10), 3309-3325.

Jeffrey, G.A., and Saenger, W., 1991, *Hydrogen Bonding in Biological Structures*. Springer Berlin Heidelberg.

Ji, Y., Li, B., Qiao, M., Li, J., Xu, H., Zhang, L., and Zhang, X., 2020, Advances on the in vivo and in vitro glycosylations of flavonoids. *Appl. Microbiol. Biotechnol*, 104(15), 6587–6600.

Jiménez-Avalos, G., Vargas-Ruiz, A.P., Delgado-Pease, N.E., Olivos-Ramirez, G.E., Sheen, P., Fernández-Díaz, M., Quiliano, M., Zimic, M., Agurto-Arteaga, A., Antiparra, R., Ardiles-Reyes, M., Calderon, K., Cauna-Orocollo, Y., de Grecia Cauti-Mendoza, M., Chipana-Flores, N., Choque-Guevara, R., Chunga-Girón, X., Criollo-Orozco, M., de La Cruz, L., Ygnacio-Aguirre, F., 2021, Comprehensive virtual screening of 4.8 k flavonoids reveals novel

insights into allosteric inhibition of SARS-CoV-2 MPRO. *Sci. Rep.*, 11(1), 15452.

Jin, Z., Liu, J.Y., Feng, R., Ji, L., Jin, Z.L., & Li, H.B., 2020, Drug treatment of coronavirus disease 2019 (COVID-19) in China, *Eur. J. Pharmacol.*, 883, 173326.

Jo, S., Kim, H., Kim, S., Shin, D.H., and Kim, M., 2019, Characteristics of flavonoids as potent MERS-CoV 3C-like protease inhibitors, *Chem. Biol. Drug. Des.*, *94*(6), 2023–2030.

Jurd, L., 1962, The Selective Alkylation of Polyphenols. II. Methylation of 7-, 4'-, and 3'-Hydroxyl Groups in Flavonols, *J. Org. Chem. Res.*, 27(4), 1294–1297.

Khalid, A., Kalsoom, S., and Riaz, N., 2013, Design and Molecular Docking of Antioxidant Lead Compound and its Analogues Acting as Human Tyrosine Kinase Inhibitors, *IOSR- J. Pharm. Biol. Sci.*, 5, 75–80.

Khan, S. A., Zia, K., Ashraf, S., Uddin, R., and Ul-Haq, Z., 2021, Identification of chymotrypsin-like protease inhibitors of SARS-CoV-2 *via* integrated computational approach, *J. Biomol. Struct. Dyn.*, 39 (7), 2607–2616.

Kohn, W., and Sham, L.J., 1965, Self-Consistent Equations Including Exchange and Correlation Effects, *Phys. Rev.*, *140*(4A), A1133–A1138.

Konwar, M., and Sarma, D., 2021, Advances in developing small molecule SARS 3CLpro inhibitors as potential remedy for corona virus infection, *Tetrahedron*, 77, 131761.

Kramer, B., Rarey, M., and Lengauer, T., 1999, Evaluation of the FLEXX incremental construction algorithm for protein-ligand docking, *Proteins: Struct. Funct. Genet.*, 37(2), 228–241.

Kubinyi, H., 2002, Chemical Similarity and Biological Activities, *J. Braz. Chem. Soc.*, *13*(6), 717-726

Kushwaha, P.P., Singh, A.K., Bansal, T., Yadav, A., Prajapati, K.S., Shuaib, M., and Kumar, S., 2021, Identification of Natural Inhibitors Against SARS-CoV-2 Drugable Targets Using Molecular Docking, Molecular Dynamics Simulation, and MM-PBSA Approach, *Front. Cell. Infect. Microbiol.*, 11, 730288.

Lalani, S., and Poh, C.L., 2020, Flavonoids as Antiviral Agents for Enterovirus A71 (EV-A71), *Viruses.*, 12(2), 184.

Leach, A.R., Shoichet, B.K., and Peishoff, C.E., 2006, Prediction of Protein−Ligand Interactions. Docking and Scoring: Successes and Gaps, *J. Med. Chem.*, 49(20), 5851–5855.

Lee, E.C., Hong, B.H., Lee, J.Y., Kim, J.C., Kim, D., Kim, Y., Tarakeshwar, P., and Kim, K.S., 2005, Substituent Effects on the Edge-to-Face Aromatic Interactions, *J. Am. Chem. Soc.*, 127(12), 4530–4537.

Leidner, F., Kurt Yilmaz, N., Paulsen, J., Muller, Y.A., and Schiffer, C.A., 2018, Hydration Structure and Dynamics of Inhibitor-Bound HIV-1 Protease, *J. Chem. Theory Comput.*, 14(5), 2784–2796.

Li, J.Y., You, Z., Wang, Q., Zhou, Z.J., Qiu, Y., Luo, R., and Ge, X.Y., 2020, The epidemic of 2019-novel-coronavirus (2019-nCoV) pneumonia and insights for emerging infectious diseases in the future, *Microbes Infect.*, 22(2), 80–85.

Li, Q., and Kang, C., 2020, Progress in Developing Inhibitors of SARS-CoV-2 3C-Like Protease, *Microorganisms*, 8(8), 1250.

Liu, K., Watanabe, E., and Kokubo, H., 2017, Exploring the stability of ligand binding modes to proteins by molecular dynamics simulations, *J. Comput. Aided. Mol. Des.*, 31 (2), 201–211.

Lu, H., 2020, Drug treatment options for the 2019-new coronavirus (2019-nCoV). *Biosci. Trends*, 14(1), 69–71.

Lu, R., Zhao, X., Li, J., Niu, P., Yang, B., Wu, H., Wang, W., Song, H., Huang, B., Zhu, N., Bi, Y., Ma, X., Zhan, F., Wang, L., Hu, T., Zhou, H., Hu, Z., Zhou, W., Zhao, L., Tan, W., 2020, Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding, *The Lancet*, 395(10224), 565–574.

Ma, Y., Tao, Y., Qu, H., Wang, C., Yan, F., Gao, X., and Zhang, M., 2022, Exploration of plant-derived natural polyphenols toward COVID-19 main protease inhibitors: DFT, molecular docking approach, and molecular dynamics simulations, *RSC Advances*, 12 (9), 5357–5368.

Maffucci, I., and Contini, A., 2013, Explicit Ligand Hydration Shells Improve the Correlation between MM-PB/GBSA Binding Energies and Experimental Activities, *J. Chem. Theory Comput.*, 9(6), 2706–2717.

Maleki, S.J., Crespo, J.F., and Cabanillas, B, 2019, Anti-inflammatory effects of flavonoids. *Food Chem.*, 299, 125124.

Maragakis, P., Lindorff-Larsen, K., Eastwood, M.P., Dror, R.O., Klepeis, J.L., Arkin, I.T., Jensen, M.Ø., Xu, H., Trbovic, N., Friesner, R.A., Palmer, A.G., and Shaw, D.E., 2008, Microsecond Molecular Dynamics Simulation Shows Effect of Slow Loop Dynamics on Backbone Amide Order Parameters of Proteins. *J. Phys. Chem. B.*, 112(19), 6155–6158.

Martínez-Ceniceros, M.C., Landeros-Martínez, L.L., Sánchez-Bojorge, N.A., Sandoval-Salas, F., Piñón-Castillo, H.A., Hernández-Ochoa, L.R., and Rodríguez-Valdez, L.M., 2020, A Potential Inhibition Process of Ricin Protein with the flavonoids Quercetin and Epigallocatechin Gallate. A Quantum-Chemical and Molecular Docking Study. *Processes*, 8(11), 1393.

Mbikay, M., and Chrétien, M., 2022, Isoquercetin as an Anti-Covid-19 Medication: A Potential to Realize. *Front. Pharmacol.*, 13, 830205.

Medina, J.S., Prosmiti, R., Villarreal, P., Delgado-Barrio, G., Winter, G., González, B., Alemán, J.V., and Collado, C., 2011, Molecular dynamics simulations of

rigid and flexible water models: Temperature dependence of viscosity, *Chem. Phys.*, 388(1–3), 9–18.

Mena-Ulecia, K., Tiznado, W., and Caballero, J., 2015, Study of the Differential Activity of Thrombin Inhibitors Using Docking, QSAR, Molecular Dynamics, and MM-GBSA, *PLOS ONE.*, 10(11), e0142774.

Meyer, E.A., Castellano, R.K., & Diederich, F., 2003, Interactions with Aromatic Rings in Chemical and Biological Recognition, *Angew. Chem. Int. Ed.*, 42(11), 1210–1250.

Mittal, L., Kumari, A., Srivastava, M., Singh, M., and Asthana, S., 2021, Identification of potential molecules against COVID-19 main protease through structure-guided virtual screening approach. *J. Biomol. Struct. Dyn.*, 39(10), 3662–3680.

Mizera, M., Lewadowska, K., Talaczyńska, A., and Cielecka-Piontek, J., 2015, Computational study of influence of diffuse basis functions on geometry optimization and spectroscopic properties of losartan potassium, *Spectrochim. Acta A Mol. Biomol. Spectrosc.*, 137, 1029–1038.

Mollica, L., Theret, I., Antoine, M., Perron-Sierra, F., Charton, Y., Fourquez, J.M., Wierzbicki, M., Boutin, J., Ferry, G., Decherchi, S., Bottegoni, G., Ducrot, P., and Cavalli, A., 2016, Molecular Dynamics Simulations and Kinetic Measurements to Estimate and Predict Protein-Ligand Residence Times, *J. Med. Chem.*, 59(15), 7167-7176.

Molsoft, L.L.C., 2018, Drug-Likeness and molecular property prediction. http://molsoft.com/mprop/ (Diakses pada 18 Februari, 2022).

Mouffouk, C., Mouffouk, S., Mouffouk, S., Hambaba, L., and Haba, H., 2021, Flavonols as potential antiviral drugs targeting SARS-CoV-2 proteases (3CL^{pro} and PL^{pro}), spike protein, RNA-dependent RNA polymerase (RdRp) and angiotensin-converting enzyme II receptor (ACE2), *Eur. J. Pharmacol.*, 891, 173759.

Mukesh, B., and Rakesh, K., 2011, Molecular Docking: A Review, *Int J Res Ayurveda Pharm.*, 2, 1746-1751.

Nabavi, S.F., Braidy, N., Habtemariam, S., Orhan, I.E., Daglia, M., Manayi, A., Gortzi, O., and Nabavi, S. M., 2015, Neuroprotective effects of chrysin: From chemistry to medicine. *Neurochem. Int.*, 90, 224–231.

Nguyen, T.T.H., Woo, H.J., Kang, H.K., Nguyen, V.D., Kim, Y.M., Kim, D.W., Ahn, S.A., Xia, Y., and Kim, D., 2012, Flavonoid-mediated inhibition of SARS coronavirus 3C-like protease expressed in Pichia pastoris. *Biotechnol. Lett.*, 34(5), 831–838.

Noureddine, O., Issaoui, N., and Al-Dossary, O., 2021, DFT and molecular docking study of chloroquine derivatives as antiviral to coronavirus COVID-19 J, *King Saud Univ. Sci*., 33(1), 101248.

Olubiyi, O.O., Olagunju, M., Keutmann, M., Loschwitz, J., and Strodel, B., 2020, High Throughput Virtual Screening to Discover Inhibitors of the Main Protease of the Coronavirus SARS-CoV-2, *Molecules*, 25 (14), 3193.

Orfali, G.di C., Duarte, A.C., Bonadio, V., Martinez, N.P., de Araújo, M.E.M.B., Priviero, F.B.M., Carvalho, P.O., and Priolli, D.G., 2016, Review of anticancer mechanisms of isoquercitin, *World. J. Clin. Oncol.*, 7 (2), 189.

Panagiotou, E., 2015, The linking number in systems with Periodic Boundary Conditions, *J. Comput. Phys.*, 300, 533–573.

Papajak, E., and Truhlar, D.G. (2010). Efficient Diffuse Basis Sets for Density Functional Theory. *J. Chem. Theory Comput.*, 6(3), 597–601.

Park, J.Y., Yuk, H.J., Ryu, H.W., Lim, S.H., Kim, K.S., Park, K.H., Ryu, Y. B., and Lee, W. S., 2017, Evaluation of polyphenols from *Broussonetia papyrifera* as coronavirus protease inhibitors, *J. Enzyme Inhib. Med. Chem.*, 32(1), 504–512.

Patel, J.S., Berteotti, A., Ronsisvalle, S., Rocchia, W., and Cavalli, A., 2014, Steered Molecular Dynamics Simulations for Studying Protein–Ligand Interaction in Cyclin-Dependent Kinase 5, *J. Chem. Inf. Model.*, 54(2), 470–480.

Patil, R., Das, S., Stanley, A., Yadav, L., Sudhakar, A., and Varma, A.K., 2010, Optimized Hydrophobic Interactions and Hydrogen Bonding at the Target-Ligand Interface Leads the Pathways of Drug-Designing, *PLoS ONE*, 5(8), e12029.

Pirolli, D., Sciandra, F., Bozzi, M., Giardina, B., Brancaccio, A., and de Rosa, M. C., 2014, Insights from Molecular Dynamics Simulations: Structural Basis for the V567D Mutation-Induced Instability of Zebrafish Alpha-Dystroglycan and Comparison with the Murine Model, *PLoS ONE*, 9(7), e103866.

Pollard, C.A., Morran, M.P., and Nestor-Kalinoski, A.L., 2020, The COVID-19 pandemic: a global health crisis, *Physiol. Genomics.*, 52(11), 549–557.

Pongajow, N.T., Juliandri, and Hastiawan, I., 2017, Penentuan Geometri dan Karakteristik Ikatan Senyawa Kompleks Ni (II)-Dibutilditiokarbamat dengan Metode Density Functional Theory. Indones. J. Appl. Sci., 7(2), 33-36.

Poulikakos, D., Arcidiacono, S., and Maruyama, S., 2003, Molecular dynamics simulation in nanoscale heat transfer: A review. *Nanoscale Microscale Thermophys. Eng*, 7, 181–206.

Proença, C., Freitas, M., Ribeiro, D., Tomé, S.M., Oliveira, E.F.T., Viegas, M.F., Araújo, A.N., Ramos, M.J., Silva, A.M.S., Fernandes, P.A., and Fernandes, E., 2019, Evaluation of a flavonoid library for inhibition of pancreatic α-amylase towards a structure–activity relationship. *J. Enzyme Inhib. Med. Chem.*, 34(1), 577–588.

Qiu, X., Kroeker, A., He, S., Kozak, R., Audet, J., Mbikay, M., and Chrétien, M., 2016, Prophylactic Efficacy of Quercetin 3-β- *O* - Glucoside against Ebola Virus Infection, *Antimicrob. Agents Chemother*, 60(9), 5182–5188.

Rai, H., Barik, A., Singh, Y.P., Suresh, A., Singh, L., Singh, G., Nayak, U.Y., Dubey, V.K., and Modi, G., 2021, Molecular docking, binding mode analysis, molecular dynamics, and prediction of ADMET/toxicity properties of selective potential antiviral agents against SARS-CoV-2 main protease: an effort toward drug repurposing to combat COVID-19. *Mol. Divers.*, 25(3), 1905–1927.

Raju, R.K., Bloom, J.W.G., An, Y., and Wheeler, S.E., 2011, Substituent Effects on Non-Covalent Interactions with Aromatic Rings: Insights from Computational Chemistry, *Chem Phys Chem*, 12(17), 3116–3130.

Ramachandran, K.I., Deepa, G., and Namboori, Dr.K., 2008, *Computational Chemistry and Molecular Modeling- Principles and applications*, Springer International, Germany.

Ren, X., Shen, L.L., Muraoka, O., and Cheng, M., 2011, Synthesis of quercetin 3-O-[6"-O-(trans-p-coumaroyl)]-β-D- Glucopyranoside. *J. Carbohydr. Chem.*, 30(3), 119–131.

Rice-Evans, C., 2001, Flavonoid Antioxidants, *Curr. Med. Chem.*, *8*(7), 797–807.

Ryu, Y.B., Jeong, H.J., Kim, J.H., Kim, Y.M., Park, J.Y., Kim, D., Naguyen, T.T.H., Park, S.J., Chang, J.S., and Park, K.H., 2010, Biflavonoids from Torreya nucifera displaying SARS-CoV $3CL^{pro}$ inhibition. *Bioorg. Med. Chem.*, 18(22), 7940–7947.

Sabe, V.T., Ntombela, T., Jhamba, L.A., Maguire, G.E.M., Govender, T., Naicker, T., and Kruger, H.G., 2021, Current trends in computer aided drug design and a highlight of drugs discovered via computational techniques: A review. *Eur. J. Med. Chem.*, 224, 113705.

Salentin, S., Haupt, V.J., Daminelli, S., and Schroeder, M., 2014, Polypharmacology rescored: Protein–ligand interaction profiles for remote binding site similarity assessment, *Prog. Biophys. Mol. Biol.*, 116(2–3), 174–186.

Schreiner, W., Karch, R., Knapp, B., and Ilieva, N., 2012, Relaxation Estimation of RMSD in Molecular Dynamics Immunosimulations, *Comput. Math. Methods. Med.*, 2012, 1–9.

Seleem, D., Pardi, V., and Murata, R.M., 2017, Review of flavonoids: A diverse group of natural compounds with anti-Candida albicans activity in vitro, *Arch. Oral Biol.*, 76, 76–83.

Slámová, K., Kapešová, J., and Valentová, K., 2018, Sweet Flavonoids: Glycosidase-Catalyzed Modifications, *Int. J. Mol. Sci*., 19 (7), 2126.

Soumia, M., Hanane, Z., Benaissa, M., Younes, F.Z., Chakib, A., Mohammed, B., 2020, Towards potential inhibitors of COVID-19 main protease M^{pro} by virtual

screening and molecular docking study, *J. Taibah Univ. Sci.*, 14 (1), 1626–1636.

Sousa, S.F., Fernandes, P.A., and Ramos, M.J., 2007, General Performance of Density Functionals, *J. Phys. Chem. A*, 111, 10439-10452.

Spitznagel, G.W., Clark, T., von Rague Schleyer, P., and Hehre, W.J., 1987, An Evaluation of the Performance of Diffuse Function-Augmented Basis Sets for Second Row Elements, Na-Cl, *J. Comput. Chem.*, 1109-1116.

Stopa, J.D., Neuberg, D., Puligandla, M., Furie, B., Flaumenhaft, R., and Zwicker, J. I., 2017, Protein disulfide isomerase inhibition blocks thrombin generation in humans by interfering with platelet factor V activation. *JCI Insight*, *2*(1), e89373.

Su, H., Yao, S., Zhao, W., Li, M., Liu, J., Shang, W., Xie, H., Ke, C., Hu, H., Gao, M., Yu, K., Liu, H., Shen, J., Tang, W., Zhang, L., Xiao, G., Ni, L., Wang, D., Zuo, J., Xu, Y., 2020, Anti-SARS-CoV-2 activities in vitro of Shuanghuanglian preparations and bioactive ingredients, *Acta Pharmacol. Sin.*, 41(9), 1167–1177.

Su, H., Yao, S., Zhao, W., Zhang, Y., Liu, J., Shao, Q., Wang, Q., Li, M., Xie, H., Shang, W., Ke, C., Feng, L., Jiang, X., Shen, J., Xiao, G., Jiang, H., Zhang, L., Ye, Y., and Xu, Y., 2021, Identification of pyrogallol as a warhead in design of covalent inhibitors for the SARS-CoV-2 3CL protease. *Nat. Commun.*, 12(1), 3623.

Syahri, J., Bambang, P., and Armunanto, R., 2016, Design of New Potential Antimalaria Compound Based on QSAR Analysis of Chalcone Derivatives. *Int. J. Pharm. Sci. Res.*, 36, 71–76.

Takahashi, O., Kohno, Y., and Nishio, M., 2010, Relevance of Weak Hydrogen Bonds in the Conformation of Organic Compounds and Bioconjugates: Evidence from Recent Experimental Data and High-Level *ab Initio* MO Calculations. *Chem. Rev.*, 110(10), 6049–6076.

Tang, H.J., Li, W., Zhou, M., Peng, L.Y., Wang, J.X., Li, J.H., and Chen, J., 2018, Design, synthesis and biological evaluation of novel xanthine oxidase inhibitors bearing a 2-arylbenzo[b]furan scaffold. *Eur. J. Med. Chem.*, 151, 849–860.

Tolosa, S., Sansón, J.A., and Hidalgo, A., 2019, Theoretical Study of Adenine to Guanine Transition Assisted by Water and Formic Acid Using Steered Molecular Dynamic Simulations, *Front. Chem.*, 7, 414.

Vieth, M., Hirst, J.D., Kolinski, A., and Brooks, C.L., 1998, Assessing energy functions for flexible docking, *J. Comput. Chem.*, 19(14), 1612–1622.

Vijayakumar, S., Manogar, P., Prabhu, S., and Sanjeevkumar Singh, R.A., 2018, Novel ligand-based docking; molecular dynamic simulations; and absorption, distribution, metabolism, and excretion approach to analyzing potential

acetylcholinesterase inhibitors for Alzheimer's disease, *J. Pharm. Anal.*, 8(6), 413–420.

Veerasamy, R., Rajak, H., Jain, A., Sivadasan, S., Varghese, C.P., and Agrawal, R.K., 2011, Validation of QSAR Models – Strategies and Importance, *Int. J. Drug. Des. Discov.*, 2, 511-519.

Walls, A.C., Park, Y.J., Tortorici, M.A., Wall, A., McGuire, A.T., and Veesler, D., 2020, Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein, *Cell*, 181(2), 281-292.e6.

Wang, C.-Z., Calway, T.D., Wen, X.-D., Smith, J., Yu, C., Wang, Y., Mehendale, S.R., and Yuan, C.-S., 2013, Hydrophobic flavonoids from Scutellaria baicalensis induce colorectal cancer cell apoptosis through a mitochondrial-mediated pathway, *Int. J. Oncol*, 42 (3), 1018–1026.

Wang, T., Li, Q., and Bi, K., 2018, Bioactive flavonoids in medicinal plants: Structure, activity and biological fate, *Asian J. Pharm. Sci.*, 13(1), 12–23.

Wang, W., Li, Q., Wei, Y., Xue, J., Sun, X., Yu, Y., Chen, Z., Li, S., and Duan, L., 2017, Novel carbazole aminoalcohols as inhibitors of β -hematin formation: Antiplasmodial and antischistosomal activities, *Int. J. Parasitol. Drugs Drug., Resist*, 7 (2), 191–199.

Wang, L., Cheng, G., 2022, Sequence Analysis of the Emerging SARS-CoV-2 variant Omicron in South Africa, *J. Med. Virol.*, 94, 1738-1733.

Wu, A., Peng, Y., Huang, B., Ding, X., Wang, X., Niu, P., Meng, J., Zhu, Z., Zhang, Z., Wang, J., Sheng, J., Quan, L., Xia, Z., Tan, W., Cheng, G., & Jiang, T., 2020, Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China, *Cell. Host. Microbe.*, 27(3), 325–328.

Xiao, J., 2017, Dietary flavonoid aglycones and their glycosides: Which show better biological significance?, *Critical Reviews in Food Science and Nutrition*, 57(9), 1874–1905.

Yesselman, J.D., Horowitz, S., Brooks, C.L., and Trievel, R.C., 2015, Frequent side chain methyl carbon-oxygen hydrogen bonding in proteins revealed by computational and stereochemical analysis of neutron structures. *Proteins: Struct. Funct. Genet.*, 83(3), 403–410.

Young, D.C., 2001, *Computational Chemistry: A Practical Guide for Applying Techniques to Real-World Problems,* John Wiley & Sons, Inc., New York.

Zakaryan, H., Arabyan, E., Oo, A., and Zandi, K., 2017, Flavonoids: promising natural compounds against viral infections. *Arch. Virol.*, 162(9), 2539–2551.

Zhang, L., Lin, D., Sun, X., Curth, U., Drosten, C., Sauerhering, L., Becker, S., Rox, K., and Hilgenfeld, R., 2020, Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved α-ketoamide inhibitors, *Science*, 368(6489), 409–412.

Zou, L., Ruan, F., Huang, M., Liang, L., Huang, H., Hong, Z., Yu, J., Kang, M., Song, Y., Xia, J., Guo, Q., Song, T., He, J., Yen, H.-L., Peiris, M., & Wu, J., 2020, SARS-CoV-2 Viral Load in Upper Respiratory Specimens of Infected Patients. *N. Engl. J. Med.*, 382(12), 1177-1179.