

REFERENCE

- Al-Alak, S. K., AL-Oqaili, R. M. S., Mohammed, B. B., & Abd-Alkhalik, N. (2015). Antibacterial activity of Hibiscus rosa-sinensis extract and synergistic effect with amoxicillin against some human pathogens. *Am J Phytomed Clin Ther*, 3(10), 020-027.
- Aldridge, B. B., Fernandez-Suarez, M., Heller, D., Ambravaneswaran, V., Irimia, D., Toner, M., & Fortune, S. M. (2012). Asymmetry and aging of mycobacterial cells lead to variable growth and antibiotic susceptibility. *Science*, 335(6064), 100-104.
- Andriani, R. A. L., & Ahmad, Z. (2020). The Effect of KatG S315t M. Tuberculosis Gene Mutation on Conversion Rate of MDR-TB Patients with Shorter-Course Treatment. *Bioscientia Medicina: Journal of Biomedicine and Translational Research*, 4(4), 1-7.
- Angelova, V. T., Valcheva, V., Pencheva, T., Voynikov, Y., Vassilev, N., Mihaylova, R., ... & Shivachev, B. (2017). Synthesis, antimycobacterial activity and docking study of 2-aryloyl-[1] benzopyrano [4, 3-c] pyrazol-4 (1H)-one derivatives and related hydrazide-hydrazones. *Bioorganic & medicinal chemistry letters*, 27(13), 2996-3002.
- Babu, S., & Jayaraman, S. (2020). An update on β -sitosterol: A potential herbal nutraceutical for diabetic management. *Biomedicine & Pharmacotherapy*, 131, 110702.
- Banerjee, P., Eckert, A. O., Schrey, A. K., & Preissner, R. (2018). ProTox-II: a webserver for the prediction of toxicity of chemicals. *Nucleic acids research*, 46(W1), W257-W263.
- Benkert, P., Biasini, M., & Schwede, T. (2011). Toward the estimation of the absolute quality of individual protein structure models. *Bioinformatics*, 27(3), 343-350.
- Bhaskar, A., & Vidhya, V. G. (2012). Hypoglycemic and hypolipidemic activity of Hibiscus rosa sinensis Linn on streptozotocin-induced diabetic rats. *International Journal of Diabetes in Developing Countries*. <https://doi.org/10.1007/s13410-012-0096-9>
- Binkowski, T. A., Naghibzadeh, S., & Liang, J. (2003). CASTp: computed atlas of surface topography of proteins. *Nucleic acids research*, 31(13), 3352-3355.
- Bollela, V. R., Namburete, E. I., Feliciano, C. S., Macheque, D., Harrison, L. H., & Caminero, J. A. (2016). Detection of katG and inhA mutations to guide isoniazid and ethionamide use for drug-resistant tuberculosis. *The international journal of tuberculosis and lung disease*, 20(8), 1099-1104.
- Bortolato, A., Fanton, M., Mason, J. S., & Moro, S. (2013). Molecular docking methodologies. In *Biomolecular Simulations* (pp. 339-360). Humana Press, Totowa, NJ.
- Buckle, J. (2016). Essential oil toxicity and contraindications. *Clinical Aromatherapy (Third Edition) Essential Oils in Healthcare; Churchill Livingstone: London, UK*,
- Chen, V. B., Arendall, W. B., Headd, J. J., Keedy, D. A., Immormino, R. M., Kapral, G. J., ... & Richardson, D. C. (2010). MolProbity: all-atom structure validation for macromolecular crystallography. *Acta Crystallographica Section D: Biological Crystallography*, 66(1), 12-21.
- Chughtai, B., Forde, J. C., Thomas, D. D. M., Laor, L., Hossack, T., Woo, H. H., ... & Kaplan, S. A. (2016). Benign prostatic hyperplasia. *Nature reviews Disease primers*, 2(1), 1-15.
- Chiang, S. S., & Starke, J. R. (2018). Mycobacterium tuberculosis. In *Principles and Practice of Pediatric Infectious Diseases* (pp. 790-806). Elsevier.
- Chitralla, K. N., Yeguvapalli, S. (2014). Computational Screening and Molecular Dynamic Simulation of Breast Cancer Associated Deleterious non-Synonymous Single Nucleotide Polymorphisms in TP53 Gene. *PloS One* 9, 1–18. doi: 10.1371/journal.pone.0104242
- Daina, A., Michielin, O., & Zoete, V. (2017). SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. *Scientific reports*, 7(1), 1-13. <https://www.nature.com/articles/srep42717>

- Dallakyan, S., & Olson, A. J. (2015). Small-molecule library screening by docking with PyRx. In *Chemical biology* (pp. 243-250). Humana Press, New York, NY.
- Doogue, M. P., & Polasek, T. M. (2013). The ABCD of clinical pharmacokinetics. *Therapeutic advances in drug safety*, 4(1), 5-7.
- Efendi, A., Hasibuan, M., Sihombing, E., & Wulandari, T. (2021, August). Bunga Kembang Sepatu Dikreasikan Untuk Kesehatan. In *SENKIM: Seminar Nasional Karya Ilmiah Multidisiplin* (Vol. 1, No. 1, pp. 129-135).
- Evangelina, I. A., Herdiyati, Y., Laviana, A., Rikmasari, R., & Zubaedah, C. (2021). Bio-Mechanism inhibitory prediction of β -sitosterol from Kemangi (*Ocimum basilicum* L.) as an inhibitor of MurA enzyme of oral bacteria: In vitro and in silico Study. *Advances and Applications in Bioinformatics and Chemistry: AABC*, 14, 103.
- Gandhi, S. P., Lokhande, K. B., Swamy, V. K., Nanda, R. K., & Chitlange, S. S. (2019). Computational data of phytoconstituents from *Hibiscus rosa-sinensis* on various anti-obesity targets. *Data in brief*, 24, 103994.
- Ganeshpurkar, A., & Saluja, A. K. (2017). The pharmacological potential of rutin. *Saudi pharmaceutical journal*, 25(2), 149-164.
- Grandvalet, C., Gominet, M., & Lereclus, D. (2001). Identification of genes involved in the activation of the *Bacillus thuringiensis* inhA metalloprotease gene at the onset of sporulation. The GenBank/EMBL/DDBJ accession number for the sequence reported in this paper is AF287346. *Microbiology*, 147(7), 1805-1813.
- Harisna, A. H., Nurdiansyah, R., Syaifie, P. H., Nugroho, D. W., Saputro, K. E., Prakoso, C. D., ... & Mardiyati, E. (2021). In silico investigation of potential inhibitors to main protease and spike protein of SARS-CoV-2 in propolis. *Biochemistry and Biophysics Reports*, 26, 100969.
- Hazarika, Z., Rajkhowa, S., & Jha, A. N. (2020). Role of Force Fields in Protein Function Prediction. In *Homology Molecular Modeling-Perspectives and Applications*. IntechOpen.
- Huber, R. (1987). Flexibility and rigidity, requirements for the function of proteins and protein pigment complexes. Eleventh Keilin memorial lecture. *Biochemical Society Transactions*, 15(6), 1009-1020.
- Indah, M., Budijanto, D., Kurniawan, R., Kurniasih, N., & Mulya, D. (2018). Tuberkulosis. pusdatin.kemkes.go.id. Retrieved 3 November 2021, from <https://pusdatin.kemkes.go.id/resources/download/pusdatin/infodatin/infodatin-tuberkulosis-2018.pdf>.
- Indonesia commitment to eliminate TB by 2030 supported by the highest-level government. (2021). Retrieved 3 June 2022, from <https://www.who.int/indonesia/news/detail/28-11-2021-indonesia-commitment-to-eliminate-tb-by-2030-supported-by-the-highest-level-government>
- InhA (enoyl-ACP). (2022). Retrieved 2 June 2022, from <https://www.ncbi.nlm.nih.gov/protein/P9WGR1.1?report=graph>
- Jabeen, A., Mohamedali, A., & Ranganathan, S. (2019). Protocol for protein structure modelling. In *Encyclopedia of bioinformatics and computational biology: ABC of Bioinformatics* (pp. 252-272). Elsevier.
- Jamroz, M., Kolinski, A., & Kmiecik, S. (2013). CABS-flex: server for fast simulation of protein structure fluctuations. *Nucleic acids research*, 41(W1), W427-W431.
- Jesus, R. S., Piana, M., Freitas, R. B., Brum, T. F., Alves, C. F., Belke, B. V., ... & Bauermann, L. D. F. (2018). In vitro antimicrobial and antimycobacterial activity and HPLC-DAD screening of phenolics from *Chenopodium ambrosioides* L. *Brazilian journal of microbiology*, 49, 296-302.
- Jian, J., Yang, X., Yang, J., & Chen, L. (2018). Evaluation of the GenoType MTBDRplus and MTBDRsl for the detection of drug-resistant *Mycobacterium tuberculosis* on isolates from Beijing, China. *Infection and Drug Resistance*, 11, 1627.

- Jilani, T. N., Avula, A., Gondal, A. Z., & Siddiqui, A. H. (2020). Active tuberculosis. StatPearls [Internet].
- JOYLAXMI, U., & CHOUDHURY, M. (2015). In silico study for Identification of drug like inhibitor from natural compounds against InhA reductase of Mycobacterium tuberculosis. *International Journal Of Pharmacy And Pharmaceutical Sciences*, 7(8), 87-90. Retrieved 24 October 2021, from <https://innovareacademics.in/journals/index.php/ijpps/article/download/4094/pdf/997>.
- KatG [Mycobacterium tuberculosis] - Protein - NCBI. Retrieved 2 June 2022, from <https://www.ncbi.nlm.nih.gov/protein/AVV29661.1?report=graph>
- Kelley, L. A., Mezulis, S., Yates, C. M., Wass, M. N., & Sternberg, M. J. (2015). The Phyre2 web portal for protein modeling, prediction and analysis. *Nature protocols*, 10(6), 845-858.
- Kannan, R., Alharbi, N. S., Kadaikunnan, S., Rajaram, S. K., & Alexander, R. A. (2016). Insilico Analysis of Phytoconstituents from Allium sativum as Potential Inhibitors of Inha in Mycobacterium tuberculosis. *Brazilian Archives of Biology and Technology*, 59.
- Kementerian Kesehatan Republik Indonesia. Kemkes.go.id. (2021). Retrieved 24 August 2021, from <https://www.kemkes.go.id/article/view/21032500001/jadikan-penerus-bangsa-bebas-tbc-dimulai-dari-diri-sendiri-dan-keluarga.html>.
- Kumar, B. A., Lakshman, K., Jayaveera, K. N., Krishna, N. V., Manjunath, M., & Suresh, M. (2009). Estimation of rutin and quercetin in Amaranthus viridis Linn by HPLC. *Asian J. Exp. Sci*, 23(1), 51-54.
- Kusdianingrum, D., Yustiantara, S., & Yowani, S. C. (2014). AMPLIFIKASI DAN IDENTIFIKASI MUTASI REGIO PROMOTER inhA PADA ISOLAT Mycobacterium tuberculosis MULTIDRUG RESISTANCE DENGAN TEKNIK POLYMERASE CHAIN REACTION
- Ladda, P. L., & Magdum, C. S. (2018). Antitubercular activity and isolation of chemical constituents from plant Vitex negundo Linn. *Iranian Journal of Pharmaceutical Research: IJPR*, 17(4), 1353..
- Lee, S. H. (2016). Tuberculosis infection and latent tuberculosis. *Tuberculosis and respiratory diseases*, 79(4), 201-206.
- Lipinski, C. A., Lombardo, F., Dominy, B. W., & Feeney, P. J. (1997). Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. *Advanced drug delivery reviews*, 23(1-3), 3-25.
- Liu, X., Shi, D., Zhou, S., Liu, H., Liu, H., & Yao, X. (2018). Molecular dynamics simulations and novel drug discovery. *Expert opinion on drug discovery*, 13(1), 23-37.
- Lu, S. et al. (2020). "CDD/SPARCLE: the conserved domain database in 2020." *Nucleic Acids Res.* 48(D1):D265-D268.
- Magdalita, Pablito & Valdoz, Jonard & San Pascual, Alangelico & Sotto, Rachel. (2019). Phenotypic evaluation of floral characteristics for predicting the components of longer floral retention in Hibiscus rosa sinensis L. hybrids.
- Maitriani, L. K. B., Wirajana, I. N., & Yowani, S. C. (2015). Desain primer untuk amplifikasi fragmen gen inha isolat 134 multidrug resistance tuberculosis (mdr-tb) dengan metode polymerase chain reaction. *Cakra Kimia (Indonesian E-Journal of Applied Chemistry)*, 3(2), 89-96.
- Maiolini, M., Gause, S., Taylor, J., Steakin, T., Shipp, G., Lamichhane, P., ... & Deshmukh, R. R. (2020). The war against tuberculosis: A review of natural compounds and their derivatives. *Molecules*, 25(13), 3011.
- Mak, Y. W., Chuah, L. O., Ahmad, R., & Bhat, R. (2013). Antioxidant and antibacterial activities of hibiscus (*Hibiscus rosa-sinensis* L.) and Cassia (*Senna bicapsularis* L.) flower extracts. *Journal of King Saud University-Science*, 25(4), 275-282.

- Master, S., Zahrt, T. C., Song, J., & Deretic, V. (2001). Mapping of Mycobacterium tuberculosis katG promoters and their differential expression in infected macrophages. *Journal of bacteriology*, 183(13), 4033-4039.
- Meng, X. Y., Zhang, H. X., Mezei, M., & Cui, M. (2011). Molecular docking: a powerful approach for structure-based drug discovery. *Current computer-aided drug design*, 7(2), 146-157.
- Migliori, G. B., & Zumla, A. (2017). Antituberculosis agents. In *Infectious Diseases* (pp. 1264-1276). Elsevier.
- Ministry of Agriculture, Food, and Fisheries. (2022). *Pesticide Toxicity and Hazard* (pp. 2-3). British Columbia: Ministry of Agriculture, Food, and Fisheries.
- MUHAMMAD, A. H. S. P. (2016). *PENAMBATAN MOLEKUL SENYAWA BIOAKTIF FLAVONOID TERHADAP RNA-POLYMERASE Mycobacterium tuberculosis* (Doctoral dissertation, Universitas Andalas).
- MULTISPECIES: 3-oxoacyl-ACP reductase FabG1 [Mycobacterium tuberculosis - Protein - NCBI. (2022). Retrieved 31 March 2022, from [https://www.ncbi.nlm.nih.gov/protein/WP_003898892.1?report=genbank&log\\$=pr_otalign&blast_rank=1&RID=3GAJ8VU201N](https://www.ncbi.nlm.nih.gov/protein/WP_003898892.1?report=genbank&log$=pr_otalign&blast_rank=1&RID=3GAJ8VU201N)
- Mysinger, M. M., Carchia, M., Irwin, J. J., & Shoichet, B. K. (2012). Directory of useful decoys, enhanced (DUD-E): better ligands and decoys for better benchmarking. *Journal of medicinal chemistry*, 55(14), 6582-6594.
- Narita, M., & Spitters, C. (2016). Tuberculosis in Travelers and Immigrants. *The Travel and Tropical Medicine Manual E-Book*, 356.
- Niehaus, A., Mlisana, K., Gandhi, N., Mathema, B., & Brust, J. (2015). High Prevalence of inhA Promoter Mutations among Patients with Drug-Resistant Tuberculosis in KwaZulu-Natal, South Africa. *PLOS ONE*, 10(9), e0135003. <https://doi.org/10.1371/journal.pone.0135003>
- Ning, Y., Jin, B., Liang, Y., & Qin, G. (2019). Pore-Scale Modeling and Simulation in Shale Gas Formations. In *Petrophysical Characterization and Fluids Transport in Unconventional Reservoirs* (pp. 217-246). Elsevier.
- Nsofor, C. A., Jiang, Q., Wu, J., Gan, M., Liu, Q., Zuo, T., ... & Gao, Q. (2017). Transmission is a noticeable cause of resistance among treated tuberculosis patients in Shanghai, China. *Scientific reports*, 7(1), 1-6.
- Ododo, M. M., Choudhury, M. K., & Dekebo, A. H. (2016). Structure elucidation of β -sitosterol with antibacterial activity from the root bark of *Malva parviflora*. *SpringerPlus*, 5(1), 1-11.
- Oduselu, G. O., Ajani, O. O., Ajamma, Y. U., Brors, B., & Adebisi, E. (2019). Homology modelling and molecular docking studies of selected substituted Benzo [d] imidazol-1-yl) methyl) benzimidamide scaffolds on Plasmodium falciparum adenylosuccinate lyase receptor. *Bioinformatics and biology insights*, 13, 1177932219865533.
- Pantsar, T., & Poso, A. (2018). Binding affinity via docking: fact and fiction. *Molecules*, 23(8), 1899.
- Parikesit, A. A., & Nurdiansyah, R. (2021). Natural products repurposing of the H5N1-based lead compounds for the most fit inhibitors against 3C-like protease of SARS-CoV-2. *J Pharm Pharmacogn Res*, 9(5), 730-745.
- Patel, K., & Patel, D. K. (2019). The beneficial role of rutin, a naturally occurring flavonoid in health promotion and disease prevention: a systematic review and update. *Bioactive food as dietary interventions for arthritis and related inflammatory diseases*, 457-479.
- Pawelczyk, J., & Kremer, L. (2014). The molecular genetics of mycolic acid biosynthesis. *Microbiology spectrum*, 2(4), 2-4.
- PubChem. (2022). Retrieved 22 May 2022, from <https://pubchem.ncbi.nlm.nih.gov/>

- QMEAN. (2022). Retrieved 31 March 2022, from <https://swissmodel.expasy.org/qmean/help>
- Raduan, S. Z., Abdul Aziz, M. W. H., Roslida, A. H., Zakaria, Z. A., Zuraini, A., & Hakim, M. N. (2013). Anti-inflammatory effects of *Hibiscus rosa-sinensis* L. and *Hibiscus rosa-sinensis* var. *alba* ethanol extracts. *Int J Pharm Pharm Sci*, 5(4), 754-762.
- Ramachandran, G. N., Ramakrishnan, C., & Sasisekharan, V. (1963). Stereochemistry of polypeptide chain configurations. *Journal of molecular biology*, 7, 95–99. [https://doi.org/10.1016/s0022-2836\(63\)80023-6](https://doi.org/10.1016/s0022-2836(63)80023-6)
- RAO, S., SAYEEDA, M., PRAKASH, T., AP, P., IMRAN, S., & RAVI, L. (2020). CONSTRUCTION OF COMPUTATIONAL 3D STRUCTURES OF PROTEIN DRUG TARGETS OF MYCOBACTERIUM TUBERCULOSIS. *Asian Journal of Pharmaceutical and Clinical Research*, 82-85.
- Rivero-Cruz, I., Acevedo, L., Guerrero, J. A., Martínez, S., Pereda-Miranda, R., Mata, R., ... & Timmermann, B. N. (2005). Antimycobacterial agents from selected Mexican medicinal plants. *Journal of pharmacy and Pharmacology*, 57(9), 1117-1126.
- Romm, A., Lee, L., & Hobbs, C. (2010). Pregnancy: third trimester. *Botanical medicine for women's health*. St. Louis: Churchill Livingstone, 386.
- Roy, K., Kar, S., & Das, R. N. (2015). Other related techniques. *Understanding the Basics of QSAR for Applications in Pharmaceutical Sciences and Risk Assessment*, 357.
- Ruban, P., & Gajalakshmi, K. (2012). In vitro antibacterial activity of *Hibiscus rosa-sinensis* flower extract against human pathogens. *Asian pacific journal of tropical biomedicine*, 2(5), 399-403.
- Saeidnia, S., Manayi, A., Gohari, A. R., & Abdollahi, M. (2014). The story of beta-sitosterol-a review. *European journal of medicinal plants*, 4(5), 590.
- Safwat, N. A., Kashaf, M. T., Aziz, R. K., Amer, K. F., & Ramadan, M. A. (2018). Quercetin 3-O-glucoside recovered from the wild Egyptian Sahara plant, *Euphorbia paralias* L., inhibits glutamine synthetase and has antimycobacterial activity. *Tuberculosis*, 108, 106-113.
- Salamah, A., Prihatiningsih, R., Rostina, I., & Dwiranti, A. (2018). Comparative morphology of single and double flowers in *Hibiscus rosa-sinensis* L.(Malvaceae): A homeosis study. In *AIP Conference Proceedings* (Vol. 2023, No. 1, p. 020136). AIP Publishing LLC.
- Sasikumar, K., Ghosh, A. R., & Dusthacker, A. (2018). Antimycobacterial potentials of quercetin and rutin against *Mycobacterium tuberculosis* H37Rv. *3 Biotech*, 8(10), 1-6.
- Secondary Structure and Backbone Conformation | SWISS-MODEL. (2022). Retrieved 31 March 2022, from <https://swissmodel.expasy.org/course/text/chapter1.htm>
- Seifert M, Catanzaro D, Catanzaro A, Rodwell TC. (2015). Genetic Mutations Associated with Isoniazid Resistance in *Mycobacterium tuberculosis*: A Systematic Review. *PLoS ONE* 10(3): e0119628. <https://doi.org/10.1371/journal.pone.0119628>
- Seung, K. J., Keshavjee, S., & Rich, M. L. (2015). Multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis. *Cold Spring Harbor perspectives in medicine*, 5(9), a017863.
- Seyyednejad, S. M., Koochak, H., Darabpour, E., & Motamedi, H. (2010). A survey on *Hibiscus rosa-sinensis*, *Alcea rosea* L. and *Malva neglecta* Wallr. as antibacterial agents. *Asian Pacific Journal of Tropical Medicine*, 3(5), 351-355.
- Sharma, S. K., Kumar, G., Kapoor, M., & Surolia, A. (2008). Combined effect of epigallocatechin gallate and triclosan on enoyl-ACP reductase of *Mycobacterium tuberculosis*. *Biochemical and biophysical research communications*, 368(1), 12-17.
- Shaw, D. J., Robb, K., Vetter, B. V., Tong, M., Molle, V., Hunt, N. T., & Hoskisson, P. A. (2017). Disruption of key NADH-binding pocket residues of the *Mycobacterium tuberculosis* InhA affects DD-CoA binding ability. *Scientific reports*, 7(1), 1-7.
- Simon, S., & Listiawan, I. (2003). Molecular based detection for drug resistance in *mycobacterium tuberculosis*. *Medical Journal of Indonesia*, 12(4), 259-70.