

SKRIPSI

**EVALUASI POTENSI EKSTRAK ETANOL *Spirulina platensis* SEBAGAI
BAHAN TABIR SURYA DAN ANTI TIROSINASE SECARA *IN VITRO* DAN
*IN SILICO***

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Sebuah skripsi yang diajukan untuk memenuhi sebagian syarat memperoleh gelar
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PERNYATAAN

Dengan ini menyatakan bahwa skripsi dengan judul ‘**Evaluasi Potensi Ekstrak Etanol *Spirulina platensis* Sebagai Bahan Tabir Surya dan Anti Tirosinase secara *In vitro* dan *In silico***’ ini beserta seluruh isinya adalah benar-benar karya saya sendiri. Saya tidak melakukan penjiplakan atau pengutipan dengan cara-cara yang tidak sesuai dengan etika ilmu yang berlaku dalam masyarakat keilmuan. Atas pernyataan ini, saya siap menanggung resiko/sanksi apabila dikemudian hari ditemukan adanya pelanggaran etika keilmuan atau ada klaim dari pihak lain terhadap keaslian karya saya ini.

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ABSTRAK

Penggunaan tabir surya yang mengandung anti tirosinase merupakan salah satu upaya untuk mencegah kerusakan kulit dari radiasi ultraviolet (UV) berlebih yang dapat menyebabkan hiperpigmentasi. Saat ini, penggunaan bahan alami sebagai agen fotoprotektif kulit banyak dikembangkan karena dinilai memiliki efek samping yang relatif rendah. Pada penelitian ini dilakukan analisis potensi ekstrak etanol *Spirulina platensis* sebagai kandidat sediaan bahan tabir surya dan anti tirosinase menggunakan pendekatan *in vitro* dan *in silico*. Karakteristik ekstrak etanol ditentukan menggunakan FTIR, screening fitokimia, dan penentuan total senyawa fenolik. Potensi tabir surya ditentukan melalui pengujian aktivitas antioksidan dan penentuan nilai SPF (*Sun Protection Factor*). Potensi anti tirosinase ditentukan melalui uji aktivitas inhibisi tirosinase secara *in vitro* dan *in silico*. Pengujian fitokimia dan FTIR menunjukkan bahwa ekstrak etanol *Spirulina platensis* mengandung senyawa fenolik dengan total kandungan fenolik sebesar 75,99 mg GAE/g ekstrak; IC50 terhadap DPPH sebesar 118,78 mg/L; inhibisi tirosinase 47,68 % (500 mg/L); dan nilai SPF terbaik tabir surya hasil formulasi yaitu 23,34. Pengujian *in silico* menunjukkan bahwa senyawa fenolik berinteraksi dengan tirosinase melalui ikatan hidrogen, ikatan hidrofobik, gaya van der Waals, dan interaksi akseptor logam. Beberapa senyawa fenolik seperti asam galat, asam vanilat, asam siringat, asam protokatekhuat, dan asam kafeat diprediksi memiliki aktivitas inhibisi yang lebih tinggi dibandingkan dengan asam kojat yang biasa digunakan sebagai inhibitor komersial tirosinase. Berdasarkan hasil penelitian dapat disimpulkan bahwa senyawa fenolik dari ekstrak etanol *S. platensis* memiliki potensi sebagai bahan aktif tabir surya yang dapat mencegah efek berbahaya dari radiasi UV dan kandidat anti tirosinase dengan prediksi mekanisme inhibisi kompetitif.

Kata Kunci: anti tirosinase, antioksidan, molekuler docking, *Spirulina platensis*, *Sun Protection Factor* (SPF).

ABSTRACT

The use of sunscreen containing anti-tyrosinase is one of the efforts to prevent skin damage from excessive ultraviolet (UV) radiation which can cause hyperpigmentation. Currently, the use of natural ingredients as skin photoprotective agents is widely developed because it is considered to have relatively low side effects. In this study, an analysis of the potential of *Spirulina platensis* ethanol extract as a candidate for sunscreen and anti-tyrosinase preparations were carried out using in vitro and in silico approaches. The characteristics of the ethanol extract were determined using FTIR, phytochemical screening, and determination of total phenolic compounds. The potential of sunscreen is evaluated by measuring an antioxidant activity and the value of the Sun Protection Factor (SPF). Anti-tyrosinase activities was determined by in vitro and in silico tests of tyrosinase inhibitory activity. Phytochemical and FTIR tests showed that the ethanol extract of *Spirulina platensis* contained phenolic compounds with a total phenolic content of 75.99 mg GAE/g extract. The DPPH assay showed an extract IC₅₀ of 118.78 mg/L and tyrosinase inhibition of 47.68 % (500 mg/L). The highest SPF value of formulated sunscreen is 23.34. In silico study showed that phenolic compounds interact with tyrosinase through hydrogen bonds, hydrophobic bonds, van der Waals forces, and metal-acceptor interaction. Several phenolic compounds such as gallic acid, vanillic acid, syringic acid, protocatechuic acid, and caffeic acid are predicted to have higher inhibitory activity than those of kojic acid which is commonly used as a commercial tyrosinase inhibitor. All in all, it can be concluded that the phenolic compounds from the ethanolic extract of *S. platensis* have potential as active sunscreen ingredients that can prevent the harmful effects of UV radiation and anti-tyrosinase candidates by predicting competitive inhibition mechanisms.

Keywords: anti-tyrosinase, antioxidant, molecular docking, *Spirulina platensis*, Sun Protection Factor (SPF).

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DAFTAR PUSTAKA

- Agarwal, P., Singh, M., Singh, J., & Singh, R. P. (2019). Microbial Tyrosinases: A Novel Enzyme, Structural Features, and Applications. In *Applied Microbiology and Bioengineering* (pp. 3–19). Elsevier.
<https://doi.org/10.1016/b978-0-12-815407-6.00001-0>
- Aksoy, L., Kolay, E., Ağılönü, Y., Aslan, Z., & Kargioğlu, M. (2013). Free radical scavenging activity, total phenolic content, total antioxidant status, and total oxidant status of endemic Thermopsis turcica. *Saudi Journal of Biological Sciences*, 20(3), 235–239.
<https://doi.org/10.1016/j.sjbs.2013.02.003>
- Alkilani, A. Z., McCrudden, M. T. C., & Donnelly, R. F. (2015). Transdermal drug delivery: Innovative pharmaceutical developments based on disruption of the barrier properties of the stratum corneum. *Pharmaceutics*, 7(4), 438–470. <https://doi.org/10.3390/pharmaceutics7040438>
- Ancans, J., Tobin, D. J., Hoogduijn, M. J., Smit, N. P., Wakamatsu, K., & Thody, A. J. (2001). Melanosomal pH controls rate of melanogenesis, eumelanin/phaeomelanin ratio and melanosome maturation in melanocytes and melanoma cells. *Experimental Cell Research*, 268(1), 26–35.
<https://doi.org/10.1006/excr.2001.5251>
- Andria, F. A., & Rahmaningsih, S. (2018). Trends in the Uses of Spirulina Microalga: A mini-review. *Jurnal Ilmiah Perikanan Dan Kelautan*, 10(2), 95–105.
- Aouir, A., Amiali, M., Bitam, A., Benchabane, A., & Raghavan, V. G. (2017). Comparison of the biochemical composition of different Arthrobacteria platensis strains from Algeria, Chad and the USA. *Journal of Food Measurement and Characterization*, 11(2), 913–923.
<https://doi.org/10.1007/s11694-016-9463-4>
- Apostică, A. G., Ichim, T., Radu, V. M., & Bulgariu, L. (2018). Simple and Rapid Spectrophotometric Method for Phenol Determination in Aqueous Media. *Bulletin of the Polytechnic Institute of Jassy*, 64(3), 9–18.

- Arwansyah, A., Ambarsari, L., & Sumaryada, T. I. (2014). Simulasi Docking Senyawa Kurkumin dan Analognya Sebagai Inhibitor Reseptor Androgen pada Kanker Prostat. *Current Biochemistry*, 1(1), 11–19.
<https://doi.org/10.29244/cb.1.1.11-19>
- Ashour, A. S., El Aziz, M. M. A., & Gomha Melad, A. S. (2019). A review on saponins from medicinal plants: chemistry, isolation, and determination. *Journal of Nanomedicine Research*, 7(4), 282–288.
<https://doi.org/10.15406/jnmr.2019.07.00199>
- Azimuddin, R. M., Norzalina, Z., Hana, F. N., Afifah, S. A. S. N., & Ashari, S. E. (2021). Preliminary Study: Molecular Docking, Optimization and Characterization of Kojic Monooleate Nanoemulsion for Cosmeceuticals Application. *Journal of Sustainability Science and Management*, 16(8), 158–176. <https://doi.org/10.46754/jssm.2021.12.011>
- Becker, L. C., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D. C., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., Gill, L. J., & Heldreth, B. (2019). Safety Assessment of Glycerin as Used in Cosmetics. *International Journal of Toxicology*, 38(3_suppl), 6S-22S.
<https://doi.org/10.1177/1091581819883820>
- Bellahcen, T. O., Aamiri, A., Touam, I., Hmimid, F., Amrani, A. El, Cherif, A., & Cherki, M. (2020). Evaluation of Moroccan microalgae: Spirulina platensis as a potential source of natural antioxidants. *Journal of Complementary and Integrative Medicine*, 17(3), 1–14. <https://doi.org/10.1515/jcim-2019-0036>
- Bikadi, Z., & Hazai, E. (2009). Application of the PM6 semi-empirical method to modeling proteins enhances docking accuracy of AutoDock. *Journal of Cheminformatics*, 1(1), 1–16. <https://doi.org/10.1186/1758-2946-1-15>
- Blaustein, A. R., & Searle, C. (2013). Ultraviolet Radiation. *Encyclopedia of Biodiversity: Second Edition*, May, 296–303. <https://doi.org/10.1016/B978-0-12-384719-5.00147-7>
- Carrer, V., Alonso, C., Pont, M., Zanuy, M., Córdoba, M., Espinosa, S., Barba, C., Oliver, M. A., Martí, M., & Coderch, L. (2020). Effect of propylene glycol

- on the skin penetration of drugs. *Archives of Dermatological Research*, 312(5), 337–352. <https://doi.org/10.1007/s00403-019-02017-5>
- Cepoi, L., Rudi, L., Miscu, V., Cojocari, A., Chiriac, T., & Sadovnic, D. (2009). Antioxidative activity of ethanol extracts from *Spirulina platensis* and *Nostoc linckia* measured by various methods. *Analele Universității Din Oradea, Fascicula Biologie*, 16(2), 43–48.
http://www.bioresearch.ro/bioresearch/2009-2/043-48_Cepoi.pdf
- Chae, S. Y., Jang, M. K., & Nah, J. W. (2005). Influence of molecular weight on oral absorption of water soluble chitosans. *Journal of Controlled Release*, 102(2), 383–394. <https://doi.org/10.1016/j.jconrel.2004.10.012>
- Chang, T. S. (2009). An updated review of tyrosinase inhibitors. *International Journal of Molecular Sciences*, 10(6), 2440–2475.
<https://doi.org/10.3390/ijms10062440>
- Chatatikun, M., & Chiabchalard, A. (2013). Phytochemical screening and free radical scavenging activities of orange baby carrot and carrot (*Daucus carota Linn.*) root crude extracts. *Journal of Chemical and Pharmaceutical Research*, 5(4), 97–102.
- Coimbra, J. T. S., Feghali, R., Ribeiro, R. P., Ramos, M. J., & Fernandes, P. A. (2020). The importance of intramolecular hydrogen bonds on the translocation of the small drug piracetam through a lipid bilayer. *RSC Advances*, 11(2), 899–908. <https://doi.org/10.1039/d0ra09995c>
- D’Orazio, J., Jarrett, S., Amaro-Ortiz, A., & Scott, T. (2013). UV radiation and the skin. *International Journal of Molecular Sciences*, 14(6), 12222–12248.
<https://doi.org/10.3390/ijms140612222>
- Damogalad, V., Jaya Edy, H., & Sri Supriati, H. (2013). Formulasi Krim Tabir Surya Ekstrak Kulit Nanas (Ananas Comosus L Merr) Dan Uji in Vitro Nilai Sun Protecting Factor (Spf). *PHARMACON Jurnal Ilmiah Farmasi – UNSRAT*, 2(02), 2302–2493.
- Dar, A. M., & Mir, S. (2017). Molecular Docking: Approaches, Types,

- Applications and Basic Challenges. *Journal of Analytical & Bioanalytical Techniques*, 08(02). <https://doi.org/10.4172/2155-9872.1000356>
- Dhorajiwala, T. M., Halder, S. T., & Samant, L. (2019). Comparative in silico molecular docking analysis of l-threonine-3-dehydrogenase, a protein target against African trypanosomiasis using selected phytochemicals. *Journal of Applied Biotechnology Reports*, 6(3), 101–108.
<https://doi.org/10.29252/JABR.06.03.04>
- Di Muzio, E., Toti, D., & Polticelli, F. (2017). DockingApp: a user friendly interface for facilitated docking simulations with AutoDock Vina. *Journal of Computer-Aided Molecular Design*, 31(2), 213–218.
<https://doi.org/10.1007/s10822-016-0006-1>
- Dianursanti, Nugroho, P., & Prakasa, M. B. (2020). Comparison of maceration and soxhletation method for flavonoid production from Spirulina platensis as a sunscreen's raw material. *AIP Conference Proceedings*, 2230.
<https://doi.org/10.1063/5.0002806>
- Dijkhoff, I. M., Drasler, B., Karakocak, B. B., Petri-Fink, A., Valacchi, G., Eeman, M., & Rothen-Rutishauser, B. (2020). Impact of airborne particulate matter on skin: A systematic review from epidemiology to in vitro studies. *Particle and Fibre Toxicology*, 17(1), 1–29. <https://doi.org/10.1186/s12989-020-00366-y>
- Dolorosa, M. T., Nurjanah, Purwaningsih, S., Anwar, E., & Hidayat, T. (2019). Tyrosinase inhibitory activity of Sargassum plagyophyllum and Eucheuma cottonii methanol extracts. *IOP Conference Series: Earth and Environmental Science*, 278(1). <https://doi.org/10.1088/1755-1315/278/1/012020>
- Ekins, S., Mestres, J., & Testa, B. (2007). In silico pharmacology for drug discovery: Methods for virtual ligand screening and profiling. In *British Journal of Pharmacology* (Vol. 152, Issue 1, pp. 9–20).
<https://doi.org/10.1038/sj.bjp.0707305>
- Elkhyat, A., Courderot-Masuyer, C., Gharbi, T., & Humbert, P. (2004). Influence of the hydrophobic and hydrophilic characteristics of sliding and slider

- surfaces on friction coefficient: I vivo human skin friction comparison. *Skin Research and Technology*, 10(4), 215–221. <https://doi.org/10.1111/j.1600-0846.2004.00085.x>
- Feng, X. X., Yu, X. T., Li, W. J., Kong, S. Z., Liu, Y. H., Zhang, X., Xian, Y. F., Zhang, X. J., Su, Z. R., & Lin, Z. X. (2014). Effects of topical application of patchouli alcohol on the UV-induced skin photoaging in mice. *European Journal of Pharmaceutical Sciences*, 63, 113–123. <https://doi.org/10.1016/j.ejps.2014.07.001>
- Ferdaus, J. (2015). *Extraction of Secondary Metabolites, Phytochemical Screening and The Analysis of Antibacterial Activity in Spirulina platensis*. BRAC University.
- Fiume, M. M., Heldreth, B., Bergfeld, W. F., Belsito, D. V., Hill, R. A., Klaassen, C. D., Liebler, D., Marks, J. G., Shank, R. C., Slaga, T. J., Snyder, P. W., & Andersen, F. A. (2013). Safety Assessment of Triethanolamine and Triethanolamine-Containing Ingredients as Used in Cosmetics. *International Journal of Toxicology*, 32(May), 59S-83S. <https://doi.org/10.1177/1091581813488804>
- Fujisawa, T., Narikawa, R., Okamoto, S., Ehira, S., Yoshimura, H., Suzuki, I., Masuda, T., Mochimaru, M., Takaichi, S., Awai, K., Sekine, M., Horikawa, H., Yashiro, I., Omata, S., Takarada, H., Katano, Y., Kosugi, H., Tanikawa, S., Ohmori, K., ... Ohmori, M. (2010). Genomic structure of an economically important cyanobacterium, arthrospira (Spirulina) platensis NIES-39. *DNA Research*, 17(2), 85–103. <https://doi.org/10.1093/dnares/dsq004>
- Gabr, G. A., El-Sayed, S. M., & Hikal, M. S. (2020). Antioxidant Activities of Phycocyanin: A Bioactive Compound from Spirulina platensis. *Journal of Pharmaceutical Research International*, March, 73–85. <https://doi.org/10.9734/jpri/2020/v32i230407>
- Geoffrey, K., Mwangi, A. N., & Maru, S. M. (2019). Sunscreen products: Rationale for use, formulation development and regulatory considerations.

- Saudi Pharmaceutical Journal*, 27(7), 1009–1018.
<https://doi.org/10.1016/j.jsps.2019.08.003>
- Gheda, S. F., Abo-Shady, A. M., Abdel-Karim, O. H., & Ismail, G. A. (2021). Antioxidant and antihyperglycemic activity of arthrospira platensis (Spirulina platensis) methanolic extract: In vitro and in vivo study. *Egyptian Journal of Botany*, 61(1), 71–93.
<https://doi.org/10.21608/ejbo.2020.27436.1482>
- Głowiak, E. D., Irimia-Vladu, M., Bauer, S., & Sariciftci, N. S. (2013). Hydrogen-bonds in molecular solids-from biological systems to organic electronics. *Journal of Materials Chemistry B*, 1(31), 3742–3753.
<https://doi.org/10.1039/c3tb20193g>
- Goswami, P. K., Samant, M., Srivastava, R., Kantivan, P., & Email, G. (2013). Natural Sunscreen Agents: A Review. *Scholars Academic Journal of Pharmacy (SAJP) Sch. Acad. J. Pharm*, 2(6), 458–463.
www.saspublisher.com
- Guedes, A. C., Amaro, H. M., & Malcata, F. X. (2011). Microalgae as sources of carotenoids. *Marine Drugs*, 9(4), 625–644.
<https://doi.org/10.3390/md9040625>
- Habib, M. A. B., Parvin, M., Huntington, T. C., & Hasan, M. R. (2008). A review of culture, production and use of Spirulina as food for humans and feeds for domestic animals and fish. In *FAO Fisheries and Aquaculture Circular. No. 1034. Rome, FAO*. 33p. (Issue 1034). <http://agris.fao.org/agris-search/search/display.do?f=2010/XF/XF0906.xml;XF2009437877>
- Hall, D. R., Kozakov, D., & Vajda, S. (2012). Analysis of protein binding sites by computational solvent mapping. *Methods in Molecular Biology*, 819(1), 13–27. https://doi.org/10.1007/978-1-61779-465-0_2
- Hasan, T., Jahan, E., Ahmed, K. S., Hossain, H., Siam, S. M. M., Nahid, N., Mazumder, T., Shuvo, M. S. R., & Daula, A. F. M. S. U. (2022). Rutin hydrate and extract from Castanopsis tribuloides reduces pyrexia via inhibiting microsomal prostaglandin E synthase-1. *Biomedicine and*

- Pharmacotherapy*, 148(February), 112774.
<https://doi.org/10.1016/j.biopha.2022.112774>
- Holtrop, F., Visscher, K. W., Jupp, A. R., & Slootweg, J. C. (2020). Steric attraction: A force to be reckoned with. In *Advances in Physical Organic Chemistry* (1st ed., Vol. 54). Elsevier Ltd.
<https://doi.org/10.1016/bs.apoc.2020.08.001>
- Hoseini, S. M., Khosravi-Darani, K., & Mozafari, M. R. (2013). Nutritional and Medical Applications of Spirulina Microalgae. *Mini-Reviews in Medicinal Chemistry*, 13(8), 1231–1237.
<https://doi.org/10.2174/1389557511313080009>
- Igarashi, T., Nishino, K., & Nayar, S. K. (2007). The appearance of human skin: A survey. *Foundations and Trends in Computer Graphics and Vision*, 3(1), 1–95. <https://doi.org/10.1561/0600000013>
- Julia, G. I., & Komari, N. (2022). *Chemica Isola Virtual Screening Peptida Aktif Antikanker dari Myosin Ikan Gabus (Channa striata)*. 2(1), 84–93.
- Jun, M., Fu, H. Y., Hong, J., Wan, X., Yang, C. S., & Ho, C. T. (2003). Comparison of antioxidant activities of isoflavones from kudzu root (*Pueraria lobata Ohwi*). *Journal of Food Science*, 68(6), 2117–2122.
<https://doi.org/10.1111/j.1365-2621.2003.tb07029.x>
- Khedidja, B., Madjda, B., & Abderrahmane, G. (2018). Antiallergy Drugs as Potent Inhibitors of Lipase with Structure-activity Relationships and Molecular Docking. *Anti-Inflammatory & Anti-Allergy Agents in Medicinal Chemistry*, 17(2), 95–101.
<https://doi.org/10.2174/1871523017666180910120150>
- Kumar, A., Ramamoorthy, D., Verma, D. K., Kumar, A., Kumar, N., Kanak, K. R., Marwein, B. M., & Mohan, K. (2022). Antioxidant and phytonutrient activities of Spirulina platensis. *Energy Nexus*, 6(April), 100070.
<https://doi.org/10.1016/j.nexus.2022.100070>
- Kushwaha, D., Verma, Y., Ramteke, P. W., & Prasad, V. M. (2020). Evaluation

- of Total Phenolic and Flavonoids Content and their Relation with Antioxidant Properties of Tagetes patula Varieties, Through DPPH Assay. *International Journal of Current Microbiology and Applied Sciences*, 9(2), 2356–2363. <https://doi.org/10.20546/ijcmas.2020.902.268>
- Lee, K. K., Cho, J. J., Park, E. J., & Choi, J. D. (2001). Anti-elastase and anti-hyaluronidase of phenolic substance from Areca catechu as a new anti-ageing agent. *International Journal of Cosmetic Science*, 23(6), 341–346. <https://doi.org/10.1046/j.0412-5463.2001.00102.x>
- Li, Y., Meng, Q., Yang, M., Liu, D., Hou, X., Tang, L., Wang, X., Lyu, Y., Chen, X., Liu, K., Yu, A. M., Zuo, Z., & Bi, H. (2019). Current trends in drug metabolism and pharmacokinetics. *Acta Pharmaceutica Sinica B*, 9(6), 1113–1144. <https://doi.org/10.1016/j.apsb.2019.10.001>
- Lin, F. R., Niparko, J. K., & Ferrucci, and L. (2014). 基因的改变NIH Public Access. *Bone*, 23(1), 1–7. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3624763/pdf/nihms412728.pdf>
- Liquan, Z. (2012). The atmospheric propagation simulation characteristic of the solar blind ultraviolet light. *Applied Mechanics and Materials*, 229–231, 2623–2628. <https://doi.org/10.4028/www.scientific.net/AMM.229-231.2623>
- Liu, J. J., & Fisher, D. E. (2010). Lighting a path to pigmentation: Mechanisms of MITF induction by UV. *Pigment Cell and Melanoma Research*, 23(6), 741–745. <https://doi.org/10.1111/j.1755-148X.2010.00775.x>
- Lolowang, F., Suryanto, E., & Citraningtyas, G. (2017). Aktivitas Antioksidan Dari Ekstrak Residu Empelur Batang Sagu Baruk (Arenga Microcarpha). *Pharmacon*, 6(4), 139–148.
- López-Castillo, N. N., Rojas-Rodríguez, A. D., Porta, B. M., & Cruz-Gómez, M. J. (2013). Process for the Obtention of Coumaric Acid from Coumarin: Analysis of the Reaction Conditions. *Advances in Chemical Engineering and Science*, 03(03), 195–201. <https://doi.org/10.4236/aces.2013.33025>

- Maciel, L. F., da Oliveira, C. S., da Bispo, E. S., & da Miranda, M. P. S. (2011). Antioxidant activity, total phenolic compounds and flavonoids of mangoes coming from biodynamic, organic and conventional cultivations in three maturation stages. *British Food Journal*, 113(9), 1103–1113.
<https://doi.org/10.1108/00070701111180319>
- Mahmoudpour, M., Javaheri-Ghezeldizaj, F., Yekta, R., Torbati, M., Mohammadzadeh-Aghdash, H., Kashanian, S., & Ezzati Nazhad Dolatabadi, J. (2020). Thermodynamic analysis of albumin interaction with monosodium glutamate food additive: Insights from multi-spectroscopic and molecular docking approaches. *Journal of Molecular Structure*, 1221, 128785.
<https://doi.org/10.1016/j.molstruc.2020.128785>
- Mancebo, S. E., Hu, J. Y., & Wang, S. Q. (2014). Sunscreens: A review of health benefits, regulations, and controversies. *Dermatologic Clinics*, 32(3), 427–438. <https://doi.org/10.1016/j.det.2014.03.011>
- Mane, R. S., & Chakraborty, B. (2018). Phytochemical screening of Spirulina platensis extracts from Rankala Lake Phytochemical screening of Spirulina platensis extracts from Rankala Lake. *Journal of Algal Biomass Utilization*, 9(4), 38–40.
https://www.academia.edu/37991345/Phytochemical_screening_of_Spirulina_platensis_extracts_from_Rankala_Lake_Kolhapur_India
- Mapoung, S., Arjsri, P., Thippraphan, P., Semmarath, W., Yodkeeree, S., Chiewchanvit, S., Piyamongkol, W., & Limtrakul, P. (2020). Photochemoprotective effects of Spirulina platensis extract against UVB irradiated human skin fibroblasts. *South African Journal of Botany*, 130, 198–207. <https://doi.org/10.1016/j.sajb.2020.01.001>
- Mebs, S., & Beckmann, J. (2022). In silico activation of dinitrogen with a light atom molecule. *Physical Chemistry Chemical Physics*.
<https://doi.org/10.1039/d2cp02516g>
- Meng, X.-Y., Zhang, H.-X., Mezei, M., & Cui, M. (2012). Molecular Docking: A Powerful Approach for Structure-Based Drug Discovery. *Current Computer*

- Aided-Drug Design*, 7(2), 146–157.
<https://doi.org/10.2174/157340911795677602>
- Mishra, A. P., Saklani, S., Milella, L., & Tiwari, P. (2014). Formulation and evaluation of herbal antioxidant face cream of Nardostachys jatamansi collected from Indian Himalayan region. *Asian Pacific Journal of Tropical Biomedicine*, 4(Suppl 2), S679–S682.
<https://doi.org/10.12980/APJTB.4.2014APJTB-2014-0223>
- Molyneux P. (2004). The Use of The Stable Free Radical Diphenylpicryl-Hydrayl (DPPH) for Estimating Anti-Oxidant Activity. *Songklanakarin Journal of Science and Technology*, 26(May), 211–219.
- Muhtadi, S. (2021). Antioxidant Activity of Sunflower (*Helianthus Annuus* L.) Ethanolic Extract with DPPH Method and Determination of Total Phenolic and Flavonoid Levels. *Journal of Nutraceuticals and Herbal Medicine*, 4(1), 31–42.
- Muttaqin, F. Z. (2019). Molecular Docking and Molecular Dynamic Studies of Stilbene Derivative Compounds As Sirtuin-3 (Sirt3) Histone Deacetylase Inhibitor on Melanoma Skin Cancer and Their Toxicities Prediction. *Journal of Pharmacopolium*, 2(2), 112–121. <https://doi.org/10.36465/jop.v2i2.489>
- Ngu, E. L., Ko, C. L., Tan, C. Y., Wong, K. H., Phang, S. M., & Yow, Y. Y. (2021). Phytochemical profiling and in vitro screening for neuritogenic and antioxidant activities of spirulina platensis. *Indian Journal of Pharmaceutical Education and Research*, 55(3), 812–822.
<https://doi.org/10.5530/ijper.55.3.154>
- Nn, A. (2015). A Review on the Extraction Methods Use in Medicinal Plants, Principle, Strength and Limitation. *Medicinal & Aromatic Plants*, 04(03), 3–8. <https://doi.org/10.4172/2167-0412.1000196>
- Noel, V. T., Dlzar, D. G., A, S. M. D., Rawa, R. I., & Lanya, K. J. (2021). Antibacterial effects of the organic crude extracts of freshwater algae of Sulaymaniyah, Kurdistan Region, Iraq. *Journal of Medicinal Plants Research*, 15(4), 178–187. <https://doi.org/10.5897/jmpr2021.7117>

- Pace, C. N., Fu, H., Fryar, K. L., Landua, J., Trevino, S. R., Schell, D., Thurlkill, R. L., Imura, S., Scholtz, J. M., Gajiwala, K., Sevcik, J., Urbanikova, L., Myers, J. K., Takano, K., Hebert, E. J., Shirley, B. A., & Grimsley, G. R. (2014). Contribution of hydrogen bonds to protein stability. *Protein Science*, 23(5), 652–661. <https://doi.org/10.1002/pro.2449>
- Pan, F., Li, J., Zhao, L., Tuersuntuoheti, T., Mehmood, A., Zhou, N., Hao, S., Wang, C., Guo, Y., & Lin, W. (2021). A molecular docking and molecular dynamics simulation study on the interaction between cyanidin-3-O-glucoside and major proteins in cow's milk. *Journal of Food Biochemistry*, 45(1), 1–10. <https://doi.org/10.1111/jfbc.13570>
- Portugal-Cohen, M., Soroka, Y., Ma'or, Z., Oron, M., Zioni, T., Brégégère, F. M., Neuman, R., Kohen, R., & Milner, Y. (2009). Protective effects of a cream containing Dead Sea minerals against UVB-induced stress in human skin. *Experimental Dermatology*, 18(9), 781–788. <https://doi.org/10.1111/j.1600-0625.2009.00865.x>
- Pratama, G. M. C. T., Hartawan, I. G. N. B. R. M., Indriani, I. G. A. T., Yusrika, U., Suryantari, S. A. A., Satyarsa, A. B. S., Sudarsa, P. S. S., & Sanglah, U. R. (2020). Potensi Ekstrak Spirulina platensis sebagai Tabir Surya terhadap Paparan Ultraviolet B. *Journal of Medicine and Health*, 2(6), 205–217.
- Rahim, A., Çakir, C., Ozturk, M., Şahin, B., Soulaimani, A., Sibaoueih, M., Nasser, B., Eddoha, R., Essamadi, A., & El Amiri, B. (2021). Chemical characterization and nutritional value of Spirulina platensis cultivated in natural conditions of Chichaoua region (Morocco). *South African Journal of Botany*, 141, 235–242. <https://doi.org/10.1016/j.sajb.2021.05.006>
- Ramawat, K. G., & Mérillon, J. M. (2013). Natural products: Phytochemistry, botany and metabolism of alkaloids, phenolics and terpenes. *Natural Products: Phytochemistry, Botany and Metabolism of Alkaloids, Phenolics and Terpenes*, 1–4242. <https://doi.org/10.1007/978-3-642-22144-6>
- Ribeiro, A. J. M., Tyzack, J. D., Borkakoti, N., Holliday, G. L., & Thornton, J. M. (2020). A global analysis of function and conservation of catalytic residues

- in enzymes. *Journal of Biological Chemistry*, 295(2), 314–324. <https://doi.org/10.1074/jbc.REV119.006289>
- Sahin, S. C. (2018). The potential of *Arthrospira platensis* extract as a tyrosinase inhibitor for pharmaceutical or cosmetic applications. *South African Journal of Botany*, 119, 236–243. <https://doi.org/10.1016/j.sajb.2018.09.004>
- Sanjaya, I. G. M. S. A. S. (2014). Kajian Teoritis Untuk Menentukan Cela Energi Kompleks 8-Hidroksiquinolin Terkonjugasi Logam Besi Dengan Menggunakan Teori Kerapatan Fungsional. *UNESA Journal of Chemistry Vol.*, 3(2), 1–10.
- Santiago, A., & Moreira, R. (2020). Drying of edible seaweeds. In *Sustainable Seaweed Technologies*. Elsevier Inc. <https://doi.org/10.1016/b978-0-12-817943-7.00004-4>
- Sayre, R. M., Agin, P. P., LeVee, G. J., & Marlowe, E. (1979). a Comparison of in Vivo and in Vitro Testing of Sunscreening Formulas. *Photochemistry and Photobiology*, 29(3), 559–566. <https://doi.org/10.1111/j.1751-1097.1979.tb07090.x>
- Sebastian, -S, Xavier, -S, Daniel, J. C., Arockianathan, P. M., Sathish, M., Reka, U., & Joseph', S. (2017). Molecular Docking Studies of Some Selective Cancer Protein With 6-Hydroxyflavanone: a Theoretical Predication for Protein-Ligand Binding Site. *Joseph's Journal of Humanities and Science*, 4(January), 71–75. <http://sjctnc.edu.in/6107-2/>
- Septiana, E., Rahmawati, S. I., Izzati, F. N., & Simanjuntak, P. (2020). ANTIOXIDANT ACTIVITY, TOTAL PHENOLIC, AND FLAVONOID CONTENTS OF THE EXTRACT OF ENDOPHYTIC FUNGI DERIVED FROM TURMERIC (*Curcuma longa*) LEAVES. *Journal of Pharmaceutical Sciences and Community*, 16(2), 78–85. <https://doi.org/10.24071/jpsc.001953>
- Shovyana, H. H., & Zulkarnain, K. A. (2013). Stabilitas Fisik dan Aktivitas Krim W/O Ekstrak Etanolik Buah Mahkota Dewa (*Phaleria macrocarph*(scheff.) Boerl,) Sebagai Tabir Surya. *Traditional Medicine Journal*, 18(2), 2013.

- Siti Halimatul Munawaroh, H., Gumilar, G. G., Nurjanah, F., Yuliani, G., Aisyah, S., Kurnia, D., Wulandari, A. P., Kurniawan, I., Ningrum, A., Koyande, A. K., & Show, P. L. (2020). In-vitro molecular docking analysis of microalgae extracted phycocyanin as an anti-diabetic candidate. *Biochemical Engineering Journal*, 161(April), 107666. <https://doi.org/10.1016/j.bej.2020.107666>
- Steinbrenner, H., Ramos, M. C., Stuhlmann, D., Sies, H., & Brenneisen, P. (2003). UVA-mediated downregulation of MMP-2 and MMP-9 in human epidermal keratinocytes. *Biochemical and Biophysical Research Communications*, 308(3), 486–491. [https://doi.org/10.1016/S0006-291X\(03\)01430-X](https://doi.org/10.1016/S0006-291X(03)01430-X)
- Sumaiyah, Masfria, & Dalimunthe, A. (2018). Determination of total phenolic content, total flavonoid content, and antimutagenic activity of ethanol extract nanoparticles of rhaphidophora pinnata (L.f) schott leaves. *Rasayan Journal of Chemistry*, 11(2), 505–510. <https://doi.org/10.7324/RJC.2018.1122068>
- Trott, O., & Olson, A. J. (2009). Software News and Update AutoDock Vina: Improving the Speed and Accuracy of Docking with a New Scoring Function, Efficient Optimization, and Multithreading. *Journal of Computational Chemistry*, 31(2), 455–461. <https://doi.org/10.1002/jcc>
- Yanuarti, R., Nurjanah, N., Anwar, E., & Pratama, G. (2017). Kandungan Senyawa Penangkal Sinar Ultra Violet dari Ekstrak Rumput Laut Eucheuma cottonii dan Turbinaria conoides. *Biosfera*, 34(2), 51. <https://doi.org/10.20884/1.mib.2017.34.2.467>
- Zarkogianni, M., & Nikolaidis, N. (2016). Determination of Sun Protection Factor (SPF) and Stability of Oil-in-Water Emulsions Containing Greek Red Saffron (*Crocus Sativus L.*) as a Main Antisolar Agent. *International Journal of Advanced Research in Chemical Science*, 3(7), 1–7. <https://doi.org/10.20431/2349-0403.0307001>
- Zeb, A. (2020). Concept, mechanism, and applications of phenolic antioxidants in foods. *Journal of Food Biochemistry*, 44(9), 1–22.

<https://doi.org/10.1111/jfbc.13394>

Zghari, B., Doumenq, P., Romane, A., & Boukir, A. (2017). GC-MS, FTIR and ¹H ,¹³C NMR structural analysis and identification of phenolic compounds in olive mill wastewater extracted from oued oussefrou effluent (Beni Mellal-Morocco). *Journal of Materials and Environmental Science*, 8(12), 4496–4509. <https://doi.org/10.26872/jmes.2017.8.12.475>

Zhang, S., & Duan, E. (2018). Fighting against Skin Aging: The Way from Bench to Bedside. In *Cell Transplantation* (Vol. 27, Issue 5, pp. 729–738). SAGE Publications Ltd. <https://doi.org/10.1177/0963689717725755>