

## **BAB V**

### **KESIMPULAN DAN SARAN**

#### **5.1 Kesimpulan**

Kesimpulan dari penelitian ini adalah sebagai berikut:

1. C-PC tidak terekstrak dengan baik dengan metode SFE, sehingga metode SFE belum dapat menjadi alternatif dari metode maserasi pada kondisi operasi penelitian ini.
2. Penggunaan *co-solvent* pada metode SFE meningkatkan perolehan dan aktivitas antioksidan ekstrak.
3. Titik optimum tekanan operasi metode SFE terletak pada 25 MPa, di mana akan didapatkan perolehan dan aktivitas antioksidan ekstrak tertinggi.
4. Semakin tinggi laju alir CO<sub>2</sub>, maka perolehan dan aktivitas antioksidan ekstrak pada metode SFE akan meningkat.
5. Kondisi operasi terbaik untuk mendapatkan perolehan (3,2832 %) dan aktivitas antioksidan ekstrak tertinggi (IC<sub>50</sub> 658,7925 ppm) adalah dengan penggunaan *co-solvent* etanol 10 %-v/v CO<sub>2</sub>, tekanan 25 MPa, dan laju alir CO<sub>2</sub> 12 mL/min.
6. Tahap *pre-treatment* ultrasonikasi dapat meningkatkan perolehan C-PC, serta perolehan dan aktivitas antioksidan ekstrak
7. Metode maserasi memberikan perolehan C-PC (47,6280 %) dan aktivitas antioksidan ekstrak (IC<sub>50</sub> 85,9929 ppm) yang lebih tinggi dibandingkan metode SFE.

#### **5.2 Saran**

Saran dari penelitian ini adalah sebagai berikut:

1. Perlu digunakan *co-solvent* etanol p.a. (100 %) atau *buffer* untuk menjaga pH dari pelarut agar tidak terjadi degradasi C-PC.
2. *Pre-treatment* ultrasonikasi dapat dilakukan dengan frekuensi, temperatur, dan intensitas yang lebih tinggi.
3. Waktu operasi ultrasonikasi dapat dibagi ke dalam beberapa siklus dengan waktu yang pendek, sehingga dapat memberikan jeda waktu untuk pendinginan agar tidak terjadi degradasi protein (antioksidan).
4. Ultrasonikasi juga dapat dilakukan dengan jenis alat *ultrasonic probe* yang intensitas ultrasonikasinya lebih tinggi dan mampu memberikan perolehan ekstraksi padat-cair yang lebih tinggi dibandingkan *ultrasonic bath*.

5. Pelarut yang digunakan pada tahap ultrasonikasi dapat disesuaikan dengan komponen yang akan diekstrak dan menghindari penggunaan alkohol karena dapat menyebabkan denaturasi protein dalam jumlah banyak, seperti *buffer* sodium fosfat pH 7 untuk C-PC.

## DAFTAR PUSTAKA

- Abd El-Baky, H. H., El Baz, F. K., & El-Baroty, G. S. (2008). Characterization of nutraceutical compounds in blue green alga *Spirulina maxima*. *Journal of Medicinal Plants Research*, 2(10), 292–300.
- Abrahamsson, A. V., Cunico, L. P., Nilsson, B., & Turner, C. (2018). Multicomponent inverse modeling of supercritical fluid extraction of carotenoids, chlorophyll A, ergosterol and lipids from microalgae. *The Journal of Supercritical Fluids*, 139, 53–61.
- Akowuah, G. A., Mariam, A., & Chin, J. H. (2009). The effect of extraction temperature on total phenols and antioxidant activity of *Gynura procumbens* leaf. *Pharmacognosy Magazine*, 4(17), 81–85.
- Alvarez-Rivera, G., Bueno, M., Ballesteros-Vivas, D., Mendiola, J. A., & Ibañez, E. (2019). Pressurized liquid extraction. In C. F. Poole (Ed.), *Liquid-Phase Extraction* (pp. 376–394). Elsevier Inc.
- Antelo, F. S., Costa, J. A. V., & Kalil, S. J. (2008). Thermal degradation kinetics of the phycocyanin from *Spirulina platensis*. *Biochemical Engineering Journal*, 41(1), 43–47. <https://doi.org/10.1016/j.bej.2008.03.012>
- Arsad, N. H., Yunus, M. A. C., Zaini, M. A. A., Rahman, Z. A., & Idham, Z. (2016). Effect of operating conditions of supercritical carbon dioxide on piper betle leave oil yield and antioxidant activity. *International Journal of Applied Chemistry*, 12(4), 741–751.
- Atsumi, S., Higashide, W., & Liao, J. C. (2009). Direct photosynthetic recycling of carbon dioxide to isobutyraldehyde. *Nature Biotechnology*, 27(12), 1177–1180.
- Augustynska, D., Jemioła-Rzemiąska, M., Burda, K., & Strzałka, K. (2015). Influence of polar and nonpolar carotenoids on structural and adhesive properties of model membranes. *Chemico-Biological Interactions*, 239, 19–25.
- Azmir, J., Zaidul, I. S. M., Rahman, M. M., Sharif, K. M., Mohamed, A., Sahena, F., Jahurul, M. H. A., Ghafoor, K., Norulaini, N. A. N., & Omar, A. K. M. (2013). Techniques for extraction of bioactive compounds from plant materials: A review. *Journal of Food Engineering*, 117(4), 426–436.
- Baineni, R., Gulati, R., & Kumar, C. G. (2017). Vitamin A toxicity presenting as bone pain. In *Archives of Disease in Childhood* (Vol. 102, Issue 6).
- Barad, M. (2007). Anatomical, Molecular, and Cellular Substrates of Fear Extinction. In *Fear and learning: From basic processes to clinical implications*. (Issue September).

- Becker, W. (2004). Microalgae in human and animal nutrition. In A. Richmond (Ed.), *Handbook of Microalgal Culture: Biotechnology and Applied Phycology* (pp. 312–351). Blackwell Publishing Ltd.
- Bennett, A., & Bogorad, L. (1973). Complementary Chromatic Adaptation in A Filamentous Blue-Green Alga. *The Journal of Cell Biology*, 58, 419–435.
- Bharte, S., & Desai, K. (2018). Techniques for harvesting, cell disruption and lipid extraction of microalgae for biofuel production. *Biofuels*, 7269, 1–21.
- Bone, K., & Mills, S. (Eds.). (2013). Principles of Herbal Pharmacology: Modern Herbal Medicine. In *Principles and Practice of Phytotherapy* (2nd ed., pp. 17–82). Elsevier Ltd.
- Brandts, J. F., & Hunt, L. (1967). The Thermodynamics of Protein Denaturation . 111 . The Denaturation of Ribonuclease in Water and in Aqueous Urea and Aqueous Ethanol Mixtures. *Journal of the American Chemical Society*, 89(19), 4826–4838.
- Campomanes, A. M. F., Rostagno, M. A., Quispe, J. J. C., & Meireles, M. A. A. (2015). Supercritical fluid extraction of polyphenols from lees: overall extraction curve , kinetic data and composition of the extracts. *Bioresources and Bioprocessing*, 2(45), 13.
- Capuzzo, A., Maffei, M. E., & Occhipinti, A. (2013). Supercritical fluid extraction of plant flavors and fragrances. *Molecules*, 18(6), 7194–7238.
- Chaiklahan, R., Chirasuwan, N., & Bunnag, B. (2012). Stability of phycocyanin extracted from Spirulina sp.: Influence of temperature, pH and preservatives. *Process Biochemistry*, 47(4), 659–664. <https://doi.org/10.1016/j.procbio.2012.01.010>
- Chen, J. C., Liu, K. S., Yang, T. J., Hwang, J. H., Chan, Y. C., & Lee, I. Te. (2012). Spirulina and C-phycocyanin reduce cytotoxicity and inflammation-related genes expression of microglial cells. *Nutritional Neuroscience*, 15(6), 252–256.
- Chester, T. L., Bowling, D. J., Innis, D. P., & Pinkston, J. D. (1990). Capillary Supercritical Fluid Chromatography at Pressures above 400 atm. *Analytical Chemistry*, 62(13), 1299–1301.
- Ciko, A. M., Jokić, S., Šubarić, D., & Jerković, I. (2018). Overview on the application of modern methods for the extraction of bioactive compounds from marine macroalgae. *Marine Drugs*, 16(10).
- Colla, L. M., Bertol, C. D., Ferreira, D. J., Bavaresco, J., Costa, J. A. V, & Bertolin, T. E. (2017). Thermal and photo-stability of the antioxidant potential of Spirulina platensis

- powder. *Brazilian Journal of Biology*, 77(2), 332–339.
- Conde-Hernández, L. A., Espinosa-Victoria, J. R., Trejo, A., & Guerrero-Beltrán, J. (2017). CO<sub>2</sub>-supercritical extraction, hydrodistillation and steam distillation of essential oil of rosemary (*Rosmarinus officinalis*). *Journal of Food Engineering*, 200, 81–86.
- Coulombier, N., Nicolau, E., Le Déan, L., Antheaume, C., Jauffrais, T., & Lebouvier, N. (2020). Impact of light intensity on antioxidant activity of tropical microalgae. *Marine Drugs*, 18(2). <https://doi.org/10.3390/md18020122>
- Crespi, F., Gavagnin, G., Sánchez, D., & Martínez, G. S. (2018). Analysis of the Thermodynamic Potential of Supercritical Carbon Dioxide Cycles: A Systematic Approach. *Journal of Engineering for Gas Turbines and Power*, 140(5).
- Cussler, E. L. (2009). *Diffusion Mass Transfer in Fluid Systems* (3rd ed.). Cambridge University Press.
- Danlami, J. M., Arsal, A., Zaini, M. A. A., & Sulaiman, H. (2014). A comparative study of various oil extraction techniques from plants. *Reviews in Chemical Engineering*, 30(6), 605–626.
- de Castro, M. D. L., Valcárcel, M., & Tena, M. T. (1994). Analytical Supercritical Fluid Extraction. In *Analytical Supercritical Fluid Extraction*. Springer-Verlag Berlin Heidelberg.
- Dejsungkranont, M., Chen, H. H., & Sirisansaneeyakul, S. (2017). Enhancement of antioxidant activity of C-phycocyanin of Spirulina powder treated with supercritical fluid carbon dioxide. *Agriculture and Natural Resources*, 51(5), 347–354. <https://doi.org/10.1016/j.anres.2017.12.001>
- Deniz, I., Ozen, M. O., & Yesil-Celiktas, O. (2016). Supercritical fluid extraction of phycocyanin and investigation of cytotoxicity on human lung cancer cells. *Journal of Supercritical Fluids*, 108, 13–18. <https://doi.org/10.1016/j.supflu.2015.10.015>
- Dent, M., Dragović-Uzelac, V., Penić, M., Brnić, M., Bosiljkov, T., & Levaj, B. (2013). The effect of extraction solvents, temperature and time on the composition and mass fraction of polyphenols in dalmatian wild sage (*Salvia officinalis* L.) extracts. *Food Technology and Biotechnology*, 51(1), 84–91.
- Do, Q. D., Angkawijaya, A. E., Tran-Nguyen, P. L., Huynh, L. H., Soetaredjo, F. E., Ismadji, S., & Ju, Y. H. (2014). Effect of extraction solvent on total phenol content, total flavonoid content, and antioxidant activity of *Limnophila aromatica*. *Journal of Food and Drug Analysis*, 22(3), 296–302.

- Duarte, K., Justino, C. I. L., Gomes, A. M., Rocha-Santos, T., & Duarte, A. C. (2014). Green analytical methodologies for preparation of extracts and analysis of bioactive compounds. In *Comprehensive Analytical Chemistry* (Vol. 65, pp. 59–78). Elsevier B.V.
- Duarte, Kátia, Justino, C. I. L., Pereira, R., Freitas, A. C., Gomes, A. M., Duarte, A. C., & Rocha-Santos, T. A. P. (2014). Green analytical methodologies for the discovery of bioactive compounds from marine sources. *Trends in Environmental Analytical Chemistry*, 3(4), 43–52.
- El-Baky, H. H. A., El Baz, F. K., & El-Baroty, G. S. (2003). Spirulina Species as a Source of Carotenoids and α-Tocopherol and its Anticarcinoma Factors. *Biotechnology (Faisalabad)*, 2(3), 222–240.
- Esquivel-Hernández, D. A., Rodríguez-Rodríguez, J., Cuéllar-Bermúdez, S. P., García-Pérez, J. S., Mancera-Andrade, E. I., Núñez-Echevarría, J. E., Ontiveros-Valencia, A., Rostro-Alanis, M., García-García, R. M., Torres, J. A., Chen, W. N., & Parra-Saldívar, R. (2017). Effect of Supercritical Carbon Dioxide Extraction Parameters on the Biological Activities and Metabolites Present in Extracts from *Arthrospira platensis*. *Marine Drugs*, 15(174), 1–18.
- Figueira, F. da S., Moraes, C. C., & Kalil, S. J. (2018). C-phycocyanin purification: Multiple processes for different applications. *Brazilian Journal of Chemical Engineering*, 35(3), 1117–1128. <https://doi.org/10.1590/0104-6632.20180353s20170160>
- Furmaniak, M. A., Misztak, A. E., Franczuk, M. D., Wilmette, A., Waleron, M., & Waleron, K. F. (2017). Edible cyanobacterial genus *Arthrospira*: Actual state of the art in cultivation methods, genetics, and application in medicine. *Frontiers in Microbiology*, 8(DEC), 1–21.
- 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*, 32(2), 73–85.
- García-Pérez, J. S., Cuéllar-Bermúdez, S. P., Arévalo-Gallegos, A., Salinas-Salazar, C., Rodríguez-Rodríguez, J., de la Cruz-Quiroz, R., Iqbal, H. M. N., & Parra-Saldívar, R. (2018). Influence of Supercritical CO<sub>2</sub> Extraction on Fatty Acids Profile, Volatile Compounds and Bioactivities from *Rosmarinus officinalis*. *Waste and Biomass Valorization*, 1–11.
- García-Pérez, J. S., Robledo-Padilla, F., Cuellar-Bermudez, S. P., Arévalo-Gallegos, A.,

- Parra-Saldivar, R., Zavala-Yoe, R., Ramirez-Mendoza, R. A., & Iqbal, H. M. N. (2017). Thermodynamics and statistical correlation between supercritical-CO<sub>2</sub> fluid extraction and bioactivity profile of locally available Mexican plants extracts. *Journal of Supercritical Fluids*, 122, 27–34.
- Guan, S. C. (2016). *EXTRACTING PHYCOCYANIN FROM SPIRULINA AND HYDROTHERMAL LIQUEFACTION OF ITS RESIDUES TO PRODUCE BIO-CRUIDE OIL*. University of Illinois.
- Guerin, M., Huntley, M. E., & Olaizola, M. (2003). Haematococcus astaxanthin: Applications for human health and nutrition. *Trends in Biotechnology*, 21(5), 210–216.
- Hadiyanto, S. H. (2016). Response surface optimization of ultrasound assisted extraction (UAE) of phycocyanin from microalgae *Spirulina platensis*. *Emirates Journal of Food and Agriculture*, 28(4), 227–234.
- Hadiyanto, Sutrisnorhadi, Sutanto, H., & Suzery, M. (2016). Phyocyanin extraction from microalgae *Spirulina platensis* assisted by ultrasound irradiation: Effect of time and temperature. *Songklanakarin Journal of Science and Technology*, 38(4), 391–398.
- Handa, Sukdev S. (2008). An Overview of Extraction Techniques for Medicinal and Aromatic Plants. In Sukhdev S. Handa, S. P. S. Khanuja, G. Longo, & D. D. Rakesh (Eds.), *Extraction Technologies for Medical and Aromatic Plants* (pp. 21–52). International Centre for Science and High Technology.
- Harun, R., Yip, J. W. S., Thiruvenkadam, S., Ghani, W. A. W. A. K., Cherrington, T., & Danquah, M. K. (2014). Algal biomass conversion to bioethanol-a step-by-step assessment. *Biotechnology Journal*, 9(1), 73–86.
- Herrero, M., Ibáñez, E., Señoráns, J., & Cifuentes, A. (2009). *Accelerated Solvent Extracts from Spirulina Platensis Microalga: Determination of their Antioxidant Activity and Analysis by Micellar Electrokinetic Chromatography*.
- Herrero, M., Martin-Alvarez, P. J., Senorans, F. J., Cifuentes, A., & Ibanez, E. (2005). Food Chemistry Optimization of accelerated solvent extraction of antioxidants from *Spirulina platensis* microalga. *Food Chemistry*, 93(3), 417–423.
- Huang, Y., Hong, A., Zhang, D., & Li, L. (2014). Comparison of cell rupturing by ozonation and ultrasonication for algal lipid extraction from *Chlorella vulgaris*. *Environmental Technology (United Kingdom)*, 35(8), 931–937.
- Hynstova, V., Sterbova, D., Klejdus, B., & Hedbavny, J. (2017). Separation , identification and quantification of carotenoids and chlorophylls in dietary supplements containing

- Chlorella vulgaris and Spirulina platensis using High Performance Th ... Journal of Pharmaceutical and Biomedical Analysis , identi. *Journal of Pharmaceutical and Biomedical Analysis*, 148(May 2018), 108–118.
- Ibañez, E., Herrero, M., Mendiola, J. A., & Castro-Puyana, M. (2012). Marine bioactive compounds: Sources, characterization and applications. In M. Hayes (Ed.), *Marine Bioactive Compounds: Sources, Characterization and Applications* (pp. 55–98). Springer Science+Business Media, LLC.
- Jeffrey, S. W., Wright, S. W., & Zapata, M. (2012). Microalgal classes and their signature pigments. In *Phytoplankton Pigments*. Cambridge University Press.
- Jessop, P. G., & Subramaniam, B. (2007). Gas-Expanded Liquids. *Chemical Reviews*, 107(6), 2666–2694.
- Joannes, C., Sipaut, C. S., Dayou, J., Yasir, S. M., & Mansa, R. F. (2015). The potential of using pulsed electric field (PEF) technology as the cell disruption method to extract lipid from microalgae for biodiesel production. *International Journal of Renewable Energy Research*, 5(2), 598–621.
- Kempkes, M. A., Roth, I., & Gaudreau, M. P. J. (2015). *Pulsed Electric Field (PEF) method for continuous enhanced extraction of oil and lipids from small aquatic plants*, Diversified Technologies Inc., US 9,029,108 (Patent No. US009029108B2). United States Patent.
- Khan, M. I., Shin, J. H., & Kim, J. D. (2018). The promising future of microalgae: Current status, challenges, and optimization of a sustainable and renewable industry for biofuels, feed, and other products. *Microbial Cell Factories*, 17(1), 1–21.
- King, J. W. (2014). Modern Supercritical Fluid Technology for Food Applications. *Annual Review of Food Science and Technology*, 5(1), 215–238.
- King, J. W., & Friedrich, J. P. (1990). Quantitative correlations between solute molecular structure and solubility in supercritical fluids. *Journal of Chromatography A*, 517(6460), 449–458.
- King, J. W., & Srinivas, K. (2009). Multiple unit processing using sub- and supercritical fluids. *The Journal of Supercritical Fluids*, 47, 598–610.
- Kissoudi, M., Sarakatsianos, I., & Samanidou, V. (2017). Isolation and purification of food-grade C-phycocyanin from Arthrospira platensis and its determination in confectionery by HPLC with Diode Array Detection. *Journal of Separation Science*, 41(4), 975–981.  
<https://doi.org/10.1002/jssc.201701151>

- Klejdus, B., Lojková, L., Plaza, M., Šnóblová, M., & Štěrbová, D. (2010). Hyphenated technique for the extraction and determination of isoflavones in algae: Ultrasound-assisted supercritical fluid extraction followed by fast chromatography with tandem mass spectrometry. *Journal of Chromatography A*, 1217(51), 7956–7965.
- Kobayashi, M. (2001). New Drying Technology: Low Temperature Spray Drying. *PDA Journal of GMP and Validation in Japan*, 3(1), 20–27.
- Kumar, P., Chand, S., & Maurya, P. K. (2016). Quercetin-modulated erythrocyte membrane sodium-hydrogen exchanger during human aging: correlation with ATPase's. In *Archives of Physiology and Biochemistry* (Vol. 122, Issue 3). Amity University Uttar Pradesh.
- Lange, L., & Lindedam, J. (2016). *The Fundamentals Of Bioeconomy The Biobased Society* (No. 6075–1).
- Lauceri, R., Chini Zittelli, G., Maserti, B., & Torzillo, G. (2018). Purification of phycocyanin from Arthrospira platensis by hydrophobic interaction membrane chromatography. *Algal Research*, 35(September), 333–340. <https://doi.org/10.1016/j.algal.2018.09.003>
- Lauritano, C., Andersen, J. H., Hansen, E., Albrightsen, M., Escalera, L., Esposito, F., Helland, K., Hanssen, K., Romano, G., & Ianora, A. (2016). Bioactivity screening of microalgae for antioxidant, anti-inflammatory, anticancer, anti-diabetes, and antibacterial activities. *Frontiers in Marine Science*, 3(MAY), 1–12.
- Lee, J. B., Hayashi, K., Hirata, M., Kuroda, E., Suzuki, E., Kubo, Y., & Hayashi, T. (2006). Antiviral sulfated polysaccharide from Navicula directa, a diatom collected from deep-sea water in Toyama Bay. *Biological and Pharmaceutical Bulletin*, 29(10), 2135–2139.
- Lee, R. E. (2008). *Phycology* (4th ed.). Cambridge University Press.
- Liu, D., Zeng, X. A., Sun, D. W., & Han, Z. (2013). Disruption and protein release by ultrasonication of yeast cells. *Innovative Food Science and Emerging Technologies*, 18, 132–137. <https://doi.org/10.1016/j.ifset.2013.02.006>
- Liu, Q., Huang, Y., Zhang, R., Cai, T., & Cai, Y. (2016). Medical Application of Spirulina platensis Derived C-Phycocyanin. *Evidence-Based Complementary and Alternative Medicine*, 2016.
- Liu, X., Ou, H., Xiang, Z., & Gregersen, H. (2020). Ultrasound pretreatment combined with supercritical CO<sub>2</sub> extraction of Iberis amara seed oil. *Journal of Applied Research on Medicinal and Aromatic Plants*, 18(July), 100265. <https://doi.org/10.1016/j.jarmap.2020.100265>

- Luo, C. J., Stride, E., & Edirisinghe, M. (2012). Mapping the influence of solubility and dielectric constant on electrospinning polycaprolactone solutions. *Macromolecules*, 45(11), 4669–4680.
- Machmudah, S., Shotipruk, A., Goto, M., Sasaki, M., & Hirose, T. (2006). Extraction of astaxanthin from *Haematococcus pluvialis* using supercritical CO<sub>2</sub> and ethanol as entrainer. *Industrial and Engineering Chemistry Research*, 45(10), 3652–3657.
- Marjoni, M. R., & Zulfisa, A. (2017). Antioxidant Activity of Methanol Extract/Fractions of Senggani Leaves (*Melastoma candidum* D. Don). *Pharmaceutica Analytica Acta*, 08(08), 1–6.
- Martelli, G., Folli, C., Visai, L., Daglia, M., & Ferrari, D. (2014). Thermal stability improvement of blue colorant C-Phycocyanin from *Spirulina platensis* for food industry applications. *Process Biochemistry*, 49(1), 154–159.
- Marzorati, S., Schievano, A., Idà, A., & Verotta, L. (2020). Carotenoids, chlorophylls and phycocyanin from Spirulina: supercritical CO<sub>2</sub> and water extraction methods for added value products cascade†. *Green Chemistry*, 22, 187–196.
- McHugh, D. J. (2003). Seaweeds uses as Human Foods. In *A Guide to the Seaweed Industry* (Issue 441).
- Mercer, P., & Armenta, R. E. (2011). Developments in oil extraction from microalgae \*. *European Journal of Lipid Science and Technology*, 113(5), 539–547.
- Metting, F. B. (1996). Biodiversity and application of microalgae. *Journal of Industrial Microbiology and Biotechnology*, 17(5–6), 477–489.
- Michałak, I., Dmytryk, A., Wieczorek, P. P., Rój, E., Bogus, B., Górką, B. B., Messyasz, B., Lipok, J., Mikulewicz, M., Wilk, R. B., Schroeder, G., & Chojnacka, K. (2015). Supercritical Algal Extracts: A Source of Biologically Active Compounds from Nature. *Journal of Chemistry*, 2015(597140), 14.
- Moldoveanu, S. C., & David, V. (2013). Mobile Phases and Their Properties. In *Essentials in Modern HPLC Separations* (pp. 363–447). Elsevier Inc.
- Moraes, C. C., De Medeiros Burkert, J. F., & Kalil, S. J. (2010). C-phycocyanin extraction process for large-scale use. *Journal of Food Biochemistry*, 34(SUPPL. 1), 133–148. <https://doi.org/10.1111/j.1745-4514.2009.00317.x>
- Mosca, F., Hidalgo, G. I., Villasante, J., & Almajano, M. P. (2018). Continuous or Batch Solid-Liquid Extraction of Antioxidant Compounds from Seeds of *Sterculia apetala* Plant and Kinetic Release Study. *Molecules (Basel, Switzerland)*, 23(7).

- Naviglio, D., Scarano, P., Ciaravolo, M., & Gallo, M. (2019). Rapid solid-liquid dynamic extraction (RSLDE): A powerful and greener alternative to the latest solid-liquid extraction techniques. *Foods*, 8(7), 1–21.
- Neves, Fábio de Farias Demarco, M., & Tribuzi, G. (2019). Drying and Quality of Microalgal Powders for Human Alimentation. In M. Vítová (Ed.), *Microalgae - From Physiology to Application* (pp. 1–20). IntechOpen.
- Núñez, G. A., del Valle, J. M., & Navia, D. (2017). Supercritical CO<sub>2</sub> oilseed extraction in multi-vessel plants. 3. Effect of extraction pressure and plant size on production cost. *Journal of Supercritical Fluids*, 122, 109–118.
- Nur, M. M. A., Garcia, G. M., Boelen, P., & Buma, A. G. J. (2019). Enhancement of C-phycocyanin productivity by *Arthrosira platensis* when growing on palm oil mill effluent in a two-stage semi-continuous cultivation mode. *Journal of Applied Phycology*, 31(5), 2855–2867.
- Oshadie, G., Silva, D., Abeysundara, A. T., Minoli, M., & Aponso, W. (2017). Extraction methods, qualitative and quantitative techniques for screening of phytochemicals from plants. *American Journal of Essential Oils and Natural Products*, 5(2), 29–32.
- Öztürk Ürek, R., & Tarhan, L. (2012). The relationship between the antioxidant system and phycocyanin production in *Spirulina maxima* with respect to nitrate concentration. *Turkish Journal of Botany*, 36(4), 369–377.
- Padmaja, M., & Srinivasulu, A. (2016). Influence of pH and temperature on total phenol content of *Ocimum sanctum* leaves. *Indian Journal of Pharmaceutical Science & Research*, 6(2), 69–72. [www.ijpsrjournal.com](http://www.ijpsrjournal.com)
- Park, W. S., Kim, H. J., Li, M., Lim, D. H., Kim, J., Kwak, S. S., Kang, C. M., Ferruzzi, M. G., & Ahn, M. J. (2018). Two classes of pigments, carotenoids and c-phycocyanin, in spirulina powder and their antioxidant activities. *Molecules*, 23(8), 1–11.
- Patel, A., Mikes, F., & Matsakas, L. (2018). An overview of current pretreatment methods used to improve lipid extraction from oleaginous microorganisms. *Molecules*, 23(7).
- Perumal, S., Thirunavukkarasu, A. R., & Pachiappan, P. (2015). Advances in marine and brackishwater aquaculture. In *Advances in Marine and Brackishwater Aquaculture*. Springer India.
- Picchio, V., Cammisotto, V., Pagano, F., Carnevale, R., & Chimenti, I. (2020). We are IntechOpen , the world ' s leading publisher of Open Access books Built by scientists , for scientists TOP 1 %. *Intechopen, Cell Interaction-Regulation of Immune Responses*,

- Disease Development and Management Strategies*, 1–15.
- Poole, C. F. (2003). Supercritical-fluid chromatography. In *The Essence of Chromatography* (1st ed., pp. 570–611). Elsevier Science B.V.
- Prihantini, N. B., Wardhana, W., Hendrayanti, D., Widyan, A., Ariyani, Y., & Rianto, R. (2010). Biodiversitas Cyanobacteria Dari Beberapa Situ/Danau Di Kawasan Jakarta-Depok-Bogor, Indonesia. *MAKARA of Science Series*, 12(1), 44–54.
- Psarrou, I., Oreopoulou, A., & Tsimogiannis, D. (2020). Extraction Kinetics of Phenolic Antioxidants from the Hydro Distillation Residues of Rosemary and Effect of Pretreatment and Extraction Parameters. *Molecules*, 25(4520), 1–23.
- Pulz, O., & Gross, W. (2004). Valuable products from biotechnology of microalgae. *Applied Microbiology and Biotechnology*, 65(6), 635–648.
- Qian, C., Decker, E. A., Xiao, H., & McClements, D. J. (2012). Physical and chemical stability of β-carotene-enriched nanoemulsions: Influence of pH, ionic strength, temperature, and emulsifier type. *Food Chemistry*, 132(3), 1221–1229. <https://doi.org/10.1016/j.foodchem.2011.11.091>
- Rangel-Yagui, C. D. O., Danesi, E. D. G., De Carvalho, J. C. M., & Sato, S. (2004). Chlorophyll production from *Spirulina platensis*: Cultivation with urea addition by fed-batch process. *Bioresource Technology*, 92(2), 133–141.
- Ratti, C. (2001). Hot air and freeze-drying of high-value foods: A review. *Journal of Food Engineering*, 49(4), 311–319.
- Reddy, C. M., Bhat, V. B., Kiranmai, G., Reddy, M. N., Reddanna, P., & Madhyastha, K. M. (2000). Selective inhibition of cyclooxygenase-2 by C-phycocyanin, a biliprotein from *Spirulina platensis*. *Biochemical and Biophysical Research Communications*, 277(3), 599–603.
- Richmond, A. (Ed.). (1986). *Handbook of Microalgal Mass Culture*. CRC Press.
- Rodríguez-Serrano, F., Mut-Salud, N., Álvarez, P. J., Aránega, A., Garrido, J. M., & Carrasco, E. (2015). Antioxidant Intake and Antitumor therapy: toward nutritional recommendations for optimal results. *Oxidative Medicine and Cellular Longevity*, 2016, 1–19.
- Rudra, S. G., Sarkar, B. C., & Shihhare, U. S. (2008). Thermal degradation kinetics of chlorophyll in pureed coriander leaves. *Food and Bioprocess Technology*, 1(1), 91–99.
- Salehi, B., Martorell, M., Arbiser, J. L., Sureda, A., Martins, N., Maurya, P. K., Sharifi-Rad, M., Kumar, P., & Sharifi-Rad, J. (2018). Antioxidants: Positive or Negative Actors?

- Biomolecules*, 8(4), 1–11.
- Sánchez-Camargo, A. del P., Ibáñez, E., Cifuentes, A., & Herrero, M. (2017). Bioactives Obtained From Plants, Seaweeds, Microalgae and Food By-Products Using Pressurized Liquid Extraction and Supercritical Fluid Extraction. *Comprehensive Analytical Chemistry*, 76, 27–51.
- Sanchez-Camargo, A. P., Mendiola, J. A., Ibáñez, E., & Herrero, M. (2013). Supercritical Fluid Extraction. In *Reference Module in Chemistry, Molecular Sciences and Chemical Engineering* (Vol. 1, pp. 196–230). Elsevier Inc.
- Santos, H. M., Lodeiro, C., & Capelo-Martinez, J.-L. (2009). Sonocrystallization of Fats. In J.-L. Capelo-Martinez (Ed.), *Ultrasound in Chemistry: Analytical Applications* (pp. 1–16). Wiley-VCH Verlag GmbH. <https://doi.org/10.1007/978-1-4614-7693-1>
- Sastre, R. R. (2012). Products from microalgae: An overview. In C. Posten & C. Walter (Eds.), *Microalgal Biotechnology: Integration and Economy* (pp. 13–44). Walter de Gruyter GmbH.
- Saúl García-Pérez, J., Cuéllar-Bermúdez, S. P., Arévalo-Gallegos, A., Rodríguez-Rodríguez, J., Iqbal, H. M. N., & Parra-Saldivar, R. (2016). Identification of bioactivity, volatile and fatty acid profile in supercritical fluid extracts of Mexican arnica. *International Journal of Molecular Sciences*, 17(9).
- Schenk, P. M., Thomas-Hall, S. R., Stephens, E., Marx, U. C., Mussgnug, J. H., Posten, C., Kruse, O., & Hankamer, B. (2008). Second Generation Biofuels: High-Efficiency Microalgae for Biodiesel Production. *BioEnergy Research*, 1(1), 20–43.
- Seabra, I. J., Braga, M. E. M., Batista, M. T., & De Sousa, H. C. (2010). Effect of solvent (CO<sub>2</sub>/ethanol/H<sub>2</sub>O) on the fractionated enhanced solvent extraction of anthocyanins from elderberry pomace. *Journal of Supercritical Fluids*, 54(2), 145–152. <https://doi.org/10.1016/j.supflu.2010.05.001>
- Sefrina, L. R., Briawan, D., Sinaga, T., & Permaesih, D. (2017). Estimasi Asupan Karotenoid pada Usia Dewasa di Indonesia. *Jurnal Gizi Dan Pangan*, 12(1), 1–8.
- Seyidoglu, N., Inan, S., & Aydin, C. (2017). A Prominent Superfood: Spirulina platensis. In *Superfood and Functional Food - The Development of Superfoods and Their Roles as Medicine replace* (pp. 1–27). Intech.
- Shirle, R., Ord, E. N. J., & Work, L. M. (2014). Oxidative stress and the use of antioxidants in stroke. *Antioxidants*, 3(3), 472–501.
- Silva, R. P. F. F. da, Rocha-Santos, T. A. P., & Duarte, A. C. (2016). Supercritical fluid

- extraction of bioactive compounds. *TrAC - Trends in Analytical Chemistry*, 76, 40–51.
- Silva, L. V., Nelson, D. L., Drummond, M. F. B., Dufossé, L., & Glória, M. B. A. (2005). Comparison of hydrodistillation methods for the deodorization of turmeric. *Food Research International*, 38(8–9), 1087–1096.
- Simorangkir, M., Nainggolan, B., & Silaban, S. (2019). Antioxidant activity of vacuum column chromatography fractions of ethanol extract of sarang banua (*Clerodendrum fragrans* vent willd) leaves. *Journal of Physics: Conference Series*, 1374(1), 6–11.
- Singh, J. (2008). Maceration, Percolation and Infusion Techniques for the Extraction of Medicinal and Aromatic Plants. In Sukhdev S. Handa, S. P. S. Khanuja, G. Longo, & D. D. Rakesh (Eds.), *Extraction Technologies for Medical and Aromatic Plants* (pp. 71–82). International Centre for Science and High Technology.
- Soletto, D., Binaghi, L., Lodi, A., Carvalho, J. C. M., & Converti, A. (2005). Batch and fed-batch cultivations of *Spirulina platensis* using ammonium sulphate and urea as nitrogen sources. *Aquaculture*, 243(1–4), 217–224.
- Sosa-Hernández, J. E., Escobedo-Avellaneda, Z., Iqbal, H. M. N., & Welti-Chanes, J. (2018). State-of-the-art extraction methodologies for bioactive compounds from algal biome to meet bio-economy challenges and opportunities. *Molecules*, 23(11).
- Spolaore, P., Joannis-Cassan, C., Duran, E., & Isambert, A. (2006). Commercial applications of microalgae. *Journal of Bioscience and Bioengineering*, 101(2), 87–96. <https://doi.org/10.1263/jbb.101.87>
- Srivastava, J. K., & Gupta, S. (2009). Extraction, characterization, stability and biological activity of flavonoids isolated from chamomile flowers. *Molecular and Cellular Pharmacology*, 1(3), 138–147.
- Stanier, R. Y., Sistrom, W. R., & Hansen, T. A. (1978). Proposal to place the nomenclature of the cyanbacteria (blue-green algae) under the rules of the international code of nomenclature of bacteria. *International Journal of Systematic Bacteriology*, 28(2), 335–336.
- Synder, L. R. (1974). Classification of The Solvent Properties of Common Liquids. *Journal of Chromatography*, 92(2), 223–230.
- Valderrama, J. O., Perrut, M., & Majewski, W. (2003). Extraction of Astaxantine and phycocyanine from microalgae with supercritical carbon dioxide. *Journal of Chemical and Engineering Data*, 48(4), 827–830.
- Vankar, P. S. (2004). Essential oils and fragrances from natural sources. *Resonance*, 9(4),

- 30–41.
- Vazquez-Roig, P., & Picó, Y. (2015). Pressurized liquid extraction of organic contaminants in environmental and food samples. *TrAC - Trends in Analytical Chemistry*, 71, 55–64.
- Ventura, S. P. M., Nobre, B. P., Ertekin, F., Hayes, M., Garcíá-Vaquero, M., Vieira, F., Koc, M., Gouveia, L., Aires-Barros, M. R., & Palavra, A. M. F. (2017). Extraction of value-added compounds from microalgae. In C. Gonzalez-Fernandez & R. Muñoz (Eds.), *Microalgae-Based Biofuels and Bioproducts: From Feedstock Cultivation to End-Products* (Issue December, pp. 461–483). Woodhead Publishing.
- Vonshak, A. (1997). Spirulina: Growth, Physiology and Biochemistry. In A. Vonshak (Ed.), *Spirulina Platensis (Arthrospira)* (pp. 43–65). Taylor & Francis Ltd.
- Vorobiev, E., & Lebovka, N. (Eds.). (2009). Pulsed-Electric-Fields-Induced Effects in Plant Tissues: Fundamental Aspects and Perspectives of Applications. In *Electrotechnologies for Extraction from Food Plants and Biomaterials* (pp. 39–81). Springer.
- Wan, D., Wu, Q., & Kuča, K. (2016). Spirulina. *Nutraceuticals: Efficacy, Safety and Toxicity*, 569–583.
- Wang, D., Li, Y., Hu, X., Su, W., & Zhong, M. (2015). Combined enzymatic and mechanical cell disruption and lipid extraction of green alga *Neochloris oleoabundans*. *International Journal of Molecular Sciences*, 16(4), 7707–7722.
- Wang, L., & Weller, C. L. (2006). Recent advances in extraction of nutraceuticals from plants. *Trends in Food Science and Technology*, 17(6), 300–312.
- Watson, A. S., Mortensen, M., & Simon, A. K. (2011). Autophagy in the pathogenesis of myelodysplastic syndrome and acute myeloid leukemia. *Cell Cycle*, 10(11), 1719–1725.
- Wen, D., & Olesik, S. V. (2000). Characterization of pH in liquid mixtures of methanol/H<sub>2</sub>O/CO<sub>2</sub>. *Analytical Chemistry*, 72(3), 475–480.
- Wiltshire, K. H., Boersma, M., Möller, A., & Buhtz, H. (2000). Extraction of pigments and fatty acids from the green alga *Scenedesmus obliquus* (Chlorophyceae). *Aquatic Ecology*, 34(2), 119–126.
- Wu, H. L., Wang, G. H., Xiang, W. Z., Li, T., & He, H. (2016). Stability and Antioxidant Activity of Food-Grade Phycocyanin Isolated from *Spirulina platensis*. *International Journal of Food Properties*, 19(10), 2349–2362.
- Wu, Q., Liu, L., Miron, A., Klímová, B., Wan, D., & Kuča, K. (2016). The antioxidant,

- immunomodulatory, and anti-inflammatory activities of Spirulina: an overview. *Archives of Toxicology*, 90(8), 1817–1840.
- Xia, S., Gao, B., Li, A., Xiong, J., Ao, Z., & Zhang, C. (2014). Preliminary characterization, antioxidant properties and production of chrysolaminarin from marine diatom *Odontella aurita*. *Marine Drugs*, 12(9), 4883–4897.
- Yamaguchi, K. (1996). Recent advances in microalgal bioscience in Japan, with special reference to utilization of biomass and metabolites: A review. *Journal of Applied Phycology*, 8(6), 487–502.
- Zhang, Q. W., Lin, L. G., & Ye, W. C. (2018). Techniques for extraction and isolation of natural products: A comprehensive review. *Chinese Medicine (United Kingdom)*, 13(1), 1–26.