

## **BAB 5**

### **KESIMPULAN DAN SARAN**

#### **5.1. Kesimpulan**

1. Penambahan gugus 4-kloro pada senyawa 4,4'-diklorodibenzalaseton menurunkan reaktivitas senyawa karena mempengaruhi kemudahan polarisasi gugus karbonil dari benzaldehid pada tahap adisi sehingga dibutuhkan waktu yang lebih lama untuk sintesis dengan metode dan daya yang sama daripada dibenzalaseton.
2. Aktivitas antimalaria dari senyawa 4,4'-diklorodibenzalaseton yang diuji dengan metode mikroskopis pewarnaan Giemsa 20% memberikan nilai  $IC_{50}$   $65,66\mu\text{g}/\text{ml}$  dan dikategorikan sebagai antimalaria aktif lemah.
3. Penambahan substituen 4-kloro pada 4,4'-diklorodibenzalaseton tidak memberikan nilai  $IC_{50}$  yang lebih baik dibandingkan Dibenzalaseton yang memiliki  $IC_{50}$  lebih rendah yaitu  $2,374\mu\text{g}/\text{ml}$ .
4. Senyawa 4,4'-diklorodibenzalaseton tidak memiliki efektivitas antimalaria yang lebih baik dibandingkan Klorokuin yang ditinjau dari nilai  $IC_{50}$  kedua senyawa tersebut.

#### **5.2. Saran**

1. Dilakukan uji lanjutan seperti uji *docking* dan uji aktivitas penghambatan polimerasi heme dari dibenzalaseton untuk mengetahui mekanisme kerjanya sebagai antimalaria.
2. Dilakukan sintesis dari analog kurkumin lain yang memiliki potensi sebagai obat antimalaria maupun alternatif dari klorokuin.

## DAFTAR PUSTAKA

- Ameta, C., Dashora, P., & Vyas, R., 2015, *Microwave-Assisted Organic Synthesis : A Green Chemical Approach*, Apple Academic Press, Toronto
- Andromeda, Ekawardhani, S., & Berbudi, A., 2020, The Role of Curcumin as An Antimalarial Agent, *Sys Rev Pharm*, **11(7)**:18-25
- Astuti, E., Raharjo, T. J., Manalu, P. B., Putra, I. S., Waskitha, S. S., & Solin, J., 2021, Synthesis, Molecular Docking, and Evaluation of Some New Curcumin Analogs as Antimalarial Agents, *Indones. J. Chem.*, **21(2)**:452-461
- Basco, L. K., 2007, *Field Application of In Vitro Assay for the Sensitivity of Human Malaria Parasites to Antimalarial Drugs*, World Health Organization, Geneva
- Bekbölet, M., & Getoff, N., 2002, Degradation of Chlorinated Benzaldehydes in Aqueous Solution by UV-Irradiation, *International Journal of Photoenergy*, **4(4)**:133-139
- Budiat, T., Soewandi, A., & Soegianto, L., 2019, Microwave-assisted Synthesis of Dibenzalacetone Derivatives and Study of their Potential Antioxidant Activities, *Journal of Chemistry and Pharmaceutical Research*, **11(9)**:11-16
- Bukhari, S. N. A., Jantan, I. B., Jasamai, M., Ahmad, W., & Amjad, M. W. B., 2013, Synthesis and Biological Evaluation of Curcumin Analogues, *Journal of Medical Sciences*, **13(7)**:501-513
- Carey, F. A., 2000, *Organic Chemistry*, 4<sup>th</sup> Edition, McGraw-Hill, USA
- Centers for Disease Control and Prevention (CDC), 2020, *Laboratory Identification of Parasites of Public Health Concern : Malaria*
- Chauhan, I. S., Rao, G. S., Shankar, J., Chauhan, L. K. S., Kapadia, G. J., & Singh, N., 2018, Chemoprevention of Leishmaniasis; *In-vitro* Antiparasitic Activity of Dibenzalacetone, a Synthetic Curcumin Analog Leads to Apoptotic Cell Death in *Leishmania donovani*, *Parasitology International*, **67**:627-636
- Coatney, G. R., Collins, W. E., Warren M., & Contacos, P. G., 2003, *The Primates Malaria*, CDC, Atlanta

- Dwiarso, R., 2017, *Metode Kromatografi Prinsip Dasar, Praktikum dan Pendekatan Pembelajaran Kromatografi*, Deepublish Publisher, Jogjakarta
- Fessenden, R. J., & Fessenden, J. S., 1986, *Kimia Organik Jilid II*, Edisi Ketiga, Erlangga, Jakarta
- Franco, L. L., Almeida, M. V., Silva, L. F. R., Vieira, P. P. R., Pohlit, A. M., & Valle, M. S., 2012, Synthesis and Antimalarial Activity of Dihydroperoxides and Tetraoxanes Conjugated with Bis(benzyl)acetone Derivatives, *Chem Biol Drug Des*, 79:790-797
- Fuhrhop, J. H., & Li, G., 2003, *Organic Synthesis Concepts and Methods*, 3<sup>rd</sup> Edition, Wiley-VCH, Germany
- Geary, T. G., Bonanni, L. C., Jensen, B., & Ginsburg, H., 1986, Effects of Combinations of Quinoline-Containing Antimalarials on *Plasmodium falciparum* in culture, *Ann. Trop. Med. Parasitol.*, **80(3)**:285-291
- Ginting, N., Haro, G., Lasma, M., & Wahyuni, H. S., 2019, *Penuntun Praktikum Kimia Organik*, Universitas Sumatera Utara, Medan
- Gupta, A. P., Khan, S., Manzoor, M. M., Yadav, A., Sharma, G., Anand, R., & Gupta, S. C., 2017, Anticancer Curcumin : Natural Analogues and Structure-Activity Relationship, *Studies in Natural Products Chemistry*, 52:355-401
- Handayani, S., Matsjeh, S., Anwar, C., Atun, S., & Fatimah, I., 2012, Sintesis Analog Benzalaseton Menggunakan Katalis NaOH/ZrO<sub>2</sub>-Montmorilonit dan Uji Aktivitasnya sebagai Antioksidan, *International Journal of Chemical and Analytical Science*, **3(6)**:1419-1424
- Harijanto, P. N., 2000, *Malaria : Epidemiologi, Patogenesis, Manifestasi Klinis, dan Penanganan*, EGC, Jakarta
- Haynes, W. M., Lide, D. R., & Bruno, T. J., 2017, *CRC Handbook of Chemistry and Physics*, 97<sup>th</sup> Edition, CRC Press, Boca Raton
- Hidayati, A. R., Widyawaruyanti, A., Hilkatul, I., Tanjung, M., Widiandani, T., Siswadono, Syarfruddin, D., & Hafid, A. F., 2020, Antimalarial Activity of Flavonoid Compound Isolated from Leaves of *Artocarpus altilis*, *Pharmacognosy Journal*, **12(4)**:835-84
- Kappe, C. O., & Stadler, A., 2005, *Microwave in Organic and Medicinal Chemistry*, Wiley-VCH. Weinheim

Kurnianingtyas, M. P., 2019, Pengaruh Gugus Kloro pada 4-klorobenzaldehida terhadap Sintesis 4,4'-diklorodibenzalaseton dengan Bantuan Iradiasi Gelombang Mikro, *Skripsi*, Sarjana Farmasi, Universitas Katolik Widya Mandala, Surabaya

Lewis, R. J., 1996, *Sax's Dangerous Properties of Industrial Materials*, 9<sup>th</sup> Edition Vol. 1-3, Van Nostrand Reinhold, New York

Lewis, R. J., 2007, *Hawley's Condensed Chemical Dictionary*, 15<sup>th</sup> Edition, John Wiley & Sons, New York

Maji, A. K., 2018, Drug Susceptibility Testing Methods of Antimalarial Agents, *Tropical Parasitology*, **8(2)**:70-76

McMurry, J., 2012, *Organic Chemistry*, 8<sup>th</sup> Edition, Cengage Learning, USA

Mirnasari, D. L., 2020, Perbandingan Sintesis Metode Konvensional dan Iradiasi Gelombang Mikro pada Pembuatan Senyawa 2,2'-Dihidroksidibenzalaseton, *Skripsi*, Universitas Katolik Widya Mandala, Surabaya

Mishra, S., Karmodiya, K., Surolia, N., & Surolia, A., 2008, Synthesis and exploration of novel curcumin analogues as anti-malarial agents, *Bioorganic & Medical Chemistry*, **16**:2894-2902

Mohamed, I. E., Khalid, H. E., Mohammed, S. A., Osman, E. E., Koko, W. S., Taha, K. K., Dahab, M. M., & Ismail, N. R., 2014, Anti-malarial Activity of Some Medicinal Sundanese Plants, *Journal of Forest Products & Industries*, **3(6)**:236-240

Morrison, R. T., & Boyd, R. N., 2002, *Organic Chemistry*, 6<sup>th</sup> Edition, Asoke K. Ghosh, New Delhi

Murray, L., Stewart, Lk. Tarr, S. J., Ahoudi, A. D., Diakite, M., Amambua-Ngwa, A., & Conway, D. J., 2017, Multiplication Rate Variation in the Human Malaria Parasite *Plasmodium falciparum*, *Scientific Reports*, **7(6346)**:1-8

National Toxicology Program (NTP), 1992, *National Toxicology Program Chemical Repository Database*, Research Triangle Park, North Carolina

O'Neil, M. J., 2013, *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals*, 15<sup>th</sup> Edition, Cambridge, United Kingdom

- Oxtoby, D. W., 2001, Gillis, H. P., & Nachtrieb, N. H., 2001, *Prinsip-Prinsip Kimia Modern*, Edisi Keempat, Erlangga, Jakarta
- Pavia, D. L., Lampman, G. M., Kriz, G. S., & Vyvyan, J. R., 2009, *Introducing to Spectroscopy*, 4<sup>th</sup> Edition, Cengage Learning, USA
- Anand, P., Thomas, S. G., Kunnumakkara, A. B., Sundaram, C., Harikumar, K. B., Sung, B., Tharakan, S. T., Misra, K., Priyadarsini, I. K., Rajasekharan, K. N., & Aggarwal, B. B., 2008, Biological Activities of Curcumin and Its Analogues (Congeners) Made by Man and Mother Nature, *Biochemical Pharmacology*, **76**(11):1590-1611
- Rafi, M., Heryanto, R., Septiningsih, D. A., 2017, *Atlas Kromatografi Lapis Tipis Tumbuhan Obat Indonesia*, IPB Press, Bogor
- Reyburn, H., 2010, New WHO Guidelines for the Treatment of Malaria, *BMJ*, 340:161-162
- Riddick, J. A., W. B., Bunger, & Sakano, T. K., 1985, *Techniques of Chemistry*, 4<sup>th</sup> Edition Vol. II., John Wiley & Sons, New York
- Rieckmann, K. H., Campbell, G. H., Sax, L. J., & Mrema, J. E., 1978, Drug Sensitivity of Plasmodium Falciparum. An *In Vitro* Microtechnique, *Lancet*, **7**(8054):22-23
- Saifi, M. A., Beg, T., Harrath, A. H., Altayalan, F. S. H., & Quraishy, S. A., 2013, Antimalarial Drugs: Mode of Action and Status of Resistance, *African Journal of Pharmacy and Pharmacology*, **7**(5):148-156
- Sastrohamidjojo, H., 2018, *Dasar-Dasar Spektroskopi*, Gadjah Mada University Press, Jogjakarta
- Shibeshi, M. A., Kifle, Z. D., & Atnafie, S. A., 2020, Antimalarial Drug Resistance and Novel Targets for Antimalarial Drug Discovery, *Infection and Drug Resistance*, 13:4047-4060
- Sidhu, A. B. S., Verdier-Pinard, D., & Fidock, D. A., 2002, Chloroquine Resistance in *Plasmodium falciparum* Malaria Parasites Conferred by *pfcrt* Mutations, *Science*, **298**(5591):210-213
- Silverstein, R. M., Webster, F. X., & Kiemle, J. D., 2005., *Spectrometric Identification of Organic Compounds*, 7<sup>th</sup> Edition, John Wiley & Sons, New York
- Siswandono, 2016, *Kimia Medisinal*, Edisi 2, Airlangga Universitas Press, Surabaya.

- Suresh, N., & Haldar, K., 2018, Mechanisms of artemisinin resistance in *Plasmodium falciparum* malaria. *Current Opinion in Pharmacology*, 42:46-54
- Whalen, K., Carinda, F., & Radhakrishnan, R., 2019, *Lippincott Illustrated Reviews: Pharmacology*, Seventh Edition, Wolters Kluwer, Philadelphia
- WHO, 2016, *Malaria Microscopy : Quality Assurance Manual*, World Health Organization, Geneva
- Williamson, K. L., & Masters, K. M. 2016, *Macroscale and Microscale Organic Experiments*, 7<sup>th</sup> Edition, Cengage Learning, USA
- Wockner, L. F., Hoffman, I., Webb, L., Mordmüller, B., Murphy, S. C., Kublin, J. G., O'Rourke, P., McCarthy, J. S., & Marquart, L., 2020, Growth Rate of *Plasmodium falciparum*: Analysis of Parasite Growth Data From Malaria Volunteer Infections Studies, *The Journal of Infectious Diseases*, 221:963-972
- World Health Organization, 2015, *Malaria*