

BAB 5

KESIMPULAN DAN SARAN

5.1 Kesimpulan

Berdasarkan hasil penelitian yang telah dilakukan maka dapat diambil kesimpulan sebagai berikut.

1. Ekstrak air rimpang kunyit (*Curcuma domestica* Val.) memiliki potensi menginhibisi enzim HMG-KoA reduktase dengan $IC_{50} 45,77 \pm 1,57 \mu\text{g/mL}$.
2. Aktivitas hambat ekstrak air rimpang kunyit 30.000 kali lebih kecil dibandingkan simvastatin.
3. Jumlah kurkumin dan jumlah fenol memiliki korelasi yang linier dengan aktivitas hambat ekstrak air rimpang kunyit terhadap enzim HMG-KoA reduktase.

5.2 Saran

Berdasarkan hasil penelitian yang telah dilakukan, maka disarankan untuk dilakukan penelitian lebih lanjut mengenai kinetika inhibisi ekstrak air rimpang kunyit (kompetitif, unkompesitif, non kompetitif) dalam menghambat enzim HMG-KoA reduktase.

DAFTAR PUSTAKA

- Abascal, K., Ganora, L. and Yarnell, E. 2004, The Effect of Freeze-drying and its Implications for Botanical Medicine: A Review, *Phytotherapy Research*, **19**: 655–660.
- Abbasi, M. A., Ilyas, M., Aziz-Ur-Rehman, Sonia, A., Shahwar, D., Raza, M. A., Khan, K. M., Ashraf, M., Afzal, I., and Ambreen, N. 2012, Curcumin and its derivatives: Moderate inhibitors of acetylcholinesterase, butyrylcholinesterase and trypsin, *Scientia Iranica C*, **19(6)**: 1580–1583.
- Abdel-Lateef, E., Mahmoud, F., Hammam, O., El-Ahwany, E., El-Wakil, E., Kandil, S., Abu Taleb, H., El-Sayed, M., Hassenein, H. 2016, Bioactive chemical constituents of *Curcuma longa* L. rhizomes extract inhibit the growth of human hepatoma cell line (HepG2), *Acta Pharmaceutica*, **66(3)**: 387–398.
- Ademosun, A. O., Oboh, G., Passamonti, S., Tramer, F., Ziberna, L., Boligon, A. A., and Athayde, M. L. 2015, Phenolics from Grapefruit Peels Inhibit HMG-CoA Reductase and Angiotensin-I Converting Enzyme and Show Antioxidative Properties in Endothelial EA.Hy 926 cells, *Food Science and Human Wellness*, **4(2015)**: 80–85.
- Asif, M. and Khodadadi, E. 2013, Medicinal Uses and Chemistry of Flavonoid Contents of Some Common Edible Tropical Plants, *Journal of Paramedical Sciences*, **4(3)**: 119–138.
- Badan Pengawas Obat dan Makanan RI, 2008, *Taksonomi Koleksi Tanaman Obat Kebun Tanaman Obat Citeureup*, Jakarta: Direktorat Obat Asli Indonesia.
- Badan Pengawas Obat dan Makanan RI, 2011, *Acuan Sediaan Herbal*, Ed. 1, Jakarta: Badan Pengawas Obat dan Makanan RI.
- Botham, K. M. and Mayes, P. A. 2006, Cholesterol Synthesis, Transport, & Excretion. In: *Harper's illustrated Biochemistry*. 27th Ed., LANGE Mc Graw Hill, USA.

- Botham, K. M. and Mayes, P. A. 2009, Cholesterol Synthesis, Transport, & Excretion. In: *Harper's illustrated Biochemistry*. 28th Ed., LANGE Mc Graw Hill, USA.
- Catapano, A. 2012, Pravastatin: A Different Pharmacological Profile, *Clinical Lipidology*, **7(sup 1)**: 3-9.
- Champe, P., Harvey, R. and Ferrier, D. 2010, *Lippincott's Illustrated Reviews: Biochemistry*, Wolters Kluwer, London, pp. 57-62.
- Chattopadhyay, I. , Biswas, K., Bandyopadhyay, U. and Banerjee, R. K. 2015, Turmeric and Curcumin: Biological actions and medicinal applications, *Current Science*, **87(1)**: 44-53.
- Copeland, R. A., Harpel, M. R. and Tummino, P. J. 2007, Targeting enzyme inhibitors in drug discovery, *Expert Opinion Therapy Targets*, **11(7)**: 967–978.
- Day, R. A. and Underwood, A. L. 2002, *Analisis Kimia Kuantitatif*, Ed. 6, Penerbit Erlangga, Jakarta.
- Depkes RI, 1979, *Materia Medika Indonesia Jilid III*, Jakarta: Direktorat Jenderal Pengawasan Obat dan Makanan.
- Depkes RI, 2007, *Kebijakan Obat Tradisional Nasional*, Jakarta: Departemen Kesehatan Republik Indonesia.
- Depkes RI, 2008, *Farmakope Herbal Indonesia*, Ed. 1, Jakarta: Kementerian Kesehatan RI.
- Dirjen POM, 2000, *Parameter Standar Umum Ekstrak Tumbuhan Obat*, Jakarta: Departemen Kesehatan RI.
- Duraisankar, M. and Ravindran, A. D. 2015, Identification of Curcuma longa Rhizomes by Physicochemical and TLC Fingerprint Analysis, *International Journal of PharmTech Research*, **8(6)**:198–205.
- Farnsworth, N. R. 1966, Biologycal and Phytochemical Screening of Plants, *Journal of Pharmaceutical Science*, **55(3)**:225-276.
- Fitrilia, T., Bintang, M. and Safithri, M. 2015, Phytochemical screening and

antioxidant activity of clove mistletoe leaf extracts (*Dendrophthoe pentandra* (L.) Miq), *IOSR Journal of Pharmacy*, **5(8)**: 13–18.

Flowers, P., Theopold, K., and Langley, R. 2017. Diakses pada tanggal 19 Juni 2018,
https://chem.libretexts.org/LibreTexts/Valley_City_State_University/Chem_122/Chapter_4%3A_Chemical_Kinetics/4.6%3A_Catalysis.

Fried, B. and Sherma, J. 1999, *Thin-Layer Chromatography*, 4th ed., Marcel Dekker, Inc, Basel.

Golomb, B. A. and Evans, M. A. 2008, Statin adverse effects : a review of the literature and evidence for a mitochondrial mechanism, *American journal of cardiovascular drugs: drugs, devices, and other interventions*, **8(6)**: 373–418.

Gunawan, D., dan Mulyani, S. 2004, *Ilmu Obat Alam*, Penebar Swadaya, Bogor.

Guyton, A. C. and Hall, J. E. 2006, *Textbook of Medical Physiology*, 11th ed., Elsevier Inc, Philadelphia.

Hafidz, K.A., Puspitasari, N., Azminah, Yanuar, A., Artha, Y. and Mun'im, A. 2017, HMG-CoA Reductase inhibitory activity of *Gnetum gnemon* seed extract and identification of potential inhibitors for lowering cholesterol level, *J Young Pharm*, **9(4)**: 559-565.

Harborne, J. B. 1998, *Phytochemical Methods: A Guide to Modern Techniques of Plant Analysis*, 3rd ed., Chapman & Hall, UK.

Hendayana, S. 1994, *Kimia Analitik Instrumen*, Ed. 1, IKIP Semarang Press, Semarang.

Hewlings, S. and Kalman, D. 2017, Curcumin: A Review of Its' Effects on Human Health, *Foods*, **6(10)**: 92.

Islam, B., Sharma, C., Adem, A., Aburawi, E. and Ojha, S. 2015, Insight into the mechanism of polyphenols on the activity of HMGR by molecular docking, *Drug Design, Development and Therapy*, **(9)**: 4943–4951.

- Isnawati, A. dan Adelina, R. 2015, Studi Docking Molekuler Catechin Gallate, Epicatechin Gallate, Gallocatechin Gallate, dan Epigallocatechin Gallate sebagai Obat Dislipidemia, *Jurnal Kefarmasian Indonesia*, **5(1)**: 25–32.
- Istvan, E. S., Palnitkar, M., Buchanan, S. K., and Deisenhofer, J. 2000, Crystal structure of the catalytic portion of human HMG-CoA reductase: insights into regulation of activity and catalysis, *The EMBO journal*, **19(5)**: 819–30.
- Istvan, E. and Deisenhofer, J. 2001, Structural mechanism for statin inhibition of HMG-CoA Reductase, *Science*, **292**: 5519.
- Jellinger, P. S., Handelsman, Y., Rosenblit, P. D., Bloomgarden, Z. T., Fonseca, V. A., Garber, A. J., Grunberger, G., Guerin, C. K., Bell, D. S. H., Mechanick, J. I., Pessah-Pollack, R., Wyne, K., Smith, D., Brinton, E. A., Fazio, S., and Davidson, M. 2017, American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease, *Endocrine Practice*, **23(Supplement 2)**: 1–87.
- Jung, M. A., Lee, S.Y., Han, S.H., Hong, J., Na, J.R., Lee, J.Y., Kim, Y. and Kim, S. 2015, Hypocholesterolemic effects of *Curcuma longa* L. with *Nelumbo nucifera* leaf in an in vitro model and a high cholesterol diet-induced hypercholesterolemic mouse model, *Animal Cells and Systems*, **19(2)**: 133–143.
- Kementerian Kesehatan RI, 2011, *Suplemen II Farmakope Herbal Indonesia*. Ed.1, Jakarta: Kementerian Kesehatan RI.
- Kementerian Kesehatan RI, 2013, Riset Kesehatan Dasar 2013, *Laporan Nasional 2013*, pp. 259–261.
- Kementerian Kesehatan RI, 2014, *Farmakope Indonesia*, Ed. 5, Jakarta: Kementerian Kesehatan RI.
- Khopkar, S. M. 1990, *Konsep Dasar Kimia Analitik*, Universitas Indonesia, Jakarta.

- Kiamahalleh, M. V., Najafpour-Darzi, G., Rahimnejad, M., Moghadamnia, A. A., Kiamahalleh, M. V. 2016, High performance curcumin subcritical water extraction from turmeric (*Curcuma longa* L.), *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences*, **1022**: 191–198.
- Kurien, B. T., Singh, A., Matsumoto, H., and Scofield, R. H. 2007, Solubility, chemical and photochemical stability of curcumin in surfactant solutions, *ASSAY and Drug Development Technology*, **5(4)**: 567–576.
- Lako, J., Trencerry, V.C., Wahlgqvist, M., Wattanapenpaiboon, N., Sotheeswaran, S. and Premier, R. 2007, Phytochemical flavonols, carotenoids and the antioxidant properties of a wide selection of Fijian fruit, vegetables and other readily available foods, *Food Chemistry*, **101(4)**: 1727–1741.
- Li, X., Liu, C., Duan, Z., Guo, S. 2013, HMG-CoA Reductase Inhibitors from *Monascus*-Fermented Rices, *Journal of Chemistry*.
- Lin, S. H., Huang, K.J., Weng, C.F. and Shiuan, D. 2015, Exploration of natural product ingredients as inhibitors of human HMG-CoA reductase through structure-based virtual screening, *Drug Design, Development and Therapy*, **(9)**: 3313–3324.
- Lipid Research Clinics Program, 1984, The Lipid Research Clinics Coronary Primary Prevention Trial results I. Reduction in Incidence of Coronary Heart Disease, *The Journal of the American Medical Association*, **251(3)**: 351–364.
- Malloy, M. J. and Kane, J. P. 2012, Agents Used in Dyslipidemia, in Katzung, B.G., Masters, S., Trevor, A.J., *Basic and clinical Pharmacology*. 12th ed., McGrawhill Companies, Inc, New York, pp 619–633.
- Markham, K. R. 1988, *Cara Mengidentifikasi Flavonoid*, Diterjemahkan dari Bahasa Inggris oleh Kosasih Padmawinata, ITB, Bandung.
- McKenney, J. 2003, Pharmacologic Characteristics of Statins, *Clinical Cardiology*, **26(Sup III)**: III-32-III-38.

- Minarno, E. B. 2015, Skrining Fitokimia dan Kandungan Total Flavonoid pada Buah *Carica pubescens* Lenne & K. Koch di Kawasan Bromo, Cangar, dan Dataran Tinggi Dieng, *El-Hayah*, **5(2)**:73-82.
- Mohammadi, A., Sahebkar, A., Iranshahi, M., Amini, M., Khojasteh, R., Mobarhan, M. G., Ferns, G. A. 2012, Effects of Supplementation with Curcuminoids on Dyslipidemia in Obese Patients: A Randomized Crossover Trial, *Phytotherapy Research*, **27(3)**:374-9.
- Moon, Y. S., Han, J. H., Lee, T. B., Kwon, J. W., Choi, C. H. 2014, Lipid-modulating Effects of Aqueous Extract of *Rubus occidentalis* in Hepatocarcinoma HepG2 Cells, *American Journal of Bioscience*, **2(2)**: 64-69.
- Murray, R. K., Granner, D. K., and Rodwell, V.W. 2006, *Harper's Illustrated Biochemistry*, 27th Edition, Mc Graw Hill, New York.
- National Cholesterol Education Program, 2001, 'Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report', National Institute of Health, diakses pada tanggal 13 November 2018, <https://www.nhlbi.nih.gov/files/docs/resources/heart/atp-3-cholesterol-full-report.pdf>.
- Nisar, T., Iqbal, M., Raza, A., Safdar, M., Iftikhar, F. and Waheed, M. 2015, Turmeric: A Promising Spice for Phytochemical and Antimicrobial Activities, *American-Eurasian J. Agricultural & Environment Science*, **15(7)**: 1278–1288.
- Oghenejobo, M., Opajobi, OA., Bethel, O., and Uzoegbu, U. 2017, Antibacterial Evaluation, Phytochemical Screening and Ascorbic Acid Assay of Turmeric (*Curcuma longa*), *MOJ Bioequivalence & Bioavailability*, **4(2)**: 232-239.
- Pothitirat, W. and Gritsanapan, W. 2005, Quantitative Analysis of Curcumin, Demethoxycurcumin and Bisdemethoxycurcumin in the Crude Curcuminoid Extract from *Curcuma longa* in Thailand by TLC- Densitometry, *Mahidol University Journal of Pharmaceutical Sciences*, **32**: 23–30.

- Priyadarsini, K. I. 2014, The Chemistry of Curcumin: From Extraction to Therapeutic Agent, *Molecules*, **19**: 20091–20112.
- Puttananjaiah, M.-K. H., Dhale, M. A., Gaonkar, V., Keni, S. 2011, Statins: 3-Hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase inhibitors demonstrate anti-atherosclerotic character due to their antioxidant capacity, *Biochem. Biotechnol.*, **163(2)**: 215–222.
- Rahmania, S., Sulistiyan, dan Lelono, A. A. 2017, Identification of HMG-CoA Reductase Inhibitor Active Compound in Medicinal Forest Plants, *Jurnal Kefarmasian Indonesia*, **7(2)**: 95-104.
- Reddy, V., Ahmed, F., and Urooj, A. 2012, Inhibition of 3-hydroxy-3-methylglutaryl Coenzyme A (HMG Co-A) Reductase in Liver Microsomes by *Moringa Oleifera* L. Polyphenols, *International Journal of Pharmaceutical Sciences and Research*, **3(07)**: 2510–2516.
- Ressaissi, A., Attia, N., Fale, P.L., Pacheco, R., Victor, B.L, Machuqueiro, M. and Serralheiro, M.L.M. 2017, Isoflavonoid derivates and piscicidic acid for hypercholesterolemia: cholesterol permeability, HMG-CoA Reductase inhibition and docking studies, *Archives of Pharmacal Research*, **40**: 1278-1286.
- Rohman, A. 2009, *Kromatografi untuk Analisis Obat*, Graha Ilmu, Yogyakarta.
- Sadek, P. C. 2002, *The HPLC Solvent Guide*, 2nd edition, Wiley-Interscience, New York.
- Sahabkar, A. 2014, Curcuminoids for the management of hypertriglyceridaemia, *Nature Reviews Cardiology*, **11(2)**: 1–2.
- Sahu, R. and Saxena, J. 2013, Screening of Total Phenolic and Flavonoid Content in Conventional and Non-Conventional Species of Curcuma, *Journal of Pharmacognosy and Phytochemistry*, **21(2)**: 24–26.
- Sando K. 2015, Drugs for Hyperlipidemia, in Whalen, K., Finekl, R., Panavelil, T.A., *Lippincott Illustrated Reviews: Pharmacology*, 6th ed., Wolters Kluwer, Philadelphia, pp 311-323.

- Sawant, S. and Godghate, A. G. 2013, Qualitative phytochemical screening of rhizomes of *Curcuma longa* linn, *International Journal of Science, Environment, 2(4)*: 634 – 641.
- Schachter, M. 2005, Chemical, pharmacokinetic and pharmacodynamic properties of statins: An update, *Fundamental and Clinical Pharmacology, 19(1)*: 117–125.
- Seidel, V. 2008, Initial and Bulk Extraction, In: Sarker, S. D., Latif, Z. and Gray, A. I., editors, *Natural Products Isolation* 2nd edition, Humana Press, New Jersey, USA.
- Setyowati, W.A.E., Ariani, S.R.D., Ashadi, Mulyani, B., Rahmawati, C.P. 2014, Skrining Fitokimia dan Identifikasi Komponen Utama Ekstrak Metanol Kulit Durian (*Durio zibethinus* Murr,) Varietas Petruk, *Seminar Nasional dan Pendidikan Kimia VI*, 271-280.
- Sigma-Aldrich, 2015, HMG-CoA Reductase Assay Kit, pp. 1–3, <https://www.sigmaldrich.com/catalog/product/sigma/cs1090?lang=en®ion=ID>.
- Sigma-Aldrich. 2017, HMG-CoA Reductase, <http://www.sigmaldrich.com/technicaldocuments/articles/biofiles/hmg-coa-reductase.html>
- Spangenberg, B., Poole, C. F., and Weins, Ch. 2010, *Quantitative Thin-Layer Chromatography: A Practical Survey*, Springer-Verlag Berlin Heidelberg New York, Springer Science + Business Media, Germany.
- Sogi, D. S., Sharma, S., Oberoi, D. P. S., and Wani, I. A. 2009, Effect of extraction parameters on curcumin yield from turmeric, *Journal of Food Science and Technology, 47(3)*: 300–304.
- Stahl, E. 1985, *Analisis Obat Secara Kromatografi dan Mikroskopi*. Diterjemahkan dari Bahasa Inggris oleh Padmawinata, K. dan Soediro I., ITB, Bandung.
- Stapleton, P. A., Goodwill, A. G., James, M. E., Brock, R. W., and Frisbee, J. C. 2010, Hypercholesterolemia and microvascular dysfunction: Interventional strategies, *Journal of Inflammation, 7:54*

- Tacouri, D. D., Baboolall, D. R., and Puchooa, D., 2013, In Vitro Bioactivity and Phytochemical Screening of Selected Spices Used in Mauritian Foods, *Asian Pasific Journal of Tropical Disease*, **3(4)**:253-261.
- Tanvir, E. M., Hossen, Md. S., Hossain, Md. F., Afroz, R., Gan, S. H., Khalil, Md. I., Karim, N., 2017, Antioxidant Properties of Popular Turmeric (*Curcuma longa*) Varieties from Bangladesh, *Journal of Food Quality*, **2017**:1-8
- Tiwari, P., Kumar, B., Kaur, M., Kaur, G., and Kaur, H. 2011, Phytochemical screening and extraction - A review, *Internationale Pharmaceutica Sciencia*, **1(1)**: 98–106.
- Verma, S. C., Jain, C. L., Rani, R., Pant, P., Singh, R., Padhi, M. M., and Devalla, R. B. 2012, Simple and Rapid Method for Identification of *Curcuma Longa* Rhizomes by Physicochemical and HPTLC Fingerprint Analysis, *Chemical Science Transactions*, **1(3)**:709–715.
- Voight, R. 1995, *Buku Pelajaran Teknologi Farmasi*, Diterjemahkan dari Bahasa Inggris oleh Soendari Nocrong, 5th ed, UGM Press, Yogyakarta.
- Vries, A. C., Vermeer, M. A., Bloemendaal, H., Cohen, L. H. 1993, Pravastatin and Simvastatin Differently Inhibit Cholesterol Biosynthesis in Human Lens, *Investigate Ophthalmology and Visual Science*, **34**: 377-384.
- WHO, 1999, WHO monographs on selected medicinal plants, *Essential Medicines and Health Products Information Portal*, **1**: 115–124.
- WHO, 2002, *The World Health Report*, Geneva, pp. 58-59.
- WHO, 2017, *WHO guidelines on good herbal processing practices (GHPP) for herbal medicines*, Geneva.
- Winarto, W. P., 2004, *Khasiat dan Manfaat Kunyit*, AgroMedia Pustaka, Jakarta.
- Wulandari, L. 2011, *Kromatografi Lapis Tipis*, PT. Taman Kampus Presindo, Jember.