BAB 7

KESIMPULAN DAN SARAN

7.1. Kesimpulan

Berdasarkan hasil penelitian yang telah dilakukan dapat disimpulkan bahwa:

1. Konsentrasi hambat minimum *Curcuminoid* dengan nanopartikel silika terhadap bakteri *Staphylococcus epidermidis* adalah 32000 µg/mL.

7.2. Saran

1. Konsentrasi *Curcuminoid* dengan nanopartikel silika lebih ditingkatkan agar konsentrasi bunuh minimum dapat ditentukan.
2. Menggunakan teknik *loading* tanpa menggunakan proses pemanasan pada saat tahap formulasi *loading Curcuminoid* ke dalam nanopartikel silika.
3. Melakukan penelitian modifikasi nanopartikel silika agar dapat mengalami degradasi setelah masuk ke dalam sel bakteri sehingga dapat memungkinkan pelepasan *Curcuminoid* secara maksimal.
4. Melakukan penelitian mengenai uji toksisitas *Curcuminoid* dengan nanopartikel.

5. Melakukan penelitian mengenai uji stabilitas *Curcuminoid* dengan nanopartikel pada pH dan suhu tertentu.
6. Melakukan penelitian mengenai peranan *Curcuminoid* dengan nanopartikel sebagai desinfeksi topikal pre-operasi.

DAFTAR PUSTAKA

1. Carroll KC, Butel J, Mietzner TA. Jawetz, Melnick, & Adelberg's Medical Microbiology. 27th ed. Carroll KC, Hobden JA, Miller S, Morse SA, Mietzner TA, editors. New york: McGraw-Hill Education; 2015. 864 p.
2. D. Fey P. Staphylococcus Epidermidis Methods and Protocols. Vol. 1106, Methods in Molecular Biology. 2014.
3. Büttner H, Mack D, Rohde H. Structural basis of Staphylococcus epidermidis biofilm formation: mechanisms and molecular interactions. Front Cell Infect Microbiol [Internet]. 2015;5(February):1–15. Available from: http://journal.frontiersin.org/Article/10.3389/fcimb.2015.00014/abstract
4. Crossley KB, Jefferson KK, Archer GL, Fowler VG. Staphylococci in Human Disease. 2nd ed. Vol. 53, Journal of Chemical Information and Modeling. Blackwell Publishing; 2009. 310-332 p.
5. Kleinschmidt S, Huygens F, Faoagali J, Rathnayake IU, Hafner LM. Staphylococcus epidermidis as a cause of bacteremia. Future Microbiol [Internet]. 2015;10(11):1859–79. Available from:

http://www.futuremedicine.com/doi/10.2217/fmb.15.98

6. Mendes RE, Deshpande LM, Costello AJ, Farrell DJ. Molecular epidemiology of Staphylococcus epidermidis clinical isolates from U.S. hospitals. Antimicrob Agents Chemother. 2012;56(9):4656–61.

7. Becker K, Heilmann C, Peters G. Coagulase-negative staphylococci. Clin Microbiol Rev. 2014;27(4):870–926.

8. Otto M. Molecular basis of Staphylococcus epidermidis infections. Semin Immunopathol. 2012;34(2):201–14.

9. Gordon RJ, Miragaia M, Weinberg AD, Lee CJ, Rolo J, Giacalone JC, et al. Staphylococcus epidermidis colonization is highly clonal across US cardiac centers. J Infect Dis. 2012;205(9):1391–8.

10. Otto M. Staphylococcus epidermidis - The “accidental” pathogen. Nat Rev Microbiol. 2009;7(8):555–67.

11. Sahal G, Bilkay IS. Multi drug resistance in strong biofilm forming clinical isolates of Staphylococcus epidermidis. Braz J Microbiol [Internet]. 2014;45(2):539–44. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25242939%5Cnhttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC4166280

12. Kali A, Bhuvaneshwar D, Charles P V., Seetha K. Antibacterial synergy of curcumin with antibiotics against biofilm producing clinical bacterial isolates. J Basic Clin Pharm [Internet]. 2016;7(3):93. Available from: http://www.jbclinpharm.org/text.asp?2016/7/3/93/183265

13. Bandaranayake WM. Quality Control , Screening , Toxicity , and Regulation of Herbal Drugs. In: Modern Phytomedicine Turning Medicinal Plants into Drugs. I. Weinheim, Germany: Wiley-VCH Verlag GmbH & Co. KGaA; 2006. p. 25–58.

14. Perdagangan K. Obat Herbal Tradisional. War Ekspor. 2014;(September 2014):1–20.

15. Zorofchian Moghadamtousi S, Abdul Kadir H, Hassandarvish P, Tajik H, Abubakar S, Zandi K. A review on antibacterial, antiviral, and antifungal activity of curcumin. Biomed Res Int. 2014;2014.

16. Kementrian Kesehatan RI. 100 Top Tanaman Obat Indonesia. Kementrian Kesehatan RI - Balai Besar Litbang; 2011. 62-63 p.

17. Araújo CC, Leon LL. Biological activities of Curcuma longa L. Mem Inst Oswaldo Cruz [Internet]. 2001 Jul;96(5):723–8. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/11500779

18. Simanjuntak P. Studi Kimia dan Farmakologi Tanaman Kunyit (Curcuma longa L) Sebagai Tumbuhan Obat Serbaguna. Lemb Ilmu Pengetah Indones [Internet]. 2012;17(2):103. Available from: http://download.portalgaruda.org/article.php?article=293764&val=6157&title=STUDI KIMIA DAN FARMAKOLOGI TANAMAN KUNYIT (Curcuma longa L) SEBAGAI TUMBUHAN OBAT SERBAGUNA

19. Bhawana, Basniwal RK, Buttar HS, Jain VK, Jain N. Curcumin Nanoparticles : Preparation , Characterization , and Antimicrobial Study. J Agric Food Chem. 2011;59:2056–61.

20. Pangemanan A, Fatimawali, Budiarso F. Uji daya hambat ekstrak rimpang kunyit (Curcuma longa) terhadap pertumbuhan bakteri Staphylococcus aureus dan Pseudomonas sp. J e-Biomedik. 2016;4(1):81–5.

21. Anwar E, Iswandana R, Mun'im A. Uji Penetrasi Secara In Vitro dan Uji Stabilitas Fisik Sediaan Krim, Salep, dan Gel, Yang Mengandung Kurkumin dari Kunyit (Curcuma longa L.). J Bahan Alam Indones. 2011;7(7):370–4.

22. Bone K, Mills S. Herbal therapeutic systems. In: Principles

and Practice of Phytotherapy [Internet]. 2nd ed. London: Elsevier; 2013. p. 3–16. Available from: http://linkinghub.elsevier.com/retrieve/pii/B9780443069925000013

23. Karaman M, Firinci F, Arikan AZ, Bahar I. Effects of imipenem, tobramycin and curcumin on biofilm formation of Pseudomonas aeruginosa strains. Mikrobiyol Bul. 2013;47:192–4.

24. Singh RP, Jain D a. Evaluation of antimicrobial activity of curcuminoids isolated from turmeric. Int J Pharm Life Sci. 2012;3(1):1368–76.

25. Gaikwad A, Bodhankar M, Ittadwar A, Waikar S. Antibacterial activity of isoflavone extracted from Curcuma longa linn. Zingeberaceae. ISOI J Microbiol Biotechnol Food Sci. 2014;1(1):6–9.

26. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of Curcumin : Problems and Promises. Mol Pharm. 2007;4(6):807–18.

27. Bitar A, Ahmad NM, Fessi H, Elaissari A. Silica-based nanoparticles for biomedical applications. Drug Discov Today [Internet]. 2012;17(19–20):1147–54. Available from:

http://dx.doi.org/10.1016/j.drudis.2012.06.014

28. Tang L, Cheng J. Nonporous Silica Nanoparticles for Nanomedicine Application. Nano Today. 2013;8(3):290–312.

29. Liberman A, Mendez N, Trogler WC, Kummel AC. Synthesis and surface functionalization of silica nanoparticles for nanomedicine. Surf Sci Rep. 2014;69(2–3):132–58.

30. ITIS Standard Report Page: Staphylococcus epidermidis [Internet]. [cited 2018 Mar 17]. Available from: https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=377#null

31. Murray PR, Rosenthal KS, Pfaller MA. Medical Microbiology. 8th ed. Philadelphia: Elsevier Ltd; 2016. 170-181 p.

32. Kleinschmidt S, Huygens F, Faoagali J, Rathnayake IU, Hafner LM. *Staphylococcus epidermidis* as a cause of bacteremia. Future Microbiol [Internet]. 2015;10(11):1859–79. Available from: http://www.futuremedicine.com/doi/10.2217/fmb.15.98

33. Beveridge TJ. Use of the Gram stain in microbiology. Biotech Histochem. 2001;76(111–118).

34. Leboffe MJ, Pierce BE. A Photographic Atlas for the

Microbiology Laboratory. 4th Editio. United States: Morton Publishing Company; 2011.

35. Todar K. Staphylococcus aureus and Staphylococcal Disease. In: Todar’s Online Textbook of Bacteriology. Wisconsin: University of Wisconsin-Madison Department of Bacteriology; 2005.

36. Waluyo L. Mikrobiologi Umum. 2nd ed. Malang: Universitas Muhamadiyah Malang; 2005.

37. Catalase test: principle, uses, procedure and results - [Internet]. 2013 [cited 2018 Apr 25]. Available from: https://microbeonline.com/catalase-test-principle-uses-procedure-results/

38. Tille PM. Bailey & Scott’s Diagnostic Microbiology. 14th Editi. St. Louis: Elsevier; 2017.

39. Sharp SE, Searcy C. Comparison of mannitol salt agar and blood agar plates for identification and susceptibility testing of Staphylococcus aureus in specimens from cystic fibrosis patients. J Clin Microbiol. 2006;44(12):4545–6.

40. Shields P, Tsang AY. Mannitol Salt Agar Plates Protocols. ASM Microbe Libr. 2006;6(13):3–5.

41. Fey PD, Olson ME. Current concepts in biofilm formation of

Staphylococcus epidermidis. Future Microbiol [Internet]. 2010;5(6):917–33. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2903046&tool=pmcentrez&rendertype=abstract

42. Rogers KL, Fey PD, Rupp ME. Coagulase-Negative Staphylococcal Infections. Infect Dis Clin North Am. 2009;23(1):73–98.

43. Vuong C, Otto M. Staphylococcus epidermidis Infections. 2002;4(4):481–9.

44. Costerton J, Z L, Caldwell D, DR K, HM L. Microbial biofilms. Annu Rev Microbiol. 1995;49:711–45.

45. Costerton J, Stewart P, Greenberg E. Bacterial biofilms: a common cause of persistent infections. Science (80-). 1999;284(5418):1318–22.

46. Mack D, Davies AP. Staphylococcus epidermidis Biofilms: Functional Molecules, Relation to Virulence, and Vaccine Potential. Sci Transl Med [Internet]. 2017;9(397):eaal4651. Available from: http://stm.sciencemag.org/lookup/doi/10.1126/scitranslmed.aal4651

47. Rohde H, Frankenberger S, Mack D. Structure function and

contribution of polysaccharide intercellularadhesin (PIA) to Staphylococcus epidermidis biofilm formation and pathogenesis of biomaterial-associated infections. Eur J cell Biol. 2010;89:103–11.

48. Heilmann C. Adhesion mechanisms of staphylococci. Adv Exp Med bioogy. 2011;715:105–23.

49. Vuong C, Kocianova S, Voyrich J, Yao Y, Fishcer E. A crucial role for exopolysaccharide modification in bacterial biofilm formation, immune evasion, and virulence. J Biol Chem. 2004;279(52):54881–6.

50. Fey PD, Ulphani J, Gotz F. Characterization of the relationship between polysaccharide intercellular adhesin and hemagglutination in Staphylococcus epidermidis. J Infect Dis. 1999;179:1561–4.

51. Rupp ME, Fey PD. In vivo models to evaluate adhesion and biofilm formation by Staphylococcus epidermidis. methods Enzymol. 2001;336:206–15.

52. T.F. M, G.A O. Mechanisms of biofilm resistance to antimicrobial agents. Trends Microbiol. 2001;9(1):34–9.

53. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, Grady NPO, et al. Clinical Practice Guidlines for the Diagnosis and

Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis. 2014;49(1):1–45.

54. Raad I, Hanna H, Maki D. Raad, I., Hanna, H. & Maki, D. Intravascular catheterrelated infections: advances in diagnosis, prevention, and management. Lancet Infect. Dis. 7, 645–657 (2007). lancet Infect Dis. 2007;7(10):645–57.

55. ITIS Standard Report Page: Curcuma longa [Internet]. [cited 2018 Mar 5]. Available from: https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=42394#null

56. Pertanian BP dan P. Ayo Mengenal Tanaman Obat. Jakarta: IAARD Press; 2012.

57. Agoes HA. Tanaman Obat Indonesia Buku 2. Jakarta: Salemba Medika; 2010.

58. Hortikultura BPS dan DJ. Produksi, Luas Panen, dan Produktivitas Biofarmaka di Indonesia. 2016.

59. Li S, Yuan W, Deng G, Wang P, Yang P, Aggarwal BB. Chemical Composition and Product Quality Control of Turmeric (Curcuma longa L .). Pharm Crop. 2011;2:28–54.

60. Muti’ah R. Evidence Based Kurkumin dari Tanaman Kunyit

(Curcuma longa) Sebagai Terapi Kanker Pada Pengobatan Modern. J Islam Pharm [Internet]. 2017 Apr 14;1(1):28. Available from: http://ejournal.uin-malang.ac.id/index.php/jip/article/view/4178

61. Heinrich M, Barnes J, Gibbons S, Williamson EM. Fundamentals of Pharmacognosy and Phytotherapy. 3rd ed. London: Elsevier Ltd; 2012. 279-280 p.

62. Labban L. Medicinal and pharmacological properties of Turmeric (Curcuma longa): A review. Int J Pharm Biomed Res [Internet]. 2014;5(1):17–23. Available from: http://www.pharmainterscience.com/Docs/IJPBS-2014-05-103.pdf

63. Lawhavinit OA, Kongkathip N, Kongkathip B. Antimicrobial activity of curcuminoids from Curcuma Longa L. on pathogenic bacteria of shrimp and chicken. Kasetsart J - Nat Sci. 2010;44(3):364–71.

64. Niamsa N, Sittiwet C. Antimicrobial Activity of Curcuma longa Aqueous Extract. J Pharmacol Toxicol [Internet]. 2009 Apr 1;4(4):173–7. Available from: http://www.scialert.net/abstract/?doi=jpt.2009.173.177

65. Indriana. Uji Banding Efektivitas Ekstrak Rimpang Temu

Kunci (Kaemferia pandurata Roxb) 10% dengan Ketokonazol 2% Secara In Vitro Terhadap Pertumbuhan Candida albicans Pada Kandidiasis vaginalis. Artikel Ilmiah Hasil Penelitian Mahasiswa. UNIVERSITAS DIPONEGORO; 2006.

66. Řezanka T, Čejková A, Masák J. Natural products: Strategic tools for modulation of biofilm formation. Vol. 38, Studies in Natural Products Chemistry. 2012. 269-303 p.

67. Zhou X, Li Y. Atlas of Oral Microbiology: From Healty Microflora to Disease. London: Academic Press; 2015. 68 p.

68. Pundir RK, Jain P. Comparative Studies On The Antimicrobial Activity Of Black Pepper (Piper Nigrum) And Turmeric (Curcuma Longa). Int J Appl Biol Pharm Technol. 2010;1(2):491–501.

69. Agoes G. Teknologi Bahan Alam. Bandung: Penerbit Istitut Teknologi Bandung; 2007. 10-29 p.

70. Mukhriani. Ekstraksi, pemisahan senyawa, dan identifikasi senyawa aktif. J Kesehat. 2014;VII(2):361–7.

71. Kulkarni SJ, Maske KN, Budre MP, Mahajan RP. Extraction and purification of curcuminoids from Turmeric (curcuma longa L.). Int J Pharmacol Pharm Technol. 2012;1(12):2277–3436.

72. Priyadarsini KI. The chemistry of curcumin: From extraction to therapeutic agent. Molecules. 2014;19(12):20091–112.

73. Pal SL, Jana U, Manna PK, Mohanta GP, Manavalan R. Nanoparticles: An Overview of Preparation and Characterization. J Appl Pharm Sci [Internet]. 2011;1(6):228–34. Available from: http://pharmacy.novelscience.info/index.php/nvp/article/viewArticle/13953

74. Bei D, Meng J, Youan BC. Engineering nanomedicines for improved melanoma therapy: progress and promises. Nanomedicine (Lond). 2013;5(9):1385–99.

75. Ficai A, Grumezescu AM. Nanostructures for antimicrobial therapy [Internet]. 2017. 722 p. Available from: https://books.google.com.sg/books?id=wM78DAAAQBAJ&pg=PA205&lpg=PA205&dq=fda+approved+amps&source=bl&ots=a6vosIZG_c&sig=Z0S3THTwfXu84KTU-9zrEYakMDw&hl=en&sa=X&ved=0ahUKEwiC5ajjjKfVAhWEw7wKHdcuD2IQ6AEIVzAJ#v=onepage&q=fda approved amps&f=false

76. Slowing II, Vivero-Escoto JL, Wu C-W, Lin VS-Y. Mesoporous silica nanoparticles as controlled release drug

delivery and gene transfection carriers☆. Adv Drug Deliv Rev [Internet]. 2008 Aug 17;60(11):1278–88. Available from: http://linkinghub.elsevier.com/retrieve/pii/S0169409X08000951

77. Vivero-Escoto JL, Slowing II, Trewyn BG, Lin VS-Y. Mesoporous Silica Nanoparticles for Intracellular Controlled Drug Delivery. Small [Internet]. 2010 Sep 20;6(18):1952–67. Available from: http://doi.wiley.com/10.1002/smll.200901789

78. Wanyika H, Gatebe E, Kioni P, Tang Z, Gao Y. Mesoporous Silica Nanoparticles Carrier for Urea: Potential Applications in Agrochemical Delivery Systems. J Nanosci Nanotechnol [Internet]. 2012;12(3):2221–8. Available from: http://www.ingentaconnect.com/content/10.1166/jnn.2012.5801

79. Tang F, Li L, Chen D. Mesoporous silica nanoparticles: Synthesis, biocompatibility and drug delivery. Adv Mater. 2012;24(12):1504–34.

80. Hoffmann F, Cornelius M, Morell J, Fröba M. Silica-based mesoporous organic-inorganic hybrid materials. Angew Chemie - Int Ed. 2006;45(20):3216–51.

81. Hartono SB, Hadisoewignyo L, Yang Y, Meka AK, Yu C. Amine functionalized cubic mesoporous silica nanoparticles as an oral delivery system for curcumin bioavailability enhancement. Nanotechnology [Internet]. 2016;27(50):1–7. Available from: http://dx.doi.org/10.1088/0957-4484/27/50/505605

82. Black JG, Black LJ. Microbiology: Principles and Explorations. Libr Congr. 2013;975.

83. Cos P, Vlietinck AJ, Berghe D Vanden, Maes L. Anti-infective potential of natural products: How to develop a stronger in vitro "proof-of-concept." J Ethnopharmacol. 2006;106(3):290–302.

84. Parhusip A. Kajian Mekanisme Antibakteri Ekstrak Andaliman (Zanthoxylum acantahopodium) Terhadap Bakteri Patogen Pangan. Institut Pertanian Bogor; 2006.

85. Sari YD, Djannah SN, Nurani LH. Uji Aktivitas Antibakteri Infusa Daun Sirsak (Annona muricata L.) Secara In Vitro Terhadap Staphylococcus aureus ATCC 25923 dan Escherichia coli ATCC 35218 Serta Profil Kromatografi Lapis Tipisnya. Kes Mas. 2010;4(3):218–38.

86. Capoor MR, Nair D, Posti J, Singhal S, Deb M, Aggarwal P,

et al. Minimum inhibitory concentration of carbapenems and tigecycline against Salmonella spp. J Med Microbiol. 2009;58(3):337–41.

87. Samaranayake L. Essential Microbiology for Denstistry. 4th ed. St. Louis: Churcill Livingstone Elsevier; 2012. 58-59 p.

88. Cockerill FR. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. Clin Lab Stand Inst [Internet]. 2012;32(2). Available from: http://www.contempclindent.org/text.asp?2011/2/4/287/91790

89. Adahoun MA, Al-Akhras MAH, Jaafar MS, Bououdina M. Enhanced anti-cancer and antimicrobial activities of curcumin nanoparticles. Artif Cells, Nanomedicine Biotechnol. 2017;45(1):98–107.

90. Aneja KR. Experiments in Microbiology and Plant Pathology and Biotechnology. 4th ed. New Delhi: New Age International Pvt. Ltd.; 2003. 216 p.

91. Institute C and LS. Performance Standards for Antimicrobial. 27th editi. United States: Clinical and Laboratory Standards Institute; 2017.

92. Kharat M, Du Z, Zhang G, McClements DJ. Physical and

Chemical Stability of Curcumin in Aqueous Solutions and Emulsions: Impact of pH, Temperature, and Molecular Environment. J Agric Food Chem [Internet]. 2017 Mar 16;65(8):1525–32. Available from: http://pubs.acs.org/doi/10.1021/acs.jafc.6b04815

93. Sharmiladevi S, Shanmuga Priya A, Sujitha M V. Synthesis of mesoporous silica nanoparticles and drug loading for gram positive and gram-negative bacteria. Int J Pharm Pharm Sci. 2016;8(5):196–201.

94. Shahbazi MA, Herranz B, Santos HA. Nanostructured porous Si-based nanoparticles for targeted drug delivery. Biomatter. 2012;2(4):296–312.

95. Gao W, Thamphiwatana S, Angsantikul P. Nanoparticle Approaches against Bacterial Infections. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2014;6(6):532–547.

96. Sasirekha B, M. Megha D, S. Sharath M, Soujanya R. Study on Effect of Different Plant Extracts on Microbial Biofilms. Asian J Biotechnol [Internet]. 2015 Jan 1;7(1):1–12. Available from: http://www.scialert.net/abstract/?doi=ajbkr.2015.1.12