



**AKTIVITAS ANTIBAKTERI KOMBUCHA DAUN
SIRSAK (*Annona muricata* Linn.) PADA BAKTERI
Escherichia coli DAN *Salmonella typhi***

SKRIPSI

**Untuk Memenuhi Persyaratan
Memperoleh Gelar Sarjana Kedokteran**



**KALYANA PALUPI
21701101019**

**PROGRAM STUDI KEDOKTERAN
FAKULTAS KEDOKTERAN
UNIVERSITAS ISLAM MALANG
2021**



**AKTIVITAS ANTIBAKTERI KOMBUCHA DAUN
SIRSAK (*Annona muricata* Linn.) PADA BAKTERI
Escherichia coli DAN *Salmonella typhi***

SKRIPSI

**Untuk Memenuhi Persyaratan
Memperoleh Gelar Sarjana Kedokteran**



Oleh ★★★★★

UNISMA ★★★★★

KALYANA PALUPI

21701101019

**PROGRAM STUDI KEDOKTERAN
FAKULTAS KEDOKTERAN
UNIVERSITAS ISLAM MALANG
2021**



**AKTIVITAS ANTIBAKTERI KOMBUCHA DAUN
SIRSAK (*Annona muricata* Linn.) PADA BAKTERI
Escherichia coli DAN *Salmonella typhi***

SKRIPSI

**Untuk Memenuhi Persyaratan
Memperoleh Gelar Sarjana Kedokteran**



**KALYANA PALUPI
21701101019**

**PROGRAM STUDI KEDOKTERAN
FAKULTAS KEDOKTERAN
UNIVERSITAS ISLAM MALANG
2021**

RINGKASAN

Kalyana Palupi. Fakultas Kedokteran, Universitas Islam Malang, Oktober 2021. Aktivitas Antibakteri Kombucha Daun Sirsak (*Annona muricata* Linn.) Pada Bakteri *Escherichia coli* dan *Salmonella typhi*. **Pembimbing 1:** Dini Sri Damayanti. **Pembimbing 2:** Reza Hakim

Pendahuluan: Kombucha sebagai minuman fermentasi yang bersifat probiotik, yang bahan dasarnya dapat diganti dengan daun sirsak. Salah satu syarat probiotik adalah memiliki aktivitas antibakteri. Daun sirsak telah terbukti memiliki aktivitas antibakteri. Tujuan penelitian ini adalah untuk mengetahui aktivitas antibakteri kombucha daun sirsak (*Annona muricata* Linn.) terhadap bakteri *Escherichia coli* dan *Salmonella typhi*.

Metode: Kombucha daun sirsak di buat dengan merebus 1000 mL air, 100 gram gula pasir dan 5 gram serbuk daun sirsak selama 5 menit. Kemudian di tambahkan 24 gram *Symbiotic Culture of Bacteria and Yeast* (SCOBY) dan di fermentasi selama 14 hari. Kombucha diambil dan diencerkan pada konsentrasi 25, 50 dan 100% dilakukan uji zona hambat dengan pengulangan 3 kali. Zona hambat diukur dengan metode difusi tipe sumuran. Pengukuran zona hambat menggunakan aplikasi *software OptiLab* versi 1,5. Analisa data menggunakan uji *One Way ANOVA* yang dilanjutkan dengan *Post-Hoc Tukey* dengan signifikansi $p < 0,05$.

Hasil dan Pembahasan: Daya hambat kombucha daun sirsak konsentrasi pada 25, 50, 100% terhadap *Escherichia coli* secara berturut-turut adalah sebagai berikut $7,3 \pm 0,9$; $9,2 \pm 0,8$; $12,3 \pm 0,3$ mm ($p=0,05$). Sedangkan gentamisin mampu menghambat pertumbuhan *Escherichia coli* sebesar $14,7 \pm 1,2$ mm. Sedangkan daya hambat kombucha daun sirsak konsentrasi pada 25, 50, 100% terhadap *Salmonella typhi* secara berturut-turut adalah $5,23 \pm 3,7$; $8,47 \pm 0,3$; $10,36 \pm 0,7$ mm ($p=0,05$). Sedangkan gentamisin mampu menghambat pertumbuhan *Salmonella typhi* sebesar $11,3 \pm 1,6$ mm. Hal ini terjadi karena kombucha daun sirsak mengandung asam organik (asam asetat, asam glukonat dan asam laktat), etanol, flavonoid dan bakteri asam laktat yang mampu menghambat pertumbuhan bakteri patogen.

Kesimpulan: Kombucha daun sirsak konsentrasi 100% efektif menghambat *Escherichia coli* dengan derajat kuat. Sedangkan kombucha daun sirsak konsentrasi 50% efektif menghambat pertumbuhan *Salmonella typhi* dengan derajat kuat. Kombucha daun sirsak lebih efektif menghambat *Salmonella typhi* dibandingkan *Escherichia coli*.

Kata Kunci: Kombucha, *Annona muricata* L, *Escherichia coli*, *Salmonella typhi*

SUMMARY

Kalyana Palupi. Faculty of Medicine, University of Islam Malang, October 2021. Kombucha Antibacterial Activity of Soursop Leaf (*Annona muricata* Linn.) on *Escherichia coli* and *Salmonella typhi* Bacteria. **Supervisor 1:** Dini Sri Damayanti. **Supervisor 2:** Reza Hakim

Introduction: Kombucha is a probiotic fermented drink, the basic ingredients of which can be replaced with soursop leaves. One of the requirements for probiotics is to have antibacterial activity. Soursop leaves have been shown to have antibacterial activity. The purpose of this study was to determine the antibacterial activity of soursop leaf kombucha (*Annona muricata* Linn.) against *Escherichia coli* and *Salmonella typhi*.

Method: Soursop leaf kombucha is made by boiling 1000 mL of water, 100 grams of sugar and 5 grams of soursop leaf powder for 5 minutes. Then 24 grams of Symbiotic Culture of Bacteria and Yeast (SCOBY) were added and fermented for 14 days. Kombucha was taken and diluted at concentrations of 25, 50 and 100%. Inhibition zone test was performed with 3 repetitions. The zone of inhibition was measured by the well type diffusion method. Inhibition zone measurement using OptiLab version 1.5 software application. Data analysis used One Way ANOVA test followed by Post-Hoc Tukey with a significance of $p < 0.05$.

Result and Discussion: The inhibitory power of soursop leaf kombucha at concentrations of 25, 50, 100% against *Escherichia coli*, respectively, was 7.3 ± 0.9 ; 9.2 ± 0.8 ; 12.3 ± 0.3 mm ($p=0.05$). Meanwhile, gentamicin was able to inhibit the growth of *Escherichia coli* by 14.7 ± 1.2 mm. Meanwhile, the concentration of kombucha in soursop leaves at 25, 50, 100% against *Salmonella typhi* was 5.23 ± 3.7 ; 8.47 ± 0.3 ; 10.36 ± 0.7 mm ($p=0.05$). Meanwhile, gentamicin was able to inhibit the growth of *Salmonella typhi* by 11.3 ± 1.6 mm. This happens because soursop leaf kombucha contains organic acids (acetic acid, gluconic acid and lactic acid), ethanol, flavonoids and lactic acid bacteria which can inhibit the growth of pathogenic bacteria.

Conclusion: Soursop leaf kombucha with 100% concentration effectively inhibited *Escherichia coli* with a strong degree. Meanwhile, soursop leaf kombucha with a concentration of 50% was effective in inhibiting the growth of *Salmonella typhi* with a strong degree. Soursop leaf kombucha is more effective at inhibiting *Salmonella typhi* than *Escherichia coli*.

Keyword: Kombucha, *Annona muricata* L, *Escherichia coli*, *Salmonella typhi*

BAB I PENDAHULUAN

1.1 Latar Belakang

Penyakit diare merupakan penyakit endemis di Indonesia dengan potensial kejadian luar biasa (KLB) yang tinggi (Kementerian Kesehatan RI, 2019). Prevalensi diare menurut Kemenkes RI mengalami peningkatan pada tahun 2018 dari tahun 2017 (Kementerian Kesehatan RI, 2019). Data menurut Parija (2012), terdapat 600 juta orang terinfeksi bakteri *Escherichia coli* dengan angka kematian 700.000 pertahun, sedangkan *Salmonella typhi* menginfeksi sekitar 13 juta pasien dengan angka kematian 600.000 pertahun (Parija, 2012). Kedua bakteri ini sering menjadi masalah di negara berkembang seperti India, Afrika, Timur Tengah, Amerika Selatan dan Asia Tenggara termasuk Indonesia (Parija, 2012), sehingga penanganan diare akibat infeksi bakteri *Escherichia coli* dan *Salmonella typhi* perlu di perhatikan.

Terapi antibiotik merupakan pengobatan lini pertama penyakit infeksi (WHO, 2017). Namun penggunaan antibiotik yang tidak benar seperti mengkonsumsi dalam jangka waktu yang panjang mengakibatkan penurunan normal flora (*Bifidobacterium*, *Lactobacillus* dan *Bacteroides*) dan peningkatan mikroba patogen seperti bakteri Gram-negatif enterik aerob (Noverr and Huffnagle, 2013). Bakteri patogen yang menempel pada sel epitel usus kemudian menginvasi mukosa dan memproduksi toksin sehingga menyebabkan diare (Robbins, 2012). Salah satu cara untuk mempertahankan keseimbangan mikrobiota normal usus dan patogen adalah dengan mengkonsumsi probiotik (Gourbeyre *et al*, 2011).

Probiotik adalah mikroorganisme hidup yang apabila dikonsumsi dalam jumlah yang cukup akan memberi manfaat untuk kesehatan manusia dan bersifat non-patogen (FAO and WHO, 2002). Salah satu minuman probiotik adalah kombucha (Kozyrovska *et al.*, 2012). Kombucha adalah minuman tradisional berbahan dasar teh yang difermentasi oleh *Symbiotic Culture of Bacteria and Yeast* (SCOBY) (Laureys *et al.*, 2020). Dalam proses fermentasi, SCOBY mampu mengubah larutan dan gula menjadi minuman berkarbonasi ringan yang memiliki rasa sedikit asam yang menyegarkan dan mengandung asam organik (asam asetat, asam glukonat, asam glukuronat dan asam laktat), vitamin, etanol, protein, polifenol, mineral dan anion (Villarreal-Soto *et al.*, 2018). Syarat mikroba dinyatakan sebagai probiotik adalah memiliki aktivitas antibakteri terhadap mikroba patogen, aktivitas antioksidan, memiliki pH antara 3 hingga 5, tahan terhadap asam, tahan terhadap garam empedu, mampu menempel pada permukaan epitel sel usus, dan memiliki aktivitas *bile salt hydrolase* (Kechagia *et al.*, 2013).

Bahan dasar pembuatan kombucha dapat diganti menggunakan daun sirsak. Daun sirsak yang memiliki kandungan senyawa aktif tannin, saponin, terpenoid, steroid, fenol, flavonoid, flavonol glikosida, alkaloid dan asetogenin telah terbukti memiliki aktivitas antibakteri melalui mekanisme mengganggu sintesa DNA, dan merusak membran sel bakteri (Iyanda-Joel *et al.*, 2019). Namun sediaan daun sirsak dalam kombucha belum diteliti, sehingga perlu dilakukan penelitian untuk membuktikan keefektifan kombucha daun sirsak sebagai antibakteri melalui pengujian zona hambat (*Zone of Inhibition*) metode difusi tipe sumuran pada kultur bakteri *Escherichia coli* dan *Salmonella typhi*.

1.2 Rumusan Masalah

1. Apakah kombucha daun sirsak (*Annona muricata* Linn.) efektif dalam menghambat pertumbuhan bakteri *Escherichia coli*?
2. Apakah kombucha daun sirsak (*Annona muricata* Linn.) efektif dalam menghambat pertumbuhan bakteri *Salmonella typhi*?

1.3 Tujuan

1. Mengetahui efektivitas kombucha daun sirsak (*Annona muricata* Linn.) dalam menghambat pertumbuhan bakteri *Escherichia coli*.
2. Mengetahui efektivitas kombucha daun sirsak (*Annona muricata* Linn.) dalam menghambat pertumbuhan bakteri *Salmonella typhi*.

1.4 Manfaat

1.4.1 Manfaat Teoritis

Penelitian ini diharapkan kombucha daun sirsak dapat menghambat pertumbuhan bakteri *Escherichia coli* dan *Salmonella typhi* sehingga dapat dikembangkan sebagai antibakteri kedepannya.

1.4.2 Manfaat Praktis

Kombucha daun sirsak (*Annona muricata* Linn.) dapat dijadikan sebagai produk yang dapat dipasarkan dimasyarakat.

BAB VII PENUTUP

7.1 Kesimpulan

1. Kombucha daun sirsak dengan konsentasi 100% efektif dalam menghambat pertumbuhan bakteri *Escherichia coli*.
2. Kombucha daun sirsak dengan konsentasi 50% efektif dalam menghambat pertumbuhan bakteri *Salmonella typhi*.
3. Kombucha daun sirsak lebih mudah menghambat bakteri *Salmonella typhi* dibandingkan bakteri *Escherichia coli*.

7.2 Saran

Adapun beberapa saran untuk meningkatkan penelitian ini di masa mendatang yaitu

- 1) Melakukan eksplorasi dengan variasi lama perebusan.
- 2) Melakukan eksplorasi dengan menggunakan jumlah serbuk daun sirsak, jumlah gula, dan berat SCOBY yang berbeda.
- 3) Melakukan fermentasi dengan variasi lama 7, 14, dan 21 hari.
- 4) Menggunakan kontrol positif dengan antibiotik lain yang cara kerjanya pada dinding sel dan DNA bakteri, untuk mengetahui mekanisme kerja yang mendekati dengan cara kerja kombucha daun sirsak dalam menghambat pertumbuhan bakteri.
- 5) Melakukan pengujian secara *in vivo* pada hewan coba, untuk membuktikan kombucha daun sirsak dapat dijadikan sebagai probiotik.

DAFTAR PUSTAKA

- Alzeer, J. and Abou Hadeed, K. 2016. *Ethanol and its Halal status in food industries*, **Trends in Food Science and Technology**, 58, pp. 14–20.
- Arthur, F. K. N., Woode, E., Terlabi, Ebenezer O., and Larbie, C. 2012a. *Bilirubin lowering potential of *Annona muricata* (Linn.) in temporary jaundiced rats*, **American Journal of Pharmacology and Toxicology**, 7(2), pp. 33–40.
- Arthur, F. K. N., Woode, E., Terlabi, Ebenezer O., and Larbie, C. 2012b. *Evaluation of hepatoprotective effect of aqueous extract of *Annona muricata* (Linn.) leaf against carbon tetrachloride and acetaminophen-induced liver damage*, **International Journal of Shoulder Surgery**, 6(2), pp. 25–30.
- Battikh, H., Bakhrouf, A. and Ammar, E. 2012. *Antimicrobial effect of Kombucha analogues*, **LWT - Food Science and Technology**, 47(1), pp. 71–77.
- Bouarab-Chibane, L., Forquet, V., Lantéri, P., Clément, Y., Léonard-Akkari, L., and Oulahal, N. 2019. *Antibacterial properties of polyphenols: Characterization and QSAR (Quantitative structure-activity relationship) models*, **Frontiers in Microbiology**, 10(APR).
- Coton, M., Pawtowski, A., Taminiou, B., Deniel, F., Coulloume-labarthe, L., Fall, A., Daube, G., and Coton, E. 2017. *Unraveling microbial ecology of industrial-scale Kombucha fermentations by metabarcoding and culture-based methods*, (April), pp. 1–16.
- Delcenserie, V., Martel, D., Lamoureux, M., Amiot, J., Boutin, Y., and Roy, D. 2012. *Immunomodulatory effects of probiotics in the intestinal tract*. **Current Issues in Molecular Biology**, 10(1), pp. 37–54.
- Ettayebi, K., Errachidi, F., Jamai, L., Tahri-Jouti, M., Sendide, K., and Ettayebi, M. 2003. *Biodegradation of polyphenols with immobilized *Candida tropicalis* under metabolic induction*, **FEMS Microbiology Letters**, 223(2), pp. 215–219.
- Falahuddin, I., Apriani, I. and Nurfadilah. 2017. *Pengaruh Proses Fermentasi Kombucha Daun Sirsak (*Annona Muricata* L.) Terhadap Kadar Vitamin C*, **Biota**, 3(2), p. 90.
- Faner, R., Sibila, O., Agustí, A., Bernasconi, E., Chalmers, J. D., Huffnagle, G. B., Manichanh, C., Molyneaux, P. L., Paredes, R., Brocal, V P., Ponomarenko, J., Sethi, S., Dorca, J., and Monsó, E. 2017. *The microbiome in respiratory medicine: Current challenges and future perspectives*, **European Respiratory Journal**, 49(4).

- FAO and WHO. 2002. *Guidelines for the Evaluation of Probiotics in Food*. London Ontario, Canada.
- Folorunso, A., Akintelu, S., Oyebamiji, A. K., Ajayi, S., Abiola, B., Abdusalam, I., and Morakinyo, A. 2019. *Biosynthesis, characterization and antimicrobial activity of gold nanoparticles from leaf extracts of Annona muricata*, **Journal of Nanostructure in Chemistry**, 9(2), pp. 111–117.
- Galdeano, C. M., Cazorla, S. I., Dumit, J. M. L., Vélez, E., Perdigón, G. 2018. *Beneficial Effects of Probiotic Consumption on the Immune System*. **Annals of Nutrition & Metabolism**, 74, pp. 115–124.
- Gavamukulya, Y., Wamunyokoli, F. and El-shemy, H. A. 2017. *Annona muricata : Is the natural therapy to most disease conditions including cancer growing in our backyard? A systematic review of its research history and future prospects* *Asian Pacific Journal of Tropical Medicine*, **Asian Pacific Journal of Tropical Medicine**, 10(9), pp. 835–848.
- George, V. C., Kumar, D. R.N., Suresh, P. K., and Kumar, R. A. 2015. *Antioxidant, DNA protective efficacy and HPLC analysis of Annona muricata (soursop) extracts*, **Journal of Food Science and Technology**, 52(4), pp. 2328–2335.
- Goh, W. N., Rosma, A., Kaur, B., Fazilah, A., Karim, A. A. and Bhat, R. 2012. *Fermentation of black tea broth (kombucha): I. effects of sucrose concentration and fermentation time on the yield of microbial cellulose*, **International Food Research Journal**, 19(1), pp. 109–117.
- Gomes, A. C., Bueno, A. A., De Souza, R. G. M. H., and Mota, J. F. 2014. *Gut microbiota, probiotics and diabetes*, **Nutrition Journal**, 13(1).
- Gourbeyre, P., Denery, S. and Bodinier, M. 2011. *Probiotics, prebiotics, and synbiotics: impact on the gut immune system and allergic reactions*, **Journal of Leukocyte Biology**, 89(5), pp. 685–695.
- Hamid, R. A., Foong, C. P., Ahmad, Z. and Hussain, M. K. 2012. *Antinociceptive and anti-ulcerogenic activities of the ethanolic extract of annona muricata leaf*, *Revista Brasileira de Farmacognosia*, 22(3), pp. 630–641.
- Hermawan, A., Eliyani, H. and Tyasningsih, W. 2007. *Pengaruh ekstrak daun sirih (Piper betle L) terhadap pertumbuhan Staphylococcus aureus dan Eschericia coli dengan metode difusi disk*, **Artikel Ilmiah Surabaya**, 2.
- Hilal A. Syahrir, N., Mochamad Afendi, F. and Susetyo, B. 2016. *Efek Sinergis Bahan Aktif Tanaman Obat Berbasiskan Jejaring dengan Protein Target*, **Jurnal Jamu Indonesia**, 1(1), pp. 35–46.
- Hudzicki, J. 2016. *Kirby-Bauer Disk Diffusion Susceptibility Test Protocol*, **American Society For Microbiology**, (December 2009), pp. 1–13.

- Hur, S. J., Lee, S. Y., Kim, Y. C., Choi, I. and Kim, G. B. 2014. *Effect of fermentation on the antioxidant activity in plant-based foods*, **Food Chemistry**, 160, pp. 346–356.
- Ingram, L. 2014. *Mechanism of Lysis of Escherichia coli by Ethanol and Other Chaotropic Agents*, (May 1981).
- Iyanda-Joel, W. O., Omonigbehin, E. A., Iweala, E.E.J. and Chinedu, S. N. 2019. *Antibacterial studies on fruit-skin and leaf extracts of Annona muricata in Ota, Nigeria*, IOP Conference Series: **Earth and Environmental Science**, 331(1).
- Jandhyala, S. M., Talukdar, R., Subramanyam, C., Vuyyuru, H., Sasikala, M. and Reddy, D. N. 2015. *Role of the normal gut microbiota*, **World Journal of Gastroenterology**, 21(29), pp. 8836–8847.
- Jayabalan, R., Malbañ, R. V., Lonç, E. S., Vitas, J. S. and Sathishkumar, M. 2014. *A review on kombucha tea-microbiology, composition, fermentation, beneficial effects, toxicity, and tea fungus*, **Comprehensive Reviews in Food Science and Food Safety**, 13(4), pp. 538–550.
- Jayabalan, R., Marimuthu, S. and Swaminathan, K. 2007. *Changes in content of organic acids and tea polyphenols during kombucha tea fermentation*, **Food Chemistry**, 102(1), pp. 392–398.
- Kaiser, G. 2021. **Microbiology**. Baltimore : LibreText, pp. 75-79
- Katzung, B. G., Masters, S. B. and Trevor, A. J. 2012. *Basic & Clinical Pharmacology*. 12th edn. San Fransisco: The McGraw-Hill Companies.
- Kechagia, M., Basoulis, D., Konstantopoulou, S., Dimitriadi, D., Gyftopoulou, K., Skarmoutsou, N., and Fakiri, E. M. 2013. *Health Benefits of Probiotics: A Review*, **ISRN Nutrition**, 2013, pp. 1–7.
- Kementerian Kesehatan RI. 2019. *Profil Kesehatan Indonesia, Journal of Clinical Pathology*. **Kementerian Kesehatan Republik Indonesia**.
- Kole, A. S., Jones, H. D., Christensen, R., PharmD and Gladstein, J. 2009. *A Case of Kombucha Tea Toxicity*, **Journal of Intensive Care Medicine**, 205–207(4), p. 402.
- Kozyrovskaya, N. O., Reva, O. M., Goginyan, V. B. and Devera, J. P. 2012. *Kombucha microbiome as a probiotic: A view from the perspective of post-genomics and synthetic ecology*, **Biopolymers and Cell**, 28(2), pp. 103–113.
- Kumar, V., Abbas, A. K. and Aster, J. C. 2020. *Buku Ajar Patologi Robbins*. **10th edn, Nasional**. Edited by M. F. Ham and M. Saraswati. Jakarta.

- Kusmayati and Agustini, N. W. 2007. *Uji Aktivitas Senyawa Antibakteri dari Mikroalga (Porphyridium cruentum)*, **J Biod**, 8(1), pp. 48–53.
- Laureys, D., Britton, S. J. and De Clippeleer, J. 2020. *Kombucha Tea Fermentation: A Review*, **Journal of the American Society of Brewing Chemists**, 78(3), pp. 165–174.
- Leal, J. M., Suárez, L. V., Jayabalan, R., Oros, H., and Escalante-aburto, A. 2018. *A review on health benefits of kombucha nutritional compounds and metabolites*, **CyTA - Journal of Food**, 16(1), pp. 390–399.
- Lingga, A. R. 2016. *Uji Antibakteri Ekstrak Batang Kecombrang (Nicolaia speciosa Horan) Terhadap Staphylococcus aureus dan Escherichia coli*, **JOM Faperta**, 3(1).
- Lopez, C. L. F., Beaufort, S., Brandam, C., and Taillandier, P. 2014. *Interactions between Kluyveromyces marxianus and Saccharomyces cerevisiae in tequila must type medium fermentation*, **World Journal of Microbiology and Biotechnology**, 30(8), pp. 2223–2229.
- Menconi, A., Kallapura, G., Latorre, J. D., Morgan, M. J., Pumford, N. R., Hargis, B. M. and Tellez, G. 2014. *Identification and characterization of lactic acid bacteria in a commercial probiotic culture*. **Bioscience of Microbiota, Food and Health**, 33(1), pp. 25–30.
- Moghadamtousi, S. Z., Kadir, H. A., Paydar, M., Rouhollahi, E. and Karimian, H. 2014. *Annona muricata leaves induced apoptosis in A549 cells through mitochondrial-mediated pathway and involvement of NF- κ B*, **BMC Complementary and Alternative Medicine**, 14(1), pp. 1–13.
- Moghadamtousi, S. Z., Fadaeinasab, M., Nikzad, S., Mohan, G., Ali, H. M. and Kadir, H. A. 2015. *Annona muricata (Annonaceae): A review of its traditional uses, isolated acetogenins and biological activities*, **International Journal of Molecular Sciences**, 16(7), pp. 15625–15658.
- Moghadamtousi, S. Z., Rouhollahi, E., Hajrezaie, M., Karimian, H., Abdulla, M. A. and Kadir, H. A. 2015. *Annona muricata leaves accelerate wound healing in rats via involvement of Hsp70 and antioxidant defence*, **International Journal of Surgery**, 18, pp. 110–117.
- Mohammadi, R., Sohrabvandi, S. and Mohammad Mortazavian, A. 2012. *The starter culture characteristics of probiotic microorganisms in fermented milks*, **Engineering in Life Sciences**, 12(4), pp. 399–409.
- Mueller, E. A., Egan, A. J.F., Breukink, E., Vollmer, W. and Levin, P. A. 2019. *Plasticity of Escherichia coli cell wall metabolism promotes fitness and antibiotic resistance across environmental conditions*, **eLife**, 8, pp. 1–24.

- Muizuddin, M. and Zubaidah, E. 2015. *Studi aktivitas antibakteri kefir teh daun sirsak (annona muricata linn .) dari berbagai merk teh daun sirsak di pasaran*, **Jurnal Pangan dan Agroindustri**, 3(4), pp. 1662–1672.
- Ningsih, A. S., Ekowati, C. N., Sumard, S. and Farisi, S. 2018. *Uji Daya Antibakteri Isolat Bakteri Asam Laktat dari Kefir terhadap Bacillus sp. dan Escherichia Coli, Biosfer: Jurnal Tadris Biologi*, 9(2), pp. 217–223.
- Noverr, M. C. and Huffnagle, G. B. 2013. *Does the microbiota regulate immune responses outside the gut?*, **Trends in Microbiology**, 12(12), pp. 562–568.
- Nwokocha, C. R., Owu, D. U., Gordon, A., Thaxter, K., Mccalla, G., Ozolua, R. I. and Young, L. 2012. *Possible mechanisms of action of the hypotensive effect of Annona muricata (soursop) in normotensive SpragueDawley rats*, **Pharmaceutical Biology**, 50(11), pp. 1436–1441.
- Padayatty, S. J., Katz, A., Wang, Y., Eck, P., Kwon, O., Lee, J. H., Chen, S., Corpe, C., Levine, M., Dutta, A., and Dutta, S. K. 2003. *Vitamin C as an Antioxidant: Evaluation of Its Role in Disease Prevention*, **Journal of the American College of Nutrition**, 22(1), pp. 18–35.
- Parija, S. C. 2012. *Microbiology & Immunology*. 2nd edn. Edited by S. M. Bhattacharya *et al.* India: **Elsevier**.
- Punyaappa-path, S., Phumkhachorn, P. and Rattanachaikunsopon, P. 2015. *Nisin : Production And Mechanism Of Antimicrobial Action*. **Int J Cur Res Rev**, 7(2), pp. 47–53.
- Quinn, P. J., Markey, B. K., Leonard, F. C., FitzPatrick, E. S., Fanning, S., and Hartigan, P. J. 2002. *Veterinary Microbiology and Microbial Disease*, Iowa State University Press, Ames, Iowa, USA, p. 536pp.
- Rahayu, W. P., Nurjanah, S. and Komalasari, E. 2018. *Escherichia coli : Patogenitas, Analisis dan Kajian Risiko*, IPB Press. pp 11-48
- Rahman, H. S., Mahmoud, B. M., Othman, H. H. and Amin, K. 2018. *A Review of History, Definition, Classification, Source, Transmission, and Pathogenesis of Salmonella: A Model for Human Infection*, **Journal of Zankoy Sulaimani - Part A**, 20(3&4), pp. 11–20.
- Rechner, A. R., Smith, M. A., Kuhnle, G., Gibson, G. R., Debnam, E. S., Srail, S. K. S., Moore, K. P., and Rice-Evans, C.A. 2004. *Colonic metabolism of dietary polyphenols: Influence of structure on microbial fermentation products*, **Free Radical Biology and Medicine**, 36(2), pp. 212–225.
- Reis, J. A., Paula, A. T., Casarotti, S. N., and Penna, A.L.B. 2012. *Lactic Acid Bacteria Antimicrobial Compounds : Characteristics and Applications*, **Food Eng Rev**, 4, pp. 124–140.

- Roe, A. J., Byrne, C. O., Mclaggan, D., and Booth, I.R. 2005. *Inhibition of Escherichia coli growth by acetic acid: A problem with methionine biosynthesis and homocysteine toxicity* *Inhibition of Escherichia coli growth by acetic acid: a problem with methionine biosynthesis and homocysteine toxicity*, (August).
- Ryan, M. P., O'Dwyer, J. and Adley, C. C. 2017. *Evaluation of the Complex Nomenclature of the Clinically and Veterinary Significant Pathogen Salmonella*, **BioMed Research International**, 2017.
- Sari, Y. D. 2011. *Uji Aktivitas Antibakteri Infusa Daun Sirsak (Annona muricata L.) Secara in Vitro Terhadap Staphylococcus aureus ATCC 25923 dan Escherichia coli ATCC 35128 Serta Profil kromatografi Lapis Tipisnya*, **Kes Mas: Jurnal Fakultas Kesehatan Masyarakat Universitas Ahmad Daulan**, pp. 218–238.
- Simanjuntak, R. J. D. and Mutiara, H. 2016. *Pengaruh Pemberian Teh Kombucha Terhadap Pertumbuhan Salmonella Typhi*, **Majoriity**, 5(5), pp. 48–54.
- Stanbury, P. F., Whitaker, A. and Hall, S. J. 2013. *Principles of Fermentation Technology: Third Edition*, **Principles of Fermentation Technology: Third Edition**, pp. 1–803.
- Susanto, A. 2020. *Buku Ajar Bakteriologi (Carrier Penyakit Typus)*. Edited by A. Dr. Rifa'atul Laila Mahmudah, M.Farm.Klin. indonesia: STIKes Majapahit Mojokerto.
- Tan, W. C., Muhialdin, B. J. and Meor Hussin, A. S. 2020. *Influence of Storage Conditions on the Quality, Metabolites, and Biological Activity of Soursop (Annona muricata. L.) Kombucha*, **Frontiers in Microbiology**, 11(December), pp. 1–10.
- Velićanski, A., Cvetković, D. and Markov, S. 2013. *Characteristics of Kombucha fermentation on medicinal herbs from Lamiaceae family*, 18(1), pp. 8034–8042.
- Vijayameena, C., Subhashini, G., Loganayagi, M and Ramesh, B. 2013. *Phytochemical screening and assessment of antibacterial activity for the bioactive compounds in Annona muricata*, **International Journal of Current Microbiology and Applied Sciences**, 2(1), pp. 1–8.
- Villarreal-Soto, S. A., Beaufort, S., Bouajila, J., Souchard, J. P. and Taillandier, P. 2018. *Understanding Kombucha Tea Fermentation: A Review*, **Journal of Food Science**, 83(3), pp. 580–588.
- Watawana, M. I., Jayawardena, N., Gunawardhana, C.B., and Waisundara, V. Y. 2015. *Health , Wellness , and Safety Aspects of the Consumption of Kombucha*, 2015.

- Watawana, M. I., Jayawardena, N., Gunawardhana, C. B. and Waisundara, V. Y. 2016. *Original article Enhancement of the antioxidant and starch hydrolase inhibitory activities of king coconut water (Cocos nucifera var . aurantiaca) by fermentation with kombucha “ tea fungus ”*, pp. 490–498.
- WHO. 2017. *Prioritization Of Pathogens To Guide Discovery, Research And Development Of New Antibiotics For Drug-Resistant Bacterial Infections, Including Tuberculosis*, World Health Organization.
- Xie, Y., Yang, W., Tang, F., Chen, X. and Ren, L. 2015. *Antibacterial Activities of Flavonoids: Structure-Activity Relationship and Mechanism*, **Current Medicinal Chemistry**, 22(1), pp. 132–149.
- Yang, S., Sheng, H., Man, X., and Ping, Y. 2014. *Selected non- Saccharomyces wine yeasts in controlled multistarter fermentations with Saccharomyces cerevisiae on alcoholic fermentation behaviour and wine aroma of cherry wines*, **Food Microbiology**, 44, pp. 15–23.
- Youssef, M. Ahmed, H. Y., Zongo, A., Korin, A., Zhan, F., Hady, E., Umair, M., Shahid Riaz Rajoka, M., Xiong, Y. and Li, B. 2021. *Probiotic supplements: Their strategies in the therapeutic and prophylactic of human life-threatening diseases*, **International Journal of Molecular Sciences**, 22(20).
- Zalán, Z., Németh, E., Baráth, Á., and Halász, A. 2005. *Influence of Growth Medium on Hydrogen Peroxide and Bacteriocin Production of Lactobacillus Strains Influence of Growth Medium on Hydrogen Peroxide and Bacteriocin Production of Lactobacillus Strains*, (October).
- Zorofchian Moghadamtousi, S., Karimian, H., Rouhollahi, E., Paydar, M., Fadaeinasab, M. and Abdul Kadir, H. 2014. *Annona muricata leaves induce G1 cell cycle arrest and apoptosis through mitochondria-mediated pathway in human HCT-116 and HT-29 colon cancer cells*, **Journal of Ethnopharmacology**, 156, pp. 277–289.