

BAB V

KESIMPULAN DAN SARAN

A. Kesimpulan

Dari penelitian dan study literatur yang telah dilakukan maka dapat di ambil kesimpulan bahwa,

Satu, bakteri *Bacillus subtilis* pada berbagai galur yang berbeda mampu menghasilkan enzim fibrinolitik yang ditunjukan dengan hasil positif pada uji fibrinolitik dengan metode plat fibrin

Dua, konsentrasi dari enzim fibrinolitik yang dihasilkan oleh bakteri *Bacillus subtilis* sangat bervariasi tergantung strain bakterinya mulai dari 1,7 U/mg sampai 8645 U/mg.

Tiga, mekanisme kerja enzim fibrinolitik dari bakteri *Bacillus subtilis* pada galur yang berbeda yaitu dengan cara mengaktifkan plasminogen atau tPA (*tissue plasmin activator*) untuk memecah bekuan darah dan juga mendegradasi fibrin secara langsung hal ini di tunjukan dengan pengujian pada fibrin plate kaya plasminogen dan tanpa plasminogen yang sama-sama memiliki hasil positif.

B. Saran

Peneliti menyarankan untuk dilakukan penelitian selanjutnya mengenai isolasi dan uji aktivitas serta variasi konsentrasi efektif enzim fibrinolitik bakteri *Bacillus subtilis* dari sumber lain terutama makanan fermentasi dari daerah di Indonesia. Kemudian dilakukan karakterisasi enzim fibrinolitik dari *Bacillus subtilis* lebih lanjut dengan beberapa parameter diantaranya adalah stabilitas pH, suhu, waktu penyimpanan.

DAFTAR PUSTAKA

- A. Hatmanti, (2000), Pengenalan Bacillus SPP. *Oseana*. Vol. 25, No. 1, Hal. 31-41.
- Adrianto, A, W. (2012), *Uji Daya Antibakteri Ekstrak Daun Salam (Eugenia Polyantha Wight) dalam Pasta Gigi Terhadap Pertumbuhan Streptococcus Mutans*. Jember: Fakultas Kedokteran Gigi Universitas Jember.
- Ahmad Toto Poernomo, dkk. (2014), *Purifikasi Parcial Enzim Fibrinolitik Tempe Kacang Koro*. Produk Fermentasi Rhizopus Oryzae FNCC 6078.
- Aini, F. N., S. Sukamto, D. Wahyuni, R. G Suhesti, & Q. Ayyunin. 2013. Penghambatan Pertumbuhan *Colletotrichum Gloeosporioides* oleh *Trichoderma Harzianum*, *Trichoderma Koningii*, *Bacillus Subtilis* dan *Pseudomonas Fluorescens*. *Jurnal Pelita Perkebunan*. Vol. 29, No. 1, Hal. 44-52.
- Ali MR, Salim Hossain M, Islam MA, Saiful Islam Arman M, Sarwar Raju G, Dasgupta P, dkk. (2014), *Aspect of Thrombolytic Therapy: A Review*. Sci World J.
- Anak Agung Budhiarta. (2007), *Peran Sistem Flbrinolisis pada Berbagai Proses Fisiologis dan Patologis*. Denpasar.
- Andarwulan, N., Kusnandar, F., dan Herawati. (2011), *Analisis Pangan*. Jakarta: Dian Rakyat.
- Anonim (1994), *Difoo Manual of Dehydrated Culture Media and Reagents for Microbiological and Clinical Laboratory Prosedures*. Tenth Edition. Detroit: Michigan USA.
- Apriyantono, A., Fardiaz, D., Puspitasari, N.L., Yasni, S., Budiyanto, S., (1989), *Petunjuk Praktikum Analisi Pangan*. Bogor: IPB Press.
- Arthur, Guyton C, John, Hall E. (1997), *Fisiologi Kedokteran*. Jakarta: Penerbit Buku Kedokteran. EGC
- Ashipala, O. K., He, Q. (2007), Optimization of Fibrinolytic Enzyme Production by *Bacillus Subtilis* DC02 in Aqueous Two-Phase System (Polyethylene Glycol 4000 And Sodium Sulfate). *Biosource Technology*. Vol. 99, Hal. 4112-4119
- Askari, Arman T., Adrian W. Messerli, and A. Michael Lincoff. (2007), *Management Strategies in Antithrombotic Therapy*. Thon Wiley & Sons, LtdThe Atrium, Southern Gate, Chichester, West Sussex PO19 8 SQ. England. 166-162

- Atlas, Ronald M. (2004), *Handbook of Microbiological Media fourth Edition*. Volume 1. United States Of America: CRC Press.
- Bakta, I. M. (2007), *Hematologi Klinik Ringkas*. Jakarta: EGC.
- Becker, rhichard C., and Frederick Spancer. (2006), *Fibrinolytic and Antithrombotic Therapy: Theory, Practice, and Management*. Madison Avenue. New York: Oxford University Press.
- Bin Chen et al (2013). Journal : Isolation and identification of an effective fibrinolytic strain *Bacillus subtilis* FR-33 from the Chinese doufuru and primary analysis of its fibrinolytic enzyme. *African Journal of Microbiology Research*. 2013
- Boyer, R. F. (1993), *Modern Experimental Biochemistry*. Benjamin Cumming Publising Company. California.
- Bradford, M. M. (1976), A Rapid and Sensitive Method for The Quantitation Ofmicrogram Quantities of Protein Utilizing the Principle of Protein-Dye Bending. *Analitical Biochemistry*. Vol. 72 Hal. 248-254.
- Brooks., et al. (2008), *Mikrobiologi Kedokteran*. Ed. 23. Jakarta: EGC.
- Bruce F, Barbara CF. (2008), Mechanisms of Thrombus Formation. *N Engl J Med*. Vol. 359 Hal. 938-949.
- Buku Petunjuk Laboratorium Biosel. (2010), Yogyakarta: UGM
- C. T. Wang, B. P. Ji, B. L. R. Nout, P. L. Li, H. Ji, & L. F. Chen, (2006), Purification and characterization of a fibrinolytic enzyme of *Bacillus subtilis* DC33, isolated from Chinese traditional Douchi," *J. Ind. Microbiol. Biotechnol.* Vol. 33.
- Cheng Tao Wang. et al (2006). Journal : Purification and characterization of a fibrinolytic enzyme of *Bacillus Subtilis* DC33, isolated from Chinese traditional Douchi. *J Ind Microbiol Biotechnol* (2006) 33: 750–758
- Cheng, Guangyan, Liying He, Zhibin Sun, Zhongli Cui, Yingxiang Du, & Yi Kong, (2015), Purification and Biochemical Characterization of a Novel Fibrinolytic Enzim from *Streptomyces* SP. P3. *Journal of Microbiology and Biotechnology*. Vol. 102, Hal. 3279-328.
- Chen-Tien Chang et al (2012). Purification and biochemical properties of a fibrinolityc enyme from *Bacillus subtilis*-fermented red bean. *Journal of elsevier*. 2012
- Choi, Duk Ju., et al. (2008), Physicochemical Characteristics of Black Garlic (*Allium sativum*). *Journal Korean Soc. Food Sci Nutr*, Vol. 37, No. 4, Hal. 465-471.
- Chung, Dong-min, Nack-shick Choi, Pil Jae Maeng, Hyo Kon Chun, and Seung-ho Kim, (2010), Purification and Characterization of a Novel Fibrinolytic

- Enzim from Chive (*Allium tuberosum*). *Food Science Biotechnolog.* Vol. 19, Hal.697-702.
- COLLIN, C.H P. M. LYNE (1987), *Microbiological Method*. Fifth Edition. London: Butterworths.
- Cooper, C. L., & Payne, R. (1994). *Causes, Coping & Consequences of Stress At Work*. USA: John Wiley & Sons, Ltd.
- Cowan, S. T. (2004), *Manual For The Identification Of Medical Fungi*. London: Cambridge University Press.
- Dwidjoseputro, D. (1989), *Dasar-Dasar Mikrobiologi*. Surabaya: Djambatan
- Guyton, A. C. & John E.H. (1997), *Fisiologi Kedokteran Edisi 9*. Editor Bahasa Indonesia Irawati Setiawan. Jakarta: EGC.
- Hadioetomo, R. S. (1993) *Mikrobiologi Dasar dalam praktek: Teknik dan Prosedur Dasar Laboratorium*. PT Gramedia Pustaka Utama.
- Hakim RF, Fakhrurrazi, Wahyuda F. 2016. Pengaruh air rebusan Dun Salam (*Eugenia polyantha wight*) terhadap pertumbuhan *Enterococcus faecalis*. *JDS* 1(1):22-18
- Hatmanti, A. (2000), Pengenalan Bacillus spp. *Oseana*. Vol. 25 No. 1 Hal. 31-41.
- Hidayah N, Baarri ANA, Budiarti C. (2014), Perbedaan pola pengambilan enzim laktoperoksidase dengan menggunakan metode kromatografi. *Jurnal Teknologi Hasil Pertanian*. Vol. 7, No. 1, Hal. 27-30.
- Holt, et al. (1994), *Bergey's Manual of Determinative Bacteriology 9th Edition*. USA: Williams and Wilkins Baltimore.
- Jawetz, E., Melnick, J. L., Adelberg, E. A., 2001, Mikrobiologi Kedokteran, Edisi XXII, diterjemahkan oleh Bagian Mikrobiologi Fakultas Kedokteran Universitas Airlangga, 205-209, Penerbit Salemba Medika, Jakarta
- Jo, Hyon-Deok, Hwang A Lee, Seon-Ju Jeong, and Jeong Hwan Kim (2011) journal : Purification and Characterization of a Major Fibrinolytic Enzyme from *Bacillus amyloliquefaciens* MJ5-41 Isolated from Meju. *J. Microbiol. Biotechnol.* (2011), 21(11), 1166–1173
- K. I. Fayek, & S. T. El-Sayed, (1980), Fibrinolytic activity of an enzyme produced by *Bacillus subtilis*. *Z. Ernaehrwiss.* Vol. 19 Hal. 21-23.
- Khopkar S. (2007), *Konsep Dasar Biokimia*. Jakarta (ID): UI Press.
- Kim, S.H & Choi, N.S. (2000), Purification and Characterization of Subtilisin DJ-4 Secreted by *Bacillus* SP. Strain DJ-4 Screened from DoenJong. Biosci. Biotechnol. Biochem. Vol. 64 Hal. 1722-1725.
- Koes Irianto. (2006), *Mikrobiologi Menguak Dunia Mikroorganisme*. Jilid 2. Jakarta

- Kotb, Essam, (2012), *Fibrinolytic Bacterial Enzymes with Thrombolytic Activity*, London: Springer
- Kotb, Essam, (2013), Activity Assessment of Microbial Fibrinolytic Enzymes. *Applied Microbiology and Biotechnology*. Vol. 97, Hal. 6647-6665
- Kowalak. (2011), *Buku Ajar Patofisiologi*. Jakarta: EGC
- Lay, B. W. (1994), *Analisis Mikroba di Laboratorium*. Jakarta: Raja Grafindo Persada.
- Lowry, O. H., N. J., Rosebrough, A. L., Farr, And R. J. Randall. (1951), *Protein Measurement with The Folin Phenol Reagent*. *J. Biol. Chem.* Hal. 193-265.
- MacFaddin, J.F. (1980), *Biochemical Test for Identification of Medical Bacteria Second Ed. Baltimore*: Wiliams and Wilkins.
- Mahajan, Prafulla M, Shubhada Nayak, and Smita S Lele, (2012), Fibrinolytic Enzime from Newly Isolated Marine Bacterium *Ibacillus subtilins I ICTF-1* : Media Optimization, purification and Characterization. *Journal of Bioscience and Bioengineering*. Vol. 113, Hal. 307-314.
- Martono, H & Kuswardani, RA.T. 2007. *Stroke dan Penatalaksanaannya oleh Internis dalam Buku Ajar Ilmu Penyakit Dalam*. Jakarta: Balai Penerbit FKUI.
- Masruroh H, Ulla DM, Fransisca SN, Vita P. 2018. Analisa kadar lemak dalam susu perah sapi menggunakan gaya sentrifugasi. *METANA* 14(1):25-30
- Medicago AB. 2010. *Phosphate buffered saline* spesification sheet.
- Michos ED, Vasamreddy CR, Becker DM, Yanek LR, Moy TF, Fishman EK, et al. (2005), Women with a low Framingham risk score and a family history of premature coronary heart disease have a high prevalence of subclinical coronary atherosclerosis. *Am Hear J.* Vol. 150 No. 6 Hal. 1276–81.
- Milner, M. Dan Makise, K. (2002), *Natto and Its Active Ingredient Nattokinase A Potent and Safe Thrombolytic Agent*. Alternative and Complementary Therapies.
- Min-ju Ahn et al.(2015). Characterization of a Novel Fibrinolytic Enzyme, BsFA, from *Bacillus subtilis* ZA400 in Kimchi Reveals Its Pertinence to Thrombosis Treatment. *J. microbial. Biotechnol.* 015
- Mitchell, Richard N., (2006), *Buku Saku Dasar Patologis Penyakit Robbins & Cotran*, ed 7 Elsevier Inc., USA.
- Murni SW, Kholisoh SD,. (2011), *Produksi, Karakterisasi, dan Isolasi Lipase dari Aspergillus Niger. Pengembangan Teknologi Kimia untuk Pengolahan Sumber Daya Alam Indonesia*. Hal. 2-5.

- Muttaqin, A & Sari, K, (2009), *Asuhan Keperawatan Perioperatif: Konsep, Proses, Aplikasi*. Jakarta: Salemba Medika.
- Nascimento, Dkk, (2016) Purification of a Fibrinolytic Protease from *Mucor Subtilissimus Ucp 1262* by Aqueous Two-phase Systems. *Journal of Chromatogrphy B: Analytical technologies in the Biomedical and Life Sciences*. Vol. 1025, Hal.16-24.
- Oxoid. (2006), *Manual Oxoid*. Edisi 9. Oxoid Limited: Bandung.
- Pelczar, M.J. & E.C.S. Chan, (1986), *Penterjemah , Ratna Siri Hadioetomo dkk. Dasar-Dasar Mikrobiologi 1*. Jakarta:Universitas Indonesia Press.
- Peng, Young, Xiaojuan Yang, and Yizheng Zhang (2005), Microbial Fibrinolytic Enzimes: an Overview Of Source, Production, Properties, and Thrombolytic Acivity In Vivo. *Applied Microbiology and Biotechnology*. Vol. 69, Hal.126-132.
- Pohl, T. (1990) Concentration of protein removal of salute dalam M.P. Deutscher, Methods of Enzymology: Guide to Protein Purification. Vol. 182. New York. Academic Press.
- Prafulla M. Mahajan, Shubhada Nayak and Smita S. Lele (2012), fibrinolytic enzyme from newly isolated marine bacterium *Bacillus subtilis* ICTF-1 : media optimization, purification and characterization, journal of bioscience and bioengineering. VOL, 113 No. 3, 307-314.
- Priadi G, Fitri S, Fifi A. (2018), Enzim β -galaktosidase dari *Leuconostoc mesenteroides* indigenus: ekstraksi, purifikasi dan karakterisasi. *Jurnal Pros Sem Nas Masy Biodiv Indon*. Vol. 4 No. 2 Hal. 184-189.
- Radji, Maksum. (2010). *Buku Ajar Mikrobiologi Panduan Mahasiswa Farmasi dan Kedokteran*. Jakarta: EGC.
- Reo. Robert A. (2001). *Trust implication for perfomance and efectiveness*. European Journal.
- Rym Agrebi, et al. BSF1 fibrinolityc enzyme from a marine bacterium bacillus subtilis A26; purification, biochemical and characterization. 2009. Elsevier.
- S. H. Wang, C. Zhang, Y. L. Yang, M. Diao, and M. F. Bai, (2008), Screening of a high fibrinolytic enzyme producing strain and characterization of the fibrinolytic enzyme produced from *Bacillus subtilis* LD-8547. *World J. Microbiol. Biotechnol.*, Vol 24
- Sabiston, David C., (1995), *Buku Ajar Bedah*. Jakarta: EGC.
- Sadikin, Mohamad. (2001), *Biokimia Darah*. Jakarta: Widya Medika.

- Saepulloh, Rina SS, Krisna S. 2016. Disentegratin dinding sel mikroba lumpur biologi instalasi pengelolahan air limbah industri kertas secara termo-alkali dan sonkasi. *Jurnal Selulosa* 6(1):1-10
- Safitri, et al (2018)l, *Isolasi Bakteri Penghasil Enzim Protease Bacillus Thuringiensis Irodi Pada Oncom Merah Pasca Fermentasi 24 Jam.* Semarang. FMIPA UNIMUS.
- San-Lang Wang, Ying-Ying Wu and Tzu-Wen Liang. Journal : Purification and biochemical characterization od a nattokinase by conversion of shirmp shell with bacillus subillis TKU007. Elsevier 2011
- Sariningsih, R. (2000), *Produksi Enzim Protease oleh Bacillus subtilis BAC-4.* Bandung. Skripsi. Institut Teknologi Bandung.
- Savitz S, Caplan LR. (2005), Current Concepts Vertebrobasilar Disease. *N Engl J Med.* Vol. 352 Hal. 2618-26.
- Schwartz, Seymour I., (2000) *Intisari prinsip-prinsip Ilmu Bedah.* Jakarta: EGC.
- Scopes, R.K. (1982), *Protein Purification.* New York: Springer Verlag.
- Seong-Bo KimIet et al (2006). Purification and characterization of a fibrinolytic subtilisin-like protease of *Bacillus subtilis* TP-6 from an Indonesian fermented soybean, Tempeh. *J Ind Microbiol Biotechnol* (2006) 33: 436–444
- Setianto B. (2001), *Sindroma Koroner Akut: Patofisiologi. Dalam : Kaligis RWM, Kalim H, Yusak M, Ratnaningsih E, Soesanto AM, Hersunarti M, dkk. eds. Diagnosis dan tata laksana hipertensi, sindrom koroner akut dan gagal jantung.* Jakarta: Balai Penerbit Rumah Sakit Jantung Harapan Kita. Hal. 59-66.
- Shi H. Wang et al (2007). Journal : Screening of a high fibrinolytic enzyme producing strain and characterization of the fibrinolytic enzyme produced from *Bacillus subtilis* LD-8547. *World J Microbiol Biotechnol* (2008) 24:475–482

- Shihai Huang et al (2013). Journal : Biochemical characterisatics of a fibrinolytic enzyme purified from a marine bacterium, bacillus subtilis HQS-3. Elsevier 2013.
- Sholihati AM, Baharuddin M, Santi. (2015), *Produksi dan Uji Aktivitas Enzim Selulasedari Bakteri Bacillus Subtilis*. Al Kimia. Hal. 80-84.
- Soesanto, L. (2008), *Pengantar Pengendalian Hayati Penyakit Tanaman, Suplemen ke Gulma dan Nematoda*. Rajawali Pers.
- Stoica C. (2016) Biochemical test & Method for bacterial Identification; Catalase - Test (*On line*). <http://www.tgw1916.net/Tests/catalase.html>. Diakses tanggal 24 April 2016.
- Suhartono, M.T. (1989), *Enzim dan Bioteknologi*. Bogor: PAU IPB.
- Sumi,Ikeda, Ohsugi, (2009), *Increasingthe Production of Nattokinase and Vitamin K2 in Natto with Dipicolinic Acid, Department of Physiological Chemistry*. Kurashiki University of Science and the Arts, Kurashiki 712-8505, Japan.
- Udjianti, Wajan. (2011), *Keperawatan Kardiovaskular*. Jakarta: Salemba Medika.
- Walsh, G., and D.R. Headon. (1994), *Protein Biotechnology*. New York: John Willey and Sons.
- Waluyo, Lud. (2004), *Mikrobiologi Umum*. Malang. UMM Press.
- WHO, (2011), *Global Atlas on Cardiovascular Disease Prevention And Control*, editor, Shanti Medis, Pekka Pustaka and Bo Norrving, Published by the Word Heart Federation and the Word Stroke Organization
- WHO. (2005), WHO Study on Prevention of Recurrences of Myocardial Infarction and Stroke (WHO-PREMISE). *Bulletin of The World Health Organization*. Vol. 83 No. 11 Hal. 820-828.
- Wilkinson M Judith & Ahern R Nancy. (2013), *Buku Saku Diagnosis Keprawatan*. Jakarta: Penerbit Buku Kedokteran EGC.
- Worp VDB, Gijn VJ. Acute ischemic stroke. *N Engl J Med*. 2007;357:572-9

L

A

M

P

I

R

A

N

Lampiran 1. Gambar alat dan bahan

No	Nama	Gambar
----	------	--------

1	Sonikator	
2	Sentrifugasi	
3	Inkubator	
4	Media Na miring	
5	Media BAP	

6	Syinge	
	Pewarnaan Gram	
	Biakan bakteri	
	Jangka sorong	

Lampiran 2. Perhitungan pelet

no	Tabung kososng (Gram)	Tabung + isi (Gram)	Pelet (Gram)
1	6,380	6,660	0,280
2	6,483	6,817	0,334
3	6,425	6,649	0,224
4	6,399	6,717	0,318
5	6,586	6,895	0,309
6	6,615	6,944	0,329

7	6,443	6,867	0,424
8	6,356	6,602	0,246
9	6,445	6,797	0,352
10	6,586	6,917	0,331
11	6,608	6,835	0,227
12	6,410	6,849	0,439
13	6,444	6,790	0,346
14	6,439	6,762	0,323
15	6,417	6,653	0,236
16	6,441	6,734	0,293
17	6,470	6,715	0,245
18	6,432	6,790	0,358
19	6,516	6,832	0,316
20	6,611	6,881	0,270
21	6,476	6,683	0,207
22	6,452	6,802	0,350
total			6,757