

REFERENCE

1. Choi, J.H., et al., Thrombolytic, anticoagulant and antiplatelet activities of codiase, a bi-functional fibrinolytic enzyme from *Codium fragile*. *Biochimie* **95**, 1266--1277, 2013.
2. Bouma, B.N. & L.O. Mosnier, Thrombin activatable fibrinolysis inhibitor (TAFI) at the interface between coagulation and fibrinolysis. *Pathophysiol. Haemost Thromb.* **33** (5-6), 375--381, 2005.
3. Ariens, R.A.S, Elevated fibrinogen causes thrombosis. *Blood* **117**(18), 4687-4688, 2011.
4. Wang, C.T., et al. Purification and characterization of a fibrinolytic enzyme of *Bacillus subtilis* DC33, isolated from Chinese traditional Douchi. *J Ind Microbiol Biotechnol.* **33**(9), 750--8, 2006.
5. Organization, W.H. The World Health Report 2001. (World Health Organization) 2001.
6. Kotb, E. Activity assessment of microbial fibrinolytic enzymes. *Appl Microbiol Biotechnol.* **97**(15), 6647-6665, 2013.
7. Herrick, S., et al. Fibrinogen. *Int J Biochem Cell B.* **31**(7), 741--746, 1999.
8. Weitz, J.I., et al., Human tissue-type plasminogen activator releases fibrinopeptides A and B from fibrinogen. *J Clin Invest.* **82**(5), 1700, 1988.
9. Doolittle, R.F, Structural aspects of the fibrinogen to fibrin conversion. *Adv Protein Chem.* **27** (1)--109,1973.
10. Lorand, L. Factor XIII: structure, activation, and interactions with fibrinogen and fibrin. *Annal of the New York Aca Sci* **936**(1), 291-311, 2001.
11. Mine, Y. and Shahidi, F. Nutraceutical proteins and peptides in health and disease. CRC Press. 2005.
12. Mihara, H., et al., A novel fibrinolytic enzyme extracted from the earthworm, *Lumbricus rubellus*. *Jpn J Physiol.***41**(3), 461--472, 1991.

13. Kunamneni, A., Abdelghani, T.T. & Ellaiah, P., Streptokinase--the drug of choice for thrombolytic therapy. *J Thromb Thrombolysis* **23**(1), 9--23, 2007.
14. Maizel, A.S., & Bookstein, J.J. Streptokinase, urokinase, and tissue plasminogen activator: pharmacokinetics, relative advantages, and methods for maximizing rates and consistency of lysis. *Cardio Int Radiol.* **9**(5-6), 236--244, 1986.
15. Califf, R.M., et al., Hemorrhagic complications associated with the use of intravenous tissue plasminogen activator in treatment of acute myocardial infarction. *Amer J Med.* **85**(3), 353--359, 1988.
16. Sumi, H., et al., A novel fibrinolytic enzyme (nattokinase) in the vegetable cheese Natto; a typical and popular soybean food in the Japanese diet. *Experientia* **43**(10), 1110--1111, 1987.
17. Wang, C.T., et al., Purification and characterization of a fibrinolytic enzyme of *Bacillus subtilis* DC33, isolated from Chinese traditional Douchi. *J Indus Microbiol Biotechnol.* **33**(9), 750--758, 2006.
18. Simkhada, J.R., et al., Purification, biochemical properties and antithrombotic effect of a novel *Streptomyces* enzyme on carrageenan-induced mice tail thrombosis model. *Thrombosis Res.* **129**(2), 176--182, 2012.
19. Mahajan, P.M., Nayak, S., & Lele, S.S. Fibrinolytic enzyme from newly isolated marine bacterium *Bacillus subtilis* ICTF-1: Media optimization, purification and characterization. *J Biosci Bioeng.* **113**(3), 307--314, 2012.
20. Peng, Y., Yang, X., & Zhang, Y. Microbial fibrinolytic enzymes: an overview of source, production, properties, and thrombolytic activity *in vivo*. *Appl Microbiol Biotechnol.* **69**(2), 126--132, 2005.
21. Bode, C., Runge, M.S., & Smalling, R.W. The future of thrombolysis in the treatment of acute myocardial infarction. *Eur Heart J*, **17**(suppl E), 55--60, 1996.

22. Suzuki, Y., et al., Dietary supplementation of fermented soybean, natto, suppresses intimal thickening and modulates the lysis of mural thrombi after endothelial injury in rat femoral artery. *Life sci*, **73**(10), 1289--1298, 2003.
23. Wong, A.H.K., and Mine, Y., Novel fibrinolytic enzyme in fermented shrimp paste, a traditional Asian fermented seasoning. *J Agri Food Chem*. **52**(4), 980--986, 2004.
24. Collen, D. & Lijnen, H.R., Tissue type plasminogen activator: a historical perspective and personal account. *J Thromb Haemost*. **2**(4), 541--546, 2004.
25. Collen, D.S., Staphylokinase: a potent, uniquely fibrin-selective thrombolytic agent. *Nature Medicine* **4**(3), 279--284, 1998.
26. Duffy, M.J., Urokinase plasminogen activator and its inhibitor, PAI-1, as prognostic markers in breast cancer: from pilot to level 1 evidence studies. *Clin Chem*. **48**(8), 1194--1197, 2002.
27. Marder, V.J. & Novokhatny, V. Direct fibrinolytic agents: biochemical attributes, preclinical foundation and clinical potential. *J Thromb Haemost*. **8**(3), 433--444, 2010.
28. Anderson, J.L., et al. Multicenter reperfusion trial of intravenous anisoylated plasminogen streptokinase activator complex (APSAC) in acute myocardial infarction: controlled comparison with intracoronary streptokinase. *J Ameri Col Cardiol*. **11**(6), 1153--1163, 1988.
29. Jespers, L., et al. Structural and functional basis of plasminogen activation by staphylokinase. *Thromb Haemost*. **81**(4), 479--485, 1999.
30. Thogersen, A.M., et al. High plasminogen activator inhibitor and tissue plasminogen activator levels in plasma precede a first acute myocardial infarction in both men and women: evidence for the fibrinolytic system as an independent primary risk factor. *Circulation* **98**(21), 2241--2247, 1998.
31. Mine, Y., Kwan Wong, A.H., and Jiang, B., Fibrinolytic enzymes in Asian traditional fermented foods. *Food Research Int*. **38**(3), 243-250, 2005.

32. Fitzmaurice, D.A., Blann, A.D., and Lip, G.Y.H., Bleeding risks of antithrombotic therapy. *Bmj* **325**(7368), 828--831, 2002.
33. Pulcinelli, F.M., et al., Inhibition of platelet aggregation by aspirin progressively decreases in long-term treated patients. *J Amer Coll Cardiol.* **43**(6), 979-984, 2004.
34. Schafer, A.I., Antiplatelet therapy. *The Amer J Med.* **101**(2), 199-209, 1996.
35. Cohen, L.S., et al., *Cardiovascular Drugs.* Zaret BL, Moser M, Cohen LS. Heart Book. New York: *Hearst Books*, 283--286, 1992
36. Vassalli, J.D., Sappino, A.P., & Belin, D., The plasminogen activator/plasmin system. *J Clin Invest.* **88**(4), 1067, 1991.
37. Gately, S., et al., The mechanism of cancer-mediated conversion of plasminogen to the angiogenesis inhibitor angiostatin. *Proceedings National Aca Sci.* **94**(20), 10868--10872, 1997.
38. Smith, R.A.G., et al., Fibrinolysis with acyl-enzymes: a new approach to thrombolytic therapy. *Nature*, 1981. 290.
39. Narasaki, R., et al., & Bacilloysin MA., a novel bacterial metalloproteinase that produces angiostatin-like fragments from plasminogen and activates protease zymogens in the coagulation and fibrinolysis systems. *J Biol Chem.* **280**(14), 14278-14287, 2005.
40. Mander, P., et al., A low molecular weight chymotrypsin-like novel fibrinolytic enzyme from *Streptomyces* sp. CS624. *Process Biochem.* **46**(7), 1449--1455, 2011.
41. Mukherjee, A.K., et al. Bafibrinase: A non-toxic, non-hemorrhagic, direct-acting fibrinolytic serine protease from *Bacillus* sp. strain AS-S20-I exhibits *in vivo* anticoagulant activity and thrombolytic potency. *Biochimie* **94** , 1300-1308.2012.
42. Lourdummy, A.J.B. and Murugaian, P., Fibrinolytic Serine Protease Isolated from Earthworm *Lampito mauritii*. 2014.

43. Matsubara, K., et al. A fibrinolytic enzyme from the green alga *Codium latum* activates plasminogen. *Fish Sci.* **68**(2), 455--457, 2002.
44. Deng, Z., et al., Purification and characterization of a novel fibrinolytic enzyme from the polychaete, *Neanthes japonica* (Iznka). *Biores Technol.* **101**(6),1954--1960, 2010.
45. Park, J.W., et al., Purification and characterization of three thermostable alkaline fibrinolytic serine proteases from the polychaete *Cirriformia tentaculata*. *Process Biochem.* **48**(5), 979--987, 2013.
46. Pinto, A.n.F.M., et al. Lonofibrase, a novel $\hat{I}\pm$ -fibrinogenase from *Lonomia obliqua* caterpillars. *Thromb Research* **113**(2), 147--154, 2004.
47. Ahn, M.Y., et al. Purification and characterization of a serine protease with fibrinolytic activity from the dung beetles, *Catharsius molossus*. *Thromb Res.* **112**(5), 339--347, 2003.
48. Fujita, M., et al., Purification and characterization of a strong fibrinolytic enzyme (nattokinase) in the vegetable cheese natto, a popular soybean fermented food in Japan. *Biochem Biophys Res Communi.* **197**(3), 1340-1347, 1993.
49. Choi, H.S., & Shin, H.H., Purification and partial characterization of a fibrinolytic protease in *Pleurotus ostreatus*. *Mycologia*, 674—679, 1998
50. Noh, K.A., et al., Isolation of fibrinolytic enzyme producing strains from kimchi. *Korean Journal of Food Science and Technology* 1999.
51. Chang, C.T., et al., Potent Fibrinolytic Enzyme from a Mutant of *Bacillus subtilis* IMR-NK1. *Journal of Agricultural and Food Chemistry* **48**(8), 3210-3216. 2000.
52. Kim, S.H., and Choi, N.S., Purification and characterization of subtilisin DJ-4 secreted by *Bacillus* sp. strain DJ-4 screened from Doen-Jang. *Biosci. Biotechnol. Biochem.* **64**(8), 1722-1725, 2000.
53. Peng, Y., et al., Purification and characterization of a fibrinolytic enzyme produced by *Bacillus amyloliquefaciens* DC-4 screened from *douchi*, a

- traditional Chinese soybean food. *Comp.Biochem.Physio.B.* **134**(1),45-52, 2003.
54. Ko, J., et al., Subtilisin QK, a Fibrinolytic enzyme, inhibits the exogenous nitrite and hydrogen peroxide induced protein nitration, *in vitro* and *in vivo*. *J Biochem Mol Biol.* **38**(5), 577, 2005.
 55. Seo, J.H., and Lee, S.P., Production of fibrinolytic enzyme from soybean grits fermented by *Bacillus firmus* NA-1. *J Med Food.* **7**(4): p. 442-9, 2004.
 56. Choi, N.S., et al., Purification and characterization of a new peptidase, bacillopeptidase DJ-2, having fibrinolytic activity: produced by *Bacillus* sp. DJ-2 from Doen-Jang. *J Microbiol Biotechnol.* **15**(1), 72--79, 2005.
 57. Kim, S.B., et al., Purification and characterization of a fibrinolytic subtilisin-like protease of *Bacillus subtilis* TP-6 from an Indonesian fermented soybean, Tempeh. *J Indus Microbiol Biotechnol.* **33**(6), 436-444, 2006.
 58. Park, S.E., et al., Purification and characterization of a fibrinolytic protease from a culture supernatant of *Flammulina velutipes* mycelia. *Biosci Biotechnol Biochem.* **71**(9), 2214-2222, 2007.
 59. Wang, S.H., et al., Screening of a high fibrinolytic enzyme producing strain and characterization of the fibrinolytic enzyme produced from *Bacillus subtilis* LD-8547. *World J Microbiol Biotechnol.* **24**(4), 475-482, 2008.
 60. Lu, C.L., Chen, S., and Chen, S.N., Purification and characterization of a novel fibrinolytic protease from *Schizophyllum commune*. *J Food Drug Anal.* **18**(2), 69-76, 2010.
 61. Majumdar, S., et al., Statistical optimization for improved production of fibrin (ogen) olytic enzyme by *Bacillus cereus* strain FF01 and assessment of *in vitro* thrombolytic potential of protease enzyme. *Biocat Agricul Biotechnol.* 2014. *In Press.*
 62. Agrebi, R., et al., Fibrinolytic serine protease isolation from *Bacillus amyloliquefaciens* An6 grown on *Mirabilis jalapa* tuber powders. *Appl Biochem Biotechnol* **162**(1), 75-88, 2010.

63. Jeong, Y.k., et al., Molecular cloning and characterization of the gene encoding a fibrinolytic enzyme from *Bacillus subtilis* strain A1. *World J Microbiol Biotechnol.* **20**(7), 711-717, 2004.
64. Ko, J.H., et al., Identification of two novel fibrinolytic enzymes from *Bacillus subtilis* QK02. *Com Biochem Physiol Part C.* **137**(1), 65-74, 2004.
65. Kho, C.W., et al., Confirmation of Vpr as a fibrinolytic enzyme present in extracellular proteins of *Bacillus subtilis*. *Protein Expre Purifi*, **39**(1),1-7,2005.
66. Choi, N.S., et al., Expression and identification of a minor extracellular fibrinolytic enzyme (Vpr) from *Bacillus subtilis* KCTC 3014. *Biotechnol.Biopro.Eng.* **15**(3), 446-452, 2010.
67. Mahajan, P.M., S.V. Gokhale, and S.S. Lele. Production of nattokinase using *Bacillus natto* NRRL 3666: media optimization, scale up, and kinetic modeling. *Food Sci Biotechnol*, **19**(6),1593-1603, 2010.
68. Liu, J., et al., A simple method for the simultaneous decoloration and deproteinization of crude levan extract from *Paenibacillus polymyxa* EJS-3 by macroporous resin. *Biores Technol.* **101**(15),6077-6083,2010.
69. Hassanein, W.A., et al., Fibrinolysis and anticoagulant potential of a metallo protease produced by *Bacillus subtilis* K42. *J Biosci.* **36**(5), 773-779, 2011.
70. Choi, N.S., et al., Purification and characterization of a novel thermoacid-stable fibrinolytic enzyme from *Staphylococcus* sp. strain AJ isolated from Korean salt-fermented Anchovy-joet. *J Indus Microbiol Biotechnol.* **36**(3), 417-426, 2009.
71. Egorov, N.S., G.A. Kochetov, and N.V. KhaÄ-darova, Isolation and properties of the fibrinolytic enzyme from the *Actinomyces thermovulgaris* cultural broth. *Mikrobiologiia*, **45**, 455-459,1975.
72. Egorov, N.S., et al. [Streptomyces spheroides M8-2 strain--a producer of extracellular proteolytic enzymes possessing fibrinolytic and thrombolytic action]. in Nauchnye doklady vysshei shkoly. *Biologicheskie nauki.* 1984.

73. Chitte, R.R. and S. Dey, Potent fibrinolytic enzyme from a thermophilic *Streptomyces megasporus* strain SD5. *Lett in Applied Microbiol.* **31**(6), 405-410, 2000.
74. Simkhada, J.R., et al., A novel fibrinolytic protease from *Streptomyces sp. CS684*. *Process Biochem.* **45**(1), 88-93, 2010.
75. El-Aassar, S.A., H.M. El-Badry, and A.F. Abdel-Fattah, The biosynthesis of proteases with fibrinolytic activity in immobilized cultures of *Penicillium chrysogenum H9*. *Appl. Microbiol Biotechnol.* **33**(1), 26-30, 1990.
76. Samy, A., Production and properties of fibrinolytic enzyme in solid state cultures of *Fusarium pallidoroseum*. *Biotechnology letters*, **17**(9), 943-948, 1995.
77. Batomunkueva, B.P. and N.S. Egorov, Isolation, Purification, and Resolution of the Extracellular Proteinase Complex of *Aspergillus ochraceus* 513 with Fibrinolytic and Anticoagulant Activities. *Microbiology*, **70**(5), 519-522, 2010.
78. Xiao-Lan, L., et al., Purification and characterization of a novel fibrinolytic enzyme from *Rhizopus chinensis* 12. *Appl Microbiol Biotechnol.* **67**(2), 209-214, 2005.
79. Ueda, M., et al., Purification and characterization of fibrinolytic alkaline protease from *Fusarium sp. BLB*. *Appl Microbiol Biotechnol*, **74**(2), 331-338, 2007.
80. Wu, B., et al., Purification and characterization of a novel fibrinolytic protease from *Fusarium sp. CPCC 480097*. *J Indus Microbiol Biotechnol*, **36**(3), 451-459, 2009.
81. Matsubara, K., et al., A fibrinolytic enzyme from a marine green alga, *Codium latum*. *Phytochemistry*, **52**(6), 993-999, 1999.
82. Matsubara, K., et al., Purification and characterization of a fibrinolytic enzyme and identification of fibrinogen clotting enzyme in a marine green alga, *Codium divaricatum*. *Comp Biochem Physiol part B.* **125**(1), 137-143, 2000.

83. Montriwong, A., et al., Novel fibrinolytic enzymes from *Virgibacillus halodenitrificans* SK1-3-7 isolated from fish sauce fermentation. *Process Biochem.* **47**(12), 2379-2387, 2012.
84. Gad, R.G., fibrinolytic enzyme from bacillus amyloliquefaciens: optimisation and scale up studies. *Int J Pharma and Pharma Sci.* 2014.
85. Zeng, W., et al., Non-sterilized fermentative co-production of poly ($\hat{\Gamma}$ -glutamic acid) and fibrinolytic enzyme by a thermophilic *Bacillus subtilis* GXA-28. *Biores Technol.* **142**, 697--700, 2013.
86. Mukherjee, A.K., et al., Bafibrinase: A non-toxic, non-hemorrhagic, direct-acting fibrinolytic serine protease from *Bacillus sp.* strain AS-S20-I exhibits *in vivo* anticoagulant activity and thrombolytic potency. *Biochimie*, **94**(6), 1300--1308, 2012.
87. Mukherjee, A.K. and S.K. Rai, A statistical approach for the enhanced production of alkaline protease showing fibrinolytic activity from a newly isolated Gram-negative *Bacillus sp.* strain AS-S20-I. *N Biotechnol*, **28**(2), 182--189, 2011.
88. Bajaj, B.K., N. Sharma, and S. Singh, Enhanced production of fibrinolytic protease from *Bacillus cereus* NS-2 using cotton seed cake as nitrogen source. *Biocatal Agri Biotechnol.* **2**(3), 204--209, 2013.
89. Majumdar, S., et al., Characterization, mechanism of anticoagulant action, and assessment of therapeutic potential of a fibrinolytic serine protease (Brevithrombolase) purified from *Brevibacillus brevis* strain FF02B. *Biochimie*, **103**, 50--60, 2014.
90. Kim, W., et al., Purification and characterization of a fibrinolytic enzyme produced from Bacillus sp. strain CK 11-4 screened from Chungkook-Jang. *Appl Environ Microbiol.* **62**(7), 2482--2488, 1996.
91. Govind, N.S., et al., Protease and carotenogenesis in *Blakeslea trispora*. *Phytochemistry*, **20**(11), 2483-2485, 1981.

92. Choi, J.H., et al., Thrombolytic, anticoagulant and antiplatelet activities of codiase, a bi-functional fibrinolytic enzyme from *Codium fragile*. *Biochimie*, **95**(6), 1266--1277, 2013.
93. Si-Kyung, L., et al., Purification and characterization of a fibrinolytic enzyme from *Bacillus* sp. KDO-13 isolated from soybean paste. *J Microbiol. Biotechnol*, **11**(5), 845--852
94. Fricke, B., et al., Characterization and purification of an outer membrane metalloproteinase from *Pseudomonas aeruginosa* with fibrinogenolytic activity. *Biochimica et Biophysica Acta (BBA)*, **1454**(3), 236--250, 1999.
95. Nakamura, T., Y. Yamagata, and E. Ichishima, Nucleotide sequence of the subtilisin NAT gene, aprN, of *Bacillus subtilis* (natto). *Biosci Biotechnol Biochem*, **56**(11), 1869--1871, 1992.
96. Peng, Y., et al., Cloning and expression of a fibrinolytic enzyme (subtilisin DFE) gene from *Bacillus amyloliquefaciens* DC-4 in *Bacillus subtilis*. *Research in Microbiol*. **155**(3), 167--173. 2004.
97. Beldarrañ-n, A., et al., Multidomain structure of a recombinant streptokinase. A differential scanning calorimetry study. *Journal of Protein Chemistry*, **20**(1), 9--17, 2001.
98. Wang, S.-L., et al., Purification and characterization of protease and chitinase from *Bacillus cereus* TKU006 and conversion of marine wastes by these enzymes. *Marine Biotechnology*, **11**(3), 334--344, 2009.
99. Lu, F., et al., Purification and characterization of a novel anticoagulant and fibrinolytic enzyme produced by endophytic bacterium *Paenibacillus polymyxa* EJS-3. *Thrombosis Res*. **126**(5), e349--e355, 2010.
100. Huang, S., et al., Biochemical characteristics of a fibrinolytic enzyme purified from a marine bacterium, *Bacillus subtilis* HQS-3. *Int J Biol Macromol*, **62**, 124--130, 2013.
101. Kotb, E., Purification and partial characterization of a chymotrypsin-like serine fibrinolytic enzyme from FCF-11 using corn husk as a novel substrate. *World J Microbiol Biotechnol*, **30**(7), 2071--2080, 2014. *In press*.

102. Afifah, D.N., M. Sulchan, and D. Syah, Purification and Characterization of a Fibrinolytic Enzyme from *Bacillus pumilus* 2. g Isolated from Gembus, an Indonesian Fermented Food. *Preventive Nutrition and Food Sci.* **19**(3), 213, 2014.
103. Kotb, E., Purification and partial characterization of serine fibrinolytic enzyme from *Bacillus megaterium* KSK-07 isolated from kishk, a traditional Egyptian fermented food. *Appl Biochem Microbiol.* **51**(1),34-43,2014
104. Kotb, E., The biotechnological potential of subtilisin •like fibrinolytic enzyme from a newly isolated *Lactobacillus plantarum* KS • II in blood destaining and antimicrobials. *Biotechnol progress*, 2014 (*In press*).
105. Jeong, S.J., et al., Characterization of AprE176, a Fibrinolytic Enzyme from *Bacillus subtilis* HK176. *J Microbiol Biotechnol*, **25**(1),89-97, 2015.
106. Niles, A.L., R.A. Moravec, and T.L. Riss, Update on *in vitro* cytotoxicity assays for drug development. 2008.
107. Mukherjee, A.K. and S.P. Mackessy, Biochemical and pharmacological properties of a new thrombin-like serine protease (Russelobin) from the venom of Russell's Viper (*Daboia russelii russelii*) and assessment of its therapeutic potential, *Biochim.Biophys.Acta.* **1830**, 3476--3488, 2013.
108. Mukherjee, A.K., The pro-coagulant fibrinogenolytic serine protease isoenzymes purified from *Daboia russelii russelii* venom coagulate the blood through Factor V activation:Role of glycosylation on enzymatic activity. *PloS One*, **9**(2), e86823, 2014.
109. LaFollette, H., and Shanks, N., Two models of models in biomedical research. *The Philosophical Quarterly*, 141--160, 1995.
110. Markland, F.S., and Swenson, S., Fibrolase:trials and tribulations. *Toxins*, **2**(4), 793--808, 2011.
111. Hung, C.C., and Chiou, S.H., Fibrinogenolytic proteases isolated from the snake venom of Taiwan Habu: serine proteases with kallikrein-like and angiotensin-degrading activities. *Biochem Biophys Res Comm.* **281**(4), 1012--1018, 2001.

112. Sumi, H., N. Nakajima, and C. Yatagai, A unique strong fibrinolytic enzyme (katsuwokinase) in skipjack Shiokara a Japanese traditional fermented food. *Comp Biochem and Physiol part B*. **112**(3), 543--547, 1995.
113. Verstraete, M., et al., Thrombolytic therapy with streptokinase using a standard dosage scheme. *Brit Medical J.*, **1**(5485), 454, 1966.
114. Yan, F., et al., Thrombolytic effect of Subtilisin QK on carrageenan induced thrombosis model in mice. *J Thromb Thrombol.* **28**(4) 444--448, 2009.
115. Szemraj, J., et al., New derivative of staphylokinase SAK-RGD-K2-Hirul exerts thrombolytic effects in the arterial thrombosis model in rats. *Pharmaco. Reports*, **63**(5), 1169--1179, 2011.
116. Yuan, J., et al., Thrombolytic effects of Douchi Fibrinolytic enzyme from *Bacillus subtilis* LD-8547 *in vitro* and *in vivo*. *BMC Biotechnol.* **12**(1), 36, 2012.
117. Xu, J., et al., Thrombolytic effects *in vivo* of Nattokinase in a carrageenan-induced rat model of thrombosis. *Acta Haematol.*, **132**(2), 247--253, 2014.
118. Rovati, J.I., et al., A novel source of fibrinolytic activity: *Bionectria* sp., an unconventional enzyme-producing fungus isolated from Las Yungas rainforest (Tucumin, Argentina). *World J Microbiol Biotechnol.* **26**(1), 55-62, 2010.
119. Joo, M.H., et al., Isolation, identification, and characterization of *Bacillus* strains from the traditional Korean soybean-fermented food, Chungkookjang. *J Appl Biol Chem*, **50**, 202--210, 2007.
120. Rai, S.K., J.K. Roy, and A.K. Mukherjee, Characterisation of a detergent-stable alkaline protease from a novel thermophilic strain *Paenibacillus tezpurensis* sp. nov. AS-S24-II. *Appl Microbiol Biotechnol.* **85**(5), 1437--1450, 2010.
121. Tamura, K., et al., *MEGA4*: Molecular evolutionary genetics analysis (MEGA) software version 4.0. *Mol Biol Evol.* **24**(8), 1596--1599, 2007.

122. Das, K. and A.K. Mukherjee, Characterization of biochemical properties and biological activities of biosurfactants produced by *Pseudomonas aeruginosa* mucoid and non-mucoid strains isolated from hydrocarbon-contaminated soil samples. *Appl Microbiol Biotechnol.* **69**(2), 192--199, 2005.
123. Weisburg, W.G., et al., 16S ribosomal DNA amplification for phylogenetic study. *J Bacteriol*, **173**(2), 697--703, 1991.
124. Saitou, N., and Nei M., The neighbor-joining method: a new method for reconstructing phylogenetic trees. *Mol Biol Evol*, **4**(4), 406--425, 1987.
125. Laemmli, U.K., Cleavage of structural proteins during the assembly of the head of bacteriophage T4. *Nature*, **227**(5259), 680--685, 1970.
126. Kim, S.H., N.S. Choi, and W.Y. Lee, Fibrin zymography: a direct analysis of fibrinolytic enzymes on gels. *Anal Biochem.* **263**(1),115, 1998.
127. Mukherjee, A.K., Characterization of a novel pro-coagulant metalloprotease (RVBCMP) possessing $\alpha\beta$ -fibrinogenase and tissue haemorrhagic activity from venom of *Daboia russelli russelli* (Russell's viper): Evidence of distinct coagulant and haemorrhagic sites in RVBCMP. *Toxicon*, **51**(5), 923--933, 2008.
128. Lowry, O.H., et al., Protein measurement with the Folin phenol reagent. *J Biol Chem*, **193**(1), 265--275, 1951.
129. Dubois, M., et al., Colorimetric method for determination of sugars and related substances. *Anal Chem.* **28**(3), 350--356, 1956.
130. Roucher, V.r.F., et al., Use of UPLC-ESI-MS/MS to quantitate free amino acid concentrations in micro-samples of mammalian milk. *Springer Plus*, **2**(1), 1--11, 2013.
131. Golaz, O., et al., Identification of proteins by their amino acid composition: an evaluation of the method. *Electrophoresis* **17**(3), 573--579, 1996.
132. Doley, R., King G.F., and Mukherjee A.K., Differential hydrolysis of erythrocyte and mitochondrial membrane phospholipids by two phospholipase A₂ isoenzymes (NK-PLA₂-I and NK-PLA₂-II) from the

- venom of the Indian monocled cobra *Naja kaouthia*. *Arch Biochem Biophys.* 425 ,1--13,2004.
133. Mukherjee, A.K., et al., Characterization of a pro-angiogenic, novel peptide from Russell's viper (*Daboia russelii russelii*) venom. *Toxicon*, 277, 26--31.
 134. Saikia, D., Thakur, R., and Mukherjee, A.K., An acidic phospholipase A₂ (RVVA-PLA₂-I) purified from *Daboia russelii* venom exerts its anticoagulant activity by enzymatic hydrolysis of plasma phospholipids and by non-enzymatic inhibition of factor Xa in a phospholipids/Ca²⁺ independent manner. *Toxicon*, **57**(2011), 841--850.
 135. Horn, F., P.Ì.c. Coutinho dos Santos, and Termignoni, C., *Boophilus microplus*. Anticoagulant Protein: An Antithrombin Inhibitor Isolated from the Cattle Tick Saliva. *Archives of Biochemistry and Biophysics*, **384**(1), 68--73, 2000.
 136. Hagimori, M., et al., Improving frequency of thrombosis by altering blood flow in the carrageenan-induced rat tail thrombosis model. *Pharmacol Res.* **60**(4), 320--323, 2009.
 137. Geng, P., et al., A novel fibrin(ogen)olytic trypsin-like protease from Chinese oak silkworm (*Antheraea pernyi*): Purification and characterization. *Biochem. Biophys. Res Commu.* 2014 *In press*
 138. Hull, R.D., et al., Relation between the time to achieve the lower limit of the APTT therapeutic range and recurrent venous thromboembolism during heparin treatment for deep vein thrombosis. *Archi Int Med.***157**(22), 2562--2568.
 139. Weisel, J.W., Fibrinogen and fibrin. *Adv Prot Chem.***70**, 247--299, 2005.
 140. Pola, P., et al., Role of Fibrinogen as a Vascular Risk Factor in Atherogenesis and Thrombogenesis, in Textbook of Angiology., *Springer.* 419--426, 2000.
 141. Sahni, A., et al., Fibrinogen synthesized by cancer cells augments the proliferative effect of fibroblast growth factor2 (FGF2). *J Thromb Haemost.* **6**(1), 176-183, 2008.

142. Swenson, S. and F.S. Markland, Snake venom fibrin (ogen) olytic enzymes. *Toxicon*, **45**(8), 1021--1039, 2005.
143. Menaldo, D.L., et al., Biochemical characterization and comparative analysis of two distinct serine proteases from *Bothrops pirajai* snake venom. *Biochimie*, **94**(12), 2545--2558, 2012.
144. Sumi, H., et al., A novel fibrinolytic enzyme (nattokinase) in the vegetable cheese Natto; a typical and popular soybean food in the Japanese diet. *Experientia*, **43**(10), 1110--1111, 1987.
145. Page, M.J. and E. Di Cera, Evolution of peptidase diversity. *J Biol Chem*. **283**(44), 30010-30014, 2008.
146. Larcher, G.r., et al., Purification and characterization of a fibrinogenolytic serine proteinase from *Aspergillus fumigatus* culture filtrate. *FEBS lett*, **308**(1), 65--69, 1992.
147. Kotiranta, A., K. Lounatmaa, and M. Haapasalo, Epidemiology and pathogenesis of *Bacillus cereus* infections. *Microbes and Infec*. **2**(2),189--198, 2002.
148. Gupta, R., Q. Beg, and P. Lorenz, Bacterial alkaline proteases: molecular approaches and industrial applications. *Appl Microbiol Biotechnol*. **59**(1), 15--32, 2002.
149. Swenson, S., and Markland F.S., Jr, Snake venom fibrin(ogen)olytic enzymes. *Toxicon*, **45**(8), 1021--1039, 2005.
150. Mansiaux, Y., et al., Assignment of PolyProline II Conformation and Analysis of Sequence Structure Relationship. *PLoS One*. **6**(3), e18401, 2011
151. Mukhametova, L.I., AÄ-sina, R.B., and Varfolomeev, S.D. Characterization of urokinase type plasminogen activator modified by phenylglyoxal. *Bioorganicheskaia khimiia*, **28**(4), 308-314, 2001.
152. Reutter, W., et al. The biology of sialic acids: insights into their structure, metabolism and function in particular during viral infection. *Glycosciences, Status and Perspectives*, 245--259, 1997.

153. Rai, S.K. and Mukherjee, A.K., Statistical optimization of production, purification and industrial application of a laundry detergent and organic solvent-stable subtilisin-like serine protease (Alzwiprase) from *Bacillus subtilis* DM-04. *Biochem Eng J*, **48**(2), 173--180, 2010.
154. Lopez-Sendon, J., et al., Cardiovascular pharmacology (XIII). The efficacy of different thrombolytic drugs in the treatment of acute myocardial infarct. *Rev.Esp. Cardiol.* **48**, 407, 1995.
155. Hirsh, J., et al. Heparin: mechanism of action, pharmacokinetics, dosing considerations, monitoring, efficacy, and safety. *Chest J.* **108**(4), 258S--275S, 1995.
156. Hirsh, J., et al. Oral anticoagulants: mechanism of action, clinical effectiveness, and optimal therapeutic range. *Chest J.* **119**(1), 8S--21S, 2001.
157. Kamath, S., Blann, A.D., and Lip, G.Y.H., Platelet activation: assessment and quantification. *Eur Heart J.* **22**(17), 1561--1571, 2001.
158. Ohlmann, P., et al., ADP induces partial platelet aggregation without shape change and potentiates collagen-induced aggregation in the absence of Galphaq. *Blood*, **96**(6), 2134--2139, 2000.
159. Clemetson, K.J. and Clemetson, J.M., Platelet collagen receptors. *Thrombo and Haemost*, **86**(1),189--197, 2001.
160. Gasmi, A., et al., Further characterization and thrombolytic activity in a rat model of a fibrinogenase from *vipera lebetina* venom. *Thrombo Res.* **86**(3), 233--242,1997.
161. Yong Hong, J.I.A., et al. Jerdonase, a novel serine protease with kinin-releasing and fibrinogenolytic activity from *Trimeresurus jerdonii* venom. *Acta Biochem.* **35**, 689--694, 2003.
162. Wong, S.L., et al., The subtilisin E gene of *Bacillus subtilis* is transcribed from a sigma 37 promoter *in vivo*. Proceedings of the National Academy of Sciences, **81**(4),1184--1188, 1984.

163. Metwalli, A.A.M., de Jongh, H.H.J., and van Boekel, M.A.J.S., Heat inactivation of bovine plasmin. *Int Dairy J.* **8**(1), 47--56, 1998.
164. Dell, A., et al. Similarities and differences in the glycosylation mechanisms in prokaryotes and eukaryotes. *Int J Microbiol.* 2010.
165. Alkjaersig, N., Fletcher, A.P., and Sherry, S., The mechanism of clot dissolution by plasmin. *J Clin Invest.* **38**(7), 1086, 1959.
166. Smith, E.L., et al. Subtilisin Carlsberg V., The complete sequence; comparison with subtilisin BPN'; evolutionary relationships. *J Biol chem.* **243**(9), 2184-2191, 1968.
167. Takahashi, M., et al. The production of recombinant APRP, an alkaline protease derived from *Bacillus pumilus* TYO-67, by in vitro refolding of pro-enzyme fixed on a solid surface. *J Biochem.* **136**(4), 549-556, 2004.
168. Saikia, D., S. Majumdar, and A.K. Mukherjee, Mechanism of *in vivo* anticoagulant and hemolytic activity by a neutral phospholipase A₂ purified from *Daboia russelii russelii* venom: correlation with clinical manifestations in Russell's viper envenomed patients, *Toxicon*, **79**,291-300, 2013.
169. Bode, W., Structure and interaction modes of thrombin. *Blood Cell Mol Dis* **36**(2), 122-130, 2006.
170. Armstrong, P.W., Pharmacotherapy: Intracoronary streptokinase in acute myocardial infarction. *Nature Reviews Cardiol.* **7**(2), 67-69, 2013.
171. Marder, V.J., et al. Thrombolysis with Plasmin Implications for Stroke Treatment. *Stroke* **41**(10), S45--S49, 2010.
172. Bekemeier, H., Hirschelmann, R., and Giessler, A.J., Carrageenin-induced thrombosis in the rat and mouse as a test model of substances influencing thrombosis. *Biomed Biochim Acta.* **43**(8--9), S347-50, 1983.
173. Chan, K.c., Yin, M.c. & Chao, W.j. Effect of diallyl trisulfide-rich garlic oil on blood coagulation and plasma activity of anticoagulation factors in rats. *Food Chem Toxicol.* **45**(3), 502--507, 2007.

174. Agero, U., et al., The thrombolytic action of a proteolytic fraction (PIG10) from *Carica candamarcensis*. *Thromb Res.* **131**(4),e175-e182, 2013.
175. Agnelli, G., et al., Effects of therapeutic doses of heparin on thrombolysis with tissue-type plasminogen activator in rabbits. *Blood*, **76**(10), 2030-2036, 1990.