

## Bibliography

1. Pu, X.C.et al. A novel analgesic toxin (hannalgesin) from the venom of king cobra (Ophiophagus hannah), *Toxicon* **33** (11), 1425-1431, 1995.
2. Sudarshan, S., & Dhananjaya, B.L. Antibacterial activity of an acidic phospholipase A2 (NN-XIb-PLA2) from the venom of Naja naja (Indian cobra), *Springerplus*. **5** (112), 1-7, 2016.
3. Prinholato, d.S.et al. Antitumor potential of the myotoxin BthTX-I from Bothrops jararacussu snake venom: evaluation of cell cycle alterations and death mechanisms induced in tumor cell lines, *J Venom. Anim Toxins. Incl. Trop. Dis.* **21** 44, 2015.
4. Sabatier, J.M. Animal venoms: from deadly arsenals (toxins) to therapeutic drug candidates, *Inflamm. Allergy Drug Targets.* **10** (5), 312, 2011.
5. Lewis, R.J., & Garcia, M.L. Therapeutic potential of venom peptides, *Nat Rev Drug Discov* **2** (10), 790-802, 2003.
6. Meier, J. Venomous Snakes, in *Medical use of snake venom proteins*, Stocker, K. F., editor; CRC Press: Basel, Switzerland, 1990, 1-32.
7. Rial, R.V.et al. Evolution of wakefulness, sleep and hibernation: from reptiles to mammals, *Neurosci. Biobehav. Rev.* **34** (8), 1144-1160, 2010.
8. Sivan, J.et al. Temporal activity and dietary selection in two coexisting desert snakes, the Saharan sand viper (*Cerastes vipera*) and the crowned leafnose (*Lytorhynchus diadema*), *Zoology. (Jena)* **116** (2), 113-117, 2013.
9. Whitaker, R.; Captain, A. *Snakes of India: The field guide.*; Draco Books: Chennai, 2004.
10. Alibardi, L. Differentiation of snake epidermis, with emphasis on the shedding layer, *J Morphol.* **264** (2), 178-190, 2005.
11. Spinner, M.et al. Snake velvet black: hierarchical micro- and nanostructure enhances dark colouration in *Bitis rhinoceros*, *Sci. Rep.* **3** (1846), 1-8, 2013.
12. Spinner, M.et al. Non-contaminating camouflage: multifunctional skin microornamentation in the West African Gaboon viper (*Bitis rhinoceros*), *PLoS. ONE.* **9** (3), e91087, 2014.
13. Miller, A.K.et al. An ambusher's arsenal: chemical crypsis in the puff adder (*Bitis arietans*), *Proc. Biol Sci.* **282** (1821), 2015.
14. Feldman, A.et al. The geography of snake reproductive mode: a global analysis of the evolutionof snake viviparity, *Global Ecology and Biogeography* **24** 1433-1442, 2015.
15. Shine, R. Evolution of an evolutionary hypothesis:a history of changing ideas about the adaptive signifcanceof viviparity in reptiles, *Journal of Herpetology* **48** 147-161, 2014.
16. Shine, R. *Reproductive strategies in snakes*; 2003; pp. 995-1004.
17. Collins, J. T.; Conant, R. *A Field Guide to Reptiles and Amphibians: Eastern and Central North America (Peterson Field Guides)*; 3 ed.; Houghton Mifflin Harcourt: Boston, 1998.
18. Marvi, H.et al. Sidewinding with minimal slip: snake and robot ascent of sandy slopes, *Science* **346** (6206), 224-229, 2014.
19. Maddock, S.T.et al. A new species of death adder (Acanthophis: Serpentes: Elapidae) from north-western Australia, *Zootaxa* **4007** (3), 301-326, 2015.

20. Huang, S.et al. What are the closest relatives of the hot-spring snakes (Colubridae, Thermophis), the relict species endemic to the Tibetan Plateau?, *Mol Phylogenet. Evol* **51** (3), 438-446, 2009.
21. Tan, T.L.et al. Bitten by the "flying" tree snake, Chrysopela paradisi, *J Emerg. Med.* **42** (4), 420-423, 2012.
22. Pyron, R.A.et al. The phylogeny of advanced snakes (Colubroidea), with discovery of a new subfamily and comparison of support methods for likelihood trees, *Mol Phylogenet. Evol* **58** (2), 329-342, 2011.
23. Pawlak, J.et al. Denmotoxin, a three-finger toxin from the colubrid snake Boiga dendrophila (Mangrove Catsnake) with bird-specific activity, *J. Biol. Chem.* **281** (39), 29030-29041, 2006.
24. Urdaneta, A.H.et al. Feeding behavior and venom toxicity of coral snake Micrurus nigrocinctus (Serpentes: Elapidae) on its natural prey in captivity, *Comp Biochem. Physiol C. Toxicol. Pharmacol.* **138** (4), 485-492, 2004.
25. Greene, H.W., & Burghardt, G.M. Behavior and phylogeny: constriction in ancient and modern snakes, *Science* **200** (4337), 74-77, 1978.
26. Kardong, K.V. Colubrid snakes and duvernoy's venom glands, *Journal of Toxicology: Toxin Reviews* **21** (2), 1-19, 2002.
27. Shine, R. *Australian Snakes: A Natural History*; Cornell University Press: Ithaca, 1995.
28. McCue, M.D. Cost of Producing Venom in Three North American Pitviper Species, *Copeia* **2006** (4), 818-825, 2006.
29. Pintor, A.F.V.et al. Costs of venom production in the common death adder (Acanthophis antarcticus), *Toxicon* **56** (6), 1035-1042, 2010.
30. Smith, M.T.et al. Metabolic cost of venom replenishment by Prairie Rattlesnakes (Crotalus viridis viridis), *Toxicon* **86** 1-7, 2014.
31. Hider, R. C.; Karlsson, E.; Namiranian, S. Separation and Purification of Toxins from Snake Venom, in *Snake Toxins*, Harvey, A. L., editor; Pergamon Press Inc: New York, USA, 1991, 1-34.
32. Freitas, M.A.et al. Citrate is a major component of snake venoms, *Toxicon* **30** (4), 461-464, 1992.
33. Odell, G.V.et al. The role of venom citrate, *Toxicon* **37** (3), 407-409, 1999.
34. Friederich, C., & Tu, A.T. Role of metals in snake venoms for hemorrhagic, esterase and proteolytic activities, *Biochem. Pharmacol.* **20** (7), 1549-1556, 1971.
35. Kordis, D., & Gubensek, F. Adaptive evolution of animal toxin multigene families, *Gene* **261** (1), 43-52, 2000.
36. Menez, A. Functional architectures of animal toxins: a clue to drug design?, *Toxicon* **36** (11), 1557-1572, 1998.
37. Prasad, B.N.et al. A platelet aggregation inhibitor phospholipase A2 from Russell's viper (Vipera russelli) venom: isolation and characterization, *Toxicon* **34** (10), 1173-1185, 1996.
38. Faure, G., & Bon, C. Several isoforms of crot toxin are present in individual venoms from the South American rattlesnake Crotalus durissus terrificus, *Toxicon* **25** (2), 229-234, 1987.
39. 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.

40. Fry, B.G.et al. Early evolution of the venom system in lizards and snakes, *Nature* **439** (7076), 584-588, 2006.
41. Fry, B.G.et al. Evolution of an arsenal: structural and functional diversification of the venom system in the advanced snakes (Caenophidia), *Mol. Cell Proteomics.* **7** (2), 215-246, 2008.
42. Fry, B.G.et al. The toxicogenomic multiverse: convergent recruitment of proteins into animal venoms, *Annu. Rev. Genomics Hum. Genet.* **10** 483-511, 2009.
43. Wong, E.S., & Belov, K. Venom evolution through gene duplications, *Gene* **496** (1), 1-7, 2012.
44. Fry, B.G.et al. The structural and functional diversification of the Toxicofera reptile venom system, *Toxicon* **60** (4), 434-448, 2012.
45. Cheng, A.C.et al. A novel heparin-dependent inhibitor of activated protein C that potentiates consumptive coagulopathy in Russell's viper envenomation, *J. Biol. Chem.* **287** (19), 15739-15748, 2012.
46. Kini, R.M. Excitement ahead: structure, function and mechanism of snake venom phospholipase A2 enzymes, *Toxicon* **42** (8), 827-840, 2003.
47. Bon, C. Multicomponent neurotoxic phospholipases A<sub>2</sub>, in *Phospholipase A2 Enzyme: Structure, Function and Mechanism*, Kini, R. M., editor; John Wiley & Sons: Chichester, England, 1997, 269-285.
48. Nakayama, D.et al. Structural basis of coagulation factor V recognition for cleavage by RVV-V, *FEBS Lett.* **585** (19), 3020-3025, 2011.
49. Phillips, D. J.; Swenson, S.; Markland, F. S. Thrombin like snake venom serine proteinases, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 139-154.
50. Fox, J.W., & Serrano, S.M. Structural considerations of the snake venom metalloproteinases, key members of the M12 reprolysin family of metalloproteinases, *Toxicon* **45** (8), 969-985, 2005.
51. Du, X.Y., & Clemetson, K.J. Snake venom L-amino acid oxidases, *Toxicon* **40** (6), 659-665, 2002.
52. Chen, H.S.et al. Cloning, characterization and mutagenesis of Russell's viper venom L-amino acid oxidase: Insights into its catalytic mechanism, *Biochimie* **94** (2), 335-344, 2012.
53. Dhananjaya, B. L.; Vishwanath, B. S.; D'Souza, C. J. Snake venom nucleases, nucleotidase and phosphomonoesterases, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 155-172.
54. Aird, S.D. Ophidian envenomation strategies and the role of purines, *Toxicon* **40** (4), 335-393, 2002.
55. Kemparaju, K.; Girish, K. S.; Nagaraju, S. Hyaluronidases, a neglected class of glycosidases from snake venom, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 287-302.
56. Kudo, K., & Tu, A.T. Characterization of hyaluronidase isolated from *Agkistrodon contortrix contortrix* (Southern Copperhead) venom, *Arch. Biochem. Biophys.* **386** (2), 154-162, 2001.
57. Ahmed, M.; Rocha, J. B. T.; Morsch, V. M.; Schetinger, M. R. C. Snake venom acetylcholinesterase, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 207-220.

58. Hill, R.E., & Mackessy, S.P. Characterization of venom (Duvernoy's secretion) from twelve species of colubrid snakes and partial sequence of four venom proteins, *Toxicon* **38** (12), 1663-1687, 2000.
59. Tsetlin, V. Snake venom alpha-neurotoxins and other 'three-finger' proteins, *Eur. J. Biochem.* **264** (2), 281-286, 1999.
60. Pahari, S. et al. Expression pattern of three-finger toxin and phospholipase A2 genes in the venom glands of two sea snakes, *Lapemis curtus* and *Acalyptophis peronii*: comparison of evolution of these toxins in land snakes, sea kraits and sea snakes, *BMC. Evol. Biol.* **7** 175, 2007.
61. Pawlak, J. et al. Irditoxin, a novel covalently linked heterodimeric three-finger toxin with high taxon-specific neurotoxicity, *FASEB J.* **23** (2), 534-545, 2009.
62. Morjen, M. et al. PIVL, a snake venom Kunitz-type serine protease inhibitor, inhibits in vitro and in vivo angiogenesis, *Microvasc. Res.*, 2014.
63. Mourao, C.B., & Schwartz, E.F. Protease inhibitors from marine venomous animals and their counterparts in terrestrial venomous animals, *Mar. Drugs* **11** (6), 2069-2112, 2013.
64. Stotz, S.C. et al. Block of voltage-dependent calcium channel by the green mamba toxin calciclidine, *J. Membr. Biol.* **174** (2), 157-165, 2000.
65. Earl, S.T. et al. Identification and characterisation of Kunitz-type plasma kallikrein inhibitors unique to *Oxyuranus* sp. snake venoms, *Biochimie* **94** (2), 365-373, 2012.
66. William H.; Heyborne; Mackessy, S. P. Cysteine-rich secretory proteins in reptile venoms., in *Handbook of venoms and toxins of reptiles.*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 325-336.
67. Yamazaki, Y., & Morita, T. Structure and function of snake venom cysteine-rich secretory proteins, *Toxicon* **44** (3), 227-231, 2004.
68. Brown, R.L. et al. Pseudechotoxin: a peptide blocker of cyclic nucleotide-gated ion channels, *Proc. Natl. Acad. Sci. U. S. A* **96** (2), 754-759, 1999.
69. Ito, N. et al. Novel cysteine-rich secretory protein in the buccal gland secretion of the parasitic lamprey, *Lethenteron japonicum*, *Biochem. Biophys. Res. Commun.* **358** (1), 35-40, 2007.
70. Osipov, A.V. et al. Cobra venom contains a pool of cysteine-rich secretory proteins, *Biochem. Biophys. Res. Commun.* **328** (1), 177-182, 2005.
71. Du, X. Y.; Clemetson, J. M. Reptile C-type lectins., in *Handbook of venoms and toxins of reptiles.*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 359-375.
72. Leduc, M., & Bon, C. Cloning of subunits of convulxin, a collagen-like platelet-aggregating protein from *Crotalus durissus terrificus* venom, *Biochem. J.* **333** ( Pt 2) 389-393, 1998.
73. Calvete, J.J. et al. Snake venom disintegrins: evolution of structure and function, *Toxicon* **45** (8), 1063-1074, 2005.
74. Calvete, J.J. Structure-function correlations of snake venom disintegrins, *Curr. Pharm. Des* **11** (7), 829-835, 2005.
75. Sanz, L. et al. Molecular cloning of disintegrins from *Cerastes vipera* and *Macrovipera lebetina transmediterranea* venom gland cDNA libraries: insight into the evolution of the snake venom integrin-inhibition system, *Biochem. J.* **395** (2), 385-392, 2006.

76. Lavin, M. F.; Earl, S.; Birrell, G.; Pierre, L. S.; Guddat, L.; Jersey, J.; Masci, P. Snake venom nerve growth factors., in *Handbook of venoms and toxins of reptiles.*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 377-392.
77. Otten, U. et al. Nerve growth factor induces plasma extravasation in rat skin, *Eur. J. Pharmacol.* **106** (1), 199-201, 1984.
78. Yamazaki, Y. et al. Snake venom Vascular Endothelial Growth Factors (VEGF-Fs) exclusively vary their structures and functions among species, *J. Biol. Chem.* **284** (15), 9885-9891, 2009.
79. Aird, S.D. Taxonomic distribution and quantitative analysis of free purine and pyrimidine nucleosides in snake venoms, *Comp Biochem. Physiol B Biochem. Mol. Biol.* **140** (1), 109-126, 2005.
80. Francis, B. et al. Citrate is an endogenous inhibitor of snake venom enzymes by metal-ion chelation, *Toxicon* **30** (10), 1239-1246, 1992.
81. Kini, R.M. Structure-function relationships and mechanism of anticoagulant phospholipase A2 enzymes from snake venoms, *Toxicon* **45** (8), 1147-1161, 2005.
82. Gupta, Y.K., & Peshin, S.S. Snakebite in India: Current scenario of an old problem, *Clinical Toicology* **4** (1), 1-9, 2014.
83. Park, H.J. et al. Antiarthritic effect of bee venom: inhibition of inflammation mediator generation by suppression of NF-kappaB through interaction with the p50 subunit, *Arthritis Rheum.* **50** (11), 3504-3515, 2004.
84. Chippaux, J.P. Snake-bites: appraisal of the global situation, *Bull. World Health Organ* **76** (5), 515-524, 1998.
85. Calvete, J.J. et al. Omics meets biology: application to the design and preclinical assessment of antivenoms, *Toxins. (Basel)* **6** (12), 3388-3405, 2014.
86. Gutierrez, J.M. et al. Snakebite envenoming from a global perspective: Towards an integrated approach, *Toxicon* **56** (7), 1223-1235, 2010.
87. Harrison, R.A. et al. Snake envenoming: a disease of poverty, *PLoS. Negl. Trop. Dis.* **3** (12), e569, 2009.
88. Mohapatra, B. et al. Snakebite mortality in India: a nationally representative mortality survey, *PLoS. Negl. Trop. Dis.* **5** (4), e1018, 2011.
89. Alirol, E. et al. Snake bite in South Asia: a review, *PLoS. Negl. Trop. Dis.* **4** (1), e603, 2010.
90. Kasturiratne, A. et al. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths, *PLoS. Med.* **5** (11), e218, 2008.
91. Brunda, G., & Sashidhar, R.B. Epidemiological profile of snake-bite cases from Andhra Pradesh using immunoanalytical approach, *Indian J Med. Res.* **125** (5), 661-668, 2007.
92. Whitaker, R., & Whitaker, S. Venom, antivenom production and the medically important snakes of India, *Current Science* **103** (6), 635-643, 2012.
93. Whitaker, R., & Martin, G. Diversity and distribution of clinically important snakes of india, *Clinical Toxinology* 1-18, 2014.
94. Gutierrez, J.M. et al. Stability, distribution and use of antivenoms for snakebite envenomation in Latin America: report of a workshop, *Toxicon* **53** (6), 625-630, 2009.

95. Simpson, I.D., & Norris, R.L. Snakes of medical importance in India: is the concept of the "Big 4" still relevant and useful?, *Wilderness. Environ. Med.* **18** (1), 2-9, 2007.
96. Joseph, J.K. et al. First authenticated cases of life-threatening envenoming by the hump-nosed pit viper (*Hypnale hypnale*) in India, *Trans. R. Soc. Trop. Med Hyg.* **101** (1), 85-90, 2007.
97. Gowda, C.D. et al. Strong myotoxic activity of *Trimeresurus malabaricus* venom: role of metalloproteases, *Mol Cell Biochem.* **282** (1-2), 147-155, 2006.
98. Ariaratnam, C.A. et al. Frequent and potentially fatal envenoming by hump-nosed pit vipers (*Hypnale hypnale* and *H. nepa*) in Sri Lanka: lack of effective antivenom, *Trans. R. Soc. Trop. Med. Hyg.* **102** (11), 1120-1126, 2008.
99. Chippaux, J.P. et al. Snake venom variability: methods of study, results and interpretation, *Toxicon* **29** (11), 1279-1303, 1991.
100. Ali, S.A. et al. Venom proteomic characterization and relative antivenom neutralization of two medically important Pakistani elapid snakes (*Bungarus sindanus* and *Naja naja*), *J. Proteomics.* **89** 15-23, 2013.
101. Sunagar, K. et al. Intraspecific venom variation in the medically significant Southern Pacific Rattlesnake (*Crotalus oreganus helleri*): biodiscovery, clinical and evolutionary implications, *J. Proteomics.* **99** 68-83, 2014.
102. Queiroz, G.P. et al. Interspecific variation in venom composition and toxicity of Brazilian snakes from *Bothrops* genus, *Toxicon* **52** (8), 842-851, 2008.
103. Mora-Obando, D. et al. Proteomic and functional profiling of the venom of *Bothrops ayerbe* from Cauca, Colombia, reveals striking interspecific variation with *Bothrops asper* venom, *J. Proteomics.* **96** 159-172, 2014.
104. Alape-Giron, A. et al. Snake venomics of the lancehead pitviper *Bothrops asper*: geographic, individual, and ontogenetic variations, *J. Proteome. Res.* **7** (8), 3556-3571, 2008.
105. Daltry, J.C. et al. Diet and snake venom evolution, *Nature* **379** (6565), 537-540, 1996.
106. Menezes, M.C. et al. Sex-based individual variation of snake venom proteome among eighteen *Bothrops jararaca* siblings, *Toxicon* **47** (3), 304-312, 2006.
107. Williams, V., & White, J. Variation in the composition of the venom from a single specimen of *Pseudonaja textilis* (common brown snake) over one year, *Toxicon* **30** (2), 202-206, 1992.
108. Zelanis, A. et al. *Bothrops jararaca* venom proteome rearrangement upon neonate to adult transition, *Proteomics.* **11** (21), 4218-4228, 2011.
109. Gao, J.F. et al. Neonate-to-adult transition of snake venomics in the short-tailed pit viper, *Gloydius brevicaudus*, *J. Proteomics.* **84** 148-157, 2013.
110. Mackessy, S.P. et al. Venom of the Brown Treesnake, *Boiga irregularis*: ontogenetic shifts and taxa-specific toxicity, *Toxicon* **47** (5), 537-548, 2006.
111. Modahl, C.M. et al. Venom analysis of long-term captive Pakistan cobra (*Naja naja*) populations, *Toxicon*, 2009.
112. Furtado, M.F. et al. Sexual dimorphism in venom of *Bothrops jararaca* (Serpentes: Viperidae), *Toxicon* **48** (4), 401-410, 2006.
113. Sintiprungrat, K. et al. A comparative study of venomics of *Naja naja* from India and Sri Lanka, clinical manifestations and antivenomics of an Indian polyspecific antivenom, *J. Proteomics.* **132** 131-143, 2016.

114. Tan, K.Y. et al. Venomics, lethality and neutralization of Naja kaouthia (monocled cobra) venoms from three different geographical regions of Southeast Asia, *J. Proteomics.* **120** 105-125, 2015.
115. Barlow, A. et al. Coevolution of diet and prey-specific venom activity supports the role of selection in snake venom evolution, *Proc. Biol. Sci.* **276** (1666), 2443-2449, 2009.
116. Gibbs, H.L. et al. Proteomic analysis of ontogenetic and diet-related changes in venom composition of juvenile and adult Dusky Pigmy rattlesnakes (Sistrurus miliarius barbouri), *J Proteomics.* **74** (10), 2169-2179, 2011.
117. Richards, D.P. et al. Venom lethality and diet: differential responses of natural prey and model organisms to the venom of the saw-scaled vipers (Echis), *Toxicon* **59** (1), 110-116, 2012.
118. Detrait, J., & Duguy, R. Changes in toxicity of venin during the annual cycle in Vipera aspis L, *Ann. Inst. Pasteur (Paris)* **111** (1), 93-99, 1966.
119. Gregory-Dwyer, V.M. et al. An isoelectric focusing study of seasonal variation in rattlesnake venom proteins, *Toxicon* **24** (10), 995-1000, 1986.
120. Monteiro, R.Q. et al. Variability of bothrojaracin isoforms and other venom principles in individual jararaca (Bothrops jararaca) snakes maintained under seasonally invariant conditions, *Toxicon* **36** (1), 153-163, 1998.
121. Leon, G. et al. Pathogenic mechanisms underlying adverse reactions induced by intravenous administration of snake antivenoms, *Toxicon* **76** 63-76, 2013.
122. de Silva, H.A. et al. Adverse reactions to snake antivenom, and their prevention and treatment, *Br. J. Clin. Pharmacol.*, 2015.
123. Tan, N.H. et al. Functional venomics of the Sri Lankan Russell's viper (Daboia russelii) and its toxinological correlations, *J. Proteomics.* **128** 403-423, 2015.
124. Wong, K.Y. et al. Venom and Purified Toxins of the Spectacled Cobra (Naja naja) from Pakistan: Insights into Toxicity and Antivenom Neutralization, *Am. J Trop. Med. Hyg.*, 2016.
125. Faizet al. The greater black krait (Bungarus niger), a newly recognized cause of neuro-myotoxic snake bite envenoming in Bangladesh, *Brain A Journal of Neurology* **133** 3181-3193, 2010.
126. Deshpande, R.P. et al. Adverse drug reaction profile of anti-snake venom in a rural tertiary care teaching hospital, *J. Young. Pharm.* **5** (2), 41-45, 2013.
127. Deshmukh, V.S. et al. Study on acute adverse drug reactions on antisnake venom in a rural tertiary care hospital, *Asian journal of pharmaceutical and clinical research* **7** (5), 2014.
128. Kumar, A.V., & Gowda, T.V. Novel non-enzymatic toxic peptide of Daboia russelii (Eastern region) venom renders commercial polyvalent antivenom ineffective, *Toxicon* **47** (4), 398-408, 2006.
129. Shashidharamurthy, R., & Kemparaju, K. Region-specific neutralization of Indian cobra (Naja naja) venom by polyclonal antibody raised against the eastern regional venom: A comparative study of the venoms from three different geographical distributions, *Int. Immunopharmacol.* **7** (1), 61-69, 2007.
130. Premawardena, A.P. et al. Excessive fibrinolysis: the coagulopathy following Merrem's hump-nosed viper (Hypnale hypnale) bites, *Am. J Trop. Med. Hyg.* **58** (6), 821-823, 1998.

131. Sellahewa, K.H.et al. Efficacy of antivenom in the treatment of severe local envenomation by the hump-nosed viper (*Hypnale hypnale*), *Am. J Trop. Med. Hyg.* **53** (3), 260-262, 1995.
132. Calvete, J.J.et al. Venoms, venomics, antivenomics, *FEBS Lett.* **583** (11), 1736-1743, 2009.
133. Mackie, I.J., & Bull, H.A. Normal haemostasis and its regulation, *Blood Rev* **3** (4), 237-250, 1989.
134. Sere, K.M., & Hackeng, T.M. Basic mechanisms of hemostasis, *Semin. Vasc. Med.* **3** (1), 3-12, 2003.
135. Becker, B.F.et al. Endothelial function and hemostasis, *Z. Kardiol.* **89** (3), 160-167, 2000.
136. Dahlback, B., & Villoutreix, B.O. The anticoagulant protein C pathway, *FEBS Lett.* **579** (15), 3310-3316, 2005.
137. Girard, T.J.et al. Inhibition of factor VIIa-tissue factor coagulation activity by a hybrid protein, *Science* **248** (4961), 1421-1424, 1990.
138. Fredenburgh, J.C.et al. Antithrombin-independent anticoagulation by hypersulfated low-molecular-weight heparin, *Trends Cardiovasc. Med.* **12** (7), 281-287, 2002.
139. Dobrovolsky, A.B., & Titaeva, E.V. The fibrinolysis system: regulation of activity and physiologic functions of its main components, *Biochemistry (Mosc. )* **67** (1), 99-108, 2002.
140. Lenting, P.J.et al. Regulation of von Willebrand factor-platelet interactions, *Thromb. Haemost.* **104** (3), 449-455, 2010.
141. Jennings, L.K. Mechanisms of platelet activation: need for new strategies to protect against platelet-mediated atherothrombosis, *Thromb. Haemost.* **102** (2), 248-257, 2009.
142. Nuyttens, B.P.et al. Platelet adhesion to collagen, *Thromb. Res.* **127 Suppl 2** S26-S29, 2011.
143. Braud, S.et al. Snake venom proteins acting on hemostasis, *Biochimie* **82** (9-10), 851-859, 2000.
144. Brass, L. Understanding and evaluating platelet function, *Hematology. Am. Soc. Hematol. Educ. Program.* **2010** 387-396, 2010.
145. Brass, L.F. Thrombin and platelet activation, *Chest* **124** (3 Suppl), 18S-25S, 2003.
146. Hoffman, M., & Monroe, D.M., III A cell-based model of hemostasis, *Thromb. Haemost.* **85** (6), 958-965, 2001.
147. Rao, L.V., & Rapaport, S.I. Activation of factor VII bound to tissue factor: a key early step in the tissue factor pathway of blood coagulation, *Proc. Natl. Acad. Sci. U. S. A* **85** (18), 6687-6691, 1988.
148. Rao, L.V.et al. Studies of the activation of factor VII bound to tissue factor, *Blood* **87** (9), 3738-3748, 1996.
149. Fujikawa, K.et al. Activation of bovine factor X (Stuart factor): conversion of factor Xalpha to factor Xbeta, *Proc. Natl. Acad. Sci. U. S. A* **72** (9), 3359-3363, 1975.
150. Osterud, B., & Rapaport, S.I. Activation of factor IX by the reaction product of tissue factor and factor VII: additional pathway for initiating blood coagulation, *Proc. Natl. Acad. Sci. U. S. A* **74** (12), 5260-5264, 1977.
151. Gailani, D., & Broze, G.J., Jr. Factor XI activation in a revised model of blood coagulation, *Science* **253** (5022), 909-912, 1991.

152. Naito, K., & Fujikawa, K. Activation of human blood coagulation factor XI independent of factor XII. Factor XI is activated by thrombin and factor XIa in the presence of negatively charged surfaces, *J Biol Chem* **266** (12), 7353-7358, 1991.
153. Matafonov, A. et al. Activation of factor XI by products of prothrombin activation, *Blood* **118** (2), 437-445, 2011.
154. Hung, D.T. et al. Cloned platelet thrombin receptor is necessary for thrombin-induced platelet activation, *J Clin. Invest* **89** (4), 1350-1353, 1992.
155. Furie, B., & Furie, B.C. Mechanisms of thrombus formation, *N. Engl. J. Med.* **359** (9), 938-949, 2008.
156. Mann, K.G. et al. The dynamics of thrombin formation, *Arterioscler. Thromb. Vasc. Biol* **23** (1), 17-25, 2003.
157. Camiolo, S.M. et al. Fibrinogenolysis and fibrinolysis with tissue plasminogen activator, urokinase, streptokinase-activated human globulin, and plasmin, *Proc. Soc. Exp. Biol Med.* **138** (1), 277-280, 1971.
158. Wiman, B., & Collen, D. On the kinetics of the reaction between human antiplasmin and plasmin, *Eur. J Biochem.* **84** (2), 573-578, 1978.
159. Aoki, N., & Harpel, P.C. Inhibitors of the fibrinolytic enzyme system, *Semin. Thromb. Hemost.* **10** (1), 24-41, 1984.
160. Davie, E.W. et al. The coagulation cascade: initiation, maintenance, and regulation, *Biochemistry* **30** (43), 10363-10370, 1991.
161. Davie, E.W. et al. The role of serine proteases in the blood coagulation cascade, *Adv. Enzymol. Relat Areas Mol Biol* **48** 277-318, 1979.
162. Jackson, C.M., & Nemerson, Y. Blood coagulation, *Annu. Rev Biochem.* **49** 765-811, 1980.
163. Venkateswarlu, D. et al. Structure and dynamics of zymogen human blood coagulation factor X, *Biophys. J* **82** (3), 1190-1206, 2002.
164. Krupiczojc, M.A. et al. Coagulation signalling following tissue injury: focus on the role of factor Xa, *Int. J Biochem. Cell Biol* **40** (6-7), 1228-1237, 2008.
165. Ansell, J. Factor Xa or thrombin: is factor Xa a better target?, *J Thromb. Haemost.* **5 Suppl 1** 60-64, 2007.
166. Hara, T. et al. DX-9065a, a new synthetic, potent anticoagulant and selective inhibitor for factor Xa, *Thromb. Haemost.* **71** (3), 314-319, 1994.
167. Hara, T. et al. DX-9065a, an orally active, specific inhibitor of factor Xa, inhibits thrombosis without affecting bleeding time in rats, *Thromb. Haemost.* **74** (2), 635-639, 1995.
168. Yamashita, T. et al. The antithrombotic effect of synthetic low molecular weight human factor Xa inhibitor, DX-9065a, on He-Ne laser-induced thrombosis in rat mesenteric microvessels, *Thromb. Res.* **85** (1), 45-51, 1997.
169. Herbert, J.M. et al. DX 9065A a novel, synthetic, selective and orally active inhibitor of factor Xa: in vitro and in vivo studies, *J Pharmacol. Exp. Ther.* **276** (3), 1030-1038, 1996.
170. Lam, P.Y. et al. Structure-based design of novel guanidine/benzamidine mimics: potent and orally bioavailable factor Xa inhibitors as novel anticoagulants, *J Med. Chem* **46** (21), 4405-4418, 2003.
171. Kanagasabapathy, P. et al. Alternatives to warfarin--the next generation of anticoagulants, *Cardiovasc. Ther.* **29** (6), e80-e88, 2011.
172. Fontana, P. et al. Direct oral anticoagulants: a guide for daily practice, *Swiss. Med. Wkly.* **146** w14286, 2016.

173. Honda, Y. et al. Edoxaban, a direct factor Xa inhibitor, suppresses tissue-factor induced human platelet aggregation and clot-bound factor Xa in vitro: Comparison with an antithrombin-dependent factor Xa inhibitor, fondaparinux, *Thromb. Res.* **141** 17-21, 2016.
174. Prandoni, P. et al. Direct oral anticoagulants in the prevention of venous thromboembolism: evidence from major clinical trials, *Semin. Hematol.* **51** (2), 121-130, 2014.
175. Haas, S., & Schellong, S. New anticoagulants: from bench to bedside, *Hamostaseologie*. **27** (1), 41-47, 2007.
176. Snodgrass, M.N. et al. Efficacy and Safety of Fondaparinux in Patients With Suspected Heparin-Induced Thrombocytopenia, *Clin. Appl. Thromb. Hemost.*, 2016.
177. Harenberg, J. Development of new anticoagulants: present and future, *Semin. Thromb. Hemost.* **34** (8), 779-793, 2008.
178. Yeh, C.H. et al. Oral direct factor Xa inhibitors, *Circ. Res.* **111** (8), 1069-1078, 2012.
179. Atoda, H. et al. Coagulation factor X-binding protein from *Deinagkistrodon acutus* venom is a Gla domain-binding protein, *Biochemistry* **37** (50), 17361-17370, 1998.
180. Faure, G., & Saul, F. Structural and Functional Characterization of Anticoagulant, FXa-binding Viperidae Snake Venom Phospholipases A2, *Acta Chim. Slov.* **58** (4), 671-677, 2011.
181. Saikia, D. et al. An acidic phospholipase A(2) (RVVA-PLA(2)-I) purified from *Daboia russelli* venom exerts its anticoagulant activity by enzymatic hydrolysis of plasma phospholipids and by non-enzymatic inhibition of factor Xa in a phospholipids/Ca(2+) independent manner, *Toxicon* **57** (6), 841-850, 2011.
182. Stefansson, S. et al. The basic phospholipase A2 from *Naja nigricollis* venom inhibits the prothrombinase complex by a novel nonenzymatic mechanism, *Biochemistry* **29** (33), 7742-7746, 1990.
183. Thakur, R. et al. A new peptide (Ruviprase) purified from the venom of *Daboia russelii russelii* shows potent anticoagulant activity via non-enzymatic inhibition of thrombin and factor Xa, *Biochimie*, 2014.
184. Kini, R.M. Anticoagulant proteins from snake venoms: structure, function and mechanism, *Biochem. J.* **397** (3), 377-387, 2006.
185. Fuly, A.L. et al. Signal transduction pathways involved in the platelet aggregation induced by a D-49 phospholipase A2 isolated from *Bothrops jararacussu* snake venom, *Biochimie* **86** (9-10), 731-739, 2004.
186. Takeya, H. et al. Coagulation factor X activating enzyme from Russell's viper venom (RVV-X). A novel metalloproteinase with disintegrin (platelet aggregation inhibitor)-like and C-type lectin-like domains, *J. Biol. Chem.* **267** (20), 14109-14117, 1992.
187. Sajevic, T. et al. Haemostatically active proteins in snake venoms, *Toxicon* **57** (5), 627-645, 2011.
188. Siigur, E. et al. Factor X activator from *Vipera lebetina* snake venom, molecular characterization and substrate specificity, *Biochim. Biophys. Acta* **1568** (1), 90-98, 2001.

189. Leonardi, A.et al. Two coagulation factor X activators from Vipera a. ammodytes venom with potential to treat patients with dysfunctional factors IXa or VIIa, *Toxicon* **52** (5), 628-637, 2008.
190. Manjunatha, K.R.et al. Classification and nomenclature of prothrombin activators isolated from snake venoms, *Thromb. Haemost.* **86** (2), 710-711, 2001.
191. Kini, R.M. The intriguing world of prothrombin activators from snake venom, *Toxicon* **45** (8), 1133-1145, 2005.
192. Berger, M.et al. Purification and functional characterization of bothrojaractivase, a prothrombin-activating metalloproteinase isolated from Bothrops jararaca snake venom, *Toxicon* **51** (4), 488-501, 2008.
193. Loria, G.D.et al. Characterization of 'basparin A,' a prothrombin-activating metalloproteinase, from the venom of the snake Bothrops asper that inhibits platelet aggregation and induces defibrination and thrombosis, *Arch. Biochem. Biophys.* **418** (1), 13-24, 2003.
194. Yamada, D.et al. Isolation and characterization of carinactivase, a novel prothrombin activator in Echis carinatus venom with a unique catalytic mechanism, *J. Biol. Chem.* **271** (9), 5200-5207, 1996.
195. Rao, V.S., & Kini, R.M. Pseutarin C, a prothrombin activator from Pseudonaja textilis venom: its structural and functional similarity to mammalian coagulation factor Xa-Va complex, *Thromb. Haemost.* **88** (4), 611-619, 2002.
196. Joseph, J.S.et al. Amino acid sequence of trocarin, a prothrombin activator from Tropidodechis carinatus venom: its structural similarity to coagulation factor Xa, *Blood* **94** (2), 621-631, 1999.
197. Zhang, Y.et al. An activator of blood coagulation factor X from the venom of Bungarus fasciatus, *Toxicon* **33** (10), 1277-1288, 1995.
198. Lee, W.H.et al. Isolation and properties of a blood coagulation factor X activator from the venom of king cobra (Ophiophagus hannah), *Toxicon* **33** (10), 1263-1276, 1995.
199. Tokunaga, F.et al. The factor V-activating enzyme (RVV-V) from Russell's viper venom. Identification of isoproteins RVV-V alpha, -V beta, and -V gamma and their complete amino acid sequences, *J Biol Chem* **263** (33), 17471-17481, 1988.
200. Siigur, E.et al. Isolation, properties and N-terminal amino acid sequence of a factor V activator from Vipera lebetina (Levantine viper) snake venom, *Biochim. Biophys. Acta* **1429** (1), 239-248, 1998.
201. Segers, K.et al. Structural models of the snake venom factor V activators from Daboia russelli and Daboia lebetina, *Proteins* **64** (4), 968-984, 2006.
202. Janssen, M.et al. Purification and characterization of an antithrombin III inactivating enzyme from the venom of the African night adder (Causus rhombeatus), *Toxicon* **30** (9), 985-999, 1992.
203. Nishida, S.et al. Purification and characterization of bothrombin, a fibrinogen-clotting serine protease from the venom of Bothrops jararaca, *Biochemistry* **33** (7), 1843-1849, 1994.
204. Andrews, R.K.et al. Purification of botrocetin from Bothrops jararaca venom. Analysis of the botrocetin-mediated interaction between von Willebrand factor and the human platelet membrane glycoprotein Ib-IX complex, *Biochemistry* **28** (21), 8317-8326, 1989.

205. Yamamoto-Suzuki, Y. et al. Identification and recombinant analysis of botrocetin-2, a snake venom cofactor for von Willebrand factor-induced platelet agglutination, *Biochemistry* **51** (26), 5329-5338, 2012.
206. Usami, Y. et al. Primary structure of two-chain botrocetin, a von Willebrand factor modulator purified from the venom of Bothrops jararaca, *Proc. Natl. Acad. Sci. U. S. A* **90** (3), 928-932, 1993.
207. Hamako, J. et al. Purification and characterization of bitiscetin, a novel von Willebrand factor modulator protein from Bitis arietans snake venom, *Biochem. Biophys. Res. Commun.* **226** (1), 273-279, 1996.
208. Polgar, J. et al. Platelet activation and signal transduction by convulxin, a C-type lectin from *Crotalus durissus terrificus* (tropical rattlesnake) venom via the p62/GPVI collagen receptor, *J Biol Chem* **272** (21), 13576-13583, 1997.
209. Kanaji, S. et al. Convulxin binds to native, human glycoprotein Ib alpha, *J Biol Chem* **278** (41), 39452-39460, 2003.
210. Horii, K. et al. Convulxin forms a dimer in solution and can bind eight copies of glycoprotein VI: implications for platelet activation, *Biochemistry* **48** (13), 2907-2914, 2009.
211. Bergmeier, W. et al. Rhodocytin (aggregatin) activates platelets lacking alpha(2)beta(1) integrin, glycoprotein VI, and the ligand-binding domain of glycoprotein Ibalpha, *J Biol Chem* **276** (27), 25121-25126, 2001.
212. Navdaev, A. et al. Aggregatin, a heterodimeric C-type lectin from *Calloselasma rhodostoma* (Malayan pit viper), stimulates platelets by binding to alpha2beta1 integrin and glycoprotein Ib, activating Syk and phospholipase Cgamma 2, but does not involve the glycoprotein VI/Fc receptor gamma chain collagen receptor, *J Biol Chem* **276** (24), 20882-20889, 2001.
213. Hooley, E. et al. The crystal structure of the platelet activator aggregatin reveals a novel (alpha/beta)2 dimeric structure, *Biochemistry* **47** (30), 7831-7837, 2008.
214. Li, R. et al. L-amino acid oxidase from *Naja atra* venom activates and binds to human platelets, *Acta Biochim. Biophys. Sin. (Shanghai)* **40** (1), 19-26, 2008.
215. Stocker, K. et al. Characterization of the protein C activator Protac from the venom of the southern copperhead (*Agkistrodon contortrix*) snake, *Toxicon* **25** (3), 239-252, 1987.
216. Kisiel, W. et al. Characterization of a protein C activator from *Agkistrodon contortrix contortrix* venom, *J. Biol. Chem.* **262** (26), 12607-12613, 1987.
217. Bell, W.R., Jr. Defibrinogenating enzymes, *Drugs* **54 Suppl 3** 18-30, 1997.
218. Zhang, Y. et al. A novel plasminogen activator from snake venom. Purification, characterization, and molecular cloning, *J Biol Chem* **270** (17), 10246-10255, 1995.
219. Sanchez, E.F. et al. A novel fibrinolytic metalloproteinase, barnettlysin-I from *Bothrops barnetti* (Barnett's pitviper) snake venom with anti-platelet properties, *Biochim. Biophys. Acta* **1860** (3), 542-556, 2016.
220. Wu, W.B., & Huang, T.F. Activation of MMP-2, cleavage of matrix proteins, and adherens junctions during a snake venom metalloproteinase-induced endothelial cell apoptosis, *Exp. Cell Res.* **288** (1), 143-157, 2003.
221. Gomes, M.S. et al. Biochemical and functional characterization of Bothropoidin: the first haemorrhagic metalloproteinase from *Bothrops pauloensis* snake venom, *J Biochem.* **157** (3), 137-149, 2015.

222. Torii, S. et al. Apoxin I, a novel apoptosis-inducing factor with L-amino acid oxidase activity purified from Western diamondback rattlesnake venom, *J Biol Chem* **272** (14), 9539-9542, 1997.
223. Sakurai, Y. et al. Anticoagulant activity of M-LAO, L-amino acid oxidase purified from Agkistrodon halys blomhoffii, through selective inhibition of factor IX, *Biochim. Biophys. Acta* **1649** (1), 51-57, 2003.
224. Ouyang, C., & Huang, T.F. Inhibition of platelet aggregation by 5'-nucleotidase purified from *Trimeresurus gramineus* snake venom, *Toxicon* **21** (4), 491-501, 1983.
225. Hart, M.L. et al. Direct treatment of mouse or human blood with soluble 5'-nucleotidase inhibits platelet aggregation, *Arterioscler. Thromb. Vasc. Biol* **28** (8), 1477-1483, 2008.
226. Santoro, M.L. et al. NPP-BJ, a nucleotide pyrophosphatase/phosphodiesterase from *Bothrops jararaca* snake venom, inhibits platelet aggregation, *Toxicon* **54** (4), 499-512, 2009.
227. Banerjee, Y. et al. Hemextin AB complex--a snake venom anticoagulant protein complex that inhibits factor VIIa activity, *Pathophysiol. Haemost. Thromb.* **34** (4-5), 184-187, 2005.
228. Barnwal, B. et al. Ringhalexin from *Hemachatus haemachatus*: A novel inhibitor of extrinsic tenase complex, *Sci. Rep.* **6** 25935, 2016.
229. McDowell, R.S. et al. Mambin, a potent glycoprotein IIb-IIIa antagonist and platelet aggregation inhibitor structurally related to the short neurotoxins, *Biochemistry* **31** (20), 4766-4772, 1992.
230. Chen, W. et al. Fasxiator, a novel factor XIa inhibitor from snake venom, and its site-specific mutagenesis to improve potency and selectivity, *J Thromb. Haemost.* **13** (2), 248-261, 2015.
231. Zingali, R.B. et al. Bothrojaracin, a new thrombin inhibitor isolated from *Bothrops jararaca* venom: characterization and mechanism of thrombin inhibition, *Biochemistry* **32** (40), 10794-10802, 1993.
232. Arocás, V. et al. Bothrojaracin: a potent two-site-directed thrombin inhibitor, *Biochemistry* **35** (28), 9083-9089, 1996.
233. Assafim, M. et al. Exploiting the antithrombotic effect of the (pro)thrombin inhibitor bothrojaracin, *Toxicon* **119**, 46-51, 2016.
234. Atoda, H., & Morita, T. A novel blood coagulation factor IX/factor X-binding protein with anticoagulant activity from the venom of *Trimeresurus flavoviridis* (Habu snake): isolation and characterization, *J. Biochem. (Tokyo)* **106** (5), 808-813, 1989.
235. Atoda, H. et al. Blood coagulation factor IX-binding protein from the venom of *Trimeresurus flavoviridis*: purification and characterization, *J. Biochem.* **118** (5), 965-973, 1995.
236. Kwon, I. et al. Thrombolytic effects of the snake venom disintegrin saxatilin determined by novel assessment methods: a FeCl<sub>3</sub>-induced thrombosis model in mice, *PLoS. ONE* **8** (11), e81165, 2013.
237. Niewiarowski, S. et al. Disintegrins and other naturally occurring antagonists of platelet fibrinogen receptors, *Semin. Hematol.* **31** (4), 289-300, 1994.
238. Williams, J.A. Disintegrins: RGD-containing proteins which inhibit cell/matrix interactions (adhesion) and cell/cell interactions (aggregation) via the integrin receptors, *Pathol. Biol. (Paris)* **40** (8), 813-821, 1992.

239. Kini, R. M. Phospholipase A2 A Complex Multifunctional Protein Puzzle, in *Venom Phospholipase A2 Enzymes: Structure, Function and Mechanism*, Kini, R. M., editor; John Wiley & Sons: Chichester, England, 1997, 1-28.
240. Doley, R.; Zhou, X.; Kini, M. R. Snake Venom Phospholipase A2 Enzymes, in *Hand Book of Venoms and Toxins of Reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 173-206.
241. Jackson, J.R. et al. The role of platelet activating factor and other lipid mediators in inflammatory angiogenesis, *Biochim. Biophys. Acta* **1392** (1), 145-152, 1998.
242. Kawauchi, Y. et al. Preparation and characterization of human rheumatoid arthritic synovial fluid phospholipase A2 produced by recombinant baculovirus-infected insect cells, *J Biochem.* **116** (1), 81-87, 1994.
243. Lamraoui, A. et al. Immunopathologic effects of scorpion venom on hepatorenal tissues: Involvement of lipid derived inflammatory mediators, *Exp. Mol Pathol.* **99** (2), 286-296, 2015.
244. Nagaraju, S. et al. Venom from spiders of the genus Hippasa: biochemical and pharmacological studies, *Comp Biochem. Physiol C. Toxicol. Pharmacol.* **144** (1), 1-9, 2006.
245. Palm, N.W. et al. Bee venom phospholipase A2 induces a primary type 2 response that is dependent on the receptor ST2 and confers protective immunity, *Immunity* **39** (5), 976-985, 2013.
246. Pan, F.M. et al. Characterization of phospholipase A2 (PLA2) from Taiwan Cobra: isoenzymes and their site-directed mutants, *Biochem. Biophys. Res. Commun.* **250** (1), 154-160, 1998.
247. Six, D.A., & Dennis, E.A. The expanding superfamily of phospholipase A(2) enzymes: classification and characterization, *Biochim. Biophys. Acta* **1488** (1-2), 1-19, 2000.
248. Alape-Giron, A. et al. Elapid venom toxins: multiple recruitments of ancient scaffolds, *Eur. J. Biochem.* **259** (1-2), 225-234, 1999.
249. Valentin, E., & Lambeau, G. What can venom phospholipases A(2) tell us about the functional diversity of mammalian secreted phospholipases A(2)?, *Biochimie* **82** (9-10), 815-831, 2000.
250. Fry, M.R. et al. Role of human sperm phospholipase A2 in fertilization: effects of a novel inhibitor of phospholipase A2 activity on membrane perturbations and oocyte penetration, *Biol. Reprod.* **47** (5), 751-759, 1992.
251. Arita, H. et al. Novel proliferative effect of phospholipase A2 in Swiss 3T3 cells via specific binding site, *J. Biol. Chem.* **266** (29), 19139-19141, 1991.
252. Nakajima, M. et al. Effect of pancreatic type phospholipase A2 on isolated porcine cerebral arteries via its specific binding sites, *FEBS Lett.* **309** (3), 261-264, 1992.
253. Sommers, C.D. et al. Porcine pancreatic phospholipase A2-induced contractions of guinea pig lung pleural strips, *Eur. J. Pharmacol.* **216** (1), 87-96, 1992.
254. Vadas, P. et al. Extracellular phospholipase A2 expression and inflammation: the relationship with associated disease states, *J. Lipid Mediat.* **8** (1), 1-30, 1993.
255. Verheij, H.M. et al. Structure and function of phospholipase A2, *Rev. Physiol Biochem. Pharmacol.* **91** 91-203, 1981.

256. Balsinde, J. et al. Regulation and inhibition of phospholipase A2, *Annu. Rev. Pharmacol. Toxicol.* **39** 175-189, 1999.
257. Touqui, L., & Alaoui-El-Azher, M. Mammalian secreted phospholipases A2 and their pathophysiological significance in inflammatory diseases, *Curr. Mol. Med.* **1** (6), 739-754, 2001.
258. Dhananjaya, B.L., & Sivashankari, P.R. Snake venom derived molecules in tumor angiogenesis and its application in cancer therapy; an overview, *Curr. Top. Med. Chem.* **15** (7), 649-657, 2015.
259. Nevalainen, T.J. et al. Phospholipase A2 in cnidaria, *Comp Biochem. Physiol B Biochem. Mol Biol* **139** (4), 731-735, 2004.
260. Schaloske, R.H., & Dennis, E.A. The phospholipase A2 superfamily and its group numbering system, *Biochim. Biophys. Acta* **1761** (11), 1246-1259, 2006.
261. Fohlman, J. et al. Taipoxin, an extremely potent presynaptic snake venom neurotoxin. Elucidation of the primary structure of the acidic carbohydrate-containing taipoxin-subunit, a prophospholipase homolog, *FEBS Lett.* **84** (2), 367-371, 1977.
262. Francis, B.R. et al. Toxins isolated from the venom of the Brazilian coral snake (*Micrurus frontalis frontalis*) include hemorrhagic type phospholipases A2 and postsynaptic neurotoxins, *Toxicon* **35** (8), 1193-1203, 1997.
263. Huang, M.Z. et al. Complete amino acid sequence of an acidic, cardiotoxic phospholipase A2 from the venom of *Ophiophagus hannah* (King Cobra): a novel cobra venom enzyme with "pancreatic loop", *Arch. Biochem. Biophys.* **338** (2), 150-156, 1997.
264. Pearson, J.A. et al. Studies on the subunit structure of textilotoxin, a potent presynaptic neurotoxin from the venom of the Australian common brown snake (*Pseudonaja textilis*). 3. The complete amino-acid sequences of all the subunits, *Biochim. Biophys. Acta* **1161** (2-3), 223-229, 1993.
265. Davidson, F.F., & Dennis, E.A. Evolutionary relationships and implications for the regulation of phospholipase A2 from snake venom to human secreted forms, *J. Mol. Evol.* **31** (3), 228-238, 1990.
266. Heinrikson, R.L. et al. Amino acid sequence of phospholipase A2-alpha from the venom of *Crotalus adamanteus*. A new classification of phospholipases A2 based upon structural determinants, *J. Biol. Chem.* **252** (14), 4913-4921, 1977.
267. Scott, D. L. Phospholipase A2 structure and catalytic properties, in *Venom Phospholipase A2 Enzymes: Structure, Function and Mechanism*, Kini, R. M., editor; John Wiley & Sons: Chichester, England, 1997, 97-128.
268. Chijiwa, T. et al. Discovery of novel [Arg49]phospholipase A2 isozymes from *Protobothrops elegans* venom and regional evolution of Crotalinae snake venom phospholipase A2 isozymes in the southwestern islands of Japan and Taiwan, *Toxicon* **48** (6), 672-682, 2006.
269. Maraganore, J.M. et al. A new class of phospholipases A2 with lysine in place of aspartate 49. Functional consequences for calcium and substrate binding, *J. Biol. Chem.* **259** (22), 13839-13843, 1984.
270. Polgar, J. et al. Asp-49 is not an absolute prerequisite for the enzymic activity of low-M(r) phospholipases A2: purification, characterization and computer modelling of an enzymically active Ser-49 phospholipase A2, ecarpholin S, from the venom of *Echis carinatus sochureki* (saw-scaled viper), *Biochem. J.* **319** (Pt 3) 961-968, 1996.

271. Scott, D.L. et al. Interfacial catalysis: the mechanism of phospholipase A2, *Science* **250** (4987), 1541-1546, 1990.
272. Tsai, I.H. et al. Venom phospholipases A2 of bamboo viper (*Trimeresurus stejnegeri*): molecular characterization, geographic variations and evidence of multiple ancestries, *Biochem. J.* **377** (Pt 1), 215-223, 2004.
273. Maraganore, J.M., & Heinrikson, R.L. The role of lysyl residues of phospholipases A2 in the formation of the catalytic complex, *Biochem. Biophys. Res. Commun.* **131** (1), 129-138, 1985.
274. Fujimi, T.J. et al. A comparative analysis of invaded sequences from group IA phospholipase A(2) genes provides evidence about the divergence period of genes groups and snake families, *Toxicon* **40** (7), 873-884, 2002.
275. Fujimi, T.J. et al. Nucleotide sequence of phospholipase A(2) gene expressed in snake pancreas reveals the molecular evolution of toxic phospholipase A(2) genes, *Gene* **292** (1-2), 225-231, 2002.
276. Jeyaseelan, K. et al. Structure and phylogeny of the venom group I phospholipase A(2) gene, *Mol. Biol. Evol.* **17** (7), 1010-1021, 2000.
277. Kordis, D., & Gubensek, F. Ammodytoxin C gene helps to elucidate the irregular structure of Crotalinae group II phospholipase A2 genes, *Eur. J. Biochem.* **240** (1), 83-90, 1996.
278. Huang, M.Z. et al. Complete amino acid sequence of an acidic, cardiotoxic phospholipase A2 from the venom of *Ophiophagus hannah* (King Cobra): a novel cobra venom enzyme with "pancreatic loop", *Arch. Biochem. Biophys.* **338** (2), 150-156, 1997.
279. Armugam, A. et al. Group IB phospholipase A2 from *Pseudonaja textilis*, *Arch. Biochem. Biophys.* **421** (1), 10-20, 2004.
280. Nakashima, K. et al. Accelerated evolution of *Trimeresurus flavoviridis* venom gland phospholipase A2 isozymes, *Proc. Natl. Acad. Sci. U. S. A* **90** (13), 5964-5968, 1993.
281. Singh, S.B. et al. Phospholipase A(2) with platelet aggregation inhibitor activity from *Austrelaps superbus* venom: protein purification and cDNA cloning, *Arch. Biochem. Biophys.* **375** (2), 289-303, 2000.
282. Subburaju, S., & Kini, R.M. Isolation and purification of superbins I and II from *Austrelaps superbus* (copperhead) snake venom and their anticoagulant and antiplatelet effects, *Toxicon* **35** (8), 1239-1250, 1997.
283. Mukherjee, A.K. et al. Two acidic, anticoagulant PLA2 isoenzymes purified from the venom of monocled cobra *Naja kaouthia* exhibit different potency to inhibit thrombin and factor Xa via phospholipids independent, non-enzymatic mechanism, *PLOS ONE* **9** (8), e101334, 2014.
284. Ogawa, T. et al. Unusually high conservation of untranslated sequences in cDNAs for *Trimeresurus flavoviridis* phospholipase A2 isozymes, *Proc. Natl. Acad. Sci. U. S. A* **89** (18), 8557-8561, 1992.
285. Ogawa, T. et al. *Trimeresurus flavoviridis* venom gland phospholipase A2 isozymes genes have evolved via accelerated substitutions, *J. Mol. Recognit.* **8** (1-2), 40-46, 1995.
286. Ogawa, T. et al. Accelerated evolution of snake venom phospholipase A2 isozymes for acquisition of diverse physiological functions, *Toxicon* **34** (11-12), 1229-1236, 1996.

287. Chuman, Y. et al. Regional and accelerated molecular evolution in group I snake venom gland phospholipase A2 isozymes, *Toxicon* **38** (3), 449-462, 2000.
288. Nobuhisa, I. et al. Accelerated evolution of *Trimeresurus okinavensis* venom gland phospholipase A2 isozyme-encoding genes, *Gene* **172** (2), 267-272, 1996.
289. Ohno, M. et al. Molecular evolution of myotoxic phospholipases A2 from snake venom, *Toxicon* **42** (8), 841-854, 2003.
290. Kini, R.M., & Chan, Y.M. Accelerated evolution and molecular surface of venom phospholipase A2 enzymes, *J. Mol. Evol.* **48** (2), 125-132, 1999.
291. Chijiwa, T. et al. Interisland mutation of a novel phospholipase A2 from *Trimeresurus flavoviridis* venom and evolution of Crotalinae group II phospholipases A2, *J. Mol. Evol.* **57** (5), 546-554, 2003.
292. Kini, R.M., & Evans, H.J. Structure-function relationships of phospholipases. The anticoagulant region of phospholipases A2, *J. Biol. Chem.* **262** (30), 14402-14407, 1987.
293. Banumathi, S. et al. Structure of the neurotoxic complex vipoxin at 1.4 Å resolution, *Acta Crystallogr. D. Biol. Crystallogr.* **57** (Pt 11), 1552-1559, 2001.
294. Vernon, L.P., & Bell, J.D. Membrane structure, toxins and phospholipase A2 activity, *Pharmacol. Ther.* **54** (3), 269-295, 1992.
295. Jain, M.K., & Berg, O.G. The kinetics of interfacial catalysis by phospholipase A2 and regulation of interfacial activation: hopping versus scooting, *Biochim. Biophys. Acta* **1002** (2), 127-156, 1989.
296. Ramirez, F., & Jain, M.K. Phospholipase A2 at the bilayer interface, *Proteins* **9** (4), 229-239, 1991.
297. Edwards, S.H. et al. The crystal structure of the H48Q active site mutant of human group IIA secreted phospholipase A2 at 1.5 Å resolution provides an insight into the catalytic mechanism, *Biochemistry* **41** (52), 15468-15476, 2002.
298. Murakami, M.T. et al. Insights into metal ion binding in phospholipases A2: ultra high-resolution crystal structures of an acidic phospholipase A2 in the Ca<sup>2+</sup> free and bound states, *Biochimie* **88** (5), 543-549, 2006.
299. Rogers, J. et al. Kinetic basis for the substrate specificity during hydrolysis of phospholipids by secreted phospholipase A2, *Biochemistry* **35** (29), 9375-9384, 1996.
300. De, S.S. Physico-chemical studies on hemolysin, *J. Ind. Chem. Soc* **21** 290, 1944.
301. Faure, G., & Bon, C. Crotoxin, a phospholipase A2 neurotoxin from the South American rattlesnake *Crotalus durissus terrificus*: purification of several isoforms and comparison of their molecular structure and of their biological activities, *Biochemistry* **27** (2), 730-738, 1988.
302. Gutierrez, J.M., & Lomonte, B. Phospholipase A2 myotoxins from Bothrops snake venoms, *Toxicon* **33** (11), 1405-1424, 1995.
303. Westerlund, B. et al. The three-dimensional structure of notexin, a presynaptic neurotoxic phospholipase A2 at 2.0 Å resolution, *FEBS Lett.* **301** (2), 159-164, 1992.
304. Saul, F.A. et al. Comparative structural studies of two natural isoforms of ammodytoxin, phospholipases A2 from *Vipera ammodytes ammodytes* which

- differ in neurotoxicity and anticoagulant activity, *J. Struct. Biol.* **169** (3), 360-369, 2010.
- 305. Gubensek, F.; Krizaj, I.; Pungercar, J. Monomeric phospholipase A2 neurotoxins, in *Venom Phospholipase A2 Enzymes: Structure, Function and Mechanism*, Kini, R. M., editor; John Wiley & Sons: Chichester, England, 1997, 245-268.
  - 306. Kondo, K. et al. Characterization of phospholipase A activity of betal-bungarotoxin from *Bungarus multicinctus* venom. I. Its enzymatic properties and modification with p-bromophenacyl bromide, *J. Biochem. (Tokyo)* **84** (5), 1291-1300, 1978.
  - 307. Tsai, I.H. et al. Molecular cloning and characterization of a neurotoxic phospholipase A2 from the venom of Taiwan habu (*Trimeresurus mucrosquamatus*), *Biochem. J.* **311** (Pt 3) 895-900, 1995.
  - 308. Aird, S.D. et al. Rattlesnake presynaptic neurotoxins: primary structure and evolutionary origin of the acidic subunit, *Biochemistry* **24** (25), 7054-7058, 1985.
  - 309. Aird, S.D. et al. A complete amino acid sequence for the basic subunit of crotoxin, *Arch. Biochem. Biophys.* **249** (2), 296-300, 1986.
  - 310. Fohlman, J. et al. Taipoxin, an extremely potent presynaptic neurotoxin from the venom of the australian snake taipan (*Oxyuranus s. scutellatus*). Isolation, characterization, quaternary structure and pharmacological properties, *Eur. J. Biochem.* **68** (2), 457-469, 1976.
  - 311. Lind, P., & Eaker, D. Amino-acid sequence of the alpha-subunit of taipoxin, an extremely potent presynaptic neurotoxin from the Australian snake taipan (*Oxyuranus s. scutellatus*), *Eur. J. Biochem.* **124** (3), 441-447, 1982.
  - 312. Kini, R.M., & Iwanaga, S. Structure-function relationships of phospholipases. I: Prediction of presynaptic neurotoxicity, *Toxicon* **24** (6), 527-541, 1986.
  - 313. Curin-Serbec, V. et al. Immunological studies of the toxic site in ammodytoxin A, *FEBS Lett.* **280** (1), 175-178, 1991.
  - 314. Pungercar, J. et al. An aromatic, but not a basic, residue is involved in the toxicity of group-II phospholipase A2 neurotoxins, *Biochem. J.* **341** (Pt 1) 139-145, 1999.
  - 315. Venkatesh, M. et al. Purification, characterization, and chemical modification of neurotoxic peptide from *Daboia russelii* snake venom of India, *J Biochem. Mol Toxicol.* **27** (6), 295-304, 2013.
  - 316. Gopalakrishnakone, P.; Ponraj, D.; Thwin, M. M. Myotoxic phospholipases from snake venoms: general myoglobinuric and local myonecrotic toxins., in *Venom Phospholipase A2 Enzyme: Structure, Function and Mechanism*, Kini, R. M., editor; John Wiley & Sons: Chichester, England, 1997, 287-320.
  - 317. Gutierrez, J.M., & Ownby, C.L. Skeletal muscle degeneration induced by venom phospholipases A2: insights into the mechanisms of local and systemic myotoxicity, *Toxicon* **42** (8), 915-931, 2003.
  - 318. Mukherjee, A.K., & Maity, C.R. Biochemical composition, lethality and pathophysiology of venom from two cobras-- *Naja naja* and *N. kaouthia*, *Comp Biochem. Physiol B Biochem. Mol. Biol.* **131** (2), 125-132, 2002.
  - 319. Kini, R.M., & Iwanaga, S. Structure-function relationships of phospholipases. II: Charge density distribution and the myotoxicity of presynaptically neurotoxic phospholipases, *Toxicon* **24** (9), 895-905, 1986.

320. Lomonte, B. et al. An overview of lysine-49 phospholipase A2 myotoxins from crotalid snake venoms and their structural determinants of myotoxic action, *Toxicon* **42** (8), 885-901, 2003.
321. Huancahuire-Vega, S. et al. Chemical modifications of PhTX-I myotoxin from Porthidium hyoprora snake venom: effects on structural, enzymatic, and pharmacological properties, *Biomed. Res. Int.* **2013** 103494, 2013.
322. Mora-Obando, D. et al. Synergism between basic Asp49 and Lys49 phospholipase A2 myotoxins of viperid snake venom in vitro and in vivo, *PLoS. ONE.* **9** (10), e109846, 2014.
323. Fletcher, J.E. et al. Basic phospholipase A2 from Naja nigricollis snake venom: phospholipid hydrolysis and effects on electrical and contractile activity of the rat heart, *Toxicol. Appl. Pharmacol.* **66** (1), 39-54, 1982.
324. Huang, M.Z. et al. Effects of an acidic phospholipase A2 purified from Ophiophagus hannah (king cobra) venom on rat heart, *Toxicon* **31** (5), 627-635, 1993.
325. Dhillon, D.S. et al. Comparison of enzymatic and pharmacological activities of lysine-49 and aspartate-49 phospholipases A2 from Agkistrodon piscivorus piscivorus snake venom, *Biochem. Pharmacol.* **36** (10), 1723-1730, 1987.
326. Paramo, L. et al. Bactericidal activity of Lys49 and Asp49 myotoxic phospholipases A2 from Bothrops asper snake venom--synthetic Lys49 myotoxin II-(115-129)-peptide identifies its bactericidal region, *Eur. J. Biochem.* **253** (2), 452-461, 1998.
327. Weiss, J. et al. Conversion of pig pancreas phospholipase A2 by protein engineering into enzyme active against Escherichia coli treated with the bactericidal/permeability-increasing protein, *J. Biol. Chem.* **266** (7), 4162-4167, 1991.
328. Weiss, J. et al. Structural determinants of the action against Escherichia coli of a human inflammatory fluid phospholipase A2 in concert with polymorphonuclear leukocytes, *J. Biol. Chem.* **269** (42), 26331-26337, 1994.
329. Elsbach, P. et al. The role of intramembrane Ca<sup>2+</sup> in the hydrolysis of the phospholipids of Escherichia coli by Ca<sup>2+</sup>-dependent phospholipases, *J. Biol. Chem.* **260** (3), 1618-1622, 1985.
330. Koduri, R.S. et al. Bactericidal properties of human and murine groups I, II, V, X, and XII secreted phospholipases A(2), *J. Biol. Chem.* **277** (8), 5849-5857, 2002.
331. Sudarshan, S., & Dhananjaya, B.L. Antibacterial potential of a basic phospholipase A2 (VRV-PL-V) of Daboia russelii pulchella (Russell's Viper) venom, *Biochemistry (Mosc.)* **79** (11), 1237-1244, 2014.
332. Sudarshan, S., & Dhananjaya, B.L. The Antimicrobial Activity of an Acidic Phospholipase A(2) (NN-XIa-PLA(2)) from the Venom of Naja naja naja (Indian Cobra), *Appl. Biochem. Biotechnol.* **176** (7), 2027-2038, 2015.
333. Samy, R.P. et al. Viperatoxin-II: A novel viper venom protein as an effective bactericidal agent, *FEBS Open. Bio* **5** 928-941, 2015.
334. Vishwanath, B.S. et al. Characterization of three edema-inducing phospholipase A2 enzymes from habu (Trimeresurus flavoviridis) venom and their interaction with the alkaloid aristolochic acid, *Toxicon* **25** (5), 501-515, 1987.

335. Angulo, Y. et al. Isolation and characterization of a myotoxic phospholipase A2 from the venom of the arboreal snake Bothriechis (Bothrops) schlegelii from Costa Rica, *Arch. Biochem. Biophys.* **339** (2), 260-266, 1997.
336. Ali, S.A. et al. Sea snake Hydrophis cyanocinctus venom. I. Purification, characterization and N-terminal sequence of two phospholipases A2, *Toxicon* **37** (11), 1505-1520, 1999.
337. Yamaguchi, Y. et al. Characterization, amino acid sequence and evolution of edema-inducing, basic phospholipase A2 from Trimeresurus flavoviridis venom, *Toxicon* **39** (7), 1069-1076, 2001.
338. Roberto, P.G. et al. Cloning and identification of a complete cDNA coding for a bactericidal and antitumoral acidic phospholipase A2 from Bothrops jararacussu venom, *Protein J.* **23** (4), 273-285, 2004.
339. Magro, A.J. et al. Structure of BthA-I complexed with p-bromophenacyl bromide: possible correlations with lack of pharmacological activity, *Acta Crystallogr. D. Biol. Crystallogr.* **61** (Pt 12), 1670-1677, 2005.
340. Wang, Y.M. et al. Absence of phospholipase A(2) in most Crotalus horridus venom due to translation blockage: comparison with Crotalus horridus atricaudatus venom, *Toxicon* **56** (1), 93-100, 2010.
341. Dutta, S. et al. Anticoagulant mechanism and platelet deaggregation property of a non-cytotoxic, acidic phospholipase A2 purified from Indian cobra (Naja naja) venom: inhibition of anticoagulant activity by low molecular weight heparin, *Biochimie* **110** 93-106, 2015.
342. Rodrigues, R.S. et al. Isolation and functional characterization of a new myotoxic acidic phospholipase A(2) from Bothrops pauloensis snake venom, *Toxicon* **50** (1), 153-165, 2007.
343. Santos-Filho, N.A. et al. A new acidic myotoxic, anti-platelet and prostaglandin I2 inductor phospholipase A2 isolated from Bothrops moojeni snake venom, *Toxicon* **52** (8), 908-917, 2008.
344. Mounier, C. et al. Platelet secretory phospholipase A2 fails to induce rabbit platelet activation and to release arachidonic acid in contrast with venom phospholipases A2, *Biochim. Biophys. Acta* **1214** (1), 88-96, 1994.
345. Boffa, M.C., & Boffa, G.A. A phospholipase A2 with anticoagulant activity. II. inhibition of the phospholipid activity in coagulation. *Biochim. Biophys. Acta* **429** (3), 839-852, 1976.
346. Stefansson, S. et al. The inhibition of clotting complexes of the extrinsic coagulation cascade by the phospholipase A2 isoenzymes from Naja nigricollis venom, *Thromb. Res.* **55** (4), 481-491, 1989.
347. Atanasov, V.N. et al. Hemolytic and anticoagulant study of the neurotoxin vipoxin and its components--basic phospholipase A2 and an acidic inhibitor, *Biochemistry (Mosc.)* **74** (3), 276-280, 2009.
348. Kerns, R.T. et al. Targeting of venom phospholipases: the strongly anticoagulant phospholipase A(2) from Naja nigricollis venom binds to coagulation factor Xa to inhibit the prothrombinase complex, *Arch. Biochem. Biophys.* **369** (1), 107-113, 1999.
349. Verheij, H.M. et al. Correlation of enzymatic activity and anticoagulant properties of phospholipase A2, *Eur. J. Biochem.* **112** (1), 25-32, 1980.
350. Renetseder, R. et al. A comparison of the crystal structures of phospholipase A2 from bovine pancreas and Crotalus atrox venom, *J. Biol. Chem.* **260** (21), 11627-11634, 1985.

351. Faure, G.et al. Characterization of a human coagulation factor Xa-binding site on Viperidae snake venom phospholipases A2 by affinity binding studies and molecular bioinformatics, *BMC. Struct. Biol.* **7** 82, 2007.
352. Gutierrez, J.M.et al. Systemic and local myotoxicity induced by snake venom group II phospholipases A2: comparison between crot toxin, crot toxin B and a Lys49 PLA2 homologue, *Toxicon* **51** (1), 80-92, 2008.
353. Kini, R.M., & Evans, H.J. The role of enzymatic activity in inhibition of the extrinsic tenase complex by phospholipase A2 isoenzymes from Naja nigricollis venom, *Toxicon* **33** (12), 1585-1590, 1995.
354. Tsai, I.H.et al. cDNA cloning, structural, and functional analyses of venom phospholipases A(2) and a Kunitz-type protease inhibitor from steppe viper *Vipera ursinii renardi*, *Toxicon* **57** (2), 332-341, 2011.
355. Laing, G.D.et al. Characterisation of a purified phospholipase A2 from the venom of the Papuan black snake (*Pseudechis papuanus*), *Biochim. Biophys. Acta* **1250** (2), 137-143, 1995.
356. Saikia, D.et al. Mechanism of in vivo anticoagulant and haemolytic activity by a neutral phospholipase A(2) purified from *Daboia russelii russelii* venom: correlation with clinical manifestations in Russell's Viper envenomed patients, *Toxicon* **76** 291-300, 2013.
357. Chakraborty, A.K.et al. Purification and characterization of a potent hemolytic toxin with phospholipase A2 activity from the venom of Indian Russell's viper, *Mol. Cell Biochem.* **237** (1-2), 95-102, 2002.
358. Prijatelj, P.et al. The C-terminal and beta-wing regions of ammodytoxin A, a neurotoxic phospholipase A2 from *Vipera ammodytes ammodytes*, are critical for binding to factor Xa and for anticoagulant effect, *Biochimie* **88** (1), 69-76, 2006.
359. Osipov, A.V.et al. A new type of thrombin inhibitor, noncytotoxic phospholipase A2, from the *Naja haje* cobra venom, *Toxicon* **55** (2-3), 186-194, 2010.
360. Antonypillai, C.N.et al. Hypopituitarism following envenoming by Russell's vipers (*Daboia siamensis* and *D. russelii*) resembling Sheehan's syndrome: first case report from Sri Lanka, a review of the literature and recommendations for endocrine management, *QJM.* **104** (2), 97-108, 2011.
361. Thorpe, R.S.et al. Phylogeography of the Russell's viper (*Daboia russelii*) complex in relation to variation in the colour pattern and symptoms of envenoming, *The Herpetological Journal* **17** (4), 209-218, 2007.
362. Isbister, G.K.et al. Venom Concentrations and Clotting Factor Levels in a Prospective Cohort of Russell's Viper Bites with Coagulopathy, *PLoS Negl. Trop. Dis.* **9** (8), e0003968, 2015.
363. Phillips, R.E.et al. Paralysis, rhabdomyolysis and haemolysis caused by bites of Russell's viper (*Vipera russelli pulchella*) in Sri Lanka: failure of Indian (Haffkine) antivenom, *Q. J. Med.* **68** (257), 691-715, 1988.
364. Than, T.et al. Evolution of coagulation abnormalities following Russell's viper bite in Burma, *Br. J Haematol.* **65** (2), 193-198, 1987.
365. Silva, A.et al. Viper bites complicate chronic agrochemical nephropathy in rural Sri Lanka, *J. Venom. Anim. Toxins. Incl. Trop. Dis.* **20** 33, 2014.
366. Golay, V.et al. Spontaneous peri-nephric hematoma in a patient with acute kidney injury following Russell's viper envenomation, *Saudi. J Kidney Dis. Transpl.* **26** (2), 335-338, 2015.

367. Kularatne, S.A.et al. Revisiting Russell's viper (*Daboia russelii*) bite in Sri Lanka: is abdominal pain an early feature of systemic envenoming?, *PLoS ONE*. **9** (2), e90198, 2014.
368. Bandyopadhyay, S.K.et al. Hypopituitarism following poisonous viperbite, *J Indian Med. Assoc.* **110** (2), 120, 122, 2012.
369. Gouda, S.et al. Posterior circulation ischemic stroke following Russell's viper envenomation, *Ann. Indian Acad. Neurol.* **14** (4), 301-303, 2011.
370. Subasinghe, C.J.et al. Bilateral blindness following Russell's viper bite - a rare clinical presentation: a case report, *J. Med. Case. Rep.* **8** 99, 2014.
371. Jayanthi, G.P., & Gowda, T.V. Geographical variation in India in the composition and lethal potency of Russell's viper (*Vipera russelli*) venom, *Toxicon* **26** (3), 257-264, 1988.
372. Prasad, N.B.et al. Comparative characterisation of Russell's viper (*Daboia/Vipera russelli*) venoms from different regions of the Indian peninsula, *Biochim. Biophys. Acta* **1428** (2-3), 121-136, 1999.
373. Chandra, V.et al. Three-dimensional structure of a presynaptic neurotoxic phospholipase A2 from *Daboia russelli pulchella* at 2.4 Å resolution, *J. Mol. Biol.* **296** (4), 1117-1126, 2000.
374. Mandal, S., & Bhattacharyya, D. Two L-amino acid oxidase isoenzymes from Russell's viper (*Daboia russelli russelli*) venom with different mechanisms of inhibition by substrate analogs, *FEBS J.* **275** (9), 2078-2095, 2008.
375. Chen, H.S.et al. P-III hemorrhagic metalloproteinases from Russell's viper venom: cloning, characterization, phylogenetic and functional site analyses, *Biochimie* **90** (10), 1486-1498, 2008.
376. Mukherjee, A.K. Characterization of a novel pro-coagulant metalloprotease (RVBCMP) possessing alpha-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.
377. Bhattacharjee, P., & Bhattacharyya, D. Factor V activator from *Daboia russelli russelli* venom destabilizes beta-amyloid aggregate, the hallmark of Alzheimer disease, *J. Biol. Chem.* **288** (42), 30559-30570, 2013.
378. Mitra, J., & Bhattacharyya, D. Phosphodiesterase from *Daboia russelli russelli* venom: Purification, partial characterization and inhibition of platelet aggregation, *Toxicon* **88** 1-10, 2014.
379. Mukherjee, A.K.et al. Characterization of a pro-angiogenic, novel peptide from Russell's viper (*Daboia russelii russelii*) venom, *Toxicon* **77** 26-31, 2014.
380. Thakur, R.et al. A new peptide (Ruviprase) purified from the venom of *Daboia russelii russelii* shows potent anticoagulant activity via non-enzymatic inhibition of thrombin and factor Xa, *Biochimie* **105** 149-158, 2014.
381. Bhat, M.K.et al. Structure-function relationships among neurotoxic phospholipases: NN-XIII-PLA2 from Indian cobra (*Naja naja naja*) and VRV PL-V from Russell's viper (*Vipera russelli*) venoms, *Toxicon* **29** (1), 97-105, 1991.
382. Kasturi, S., & Gowda, T.V. Analysis of *Vipera russelli* venom using polyclonal antibodies prepared against its purified toxic phospholipase A2 VRV PL-V, *Biochem. Int.* **27** (1), 155-164, 1992.

383. Jayanthi, G.P. et al. Dissociation of catalytic activity and neurotoxicity of a basic phospholipase A2 from Russell's viper (*Vipera russelli*) venom, *Toxicon* **27** (8), 875-885, 1989.
384. Vishwanath, B.S. et al. Purification and partial biochemical characterization of an edema inducing phospholipase A2 from *Vipera russelli* (Russell's viper) snake venom, *Toxicon* **26** (8), 713-720, 1988.
385. Kasturi, S. et al. Antibodies to a phospholipase A2 from *Vipera russelli* selectively neutralize venom neurotoxicity, *Immunology* **70** (2), 175-180, 1990.
386. Babu, A.S., & Gowda, T.V. Effects of chemical modification on enzymatic and toxicological properties of phospholipases A2 from *Naja naja naja* and *Vipera russelli* snake venoms, *Toxicon* **29** (10), 1251-1262, 1991.
387. Gowda, V.T. et al. Primary sequence determination of the most basic myonecrotic phospholipase A2 from the venom of *Vipera russelli*, *Toxicon* **32** (6), 665-673, 1994.
388. Gowda, T.V., & Middlebrook, J.L. Monoclonal antibodies to VRV-PL-VIIIa, a basic multitoxic phospholipase A2 from *Vipera russelli* venom, *Toxicon* **32** (8), 955-964, 1994.
389. Uma, B., & Veerabasappa, G.T. Molecular mechanism of lung hemorrhage induction by VRV-PL-VIIIa from Russell's viper (*Vipera russelli*) venom, *Toxicon* **38** (8), 1129-1147, 2000.
390. Sudharshan, S., & Dhananjaya, B.L. Antibacterial potential of a basic phospholipase A2 (VRV-PL-VIIIa) from *Daboia russelii pulchella* (Russell's viper) venom, *J Venom. Anim. Toxins. Incl. Trop. Dis.* **21** 17, 2015.
391. Saikia, D. et al. Differential mode of attack on membrane phospholipids by an acidic phospholipase A(2) (RVVA-PLA(2)-I) from *Daboia russelli* venom, *Biochim. Biophys. Acta* **1818** (12), 3149-3157, 2012.
392. Kole, L. et al. Purification and characterization of an organ specific haemorrhagic toxin from *Vipera russelli russelli* (Russell's viper) venom, *Indian J. Biochem. Biophys.* **37** (2), 114-120, 2000.
393. Chakrabarty, D. et al. Purification and partial characterization of a haemorrhagin (VRH-1) from *Vipera russelli russelli* venom, *Toxicon* **31** (12), 1601-1614, 1993.
394. Chakrabarty, D. et al. Haemorrhagic protein of Russell's viper venom with fibrinolytic and esterolytic activities, *Toxicon* **38** (11), 1475-1490, 2000.
395. Thakur, R. et al. Elucidation of procoagulant mechanism and pathophysiological significance of a new prothrombin activating metalloprotease purified from *Daboia russelii russelii* venom, *Toxicon* **100** 1-12, 2015.
396. Risch, M. et al. Snake venomics of the Siamese Russell's viper (*Daboia russelli siamensis*) -- relation to pharmacological activities, *J. Proteomics.* **72** (2), 256-269, 2009.
397. Zelanis, A. et al. Analysis of the ontogenetic variation in the venom proteome/peptidome of *Bothrops jararaca* reveals different strategies to deal with prey, *J. Proteome. Res.* **9** (5), 2278-2291, 2010.
398. Warrell, D.A. Snake venoms in science and clinical medicine. 1. Russell's viper: biology, venom and treatment of bites, *Trans. R. Soc. Trop. Med. Hyg.* **83** (6), 732-740, 1989.

399. LOWRY, O.H. et al. Protein measurement with the Folin phenol reagent, *J Biol. Chem.* **193** (1), 265-275, 1951.
400. Laemmli, U.K. Cleavage of structural proteins during the assembly of the head of bacteriophage T4, *Nature* **227** (5259), 680-685, 1970.
401. Joubert, F.J., & Taljaard, N. Purification, some properties and amino-acid sequences of two phospholipases A (CM-II and CM-III) from *Naja naja kaouthia* venom, *Eur. J. Biochem.* **112** (3), 493-499, 1980.
402. Doley, R., & Mukherjee, A.K. Purification and characterization of an anticoagulant phospholipase A(2) from Indian monocled cobra (*Naja kaouthia*) venom, *Toxicon* **41** (1), 81-91, 2003.
403. LANGDELL, R.D. et al. Effect of antihemophilic factor on one-stage clotting tests; a presumptive test for hemophilia and a simple one-stage antihemophilic factor assay procedure, *J. Lab Clin. Med.* **41** (4), 637-647, 1953.
404. Pla, D. et al. Second generation snake antivenomics: comparing immunoaffinity and immunodepletion protocols, *Toxicon* **60** (4), 688-699, 2012.
405. George, A. et al. Viper bite poisoning in India: a review with special reference to renal complications, *Ren Fail.* **10** (2), 91-99, 1987.
406. Woodhams, B.J. et al. Differences between the venoms of two sub-species of Russell's viper: *Vipera russelli pulchella* and *Vipera russelli siamensis*, *Toxicon* **28** (4), 427-433, 1990.
407. Jeyarajah, R. Russell's viper bite in Sri Lanka. A study of 22 cases, *Am. J. Trop. Med. Hyg.* **33** (3), 506-510, 1984.
408. Hung, D.Z. et al. Russell's viper snakebite in Taiwan: differences from other Asian countries, *Toxicon* **40** (9), 1291-1298, 2002.
409. Gawarammana, I.B. et al. Parallel infusion of hydrocortisone +/- chlorpheniramine bolus injection to prevent acute adverse reactions to antivenom for snakebites, *Med. J. Aust.* **180** (1), 20-23, 2004.
410. Das, R.R. et al. High-dose versus low-dose antivenom in the treatment of poisonous snake bites: A systematic review, *Indian J. Crit Care Med.* **19** (6), 340-349, 2015.
411. Calvete, J.J. et al. Snake venomics and antivenomics of *Bothrops colombiensis*, a medically important pitviper of the *Bothrops atrox-asper* complex endemic to Venezuela: Contributing to its taxonomy and snakebite management, *J. Proteomics.* **72** (2), 227-240, 2009.
412. Boldrini-Franca, J. et al. Snake venomics and antivenomics of *Crotalus durissus* subspecies from Brazil: assessment of geographic variation and its implication on snakebite management, *J. Proteomics.* **73** (9), 1758-1776, 2010.
413. Lomonte, B., & Carmona, E. Individual expression patterns of myotoxin isoforms in the venom of the snake *Bothrops asper*, *Comp Biochem. Physiol B* **102** (2), 325-329, 1992.
414. Singh, A. et al. Acute pulmonary edema as a complication of anti-snake venom therapy, *Indian J. Pediatr.* **68** (1), 81-82, 2001.
415. Kalantri, S. et al. Clinical predictors of in-hospital mortality in patients with snake bite: a retrospective study from a rural hospital in central India, *Trop. Med. Int. Health* **11** (1), 22-30, 2006.

416. Rombouts, I.et al. Improved identification of wheat gluten proteins through alkylation of cysteine residues and peptide-based mass spectrometry, *Sci. Rep.* **3** 2279, 2013.
417. Ouyang, C., & Teng, C.M. Fibrinogenolytic enzymes of *Trimeresurus mucrosquamatus* venom, *Biochim. Biophys. Acta* **420** (2), 298-308, 1976.
418. Jeng, T.W.et al. Search for relationships among the hemolytic, phospholipolytic, and neurotoxic activities of snake venoms, *Proc. Natl. Acad. Sci. U. S. A* **75** (2), 600-604, 1978.
419. Mukherje, A.K.et al. Some biochemical properties of Russell's viper (*Daboia russelli*) venom from Eastern India: correlation with clinico-pathological manifestation in Russell's viper bite, *Toxicon* **38** (2), 163-175, 2000.
420. Vishwanath, B.S., & Gowda, T.V. Interaction of aristolochic acid with *Vipera russelli* phospholipase A2: its effect on enzymatic and pathological activities, *Toxicon* **25** (9), 929-937, 1987.
421. KONDO, H.et al. Studies on the quantitative method for determination of hemorrhagic activity of Habu snake venom, *Jpn. J. Med. Sci. Biol.* **13** 43-52, 1960.
422. van de Loosdrecht, A.A.et al. A tetrazolium-based colorimetric MTT assay to quantitate human monocyte mediated cytotoxicity against leukemic cells from cell lines and patients with acute myeloid leukemia, *J. Immunol. Methods* **174** (1-2), 311-320, 1994.
423. Doley, R., & Kini, R.M. Protein complexes in snake venom, *Cell Mol. Life Sci.* **66** (17), 2851-2871, 2009.
424. Mancheva, I.et al. Sequence homology between phospholipase and its inhibitor in snake venom. The primary structure of phospholipase A2 of vipoxin from the venom of the Bulgarian viper (*Vipera ammodytes ammodytes*, Serpentes), *Biol. Chem. Hoppe Seyler* **368** (4), 343-352, 1987.
425. Wang, Y.M.et al. Characterization and molecular cloning of neurotoxic phospholipases A2 from Taiwan viper (*Vipera russelli formosensis*), *Eur. J. Biochem.* **209** (2), 635-641, 1992.
426. Maung, M.T.et al. A major lethal factor of the venom of Burmese Russell's viper (*Daboia russelli siamensis*): isolation, N-terminal sequencing and biological activities of daboia toxin, *Toxicon* **33** (1), 63-76, 1995.
427. Kasturi, S., & Gowda, T.V. Purification and characterization of a major phospholipase A2 from Russell's viper (*Vipera russelli*) venom, *Toxicon* **27** (2), 229-237, 1989.
428. Jan, V.M.et al. Phospholipase A2 diversity and polymorphism in European viper venoms: paradoxical molecular evolution in Viperinae, *Toxicon* **50** (8), 1140-1161, 2007.
429. Tsai, I.H.et al. Two types of Russell's viper revealed by variation in phospholipases A2 from venom of the subspecies, *Toxicon* **34** (1), 99-109, 1996.
430. Oyama, E., & Takahashi, H. Purification and characterization of a thrombin-like enzyme, elegaxobin, from the venom of *Trimeresurus elegans* (Sakishima-habu), *Toxicon* **38** (8), 1087-1100, 2000.
431. Fox, J.W., & Serrano, S.M. Insights into and speculations about snake venom metalloproteinase (SVMP) synthesis, folding and disulfide bond formation and their contribution to venom complexity, *FEBS J.* **275** (12), 3016-3030, 2008.

432. Fox, J.W., & Serrano, S.M. Timeline of Key Events in Snake Venom Metalloproteinase Research, *J. Proteomics.*, 2009.
433. Fox, J. W.; Serrano, S. M. Snake venom metalloprotease, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 95-113.
434. Grant, G.A. et al. Amino acid sequence of kappa-flavitoxin: establishment of a new family of snake venom neurotoxins, *Biochemistry* **27** (10), 3794-3798, 1988.
435. Gutierrez, J.M., & Rucavado, A. Snake venom metalloproteinases: their role in the pathogenesis of local tissue damage, *Biochimie* **82** (9-10), 841-850, 2000.
436. Takeda, S. et al. Crystal structure of RVV-X: An example of evolutionary gain of specificity by ADAM proteinases, *FEBS Lett.* **581** (30), 5859-5864, 2007.
437. Fujikawa, K. et al. Bovine factor X 1 (Stuart factor). Mechanism of activation by protein from Russell's viper venom, *Biochemistry* **11** (26), 4892-4899, 1972.
438. Tan, N. H.; Fung, S. Y. Snake venom L-amino acid oxidases, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 221-235.
439. Suhr, S.M., & Kim, D.S. Identification of the snake venom substance that induces apoptosis, *Biochem. Biophys. Res. Commun.* **224** (1), 134-139, 1996.
440. Samel, M. et al. Isolation and characterization of an apoptotic and platelet aggregation inhibiting L-amino acid oxidase from Vipera berus berus (common viper) venom, *Biochim. Biophys. Acta* **1764** (4), 707-714, 2006.
441. Aird, S.D. et al. Quantitative high-throughput profiling of snake venom gland transcriptomes and proteomes (Ovophis okinavensis and Protobothrops flavoviridis), *BMC Genomics* **14** 790, 2013.
442. Russell, F.E. et al. Zootoxicological properties of venom phosphodiesterase., *Toxicon* **1** 99-108, 1963.
443. Zhong, S.R. et al. Characterization and molecular cloning of dabocetin, a potent antiplatelet C-type lectin-like protein from Daboia russellii siamensis venom, *Toxicon* **47** (1), 104-112, 2006.
444. Andrews, R.K. et al. Binding of a novel 50-kilodalton alboaggregin from Trimeresurus albolabris and related viper venom proteins to the platelet membrane glycoprotein Ib-IX-V complex. Effect on platelet aggregation and glycoprotein Ib-mediated platelet activation, *Biochemistry* **35** (38), 12629-12639, 1996.
445. Asazuma, N. et al. The snake venom toxin alboaggregin-A activates glycoprotein VI, *Blood* **97** (12), 3989-3991, 2001.
446. Dormann, D. et al. Alboaggregin A activates platelets by a mechanism involving glycoprotein VI as well as glycoprotein Ib, *Blood* **97** (4), 929-936, 2001.
447. Guo, C.T. et al. Trypsin and chymotrypsin inhibitor peptides from the venom of Chinese Daboia russellii siamensis, *Toxicon* **63** 154-164, 2013.
448. Qiu, Y. et al. Molecular cloning and antifibrinolytic activity of a serine protease inhibitor from bumblebee (*Bombus terrestris*) venom, *Toxicon* **63** 1-6, 2013.
449. Schweitz, H. et al. Calciclidine, a venom peptide of the Kunitz-type protease inhibitor family, is a potent blocker of high-threshold Ca<sup>2+</sup> channels with a

- high affinity for L-type channels in cerebellar granule neurons, *Proc. Natl. Acad. Sci. U. S. A* **91** (3), 878-882, 1994.
450. Sanz-Soler, R. et al. Recombinant expression of mutants of the Frankenstein disintegrin, RTS-o-cellatusin. Evidence for the independent origin of RGD and KTS/RTS disintegrins, *Toxicon* **60** (4), 665-675, 2012.
451. Calvete, J. J.; Juarez, P.; Sanz, L. Snake venomics and disintegrins portrait and evolution of a family of snake venom integrin antagonist, in *Handbook of venoms and toxins of reptiles*, Mackessy, S. P., editor; CRC Press: Boca Raton, 2010, 337-358o.
452. Yamazaki, Y. et al. Snake venom vascular endothelial growth factors (VEGFs) exhibit potent activity through their specific recognition of KDR (VEGF receptor 2), *J. Biol. Chem.* **278** (52), 51985-51988, 2003.
453. Li, A.K. et al. Nerve growth factor: acceleration of the rate of wound healing in mice, *Proc. Natl. Acad. Sci. U. S. A* **77** (7), 4379-4381, 1980.
454. Rokyta, D.R. et al. The venom-gland transcriptome of the eastern diamondback rattlesnake (*Crotalus adamanteus*), *BMC Genomics* **13** 312, 2012.
455. Kini, R.M. Platelet aggregation and exogenous factors from animal sources, *Curr. Drug Targets. Cardiovasc. Haematol. Disord.* **4** (4), 301-325, 2004.
456. Joseph, J.S. et al. Amino acid sequence of trocarin, a prothrombin activator from *Tropidodactylus carinatus* venom: its structural similarity to coagulation factor Xa, *Blood* **94** (2), 621-631, 1999.
457. Ward, M. Pyridylethylation of Cysteine Residues, in *The Protein Protocols Handbook*, 3rd ed.; John M. Walker, editor; Humana Press: New York, 2002, 461-463.
458. Crimmins, D. L.; Mische, S. M.; Denslow, N. D. Chemical cleavage of proteins in solution, in *Current Protocols in Protein Science*, Coligan John E; Dunn Ben M; Speicher David W; and Wingfield Paul T, editors; Wiley Online Library: New Jersey, 2005, 1-11.
459. Milner, S.J. et al. Optimization of the hydroxylamine cleavage of an expressed fusion protein to produce recombinant human insulin-like growth factor (IGF)-I, *Biotechnol. Bioeng.* **50** (3), 265-272, 1996.
460. Larkin, M.A. et al. Clustal W and Clustal X version 2.0, *Bioinformatics*. **23** (21), 2947-2948, 2007.
461. Tamura, K. et al. MEGA5: molecular evolutionary genetics analysis using maximum likelihood, evolutionary distance, and maximum parsimony methods, *Mol. Biol. Evol.* **28** (10), 2731-2739, 2011.
462. Saitou, N., & Nei, M. The neighbour joining method: A new method for reconstructing phylogenetic trees., *Mol Biol Evol* **4** (4), 406-425, 1987.
463. Kelly, S.M. et al. How to study proteins by circular dichroism, *Biochim. Biophys. Acta* **1751** (2), 119-139, 2005.
464. Louis-Jeune Cet al. Prediction of protein secondary structure from circular dichroism using theoretically derived spectra, *Proteins. Structure, Function, and Bioinformatics* **80** (2), 2011.
465. Scott, D.L., & Sigler, P.B. Structure and catalytic mechanism of secretory phospholipases A2, *Adv. Protein Chem.* **45** 53-88, 1994.
466. Fleer, E.A. et al. Modification of carboxylate groups in bovine pancreatic phospholipase A2. Identification of aspartate-49 as Ca<sup>2+</sup>-binding ligand, *Eur. J. Biochem.* **113** (2), 283-288, 1981.

467. Gasteiger E; Hoogland C; Gattiker A; Duvaud S; Wilkins M.R; Appel R.D; Bairoch A Protein Identification and Analysis Tools on the ExPASy Server; in *The Proteomics Protocols Handbook*, John M.Walker, editor; Humana Press: New York, 2005, 571-607.
468. Tsai, I.H. et al. Venom phospholipases of Russell's vipers from Myanmar and eastern India--cloning, characterization and phylogeographic analysis, *Biochim. Biophys. Acta* **1774** (8), 1020-1028, 2007.
469. Scott, D.L. et al. Structures of free and inhibited human secretory phospholipase A2 from inflammatory exudate, *Science* **254** (5034), 1007-1010, 1991.
470. Maduwage, K. et al. The in vitro toxicity of venoms from South Asian hump-nosed pit vipers (Viperidae: Hypnale), *J. Venom. Res.* **2** 17-23, 2011.
471. Lundblad, R. L. Modification of Heterocyclic Amino Acids: Histidine and Tryptophan, in *Chemical modification of biological polymers*, CRC Press: Florida, 2011, 167-214.
472. Banerjee, Y. et al. Hemextin AB complex, a unique anticoagulant protein complex from *Hemachatus haemachatus* (African Ringhals cobra) venom that inhibits clot initiation and factor VIIa activity, *J. Biol. Chem.* **280** (52), 42601-42611, 2005.
473. Eckly, A. et al. Mechanisms underlying FeCl<sub>3</sub>-induced arterial thrombosis, *J. Thromb. Haemost.* **9** (4), 779-789, 2011.
474. Wang, X. et al. Effects of factor IX or factor XI deficiency on ferric chloride-induced carotid artery occlusion in mice, *J. Thromb. Haemost.* **3** (4), 695-702, 2005.
475. Wu, W. et al. The kunitz protease inhibitor domain of protease nexin-2 inhibits factor XIa and murine carotid artery and middle cerebral artery thrombosis, *Blood* **120** (3), 671-677, 2012.
476. Valgas, C. et al. Screening methods to determine antibacterial activity of natural products, *Brazilian Journal of Microbiology* **38** 369-380, 2007.
477. Gutierrez, J.M. et al. Impact of regional variation in *Bothrops asper* snake venom on the design of antivenoms: integrating antivenomics and neutralization approaches, *J. Proteome. Res.* **9** (1), 564-577, 2010.
478. Kini, R.M., & Evans, H.J. A model to explain the pharmacological effects of snake venom phospholipases A2, *Toxicon* **27** (6), 613-635, 1989.
479. Dennis, E.A. Phospholipase A2 in eicosanoid generation, *Am. J. Respir. Crit Care Med.* **161** (2 Pt 2), S32-S35, 2000.
480. Donato, N.J. et al. Regulation of epidermal growth factor receptor activity by crotoxin, a snake venom phospholipase A2 toxin. A novel growth inhibitory mechanism, *Biochem. Pharmacol.* **51** (11), 1535-1543, 1996.
481. Gopalakrishnakone, P., & Hawgood, B.J. Morphological changes induced by crotoxin in murine nerve and neuromuscular junction, *Toxicon* **22** (5), 791-804, 1984.
482. Hendon, R.A., & Tu, A.T. The role of crotoxin subunits in tropical rattlesnake neurotoxic action, *Biochim. Biophys. Acta* **578** (1), 243-252, 1979.
483. Landucci, E.C. et al. Crotoxin induces aggregation of human washed platelets, *Toxicon* **32** (2), 217-226, 1994.
484. Rudd, C.J. et al. In vitro comparison of cytotoxic effects of crotoxin against three human tumors and a normal human epidermal keratinocyte cell line, *Invest New Drugs* **12** (3), 183-184, 1994.

485. Sampaio, S.C. et al. Contribution of crotoxin for the inhibitory effect of *Crotalus durissus terrificus* snake venom on macrophage function, *Toxicon* **41** (7), 899-907, 2003.
486. Sampaio, S.C. et al. Inhibitory effect of phospholipase A(2) isolated from *Crotalus durissus terrificus* venom on macrophage function, *Toxicon* **45** (5), 671-676, 2005.
487. Yan, C.H. et al. Autophagy is involved in cytotoxic effects of crotoxin in human breast cancer cell line MCF-7 cells, *Acta Pharmacol. Sin.* **28** (4), 540-548, 2007.
488. Zhang, H.L. et al. Opiate and acetylcholine-independent analgesic actions of crotoxin isolated from *crotalus durissus terrificus* venom, *Toxicon* **48** (2), 175-182, 2006.
489. Soares A.M., & Giglio, J.R. Chemical modifications of phospholipase A2 enzymes from snake venom : effects on catalytic and pharmacological properties, *Toxicon* **42** 855-868, 2003.
490. Zhao, H. et al. Structure of a snake venom phospholipase A2 modified by p-bromo-phenacyl-bromide, *Toxicon* **36** (6), 875-886, 1998.
491. Jiang, M.S. et al. Effects of divalent cations on snake venom cardiotoxin-induced hemolysis and 3H-deoxyglucose-6-phosphate release from human red blood cells, *Toxicon* **27** (12), 1297-1305, 1989.
492. Brown, A.M. et al. Neurotoxins that act selectively on voltage-dependent cardiac calcium channels, *Circ. Res.* **61** (4 Pt 2), I6-I9, 1987.
493. Chang, C.C., & Lee, C.Y. Isolation of neurotoxins from the venom of *Bungarus multicinctus* and their modes of neuromuscular blocking action, *Arch. Int. Pharmacodyn. Ther.* **144** 241-257, 1963.
494. Azevedo, F.V. et al. Human breast cancer cell death induced by BnSP-6, a Lys-49 PLA(2) homologue from *Bothrops pauloensis* venom, *Int. J Biol Macromol.* **82** 671-677, 2016.
495. Roy, A. et al. I-TASSER: a unified platform for automated protein structure and function prediction, *Nat. Protoc.* **5** (4), 725-738, 2010.
496. Li, Y., & Zhang, Y. REMO: A new protocol to refine full atomic protein models from C-alpha traces by optimizing hydrogen-bonding networks, *Proteins* **76** (3), 665-676, 2009.
497. Zhang, Y. I-TASSER server for protein 3D structure prediction, *BMC Bioinformatics.* **9** (1), 40, 2008.
498. Yang, J. et al. The I-TASSER Suite: protein structure and function prediction, *Nat. Methods* **12** (1), 7-8, 2015.
499. Girish , V. *Exactin-A specific inhibitor of FX activation by extrinsic tenase complex isolated from Hemachatus haemachatus venom*, PhD Thesis, National University of Singapore, Singapore, 2012.
500. Zhang, Y. et al. Nitrophorin-2: a novel mixed-type reversible specific inhibitor of the intrinsic factor-X activating complex, *Biochemistry* **37** (30), 10681-10690, 1998.
501. Mathur, A., & Bajaj, S.P. Protease and EGF1 domains of factor IXa play distinct roles in binding to factor VIIIa. Importance of helix 330 (helix 162 in chymotrypsin) of protease domain of factor IXa in its interaction with factor VIIIa, *J. Biol. Chem.* **274** (26), 18477-18486, 1999.
502. Koh, C.Y. et al. Variegin, a novel fast and tight binding thrombin inhibitor from the tropical bont tick, *J. Biol. Chem.* **282** (40), 29101-29113, 2007.

503. Darden, T. A.; Cheatham, T. E.; Simmerling, C. L.; Wang, J.; Duke, R. E.; Luo, R.; Walker, R. C.; Zhang, W.; Roberts, B.; Roitberg, A.; Seabra, G.; Swails, J.; Götz, A. W.; Kolossváry, I.; Wong, K. F.; Vanice, J.; Wolf, R. M.; Liu, J.; Wu, X.; Brozell, S. R.; Steinbrecher, T.; Gohlke, H.; Cai, Q.; Ye, X.; Mathews, D. H.; Cui, G.; Roe, D. R.; Seetin, M. G.; Salomon-Ferrer, R.; Sagu, C.; Babin, V.; Gusaro, S.; Kovalenko, A.; Kollman, P. A. *Amber* 12. 2012.
504. Duhovny D, N. R. W. H. Efficient Unbound Docking of Rigid Molecules., 2452 ed.; In Gusfield et al, editor; Springer Verlag: Berlin, 2002, 185-200.
505. Schneidman-Duhovny, D. et al. PatchDock and SymmDock: servers for rigid and symmetric docking, *Nucleic Acids Res.* **33** (Web Server issue), W363-W367, 2005.
506. Zhang, C. et al. Determination of atomic desolvation energies from the structures of crystallized proteins, *J. Mol. Biol.* **267** (3), 707-726, 1997.
507. Mashiach, E. et al. FireDock: a web server for fast interaction refinement in molecular docking, *Nucleic Acids Res.* **36** (Web Server issue), W229-W232, 2008.
508. Andrusier, N. et al. FireDock: fast interaction refinement in molecular docking, *Proteins* **69** (1), 139-159, 2007.
509. Kruger, D.M., & Gohlke, H. DrugScorePPI webserver: fast and accurate in silico alanine scanning for scoring protein-protein interactions, *Nucleic Acids Res.* **38** (Web Server issue), W480-W486, 2010.
510. Sobolev V. et al. SPACE: a suite of tools for protein structure prediction and analysis based on complementarity and environment, *Nucl. Acids Res* **33** 39-43, 2005.
511. Dabigatran (Pradaxa): deep vein thrombosis and pulmonary embolism. Warfarin remains the standard drug, *Prescrire. Int.* **24** (161), 150, 2015.
512. Groszek, B., & Piszczeck, P. [Vitamin K antagonists overdose], *Przegl. Lek.* **72** (9), 468-471, 2015.
513. Lei, L. et al. Coumarin derivatives from Ainsliaea fragrans and their anticoagulant activity, *Sci. Rep.* **5** 13544, 2015.
514. Stepanyan, G. et al. Safety of new oral anticoagulants for patients undergoing atrial fibrillation ablation, *J. Interv. Card Electrophysiol.* **40** (1), 33-38, 2014.
515. Huber, K. et al. Antiplatelet and anticoagulation agents in acute coronary syndromes: what is the current status and what does the future hold?, *Am. Heart J.* **168** (5), 611-621, 2014.
516. Ameln-Mayerhofer, A. [Management of bleeding complications associated with NOAC], *Med. Monatsschr. Pharm.* **38** (10), 389-393, 2015.
517. Death Associated with Inadequate Reassessment of Venous Thromboembolism Prophylaxis at and after Hospital Discharge, *Alta. RN.* **71** (3), 26-28, 2015.
518. Kini, R.M. Toxins in thrombosis and haemostasis: potential beyond imagination, *J. Thromb. Haemost.* **9 Suppl 1** 195-208, 2011.
519. Li, J. et al. Bivalirudin Anticoagulant Therapy With or Without Platelet Glycoprotein IIb/IIIa Inhibitors During Transcatheter Coronary Interventional Procedures: A Meta-Analysis, *Medicine (Baltimore)* **94** (32), e1067, 2015.
520. Liu, Z. et al. A novel stearic acid-modified hirudin peptidomimetic with improved pharmacokinetic properties and anticoagulant activity, *Sci. Rep.* **5** 14349, 2015.

521. Hao, Z.et al. Fibrinogen depleting agents for acute ischaemic stroke, *Cochrane Database. Syst. Rev.* **3**, 2012.
522. Esfandi, A.et al. Comparison between the Outcomes of Intracoronary and Intravenous Administration of Eptifibatide during Primary Percutaneous Coronary Intervention in Patients with Acute ST-Elevation Myocardial Infarction, *J. Atheroscler. Thromb.*, 2015.
523. Sun, Z.et al. Intracoronary injection of tirofiban prevents microcirculation dysfunction during delayed percutaneous coronary intervention in patients with acute myocardial infarction, *Int. J. Cardiol.* **208** 137-140, 2016.
524. Marsh, N., & Williams, V. Practical applications of snake venom toxins in haemostasis, *Toxicon* **45** - (8), 1171-1181, 2005.
525. Matsui, T.et al. Snake venom proteases affecting hemostasis and thrombosis, *Biochim. Biophys. Acta* **1477** (1-2), 146-156, 2000.
526. Joseph, R.et al. Hypotensive agents from snake venoms, *Curr. Drug Targets. Cardiovasc. Haematol. Disord.* **4** (4), 437-459, 2004.
527. Kini, R.M., & Banerjee, Y. Dissection approach: a simple strategy for the identification of the step of action of anticoagulant agents in the blood coagulation cascade, *J. Thromb. Haemost.* **3** (1), 170-171, 2005.
528. Miesczanek, J.et al. Ancylostoma ceylanicum anticoagulant peptide-1: role of the predicted reactive site amino acid in mediating inhibition of coagulation factors Xa and VIIa, *Mol. Biochem. Parasitol.* **137** (1), 151-159, 2004.
529. Francischetti, I.M.et al. Ixolaris, a novel recombinant tissue factor pathway inhibitor (TFPI) from the salivary gland of the tick, *Ixodes scapularis*: identification of factor X and factor Xa as scaffolds for the inhibition of factor VIIa/tissue factor complex, *Blood* **99** (10), 3602-3612, 2002.
530. Miesczanek, J.et al. Anticoagulant peptides from *Ancylostoma caninum* are immunologically distinct and localize to separate structures within the adult hookworm, *Mol. Biochem. Parasitol.* **133** (2), 319-323, 2004.
531. Ribeiro, J.M.et al. Purification and characterization of prolixin S (nitrophorin 2), the salivary anticoagulant of the blood-sucking bug *Rhodnius prolixus*, *Biochem. J.* **308** ( Pt 1) 243-249, 1995.
532. Isawa, H.et al. The insect salivary protein, prolixin-S, inhibits factor IXa generation and Xase complex formation in the blood coagulation pathway, *J. Biol. Chem.* **275** (9), 6636-6641, 2000.
533. Rudolph, A.E.et al. Definition of a factor Va binding site in factor Xa, *J. Biol. Chem.* **276** (7), 5123-5128, 2001.
534. Norledge, B.V.et al. The tissue factor/factor VIIa/factor Xa complex: a model built by docking and site-directed mutagenesis, *Proteins* **53** (3), 640-648, 2003.