IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023

A Brief on Exploring Knowledge about Vaccine Generation from Snake Venom

Nilam Vitthal Ichake, Dhanashree Prakash Karande, Pooja Shankar Mehetre, Seema Vikas Ghode, Mr. Shubham Gadge
Samarth Institute of Pharmacy, Belhe, Maharashtra, India

Abstract: *As expected, several new variants of Severe Acute Respiratory Syndrome-CoronaVirus-2 (SARS-CoV-2) emerged and have been detected around the world throughout this Coronavirus Disease of 2019 (COVID-19) pandemic. Currently, there is no specific developed drug against COVID-19 and the challenge of developing effective antiviral strategies based on natural agents with different mechanisms of action becomes an urgent need and requires identification of genetic differences among variants. Such data is used to improve therapeutics to combat SARS-CoV-2 variants. Nature is known to offer many bio therapeutics from animal venoms, algae and plant that have been historically used in traditional medicine. Among these bio resources, snake venom displays many bioactivities of interest such as antiviral, antiplatelet, antithrombotic, anti-inflammatory, antimicrobial and antitumor. COVID-19 is a viral respiratory sickness due to SARS-CoV-2 which induces thrombotic disorders due to cytokine storm, platelet hyper activation and endothelial dysfunction. Wnt dependency and Lgr5 expression define multiple mammalian epithelial stem cell types. Under defined growth factor conditions, such adult stem cells (ASCs) grow as 3D organoids that recapitulate essential features of the pertinent epithelium. Here, we establish long-term expanding venom gland organoids from several snake species. The newly assembled transcriptome of the Cape coral snake reveals that organoids express high levels of toxin transcripts. Single-cell RNA sequencing of both organoids and primary tissue identifies distinct venom-expressing cell types as well as proliferative cells expressing homologs of known mammalian stem cell markers. A hard-wired regional heterogeneity in the expression of individual venom components is maintained in organoid cultures. Harvested venom peptides reflect crude venom composition and display biological activity. This study extends organoid technology to reptilian tissues and describes an experimentally tractable model system representing the snake venom gland*

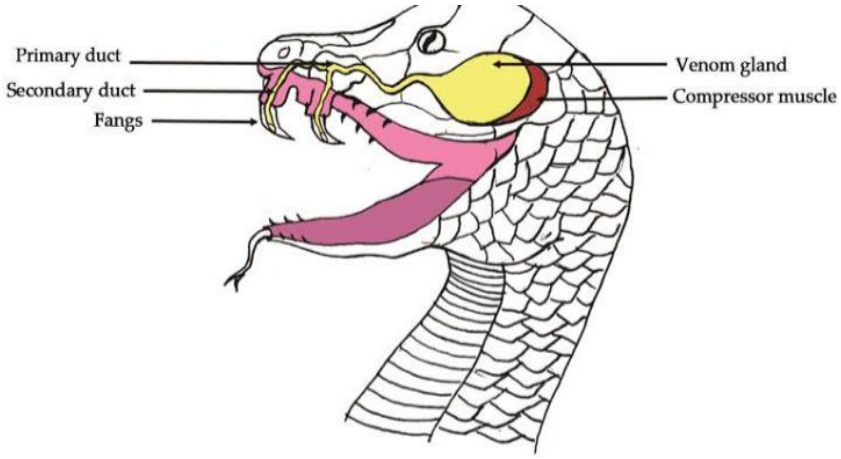
This review aims to:
(1) present an overview on the infection, the developed thrombi-inflammatory responses and mechanisms of induced thrombosis of COVID-19 compared to other similar pathogenesis; (2) underline the role of natural compounds such as anticoagulant, antiplatelet and thrombolytic agents; (3) investigate the management of coagulopathy related to COVID-19 and provide insight on therapeutic such as venom compounds. We also summarize the updated advances on antiviral proteins and peptides derived from snake venoms that could weaken coagulopathy characterizing COVID-19.

Keywords: SARS-CoV-2 variants, COVID-19, Snake venoms, Coagulopathy, Antiplatelet peptides, Antithrombotic compounds.

I. INTRODUCTION

Objective
To investigate whether a DNA immunoassay method targeting the large bleeding molecule prothrombin activator-like metalloproteinase derived from the venom of Chis ocellatus (E. ocellatus) can support stimulation more specifically and whether its relevance to today's system is equivalent to an antibiotic. For reaction.

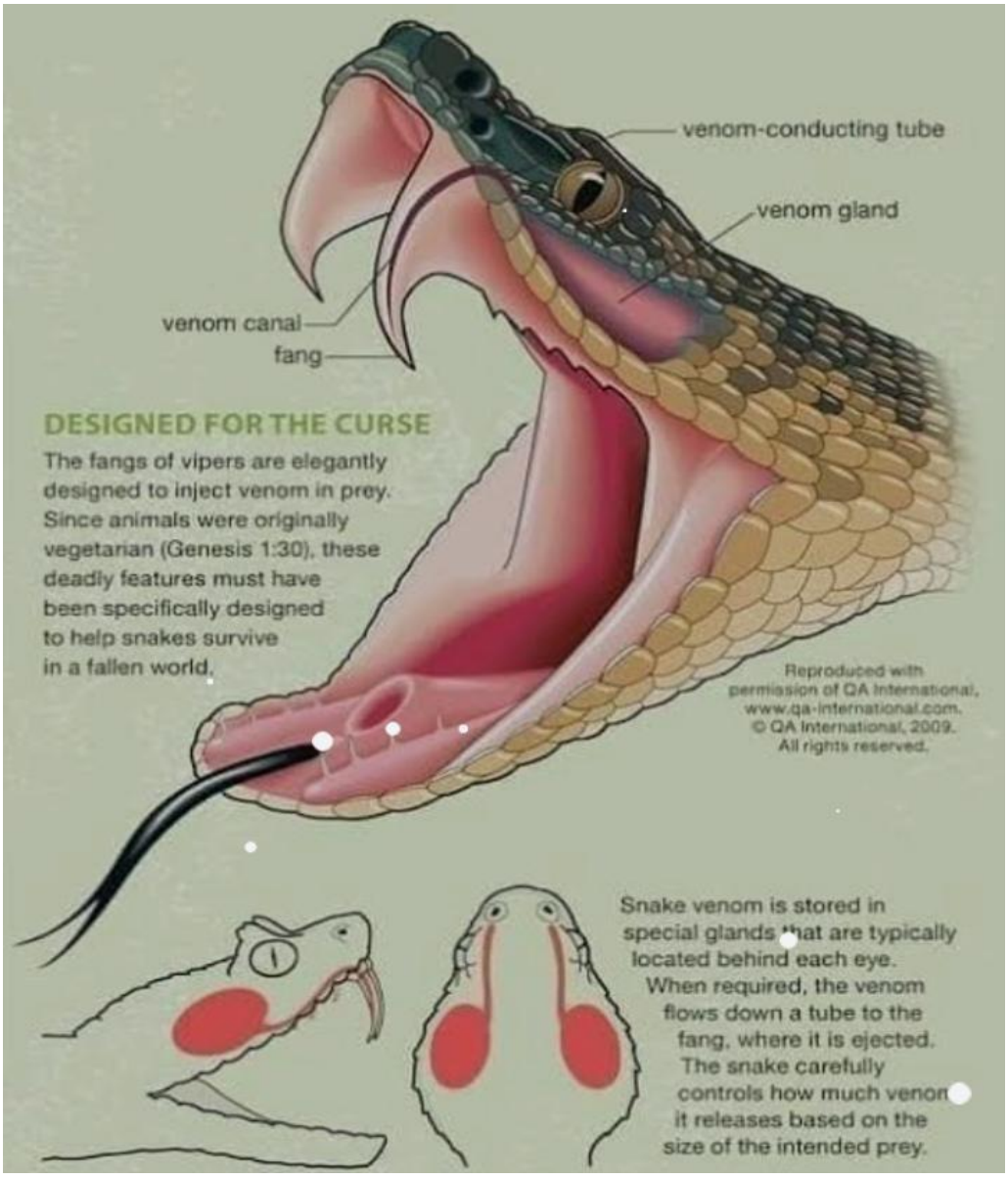
IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023



Poisoning from snake bites is still the most common public health problem in many countries, especially tropical and subtropical countries (1). Echis ocellatus (E. ocellatus) is the most abundant and important snake species in West Africa and is considered the deadliest snake in the world [2]. The exact frequency of snake bites is difficult to determine and is often underestimated, but in some areas of the Nigerian savanna, victims of E. ocellatus poisoning can account for more than 10% of hospital beds [2]. In the Benue valley of Nigeria, for example, the estimated incidence is 497 per 100 000 populations per year with 10%–20% untreated mortality [3]. Furthermore, in Northern Nigeria, E. ocellatus is accountable for 95% of all envenoming by snakes [4] causing hundreds of deaths annually. Local effects of Echis viper envenoming apart of haemorrhage include swelling, pain, blistering, and which in extreme cases, may lead to necrosis, permanent deformity, and even amputation of the affected limb [5]. Systemic effects include potentially lethal consumption coagulopathy, haemorrhage and hypovolaemic shock [6]. The only effective treatment is the administration of conventional antivenoms [7] that suffer from shortages imposed by the mode of preparation. Antivenoms are prepared by purifying the sera of large animals, typically horses, hyperimmunized with either individual or a range of venoms [8]. Since venoms contain numerous molecules, only some of which are toxic, antivenoms raised against these molecules consist of numerous antibodies with no known therapeutic functions [4]. Furthermore, because the toxicity of a venom molecule is unrelated to its immunogenic potential, the most potent antibodies in antivenoms are not necessarily targeted to the most pathogenic molecules [9]. In addition, an antivenom production system with less dependence upon snake collection, venom extraction and maintenance to give venoms for immunization would decrease the hazards as well as costs of conventional procedures. To explore whether a DNA immunization approach targeting the major haemorrhage molecule of a prothrombin activator-like metalloproteinase from E. ocellatus venom could be conceived to inspire antibodies with more prominent specificity and equal adequacy to current conventional antivenoms systems. The notably T helper 2-type polarized immune response accomplished by GeneGun DNA delivery technique over intramuscular injection of DNA [10], [11] was exploited here to advance antibody initiation against a toxin present in the venom of E. ocellatus. We utilized DNA encoding the carboxyl-disintegrin and cysteine-rich (DC) domains (EoDC-2) of EoMP-6 (GenBank accession number: AY261531), a prothrombin activator-like metalloproteinase in the venom of E. ocellatus for the DNA immunization.

The significant of this finding based on that (i) although anti-EoDC-2 antibody was generated against E. ocellatus it shows another approach with great potential to neutralise the local hemorrhagic activity significantly induced by venoms of other snake species involved in this investigation; (ii) the potential of having antivenom generated against one part (the non-catalytic domain) as opposed to the whole molecule to neutralise its hemorrhagic activity is of crucial importance as it represents a novel approach with greater immunological specificity and fewer hazards if any than conventional systems of antivenom production, by exposure large animals that usually being used for the current antivenom production to a less injurious than expression of the whole molecule containing the catalytic metalloprotease domain. Hence, we report here that our preliminary results may hold a promising future for antivenom development.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023



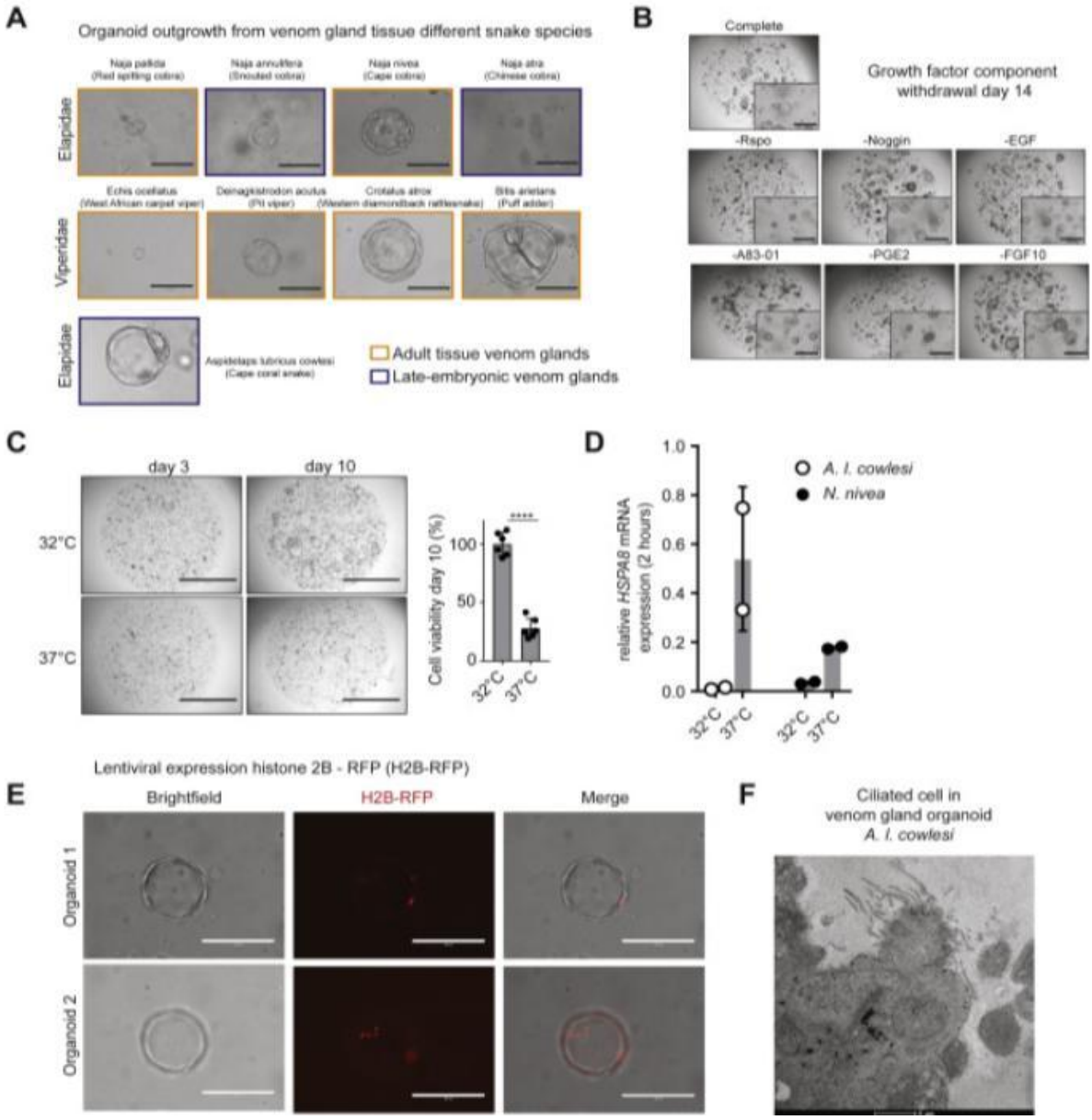
Antibodies generated against the E. ocellatus venom prothrombin activator-like metalloprotease and more specific against its DC domains, named EoDC-2, prove to modulate and inhibit the catalytic activity both in vitro and in vivo of venom MDCs. These preliminary findings may have great potential for antivenom development in which anti-Eo-DC antibody, constitutively expressed inhibitor of viper venom-induced haemorrhage. Preclinical antivenom efficacy assays are required to be conducted in order to gain insight into the provision of these antibodies with the possibility of better advantages over the current equine and ovine antivenoms. This will have significant contribution to improve the treatment of systemic and necrosis effects that exerted by the saw scaled viper E. ocellatus envenoming.

Method

isolated DNA EoMP-6 was used as template for PCR amplification using forward and reverse primers specific for EoDC-2. An approximately 700 bp PCR product was obtained and cloned into the pSecTag-B expression vector, from which anti-EoDC-2 antibodies were generated and examined for their effectiveness in blood localization in vitro and in vivo.

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023

Establishment of Organoid Culture Conditions for Snake Venom Gland



Schematic representation of the derivation of venom gland organoids from late embryonic (~7–2 days before hatching) A. l. cowlesi (n = 7) (see also Figure S1A).
Time course of organoid expansion after seeding of cells from a single A. l. cowlesi venom gland in BME (passage 0) until passage 17. Scale bars, 1,000 µm.© Haematoxylin and eosin (H&E) stain of late embryonic A. l. cowlesi venom gland and organoids. Scale bars, 50 µm.
Schematic representation of medium component dropout screen on primary tissue outgrowth. Quantification of relative cell viability per condition after 14 days, normalized to complete expansion medium (see also Figure S1B). Data points represent biological replicates. ** = $p \leq 0.01$.€ Immunofluorescent staining of organoid for DNA (DAPI), tubulin (green), and actin (blue). Scale bars, 50 µm

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023

II. RESULTS

Our results show that the product produced against EoDC-2 (a) exerts a positive effect by interfering with the interaction of recombinant disintegrin "EoDC-2" isolated from E. coli. Ocellatus as well as other viper species to the α2β1-integrins on platelets; (b) complete inhibition of the catalytic site of the metalloproteinase molecules in vitro using an adaptation antibody zymography assay. Furthermore, it has a polyspecific potential and constitutively expressed significant inhibition by cross-reaction and neutralised venom-induced local haemorrhage exerted by different viper species in vivo. The potential characteristic of EoDC-2 against one part (the non-catalytic domain) as opposed to the whole molecule to neutralise its haemorrhagic activity is of crucial importance as it represents a novel approach with greater immunological specificity and fewer hazards, if any, than conventional systems of antivenom production, by exposure large animals that usually being used for the current antivenom production to a less injurious than expression of the whole molecule containing the catalytic metalloprotease domain. Hence, we report for the first time that our preliminary results hold a promising future for antivenom development.

III. CONCLUSION

Antibodies generated against the E. Eyespot venom prothrombin activator-like metalloprotease and disintegrin cysteine-rich domain modulate and inhibit the catalytic activity of disintegrin cysteine-rich molecules in vitro and in vivo. Therefore, the production of venom-specific toxin antibodies through DNA injection provides a more appropriate treatment for snake poisoning than antibiotics.

REFERENCES

[1] S.S. Hasson, M.S. Al-Balushi, E.A. Said, O. Habbal, M.A. Idris, R.A. Mothana, et al.Neutralisation of local haemorrhage induced by the saw-scaled viper Echiscarinatussochureki venom using ethanolic extract of Hibiscus aethiopicusL,Evid Based Complement Alternat Med, 2012 (2012), p. 540671

[2] S.S. Hasson, R.A. Mothana, T.A. Sallam, M.S. Al-balushi, M.T. Rahman, A.A. Al-JabriSerine protease variants encoded by Echis ocellatus venom gland cDNA: cloning and sequencing analysisJ Biomed Biotechnol, 2010 (2010)Pii: 134232

[3] A.G. Habib, M. Lamorde, M.M. Dalhat, Z.G. Habib, A. KuznikCost-effectiveness of antivenoms for snakebite envenoming in NigeriaPLoSNegl Trop Dis, 9 (1) (2015), p. e3381

[4] R.D. Theakston, G.D. Laing,Diagnosis of snakebite and the importance of immunological tests in venom researchToxins, 6 (5) (2014), pp. 1667-1695

[5] A.G.Habib,Public health aspects of snakebite care in West Africa: perspectives from Nigeria ,J Venom Anim Toxins Incl Trop Dis, 19 (1) (2013), p. 27

[6] C.W. Hwang, F.E. Flach,Recurrent coagulopathy after rattlesnake bite requiring continuous intravenous dosing of antivenom.

[7] B.Lomonte, W.C. Tsai, J.M. Ureña-Diaz, L. Sanz, D. Mora-Obando, E.E. Sánchez, et al.Venomics of New World pit vipers: genus-wide comparisons of venom proteomes across Agkistrodon,J Proteomics, 96 (2014), pp. 103-116

[8] T.Hifumi, A. Sakai, Y. Kondo, A. Yamamoto, N. Morine, M. Ato, et al.Venomous snake bites: clinical diagnosis and treatment,J Intensive Care, 3 (1) (2015), p. 16

[9] L.M. Alvarenga, M. Zahid, A. di Tommaso, M.O. Juste, N. Aubrey, P. Billiald, et al.Engineering venom's toxin-neutralizing antibody fragments and its therapeutic potentialToxins (Basel), 6 (8) (2014), pp. 2541-2567

[10]T.Y. Weng, M.C. Yen, C.T. Huang, J.J. Hung, Y.L. Chen, W.C. Chen, et al.DNA vaccine elicits an efficient antitumor response by targeting the mutant Kras in a transgenic mouse lung cancer model,GeneTher, 21 (10) (2014), pp. 888-896

[11] G.W. Sledge, E.P. Mamounas, G.N. Hortobagyi, H.J. Burstein, P.J. Goodwin, A.C. Wolff ,Past, present, and future challenges in breast cancer treatment,J Clin Oncol, 32 (19) (2014), pp. 1979-1986

[12] S.S. Hasson, R.D. Theakston, R.A. Harrison,Cloning of a prothrombin activator-like metalloproteinase from the West African saw-scaled viper, Echisocellatus,Toxicon, 42 (6) (2003), pp. 629-634

[13] C.Marcinkiewicz,Applications of snake venom components to modulate integrin activities in cell-matrix interactions,Int J Biochem Cell Biol, 45 (9) (2013), pp. 1974-1986

IJARSCT
ISSN (Online) 2581-9429
International Journal of Advanced Research in Science, Communication and Technology (IJARSCT)
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
Impact Factor: 7.301
Volume 3, Issue 2, December 2023

[14] A.S.KamigutiPlatelets as targets of snake venom metalloproteinases,Toxicon, 45 (8) (2005), pp. 1041-1049
[15] I.Tanjoni, D. Butera, L. Bento, M.S. Della-Casa, R. Marques-Porto, H.A. Takehara, et al.Snake venom metalloproteinases: structure/function relationships studies using monoclonal antibodies,Toxicon, 42 (7) (2003), pp. 801-808
[16] I.P. Nascimento, L.C. Leite,Recombinant vaccines and the development of new vaccine strategies,Braz J Med Biol Res, 45 (12) (2012), pp. 1102-1111
[17] D.Lema, A. Garcia, J.B. De Sanctis,HIV vaccines: a brief overview,Scand J Immunol, 80 (1) (2014), pp. 1-11
[18] Late breaking abstracts: presented at the American Society of Gene & Cell Therapy's 16th Annual Meeting, May 15–18, 2013, Salt Lake City, Utah,MolTher, 21 (9) (2013), pp. e1-46
[19] S. Parasuraman, R. Raveendran, R. Kesavan,Blood sample collection in small laboratory animals,JPharmacolPharmacother, 1 (2) (2010), pp. 87-93
[20] S.S. Hasson, A.A. Al-Jabri, T.A. Sallam, M.S. Al-Balushi, R.A. Mothana,Antisnake venom activity of Hibiscus aethiopicus L. against Echis ocellatus and Naja n. nigricollisJToxicol, 2010 (2010), p. 837864,View in ScopusGoogle Scholar
[21] S.M. Serrano, J. Kim, D. Wang, B. Dragulev, J.D. Shannon, H.H. Mann, et al.The cysteine-rich domain of snake venom metalloproteinases is a ligand for von Willebrand factor A domains: role in substrate targeting,J Biol Chem, 281 (2010), pp. 39746-39756