

ABSTRACT FORM ECAT SYMPOSIUM 8 – 9 NOVEMBER 2018

Name:

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Title:

The use of snake venoms in the coagulation laboratory

Abstract:

Snake venoms are modified digestive juices containing zootoxins that function as offensive weapons to incapacitate and immobilise prey items, as defensive weapons to protect from predators, and to aid digestion. Broadly, venoms can be neurotoxic, cytotoxic, cardiotoxic or haemotoxic, and it is intriguing that evolution of the latter unravelled many of the crucial steps in vertebrate haemostasis long before human study did the same. Not to be outdone, albeit a few million years later, human study continues to unravel the complexities of snake venoms and the knowledge gained thus far has permitted us to employ snake venoms in diagnostic haemostasis testing for some decades. More recently, therapeutic applications are being realised for some snake venom fractions.

Most venomous snakes produce venom containing a cocktail of toxins, but very generally, viper venoms tend towards being haemotoxic and elapid (cobra family) venoms tend towards neurotoxicity. Use of some viper venoms is commonplace in small and large haemostasis laboratories alike, such as Common Lancehead (*Bothrops atrox*) venom to check for suspected presence of heparin, Southern Copperhead (*Agkistrodon contortrix contortrix*) venom in clotting or chromogenic-based protein C activity assays, and the almost ubiquitous Russell's Viper (*Daboia russelli*) venom for lupus anticoagulant detection. Russell's viper venom has other diagnostic applications, such as direct FX activation in protein S activity and activated protein C resistance assays. The FV activator from Russell's Viper venom is also used in conjunction with Noscamin, a FII activator from Tiger Snake (*Notechis scutatus scutatus*) venom in an activated protein C resistance assay that is unaffected by lupus anticoagulants and most therapeutic anticoagulants, including direct FXa inhibitors. The Russell's viper venom FV activator is also employed in the prothrombinase induced clotting time assay for monitoring direct and indirect inhibitors of FIIa and FXa.

Snake venom FII activators with different co-factor requirements have been employed in lupus anticoagulant detection. Textarin, a fraction of Australian Eastern Brown Snake (*Pseudonaja textilis*) venom, which requires FV, phospholipid and Ca^{++} as cofactors, can be used as a screening test with dilute phospholipid. Instead of a high concentration phospholipid confirmatory test it is paired with Ecarin venom from the Saw-scaled Viper (*Echis carinatus*), which is co-factor independent and thus cannot be affected by lupus anticoagulants. Alternatively, the phospholipid and Ca^{++} dependent FII activator from Coastal Taipan (*Oxyuranus scutellatus*) venom can be used in the screening test. These venoms were initially proposed for lupus anticoagulant testing because they are unaffected by vitamin K antagonist anticoagulation since they can activate the undercarboxylated FII, giving them a diagnostic advantage over conventional assays. Limited availability precluded wide adoption of the assays but the arrival of direct FXa inhibitors in the anticoagulant armoury has prompted a resurgence of interest in them since direct FII activation bypasses FXa inhibition.

Use of snake venom in diagnostics for primary haemostasis is less well established despite a myriad of venoms that are known to act on von Willebrand factor and platelets. Probably the most widely known is Botrocetin from the Brazilian Pit Viper, or Jararaca (*Bothrops jararaca*) venom, which can adopt a similar role to ristocetin in a von Willebrand factor activity assay, and it can also be used to help distinguish between von Willebrand disease and Bernard-Soulier Syndrome in platelet aggregation studies. Also available for platelet function studies is Convulxin, from the South American Rattlesnake, or Cascabel (*Crotalus durissus terrificus*), which activates mammalian platelets by binding and clustering glycoprotein VI.

