AIM AND SCOPE OF THE PRESENT INVESTIGATION

Envenomation by snakes include subcutaneous/intramuscular injection of venom into the prey or human victims that results in complicated pathology comprising of both local and systemic effects. The systemic toxicity may include neurotoxicity (post/pre synaptic), myotoxicity, coagulant (pro/anti), cardiotoxicity, hemorrhage associated with internal organs and hypotensive or rarely hypertensive effects. The local toxicity includes edema, hemorrhage, dermonecrosis, myonecrosis and inflammation at the site of bite (Shashidhara murthy et al., 2002 and references there in).

The systemic toxins targeting vital organs leading to fatal toxicity are extensively studied as a matter of fact that some of them serve as drugs or prototypes for drug designing and some as tools to uncover many unsolved physiological events (Kini, 1998; Menez, 1998). Induction of systemic effects depends on the concentration and rate at which the toxins diffused from the site of bite to their sites(s) of action. This process is facilitated through the degradation of local tissues (Anai et al., 2002; Girish et al., 2002). Matrix degrading hemorrhagic metalloproteases and hyaluronidases are the principal agents that damage the tissue at the bitten region. The hemorrhagic metalloproteinases degrade the structural protein scaffold of the extracellular matrix, while hyaluronidases degrade the hyaluronic acid in to small fragments. The degradation of extracellular matrix components not only destroys the mechanical support of the tissue but also makes the extracellular matrix smooth and fragile that result in easy diffusion of systemic toxins into the circulating blood, a property referred to as “spreading property”. Despite the key role played as a “spreading factors” during envenomation, hemorrhagic metalloproteases and hyaluronidases are the least studied enzymes from snake venoms. These enzymes are non-lethal by themselves and that could be the reason for lack of interest. In recent years spreading property has drawn the attention of venom researchers as a matter of fact that the presence or absence of the property can make the venom/toxin in to a more toxic or less toxic form.

Anti-venom therapy is the current best and successful therapy available to treat the threatening fatal systemic toxicity while, it is less effective or ineffective against local toxicity (Lomonte et al., 1996; Guitterrez et al., 1998; Leon et al., 2000). Tissue destruction would continue even after the neutralization of systemic toxicity. This would result in severe morbidity and occasionally requires amputation of the affected limbs. The progressive necrosis is common especially during Viper bites. Therefore, in order to overcome this limitation strategically, a thorough characterization of agents responsible for local tissue damage and inhibitors for these locally acting enzymes especially from plant sources is essential. It is likely that the inhibitors of these enzymes would minimize not only the local tissue damage but also the rate of spreading of systemic toxins. Recent studies confirmed that the natural inhibitors of locally acting enzymes, in addition to complete neutralization of local tissue damage also increased the survival time of experimental mice by retarding the easy diffusion of systemic toxins (Escalante et al., 2000; Leon et al., 2000; Anai et al., 2002; Yingprasertchai et al., 2003; Girish et al., 2009 and references there in). In the recent past, a locally acting hemorrhagic metalloprotease complex (HC) was isolated and characterized from *Daboia russellii* venom (Ushanandini Ph.D. thesis, 2006).

Therefore, the present study was undertaken to,

- To screen some of the well known Indian medicinal plants against the local toxicity of Viper bites.
- To isolate and characterize the locally acting enzyme, especially the hyaluronidase from the *Daboia russellii* venom.
- To understand the spreading property of both hayluronidase and hemorrhagic metalloprotease (HC) and inhibition and hence the spreading property of these enzymes by plant isolates.
- To establish the beneficial effects of inhibition of spreading property of *Daboia russellii* venom in the management of both local and systemic effects.