

Insect larvae as Biofactories to produce sphingomyelinase D for *Loxosceles* antivenom development

Loxosceles species, commonly named “violin” spiders, are widely spread venomous spiders. Clinical cases of *Loxosceles* bites are more commonly reported in the Americas, particularly in Argentina, Brazil, Chile and Perú. Most accidents are characterized by dermonecrotic lesions, often referred to as necrotic or gangrenous arachnidism. However, in about 10% of the cases a more serious presentation occurs, characterized by a systemic evolution of the pathology that can result in a fatal outcome, mostly in children and elders. Antivenom against *Loxosceles* species is being produced in the Americas since the early 1960s. Its Active Pharmaceutical Ingredients are immunoglobulins or their fragments obtained from equine plasma of animals hyperimmunized with spiders’ venom. Venom extraction, a very laborious task with very low yields per spider, is the most relevant production bottleneck. Herein we optimized a biotechnological process based on *Spodoptera frugiperda* larvae as biofactories to obtain a recombinant version from *L. laeta* sphingomyelinase D (rSmase). The rSmase was recovered high purity level (94.5%) in one-chromatographic step at low cost. Our version of rSmase was able to induce a neutralizing humoral response in horses’ sera. The amount of venom of 17000 spiders could be replaced with rSmase from 1600 insect larvae. The use of rSmase is expected to change traditional antivenom production.