Table 1 Toxins purified from SpV to date

Molecule Function	Toxin Name	Chemical Aspects	Functional Characteristics	Source
Protease	Sp-GP	≈72 kDa N-terminally blocked	Gelatinolytic activity	[20]
Cytolysin	Sp-CTx	Glycoprotein Dimeric constitution (subunits ≈ 65 kDa)	Hemolytic activity — cell membrane pore formation Cardiovascular biphasic response in vivo — initial systolic and diastolic pressure increase followed by decrease Positive inotropic effect on cardiac muscle Increase of Ca^{2+} current on isolated cardiomyocytes Vasoconstriction — coronary bed Vasodilation — aortic ring	[24] [25] [26]
B-type lectin	Plumeribetin	Homotetramer (monomer — 13.157 kDa) N-terminally blocked High content of anti-parallel strands	Integrin inhibitory activity Attenuation of cell-collagen contacts and cell spreading	[27]
C-Type lectin	Sp-LC 1 2 3 4 5	16.981 kDa 16.982 kDa 16.975 kDa 16.841 kDa 16.842 kDa	Hemagglutinating activity Recognizes the sugar motif (Gal-β(1 → 4)GlcNAc)	[28]

are novel to fish venoms. A preliminary analysis of expressed sequence tags (EST) obtained through a cDNA library from *S. plumieri* venom revealed that about 30% of the sequences had no similarities with previously described ones, suggesting the presence of unknown genes of potential relevance in the venom gland. In addition, the screening of the library with antibodies against a lectin fraction from *S. plumieri* venom has shown that lectin-like genes account for 12% of all transcripts, a finding confirmed by extensive *in silico* analysis [61]. These constitute the very first steps towards the unraveling of the molecular diversity contained in fish venoms.

Neutralization of *S. plumieri* toxic activities

Although there is no antivenom available for the envenoming by *S. plumieri*, the commercial antivenom raised against the venom of the stonefish *Synanceia trachynis* (SFAV) — a horseFab'2 preparation made by CSL in Melbourne, Australia [63] — evoked a cross-reactive immune response to SpV.

SFAV neutralizes all known clinical effects of serious *S. trachynis* envenomation [64], and is also efficient in neutralising the inflammatory and cardiovascular responses as as well as the hemolytic activity induced by *S. plumieri* in mice [29], suggesting that the compounds responsible for these effects share similar biochemical and antigenic properties to those found in stonefish venom. This antivenom also neutralises some of the toxic effects of other stonefish (*S. verrucosa*), lionfish (*Pterois volitans, P. lunulata, P. antennata and Dendrochirus zebra*) and soldierfish (*Gymnapistes marmoratus*) [51, 65, 66].

This is in accordance with the hypothesis that venomous fishes belonging to different genera or inhabiting different regions may share venom compounds with similar antigenic properties [1].

Conclusions

In conclusion, despite all the progress made recently, many questions remain to be answered, not only with respect to the physio-pharmacological effects and the precise action mechanism of some of the components already described, but also as to the considerable number of molecules still unexplored in the venom of *S. plumieri*. The study and exploration of the full potential contained in fish venoms can contribute to a better understanding of complex physiological processes — such as the very pain induced by the envenomation — and to the discovery of new drugs, not to mention the development of more effective ways to treat the injuries caused by these animals.

Abbreviations

AM: Alveolar macrophages; CPP: Coronary perfusion pressure; ECM: Extracellular matrix; EST: Expressed sequence tags; MALDI-TOF: Matrix-assisted laser desorption/ionization – time of flight; MAP: Mean arterial pressure; RP-HPLC: Reverse phase high performance liquid chromatography; SINAN: Notifiable diseases information system; Sp-GP: *Scorpaena plumieri* gelatinolytic protease; SpV: *S. plumieri* venom extract; UFES: Federal University of espírito santo

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