STRUCTURAL AND BIOLOGICAL COMPARISON OF *BOTHROPS* *JARARACA* DISINTEGRINS AND THEIR DERIVED-PEPTIDES

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Platelet integrins are molecules involved in the recognition of plasma and extracellular matrix components, essential for platelet adhesion and aggregation during haemostasis and arterial thrombosis. Disintegrins are cysteine-rich venom peptides that inhibit integrin ??sub?IIb?3sub>??sub?$_3$?3sub>-dependent platelet aggregation via an Arg-Gly-Asp (RGD) motif. Herein we compared two Bothrops jararaca disintegrins, jarastatin and jararacin, characterizing their inhibitory and structural properties towards ADP and thrombin-induced human platelets aggregation. We also tested six synthetic cyclic peptides designed to mimicry the RGD-loop of jarastatin (CRRARGDDMDDYC, CRARGDDMDDC and CARGDDMDC) and jararacin (CRRARGDNPDDRC, CRARGDNPDDC and CARGDNPDC). Initially, we isolated and identified the disintegrins (jarastatin-7,55kDa and jararacin-7,35kDa), through chromatography columns and MALDI-ToFMS. These peptides are potent inhibitors of ADP-induced platelet aggregation (jarastatin IC₅₀=0.3µM and jararacin-IC₅₀=75nM), Nevertheless all cyclic peptides showed no activity. Disintegrins biological activity was higher against thrombin-stimulated platelets (jarastatin-IC₅₀=120nM and jararacin-IC₅₀=29nM). Moreover, the jarastatin peptide CRRARGDDMDDYC displayed activity (IC₅₀=66µM) similar to jararacin peptides CRARGDNPDDC (IC₅₀=65µM) and CARGDNPDC (IC₅₀=57µM). Homology models revealed significant differences between disintegrins and peptides, especially in the RGD loop. This feature might be responsible for the diminished response observed within disintegrin peptides. By exploring the inhibitory platelet aggregation and structural properties of these disintegrins, we may identify the potential of these molecules as new antiplatelets drugs prototypes. (Support: FAPERJ, CNPq, UFF) Disintegrin, homology-models, platelet.