EVALUATION OF ANTITHROMBOTIC PROFILE OF CYCLIC RGD SYNTHETICS PEPTIDES
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Introduction and objectives: Thrombosis can occur in the arterial or venous circulation, being the most common cause of cardiovascular disease-associated death. Despite current treatments are effective, they have significant side effect of bleeding. Thus, the search for more effective and safe therapies is need. The aim of this study was to analyze the antiplatelet and antithrombotic profile of five-cyclic RGD peptides (Ser-Jast, Ser-Jarc, Arg-Jarc, Jast-Loop and Jarc-Loop) derived from the RGD loop of jararacin and jarastatin from the Bothrops jararaca snake venom. Methods: Primarily, each peptide was analyzed in platelet aggregation assay using human platelets induced by ADP, thrombin and collagen. Then for the most active was investigated in a model of ferric chloride-induced arterial thrombosis in mice. Results: Peptides showed an IC50 of 24.35, 18.76, 40.08 µM, for Ser-Jarc, Arg-Jarc, Jarc-Loop, and 137.80, 106.50 µM for Ser-Jast and Jast-Loop, respectively for platelet aggregation induced by ADP. All peptides also inhibit platelet aggregation induced by thrombin showing that Ser-Jarc, Arg-Jarc, Jarc-Loop had similar IC50 while Ser-Jast and Jast-Loop showed an IC50 of 63.91 and 49.48 µM, respectively. In addition, the collagen-induced platelet aggregation assay showed to be less effective with values of IC50s around 100µM for Jarc peptides. Finally, the evaluation of antithrombotic effect of Ser-Jarc peptide (1 and 5 mg/kg) and Ser-Jarc + Arg-Jarc (1:1) were performed (25 mg/kg). These treatments did not prolong the occlusion time of the artery in significant manner, but the dose of 5 mg/kg was able to maintain the initial flow of animals longer than control. Conclusion: Thus, it was possible to observe the synthetic peptides exhibit antiplatelet activity in a dose-dependent manner in vitro, but the change of structure the peptides did not increased their activity, peptides based on Jarc showed to have better activity, nevertheless the antithrombotic effects should be further investigate.

Keywords: Disintegrin, Synthetic peptide and Arterial thrombosis.