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Synthetic Tripeptides (RGD Analogs) Incorporating Moiety of Salicylic-Derivatives Strongly Inhibit Platelet Function *in vitro*

Y. Sarigiannis[1], G. Stavropoulos[1], M. Liakopoulou-Kyriakides[2] and P.E. Makris[3]

[1]Dept. of Chemistry, University of Patras, Patra, [2]Dept. of Chemical Engineering, Aristotle University of Thessaloniki, [3]Haeamostasis and Thrombosis Unit, A' Medical Propedeutic Clinic, Medical School, Aristotle University, Thessaloniki, Greece

AIM

Various polypeptides, imitating RGD receptors or glycoproteins' complexes, mainly GpIIb/IIIa, antagonists, have been reported to show inhibitory activity on human platelet aggregation. Here we report the effect on platelet function in vitro of a series of RGD analogs incorporating moiety of salicylic-derivatives.

METHODS

Five synthetic tripeptides of the general form X^1-2-OH-C_6H_5-CO-Arg(X^2)-Gly-Asp(X^3)-NH_2 (where X^1; H, Br, Cl, X^2; H, NO_2, X^3; H, Me, Bzl) were prepared by the conventional solution technique and/or by solid phase synthesis. All five RGD analogs at concentration ≤1.7 mM were tested in a Chronolog- P.I.C.A Aggregometer for in vitro inhibition of platelet aggregation induced by Collagen, ADP and Thrombin. Platelet Rich Plasma was prepared from healthy donors (Laboratory personel). MDA (manohyl dialdehyde) production was measured by Thiobarbituric acid reagent substances. In order to confirm these results, flow cytometry with monoclonal antibodies against GpIb, GpIIb/IIIa, GpIIIa and GMP140, was used.

RESULTS AND CONCLUSIONS

It was found that RGD analog incorporating bromine in the salicyl nucleus presents strong inhibitory activity against Collagen, ADP and Thrombin. Production of MDA is strongly inhibited by the same tripeptide (incorporating bromine). Flow cytometric determination of receptors of glycoprotein complexes further confirmed the inhibitory effect on platelet GpIIb-IIIa caused by this peptide. Synthetic RGD tripeptide incorporating bromine strongly inhibits platelet aggregation induced by Collagen, ADP and Thrombin. This effect is due to the inhibition of thromboxane A2 production (measured by MDA production) and it is further confirmed by the reduction of glycoproteins' receptors, expressed by the complex IIb-IIIa.