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MOLECULAR DOCKING STUDY OF A NUCLEOTIDASE PURIFIED FROM CERASTES CERASTES VENOM: PROSPECT OF USE IN THE TREATMENT OF CD 73 DEFICIENCY

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ABSTRACT

Background: Deficiency in ecto-5′ -nucleotidase CD73 alters thromboregulation and affects coronary vascular tone and platelet activation. Previous studies reported that the treatment with soluble 5’ -nucleotidase inhibited platelet aggregation and may be clinically beneficial in vascular leakage, myocardial or acute lung injury. Therefore, in this study, we purified and characterized a nucleotidase CD73-like “Cc-5’NTase” from Cerastes cerastes venom.

Methods: The aggregation was explored by induction with the agonists after 5-min of platelet incubation with the purified molecule. Anticoagulant effect of Cc-5’NTase was tested by i.p. injection to mice. Cc-5’NTase 3D structure was modeled by homology to a human ecto-2 5’-nucleotiase (4h1S.pdb). Molecular docking was performed using the Glide tool in Schrodinger software.

Results: Cc-5’NTase is a 70 kDa enzyme, structured into 13 α-helices and 26 β-strands. It displayed anti-platelet and anticoagulant activities that probably involve hydrolysis of ADP, prevention of its binding to P2Y receptors and the binding of resulting adenosine to its P1 receptor. Molecular docking study showed that pharmacological effects of Cc-5’NTase were mediated by targeting; ADP via six hydrogen bonds established with Tyr351, Leu573, Tyr288, Ser60 and two with Val265, AMP via six hydrogen bonds established with Asn251, Thr253, His362, Gly448 and two with Arg53 and ATP via five hydrogen bonds established with Asn125, Asn252, Leu192 and two with Arg401 as well as three salt bridges linked with Arg360 and Arg401.

Conclusion: According to these data, Cc-5’NTase could constitute an alternative pharmacological tool to treat pathologies due to the loss of CD73 functions.

KEYWORDS: Nucleotidase, Molecular docking, Anti-platelet, Anticoagulant, Treatment of CD73 deficiency

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