Anti-Plasmodium Effects of Angiotensin II Analogues

Chamlian, M.[1], Maciel, C.M.[2], Capurro, M.L.[2], Miranda, A.[3], Oliveira, V.X.Jr.[1]

[1]Centro de Ciências Naturais e Humanas, Universidade Federal do ABC, [2]Departamento de Parasitologia, Universidade de São Paulo, [3]Departamento de Biofísica, Universidade Federal de São Paulo, São Paulo, Brazil.

Malaria is a major parasitic disease affecting around 300-500 million people in the world. The efforts to control this disease are hampered by drug resistance in parasites, insecticide resistance in mosquitoes, and the lack of an effective vaccine. Recently, we performed a study, which showed that the Angiotensin II (AII) and some analogues are highly active against immature and mature sporozoites of *Plasmodium gallinaceum*. In an attempt to increase the biological activity, we synthesized and tested two series of AII analogues with an i-(i+2) and i-(i+3) lactam bridge scaffold. Analogues were synthesized by solid phase method on Merrifield's resin and cyclized using activator BOP reagent. Peptides were cleaved from the resin using HF anhydrous, purified by RP-HPLC and characterized by mass spectroscopy, amino acid analysis and capillary electrophoresis. In the bioassays experiments the sporozoites showed nuclear fluorescence, indicative of cell damage, after 60 minutes incubation with cyclic analogues VC-5, VC-17 and VC-19, which present the introduction of the side-chain to side-chain bridging element in the N-terminal portion, and with the linear peptides VC-12, VC-26 and VC-28, that present the insertion of Asp and Lys residues in the C-terminal portion. These results suggest that the position of the lactam bridge in the sequence is important for the association of the molecule with the sporozoite membrane; and that biological effect could be increase with the addition of charged residues. This kind of approach may offer the basis for development the new drugs for malaria prevention and chemotherapy.
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