

## Angiotensin II short linear derivative peptides as antiplasmodial drugs

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**Introduction:** Antiplasmodial activities of angiotensin II and its analogues have been extensively investigated in *Plasmodium gallinaceum* and *Plasmodium falciparum* parasite species. Due to its vasoconstrictor property angiotensin II, it cannot be used as an anti-malarial drug. **Objective:** In this work, Ang II derivative peptides were synthesized and tested *in vitro* in order to find a short bioactive peptide that influence on parasite-membrane interaction on both *P. gallinaceum* and *P. falciparum* parasite species. **Methodology:** This work presents the solid-phase syntheses and liquid chromatography and mass spectrometry characterization of ten linear peptides related to angiotensin II against mature *P. gallinaceum* sporozoites and erythrocyte invasion by *P. falciparum*. Conformational analyses were performed by circular dichroism. IC<sub>50</sub> and haemolytical assays were performed to identify the ideal concentration and viability used on the biological experiments. The contractile responses assays of the analogues were made to evaluate if they are promising candidates to be applied as antiplasmodial drugs. **Results:** The results indicate two short-peptides constituted by hydrophobic residues (5 and 6) with antiplasmodial activity in these models, 89 and 94% of biological activity against *P. gallinaceum* sporozoite, respectively, and around 50 % of activity against *P. falciparum*. Circular dichroism spectra suggested that all the peptides adopted  $\beta$ -turn conformation in different solutions, except peptide 3. Besides the biological assays IC<sub>50</sub>, the haemolysis assays and contractile response activities were applied for peptides 5 and 6, which did not present expressive results. **Conclusion:** The hydrophobic portion and the arginine, tyrosine, proline, and phenylalanine, when present on peptide primary sequence, tend to increase the antiplasmodial activity. This class of peptides can be explored, as anti-malarial drugs, after *in vivo* model tests.

Keywords: Malaria, *P. falciparum*, Angiotensin II, Peptides, *P. gallinaceum*

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