



Antimalarial activity of cyclolinopeptide a and its analogues.

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Streszczenie

Cyclolinopeptide A (CLA) is an immunosuppressive peptide of the sequence c-(-Leu-Ile-Ile-Leu-Val-Pro-Pro-Phe-Phe-), isolated from linseed. Since another cyclic, hydrophobic, immunosuppressive peptide, cyclosporin A, has potent antimalarial activity, CLA and a series of its analogues were synthesized on solid phase and tested for inhibition of the human malarial parasite *Plasmodium falciparum* in culture. The results were compared with the influence of these agents on humoral and cellular immune responses. There was no clear correlation between the structure of the peptides, their immunosuppressive activity, and their antimalarial activity. However, the antimalarial activity of the peptides was apparently connected with the strong hydrophobic nature of CLA. Substitution of a less hydrophobic residue into the peptide chain led to a decrease in or even loss of detectable activity, although such peptides retained the immunosuppressive properties. A possible explanation is that the antimalarial effect of CLA and analogues may result from their influence on cell membranes rather than on some specific receptor such as cyclophilin. In agreement with this idea, binding of CLA to purified *P. falciparum* cyclophilin was not detected except at very high concentrations. Substitution of D-aromatic residues into the CLA molecule led to a decrease in immunosuppressive activity but had little effect on antimalarial activity, which for these peptides was of the same order as for CLA. We have therefore demonstrated that the cyclolinopeptides are a class of compound not previously shown to have antimalarial activity, and that in a series of analogues there was no correlation between antimalarial and immunosuppressive effects.