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Potential use of 13-mer peptides based on phospholipase and oligoarginine as leishmanicidal agents

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Highlights

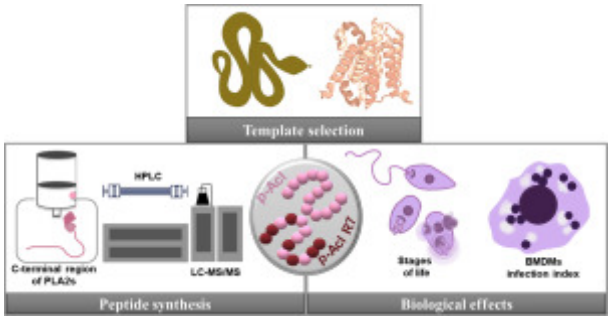
- 13-mer peptides based on phospholipase and oligoarginine sequences are promising leishmanicidal compounds.
- Arginine may confer better antileishmanial activity to cationic peptides than lysine residues.
- 13-mer leishmanicidal peptides interfere with cell membrane permeabilization.
- 13-mer peptides showed low toxicity to mammalian cells.

Abstract

Phospholipase A_2 toxins present in snake venoms interact with biological membranes and serve as structural models for the design of small peptides with anticancer, antibacterial and antiparasitic properties. Oligoarginine peptides are capable of increasing cell membrane permeability (cell penetrating peptides), and for this reason are interesting delivery systems for compounds of pharmacological interest. Inspired by these two families of bioactive molecules, we have synthesized two 13-mer peptides as potential antileishmanial leads gaining insights into structural features useful for the future design of more potent peptides. The peptides included p-Acl, reproducing a natural segment of a Lys49 PLA_2 from *Agkistrodon contortrix laticinctus* snake venom, and its p-AclR7 analogue where all seven lysine residues were replaced by arginines. Both peptides were active against promastigote and amastigote forms of *Leishmania* (*L.*) *amazonensis* and *L.* (*L.*) *infantum*,

while displaying low cytotoxicity for primary murine macrophages. Spectrofluorimetric studies suggest that permeabilization of the parasite's cell membrane is the probable mechanism of action of these biomolecules. Relevantly, the engineered peptide p-AclR7 was more active in both life stages of *Leishmania* and induced higher rates of ethidium bromide incorporation than its native template p-Acl. Taken together, the results suggest that short peptides based on phospholipase toxins are potential scaffolds for development of antileishmanial candidates. Moreover, specific amino acid substitutions, such those herein employed, may enhance the antiparasitic action of these cationic peptides, encouraging their future biomedical applications.

Graphical abstract



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Keywords

Leishmanicidal activity; Oligoarginine; Peptide; Phospholipase

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