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ACCEPTED MANUSCRIPT

LmrBPP9: a synthetic bradykinin-potentiating peptide from *Lachesis muta rhombeata* venom that inhibits the angiotensin-converting enzyme activity in vitro and reduces the blood pressure of hypertensive rats

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Graphical abstract



Highlights

- Lachesis muta rhombeata venom has several compounds with ACE-inhibitory activity.
- BPPs may play a key role in the envenoming by this species.
- LmrBPP9 presents ACE-inhibition activity in vitro.
- LmrBPP9 shows hypotensive effect in hypertensive 2K1C rats.
- LmrBPP9 has a potential to be a model for the development of new hypotensive drugs.

Abstract

Bradykinin-potentiating peptides (BPPs) are an important group of toxins present in *Lachesis muta rhombeata* venom. They act directly at renin-angiotensin-aldosterone system, through the inhibition of angiotensin-converting enzyme (ACE). This action may contribute to the hypotensive shock observed during the envenoming by this species. Thus, the main goal of this study was the solid-phase synthesis of a BPP found in *L. m. rhombeata* venom and its in vitro and in vivo characterization in relation to ACE inhibition and hypotensive activity, respectively. The LmrBPP9 peptide was synthesized using an automated solid-phase peptide synthesizer and purified by reversed-phase fast protein liquid chromatography (FPLC). The in vitro IC50 of the synthetic peptide is $4.25 \pm 0.10 \mu$ M, showing a great

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