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In vivo Leishmanicidal Activity of Beauvericin Produced by the Fungus Aspergillus terreus P63

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Beauvericin is a bioactive cyclic hexadepsipeptide produced by the marine-derived fungus *Aspergillus terreus* P63, previously reported to exhibit potent antileishmanial activity *in vitro*. Leishmaniasis remains a neglected tropical disease with significant global health impact, and current treatments are limited by toxicity, drug resistance, and variable efficacy. The discovery of novel natural products with selective leishmanicidal activity is therefore a pressing need. This study aimed to re-isolate and purify beauvericin from *A. terreus* P63 using chromatographic methods, and to conduct preliminary *in vivo* assays to investigate its potential mechanism(s) of action. Solid-state fermentation was performed for 30 days, followed by methanolic extraction, sequential solvent partitioning, silica gel and Sephadex® LH-20 column chromatography, and final purification by HPLC-UV. Beauvericin was identified by HPLC-UV-MS, showing the $[M+H]^+$ ion at m/z 784, consistent with literature data, and confirmed by ^1H NMR spectroscopy. The isolation procedure yielded over 300 mg of the pure compound. In preliminary *in vivo* assays against *Leishmania amazonensis promastigotes*, beauvericin induced approximately a 20% increase in lipid peroxidation compared to untreated controls, indicating a mild oxidative stress response. These findings suggest that oxidative membrane damage may contribute to its leishmanicidal mechanism, potentially leading to loss of parasite membrane integrity and cell death. The results demonstrate the successful isolation of beauvericin and provide mechanistic insights into its biological activity, reinforcing its potential as a promising lead compound for the development of innovative therapies against leishmaniasis. Further studies are underway to confirm these observations, to investigate the possible *in vivo* mechanism-of-action of beauvericin (possibly related to its ability to chelate metals and/or to promote the permeation of membrane cells) and to fully elucidate its therapeutic applicability. The authors gratefully acknowledge the support from their institutions and funding from FAPESP, CAPES and CNPq.

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