P2270

Abstract (poster session)

Necrodane-oxygenated therpenes underline the strong effect of Lavandula luisieri on cutaneous, mucocutaneous and visceral representative Leishmania sp.

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Leishmaniasis remains a highly prevalent worldwide infection and available treatment is limited as they are toxicity, expensive, promotes side effects, rate of relapse and low compliance. New therapeutic agents from natural sources is a very effective and successful strategy to develop new therapies, as isolated compounds might be used pure, manipulated by hemisynthesis or as prototypes, mainly on phytochemicals with high druglikness and drugability. The present work focused on the discovery of new anti-Leishmania agents from Lavandula luisieri volatile extracts. Volatile extract were analysed by GC and GC-MS and the antileishmanial activity of extract and pure volatile compounds (alpha-pinene, 1,8-cineole, linalool) was performed on L. infantum, L. tropica and L. major promastigotes cultures. Viability was assessed by tetrazolium-dye colorimetric method and expressed as concentration that inhibits parasite viability by 50% (IC50). Effects on promastigotes were analyzed by flow cytometry in order to assess mitochondrial transmembrane electrochemical gradient (JC-1), analyze phosphatidylserine externalization (annexin V–FITC, propidium iodide) and evaluate cell cycle (DNase-free, RNase, PI). Morphological and ultrastructural studies were performed by light, scanning and transmission electron microscopy. Lavandula luisiri volatile extract revealed a strong anti-Leishmania effect under 65 microg/ml in all tested species. The most prominent activity was assessed on L. major with IC50 of 31 microg/ml. It was observed modifications on normal cell shape, mitochondrial and kinetoplast swelling; increased number of autophagosomal structures, cytoplasmic vacuolizations and important nuclear modifications. The leishmanicidal activity of volatile extract was mediated partially via apoptosis as evidenced by externalization of phosphatidylserine, loss of mitochondrial membrane potential, and a very marked cell-cycle arrest at the G(0)/G(1) phase. Other important finding was related to the activity of the tested pure therpenes, Alpha-pinene, 1,8-cineole, and linalool, as they do not justified the strong activity of the volatile extract as Alpha-pinene was the only with activity against promastigotes (IC50 of 161 microg/ml). In fact, new necrodane oxygeneted compounds, under study seems be the responsible for this promising effect and justifies the undergoing work to identify these new agents for leishmaniasis treatment. This work was supported FCT POCTI (FEDER).