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Abstract (poster session)

Aloesaponol III 8-methyl ether of Eremurus plant extracts as a new potential antiprotozoal drug: activity on Leishmania infantum and Trypanosoma brucei brucei

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Trypanosomiasis and leishmaniasis are responsible for considerable mortality and morbidity, affecting more than 500 million of people in the world. The therapy available is hampered due to marked toxic side effects of the anti-parasitic drugs and by emergence of drug resistance. Research of novel drugs from natural sources are reliable option .So, this study provides a biological screening of different plant extracts from the genus Eremurus, widespread in western and central Asia, on Leishmania and Trypanosoma parasites. The ethanolic extracts of Eremurus persicus, E. spectabilis, E. sp were analyzed by HPLC and the molecule aloesaponol 8-methyl ether was isolated from E. persicus by flash chromatography. L. Infantum Nicolle (zymodeme MON-1) promastigotes were cultured at 26 °C in RPMI 1640 medium with 10% FBS and trypomastigotes of T. b. brucei were cultures in HMI-9 medium at 37 °C. The extracts activity was evaluated by MTT colorimetric method and alamar blue, used as viability assays. Effects on promastigotes were also analyzed by flow cytometry in order to assess mitochondrial transmembrane electrochemical gradient, to analyze phosphatidylserine externalization and to evaluate cell cycle. The alterations on morphology and DNA integrity were also studied. Cytotoxicity assays were done on macrophages cell line (RAW 264.7). Ethanolic extracts of E. persicus, E. spectabilis, E. sp had no activity against the tested protozoa, while aloesaponol 8-methyl ether was active with IC50 of 17 µg/mL (T. b. brucei) and 73 µg/mL (L. infantum). The morphological assay showed that the promastigotes treated with IC50 concentrations of the isolated compound did not showed changes after 2 hours of incubation. However, after 4 hours was possible to note aberrant forms and rounded and decreased of cell movement. These morphological changes were evident after 7 and 24 hours of exposure. Aloesaponol III 8-methyl ether doesn’t provoke fragmentation of a DNA and the results obtained by the flow cytometry point out a decrease of the mitochondrial transmembrane potential. The compound was not toxic to macrophages until concentrations of 3x IC50. This work leads us to propose the aloesaponol III 8-methyl ether as compound active against Leishmania and Trypanosoma as well as a valuable source for the development of new molecules for these protozoa infections. Acknowledgements:This work was supported FCT POCTI (FEDER).