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GROWTH INHIBITION AND ULTRASTRUCTURAL CHANGES INDUCED BY LICHENIC SUBSTANCES ON *LEISHMANIA CHAGASI IN VITRO*

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Leishmaniasis is an increasing public health problem in Brazil. The only drug of choice for both visceral and cutaneous leishmaniasis is sodium stibogluconate (Sb^V), a 40 years old drug. Although resistant *Leishmania* strains are still rare, there is a growing number of cases were the conventional treatment fails. On the other side, compliance to i.m. Sb^V treatment in cutaneous cases is rarely achieved, specially in rural areas, far from the medical continuous surveillance. New drugs that could be used either as topic unguents or orally are needed. In this work we describe the action of six lichen substances on *Leishmania chagasi*, the etiological agent of kala-azar in the Americas. The following substances were tested: fumarprotocetaric , protocetaric, secalonic, hypostitic and difractaric acids and atranorine. Density readings were obtained daily from promastigote cultures on LIT medium, at 26 ^oC, containing up to 40 µg/ml of one of the substances. A >50% growth inhibition was observed only when atranorine and difractaric acids were used at concentrations of 30 and 40 µg/ml, atranorine being always more effective than difractaric acid. Promastigotes from atranorine- and difractaric acid-containg cultures and from control cultures were fixed with glutaraldehyde and prepared for transmission electron microscopy by standard techniques. Mielin whorls in abnormal mitochondria were observed in many cells treated with atranorine, in both concentrations, and in some of the promastigotes from difractaric acid-containing cultures, but was rarely observed in control cultures. Other cell structures were apparently not affected. Our results points toward those two lichenic substances as potential new drugs in leishmaniasis.

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GROWTH INHIBITION OF *LEISHMANIA (LEISHMANIA) AMAZONENSIS* BY AUSTRALIAN SNAKE VENOMS

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Cutaneous leishmaniasis is an endemic disease, mostly found in tropical and subtropical regions. In Brazil, it is registrated 26000 new cases/year considering all their clinical forms. The actual treatment is based on some toxic drugs such as pentamidine and antimonials. The aim of this project is to determine Australian snake venoms with anti-*leishmania* activity on *Leishmania (Leishmania) amazonensis*. *Acanthophis antarcticus, Agkistrodon bilineatus, Hoplocephalus stephensi, Naja melanoleuca, Notechis ater niger, Notechis scutatus,. Oxyuranus microlepidotus, Oxyuranus scutellatus, Pseudechis australis, Pseudechis colletti, Pseudechis guttatus, Pseudechis porphyriacus and Pseudonaja textilis* venoms were incubated at the concentration of 40µg/mL in 25mM EDTA with $3{,}0x10^6$parasites/mL. Promastigotes from *L.(L.) amazonensis* were grown in RPMI 1640 medium without phenol red plus 10 % fetal bovine serum at 25^OC. The parasites viability was measured by a colorimetric assay based on the conversion of MTT (3-[4,5-Dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide) (5mg/ml) in colored (570nm) formazan. *A.bilineatus, H.stephensi N.melanoleuca, P.australis, P.colletti, P.guttatus* and *P. porphyriacus* venoms showed anti-*Leishmania* activity and even after irradiation with 2000 Gy dose, they still kept their inhibition growth activity. The L-amino acid oxidase (LAO) activity was tested in all venoms , using RPMI as substrate and peroxidase and OPD (o-Phenylenediamine) as revealing reagents. The same venoms, including the irradiated one, that presented the anti-*leishmania* activity, showed LAO activity. These data suggest that the anti-*leishmanial* effect could be related by L-amino acid oxidase activity.

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IMMUNESUPPRESSION REDUCES THE ACTIVITY OF STEROL BIOSYNTHESIS INHIBITORS (SCH56592 AND DO870) BUT NOT BENZNIDAZOLE (BZ) IN MICE ACUTELY INFECTEDWITH *TRYPANOSOMA CRUZI*

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