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CYTOTOXICITY EVALUATION *IN VITRO* OF METHANOLIC EXTRACT OF *Calophyllum brasiliense* LEAVES ON MACROPHAGES AND AGAINST PROMASTIGOTE FORMS OF *LEISHMANIA* SPP

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INTRODUCTION

Leishmaniasis is an infectious disease caused by parasites of the *Leishmania* genus, with a wide spectrum of clinical manifestations encompassing from cutaneous to visceral forms, with an estimate of more than one million new cases annually. There are few therapeutic options, which are highly toxic and causes severe side effects. The search for alternative drugs becomes an important and urgent issue. In this sense, *Calophyllum brasiliense* (CB) has been used in folk medicine in Brazilian rain forests for leishmaniasis treatment, besides reported biological activities. Thus, this study aimed to evaluate *in vitro* the cytotoxicity of methanolic extract of cultivated CB on bone-marrow-derived macrophages (BMDM), and the direct action against *L. amazonensis* (*L.a.*) and *L. infantum* (*L.i.*) promastigote forms.

MATERIAL AND METHODS

The methanolic extract was obtained from CB leaves (Niqfar-UNIVALI) (SisGen number A56F049). The MTT assay was performed to assess cell viability using BMDM of BALB/c mice (CEUA/UNIVALI: 026/21). Cells (1×10^6 cells/well) were treated with different concentrations of CB (50 - 300 µg/mL) for 24h. To evaluate the direct action of CB against promastigote forms *L.a.* (WHOM/BR/75/JOSEFA) and *L.i* (MCAN/BR/97/p142), 10^6 cells/mL were incubated with different concentrations of CB (25 – 100 µg/mL). Viable promastigotes were counted after 24, 48, 72, and 96h of treatment.

RESULTS

The results showed that the concentration above 200 µg/mL of CB presented toxicity on BMDM, with a CC50 (50% cytotoxic concentration) of 325.2 ug/mL. Antipromastigote assay showed *L.a.* more susceptibility to CB when compared to *L.i.* It was possible to verify the direct effect of CB against *L.a.* at the lowest concentration of 25 µg/mL after 48h of treatment and this effect lasted until 96h, with an IC50 of 20.5 µg/mL, showing a selectivity index (SI) more than 15 times higher. In *L.i.* after 24h, there is already a reduction in the number of parasites at concentrations of 50 and 100 µg/mL, however after 96h of treatment only the highest concentration was able to reduce by 60%, with an IC50 of 76.8 µg/mL, showing a SI 4 times higher over the *L.i.*

CONCLUSIONS

Knowing that CB has anti-*Leishmania* action and is not toxic to cells, phytochemical studies are in progress to determine the active principles so that new assays can be carried out in the experimental model of leishmaniasis.

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