culture 20/96 (21%) of the samples. In addition, PCR was able to detect VL of 19 patients (19.8%) which were negative by microscopy. PCR of DNA extracted from Giemsa-stained bone-marrow slides is a suitable tool for confirming diagnosis in patients with VL and may be useful in the diagnosis of difficult cases. Bone-marrow smears were easily stored, and can be easily sent to research centers where PCR is available. This makes PCR is good option for diagnosis in the field.

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ISOLATED AND PURIFIED NOVEL ANTILEISHMANIAL DRUG CANDIDATE FROM *HIMATANTHUS SUCUUBA*

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Cutaneous Leishmaniasis is a major parasitic disease worldwide health problem. Although a number of antileishmanial drugs are available, painful and lengthy treatments with standard drugs such as Antimonials and Amphotericin B remain being used even though it is well known that they have toxic side effects and growing chemotherapy failure, reasons why new drugs are actually needed. In previous studies, we have isolated, purified and bioassayed a spirolactone iridoid compound, Plumericin, from the Amazonian plant *Himatanthus suucuba*. Results, using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) micromethod, showed that Plumericin has a potent antileishmanial activity. Thus, *in vitro* axenically cultured amastigotes disclosed an IC_{50} value of 0.21 µM versus 0.52 µM of Amphotericin B. In addition, Plumericin also demonstrated lower citotoxicity when challenging healthy peritoneal mice macrophages *in vitro* than with Amphotericin B (IC50 of 1.86 µM versus >10 µM, respectively). Those potential positive features prompted us to identify its biochemical target in the amastigote form. Plumericin effects on *Leishmania amazonensis* DNA and RNA nucleic acids metabolism were studied by comparing the incorporation of labeled analogues [^{3}H] thymidine and [^{3}H] uridine, respectively, after treating axenic amastigotes for 30 minutes with Plumericin. Interestingly, Plumericin was also active on inhibiting cellular DNA synthesis with a subsequent recovery, but especially on the inhibition of cellular RNA synthesis which after 120 minutes of evaluation, it maintained a progressive decrease of RNA precursor molecules incorporation. Therefore, Plumericin would severely interfere in nucleic acids metabolism of the parasite. If so, we propose this compound as an interesting anti-leishmanial drug candidate for future studies.

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ORGAN SPECIFIC ACCUMULATION AND DISTRIBUTION OF STRUCTURALLY RELATED ANTI-TRYPANOSOMAL COMPOUNDS: A POSSIBLE ROLE IN RENAL TOXICITY

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Human African trypanosomiasis (HAT), also called African sleeping sickness, is a neglected tropical parasitic disease occurring in sub-Saharan Africa. HAT progresses through a relatively asymptomatic, hemolymphatic first stage into a fatal central nervous system (CNS) infection in the second stage. Current treatments for second stage HAT are limited by severe toxicity and lack of efficacy. Diamidine compounds such as pentamidine and furamidine are potent anti-trypanosomal molecules. Clinical trials of pafuramidine, a prodrug of furamidine for potential use in first stage HAT, were recently terminated due to unexpected delayed nephrotoxicity. CPD0801 is a related diamidine compound in development by the UNC based Consortium for Parasitic Drug Development. CPD0801 is curative in the second stage of a HAT murine model, and is currently under development as a treatment for second stage human disease. Rats were administered furamidine or CPD0801 (10 µmol/kg; single bolus dose) through a femoral vein cannula. Kidneys and livers were harvested for fluorescence microscopy and HPLC-MS/MS quantification. Livers contained similar quantities of both compounds while exhibiting slightly different distribution patterns. In contrast, CPD0801 accumulated in kidney at concentrations approximately 10 times less than furamidine when measured 48 hours after a single dose. Mechanistically-relevant, differential renal distribution patterns were also observed. Dissimilarities in kidney accumulation and distribution over time should reveal potential mechanistic differences in uptake and/or excretion of the compounds. Additional distribution/localization studies using the prodrug forms of CPD0801 and furamidine (pafuramidine) are in progress. The low accumulation and distribution of CPD0801 compared to furamidine may indicate a lesser risk of delayed nephrotoxicity in humans.

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ANTIBODY DROP IN NEWBORNS CONGENITALLY INFECTED BY *TRYPANOSOMA CRUZI* TREATED WITH BENZNIDAZOLE

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Vector control leads to drastic drop of the prevalence of Chagas disease in Latin America, giving importance to congenital Chagas disease. Diagnosis and treatment of infected newborns becomes a priority. Recovery is confirmed by the disappearance of *T. cruzi* antibodies several months after the treatment. During a trial aiming at comparing two treatment modes of congenital Chagas disease, we compared the decrease of antibody titers in congenitally infected newborns after treatment and evaluate the time to recovery. The decrease of *T. cruzi* antibody titers measured by ELISA tests was followed during the first year of life in congenitally infected newborns treated with different doses of benznidazole and compared to *T. cruzi* antibody titers in non infected newborns. Confirmation of recovery was given by two negative serological tests: Chagas Stat-Pak® (immunochromatography) and Chagatest® v3.0 (ELISA). In non infected infants from infected mothers, antibodies from maternal origin disappeared in less than 8 months while in infected infants *T. cruzi* antibodies decreased more slowly and disappeared in 9 to 16 months allowing to confirm the recovery. All Chagas Stat-Pak® tests were negative before the 9th month while about 10% of ELISA tests remained positive at the 12th month. Recovery may be confirmed in most cases at 10 months. The Chagas Stat-Pak® test appeared to give a reliable response earlier than the Chagatest® v3.0 ELISA. The decrease rate of antibodies does not depend on treatment modes.

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ACUTE INFECTION WITH *TRYPANOSOMA CRUZI* IN WISTAR RATS INDUCES GROWTH RETARDATION AND DEVELOPMENT OF MORPHOLOGICAL ANOMALIES IN THEIR FETUSES

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The present study shows the development of the fetuses in two groups of Wistar rats. Rats (R) were injected intraperitonealy with 2x10^5 of bloodstream trypomastigotes I/PAS/VE/00/PLANALTO and ASM *Trypanosoma cruzi* strains. To obtain pregnancies, rats were maintained in estrus the menstrual cycles and them mated with males at days 12 after infection, noninfected pregnancy rats were used as control. The results showed high levels of parasitemia in the rats between days 12 to 34 of infection with 0, 6, 12 and 20 days of gestation. Some of the rats were sacrificed and the number and aspects of fetuses extracted was revised. Between 1 and 8 fetuses were collected from 4 infected rats with PLANALTO *T. cruzi* strain; R1 showed 4 fetuses in right side and 4 immobile fetuses in left side of uterus (intrauterine growth retardation was seen in these fetuses), R2 showed fetal resorptions and placenta remains in right side and 1 fetus in left side of uterus, R3 showed 3 fetus in right side and 2 fetus dead in left side of uterus together to inflammated and necrosed placenta, and R4 showed 1 fetus in right side and 3 fetus in