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Is that possible to prevent parasitic iatrogenic blood bank transmission?

Chagas disease (CD) is neglected tropical disease (NTD) that affects over 6 million people mainly in the poorest areas of Latin America. CD also represents a public health concern in non-endemic areas such as North America, Asia, Oceania and Europe due to the human migration and globalization. This NTD has two clinical phases: the acute phase, usually presenting oligosymptomatic symptoms followed by a long chronic stage displaying a sub patent parasitism but that after years or even decades can evolute to progressive cardiac and digestive abnormalities. The etiological agent is the protozoa parasite called *Trypanosoma cruzi* that is primarily transmitted by insect bugs (popularly named "barbeiros" and "vinchucas"). However, other routes include blood transfusion, organ transplantation, laboratory accidents, congenital transmission, and ingestion of contaminated food.

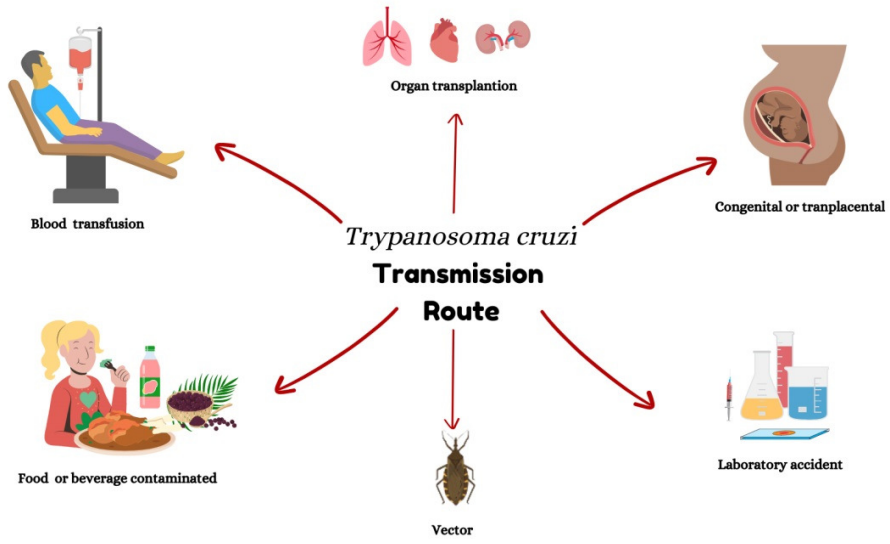

Fig. 1. Routes of Trypanosoma cruzi Transmission.

The available chemotherapy is based on two very old nitro-derivatives, named benznidazole and nifurtimox. Both are not effective specially at the later disease stage and induce several side effects demanding the identification of new drugs to treat this potentially fatal disease that kills more people in Latin America than any other parasitic infection, including malaria. Another challenge is related to the iatrogenic transmission mainly related to blood transfusions. Given the large number of asymptomatic, undiagnosed, and untreated infected people, the iatrogenic transmission still poses as a relevant transmission route for *T. cruzi*, specially in very hot endemic areas of Latin America, justifying the search for new chemoprophylactic agents. An old stain named crystal violet has been previously used for pathogen reduction, but it displays undesirable side-effects. Amidine-containing compounds such as pentamidine are DNA minor groove binders with a broad spectrum of activities against human and veterinary pathogens. Due to their poor bioavailability and toxicity, many analogues, and derivatives, have been synthesized such as the 'reversed amidines' also known as arylimidamides (AIAs) that are very active several parasites, particularly *T. cruzi*.

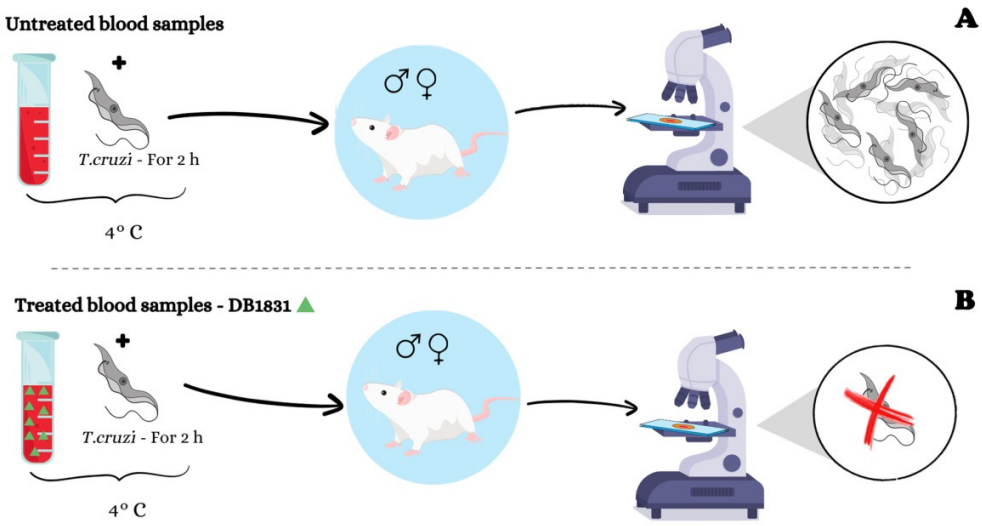

Fig. 2. Experimental Design: A – Untreated blood samples incubated for 2 hours/4°C with Trypanosoma cruzi bloodstream forms and than used to infect male and female mice. B- Blood samples were incubated for 2 hours/4°C with Trypanosoma cruzi bloodstream forms in the presence of 96 µM of the AIA DB1831 and then used to infect male and female mice. In both groups (A and B), their blood were collected from the animal tails to inspected the parasitism by light microscopy observation.

Presently we performed a stablished protocol to assess drug activity for blood bank purposes by the incubation of bloodstream trypomastigotes (BT) of *T.cruzi* kept at 4º C in a cell culture medium supplemented with 96 % of mouse blood in the presence of the studied AIAs. We found that the AIAs (such as DB1831) at 96 µM prevented the infection of male and female Swiss mice inoculated with blood samples spiked with BT, suppressing the circulating parasitism, referred as parasitemia. This experimental approach also protected the animals against mortality induced by the parasite infection. Our results are very promising and justify additional studies to confirm the potential use of AIAs in the chemoprophylaxis for blood bank use.

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Publication

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