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SUMMARY OF THESIS

BORBOREMA, Samanta Etel Treiger - **Biodistribuição do antimoniato de meglumina em animais sadios e infectados com *Leishmania (L.) chagasi.* São Paulo, 2005. (Dissertação de Mestrado - Instituto de Pesquisas Energéticas e Nucleares/IPEN).**

MEGLUMINE ANTIMONIATE BIODISTRIBUTION IN HEALTHY AND *L. (L.) chagasi* INFECTED BALB/c MICE

Pentavalent antimony, as meglumine antimoniate (Glucantime®) or sodium stibogluconate (Pentostam®), is the main treatment for leishmaniasis, a complex of diseases caused by protozoan parasite *Leishmania,* an endemic and neglected threat in Brazil. Despite over half a century of clinical use of these antileishmanial agents, their mechanism of action, toxicity and pharmacokinetics data remain mostly unknown. The analytical methods for determination of the amount of antimony in biological systems remain complex and with low sensitivity. Radiotracer studies performed on animals have the potential to play a major role in pharmaceutical development. The aim of this study was to obtain a radiotracer, by neutron irradiation of antimony, with suitable physics and biological properties, allowing easy determination of its biodistribution. Meglumine antimoniate (Glucantime®, Aventis, S. Paulo, Brazil) was neutron irradiated inside the IEA-R1 nuclear reactor, producing two radioisotopes ^{122}Sb and ^{124}Sb, with high radionuclidic purity and good specific activity. This compound presented the same antileishmanial activity as the native compound; either *in vitro* and *in vivo* treatment. In its biodistribution studies, it was found higher uptake in the liver of healthy or infected mice and elimination is mostly by biliary excretion with a small and fast proportion of the drug excreted by kidney. Free pentavalent antimony showed fast elimination predominant by kidney and great proportion of the drug is excreted by biliary route. The serum kinetic curve is bi-exponential, showing two compartments, a distribution in the central compartment and other associated to drug equilibrium and excretion. The use of the radiotracers, easily created by neutron irradiation, could be an interesting tool to solve important questions in antimonials pharmacology.

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*This book is available at the Library of the Instituto de Medicina Tropical de São Paulo