M-020-23 **UPTAKE AND ANTILEISHMANIAL ACTIVITY OF MEGLUMINE ANTIMONIATE-CONTAINING LIPOSOMES IN Leishmania (Leishmania) major-INFECTED MACROPHAGES**

Autores: Borborema SET (IPEN-CNEN, SP, Brazil.) ; Schwendener RA (IMCR-UZ, Zurich, Switzerland.) ; Osso Jr JA (IPEN-CNEN, SP, Brazil.) ; Andrade Jr HF (IMTSP-USP, SP, Brazil) ; Nascimento N (IPEN-CNEN, SP, Brazil)

Resumo

Leishmaniasis is a parasitic disease caused by the intramacrophage protozoa Leishmania spp. and may be fatal if left untreated. Although pentavalent antimonials are toxic and their mechanism of action is unclear, they remain the first-line drugs for treatment of leishmaniasis. An effective therapy could be achieved by delivering antileishmanial drugs to the site of infection. Compared with free drugs, antileishmanial agent-containing liposomes are more effective, less toxic and have fewer adverse side effects. The aim of this study was to develop novel meglumine antimoniate (MA)-containing liposome formulations and to analyse their antileishmanial activity and uptake by macrophages. Meglumine antimoniate (Glucantime®, Aventis, SP, Brazil) was encapsulated in liposome formulations with and without phosphatidylserine. Intracellular analyses were performed in infected and non-infected macrophages. Determination of the 50% inhibitory concentration (IC50) values showed that MA-containing liposomes were =10-fold more effective than the free drug, with a 5-fold increase in selectivity index, higher activity and reduced macrophage toxicity. The concentration required to kill 100% of intracellular amastigotes was =40-fold lower when MA was encapsulated in liposomes containing phosphatidylserine compared with the free drug. Fluorescence microscopy analysis revealed increased uptake of fluorescent liposomes in infected macrophages after short incubation times compared with non-infected macrophages. In conclusion, these data suggest that MA encapsulated in liposome formulations is more effective against Leishmania-infected macrophages than the non-liposomal drug. Development of liposome formulations is a valuable approach to the treatment of infectious diseases involving the mononuclear phagocyte system.