INNOVATIVE LIPOSOMAL NANOFORMULATION CO-INCORPORATING AMPHOTERICIN B AND MILTEFOSINE FOR THE THERAPY OF VISCERAL LEISHMANIASIS

Virgínia Mendes Russo Vallejos[1*], Guilherme Santos Ramos[1*], Helane Lúcia Oliveira de Morais[1], Gabriel Silva Marques Borges[2], Marta Marques Gontijo Aguiar[2], Christian Fernandes[2], Ricardo Toshio Fujiwara[3], Lucas Antônio Miranda Ferreira[2], Frédéric Frézard[1].

[1]Department of Physiology and Biophysics, Institute of Biological Sciences, Federal University of Minas Gerais, Brazil. [2]Faculty of Pharmacy, Federal University of Minas Gerais, Brazil. [3]Department of Parasitology, Institute of Biological Sciences, Federal University of Minas Gerais, Brazil. [*]Both authors share first authorship.
Federal University of Minas Gerais (UFMG), Belo Horizonte (MG), Brazil; e-mail: mendesvc@yahoo.com.br

Liposomal amphotericin B (AmB) or AmBisome® and oral miltefosine (Milt) are two major therapeutic options for visceral leishmaniasis (VL). Nevertheless, the clinical efficacy of these drugs is limited in severe cases of HIV/VL co-infection and cutaneous leishmaniasis (CL). Previously, our group introduced a novel method for encapsulation of AmB into pre-formed liposomes. Considering the great potential of drug combination for further improving leishmaniasis chemotherapy, the aim of this work was to develop a novel liposomal nanoformulation co-incorporating AmB and Milt and evaluate its therapeutic efficacy in a hamster model of VL. AmB was incorporated into pre-formed PEGylated liposomes containing Milt. The mixed PEGylated formulation showed vesicles with diameter of 135 (±14) nm and low polydispersity index (PI<0.3), with AmB encapsulation efficiency of 90%. The mixed PEGylated formulation was compared to PEGylated formulations containing solely AmB or Milt and to AmBisome® in *L. infantum*-infected hamsters for its effects on the parasite load in liver and spleen after 10 doses of treatment, given every day by IP route (5 mg/kg of AmB and 3.9 mg/kg of Milt). Animals, either untreated or treated IP with empty PEGylated liposomes, were used as negative controls. Treatments with mixed AmB/Milt liposomal formulation, liposomal AmB formulation and AmBisome®. promoted significant parasite supression in the liver in comparison untreated control. The mixed formulation showed the highest level of parasite reduction (94.3%), compared to Ambisome® (88.3%) and PEGylated liposomal AmB (84,2%). Significant reduction was also observed in the spleen, at a similar level, for all AmB/Milt liposomal formulations. This study supports the increased efficacy of the mixed PEGylated formulation and its potential for the treatment of severe cases of VL and for situations where there has been therapeutic failure with the use of Milt or AmB alone.

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