ORAL LIPOSOMAL FORMULATION WITH AMPHOTERICIN B FOR THE TREATMENT OF CUTANEOUS LEISHMANIASIS IN HAMSTER MODEL

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Leishmaniasis is a neglected disease with few treatment options that are flawed or toxic. Liposomal amphotericin B is the most effective therapeutic agent for VL, but has limited efficacy in CL and HIV/VL coinfection, restricted to parenteral route. Our hypothesis is that PEGylated liposomes can improve therapeutic efficacy by prolonging blood circulation time and improving stability in gastric fluid. We evaluate the effect of PEGylation of liposomal AmB on its stability in simulated gastric fluid and oral efficacy in hamsters with CL. AmB formulations in conventional and PEGylated liposomes were characterized for particle size, encapsulation efficiency/quantification of AmB and AmB aggregation state at room temperature and after incubation for 2h at 37ºC in acidic solution. The release kinetics of formulations before and after heat curing were also compared. Hamsters were infected with *L. amazonensis* and treated with AmB liposomal orally at daily doses of 5 mg/kg for 10 days. Treatment efficacy was assessed by recording lesion size and parasite load in comparison to oral miltefosine. AmB formulations presented mean diameters between 110 and 130 nm, drug encapsulation efficiencies greater than 98% and CD spectra consistent with a non-aggregated form. PEGylated formulation showed greater stability than the conventional when exposed to acidic environment. Treatment of infected hamsters with PEGylated formulation promoted significant reduction in lesion size compared to untreated group at level more pronounced than with the conventional one and equivalent to miltefosine. Statistically significant suppression of parasite load was observed in lesions of animals treated with miltefosine and PEGylated formulation in relation to conventional, with this suppression greater in PEGylated formulation. This work demonstrates that PEGylation of liposomal AmB increases its stability in simulated gastric fluid and its oral efficacy in a hamster model of CL.

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