Schistosomicidal activity of oxamniquine encapsulated inn sterically stabilized liposomes: influence of the route of administration

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We reported previously that liposome-encapsulated oxamniquine was more effective than free oxamniquine (OXA) for the treatment of experimental schistosomiasis, particularly when administered subcutaneously at a time close to the infection. Indeed, the conventional liposome preparation used in this study was ineffective when administered 35 days after infection (10 mg OXA/Kg), either by the subcutaneous or the intraperitoneal route. The aim of our present work is to look for more efficient liposome preparations. Here, we investigated the efficiency of sterically stabilized liposomes (SSL) which, contrary to conventional liposomes, escape from macrophage uptake and degradation. Therefore, these liposomes are expected to prolong the drug presence in vivo. SSL were made from distearoylphosphatidylcholine, cholesterol and polyethylene-phosphatidylethanolamine at a molar ratio of 5:4:0.3 and were calibrated through polycarbonate membranes with 0.1 micrometer pore diameter. A transmembrane gradient of ammonium sulfate was used for the encapsulation of OXA. This procedure led to high drug encapsulation efficiency (>90%) and drug to lipid molar ratio (1/10). Moreover, liposomes were found to efficiently retain encapsulated OXA in dialysis conditions at 37^{o}C. Four groups of 10 mice SWISS (male, adult, weighting 30 g) were infected with about 80 cercarias of *Schistosoma mansoni* (LE). 35 days after infection, a first group received Liposome-entrapped OXA (LOXA) at 20 mg OXA/kg by the intraperitoneal route, a second group received LOXA at 20 mg OXA/kg by subcutaneous route, a third group received OXA at 20 mg OXA/kg by subcutaneous route, and the last group remains without treatment (control group). Two weeks after treatment, animals were sacrificed and parasites recovered and counted. LOXA provoked a significant reduction in parasite count when compared to control group, only when the preparation was administered by the intraperitoneal route. Since the proportion of liposomes that reach the circulation is much higher when those are given intraperitoneally (than subcutaneously), we can propose that liposomes have to reach the circulation to be effective. This would not be surprising as parasites are located in the circulation 5 weeks after the infection. Strikingly, OXA was found to be superior to LOXA when both preparations were given subcutaneously. This discrepancy may be attributed to the fact that encapsulated oxamniquine was released very slowly and locally. In conclusion, our data suggests that sterically stabilized liposomes have to reach the circulation to act as an effective drug delivery system for oxamniquine.

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