Short- and Long-Term Efficacy of Hexadecylphosphocholine against Established *Leishmania infantum* Infection in BALB/c Mice

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In the immunocompetent host, visceral leishmaniasis (VL) is a fatal disease if untreated. In immunosuppressed patients, VL is an opportunistic infection for which there is no effective treatment for relapses. Here we report on the long-term activity of orally administered hexadecylphosphocholine (HDPC) against established *Leishmania infantum* infection in BALB/c mice. HDPC is a synthetic phospholipid with antiproliferative properties that has been extensively studied for its cancerostatic activity. Its short-term leishmanicidal effects in mice recently infected with viscerotropic *Leishmania* species have been previously reported. First, we show that 5 days of oral therapy with HDPC (20 mg/kg of body weight/day) led to amastigote suppression in the liver and the spleen of 94 and 78%, respectively (versus 85 and 55% suppression by meglumine antimonate in the liver and spleen, respectively), in mice infected 6 weeks before treatment and examined 3 days after the end of treatment. These results demonstrate the short-term efficacy of HDPC against an established *Leishmania* infection. Next, the long-term efficacy of HDPC was examined. In HDPC-treated mice both the hepatic and splenic amastigote loads were significantly reduced (at least 89%) 10, 31, and 52 days after the end of the treatment. In the treated mice, the increase of the splenic load was significantly slower than that in the untreated mice, demonstrating that the HDPC-
exerted inhibition of *Leishmania* growth persisted for at least 7 to 8 weeks. Orally administered HDPC—the safe doses and side effects of which are at least partially known—appears to be a promising candidate for the treatment of VL.

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