Effect of Myriocin on *Leishmania (Viannia) braziliensis*

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Sphingolipids have been related with several biological processes, such as intracellular transport, modulation of signal transduction and apoptosis. Since inositol phosphorylceramide (IPC) is the major sphingolipid expressed in promastigotes of *Leishmania*, the biosynthetic pathway of IPC was investigated. The effect of myriocin on *Leishmania (Viannia) braziliensis* promastigote growth, morphology and sphingolipid synthesis was investigated. Myriocin acts by blocking the first step of sphingolipid synthesis (serine + palmitate forming 3-ketodihydrosphingosine, 3-KDS). A significant reduction of parasites growth was observed when promastigotes were incubated for 3 days with 1 µM and 2.5 µM myriocin (49 % and 51%, respectively). Addition of 5 µM 3-KDS in promastigote cultures reduced the inhibitory effect of myriocin, i.e., promastigotes grown in presence of 1 µM myriocin plus 5 µM 3-KDS, and 2.5 µM myriocin plus 5 µM 3-KDS, showed a reduction of growth rate of 38.5%. These results indicate that addition of 3-KDS to parasite culture partially revert the blocking effect of myriocin. Morphologic examination of myriocin-treated promastigotes showed that the parasites present a more rounded form than control parasites. On the other hand, when parasites are incubated with 2.5 µM myriocin plus 5 µM 3-KDS the morphology resembles those of control parasites. In order to confirm that myriocin growth inhibition is due to serine-palmitoyl synthase inhibition, IPCs of promastigotes were fractionated by HPTLC and was quantified. As expected it was detected a decrease of 56 and 66% of IPC expression in the presence of 1 µM and 2.5 µM of myriocin. In agreement with these data, addition of 5 µM of 3-KDS led to a partial reversion of IPC synthesis.

Keywords: *Leishmania (Viannia) braziliensis*; sphingolipid; myriocin; 3-ketodihydrosphingosine

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