Effect of digoxin derivatives in promastigotes and amastigotes of *Leishmania (Leishmania) infantum chagasi*

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Leishmaniasis are part of the group of neglected diseases and are caused by parasites of *Leishmania* genus and transmitted to the vertebrate host through infected female phlebotomine sand flies. These diseases are characterized by cutaneous, mucocutaneous or visceral forms. *Leishmania infantum* is responsible for the most severe form of the disease, the visceral leishmaniasis, and may lead to death if untreated. The treatments currently used present serious collateral effects. Other problem is the existence of resistant species; therefore, it is necessary to find new compounds to avoid those problems. *Leishmania* has a single mitochondrion per cell, which occupies about 12% of the cell volume and is associated with kinetoplast. Mitochondria is responsible for oxidative metabolism and the study of compounds effect on this organelle has helped to establish the mechanism of action and the cytotoxic potential. Digoxin is a glycoside derived from the *Digitalis lanata* plant and it is one of the older drugs for heart treatments in use until the present time and there is still no description in the literature on its effects or its derivatives on *Leishmania* spp., which makes an evaluation of them interesting. The objective of this study was evaluated the effects of fifteen digoxin derivatives compounds on promastigotes and two of these compounds on amastigotes of *L. (L.) infantum chagasi*, their toxicities in different cell lines and their effects on mitochondrial metabolism. The studies included tests to evaluate the inhibition of growth of promastigotes in the presence of compounds at different concentrations using the MTT colorimetric method. To assess the cytotoxicity of the compounds, were made tests with different cell lines (RAW 264.7, HaCat and HFF). Other tests were performed to assess the ability of these compounds in the interaction between macrophages and intracellular amastigotes. To evaluate the effects of these compounds on mitochondrial metabolism, were assessing the oxygen consumption in the presence of these compounds. The results showed that two of the fifteen compounds tested, called DGB-3 and DGB-17 showed a strong antileishmanial effect. The DGB-3 showed no toxicity across the cell lines tested and the DGB-17 showed little toxicity. The DGB-17 inhibited infection of macrophages and reduced the number of intracellular amastigotes. The two compounds showed a reduction in oxygen consumption by promastigotes performed in the presence of each compound. Therefore, the DGB-3 and the DGB-17 appear promising antileishmanial and further tests are being performed to elucidate the mechanism of action.