EVALUATION OF THE *IN* VITRO SYNERGISTIC ACTION OF ALDIMINE AND HANTZSCH ADDUCT COMPOUNDS IN THE TREATMENT OF VISCERAL LEISHMANIASIS

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Visceral leishmaniasis (VL) is a neglected tropical disease caused by *Leishmania infantum*, which can result in severe complications and death if untreated. Treatment is challenged by high costs, adverse effects, and limited efficacy. In this context, combination therapy has emerged as a promising alternative to address these issues. In preliminary screening, the compounds T5, T9 and 8A4, from the Aldimine and Hantzsch Adduct chemical groups, showed individual leishmanicidal activity. Based on the initial results, the combinations T5+8A4 (C1) and T9+8A4 (C2) were selected to test their synergistic action against both evolutionary forms of *L. infantum*. The combinations were evaluated at two concentrations: C1-120µg/mL+150µg/mL, 60µg/mL+75µg/mL, and C2-100µg/mL+150µg/mL,50µg/mL+75µg/mL. Leishmanicidal activity against promastigote forms was tested in *L. infantum* (OP46) transfected with GFP, using propidium iodide (PI) to label non-viable cells. Activity against amastigote forms was assessed in RAW 264.7 murine macrophages infected with the same promastigote species. The evaluation was performed by flow cytometry (FACS Calibur) at 24, 48 and 72 hours, with Amphotericin B as the positive control (PC) and the untreated group as the negative control (NC). For promastigote forms, both combinations significantly reduced the viability, particularly C2, after 24 and 48 hours. For amastigote forms, a reduction in the percentage of infected macrophages was observed, with C1 decreasing by 53.8% and C2 by 57.5% after 24 hours of treatment compared to NC. The parasite load analysis, measured by mean fluorescence intensity (MFI), showed a reduction at all treatment times, especially at higher concentrations. The reduction values were: C1- 89.7%, 85.5% and 78.5%, and C2- 83.9%, 86.1%, and 80.1%, respectively, compared to NC. These results suggest that the combinations of these molecules exhibit in vitro leishmanicidal activity against *L. infantum*, although further studies are needed.

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