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NEW PHOSPHOLIPIDS ANALOGUES AS CANDIDATES TO AN ANTI T. CRUZI CHEMOTERAPY: IN VITRO TEST AND ULTRA-STRUCTURAL ANALYSIS

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Chagas disease is a systemic and endemic a neglected tropical disease, caused by T. cruzi, an obligate intracellular parasite. Nowadays, 8-10 million people in Latin America suffer with this trypanosomiasis and it is considered a major parasitic disease burden in the American continent. The treatment is based on two nitroheterocyclic compounds and both are ineffective against late chronic phase of the disease. Besides, the toxicity of these compounds is high. Thus, the need for more efficient, safe, and accessible drugs is urgent. Phospholipids analogues (PAs) have been shown to be effective against malignant mammalian cells and some pathogenic protozoa as Leishmania. Here, we analyzed the effects of new phospholipids analogues on the epimastigotes, trypomastigotes and intracellular amastigotes of T. cruzi. TC 387, TC388, LDT10 and LDT137 which were able to inhibit the in vitro growth of epimastigotes and amastigotes with IC50 in the nanomolar range. Trypomastigote lysis was also observed. Ultrastructural analysis demonstrated that these compounds affected the parasite's membranes. Mitochondrial and Golgi cisternae swelling and the formation of membrane blebs, ultimately leading to parasite death, were observed. The Golgi complex of parasites, but not that of the host cells, was affected suggesting a specific mechanism of action possibly due to interference in two different phospholipid biosynthesis pathways used in the distinct cell types. Our observations show that the trypanocidal activity of the PAs investigated herein is higher than that of previously reported PAs in the literature. In conclusion, this work shows that these compounds are potent and fast acting inhibitors of the growth of the proliferative developmental forms of T. cruzi (associated with several alterations in the parasite structural organization) and cause lysis of the highly infective trypomastigote form. The effects observed support the assertion that interference with the phospholipids of the membranes is important as a potential route for the development of new therapeutic agents to treat Chagas disease.

Biography

Emile Barrias is a Researcher in the area of optical microscopy-Inmetro with emphasis on optical microscopy of biological material. She holds a Bachelor's degree in Biological Sciences from the Federal University of Rio de Janeiro (2006), a Master's degree (2008) and a PhD (2014) in Biological Sciences (Parasitology and Cell Biology Program) from the Federal University of Rio de Janeiro at Carlos Chagas Filho Institute of Biophysics. She has experience in the areas of Celullar Biology, with emphasis on Parasitology, Cell Biology of parasites, working mainly on the following topics: Trypanosoma cruzi, T. cruzi interaction-host cell and anti-parasitic chemotherapy using optical microscopy techniques, super-resolution (STORM, SIM and GSD), transmission electron microscopy, scanning electron microscopy (SEM), multiparametric cell sorting and flow cytometry publishing 15 articles in international journals and three book`s chapters. She participates in the BIPM (Celullar Analysis Working Group) research group in cellular quantification pilot studies involving microscopy techniques.

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