NATURAL PRODUCTS FROM BRAZILIAN PLANT SPECIES - A SOURCE OF NEW COMPOUNDS WITH ANTIPARASITIC ACTION

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Parasitic diseases are responsible for considerable morbidity and mortality worldwide, especially in underdeveloped and developing countries. Among them, Chagas disease, caused by *Trypanosoma cruzi*, occurs throughout Latin America countries and is closely related to low social and economic development. The clinical treatment of this disease involves the use of toxic compounds, such as benznidazole and nifurtimox. Leishmaniasis is another neglected tropical disease (NTD) that affects more than one billion people in tropical and subtropical countries, including parts of Latin America, Africa and Asia. The World Health Organization estimated 1.3 million new cases annually including 300,000 cases of visceral leishmaniasis caused by *Leishmania (L.) infantum*. The therapeutic arsenal for the treatment of leishmaniasis is limited and still unsatisfactory. The treatment is not only challenging and long, but also offers a reduced option of drugs, most of which are toxic such as antimonials, amphotericin B, pentamidine and miltefosine. Considering this problematic context and lack of interest from the pharmaceutical sector, the search for novel drugs is crucial. Based on this aspect, natural products may be considered an interesting source of new molecules for the development of scaffolds for protozoal diseases, including leishmaniasis and Chagas disease. Aiming to discover new bioactive antiparasitic compounds from the Brazilian biodiversity, several bioactive extracts from plants species belonging to Lauraceae, Annonaceae, Asteraceae, Piperaceae, and Euphorbiaceae were subjected to dereplication procedures to afford bioactive metabolites especially alkaloids, lignoids, terpenoides, lactones, and flavonoids. These compounds were evaluated *in vitro* against *T. cruzi* (trypomastigote and amastigote forms), *L. (L.) infantum* (promastigote and amastigote forms) and against NCTC cells for mammalian cytotoxicity. Furthermore, quantitative structure relationship models based on multivariate statistical analysis (MSA) and machine learning techniques (MLT) were developed for a systematic investigation of important molecular features required for selection of leader compounds (natural or semisynthetic derivatives). Additionally, in order to elucidate possible mechanisms of actions, phenotypic analyzes of compounds-treated parasites were performed: alterations in the plasma membrane permeability, plasma membrane electric potential ($\Delta\Psi p$), mitochondrial membrane potential ($\Delta\Psi m$), and induction of ROS. Therefore, the obtained natural products and/or semisynthetic derivatives could represent promising scaffolds for drug design studies for leishmaniasis and Chagas disease treatment.

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