Trypanosoma cruzi and Naphthoimidazoles: Proteomic Approach regarding their Mechanism of Action

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In an effort to develop alternative drugs for Chagas disease derivatives of natural quinones were synthesized and screened on *Trypanosoma cruzi*. The most active were the naphthoimidazoles N1, N2 and N3 derived from ß-lapachone. In trypanosomatids, transcription is not a regulatory step in gene expression, increasing the importance of proteomic approach for the understanding of drugs mechanism of action. In this work, we focused in the proteomic analysis of *T. cruzi* epimastigotes using two-dimensional electrophoresis (2D) and mass spectrometry. Four experimental groups were selected: control and treated with naphthoimidazoles N1, N2 and N3. The 2D gel optimal resolution was determined using different conditions for protein extraction, pH range and sample buffer for protein solubilization. The optimized conditions for 2D electrophoresis were: freeze-thaw lysis as cell disruption method, 4-7 (18 cm) as pH separation range and 7M urea, 2M thiourea, 4% CHAPS, 60 mM DTT and 1% ampholytes as sample buffer. The gels were stained by Colloidal Coomassie Blue and automatically analyzed by Image Master® Platinum Software. Around 617 proteins were detected in each gel and the control group showed over expression in approximately 20 spots. In gel digestion followed by mass spectrometric analysis will reveal the protein identification of these spots. The present study shall identify proteins implicated in the parasite's response to treatment with the three naphthoimidazoles and its implications in parasite biology.

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