Insights into 1,4-Diamino-2-butaneone Cytotoxicity to *Trypanosoma cruzi* and Mammalian Cells

Soares CO¹, Bechara EJH², Colli, W¹, Alves MJM¹

¹Depto Bioquímica, Instituto de Química, USP, São Paulo, SP. ²Depto de Ciências Exatas e da Terra, UNIFESP, Diadema, SP.

The putrescine analogue 1,4-diamino-2-butaneone (DAB) is highly toxic to various microorganisms including *Trypanosoma cruzi*. *In vitro*, DAB undergoes Fe(II)- and Cu(II)-catalyzed oxidation yielding ROS and a highly toxic α-oxoaldehyde. *In vivo*, DAB decreases the viability of LLC-MK2 Rhesus cells, associated to redox and stress responses changes. Here, we study the role of thiols in DAB cytotoxicity to mammalian cells and evaluate DAB pro-oxidant effects to trypomastigotes and intracellular *T. cruzi* amastigotes. Treatment of culture cells with DAB (IC₅₀ ca. 1.5 mM) increases ROS production and depletes reduced thiols, in parallel to an increment in SOD activity. Further, pre-treatment with BSO (100-500 µM) potentiates DAB cytotoxicity whereas NAC (5 mM) protects cells against the oxidative stress. Accordingly, DAB (0.05 – 5 mM) treatment of trypomastigotes, the infective stage of *T. cruzi*, leads to a decline in parasite viability (IC₅₀ ca. 0.2 mM DAB, 4 h incubation), changes in the morphology, and thiol redox imbalance combined with increased TcSOD activity. Medium supplementation with catalase (2.5 µM) protects trypomastigotes against DAB while host cell invasion by trypomastigotes is hampered by DAB. Also, intracellular amastigotes showed to be susceptible to DAB toxicity. Altogether, the current data support the hypothesis that oxidative stress contributes to DAB cytotoxicity to mammalian host cells and *T. cruzi*. Support: FAPESP, CNPq, INCT Redoxoma.