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ACET-1 causes different biochemical responses in parasitic forms of *Trypanosoma cruzi*

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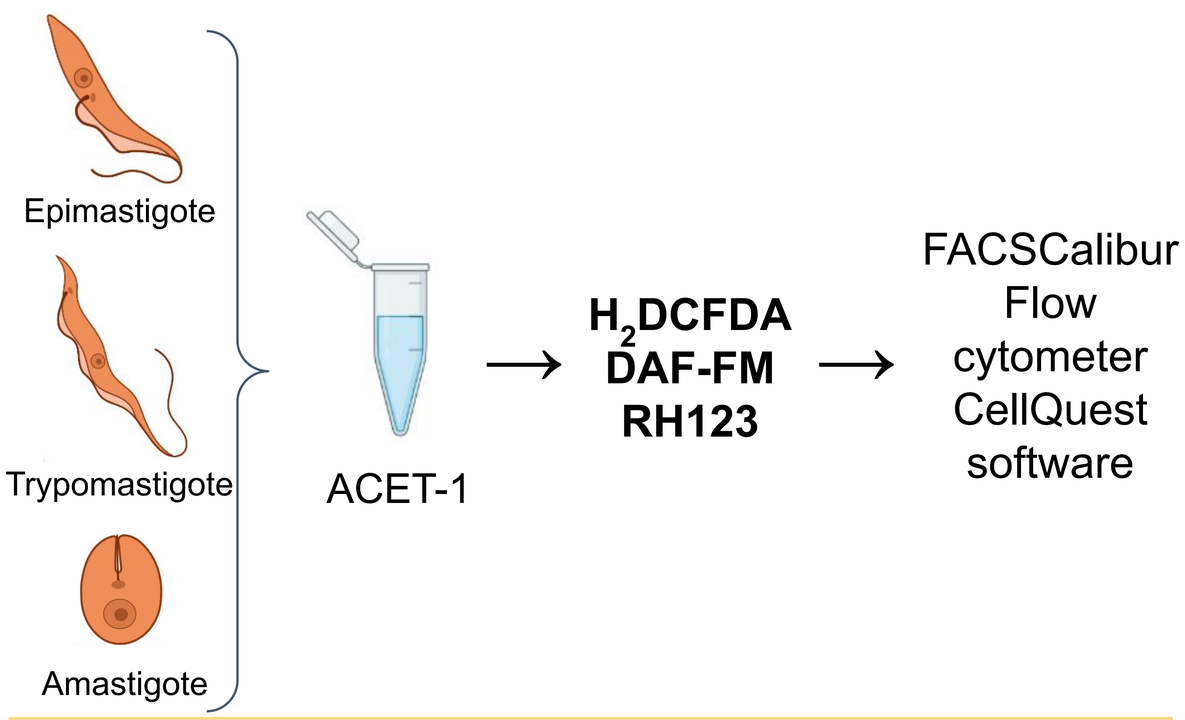
Introduction

Chagas disease is caused by infection with the protozoan parasite *Trypanosoma cruzi*, an uniflagellate pathogen that causes significant morbidity and death among millions in the world. There are approximately 7 million infections and 14,000 deaths each year from Chagas disease worldwide (1). The parasite in nature exists in different populations of vertebrate hosts such as humans, wild animals, and domestic animals, and invertebrates, such as insect vectors (triatomines). *T. cruzi* has morphological and functional variations, alternating between stages that undergo binary division and non-replicative and infective forms. As replicative forms are included the epimastigotes present in the digestive tract of the vector insect (non-infective) and amastigotes (infective) observed inside mammalian cells. The non-replicative and infective forms, the metacyclic trypomastigotes, are found in the feces and urine of the vector insect and the trypomastigotes circulating in the blood of mammals (2,3). Despite continuous efforts, the current treatment is unsatisfactory, especially in the chronic phase of the disease, besides high toxic. In response, our research group demonstrated interesting trypanocidal activity of the thiophene substance ACET-1 on the main parasitic forms of *T. cruzi*: epimastigote, amastigote and trypomastigote.

Objectives

Based on that, this work aimed to evaluate the biochemical effects of ACET-1 on *T. cruzi* in order to investigate the mechanism of action of this thiophenic substance.

Methodology



Results

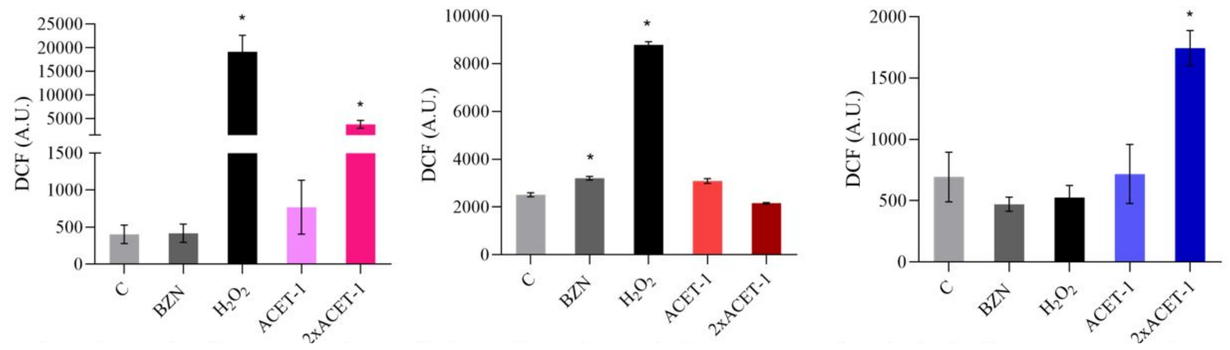


Figure 1: Total reactive oxygen species in parasitic forms of *T. cruzi* treated with ACET-1 for 24h and stained with H_2DCFDA. Epimastigotes (pink) were treated with 46.6 and 92.8 µM ; Trypomastigotes (red) were treated with 75.9 and 151.8 µM; Amastigotes (blue) were treated with 115.2 and 230.4 µM. Control group were untreated cells and positive control were treated with 1mM of H_2O_2.

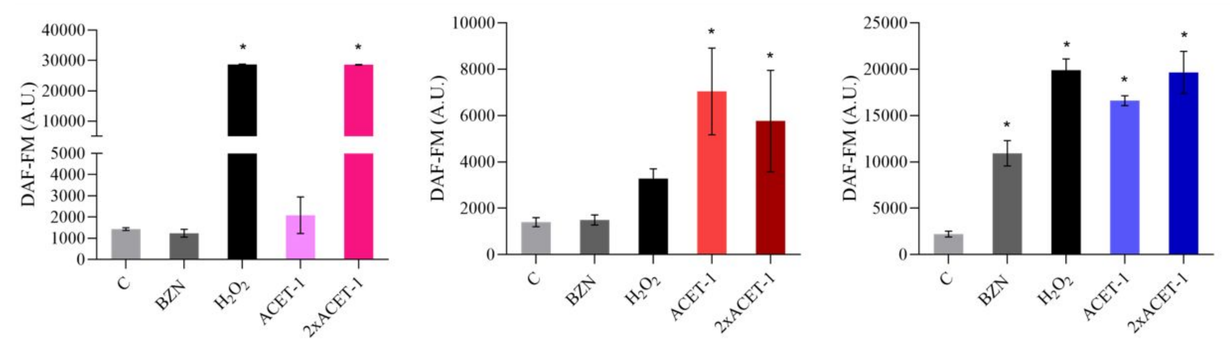


Figure 2: Oxid nitric presence in parasitic forms of *T. cruzi* treated with ACET-1 for 24h and stained with DAF-FM. Epimastigotes (pink) were treated with 46.6 and 92.8 µM ; Trypomastigotes (red) were treated with 75.9 and 151.8 µM; Amastigotes (blue) were treated with 115.2 and 230.4 µM. Control group were untreated cells and positive control were treated with 1 mM of H_2O_2.

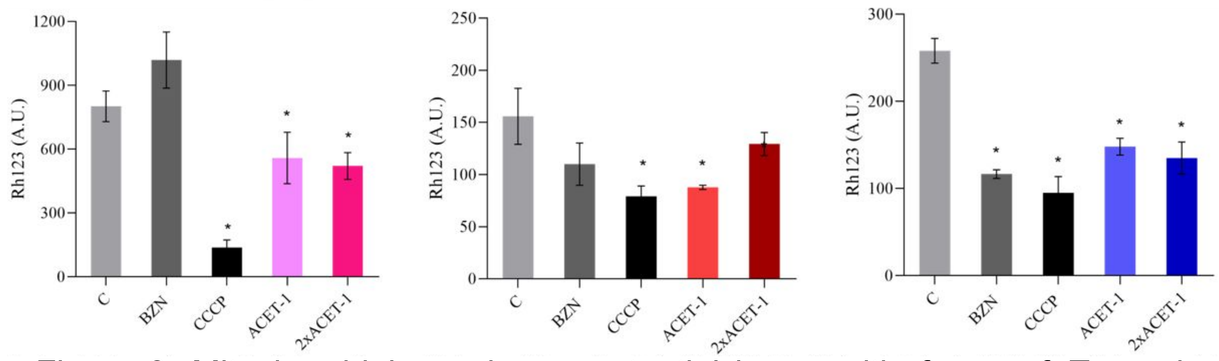


Figure 3: Mitochondrial membrane potential in parasitic forms of *T. cruzi* treated with ACET-1 for 24h and stained with RH123. Epimastigotes (pink) were treated with 46.6 and 92.8 µM ; Trypomastigotes (red) were treated with 75.9 and 151.8 µM; Amastigotes (blue) were treated with 115.2 and 230.4 µM. Control group were untreated cells and positive control were treated with 100 µM of CCCP.

Conclusions

Our results showed different biochemical alterations in differents parasitic forms after the treatment with the same substance (ACET-1), evidencing the metabolic differences of each of the forms.

References

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(3) Coura, J.R.; Viñas, P.A; Chagas disease: a new worldwide challenge. Nature; 465(7301): S6-7, 2010.

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