Abstract

Docking Study on T. cruzi Trypanothione Reductase and Iron-Superoxide Dismutase Isoforms of a Series of Imidazole-Based Derivatives as an Approach towards the Design of New Potential Inhibitors †

Iván Beltrán-Hortelano 1,2,3, María Font 1,3, Silvia Galiano 1,2 and Silvia Pérez-Silanes 1,2,*

1 Instituto de Salud Tropical (ISTUN), Universidad de Navarra, Campus Universitario, 31008 Pamplona, Spain; ibeltran@alumni.unav.es (I.B.-H.); mfont@unav.es (M.F.); sgaliano@unav.es (S.G.)
2 Sección Síntesis Orgánica, Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia y Nutrición, Universidad de Navarra, Campus Universitario, 31008 Pamplona, Spain
3 Sección Modelización Molecular, Departamento de Química Orgánica y Farmacéutica, Facultad de Farmacia y Nutrición, Universidad de Navarra, Campus Universitario, 31008 Pamplona, Spain

* Correspondence: sperez@unav.es; Tel.: +34-948425600
† Presented at the 1st Molecules Medicinal Chemistry Symposium, Barcelona, Spain, 8 September 2017.

Chagas disease (CD) or American trypanosomiasis is a widespread parasitic disease throughout the world. It is part of the group of 17 Neglected Tropical Diseases (NTD), classified by the World Health Organization (WHO) [1]. CD is caused by the flagellate protozoan parasite Trypanosoma cruzi (T. cruzi), which is mainly transmitted to humans by the faeces of blood-sucking Triatoma insects. Nowadays, CD is one of the most significant health problems in Central and South America in terms of epidemiological and human health repercussions. CD is potentially lethal (12,000 deaths/year), so it involves significant socioeconomic repercussions for the concerned countries [2]. Currently, only two drugs are available to treat CD in the acute phase: Nifurtimox (NFX) and Benznidazol (BNZ). However, both of them have significant toxic effects and variable clinical efficacy during the chronic phase of CD [3]. For those reasons, there is an urgent necessity to find new compounds that are safer, more effective and more affordable than the existing ones to eradicate T. cruzi, preventing the progression and reducing the risk of transmission of this disease.

Despite efforts, actions and strategies by the WHO and several organizations, the research of new potential treatments against CD remains a challenge in drug discovery programmes [4]. Nowadays, one of the strategies is based on the search for molecules enabling interference with enzymes that are involved in the survival of the parasite. Thus, many enzymes have been studied and reported as potential targets for the discovery and design of new compounds for the treatment of CD [5].

Due to the intracellular nature of the parasite, it is highly sensitive to Reactive Oxygen Species (ROS), so our research group focuses on two targets that protect it against oxidative damage: trypanothione reductase (TR) and iron-superoxide dismutases (Fe-SODs) isoforms (one cytosolic and one mitochondrial). Therefore, we design and synthesize new potential inhibitors against these two targets for the therapy of CD [6]. In this context, we carried out a docking study of a new series of imidazole-based derivatives with the ability to inhibit these two exclusive targets that regulate T. cruzi redox metabolism.

Acknowledgments: The author is grateful to the Instituto de Salud Tropical de la Universidad de Navarra (ISTUN) for a grant.

Author Contributions: These authors have contributed equally to this work.

Conflicts of Interest: The authors confirm that this work has no conflict of interest.
References


© 2017 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (http://creativecommons.org/licenses/by/4.0/).