

Abstract

# Synthesis and In Vitro Antiparasitic Activity of Novel Arylamine Mannich Base-Type Derivatives against *Trypanosoma cruzi* and *Leishmania* spp. <sup>†</sup>

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Chagas disease and Leishmaniasis are trypanosomatid diseases considered as neglected tropical diseases by the WHO. These diseases are caused by *T. Cruzi* and *Leishmania* spp. that affect hundreds of millions of people all over the world [1]. Although the number of people affected has decreased, these infections are still threatening to human life. Governmental and non-governmental organizations have proposed big challenges with the commitment to meet the needs of these patients. One of the most important challenges is the search for new, safe, effective and affordable drugs to combat these diseases as the current therapeutic arsenal is inadequate and insufficient [2].

In this context, our research group has been working on the discovery of new Mannich base-type derivative compounds as promising molecules for new anti-trypanosomatid agents [3].

Considering the target product profile of these diseases and the results found to date, we persist in the search of potentially trypanocidal compounds; therefore, thirty-three new derivatives have been synthesized by different, simple and cheap synthetic routes.

All compounds have been tested in vitro against the epimastigote form in three different *T. cruzi* strains (SN3, Arequipa and Tulahuén) for Chagas disease and in the promastigote form in *L. braziliensis*, *L. donovani* and *L. infantum*. The cytotoxicity has also been determined using Vero and THP-1 mammalian cell lines to establish their selectivity index (SI). Subsequently, the activity of the selected compounds is being carried out in the intracellular forms of the parasites. The results obtained from this evaluation will be shown in this Symposium.

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## References

1. World Health Organization (WHO). Vector-Borne Disease. Available online: <http://www.who.int/mediacentre/factsheets/fs387/en/> (accessed on 20 March 2017).

2. Paucar, R.; Moreno-Viguri, E.; Pérez-Silanes, S. Challenges in Chagas Disease Drug Discovery: A Review. *Curr. Med. Chem.* **2016**, *23*, 3154–3170.
3. Moreno-Viguri, E.; Jiménez-Montes, C.; Martín-Escolano, R.; Santivañez-Veliz, M.; Martín-Montes, A.; Azqueta, A.; Jimenez-Lopez, M.; Ledesma, S.Z.; Cirauqui, N.; de Ceráin, A.L.; et al. In Vitro and in Vivo Anti-Trypanosoma cruzi Activity of New Arylamine Mannich Base-Type Derivatives. *J. Med. Chem.* **2016**, *59*, 10929–10945.



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