

11th International Conference on

Medicinal Chemistry & Pharmaceutical Technology

April 01-02, 2019 | Prague, Czech Republic

Drug repurposing as effective strategy to fight neglected tropical diseases

Neglected tropical diseases (NTDs) represent a major health problem and huge economic burden in developing countries. Among them, trypanosomatid diseases, including leishmaniases, Chagas disease and African sleeping sickness, are categorized by WHO as the most challenging NTDs affecting more than 20 million people worldwide. Additionally, they are expanding their frontiers worldwide and becoming relevant global health concerns. New treatment options against these diseases are lacking due to the poor interest of big Pharma towards such neglected therapeutic area, and the current chemotherapy is based on few old drugs endowed with limited efficacy and high toxicity. Thus, the search for new effective agents able to overcome these limits is always a hot topic.

Drug repurposing represents one of the most prominent and successful strategies to furnish new compounds and tools for the treatment of diseases for which no or very few drugs are available. We applied this approach to find agents able to defeat NTDs. According to this, our inhouse series of azole antifungal drugs designed several years ago, which showed good activity both *in vitro* against *C. albicans* and spp, and *in vivo* in rabbit model of cutaneous fungal infection were screened against clinically relevant parasites. A number of them displayed nanomolar activities against *T. cruzi*, resulting much more active than the reference drug and showing high selectivity towards parasite. Interestingly, the most active derivative displayed efficacy in *in vivo* model of infection. Starting from these data, we designed and synthesized a new series of azole compounds endowed with nanomolar potencies against *T. cruzi* and capable to effectively reduce parasitemia higher than 99% in 4-day *in vivo* models.

Key words: neglected tropical diseases, trypanosomatid diseases, azole

Biography

Roberto Di Santo is Full Professor in Medicinal Chemistry at University of Rome "La Sapienza". He is engaged in drug design and Discovery of new chemotherapeutic agents. His current focus is on the Discovery of antimicrobial agents with attention to new chemical entities useful to defeat microbial neglected diseases. He is the director of Drug Design and Discovery Laboratory in Chemistry and Technology of Drugs Department of Rome University "La Sapienza". He has published more than 130 papers on high impact peer reviewed journals and has been serving as an editorial board member of repute.

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