Antimicrob Agents Chemother. 2022 Nov 15;66(11):e0028422. doi: 10.1128/aac.00284-22.
Epub 2022 Oct 31.

Drug Repurposing in Chagas Disease: Chloroquine Potentiates Benznidazole Activity against Trypanosoma cruzi *In Vitro* and *In Vivo*

Ramendra P Pandey [# 1 2], Marilda Savoia Nascimento [# 2 3], Caio Haddad Franco [4], Karina Bortoluci [5], Marcelo Nunes Silva [6], Bianca Zingales [6], Daniel Gibaldi [7], Leda Castaño Barrios [7], Joseli Lannes-Vieira [7], Leonardo Moro Cariste [8], Jose Ronnie Vasconcelos [8 9], Carolina Borsoi Moraes [4], Lucio H Freitas-Junior [4], Jorge Kalil [1 2], Laura Alcântara [1 2 3], Edecio Cunha-Neto [1 2]

Affiliations

PMID: 36314800 PMCID: PMC9664849 DOI: 10.1128/aac.00284-22

Free PMC article

Abstract

Drug combinations and drug repurposing have emerged as promising strategies to develop novel treatments for infectious diseases, including Chagas disease. In this study, we aimed to investigate whether the repurposed drugs chloroquine (CQ) and colchicine (COL), known to inhibit Trypanosoma cruzi infection in host cells, could boost the anti-T. cruzi effect of the trypanocidal drug benznidazole (BZN), increasing its therapeutic efficacy while reducing the dose needed to eradicate the parasite. The combination of BZN and COL exhibited cytotoxicity to infected cells and low antiparasitic activity. Conversely, a combination of BZN and CQ significantly reduced T. cruzi infection *in vitro*, with no apparent cytotoxicity. This effect seemed to be consistent across different cell lines and against both the partially BZN-resistant Y and the highly BZN-resistant Colombiana strains. *In vivo* experiments in an acute murine model showed that the BZN+CQ combination was eight times more effective in reducing T. cruzi infection in the acute phase than BZN monotherapy. In summary, our results demonstrate that the concomitant administration of CQ and BZN potentiates the trypanocidal activity of BZN, leading to a reduction in the dose needed to achieve an effective response. In a translational context, it could represent a higher efficacy of treatment while also mitigating the adverse effects of high doses of BZN. Our study also reinforces the relevance of drug combination and repurposing approaches in the field of Chagas disease drug discovery.

Keywords: Chagas disease drug discovery; benznidazole; chloroquine; drug combination; drug repurposing.

Figures

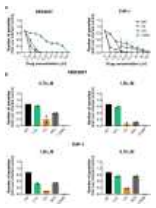

FIG 1 Activity of drugs and drug…

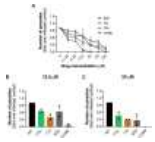

FIG 2 Activity of drugs and drug…

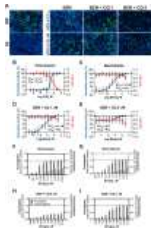

FIG 3 Efficacy of drugs and drug…

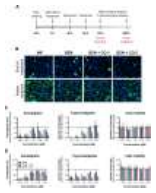

FIG 4 Dynamics of T. cruzi infection…

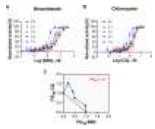

FIG 5 *In vitro* drug interactions between…

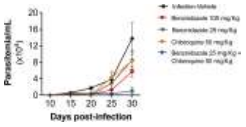

FIG 6 Therapeutic efficacy of drugs and…

Related information

MedGen
PubChem Compound (MeSH Keyword)

LinkOut – more resources

Full Text Sources
Atypon
Europe PubMed Central
PubMed Central

Medical
MedlinePlus Health Information