Title: EVALUATION OF ANTIMICROBIAL ACTIVITY OF NAPHTHOQUINONES AGAINST 
*Mycobacterium tuberculosis*

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Abstract:

Tuberculosis (TB) is an infectious disease caused mainly by *Mycobacterium tuberculosis*, 
despite being curable, is still a problem of global public health. Among the obstacles to TB 
control, is the increase in cases of patients infected by resistant strains, the long duration of 
treatment and its toxic effects. This reinforces the need to develop new drugs that increase the 
therapeutic arsenal available for the treatment of TB. The aim of this study was to evaluate the 
antimycobacterial activity of six naphthoquinones compounds. It was determined the minimum 
inhibitory concentration (200 µg/mL to 0.4 µg/mL) of the molecules by the microdilution 
method Resazurin Microtiter Assay (REMA) and the minimum concentration capable of inhibiting 90% of 
bacterial growth (IC90) of three *M. tuberculosis* strains: a pan susceptible H37Rv (ATCC 
27294); a isoniazid mono resistant (INHr), with mutation in the katG gene codon 315 Ser-Tir 
(ATCC 35822); and a rifampin mono resistant (RMPr), with mutation in the rpoB gene codon 
526 His-Tir (ATCC 35338). From six naphthoquinones, five were active against the H37Rv 
strain (IC90 between 10 and 89 µg/mL); six were active against INHr (IC90 between 10 and 44 
µg/mL) and RIFr (IC90 between 0.9 and 95 µg/mL). The most active molecule against the 
H37Rv strain was also the most active for the INHr, with IC90 of 10 µg/mL, and contains cloro 
as substituent, while the unique molecule to have a benzene ring as a substituent, had the 
lowest IC90 for the RMPr strain, of 0.9 µg/mL. These differences in antimycobacterial activity of 
naphthoquinones seem to be related to the radicals in 3-meta position. The results demonstrate 
the potential of these molecules, particularly with the cloro substituent for sensitive and INHr 
strains, and with a benzene ring for RMPr strains, and could be a scaffold for new drugs for TB 
treatment. The next step is to elucidate the mechanisms of action of these compounds.

Key-words: Antimicrobials, drug resistance, *Mycobacterium tuberculosis*

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