Poster

Repurposing of the tamoxifen metabolites in combination with tigecycline against Gram-negative bacteria

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ABSTRACT

Motivation: Emerging of multidrug-resistant (MDR) bacteria represent a matter of grave urgency and a problem for public health. Due to the emergence of resistance new strategic antimicrobial therapeutic approaches are proposed, such as drug repurposing. Tamoxifen was previously reported to present efficacy against MDR Acinetobacter baumannii and Escherichia coli [1]. The objetive of this project was to study in vitro the activity of the three major metabolites of tamoxifen (MET): N-desmethyltamoxifen, 4-hydroxytamoxifen, and endoxifen, in combination with tigecycline against colistin-susceptible (COL-S) and colistin-resistant (COL-R) A. baumannii and E. coli.

Methods: A colection of Gram-negative bacteria [8 COL-R and 1 COL-S A. baumannii, 17 COL-R and 1 COL-S E. coli] was used [2]. All strains were grown in Mueller-Hinton Broth (MHB) at 37ºC. Minimal Inhibitory Concentration (MIC) was determined for all strains by using microdilution assay. In order to determine the synergy between a mix of the three MET and tigecycline checkerboard and time-kill curves assays were performed.

Results: Tigecycline MIC range was 4-8 mg/L for all COL-R A. baumannii strains, 0.5 mg/L for COL-S A. baumannii strain and 0.125-1 mg/L for both COL-R and COL-S E. coli strains. Checkerboard analyses showed partial synergism for combination tigecycline and MET against COL-R ans COL-S A. baumannii and E. coli strains. Time-kill curves confirmed synergetic effect and inhibited partially and completely the regrowth of COL-R E. coli and A. baumannii strains, respectively.

Conclusions: Tamoxifen metabolites in combination with tigecycline showed in vitro synergetic effect against COL-R A. baumannii and E. coli strains, representing a potential new alternative for treatment of infections caused by MDR A. baumannii and E. coli.

REFERENCES

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