

**TITLE:** ANALYSIS OF THIOUREA DERIVATIVES AS POTENTIAL CANDIDATES FOR ANTIMICROBIAL AGENTS

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**ABSTRACT:**

The emergence and spread of antibiotic resistance among human pathogens are relevant problems for human health. Selective pressure associated and bacterial mechanisms of genetic evolution collaborates to increase this issue. *Staphylococcus aureus* is the most opportunistic pathogen and perhaps of greater concern because of its intrinsic virulence and ability to cause a wide variety of infections. *Staphylococcus epidermidis* constitutes the normal bacterial flora of human skin and mucous membranes. This microorganism can be easily introduced as a contaminant in medical devices. Due to the acquisition of transferred virulence factors, *Escherichia coli* can, also, cause disease. Among the pathogenic strains, there are those causing intestinal and extra-intestinal infections. Compounds 1,2,4-triazole-ciprofloxacin have been reported to exhibit antibacterial activity against Gram-positive and Gram-negative strains. There are derivatives presenting better activity than the commercially available antibiotics - ciprofloxacin and vancomycin, against *S. aureus*. We intended to verify the potential antimicrobial and anti-biofilm activities of thioureas derivatives as candidates for the treatment of infections caused by these microorganisms. Hence, new thiourea derivatives were designed as novel putative antimicrobial agents based on bioactive compounds that present the triazole ring and thiourea group in their structures. The biological activity of each compound was evaluated, where the diluted inoculum and the derivative were applied in 96-well plates at 512 µg/mL to 0.0625 µg/mL concentrations to determinate MIC, the reading was visualized by resazurin. The antimicrobial dilutions for MIC as well as the positive control were applied In TSA medium plates to check the bacterial growth and evaluate the MBC. The cytotoxicity assay was performed in 3T3 cell culture. The results were analyzed by GraphPad Prism. Among eight derivatives tested, the triazole-thiourea PLTU 01-09 showed bacteriostatic effect in the following dilutions: 16 µg/mL (*S. aureus*), 64µg/mL (*S. epidermidis*) and 128 µg/mL (*E. coli*). The bactericidal effect was observed for *S. epidermidis* and *E. coli* (128 µg/mL and 256 µg/mL, respectively). The cytotoxicity was very satisfying for this compound. Therefore, these compounds represent potential as antimicrobial agent against important pathogenic bacteria and infections of multidrug-resistant bacteria, being a candidate for pre-clinical trials.

**Keywords:** thiourea compounds, bacterial infection, antimicrobial resistance.

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