

**TITLE:** Synergistic effect between  $\beta$ -lapachone and vancomycin on *Enterococcus faecalis* strains

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**ABSTRACT:**

Enterococci are commensal microorganisms that act as opportunistic pathogens and frequently cause infections in hospitalized patients and/or who have received multiple types of antimicrobial therapy. The main human reservoir of this microorganism is the gastrointestinal tract. Enterococci have become important agents of human diseases due mainly to the antibiotics intrinsic resistance or the ability to acquire resistance through mutation. Due to the increased bacterial resistance to multiple antibiotics, there are concerns about researching for new drugs and antibacterial therapy. In this way, the aim of present study was to determine the synergistic effect of  $\beta$ -lapachone in combination with vancomycin against multiresistant *Enterococcus faecalis* strains. Initially, the Minimum Inhibitory Concentration (MIC) of three naphthoquinones (lapachol,  $\alpha$ -lapachone and  $\beta$ -lapachone) and vancomycin was determined against ten strains of *Enterococcus faecalis* with a resistant phenotype previously determined by the disk diffusion method. The study of interaction between  $\beta$ -lapachone and vancomycin was carried out by the checkerboard method on five *E. faecalis* strains. The criteria used to evaluate the synergistic activity were defined by Fractional Inhibitory Concentration Index (FIC index). All *E. faecalis* strains showed vancomycin resistance whose MICs were greater than 128  $\mu$ g/ml. Among the naphthoquinones,  $\beta$ -lapachone was shown to be more effective (MIC 320-160  $\mu$ g/ml) and was chosen for the second stage of this research. A strong synergistic effect was observed with the combination vancomycin/ $\beta$ -lapachone for all strains. The FICI values ranged from 0.31 to 0.04. The MIC reduction for vancomycin was greater than or equal to 75%.  $\beta$ -lapachone associated with vancomycin acts synergistically by inhibiting multidrug-resistant *Enterococcus faecalis* strains.

**Keywords:** Enterococci infections; naphthoquinones; vancomycin; synergistic activity.

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