

**TITLE:** SYNERGISTIC EFFECT OF  $\beta$ -LAPACHONE, OXIMA OF LAPACHOL AND OXACILLIN AGAINST CLINICAL ISOLATES OF *Staphylococcus aureus*

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**ABSTRACT:**

Bacteria of the genus *Staphylococcus* are among the pathogens that most cause nosocomial infections. This is result of the difficulty of the treatment due to the mechanisms of resistance that these microorganisms present. These infections have become a major health challenge, especially in relation to the appearance of strains resistant to the usual antimicrobial therapy. In this context, researchers are developing alternative therapies involving chemical synthesis in order to potentiate the biological activity of natural substances, as well as synergistically assist antimicrobials in the control of infectious conditions. The objective of the study was to verify the synergistic effect of semisynthetic products with Oxacillin against clinical isolates of *Staphylococcus aureus*. Para isso, foi utilizada a metodologia do *Checkerboard*. Clinical isolates of *Staphylococcus aureus* originated from human blood cultures and standardized in optical density 0,030 – 0,040 ( $1,37 \times 10^7$  UFC). The antimicrobials were distributed: the semisynthetic product in the vertical in the concentration of 8x the MIC value (column 6 to 1); the Oxacillin in the horizontal in the concentration of 4x the value of the MIC (line "A" to "F"). At the end, the bacteria were distributed in each well. The synergistic effect of each antimicrobial was performed by addition of CTT (2,3,5-triphenyltetrazolium chloride) and the combinations were determined and used for the calculation of the Inhibitory Fraction Index (IFI), by means of the following formula: IFI semisynthetic products = (MIC combined / MIC alone) or IFI antibiotic = (MIC / MIC alone). The sum of the IFIs was used to classify effects according to the following criteria: Synergism ( $\Sigma IFI \leq 0.5$ ), Additive ( $0.5 < \Sigma IFI < 1$ ), Indifferent ( $0.75 < \Sigma IFI < 4$ ) and Antagonism ( $\Sigma IFI > 4$ ). As results, it was observed that the concentrations of 7.81  $\mu\text{g/mL}$  of Lapachol Oxime and 31,25  $\mu\text{g/mL}$  of Oxacillin presented a synergistic effect, as well as the concentration of 15.62  $\mu\text{g/mL}$  of  $\beta$ -lapachona with 0,97  $\mu\text{g/mL}$  of the antibiotic. The advantages of this effect are the reduction of toxicity, the use of low doses of the drug, the prevention of the selection of resistant bacteria during therapy. Therefore the synergistic action of the substances with Oxacillin provides an extra tool in the control and eradication of multiresistant bacteria.

**Keywords:** MRSA, semisynthetic products, chemical synthesis.

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