

TITLE: OXIDATIVE STRESS RESPONSE OF *Pseudomonas aeruginosa* EXPOSED AT SUBLETHAL CONCENTRATIONS OF LANTIBIOTIC NISIN, CIPROFLOXACIN AND THEIR COMBINATIONS.

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ABSTRACT:

Pseudomonas aeruginosa is an opportunistic pathogen that exhibits a facility of adaptability in a wide range of other natural and artificial settings, including surfaces in medical facilities, and high antibiotic resistance. To reduce bacterial resistance, studies are needed with new antimicrobial drugs and especially studies to understand how these drugs act on the pathogen physiology, their targets and mechanisms of action and the response of this to different treatments, for example the response to oxidative stress in bacteria. Previously it was determined the maximum sublethal concentration (MSC) of nisin (N), ciprofloxacin (CIP), and their combination (N+CIP); (proportion of ¼ the nisin + ¼ the ciprofloxacin of the MSC) against strain of *Pseudomonas aeruginosa* ATCC 27853 from Resazurin Microtiter Assay (REMA) in Mueller Hinton Broth (MHB). To protein extraction, growth cells were harvested by centrifugation followed by extraction of proteins of *P.aeruginosa* (Control), exposed to sublethal concentrations of nisin, ciprofloxacin and their combination. The supernatant was used for determination the activity of the antioxidant enzymes: catalase (CAT), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and to mark the oxidative stress was used the quantification of lipid hydroperoxide (HP).The enzymatic activity of *P.aeruginosa* treated with the tested antimicrobials, ciprofloxacin and ciprofloxacin + nisin combination showed higher enzymatic activity in relation to the control in the three enzymes tested and also with increased levels of HP. Individual ciprofloxacin and the combination of antimicrobials was able to induce a greater ($p<0.05$) oxidative stress against *P.aeruginosa* compared with control. Already individual treatment with nisin increased the activity of the catalase enzyme in relation to the control, but did not differ in the increase of the enzymatic activity for the SOD and GSH-Px enzymes and for the HP marker. There are already studies that ciprofloxacin can cause overproduction of reactive oxygen species and cell injury. When placed in combination with nisin and with the already damaged cell it may come into contact and cause damage to the membrane and consequent instability of the cell. The action together consequently causing an electrolyte imbalance increasing the number of oxidant and antioxidant enzymes and this can become a new therapeutic target.

Key words: *Pseudomonas aeruginosa*, Oxidative stress, Nisin, Ciprofloxacin

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