**TITLE:** EVALUATION OF IN VITRO SYNERGISM BETWEEN A LIPOPEPTIDE PRODUCED BY *Paenibacillus elgii* AND COMMON ANTIBIOTICS IN THE INHIBITION OF MULTIDRUG-RESISTANT *Klebsiella pneumoniae*.

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**ABSTRACT:**

The exploration of microorganisms as a source of biologically active compounds led to the discovery of new substances with antimicrobial activity. In this group, there are the lipopeptides produced by the *Paenibacillus elgii* belonging to the pelgipeptin family, which modify the bacterial surface. *Klebsiella pneumoniae* is a Gram-negative bacterium; it is a saprophyte in humans, colonizing the gastrointestinal tract, skin, and nasopharynx. It is currenlty considered an important causative agent of community-acquired infections, due to the rapid dissemination of multidrug-resistant *K. pneumoniae* strains producing “carbapenemases”. The objective of this study was to evaluate the in vitro combination of pelgipeptin B and Chloramphenicol or Penicillin G, against a multidrug-resistant strain of *K. pneumonia*, aiming to apply lower concentration of these antimicrobials to control infections caused by this bacterium. *P. elgii* was grown in nutrient broth at 37°C for 40h. Lipopeptides were extracted from the supernatant with butanol 1:1. The organic fraction was removed and the precipitate was resuspended in deionized water. The lipopeptides were purified and quantified by HPLC. The analysis was performed by mass spectrometry, MALDI-TOF. Multidrug-resistant strain of *K. pneumoniae* was obtained from LACEN. The minimum inhibitory concentration (MIC) of the pelgipeptins and the checkerboard method were evaluated using microdilution in broth. The lipopeptides produced by *P. elgii*: pelgipeptins A, C and B were purified. They correspond to the molecular masses of 1073, 1087 and 1101, respectively. The observed MIC against multidrug-resistant *K. pneumoniae* were 16 µg/mL for pelgipeptins A and C, 32 µg/mL for pelgipeptin B. Chloramphenicol and penicillin G were used as controls, presenting MIC of 32 µg/mL, and MIC higher than 1024 µg/mL, respectively. Pelgipeptin B antimicrobial effect was evaluated in combination with chloramphenicol or penicillin G, for the synergism studies. In the first combination the pelgipeptin B presented MIC of 2 µg/mL and the chloramphenicol a MIC of 8 µg/mL, resulting in the Fractional Inhibitory Concentration Index (FICI) of 0.3125, confirming the presence of synergism. However, the combination between pelgipeptin B and penicillin G did not present additive antimicrobial activity. Thereby, there is a potential for therapeutic use of pelgipeptins associated with some common drugs for the control of infections with resistant *K. pneumoniae*.

**KEYWORDS:** Antimicrobial lipopeptides, *Klebsiella pneumoniae*, Multidrug- resistant, Paenibacillus, Pelgipeptin.

**DEVELOPMENT AGENCY:** CNPq