TITLE: PAβN (PHENYL-ARGININE-β-NAPHTHYLAMIDE) CITOTOXICITY IN ALVEOLAR MAMMARY BOVINE CELLS (MAC-T)

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ABSTRACT

The increase of resistance to antimicrobials in bacterial strains is a worldwide concern. In addition to other factors, resistance may be caused by the presence of efflux pumps, which are membrane transporters capable of reducing the accumulation of antimicrobials within the bacterial cells. The use of inhibitors of these pumps coadministered with an antimicrobial could be a treatment option. In *Escherichia coli* the major multidrug efflux system is a complex of three proteins, AcrAB-TolC, belonging to Resistance-Nodulation-Division family. Here, the aim was to verify the cytotoxicity of the efflux pump inhibitor PAβN (phenyl-arginine-β-naphthylamide) in bovine mammary alveolar cells (MAC-T). Four isolated of *E. coli* obtained from mastitis milk belonging to the Laboratory of Bacterial Diseases' bacterial collection that were ampicillin-resistant and had *acrA* and/or *acrB* genes were subjected to the MIC test of ampicillin (concentrations tested ranged from 1 to 500 µg/mL) by microdilution in broth in the presence and absence of PAβN at 50 µg/ml. The PAβN cytotoxicity at concentrations of 50 and 350 µg/ml in MAC-T was evaluated by the MTT assay. In the absence of PAβN, the isolated were resistant to ampicillin in all concentrations tested (1 to 500 µg/mL) in the MIC test; in its presence, MICs ranged from 1 to 15.6 µg/mL of ampicillin, and PAβN alone was not able to inhibit bacterial multiplication. PAβN was shown to be non-toxic to MAC-T at the concentrations tested. The concentration of 350 µg/ml is sevenfold the concentration described in the literature for PAβN use. Thus, PAβN used as an adjuvant may be an option in the treatment of bovine mastitis because it is considered safe for use in the mammary gland *in vitro*. Moreover, in its presence it would be possible to decrease the concentrations of antimicrobial drugs, thus reducing the selective pressure on microorganisms. *In vivo* experiments are the next step.

Keywords: cytotoxicity; MAC-T; mastitis; PAβN

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