

TITLE: SYNERGISM OF FRUIT SUBSTANCES OF *Garcinia brasiliensis* WITH ANTIMICROBIALS ON *Streptococcus* spp. ISOLATED FROM MASTITIS

AUTHORS: MAIA, N. L.¹; PENA, J. L.¹; OLIVEIRA, L. L. De²; SANTOS, M. H. Dos³; CARDOSO, S.⁴; BARROS, M. ¹; MOREIRA, M. A. S.¹

¹LABORATORY OF BACTERIAL DISEASES (LDBAC), PREVENTIVE VETERINARY MEDICINE AND PUBLIC HEALTH SECTOR, VETERINARY DEPARTMENT; ²GENERAL BIOLOGY DEPARTMENT; ³CHEMISTRY DEPARTMENT; ⁴MEDICINE AND NURSING DEPARTMENT.

INSTITUTION: UNIVERSIDADE FEDERAL DE VIÇOSA, MG (AV. PH ROLFS S/N, CAMPUS UNIVERSITÁRIO, CEP: 36.570-900, VIÇOSA - MG, BRAZIL).

ABSTRACT:

Bovine mastitis is a disease of high occurrence and widespread in herds around the world, making it a worrying scenario due to the impacts on public health and also on the countries' economies, especially in Brazil due its large milk production. The number of bacterial isolated resistant to a variety of pharmacological medicines has increased, mostly because of drug-indiscriminate use. The investigation of new molecules with antimicrobial potential as well as the association with traditional drugs became a great necessity. The aim of this study was to investigate the antimicrobial action of two bioactive substances, gutiferone-A (M11) and 7-epiclusianone (M6), on field isolated *Streptococcus uberis* (Su959) and *Streptococcus agalactiae* (Sa4605) obtained from animals infected with mastitis. Analyses were conducted to define the Minimum Inhibitory Concentration (MIC) of synthetic antimicrobials and bioactive molecules, with concentrations ranging from 0.6 to 125 µg/mL. Later, the presence of synergistic interactions was investigated using the Checkerboard Method from eight combinations of M11 and M6 with ampicillin and gentamicin. To assess the cell viability, was performed the MTT (3 - [- 4,5-dimethyl-thiazol-2-yl]-2,5-diphenyl tetrazolium bromide) assay, with individual exposure of each antimicrobial (synthetic and bioactive) targeting the MAC-T cells (bovine mammary epithelial cells). At MIC test, it was confirmed the antimicrobial potential of M6 and M11, besides the inefficacy of ampicillin and gentamicin in control the multiplication of both isolated. Considering the synergistic interactions, six associations showed positive synergic interaction leading to the recovery and powering the action of the synthetic antimicrobials against studied isolated previously resistant to their individual action. On MTT assay, results showed that only M11 was cytotoxic at 2xMIC and 1xMIC. However, concentrations doses equal to or lower than 0.5xMIC are needed to potentiate the action of synthetic antimicrobials, and these concentrations were no toxic to MAC-T *in vitro*. Thus, the gutiferone-A and 7-epiclusianone showed an effective antimicrobial action on the field *Streptococcus uberis* and *Streptococcus agalactiae*, in addition to being promising candidates for use in combinations with the synthetic antimicrobials ampicillin and gentamicin, in order to recover and optimize their antimicrobial action.

Keywords: Bioactive substances; disease; milk; synergism.

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