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REUNIÓN DE SOCIEDADES DE BIOCENCIAS 2021

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SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)**

**LXIX REUNIÓN ANUAL DE LA
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**LIII REUNIÓN ANUAL DE LA
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**XI REUNIÓN ANUAL DE LA
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(NANOMED-AR)**

17-20 de noviembre de 2021

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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2021

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(NANOMED-AR)**

November 17-20, 2021

RESPONSIBLE EDITORS

Dr. Alejandro Curino

Dra. Mariana Maccioni

Dra. Paula Schaiquevich

Dra. Hebe Duran

AGENTES ANTIMICROBIANOS Y ANTIPARASITARIOS

1. (035) INHIBITION OF BACTERIAL ADHERENCE TO VASCULAR CATHETER OF THE ANTIMICROBIAL PEPTIDE AP7121

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Healthcare-associated bloodstream infections are the leading cause of morbidity and mortality in hospitalized patients. Vascular catheter-related infection is its main source. Gram-positive bacteria specially *Staphylococcus* spp., are the most prevalent etiological agents. Bacterial adherence is the starting point of colonization of a surface known as biofilm development. The inhibition of this process is the primary strategy to prevent bacteremia related to medical devices. The aim of this work was to assess the inhibitory activity of the antimicrobial peptide AP7121 on the *Staphylococcus aureus* adherence in vascular catheters. The biofilm-producer strain *Staphylococcus aureus* ATCC 35556 (SA) was used. First, The MIC of AP7121 (MIC_{AP}) for SA was estimated. Upon, 20 mm segments of vascular catheter (n=3) were inoculated with 10⁴ CFU/mL of SA. Three different treatment schemes (A: simultaneous, B: previous and C: following bacterial challenge) using 1 x MIC_{AP} were tested. Control groups were included in each scheme. Statistical analysis was made using ANOVA and Kruskal-Wallis test ($p < 0.05$ was considered statistically significant). The MIC_{AP} was 0.48 mg/L. A significant bacterial reduction ($p < 0.001$) of 2 logarithms representing a decrease of 99% of viable SA cells was achieved with schemes A and B. The post-challenge treatment with AP7121 (scheme C) produced a significant reduction ($p < 0.01$) of 1 logarithm representing a decrease of 90% of viable SA cells. The results observed in this work suggest a fast antimicrobial activity of AP7121 that could be beneficial to reduce bacterial adherence on medical devices such as vascular catheter and potential decreasing bloodstream infections -associated. *In vivo* studies are needed to establish the feasibility of this proposal.

2. (043) METFORMIN INDUCES AUTOPHAGY AND UPR UNDER INTRACYSTIC GLUCOSE DEPRIVATION IN IN VITRO METACESTODES AND IN VIVO EXPERIMENTAL MODELS OF ECHINOCOCCUS GRANULOSUS

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Metformin (Met) is an experimental antiechinococcal drug (Loos et al., 2017; 2020), which inhibits the complex I of the respiratory chain in *in vitro* *Echinococcus* larval stage, resulting in an indirect AMPK activation (by an increased ADP/ATP ratio due to ATP drop) and a subsequent inhibition of TOR signaling with autophagy induction

(Loos et al., 2015, 2018). Here, we demonstrated that Met mediated the dephosphorylation of Eg-TOR in Ser³¹²², which trigger the reduction of its activity in metacestodes, responding also to exogenous insulin and rapamycin. Moreover, Met induced the overexpression of TFEB, a hub transcription factor that regulates lysosome biogenesis, lipid catabolism and autophagy in metazoa. In concordance with the mitochondrial depolarization induced by Met, an increase in total cellular Pi (an activator of PFK1) was detected, with stimulation of glycogen consumption (glycogenolysis) and, increase of glycolysis and the lactate fraction. Cumulatively, this supports the reduction in the glucose intracystic content demonstrated *in vitro*, as well as in two different experiments (50 and 250 mg/kg/day of Met) in the echinococcosis murine model. In this line of evidence, the energy starvation induced by Met causes endoplasmic reticulum stress-mediated unfolded protein response (UPR). In presence of a manose-specific lectin (Helja-FITC) and using confocal microscopy, we found that parasite cells expanded their ER volume at least 3-fold under treatment with Met. Using thapsigargin, tunicamycin and Met-treated parasites, we validated the IRE activity by XBP1 splicing and demonstrated that Met induced the mRNA of Bip/Grp78d. In this context, we described that UPR induced after Met-treatment can take place upon glucose deprivation in the parasite, suggesting that the anthelmintic effects of Met result from sustained autophagy mediated by activation of the AMPK-TOR-TFEB signaling pathway interdependent with UPR activation, especially through the IRE/XBP arm.

3. (063) DISPENSE OF ANTIBIOTICS IN ASSOCIATION WITH FIXED DOSES IN A PHARMACY OF AN UNIVERSITY SOCIAL SECURITY INSTITUTE OF CORRIENTES, 2020

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Antibiotics (ATB) are essential medicines for human health, but their massive and indiscriminate use increases the development of resistance. At the same time, in the pharmacological market they are offered in associations at fixed doses (AFD) that are not always rational, which exposes the patient to a greater risk of having adverse effects. The objective of this study was to characterize ATB in the form of AFD dispensed on an outpatient basis in an University Social Security Institute, during the year 2020. An observational, descriptive, cross-sectional study of drug use (SDU) was carried out. The dose unit (DU) was used as a quantitative indicator of outpatient dispensing and the Potential Therapeutic Intrinsic Value (PTIV) as a qualitative indicator, methodologies recommended by Laporte and Tognoni. Of a total of 1,364 outpatient dispensations of ATB, 164 (12%) were AFD, 56% for the female sex. Average age: 42 years; range: 2 to 79 years. The 164 AFD contained a total of 2356 DU, corresponding to amoxicillin + ambroxol (516 DU), norfloxacin + phenazopyridine (350 DU), clarithromycin + ambroxol (338 DU), amoxicillin + acetylcysteine (336 DU), amoxicillin + clavulanic acid + ambroxol (336 DU), amoxicillin + diclofenac (280 DU), ampicillin + dipyrone + guaifenesin (200 DU). Qualitatively, 114 (69.51%) had relative PTIV and 50 (30.48%) had unacceptable PTIV. These findings require special attention, because the consumption of this type of AFD is considered irrational according to the Laporte and Tognoni classification; generates potential risk of the appearance of adverse events and pharmacological interactions, increases health costs and their indiscriminate use can become a risk factor for the development of bacterial resistance, a current scourge that gives rise