10. NEW CHEMOTHERAPY FOR THE TREATMENT OF INFECTIOUS DISEASES

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STUDY OF CYTOTOXIC AND ANTIPROLIFERATIVE ACTIVITY OF FUNGICIDAL SAPONIN TAUROSID Sx1 ON TRANSFORMED MAMMALIAN CELLS

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Saponins taurosids from the Crimean ivy are capable of enhancing the immune response in mice to HIV surface glycoproteins and influenza virus. It was shown that saponin taurosid Sx1 has a fungicidal activity against *Candida* spp. The aim of our work was to determine cytotoxic properties of saponin taurosid Sx1 on mammalian transformed cells such as MT-4 lymphoblastoid cell line and Vero fibroblast-like cell line.

The triterpene saponin taurosid Sx1 with the structure 3-O-α-Lrhamnopyranosyl(1→2)-α-L-arabinopyranoside hederagenin isolated from the Crimean ivy *Hedera taurica* Carr. *(Araliaceae)*, lymphoblastoid tumor cells of MT-4 line and fibroblast-like cells of the Vero line were used in the study. The saponin toxicity was determined with a methyltetrazolium test (MTT).

The effects of taurosid Sx1 taken in 0.019–50.0 μg/ml concentrations on MT-4 cells were assessed. The saponin concentration of 3.13 μg/ml was shown not toxic — the number of surviving cells was 81.56%. The marked toxic effects were observed with saponin concentrations 25 and 50 μg/ml — the number of surviving cells were 68.10% and 30.43%, correspondently. For Vero cells the non-toxic saponin concentration was 0.78 μg/ml (the number of surviving cells was 84.14%). Regarding Vero cells, taurosid Sx1 exhibited cytotoxic properties at lower concentrations — at 6.25 μg/ml. The number of surviving cells was 44.15%.

Cytotoxic concentrations of taurosid Sx1 from *Hedera taurica* Carr. *(Araliaceae)* are similar to the cytotoxic concentrations of triterpene saponins from plants such as *Albizia procera* and *Lysimachia thyrsiflora* L. Saponins from these plants exhibited cytotoxic and anti-proliferative properties for transformed and normal mammal cells at concentrations close to the cytotoxic concentrations of taurosid Sx1. This result allows us to consider taurosid Sx1 as a potent anti-fungal, anti-viral and immunomodulating agent, but also as a anti-proliferative substance possessing potential antitumor effects.

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ANTIMICROBIAL AND IMMUNOMODULATING ACTIVITY OF A TOPICAL GEL CONTAINING ACTIVE PEPTIDE COMPONENTS ON THE MODEL OF EXPERIMENTAL BACTERIAL VAGINITIS

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Common methods of therapy of bacterial vaginitis are not effective due to the spread of antibiotic resistance, side effects of antibiotics and insufficient immune response. One of modern approaches to the treatment of vaginitis are based on the use synthetic analogues of natural peptides. The objective of the study was to analyze the antibacterial and immunomodulatory effects of gel preparations based on chemically synthesized peptides on the model of experimental vaginitis.

White outbred female mice were infected *per vaginum* by pathogens: *Streptococcus agalactiae* and *Staphylococcus aureus* for 5 days. Then gels containing antimicrobial peptide pentadefenin (P), immunostimulating peptide alloferon (A) and both compounds were administered to the animals (groups P, A and PA, respectively) for 5 days. The control group (C) of the infected mice did not receive therapy. During course of therapy, the composition of the vaginal microbiocenosis was assessed using a bacteriological method and quantitative PCR. The concentration of IgA in vaginal lavages and IgM in serum were determined by ELISA.

Experimental vaginitis was accompanied by a change in the vaginal biocenosis: the number of lactobacilli decreased and the content of *Gardnerella* sp., *Prevotella* sp., and *Porphyromonas* sp. increased. Because of the therapy, a gradual decrease in the vaginal contamination of pathogenic bacteria occurred. Infection with *S. agalactiae* and *S. aureus* was observed in-group C throughout the observation period. The laboratory signs of bacterial vaginosis in the C group did not disappear, unlike other groups.

The drug P showed maximum antistreptococcal and antistaphylococcal effect only in the course of treatment. However, it acted only bacteriostatically and after its cancellation (day 9), the number of pathogenic bacteria became greater than in the group C. In groups P and PA, pathogenic bacteria practically disappeared, but this occurred only on the 9–14 days of the experiment. The antimicrobial effect of a correlated with an increase in the concentration of bacteriospecific IgA in the vaginal lavages and IgM in serum. Elimination of pathogenic bacteria occurred without the development of bacterial vaginosis, complications after antibiotic therapy or infection. Peptide P, as a bacteriostatic, should be used for a long time. The effect of peptide A is manifested only after the formation of a specific immune response. Thus, the maximum therapeutic effect should be expected in case of A and P mixture application.

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ANTIMICROBIAL ACTIVITY OF SYNTHETIC ANALOGOUS OF CAPRINE PEPTIDES BACTENECINS TOWARDS DRUG-RESISTANT BACTERIA

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Antimicrobial peptides (AMPs) of the innate immune system are unique molecules, providing human and animals host defense, and prototypes of novel drugs to fight