Abstracts
of scientific conference "ACHIEVEMENTS AND PROSPECTS IN THE FIGHT AGAINST INFECTIOUS DISEASES (MICROBIOLOGY, VETERINARY, PHARMACY), May 18, 2017, Kharkov, Ukraine

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The Abstracts

SENSITIVITY OF DOMINANT PATHOGENS OF INFECTIOUS AND INFLAMMATORY COMPLICATIONS AFTER DENTAL IMPLANTATION TO ANTIBIOTICS AND ANTISEPTICS. Faustova M.O. Higher State Educational Establishment of Ukraine "Ukrainian Medical Stomatological Academy", Poltava, Ukraine

Relevance. Dental implant placement is known to provide a high level restoration of dentition anatomical and functional integrity and maximal aesthetic effect that promotes social rehabilitation of patients during and after the treatment. In more than 90% of cases the implant osseointegration in the alveolar bone is reported to be successful, but implant placement may also be accompanied by some complications that can occur during the procedure of dental implant placement as well as in the postoperative period. Representatives of the normal microflora of the oral cavity play a key role in the development of infectious and inflammatory complications. The purpose of this study was to investigate sensitivity of causative agents of infectious and inflammatory diseases occurring during dental implant placement to antibiotics and antiseptics. Materials and methods. The study involved 43 patients with peri-implant mucositis and peri-implantitis. During the study 162 clinical strains of microorganisms were isolated and identified. The cultivation of strains was carried out by standard method. Final identification was carried out with an automatic bacteriological analyzer Viteck – 2 compact bioMérieux (France) according to manufacturer's instructions. The sensitivity assessment of the derived strains to antibiotics and antiseptics was done by disc-diffusion method and double serial dilutions according to the standard procedure approved by the Order №167 of the Ministry of Public Health of Ukraine on "On Approval of Training Guidance "Assessment of the sensitivity of microorganisms to antibiotics ", dated by April, 5, 2007. Results. As a result of the study representatives of Streptococcus spp. and Staphylococcus spp. were found as dominate among another microorganisms, although Kocuria spp., Enterobacter spp. and yeast-like fungi Candida spp. were detected quite common. Investigated clinical strains of microorganisms were sensitive to fluoroquinolones (99%), but very significant number of them showed resistance to penicillins (92%), macrolides (87%) and lincosamides (77%). In turn, no clusters were resistant to the action of antiseptics. Horosten, dekasan and chlorhexidine had powerful antimicrobial effect on dominant pathogens of periimplant mucositis and periimplantitis in patients. Moreover, the effect of decametoxine-based antiseptics on S. aureus, S. sunguinis, S. warneri and K. kristinae significantly exceeded the activity of chlorhexidine. Conclusions. Most of pathogens of periimplantitis and mucositis obtaine resistance to antibiotics (penicillins, macrolides, lincosamides). But modern antiseptics horosten, decasan and chlorhexidine can produce strong antimicrobial effect on the explored clinical strains. It makes them promising for prophylaxis and treatment of infectious and inflammatory complications after dental implant placement.

DEVELOPMENT OF FORMULATION OF COMBINATION MEDICINAL PRODUCT FOR THE TREATMENT OF WOUND PROCESS PHASE I. Dovha I.M., Povolokina I.V., Nevmerzhytskyi V.V., Shulha N.M., Volianska N.O., Yudin I.P., Ivannik V.Yu., Kazmirchuk V.V. State Institution "I.I. Mechnikov Institute of Microbiology and Immunology of the National Academy of Medical Sciences of Ukraine", Kharkiv, Ukraine

Wound treatment remains one of urgent problems of medicine, which requires creation of medicinal products with broad activity spectrum. Effective wound healing depends on the wound process stage, and wound treatment should be exclusively differentiated. One of priority methods in treatment of wound infection is the use of topical therapy, in particular, ointments, which are most widely used in wound process phase I. At present, majority of ointments have focused effects, and treatment of wound phase I requires the effect on wound process in at least three directions: enhancement of efflux from the wound, inhibition of infection, anesthetization. In these circumstances, creation of multicomponent ointments containing antibacterial and anti-inflammatory substances, antioxidants, and local anesthetics, is essential. At present, over-evaluation of the role of antibiotics lead to the increased interest to antiseptic agents, representing chemical substances, having antimicrobial effects, and being used for application on affected skin, mucous membranes, cavities and wounds for the treatment and prevention of local infectious lesions and sepsis. Wound process is usually associated with pain, which is why the use of anesthetic agent in the medicinal product is necessary. Recently, active search for substances and dosage forms with prolonged antimicrobial effects is going on. Ointments with hydrophilic base, in particular, polyethylene oxide (PEO), are the most effective among topical antimicrobial medicinal products for the treatment of wound process phase I. PEO molecules in purulent wound actively sorb the wound exudate and assure the necessary osmotic effect of the medicinal product on a long-term basis. Due to the high prevalence of antibiotic-resistant strains of wound infection causative agents, as well as uncertainty of primary microbial wound contamination, the use of antibiotics is not expedient. In order to prevent the development of infection, broad spectrum antiseptic agents should be added to the product for wound treatment at wound process phase I. A promising approach in this branch is the use of combination medicinal products containing plant substances – walnut and black walnut extracts containing bioactive substances with pronounced bactericidal, anti-

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inflammatory, and reparative properties. In combination with an antiseptic agent and topical anesthetic agent, this product formulation assures all necessary effects for wound treatment at wound process phase I. Formulation development of a combination medicinal product with antimicrobial effect for wound healing provides for conduct of several studies for selection of the most active substance of plant origin – walnut or black walnut extracts, antiseptic agent, anesthetic agent, excipients, their concentrations, and establishment of osmotic activity, which is essential for exudate removal at inflammation phase. In view of the above, we have developed several medicinal formulations based on nut extracts of different composition in the form of ointment with hydrophilic base using polyethylene oxides of different molecular weight and the production technology. The following parameters have been selected during the ointment formulation development: method of addition of active ingredients, solvent, PEO 400 : PEO 1500 quantitative ratio, depending on which the experimental samples have the necessary consistency. Optimal technological parameters for the ointment manufacture – temperature regimen, stirring duration and rate – have been studied. Concentrations of active ingredients in the ointment formulation will be selected in further microbiological and pharmacological studies.

PROSPECTS OF THE USE OF CARBON DIOXIDE HOP EXTRACT IN DEVELOPMENT OF AN ANTIMICROBIAL AGENT FOR TREATMENT OF ACNE VULGARIS. Moiseienko1 T.M., Dovha1 I.M., Rudyk2 R.I., Nevmerzhytskyi1 V.V., Povolokina1 I.V., Ivannik1 V.Yu., Makarenko3 V.D., Kazmirchuk1 V.V. I.I. Mechnikov Institute of Microbiology and Immunology of the National Academy of Medical Sciences of Ukraine", Kharkiv, Ukraine1. Institute of Polissia Agriculture of the National Academy of Agricultural Sciences of Ukraine, Zhytomyr, Ukraine2. Kharkiv Medical Academy of Postgraduate Education (KMAPE)3

Inflammatory disease of sebaceous glands (*acne vulgaris* or acneiform rash) is one of the most prevalent skin diseases. *Acne vulgaris* development cause is disorder in balance of certain hormones, lipid imbalance, follicular hyperkeratosis, increased pathogenicity of bacteria, and inflammation development. Currently used *acne vulgaris* treatment methods are not always effective and safe enough. This can be explained by species diversity of skin microflora with deviant quantitative and qualitative composition in patients with acne, which causes the inflammatory process development and hair follicle duct obstruction. The most pronounced changes are manifested through increased quantitative content of *S. aureus* and *S. haemoliticus* on the skin and decreased content of epidermal Staphylococci, Propionibacteria, and other representatives of normal skin flora. An issue not less essential at present is microbial resistance to antibacterials, which also remains unsolved so far. Pathogenic and opportunistic microorganisms isolated in acne frequently possess resistance to actibacterials (erythromycin resistance of *S. epidermidis* comprises 95 %, and the same of *P. acnes* is 52 %) and increased pathogenic potential. An alternative solution of this problem is the use of plant-based medicinal products. Presence of bioactive substances of various activity directions in plants enables using them in treatment of many diseases. Common hop has become widely used in treatment of various diseases in modern medicine. Carbon dioxide hop extract obtained from hop cones deserves special attention. Its anti-inflammatory, pain-relieving, bactericidal, antiviral, and anti-allergic properties stipulate potential therapeutic efficacy of medicinal products based on carbon dioxide hop extract in *acne vulgaris*. The experimental studies of carbon dioxide hop extract conducted in laboratory of antimicrobial agents of the State Institution "Institute of Microbiology and Immunology of the National Academy of Medical Sciences of Ukraine" have shown its high antimicrobial activity against overwhelming majority of tested gram-positive and gram-negative microorganisms and *Candida* fungi. According to the results of preliminary studies, a series of model compositions with carbon dioxide hop extracts from different manufacturers has been developed. The study goal was determination of the dose of carbon dioxide hop extract in test samples on the basis of its antimicrobial activity for the treatment of *acne vulgaris*. Measurement of antimicrobial activity of test samples was performed by agar diffusion method in "well" modification versus reference microbial strains. Results of the experiment conducted are indicative that carbon dioxide hop extracts from different manufacturers exhibit almost similar bactericidal effects. According to evaluation results of the samples' antimicrobial activity, the concentration of active substance, carbon dioxide hop extract, in the new medicinal product has been selected, which should allow developing a new antimicrobial agent for the treatment of *acne vulgaris*.

THE MEASUREMENT OF BIOACTIVE WATER SOLUTIONS PHYSICAL PROPERTIES USING MICROWAVE DIELECTROMETER. Eremenko[1] Z.E., Sklyar[2] N.I., Kuznetsova[1] E.S. 1 O. Ya. Usykov Institute for Radiophysics and Electronics, National Academy of Sciences of Ukraine, Kharkiv, Ukraine. 2 State Institution «I.Mechnikov Institute of Microbiology and Immunology National Academy of Medical Sciences of Ukraine», Kharkiv, Ukraine

The monitoring studies of quantitative characterization of water solutions of biologically active substances in the substrate is the cornerstone of laboratory diagnostics in humane and veterinary medicine. The variety of biological contaminants introduced into the environment, is growing steadily, for example, antibiotics that pollute the water environment both as output by the human body in a biologically active form without almost losing their properties, and with wastewater from pharmaceutical companies. Physical technology for detecting biologically active substances is a promising area of research and has significant social and economic impact. The complex permittivity (CP) of any substance is an integral physical parameter of it. We study the CP of water contained solutions by the use of electromagnetic

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waves at microwave range. It is known that the maximum frequency dispersion (maximum sensitivity of CP determination) of free water and water solutions is on microwaves. We used the waveguide-differential dielectrometer for the CP determination of high loss liquids that was designed by us. The basis of our method is the measurement of the difference in the attenuation of electromagnetic waves and, corresponding, the wave phase difference for the waves passing through the measuremnet cells with different lengths of the dielectrometer cavity at frequency of 31,82 GHz. The absolute measurement errors of our dielectrometer were 0,5% for real CP part and 3-5% is for imaginary one. The measurement error on the reference liquid was 0,1%. We have carried out various test measurements of water solutions of biologically active substances (toxoid, antibiotics, different pH environments) using our dielectrometer. The obtained dependences of the wave phase and amplitudes in two measurement cells on penicillin (mg/ml: 20 000, 2000, 200, 20, 2) and gentamicin (mg/ml: 4000; 400; 40; 4; 0,4) concentrations in water show that the maximum changes of wave phase and amplitude are at small concentrations of solutions. But at big concentrations of solutions we observed these dependences with, practically, no change. Thus it was proved promising application device. For example, the minimum detection limit of gentamicin in water solution is 0,68 mg/ml in terms of changes in wave phase and 0,125 mg/ml in terms of the wave amplitude of the electromagnetic wave passing through the measuring cell of the dielectrometer. This minimum limit is comparable with the figures which give highly costly methods. For example, the method of immuno-affinity chromatography minimum detection limit amount of tetracycline in milk is 0,019 mg/ml, and for the method of high performance liquid chromatography with fluorescence and mass spectrometry detectors, the figure is 0,002 mg/ml.

ANALYSIS OF INFECTIOUS FACTORS THAT CAUSE THE REACTIVE ARTHRITIS AND THEIR IMPACT ON THE ACTIVITY OF NO-SYNTHASE PERIPHERAL BLOOD LYMPHOCYTES. Melnyk O.V., Korniychuk O.P. Danylo Halytsky Lviv National Medical University, Ukraine

Objective. One of the most common rheumatic diseases is reactive arthritis (ReA). For now days, actively studied the incidence of ReA from a number of infectious agents. This issue remains that unclear by some bacteria can cause illness in ReA, and raise it with varying frequency. Probably different organisms have different pathogenicity factors of arthrigenisity properties, which lead to incidence dependence of reactive arthritis on the type of pathogen. Also remains an open question whether different biochemical and immune parameters of the body by the action of various infectious factors. The aim of research were to study the species of infectious factors leading to the development of ReA and their effects on NO-synthase system blood lymphocytes. Taking of biological material to identify the causative agents of urogenital, intestinal and nasopharyngeal infections, and blood samples were performed in patients for examination and treatment of rheumatologic department of the Lviv Regional Hospital. To identify bacteria and viruses have been used PCR, ELISA and smears of microorganisms. Mononuclear cells of peripheral blood have been extracted from freshly preparing heparinized blood donors and density gradient on ficoll-triombrast of patients. The activity of inducible and endothelial NO-synthase had been determined by the method described by Peretyatko et al. (2009). The data on the etiological factors that cause the development of reactive arthritis patients had shown that the largest percentage of disease causing *Chlamidia trachomatis* (36*%), Streptococcus haemolyticus (pyogenes)* - 19%, *Chlamidia trachomatis* and *Ureaplasma urealiticus* - 5%, *Chlamidia trachomatis* and Micoplasma hominis - 5%, Trichomonas vaginalis and Chlamidia trachomatis - 3%, *Ureaplasma urealiticus* - 3% *Micoplasma hominis* - 3%, *Yersinia enterocolitica* - 1%, *Salmonella enterica* - 1%, hepatitis B and C - 10% *Cytomegalovirus* - 6%, herpes virus - 4%, *Epstein-Barr virus* - 3% HIV - 1%. Since the development of ReA are caused by various infectious factors, the question arises whether some different biochemical blood parameters, depending on the trigger. It was established that the performance of arginase activity, eNOS and iNOS with ReA, caused by different infectious factors significantly different from those in control. However, if to compare between activities of these enzymes with reactive arthritis, caused by *Chlamidia trachomatis, Ureaplasma urealiticus, Streptococcus haemolyticus* (pyogenes) or Cytomegalovirus difference between them is not found. Thus, as a result of the research found: the highest percentage growth in CEA makes chlamydial infection (36%) and activity of arginase-NO-synthase system in peripheral blood lymphocytes with CEA does not depend on the particular infectious factor. The growth and activity of arginase-iNO-synthase lymphocytes indicates changes the functional activity of immune cells that can be caused by impaired metabolic and regulatory processes in these cells caused by a bacterial or viral infection. Key words: reactive arthritis, NO-synthase, arginase-NO-synthase system.

EFFECT OF PROBIOTCS ON DIARRHEA CAUSING BACTERIA IN CHILDREN. Goma Mohamed Huwiage. Higher Institute of Medical Sciences and Technology, Algaraboulli, Libya

The study includes the effects of three probiotic products found in Libyan pharmacies on E. coli, Salmonella, Klebsiella, probiotics namely lacteol 340 mg, which is in the form of powders in powder bags and produced by the French pharmaceutical company (ADARE Pharmaceuticals S.A.S). Each bag contains 10 billion cells of Lactobacillus delbruekii live bacteria, Lateol forte, which is in the form of capsules and product by the company of the tenth of Ramadan/Egypt with a license from the French company Axcan Pharma - France. Each capsule contains 5 billion cells of Lactobacillus delbrukii and Lactobacillus fermentum bacteria. The th3 Probiotics are the protects baby in the form of oral droplets 5 ml (5 ml probiotic drops) produced by Biogayia pharmaceutical company, one dose of five oral drops contains 100 million

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bacterial cells from Lactobacillus reuteri bacteria. Key words: probiotics, Lacteol, lacteal forte, Protects baby, E. coli, Salmonella, Klebsiella. **Introduction**: Two years ago probiotics have been introduced into the Libyan pharmaceutical market and doctors described them as an alternative therapy or after treatment of bacterial diseases with doses of strong antibiotics. The question arises here. Are all our doctors in Libya have full knowledge about probiotics and what their ingredients are and when they are used and when they should be described and their high cost inside pharmacies and worldwide. The problems of the excessive use of antibiotics in children is that the antibiotic kill all types of bacteria, even beneficial ones, which are present in the digestive system and facilitate the process of digestion and know these types of beneficial bacteria and normal micro flora, which protect the body from many types of pathogenic bacteria and increased beneficial bacteria in the digestive system to help the body in the disposal of toxic substances, child is taking antibiotics often suffers from problems in his digestive system, as well as many health problems during the early age, such as weakening the immune system and reducing its ability to resist diseases in the future **Materials and method**: Three types of bacteria isolated form children Stool, which includes E. coli, Salmonella, Klebsiella, all bacteria isolated in pure bacterial cultures taken from the Reference Medical Laboratory – Tripoli. Method for sowing the probiotic in the form of a circle in the center of the nutrient agar in a Petri dish and then sowing the test strain of the microorganism with a radial stroke (1 cup Petri with nutrient medium, 2) sowing probiotic culture in the form of a circle in the center of the nutrient medium, Strain of the microorganism by a radial stroke). Probiotic cultures were incubated at 37 °C for 72 hours, and then deviated from the growth zone of probiotic culture by 1.5-2.0 mm, the cultures of test strains of bacteria and were sampled. To this end, fresh cell cultures of test strains of microorganisms were prepared by suspending their cells in a sterile 0.9% sodium chloride solution containing at least 106 cells per ml according to the standard optical turbidity. After sowing test strains of microorganisms, nutrient media with grown probiotic cultures and test strains of the investigated microorganisms were incubated in a thermostat under ordinary conditions at 37 °C for 24 hours, and then the results were taken. The presence or absence of the antagonistic activity of the probiotic with respect to the test strain of the microorganism was determined by measuring the growth inhibition zone of the corresponding test strain of the microorganism in mm, each experiment to determine the antagonistic activity of the probiotic was performed in triplicate. With each probiotic, at least 15 experiments were carried out. The obtained research data were processed by conventional statistical methods. The objective of the project: This study is the first of its kind at the level of technical institutes and universities in Libya, since Probiotic products have entered the Libyan pharmaceutical market recently for less than two years, while it is known in other countries. The lack of sufficient knowledge of such products by many the doctors. **Results**: In the practical study, it was found that the Lacteol Fort give the highest results in the area of inhibition of bacteria is estimated at 10.40 millimeters in the average reading, followed by protects Baby with a reading rate of 8.60 millimeters and after the Lacteol at a reading rate of 6.70 millimeters. **Recommendations**: It is recommended to use both lacteal fort, protects baby, to stop diarrhea in children resulting from E. coli, Salmonella and Klebsiella. .

CRYPTOSPORIDIOSIS: THE EVOLUTION OF A PARADIGM. Pokhil S. I., Timchenko O. M., Chigirinska N. A., Kostyrya I. A., Kruglova T. A., Nesterenko A. M., Yakovenko D. V. SU "Mechnikov Institute for Microbiology and Immunology NANS of Ukraine", Kharkiv, Ukraine

Human cryptosporidiosis (ICD-10 A07.2 Cryptosporidiosis) – is an emergent protozoan illness caused by protozoans of genus *Cryptosporidium*. Cryptosporidiosis is one of the vivid examples of significant consecutive change of theoretical foundations, the systems of terminology and concepts (paradigms) concerning certain (nosological) forms of infections/invasions that dominate on certain stages of medical science development and are based on accumulation of pathogen properties, epidemiological patterns of their propagation, features of the clinical course of infectious process, diagnostic methods improvement, correction of principles of disease prophylaxis and treatment. Since the time when cryptosporidia were discovered (Clarke J., 1895; Tyzzer E., 1907) and up until the year 1955, when Slavin D. had first proven the etiologic significance of *C. meleagridis* in enteritis of turkey chicks, these protozoans were not considered to be pathogens and viewed as facultative commensals of gastrointestinal tract (mainly mice). In the next 20 years the scientists had established that cryptosporidia are able to cause diseases in other domesticated and wild animals and cryptosporidiosis became a zoonotic parasitosis. First two cases of cryptosporidiosis in humans were described by Nime E. et al. and Meisel J. et al. in 1976 and 7 more such cases were established up until 1980, and 5 cases among those developed in individuals with immune deficiency state, therefore cryptosporidiosis started to be perceived as a rare acute diarrhea that is associated with immune deficiency, i.e as an acute opportunistic zoonotic parasitosis (Bird R. and Smith M., 1980). But subsequent multiple reports on severe forms of its clinical course with prolonged diarrhea in AIDS – infected patients change the perception of cryptosporidiosis in professionals to the chronic opportunistic invasion. Beginning from the second half of 80-s of the previous century, cryptosporidiosis was categorized as self-restricting protozoan gastroenteritis that often affects immune competent individuals in the high risk groups: young children, farmers and husbandry workers and individuals that visited countries/regions with high level of endemic rate of sickness with that parasitosis. Therefore, the latter started to be considered as an ubiquitously propagated zooantroponous disease with fecal-oral and airborn mechanism of pathogen infection transmission and a characteristic clinical presentation in the form of "watery diarrhea" and a wide range of severity of clinical course of the disease: from acute self-restricting subclinical and light forms (in immune competent individuals) to chronic severe infections often with lethal

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outcome (in individuals with immune disorders). Next change of paradigm of modern epidemic and clinical features and globality of cryptosporidiosis propagation and significant social, medical and economical burden caused thereby is based on multiple reports of water outbreaks of group infections with cryptosporidiosis in different countries of the world (Bulleting of WHO, 2013. – Issue. 91, №4). In the whole, in water outbreaks of parasite infections in the world studied in the beginning of this century, the level of etiologic significance of *Cryptosporidium* spp. reached 60,3 % (Baldursson S. and Karanis P., 2011). The mentioned above facts were the basis of the decision of Centre for Disease Control and Prevention of USA to include cryptosporidia to the pathogen rating group "B" of biopathogens that are the most likely to be used as a bioterrorism tool and should be taken into account during national systems of bioterrorism prevention (CDC, 1993; Putignani L. and Menichella D., 2010). Therefore, at present cryptosporidiosis is acknowledged as a global biological threat, it has ubiquitous propagation and affects wide population stratas, causes significant economic damage to the industrial animal and control of cryptosporidiosis requires purposeful and coordinated efforts of WHO organization, national health systems and veterinary medicine establishments.

THE USE OF THE CHEMILUMINESCENCE METHOD TO EVALUATE THE OXYGEN METABOLISM OF BLOOD NEUTROPHILS IN CHILDREN WITH CHRONIC HERPESVIRUS INFECTION AFTER ROUTINE VACCINATION. Smelyanskaya M. V., Peremot S. D., Kashpur N. V., Volyanskiy A. Y. Mechnikov Institute of Microbiology and Immunology Kharkiv, Ukraine

The state of the immune system plays an important role in the pathogenesis of not only acute inflammation, but also in the pathogenesis of relapses and the chronization of the process. It is proved that the first stage of pathogen invasion into epithelial cells is possible only in conditions of a decrease in the functional state of peripheral adaptive systems. One such system is the neutrophilic link of the body's immune defense. And only the next stage is the activation of systemic adaptive immunity involving cytotoxic T-lymphocytes and specific antibodies, including secretory IgA. Therefore, the role of the first line of defense involving neutrophils is fundamental for the development and completion of antigen elimination. Thus, the search for a method that makes it possible to adequately assess the ability of neutrophils to produce activated oxygen metabolites, to reveal reserve capacities of cells, is still relevant to this day. Of particular interest in this regard is the use of the chemiluminescent method, since it creates unique opportunities for dynamic observations of the neutrophil neutrophil reaction, the conditions and mechanisms of their initiation, development, and regression. Of all the methods of functional sounding of phagocytes, this method has the greatest prospects of introduction into general clinical practice. Material & methods. 95 children aged 6 years vaccinated according to the vaccination schedule (PDA and ADS) were examined and who had blood leukocyte counts of 2-3-4 by representatives of the viruses of the Herpesviridae family. These children had chronic herpesvirus infection (CHVI). The control group consisted of children (25 people), comparable in age and sex, vaccinated in full and not having a viral load of blood cells. After the planned vaccination the children with CHVI were divided into two groups depending on the presence or absence of vaccinal immunity: Group 1 - children with CHVI, in which the titres of specific antibodies (50 people) were reduced; 2 group - children with CHVI, in which JSCs were made for components of vaccines in ultra-high titles of 45 people); 3 group - control group (25 people). The method of luminol-dependent chemiluminescence (CL). To evaluate the oxygen metabolism, the evaluation of spontaneous chemiluminescence (CL) of whole heparinized blood was used. Along with this, an estimation test for the difference in spontaneous difference of light-sum (DSL test) was used to evaluate the functional activity of neutrophils - patent RU No. 2457488. The principle of the DSL test is to evaluate the oxidant potential of neutrophils; it is recorded by the change in luminol-dependent CL in the exposure of heparinized blood in vitro. The DS test allows to evaluate the functional activity of neutrophils (the phenomenon of the lack of a reserve of activation, deactivation and hyperactivation) under the influence of its own endogenous substances. Interesting data were obtained when analyzing the parameters of the DSL test, the value of which in the first group was statistically lower in comparison with the control ($p = 0.01$). Conducting a frequency analysis of the values of the DSL test revealed that negative values of the DSL test were found in patients of this group, while in 81% of them the value of spontaneous CL exceeded the upper limit of the norm (more than 8.14 c.u.). This phenomenon, confirming the presence of a negative correlation between spontaneous CL and BCC ($R = -0.72$ $p = 0.00001$), can be explained by cell hyperactivation by microbial agents *in vivo* and the lack of a reserve of their activation *in vitro*. In the second group, the value of the DSL test is statistically significantly higher ($p = 0.00029$), which indicates an increase in the neutrophil activation reserve.

INVESTIGATIONAL METHODS OF THE ANTIVIRAL ACTIVITY OF PHARMACEUTICAL DRUGS IN VITRO. Kalinichenko[1] S.V., Korotkykh[1] O. O., Makhota[2] L. S., Zvieriva[2] N. V., Torianyk1 I. I., Popova1 N. G., Melentyeva1 K. V. 1-National Academy of Medical Sciences of Ukraine Mechnikov Institute of Microbiology and Immunology; 2-Kharkiv regional Laboratory Center of the Ministry of Health of Ukraine

Diseases of viral infections represent a serious problem of both theoretical and practical medicine. The development of new antiviral drugs requires an adequate model for determining the antiviral activity of the created drugs. According to many scientists, cell culture is the most convenient model for the primary evaluation of antiviral activity of drugs *in vitro*. The study of preparations on cell culture begins with a comparative evaluation of its cytotoxic action: the determination of the maximum tolerated concentration, does not show the cytotoxic

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activity, maximum tolerated dose (MTD), the establishment of an inhibitory dose reduces the number of viable cells by 50 % (ID_{50}) and the cytotoxic dose reduces the growth Cells, or the synthesis of cellular DNA by 50 % (CD_{50}). The following indicators are used to determine the antiviral activity of the drug: ED_{50} (50 % effective dose) - indicates the concentration of an antiviral drug in which it reduces the number of plaques or the development of cytopathic action (CPA) in the infected treated culture by 50 % or the minimum inhibitory concentration (MIC) of the antiviral Drug, reduces by 50 % the number of cells with virus-specific inclusions or clusters of viral antigen. In essence, these indicators are similar. These indicators are used to determine the chemotherapeutic index (CTI) or the index of selectivity (IS). These indices are the main criteria for assessing the effectiveness of substances in the culture of cells and the appropriateness of further research. Preference is given to drugs with high IS and those that reduce the virus yield by more than 2 lg. However, the use of cell culture to test the sensitivity of viruses to chemotherapy has certain limitations: different types of cells have different effects on the reproduction of viruses; for certain viruses, there are no known cell cultures in which they are able to multiply, etc. Therefore, the following methods are used to study the antiviral activity of drugs in vitro: a method of reducing plaques (associated with the concentrations of drugs that are required to inhibit the production of the virus); the fluorescent antibody method (involves the detection of individual virus-infected cells containing a viral antigen); flow cytometry (the detection of virus-infected cells, the study of viral pathogenesis, the evaluation of the effect of antiviral compounds on the synthesis of viral antigens and nucleic acids in); the activity of compounds against those viruses that have hemagglutinating activity (orthomixo-, paramyxo- and togaviruses)); the hemodysorption reaction (the inhibitory effect of the preparations is evaluated by the reduction of the number of hemadsorbed cells); high-performance liquid chromatography (used for primary screening of protease inhibitors, in comparison with the control); enzyme immunoassay (used for the initial selection of antiviral drugs, determination of effective concentrations as well as the effect on the formation of an infectious virus); polymerase chain reaction (used both in the initial selection of chemotherapeutic drugs *in vitro* and in the screening of prototypes and preparations *in vivo*); mass spectrometry (study of substances by determining the masses of atoms and molecules entering In its composition, and their amounts); electron microscopy (this method establishes the effect of antiviral agents on the morphology of viral particles). Further studies of antiviral activity are conducted *in vivo*.

THE POSSIBILITY USING OF HISTONE DEACETYLASE INHIBITORS AND HISTONE ACETYLATION ACTIVATORS FOR STIMULATE THE PHAGOCYTOSIS COMPLETION IN TUBERCULOSIS.

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One of the most promising methods for preventing reactivation of tuberculosis is stimulation of the phagocytosis completion. At the moment, there are no pharmaceutical compositions that affect the phagocytosis completion in the pharmaceutical market. The blockade of the process of phagocytosis completion by the products of the vital activity of mycobacteria is one of the main causes of the immunity imbalance in tuberculosis patients and, accordingly, with the activation of acute form pathology. Stimulation of phagocytes for complete the phagocytosis process - digestion of mycobacteria in phagosomes is an interesting target for the development of new drugs for the prevention and therapy of tuberculosis. A new class of drugs capable of stimulating the expression necessary for the phagocytosis completion factors in phagocytes are histone deacetylase inhibitors. The most studied representative of this group of drugs is valproic acid (Fig.1).

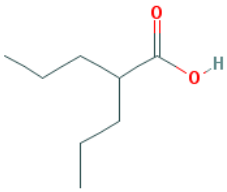

Fig.1. Valproic acid

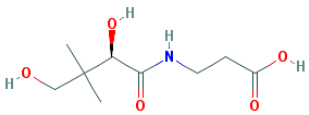

Fig.2. Pantothenic acid

Histone deacetylation inhibition leads to inhibition of histone binding to DNA, inhibition of DNA compaction, and activation of previously inactive regions in the macrophage genome. Another interesting group of drugs - inducers of histones acetylation: pantothenic acid (Fig.2) and trimethylglycine (betaine) (Fig.3).

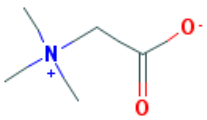

Fig.3. Betaine

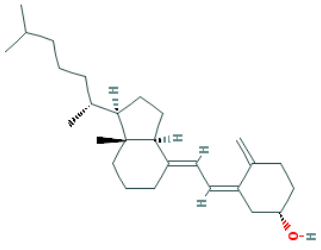

Fig. 4. Cholecalciferol (Vit.D3)

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They increase the activity of histone acetylase and increase the amount of acylated lysine residues in histones. In fact, the combination of valproic and pantothenic acid can be a means of preventing the reactivation of tuberculosis. Another tool that affects the histones deacetylation is cholecalciferol or vitamin D3 (Fig.4). The mechanism of its action is mediated by a specific nuclear receptor, through which the natural process of activation histones deacetylation and the completion of phagocytosis is triggered. The development of such a pharmaceutical composition based on several drugs for epigenetic control may be a most promising step in the fight against tuberculosis.

MICROBIOLOGICAL SUBSTANTIATION OF THE EFFECTIVENESS OF COMBINED TOPICAL THERAPY OF PSEUDOMONAS INFECTION. Palii H. K., Vovk I. M., Kovalenko I. M., Prokopchuk Z. M., Nazarchuk O.A. National Pirogov Memorial Medical University, Vinnytsya, Ukraine. microbiology@vnmu.edu.ua

The problem of struggle against local infections caused by P.aeruginosa, is quite urgent today because of certain biological properties of this genus of nonfermentative bacteria. Among these properties are such as: their innate resistance to antibiotics, multiple mechanisms realizing their innate resistance to traditional antipseudomonas antibiotics; insusceptibility of these bacteria to many of antiseptics, used for topical management of wound infection. In Ukraine, 45.5% resistant to therapy of purulent-inflammatory diseases are caused by P.aeruginosa. Above 50% opportunistic clinical strains of this pathogen also demonstrate multi-resistance to antibiotics. In recent years, alternative method of treatment of Pseudomonas mediated infection by means of specific bacteriophages is actively has being implemented in clinics. But the rate of phage-restant strains among P.aeruginosa, isolated from patients has been found to increase. The instructions for the use of this biological remedy warn of the impossibility of simultaneous local application of antiseptics and bacterial viruses. Taking into account the nature of bacterial viruses, we were interested to investigate the effect of lytic activity of antipseudomonas bacteriophage remedy against clinical strains of P.aeruginosa. We also hypothesized, that antiseptics, belonging to the group of cationic detergents, among which there was domestic one known as decamethoxinum, could not influence on the antipseudomonas effect of bacteriophage. Our supposition was to be proved in the experiment. The study was conducted on 30 clinical strains P.aeruginosa, isolated and identified in biological laboratory of the department of microbiology National Pirogov Memorial Medical University, Vinnytsya. All studied strains were isolated from patients with purulent-inflammatory complications of various locations. We used P. aeruginosa ATCC 27853 as used reference strain. In determining the susceptibility of P.aeruginosa to polyvalent antipseudomonas bacteriophage we found that in 18 strains of this bacteria happened partial lysis or they were not sensitive to the remedy. The study of activity of bacteriophage against phage-susceptible strains of P.aeruginosa under conditions of different microbial load demonstrated the decrease of its effectiveness, when the increase of concentration of bacteria from 10^3 to 10^{10} had happened. This indicated that the heterogeneity of microbial populations of sensitivity to bacteriophage and the possibility of phage-resistant variants selection would happen, if bacterial viruses were actively used for topical treatment of infections. This fact seemed about inefficiency, perhaps, of the last tool of influence on breeding resistant variants of P.aeruginosa in the wound. To aim the prediction of selective pressure of specific biodrugs on clinical strains of Pseudomonas, we studied the decamethoxinum influence on the lytic properties of bacteriophage against isolated phage-susceptible but antiseptic-resistant strains of P.aeruginosa, in nutrient media, containing detergent in amount from 500 mkg/ml to 3,9 mkg/ml. There was found the effective lytic activity of the phage, when 250 mkg/ml of decamethoxinum had been used. Therefore this antiseptics had no negative effect on the topical effectiveness of phage therapy and could be used simultaneously. The sensitivity of phage-resistant sub-populations of clinical strains were also studied in the presence of subinhibitory concentrations of decamethoxinum. Isolates of P.aeruginosa revealed their susceptibility to bacteriophage. Thus, decamethoxinum potentiates the lytic bacteriophage properties against strains of P. aeruginosa , which have moderate sensitivity to bacterial virus, and it prevents forming of phage-resistance in phage-susceptible cultures of bacteria when bacteriophage is applied. Experimentally the effectiveness of the combined impact of decametoxinun and antipseudomonas bacteriophage was confirmed.

CYTOKINE STATUS IN PATIENTS ON CHRONIC BACTERIAL AND HERPES VIRAL INFECTIONS. Gaidash I.S., Gaidash I.A., Shabelnyk O.I., Gaidash D.I., Bondarenko O.O., Pantielieiev P.G., Novytsky O.M., Liesna A.C. State Establishment "Lugansk State Medical University", Rubizhne, Ukraine

The cytokine status of a person describes the reaction of the immune system to the presence of the pathogen, as bearers of genetically alien information. The study of cytokine status allows developing pathogenetically substantiated methods of treatment of chronic diseases, both of viral and bacterial etiology. The aim of the study was to study serum concentrations of pro-inflammatory cytokines, such as interleukins (IL-1β, IL-6, IL-8) and tumor necrosis factor (TNF-α) in patients with chronic periodontitis, recurrent herpetic keratoconjunctivitis and herpes zoster. Eighty-six patients were examined, including 34 patients on chronic periodontitis, 27 patients with recurrent herpetic keratoconjunctivitis and 25 patients on shingles. The average age of patients was 43.5±2.3 years; there were 29 (33.7%) women and 57 (66.3%) men. Clinical diagnoses in the examined patients were confirmed by the appropriate laboratory methods (bacteriological ones in patients with chronic periodontitis, and method of enzyme immunodetection in patients with herpetic infections). The control group consisted of 20 virtually healthy people (7 women and 13 men) aged of 37.4±1.9 years. Determination of concentrations of IL-1β,

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IL-6, IL-8 and TNF-α was performed by the enzyme immunodetection method on the automatic immune-enzyme complex "GBG Star Fax 2100" manufactured by Awareness Technology Inc. (USA) with the use of commercial test systems by Gen-Probe Diaclone company (France). Statistical processing of obtained data was carried out by the methods of variation statistics with the use STATISTICA V. 6.0 (Statsoft Inc., USA), license No. AJAR909E415822FA. It is established that in the acute phase of chronic bacterial and herpes viral disease the content of IL-1β, IL-6, IL-8 and TNF-α in the examined patients is increased, regardless of the nature of the etiological factor. The concentration of IL-1β in the blood serum was increased, against reference standards (8.2±0.6 PG/ml) in 7.2–9.1 times ($p<0.001$), the concentration of IL-6 (at a rate of 4.3±0.2 PG/ml) increased in 5.8–7.0 times ($p<0.001$), and the concentrations of IL-8 and TNF-α exceeded the reference standards (for IL-8.8±0.3 PG/ml, TNF-α – 5.6±0.4 PG/ml) in 6.3–7.5 times and 3.7–4.6 times, respectively ($p<0.001$ for both comparisons). The degree of increase in the content of pro-inflammatory cytokines in the serum of patients with chronic bacterial and herpes viral infection coincided with the degree of severity of the disease and was the highest in severe forms of the disease. In the phase of clinical recovery the concentration of pro-inflammatory cytokines IL - 1β, IL-6, IL-8 and TNF-α in convalescents was significantly decreased. Their normalization occurred in less severe diseases (the contents of these cytokines is equal to the upper boundary of appropriate reference standards), while in moderately severe and severe disease the levels of IL-1β, IL-6, IL-8 and TNF-α exceeded the reference standards statistically significantly. The largest residual changes of pro-inflammatory cytokines occurred in patients with the hard cause of the disease. Thus, the results of the study allow to assert that the changes of cytokine status of a person in chronic bacterial (chronic periodontitis) and herpes viral infections (recurrent herpetic keratoconjunctivitis, herpes zoster) coincide with changes in indicators of cytokine status that is a stereotyped inflammatory response, and the degree of change and the dynamics of the disappearance of the negative changes of cytokine status of a person depend on the severity of the disease.

OLIGORIBONUCLEOTIDES AS INSTRUMENT FOR DEVELOPMENT OF ANTIVIRAL DRUGS WITH A WIDE RANGE OF BIOLOGICAL ACTIVITIES. Zenoviy Tkachuk. Institute of Molecular Biology and Genetics, NASU, Kyiv, Ukraine

Synthesis of new compounds that bind to active center of specific disease-associated protein with a high dissociation constant (Kd) has been the ideology of drugs development for a long time. In this manner a large number of drugs were developed on the principle of "one protein is a biologically active compound (BAC)". However, viruses, microorganisms and cells produce a resistance to such BAC very fast. It is necessary to build a new concept and to search for new BACs. We show that the synthetic 2'-5' oligoadenylates (2'-5'OAs) have a wide range of antiviral activity. By binding to capsid proteins of viruses (CPVs), the 2'-5'OAs change conformations and activities of these proteins. Study of the 2'-5'OAs bind to cytokines, protein kinases and calcium binding proteins (CBPs) showed that the 2'-5'OAs effect on conformation, affinity and activity of these proteins of the innate immune system. A more detailed study of the 2'-5'OAs binding site of CBP by the nuclear magnetic resonance (NMR) spectroscopy demonstrated changes of CBP conformation due to influence on amino acid residues in "hinge" region. It was shown by the mass spectrometry that cytokines can bind to several molecules of the 2'-5'OAs. A 5% change in the structure of the CBP alpha helix under 2'-5'OAs-CBP interaction was studied by the circular dichroism (CD) spectroscopy. This suggests that the proteins have the specific 2'-5'OAs binding regions and conformation, activity of protein can change under condition of the 2'-5'OAs-protein interaction. Results of the protein kinases study showed that the 2'-5'OAs can influence on activity of protein kinases not binding to active center of these proteins. Depending on conditions the 2'-5'OAs multidirectionally change conformation of protein kinases and thus they can inhibit or increase the activity of protein kinases. Results of the 2'-5'OAs properties study allowed to confirm ability to develop broad-spectrum antiviral drugs based on the 2'-5'OAs and it will be difficult for viruses to produce a resistance to such drugs. Monitoring of natural oligoribonucleotides (ORNs) isolated from highly purified yeast total RNA was conducted. It was demonstrated by the mass spectrometry that derived BACs have the dominant fraction with 3-8 nucleotides. Complexes of ORNs-sugars that have maximum ability to change conformation and activity of CBPs, cytokines and protein kinases were selected by fourier transform infrared (FTIR) and Raman spectroscopies. It was found that the complexes of ORNs-D-mannitol have the same properties as the synthetic 2'-5'OAs. Oligoribonucleotides-D-mannitol complexes (ORNs-D-mannitol) under the trade name Nuclex have been recently registered in Ukraine. On experimental models were studied prevention and treatment with ORNs-D-mannitol under condition of virus infection *in vivo*. It was shown that the ORNs-D-mannitol have antiviral activity against the pandemic influenza (flu), avian flu and viruses that cause acute respiratory infections (parainfluenza and adenovirus). Antiviral activity of the ORNs-D-mannitol against hepatitis (hepatitis C) and herpes (cytomegalovirus and Epstein-Barr virus) viruses was studied too. It was shown that the mechanism action of Nuclex is effects to conformation of the CPVs and cell regulatory proteins changing their structures. The wide range of antiviral activity, lack of ability of viruses to develop resistance to these drugs, high efficiency during viral co-infection, stimulation of the bone marrow stem cell migration and hepatoprotective effect allow the Nuclex to fight against a lot of viral infections of humans.

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STUDY OF THE IMMUNOLOGICAL PARAMETERS OF BLOOD OF CHILDREN OF KIROVOGRAD REGION UNDER EFFECT CHRONIC LOW LEVEL IONIZING RADIATION. Operchuk N.[1], Zadorozhna V.[2], Raksha - Slusareva O.[2] ·1 State Institution Kirovograd Oblast Laboratory Center of the Ministry of Health of Ukraine. 2 State Institution Gromashevsky Institutes of Epidemiology and Infectious Diseases of the National Academy of Medical Sciences of Ukraine

Introduction. Ukraine has areas where there is a risk of excessive exposure of certain categories of workers uranium companies and people living in the area of these enterprises. It is this area is the Kirovograd region, which is geographically located in the central Ukrainian Shield; the subsoil is very rich by uranium. This situation causes a chronic effect the natural low doses of ionizing radiation. Uranium companies located in this region. The process of development, extraction of uranium ore is characterized in that residues from waste production this cycle may adversely affect the environment and the population of people, including the course of infectious diseases. It first of all can be displayed on the child population, which is particularly sensitive to ionizing radiation and simultaneously could be in the group of viral diseases with drip mechanism of transmission. Methods. The main study groups were children aged 3 to 15 years (200 people) who live in areas where are companies of nuclear fuel cycle (Kropivnitskiy town, Mala Viska rayon). The control group consisted of children (200) of the same age who live in relatively clean areas without affecting technologically reinforced natural sources of ionizing radiation (Svitlovodsk rayon, Alexandria rayon, Svitlovodsk town, Alexandria town). Child population was divided into three age groups (3-6 years, 7-10 years and 11-14 years). Epidemiological, sanitary - statistical, demographic - sanitary, hematological methods used in this study. Results: the research found that the values of white blood cells in the age group 3-6 years amounted to 5,4 ± 0,19 g/liter, of children 7-10 years - 5,6 ± 0,2 g/liter and 5,2±0,23 g/liter of children 11-14 years. The content of peripheral blood leukocytes of children Svitlovodsk town and Svitlovodsk rayon (control group) was higher and amounted to: in the age group 3-6 years 6,5 ± 0,21 g/liter, children 7-10 years - 6 8 ± 0,28 g/liter and 6,4 ± 0,28 g/liter of children 11-14 years. Significantly higher levels of white blood cells established in a group of children of 11-14 years of Alexandria town and the Alexandria rayon. Indicators content of leukocytes children three age groups studied from the Alexandria town, Alexandria Rayon and Mala Viska Rayon amounted to 6,49 ± 0,62 g/liter, 5,87 ±0,25 g/liter and 7.3 ± 0 53 g/liter and 6,5 ± 0,27 g/liter, 7,1 ± 0,3 g/liter and 56,2 ± 0,3 g/liter and hardly differed and were higher than such in children living in the Kropivnitskiy town. Conclusions: Chronic technologically amplified by the natural low doses of ionizing radiation adversely affects peripheral blood of children of all age groups studied (content pool leukocytes).

THE INFLUENCE OF PAMMOSEPT ON A COURSE OF THE ANAPHYLACTIC SHOCK. Palii D. V., Palii H. K., Yatsula O. V. National Pirogov Memorial Medical University, Vinnytsya, Ukraine

Actuality. In recent years, in Ukraine researches medicines, which have enriched the information about their properties In recent years Ukraine researches of new antimicrobial agents have been conducted, that extended information about their properties and formed the scientific substantiation of the use of drugs. Antiseptics are known to influence on humoral and cell-mediated immune responses of a patient.Aim. Study of the influence of antiseptic drug pammosept® (PMS®) on a course of the anaphylactic shock in animals. Materials and methods. For the research there was used PMS® containing: decamethoxinum декаметоксину in terms of dry matter - 0,5 g; polyvinyl butyral (GOST 9439-85, brand PSh – 1) - 3,0 g; розчину citral alcohol 1 % (FS 42-2005-83) – 2,0 ml; ethyl 96 % (GFS 42U-001-97) - by 100 ml. Drug PMS® was a liquid with slight opalescence and lemon-scented. The absorption spectrum of the test solution is 400-600 nm with a peak wavelength 540±2 nm. PMS® should be colorless. The content of solids is 3,2 – 3,8%; density of PMS® was 0,81 – 0,82. PMS® is sterile. Antibacterial activity of PMS® was studied on 25 reference and clinical poly-resistant strains of microorganisms by means of well-known standard methods. The influence of PMS® on course of the anaphylactic shock in animals was carried out by Kh. Kh. Planeles. Cavies (48 individuals) were sensibilized with 0,5 ml of horse serum, administrated subcutaneously in the area of front abdominal wall. PMS® in dose 2 mg/kg was administrated to the animals for 4 days subcutaneously once per day. Resolving dose of the serum (0,5 ml) was administrated on 30th day of the experiment by the same way. And the appearance of primary symptoms of anaphylactic shock, terms of the dearth of control and experimental animals were registered. In the control group animal received subcutaneously 0,5 ml isotonic sodium chloride solution on a similar scheme. Results of the research. Anaphylactic shock in the animals in control group was found to appear 45-50 seconds later after administration of resolving dose of the serum. In the research group of animals primary symptoms of anaphylactic shock appeared much later (after 103 seconds), there course lasted rapidly. The dearth of animals happened after 223±9 seconds ($p < 0,01$). Conclusion. In the experiments on cavies PMS® was proved to provide desensitizing effect in the dose 2 mg/kg once per day (during 4 days), that positively characterized this drug, allows its topical use for the prophylaxis and treatment of infectious diseases of skin.

SUBSTANTIATION OF DECAMETHOXINUM USAGE IN THE STRUGGLE AGAINST ANTIBIOTIC RESISTANCE. Nazarchuk O. A. National Pirogov Memorial Medical University, Vinnytsya, Ukraine

Actuality. In modern conditions of medical care there is registered the increasing number of infectious complications, caused by *Pseudomonas aeruginosa* and

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other bacteria. Clinical strains of *P.aeruginosa* were found to have the ability of rapid forming of multiple resistance to traditionally used antibiotics. The aim. Substantiation of decamethoxinum® usage in the struggle against the resistance of *P.aeruginosa* to cefalosporins. Materials and methods. The research was carried out in bacteriological laboratory of the microbiological department of National Pirogov Memorial Medical University, Vinnytsya. There were studied 50 clinical strains of *P. aeruginosa*. Clinical isolates were received from patients, treated in burn centre of Vinnysya Regional Clinical Hospital named after N. I. Pirogov. In all microbiologically observed patients deep burns of 3rd stage (10-80 % of body surface) had been diagnosed. In the research *P. aeruginosa ATCC 27853* was used as reference strain. The sensitivity of *P.aureginosa* to ceftazidime (CFD), cefoperazone/sulbactam (CFS), cefepime (CP) was studied by standard double serial dilution method according to the recommendations of Ministry of Health of Ukraine (Order №167 from 05.04.2007 year). The sensitivity of *P.aureginosa* to cephalosporins in presence of sub-inhibitory concentrations (subMIC) of decamethoxinum (DCM) was also studied. Statistical analysis of received data was carried out by means of Statistica 7. Results and discussion. CFD and CFS were found to provide antimicrobial activity against *P. aeruginosa ATCC* 27853 when their minimal inhibitory concentrations (MIC) 3,9 mkg/ml were used. MIC of CP against reference strain were no more than 1,95 mkg/ml. Antimicrobial activity of DCM against *P.aureginosa* was found in presence of its MIC (62,5 mkg/ml) and minimal bactericidal concentration (MBcC) of decamethoxinum 125 mkg/ml. The sensitivity of clinical strains was found to MIC (89,06±12,67 mkg/ml) of DCM. Tthis antseptic was used in concentrations 162,5±16,38 mkg/ml to guarantee bactericidal activity against clinical isolates of *P. aeruginosa*. Clinical strains of *P.aureginosa* were proved to have low sensitivity to cephalosporins. CFD had low efficacy against *P. aeruginosa* (16 %). However, MBcC of CFD against majority of *P. aeruginosa* (80 %) isolates amounted to about 153,13±16,73 mkg/ml. Only 18 % of *P. aeruginosa* isolates were sensitive to CFS. MBcC of CFS against resistant strains of *P. aeruginosa* (68 %) was above 149,82±18,55 mkg/ml. The effectiveness of CP was determined in 18 % of cases. Inhibitory activity of CP on these bacteria was registered in presence of 173,44±26,17 mkg/ml. While using subMIC of DCM the reveling of sensitivity in resistant clinical strains of *P. aeruginosa* to antibiotics was found. The use of DCM recovered at all the sensitivity of *P. aeruginosa* to CFD (27,5 %), CFS (37,3 %), CP (37,5 %). The majority of resistant strains of *Pseudomonas* obtained moderate resistance to CFD (37,5 %), CFS (35,3 %), CP (22,5 %). DCM was shown, that in SubMIC it can influence on the rate of inhibitory concentrations of cephalosporin antibiotics against *P. aeruginosa*, decreasing them in CFD into 7,3±0,78 times, in CFS into 8,5±1,05 times, in CP into 8,31±1,11 times. Conclusion. Clinical strains of *Pseudomonas aeruginosa*, colonizing burn wounds, obtain resistance to ceftazidime, cefepime (80 %), cefoperazone/sulbactam (68 %). Combined use of subMIC concentrations of decamethoxinum and cephalosporins provides sensitization (into 7 – 8,5 times) or recovery of sensitivity to ceftazidime, cefoperazone/sulbactam, cefepime in resistant strains of *P. aeruginosa*, improving in this way perspectives of the use of decamethoxinum multivectoral properties for decreasing antibiotic resistance in bacteria.

SEX DIFFERENCES AND ITS CLINICAL IMPACT OF DICLOFENAC - INDUCED HEPATITIS.

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Rats model diclofenac induced hepatitis are useful for studding sex differences connected with cytochrome P450 2C11 in rats.It has been known that diclofenac (DCF) is biotransformed into chemically reactive metabolites by P450 (Cyp3a4, Cyp2c11), which bind covalently to liver microsomal proteins, including cytochrome P450 enzyme(s). Cytochrome P450 2C11 in rats was recently found to metabolize diclofenac into a highly reactive product that covalently bound to this enzyme before it could diffuse away and react with other proteins. It is recalled that the gene Cyp2c11 is a prototype gene CYP2C9 in humans, induction Cyp2c11 in rats is on the 4th week of life under the influence of pulsating pulse secretion of growth hormone, while the stable profile of growth hormone in females abolishes expression Cyp2c11 and induces specific to females Cyp2c12. There are some pharmacokinetic differences between the sexes that are likely due to oxidative metabolism and expression in CYPs, transport proteins, as well as, the hepatic canalicular transporter P-glycoprotein (P-gp) and the multidrug resistance protein MRP2 are involved in the transport of diclofenac acyl glucuronide to biliary canaliculi and the metabolite accumulates. So, the actuality of the developed model is conditioned by the gender features in the activity of metabolizing enzymes in male and female and their influence on course of Drug-induced liver injury (DILI). Mature Wistar rats weighing 200-220 g (120 females and 120 males) were injected intraperitoneally DCF at doses of 5-10 mg / kg, females - daily for 4 days, male - twice, daily. Experimental rats have showed a sex-related difference in toxic effects upon administration DCF. Administration of DCF (cumulative dose of 20 mg / kg) to males or injection females (40 mg / kg) was accompanied by a loss of 10% of the animals for 5-6 days after the last injection DCF.After three week of the experiment we recorded by ultrasound diffuse changes in the liver of animals and increasing of transaminases in their blood serum. According to histological examination hepatic parenchymal cells were filled with fat droplets, fatty degeneration of hepatocytes, and focal hepatocyte necrosis was seen in the centrilobular region. Sinusoidal capillary expansion, especially pronounced at 12 weeks after the last injection of DCF. During the 20 weeks females developed fatty degeneration of hepatocytes, signs of granular/fatty hepatocytes steatosis. The same time males exposed to DCF developed focal infiltration of portal stromal cells, necrosis of hepatocytes, signs of granular / fatty

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hepatocytes.The sexual dimorphism of liver gene expression can impact on course of experimental Diclofenac - induced hepatitis.

RESEARCH ON ANTIFUNGAL ACTIVITY OF THIAZOLIDINE DERIVATIVES. Zasidko V.V.[1], Kutsyk R.V.1, Lesyk R.B.[2] 1 Ivano-Frankivsk national medical university, Ivano-Frankivsk, Ukraine. 2 Danylo Halytsky Lviv national medical university, Lviv, Ukraine

Introduction. In the entire world the problem of fungal infections has special meaning. First of all it is connecting with global antibiotic usage. As a result of destroying bacterial forms biological space appears, which are successfully filling in with microscopic pathogenic fungi. It causes outbreak of different well-known and new fungal diseases. According to WHO's database, each fifth Earth inhabitant is infected by fungi and each tenth has clinical symptoms. The reasons for this are social factors, medical, pharmaceutical ones and others. Irrational using of a huge amount of antifungal drugs sparked appearance of a new problem - the resistance of fungi *Candida sp.* to used drugs and their further inefficiencies in clinical use. One of solution to this issue is the search for new compounds with antifungal properties. The main aim of this research is to determine the sensitivity of clinical strains of fungi *Candida sp.* to the action of synthesized thiazolidine derivatives. **Materials & Methods.**We used agar diffusion method for screening research of antifungal activity of the 330 synthesized thiazolidine derivatives (series of substances under the code "ID" or "L"). We made holes in Sabouraud agar on Petri plate, in which we brang in 20 μL solution of the test substances in concentration of 1000 μg/ml. As test microorganisms we used 5 clinical strains of *Candida* yeasts - *Candida albicans, Candida kefyr, Candida lipolytica, Candida lusitaniae* and *Candida tropicalis,* which are characterized as highly and medium resistant to fluconazole, clotrimazole and terbinafine. After incubation for 24-48 hours, we measured diameters of a zone of inhibition. Images of Petri plates were analyzed by the computer program UTHSCSA ImageTool 2.0.**Results.**As a result of performed screening of 330 thiazolidine derivates had been detected 3 substances, which have had the most powerful effect against *Candida* yeasts: **L095** – N-(4-bromphenyl)-2-(6-oxo-5,6-dihydro[1,3]-thiazolo[2,3-b][1,2,4]triazol-5-yl)acetamide. Diameters of growth inhibition zones varied from 13.81 ± 0.41 mm to 32.06 ± 0.98 mm, control – 4.2 ± 0.18 mm. **L-1558** and **L-1369** which are derivates of 6-oxo-5,6-dihydro[1,3]-thiazolo[2,3-b][1,2,4]triazol-6-one. Diameters of growth inhibition zones varied from 15.72 ± 0.23 mm to 32.52 ± 0.44 mm (for **L-1369**) and from 10.5 ± 0.25 mm to 28.77 ± 0.77 mm (for **L-1558**), control – 4.24 ± 0.08 mm. The minimum inhibitory concentrations (MIC) for selected substances were founded using serial dilution method. For strain *Candida albicans* $FCZ^{I}CTZ^{R}TER^{R}$ MIC **L095** is 6.25 μg/ml, **L-1369 –** 1.6 μg/ml and **L-1558 –** 50 μg/ml. For strain *Candida tropicalis* $FCZ^{I}CTZ^{R}TER^{R}$ MIC **L095** is > 100 μg/ml, **L-1369 –** 50 μg/ml, **L-1558 –** 100 μg/ml. For strain *Candida lipolytica* $FCZ^{R}CTZ^{R}TER^{S}$ MIC **L095** is 100 μg/ml, **L-1369 –** 0.8 μg/ml, **L-1558 –** 1.6 μg/ml. For strain *Candida kefyr* $FCZ^{I}CTZ^{R}TER^{R}$ MIC **L095** is 100 μg/ml, **L-1369 –** 50 μg/ml and **L-1558 –** 25 μg/ml. For strain *Candida lusitaniae* $FCZ^{I}CTZ^{R}TER^{I}$ MIC **L095** is 100 μg/ml, **L-1369 –** 50 μg/ml and **L-1558 –** 25 μg/ml. **Conclusion.** On a basis of thiazolidine derivates microbiological screening, we have detected leader structures, which in the future can be used for creation of new antifungal drugs for preclinical research. In addition, they can be considered as basic compounds for further modification and optimization of molecular structure and detecting of contribution of some fragments in their antifungal activity manifestation.

CLINICAL, LABORATORY AND MORPHOLOGICAL DIAGNOSTIC CRITERIA OF THE TOXOPLASMA BRAIN DAMAGE ON THE BACKGROUND OF HIV/AIDS. Kseniia Veklych . V.N. Karazin Kharkiv national university, Kharkiv

The urgency of the problem of toxoplasmosis is defined by a set of interrelated factors of a microorganism, the macroorganism and the environment. It is extremely difficult to control and radically influence the distribution of toxoplasmosis, because it's distribution in nature occurs without human intervention. Contamination occurs easily; in most cases the disease is latent. Extremely severe clinical manifestation of toxoplasmosis can be seeing in patients with AIDS, assuming the character of an aggressive infestation that can lead to rapid disability and death. **Materials and methods**. We investigated 60 patients with an established diagnosis of HIV/AIDS which have been treated in the intensive care unit of the regional clinical infectious hospital of Kharkov in 2014 – 2016. Based on the recommendations of the World Health Organization, the examination of the patient has been conducted using the general clinical and biochemical methods of investigation, CT and MRI of the brain, PCR and ELISA of the cerebrospinal fluid and blood. In the study group male (59%) mainly of young age – 25 – 38 years old were predominant. Affection of the CNS, among which affection of toxoplasmosis and herpes viral ethiology were predominant, at time of hospitalization was diagnosed in more than 60% of patients. The mortality rate in the studied patients' population was 87%, and all died patients have expressive minor signs of AIDS. 92% of patients were hospitalized in the infectious hospital with the full clinical picture of CNS injury in the later stages – more than one month from the date of occurrence of the first signs of brain damage.The debut of the toxoplasmosis brain affection in most patients (97.7%) has been provoked by various factors (mainly hypothermia, excessive mental or physical exertion) and has been accompanied by rises in body temperature to subfebrile, and neurological manifestations of the disease combined both focal and non-focal neurological symptoms, while focal symptoms were unsystematic. As the severity of patients condition has deteriorated, also has deteriorated manifestations of the central nervous system affection, that has been accompanied by the appearance of symptoms such as impaired consciousness and speech disturbances, the emergence of pathological signs from the extremities,

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severe meningeal symptoms, overtone of the muscles of the limbs of spastic type on the side of affection on the background of flaccid paresis on the opposite side. The representatives of the study population have such symptoms of CNS affection as impairment of consciousness up to semisomnus – coma I (according to Glasgow coma scale), facial asymmetry (65.5%), ptosis (80%), anisocoria (95%), a pathologic position of the eyeballs in the side of the lesion (60%), and others. From the time of administration all patients had persistent febrile and high hyperthermia resistant to the introduction of medicines. Degenerative phenomena of edema and swelling of the brain, the joining of the multiple-organ-failure syndrome progression of secondary manifestations of AIDS led to death of patients. All patients underwent routine clinical and laboratory methods of investigation, CT and MRI of the brain, PCR and ELISA of blood and CSF. Results of conducted PCR and ELISA of the CSF and blood let us detect IgG and DNA of the T. gondii in all patients (optical dencity – 1.5 – 1.8 odu; EIU – 80-90; ME – 85-95; AT – 1:1600 – 1:1800) with avidity ranged 45-50 to 65-70%. Post-mortem examination of the brain in patients with toxoplasmosis brain damage revealed affection of its various structures – the cortex, subcortical nuclei, cerebellum. Founded lesions consisted of areas of necrosis that does not exceed 2 cm in diameter, had clear contours and were painted in a dirty yellow; diffusely placed areas of cerebral infarction of various shapes, whose size ranged from 0.5 to 2.5 cm in diameter, which were placed outside the zones of necrosis; cysts of different localization, filled with transparent content, the size of which does not exceed 1.0 cm in diameter. Histological examination revealed findings that are typical for acute and chronic lesions of the brain tissue: areas of calcification, glial nodes, granulomatous proliferation of reticular cells, which were placed away from the zones of destruction of brain tissue, proliferation-inflammatory clutches around intracerebral blood vessels with stasis and clotting, sclerosis of the vascular walls, that provides development of many of the hemorrhages as in the periphery of necrosis, and the type of hemorrhagic and ischemic infarcts. Such findings as vacuolization of the cytoplasm, pericellular swelling up to the formation of optical cavities, and foci of necrosis, representing alterative manifestations of the destruction of brain cells and neuroglia were permanent. Also typical signs of toxoplasmosis CNS affection - Toxoplasma pseudocyst that were placed in fresh foci of necrosis, foci of calcification and lying loose in the tissues of the brain has been found. **Conclusions**. In patients with AIDS clinical forms of the disease with involvement of the central nervous system, leading among which is toxoplasmosis brain damage, are predominant. In this disease infiltrative - inflammatory processes in the brain that clinically manifested in the form of signs of meningoencephalitis with liquor-hypertension syndrome and non-systemic focal nervous disorders. Toxoplasmosis of the brain on the background of HIV/AIDS occurs as a progressive disease, histological examination; and histological examination of patients with this disease let find “old” and “new” morphological signs of toxoplasmosis brain damage.

EXPLORE THE POSSIBILITY INCREASE EFFICIENCY ETIOTROPIC TREATMENT OF SALMONELLOSIS BY MEANS OF L-ARGININE.

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Actuality. The salmonellosis is still constantly growing tendency in Ukraine. The prevalence of salmonellosis caused by the pathogen ability to be stored for a long time in the environment and antibiotic resistance which results in the lack of traditional treatment effectiveness. That reason motivates to look for completely new ways of treatment. Some researchers (J. Ghosh, Haque S.S.) have suggested the possibility of using L-arginine for treating salmonellosis. Haque S.S. upon completion of the research (2011-2013 years) has asserted that L-arginine as a donator of NO, has a direct antimicrobial effect and increases the effectiveness of antibiotic therapy (zone of growth inhibition *Salmonella enterica var. typhi* for L-arginine it consists of 17,5 mm, ciprofloxacin - 18,0 mm, their combination - 20,0 mm). Indian scientists conducted research on *Salmonella enterica var. typhi* and *Salmonella enterica var. typhimurium*, however, specifically in our region the most suitable option is the research on *Salmonella enterica var. enteritidis*, because of increasing of proportion Salmonella group since 2009 in it’s etiological structure. **Purpose.** determine the possibility of increasing the efficiency of antibiotic therapy by using the L-arginine on Salmonella infection. **Materials and methods.** The study was conducted by means of two strains *Salmonella enterica var. enteritidis*, cultivated from patients during outbreaks which occurred in Dolina and Kalush (Ivano-Frankivsk region) in September 2016, where 92 people have been involved in those outbreaks. To investigate the antimicrobial activity of L-arginine we used medicine "Tivortin" - 4,2 % - 100 ml. The study’s been conducted in 4 stages: The First stage - screening of antimicrobial activity of L-arginine by using agar diffusion method. In the second stage in order to study antimicrobial activity of arginine, double serial dilutions method had been applied. To determine the number of viable cells from test tubes containing 40 mg/ml and 20 mg/ml of arginine, dropouts performed on Endo medium, previously dissolving them apart at 9 and 10 times. At the third stage of the experiment, Salmonella has been grown in the environment “Endo” with arginine in concentrations of 20, 13 and 10 mg/ml respectively. Control experiments performed on environment “Endo” without arginine. At stage IV, the sensitivity evaluation of Salmonella to antibiotics (ceftriaxone, cefuroxime, chloramphenicol, gentamicin, ofloxacin) had been performed in the presence of arginine by applying a paper disc method (L-arginine dose – 0,42 mg per disc). **Results.** During the screening by means of agar diffusion method, a visible zone of the inhibition microorganism growth was absent. In the study by a method, serial dilutions in the presence of high concentrations of L-arginine (20-40 mg/ml) showed a slight bacteriostatic effect of the drug. By adding arginine to the environment “Endo” Endo in concentrations of 20, 13 and 10 mg/ml respectively, the number of Salmonella colonies decreased by 18,75 %; 12,5 % and 0 %,

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respectively (regarding the control). The greatest sensitivity to pathogens was shown in the case of ceftriaxone, the smallest – to cefuroxime and ofloxacin. By using the paper disc method, which resulted in the absence of significant discrepancy in the areas of growth delay under circumstances using disks with antibiotic and antibiotic + L-arginine. **Conclusions.** The drug L-arginine "Tivortyn" does not signify direct antimicrobial action against *Salmonella enterica var. enteritidis*. In the presence of high concentration of L-arginine (20-40 mg/ml), which impossible to achieve in serum and tissues in reality, but with a small microbial load the manifestation of bacteriostatic effect was shown clearly. L-arginine does not affect the sensitivity of Salmonella to antibiotics, thus; the therapeutic effect of L-arginine regarding Salmonella infection can not be explained by its direct antimicrobial effect.

SENSITIVITY OF ISOLATED E. COLI STRAINS TO BACTERIOPHAGUM COLI-PROTEICUM IN PATIENTS WITH PERITONITIS. Kosilova O.Y., Vovk O.O. Kharkiv National Medical University, Kharkiv, Ukraine

Fundamental researches in biology discover new horizons and perspectives in medicine, and often revive the forgotten methods of treatment of infectious diseases. These researches are up-to-date because of some problems with which modern medicine may face - crisis. Resistant to the majority or even all known antibiotics bacteria cause more and more serious problems. Despite the intensive work of pharmaceutical companies for the past 30 years new classes of antibiotics has not found yet. Phage therapy was firstly developed in the early 20th - century and seemed to be promising scientific area, although it caused a lot of debates. It is known that antibiotics suppress the normal flora in natural biocenoses of a human, they almost always provide a teratogenic effect, and the most of antibiotics are toxic, which significantly increases the list of phisicians contraindications for their usage. For this reason, there are situations where practitising using antibiotics forced to finding a compromise between their antimicrobial activity and severity of side effects. During recent years, studies devoted to finding alternative methods and synergistic antimicrobial action have been conducting. One of them is fahoterapy and fahoprofylaxis. Taking into consideration that E.coli is dominant microorganism at peritonitis, which was detected in association with representatives of the genus *Proteus* in 21,0 ± 7,8% cases because we have studied the sensitivity of microorganisms to bacteriophagum coli-proteicum. It is advisable to determine the sensitivity the remoted clinical and the museum strains of *E.coli* to bacteriophagum coli-proteicum. Analysis of the results showed that the clinical strains removed from the abdominal cavity of the adult patients with peritonitis were in 19 (76,0 ± 8,5)% cases susceptible to bacteriophagum coli-proteicum and in 6 (24,0 ± 4,7) % - less sensitive. In the analysis of *E.coli* strains isolated from children, we found that 13 (52,0 ± 9,9)% of strains were susceptible to bacteriophagum coli-proteicum, and 12 (48,0 ± 6,5)% were not sensitive. In the study of 19 the museum strains, which were stored in a lyophilized form 10 (52,0 ± 11,5)% - were susceptible and 9 (48,0 ± 6,5)% - not sensitive to bacteriophagum coli-proteicum. The strains isolated from relatively healthy people (comparative group) showed relatively high sensitivity to bacteriophagum coli-proteicum. 23 studied strains (92,0 ± 5,4)% of the 25 strains were susceptible 2 - (8,0 ± 2,8)% insensitive. The receving results indicate that studied *the E.coli* strains had high sensitivity to coli-proteicum bacteriophagum, which indicated the feasibility of its usage at peritonitis caused by *Escherichia coli*.

ASSOCIATAL INTERACTION OF MICROSYMBIONTS, MILK ACID AND OXIDIZED OXYGEN FORMS PRODUCERS. Kremenchutsky G.N., Stepansky D.A., Turlyun S.A., Stetsenko I.Y., Krushinskaya T.Y. Dnepropetrovsk Medical Academy, Ministry of Health of Ukraine, Ukraine

A model association of microsymbionts from three species of mutually biologically related microorganisms, colonizing the biotopes of the intestinal and vaginal mucosa has been developed. Two members of the association, Lactobacillus acidophilus ATCC 4356 [Campana R. et al., 2012] and Bifidobacterium animalis subsp. lactis BB-12 [Jungerson M. et al., 2014], were selected by the ability to produce lactic acid. A third microorganism, Aerococcus viridans 5m2015, by the ability to oxidize lactic acid with the production of reactive oxygen species: superoxide, hydroxyl radicals, hydrogen peroxide [Kremenchutsky G .N., 2001] with the excretion of pyruvic acid. Cultural and biochemical indices in the process of associative system components growth were studied before to model it. The stimulating effect of pyruvate on L. acidophilus ATCC 4356 and B. animalis subsp. lactis BB-12 growth was shown. Hydrogen peroxide was neutralized with the growth of A.viridans 5m2015, as a result of the chemical reaction and the antioxidant activity of aerochemical superoxide dismutase and glutathione peroxidase. There was a difference in the growth and production of metabolites between the initial combination and sequential coupling of components. In the latter case, the primary added microorganism received the advantage. This was particularly noticeable during first inoculation of A.viridans 5m2015, which began to actively oxidize the lactic acid of the nutrient medium with the production of reactive oxygen forms. With the initial application of L. acidophilus ATCC 4356 and B. animalis subsp. lactis BB-12 with a drop of pH <5, development of A.viridans 5m2015 was slowed down with a decrease in the activity of lactic acid oxidation and a decrease in the accumulation of reactive oxygen forms. It was found that with the simultaneous introduction of microassociates, all three connected components did not exert a direct antagonistic effect on each other, except for competition for nutrient substrates. Concentrations of lactic acid, pyruvate, hydrogen peroxide, superoxide formation, superoxide dismutase activity, glutathione peroxidase were determined in the microassociates interaction environment at the process of different time variants of the model development. The general antagonistic and oxidase activity of the medium was determined by the method of

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[Kremenchutsky G.N. et al., 2009] antagonistically active, low molecular weight peptides (microcines) accumulation in an environment. Total antagonistic activity of the medium was determined on 23 strains of Staphylococcus spp., 7 strains of Meningococcus spp., 5 strains of Salmonella spp. 6 strains of Pseudomonas spp. in the course of a sequential components combination and initial simultaneous development. The determinations were conducted by the diffuse method on Petri dishes with an appropriate nutrient media. A significant difference in the growth suppression zones of the opportunistic and pathogenic bacteria was found. The highest activity was shown by the environment with the joint development of simultaneously inoculated biocontiants. Somewhat less antagonistic activity was provided by the medium with sequential application of microassociates and the lowest activity was shown by the medium with individual development of L. acidophilus ATCC 4356, B. animalis subsp. Lactis BB-12 and A. viridans 5m2015. Thus, a model association of L. acidophilus ATCC 4356, B. animalis subsp. Lactis BB-12 microsymbionts, bound by metabolic processes of lactic acid production, oxidized by A. viridans 5m2015, colonizing the common biotopes was elaborated, which can be used for studying both biochemical and colonization processes in this system.

CHRONIC HEPATITIS C: ABILITY TO ASSESS THE DEGREE OF LIVER FIBROSIS BY INDEXES OF BLOOD CHEMISTRY. Nekrasova Yu., Vynokurova O., Bondar O. Kharkiv national medical university, department of Infectious Diseases, Kharkiv, Ukraine

Introduction. Around 170 million people in the world and more than 1.2 million in Ukraine are infected with hepatitis C virus (HCV). Transformation of acute hepatitis C in chronic form is seen in 75-85% of cases, and during 10-30 years for approximately 25-35% of patients with chronic hepatitis C (CHC) develops fibrosis and cirrhosis of the liver. By 2020, the growth of HCV infection is expected more than in 2 times, that will increase the number of patients with cirrhosis and liver cancer. The determining factor in the pathogenesis of chronic liver disease of various etiologies is the progression of inflammatory and fibrotic processes with formation of the cirrhosis of the liver. Assessment of the state of liver fibrosis is important for several reasons: prognosis of chronic liver disease, the selection of patients for specific (etiotropic) treatment and potential liver transplantation. Quantitative indicators of severity and rate of progression of fibrosis are the most important clinical parameter the definition of which is crucial for choosing the right therapy and to monitor its effectiveness. "Gold standard" in the diagnosis of fibrosis is liver biopsy. However, a biopsy method for assessing fibrosis has serious limitations. Recently began to use non-invasive methods of diagnosing fibrosis. These methods for assessing the degree of fibrosis in patients with hepatitis C are included in the recommendations of the European Association for the study of the liver. The evaluation stage of fibrosis through indirect serum markers can easily be done in terms of everyday clinical practice. **Objective:** to analyze the basic biochemical parameters in serum of patients with chronic hepatitis C depending on the stage of liver fibrosis (F) and necroinflammatory activity of the liver (A). **Materials and methods.** Investigated 79 patients aged from 21 to 67 diagnosed with CHC. Among them, 44 women (55.7%) and 35 men (44.3%). Patients were examined with the help of GenoFibroTest, which is constituents' diagnosis of necroinflammatory activity of the liver (A) and stage of fibrosis (F), which includes definitions: α2-macroglobulin, haptoglobin, apolipoprotein AI, bilirubin, γ-glutamyl, ALT on a scale of METAVIR. **Research results.** Was found that the level of α2-macroglobulin significantly lower ($p < 0.05$) in the F0 and F1 to F4 of leveling the playing field; ALT levels also significantly lower when compared F0 with F1, F3 and F4. When looking for correlations between parameters that were investigated, found a strong correlation between F and the level of α2-macroglobulin, which amounted to 0.74, and between A and ALT - 0.68. According to the schedule, constructed with the use of approximations determined if the value α2-macroglobulin belongs to the range 0 to 3 g / l, $F \leq 2$, if the interval α2-macroglobulin 3 to 5 g / l, $2 \leq F \leq 4$ (with a probability of 100%). If the value of ALT belongs to the range from 0 to 40 IU / L, then $A \leq 1$, and if ALT belongs to the range of 40 to 59 IU / L, then $A \leq 2$ with a probability of 100% if ALT belongs to the interval from 60 to 100 U / l, it will be determined primarily A2 with a probability of 59% if ALT belongs to the range of 100 to 650 IU / l, the probability of A3 is 91%. The method of ROC-analysis confirmed the high quality of our research, as factors AUC area under the curve between the values F and α2-macroglobulin and between A and ALT were accordingly 0.82 and 0.78. **Conclusions.** The level of α2-macroglobulin can be used in assessing the stage of fibrosis and ALT - in determining the degree of liver necroinflammatory process.

CHARACTERISTICS OF MICROBIOTA INVOLVED IN THE PROCESS OF DIABETIC FOOT. Rumynska T.M., Tymchuk I.V., Panas M.A., Korniychuk O.P., Savchenko A.A. Danylo Halytsky Lviv National Medical University Lviv, Ukraine

Diabetic foot syndrome – is a specific symptom of the foot lesions in diabetes mellitus (DM), associated with neuropathy and different grades of ischemia and infection. It represents a serious long-term complication of diabetes mellitus leading to amputations, disability, and reduced quality of life. These processes are developing by mutually bothering one another, with the serious necrotic lesions accession, characterized by a special microflora composition and occurring on the backdrop of the deep metabolic disorders and immunosuppression. **Aim.** To study the association of microorganisms and microbial sensitive to antibacterial preparations of pathogens isolated from patients with diabetes, admitted in surgery department after an ineffective conservative treatment. **Materials and methods**. Bacteriologic examination of pathogens were carried out in 20 patients with purulent necrotic lesions on the lower limbs with diabetes. Have been isolated bacterial microflora conducted in accordance with current regulations. For the purpose of had been

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isolating fungi exudate of wounds were been plated additionally on Saburo agar. Pure cultures of isolated strains were identified by biochemical properties. Determination of the sensitivity of pathogens to antimicrobial agents was carried out by disc-diffusion method. We used discs with ampicillin, amoxiclav, cephalexin, ceftriaxone, cefuroksym, tsefipimom, ciprofloxacin, lincomycin, gentamicin, tobramycin, chloramphenicol, doxycycline, imipenem, meropenem, fluconazole, clotrimazole, nystatin, amphotericin. By production of "Pharmasco" and "St. Petersburg Institute of antibiotics." **Results**. At the result of the research we had been isolated and identified nine species of microorganisms, including: *Staphylococcus aureus* - 5 (25%), Staph. MRSA - two (10%), Staph. VRSA - 2 (10%), *Klebsiella pneumoniae* - 4 (20%), *Pseudomonas aeruginosa* - 4 (20%), *Enterococcus faecalis* - 2 (10%), Enterobacter spp. - 2 (10%), *Candida albicans* - 4 (20%). Were found that microbial association of staphylococci and gram negative bacilli in 25%. Studying antibioticogram of pathogens has shown total resistance to antibiotics of the major groups except for group carbapenems and glycopeptides, where sensitivity was found to imipenem, meropenem in 16 patients (80%), vancomycin in 18 (90%). In 2 patients with *S. aureus* (VRSA strain) resistant to all antibiotics studied groups. Candida were sensitive (100%) to nystatin and amphotericin B and partially sensitive (50%) and to fluconazole (75%) to clotrimazole. **Conclusions**. The ineffectiveness of antimicrobial treatment of patients with purulent necrotic lesions on the lower limbs with diabetes was associated with resistant strains of microorganisms which were isolated from these patients. For the treatment have been recommending by carbapenems and glycopeptides, antifungal therapy clotrimazole and nystatin.

COMBINED EXPOSURE TO ULTRAVIOLET RADIATION AND BIO-CHLORINE DISINFECTANT OF MICROBIAL CONTAMINANTS OF WORKING SURFACES IN EDUCATIONAL LABORATORIES. Sus M.Yu., Korniychuk O.P. Danylo Halytsky Lviv National Medical University, Department of Microbiology, Ukraine.

Actuality: Microbiological monitoring of pollution in enclosed spaces is an important component of the system of preventive measures aimed at detecting the occurrence and spread of pathogenic microorganisms. Working surface microflora of indoor tables is more conformed and relatively stable. Microorganisms that appear at the working surface due to coughing, sneezing or talking are prevalent. The level of microbial contamination depends on sanitation of the premises, ventilation and its frequency, cleaning method and other conditions. It is important to study this issue because working surface can be an intermediary in the transmission of many infectious agents. Objective: The study of microbial contamination of working surfaces and examination of combined effects of ultraviolet (UV) radiation and disinfectant on microorganisms. Materials and Methods: The objects of the study were working surfaces of tables in 6 classrooms of Lviv National Medical University. Sampling was carried out by washings from the working surface performed before and after desinfection with bio-chlorine (diluted according to instructions) and exposure to UV radiation for 30 minutes. Inoculation was carried out under the guidance materials on the area of 100 cm^2 at the end of the day. Quantitative pollution index (total microbial count - TMC) in CFU/cm^2 and microorganism species was defined. A series of five studies was conducted. Results: The working surfaces of objects under study were relatively little contaminated. The studied samples mainly detected enterococcus (80%), epidermal staphylococcus (10.5%), sarcina and spore-forming bacilli (5%). Escherichia coli was found on only one of the studied surfaces.

The contamination level of working surfaces of tables before and after disinfection (CFU/cm^2)

Before desinfection	After desinfection		
	Bio-chlorine	UV	Bio-chlorine + UV
0.33±0.04	0.028±0.007	0	0

In one case the object turned out to be sterile after processing with bio-chlorine. A slight growth of microorganisms was identified in other cases. Basically a small amount of bacilli retained viability and enterococci were revealed in one case. Moreover, the processing of the most contaminated site with TMC of 2.44 CFU/cm2 using chemical agent resulted in the reduction of the corresponding value in only 2.2 times. Morphological changes were detected in cells of isolated cultures that restored their properties after passaging. The use of UV as well as its combination with chemical disinfectants makes it possible to achieve the effect of sterilization (no inoculation of microorganisms). Conclusion: The level of contamination should be taken into account as it requires longer exposure. The absence of inoculation of microorganisms after the disinfection does not exclude the presence of residual biological material (e.g. nucleic acids), which may have corresponding consequences in hospital settings. Improved efficacy of processing methods of environmental objects is achieved by using complex of methods: mechanical cleaning, chemical agents and the use of radiant energy.

PYOCINS AS EFFECTIVE MEANS AGAINST PSEUDOMONAS AERUGINOSA. Balko O.I., Balko O.B., Avdeeva L.V. Zabolotny institute of microbiology and virology NAS of Ukraine, Kyiv, Ukraine

Introduction. *Pseudomonas aeruginosa* can cause difficult infectious diseases with high mortality in immunocompromised patients. *P. aeruginosa* strains are characterized by high level of antibiotic resistance. The ability to form biofilm facilitates spread and increase of antibiotic resistance in *P. aeruginosa* strains and lead to transformation of disease into chronic form. It's a global

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problem, which requires new approaches for its solving. Bacteriocins are ones of the most widespread natural means of bacterial antagonism with high bactericidal activity. These substances can be considered as alternative to antibiotics in future. The aim of our work was isolation and study of bacteriocins with high level of antipseudomonal activity from different *Pseudomonas* species. **Methods.** The bacteriocins with antipseudomonal activity were obtained from 94 strains of 16 *Pseudomonas* species by nalidixic acid induction. For all these substances the antimicrobial spectrum against 38 *P. aeruginosa* strains, including 9 multiresistant clinical isolates, sensitivity to temperature and enzymes, capacity for dialysis through cellophane membranes were investigated. DNase activity of *P. aeruginosa* bacteriocins was estimated by splitting of phage λ DNA. The influence of these bacteriocins on *Pseudomonas aeruginosa* biofilm formation was studied in stationary system. **Results.** All investigated producer strains were divided into two groups. The majority of *Pseudomonas* species capable to produce substances with low and middle activity were included into the first group. The most active bacteriocins were detected among *P. mendocina*, *P. fragi* and *P. taetrolens*. They influenced on 30-50% of test cultures. Only *P. aeruginosa* strains were referred to the second group. Substances of this group were characterized by considerably higher activity, some of them influenced on 90% of used cultures. The highest antipseudomonal activity was revealed in four *P. aeruginosa* substances, active against the majority of used tests-cultures, incl. clinical isolates of *P. aeruginosa*. It was shown that these substances didn't lyse their own producer strains, didn't cause the formation of phage plagues, penetrated through cellophane membranes with 5 nm pore, lost their activity after temperature and enzyme (tripsin) treatment, weren't sensitive to DNase and RNase. These particles were high stabile during long-term storage and didn't lyse representatives of other taxonomic groups of microorganism such as *Bacillus cereus, Bacillus subtilis, Candida albicans*, *Escherichia coli*, *Salmonella enterica*, *Proteus vulgaris, Klebsiella pneumoniae*, *Staphylococcus aureus* and *Staphylococcus epidermidis*. Based on these properties the main active killer components of investigated lysates were referred to low molecular weight S-type pyocin group. PCR-analysis of *P. aeruginosa* strain-producer genome confirmed possibility of S-type pyocin synthesis, namely SI and S5 pyocins. Killer activity of four *P. aeruginosa* bacteriocins against collection cultures varied from 0,32 to 128 million Units/ml. Their activity against clinical isolates reached to 20,5 million Units/ml. These substances didn't repress each other and their mix was capable to influence simultaneously on all 38 available *P. aeruginosa* strains, including 9 multiresistant clinical isolates. The antimicrobial effect of four *P. aeruginosa* bacteriocins was caused by their DNase activity. The preventive addition of these bacteriocins into the stationary system resulted in decrease of sample area covered by *Pseudomonas aeruginosa* biofilm. **Discussion.** Thus low molecular weight S-type pyocins are characterized by narrow spectrum and high antipseudomonal activity. The researched bacteriocins influence on *P. aeruginosa* in planctonic and biofilm form. These pyocins with DNase activity are capable to cause biofilm cleavage and prevent its formation. The revealed properties of these low molecular weight S-type pyocins allow considering them as new promising antipseudomonal means with perspective for use in medicine.

OPTIMIZATION OF CULTIVATION CONDITIONS OF SELENIUM ENRICHED PROBIOTIC STRAIN LACTOBACILLUS GASSERI 55 IN LABORATORY FERMENTER. Ogirchuk K., Kisten A., Kovalenko N. Zabolotny Institute of Microbiology and Virology of the National Academy of Sciences of Ukraine. Kiev, Ukraine

Selenium is an essential mineral that is involved in the processes of antioxidant and bone tissue metabolism. In this regard, the recent increased interest in the use of organic forms of selenium in the diet of humans and animals as food supplements and functional foods. The results of our previous studies demonstrated the use of selenium-enriched probiotic strain *Lactobacillus gasseri* 55 as nontoxic dietary sources of selenium. The aim of our study was the selection of optimal parameters of cultivating the strain *L. gasseri* 55 enriched selenium under conditions close to industrial. Cultivation of the strain *L. gasseri* 55 performed in a laboratory fermenter BIOTEC (Sweden) volume of 3.2 liters on corn medium under the following conditions: temperature 37 °C, initial pH 6.5. To maintain a stable pH using 10% ammonia solution. During the cultivation observed rapid growth of *L. gasseri* 55 in the first 4 hours, after which culture growth slowed significantly, and the exponential growth of the culture began only from 16 h of fermentation. The economic coefficient at 22 hour of cultivation of the strain *L. gasseri* 55 in the selenium-enriched environment was 4.47×10^{10} CFU/g, and the substrate been used only by 63%. The results indicate a complicated adaptation of culture in the laboratory fermenter. Considering this, the optimum initial pH of cultivation of *L. gasseri* 55 in selenium-enriched environment been chosen. It was 7.0 with the highest figure ΔpH 1.8 units. Also for the growth of L. gasseri, as facultative anaerobes, it was necessary to create the absence or low concentration of oxygen in the environment and the value of redox potential (Eh) less than 100 mV. Therefore, in order to change the rheological properties of the cultivation medium 1 g/l tween-80 and 1 g/l agar-agar was included to its composition. Anaerobic conditions was been ensured by displacement of oxygen with carbon dioxide. Exponential phase for the culture, grown in medium with agar-agar, lasted until 18 h and then passed into the stationary phase of growth (Figure 1). At this point, the substrate was exhausted by 96%, but the economic coefficient was 4.47×10^{11} CFU/g. In control fermenter stationary phase of growth began in the 20th hour, the substrate was been exhausted by 100%, and the economic coefficient was 6.09×10^{10} CFU/g.

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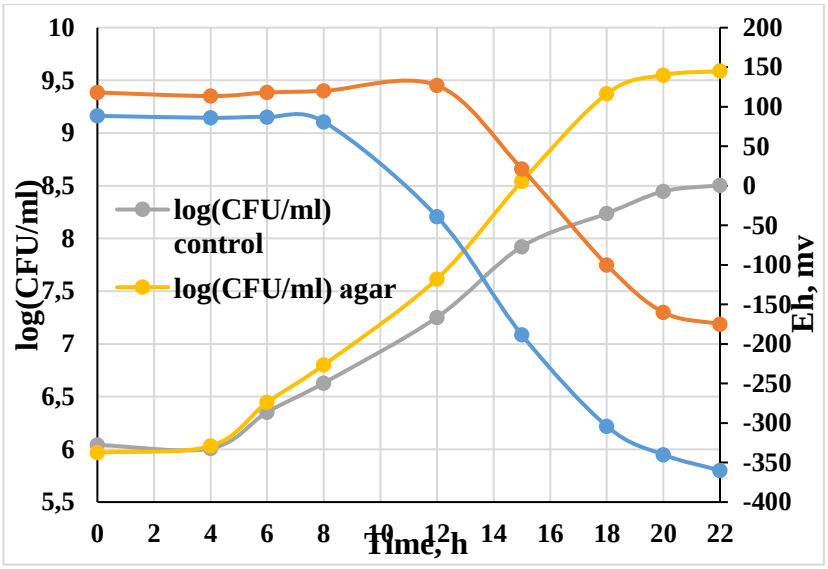
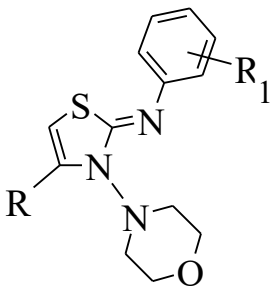


Fig.1. Growth and redox potential (Eh) during of cultivation of the strain *L. gasseri* 55 in laboratory fermenter.

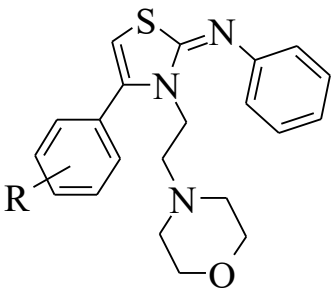
Adding to the medium agar-agar helped reduce initial Eh system at 30 mV compared with the control, resulting in a reduction of the redox potential in the medium with the agar-agar started after 7 h of cultivation, while in control - only after 12 h of growth. Dynamics of decrease redox potential functional correlates with the growth index *log (CFU/ml)*. Optimized parameters of cultivation the strain *Lactobacillus gasseri* 55 may be the basis for technology of obtaining the selenium-enriched probiotic in bioavailable, safe organic form.

NEW MORPHOLINE DERIVATIVES WITH ANTIMICROBIAL ACTIVITY. Yeromina H.O., Osolodchenko T.P., Perekhoda L.O., Ieromina Z.G. The National University of Pharmacy, Kharkiv, Ukraine

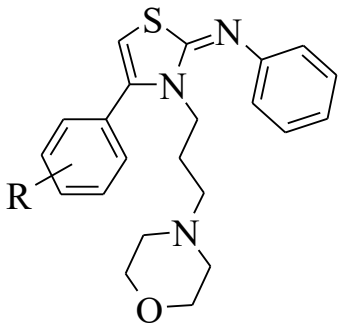
Treatment of bacterial infections today is one of the actual problem of modern medicine. The importance of antibacterial therapy is difficult to overestimate. But everywhere is fixed a steady increase in the resistance of bacteria to antimicrobial drugs. Antibiotic resistance is beyond the scope of the purely medical problem has a huge socio-economic importance and is seen as a threat to national security in developed countries. Therefore, the search for new antimicrobial agents is very important. Morpholine-containing heterocycles are well known as antimicrobial and antifungal agents. So we have been synthesized N-[4-methyl(4^1-chlorophenyl)-2-R-phenyliminothiazol-3-yl]-morpholine derivatives (Formula 1), 4-(R-phenyl)-3-[2-(4-morpholinyl)ethyl]-N-phenyl-1,3-thiazol-2(3H)-imine (Formula 2) and 4-(R-phenyl)-3-[3-(4-morpholinyl)propyl]-N-феніл-1,3-phenyl-1,3-thiazol-2(3H)-imine (Formula 3) derivatives:



Formula 1



Formula 2



Formula 3

Those synthesized morpholine-containing compounds have been screened for antimicrobial activity against gram-negative microorganisms – *Pseudomonas aeruginosa* and *Proteus vulgaris* using method of diffusion of the drug into agar by "wells". It was established, that all substances possesses a moderate antimicrobial activity against *Pseudomonas aeruginosa* and *Proteus vulgaris*.

PLANT ESSENTIAL OILS: ANTIBACTERIAL PROPERTIES AND PROSPECTS OF THEIR USE. Tishchenko I. Yu. National University of Pharmacy, Kharkiv, Ukraine

Essential oils have always attracted the attention of people, their history of use dating back to ancient times. Valuable information about the healing properties of essential oils was obtained from the great scientists of antiquity - Avicenna, Hippocrates, Galen, Plutarch. Every year practical interest to modern medicine essential oils is increasing, due to the advanced study of biologically active substances contained in plants, and their multifaceted

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effect on micro and microorganism. Plants containing essential oils are common in all climatic zones of the world. Only in CIS there are 77 families (about 1050) plants containing essential oils. The greatest number of these species includes three families: Labiatae, Umbelliferae and Compositae. Unlike refined and synthetic medicines, essential oils contain a large number of organic and inorganic substances with a broad spectrum of action. Their chemical composition is complex and is a mixture of volatile aromatic organic compounds - carbohydrates, especially a number of terpenes and their oxygen derivatives, alcohols, phenols, aldehydes and acids, esters, lactones, and some heterocyclic compounds. Essential oils can be accumulated in special structures or surface organs (glandular hairs of different types, essential oil glands, glandular spots) or in plants (secretory cells receptacle, secretory tubules and moves). In peppermint and eucalyptus they are mainly localized in leaves, in cumin, coriander, fennel - in seeds, in citrus fruits - in the skin of fruits, in cinnamon - in bark, in camphor, in cedar - in wood. As well as essential oils can be found in some plant resins and balms, which are released when the plant tissue is damaged (for example, in pine). The amount of various organic and inorganic substances that make up essential oils varies from 120 to 500. Essential oils are biologically active compounds with a wide spectrum of action in relation to the human body. First of all, it is the antiseptic activity of essential oils, which is due to their antimicrobial, antifungal action and antiviral actions. This is due to the presence of volatile oils. It is essential that phytoncides (antibiotics) of lower plants produced in the conjugate evolution of microorganisms in their competitive struggle, including pathogenic for humans and animals, act primarily on the pathogenic microflora. Phytoncides of higher plants (including carriers of essential oils) directly affect not only microorganisms, but also the immunological mechanisms of the human body (phagocytosis, inflammation, antigenic reactivity), they are able to stimulate and suppress the immune reactivity of living organisms. Volatile substances released by plants that form essential oils have acaricidal, fungicidal, antiviral or antiprotozoal effects. Nonvolatile phytoncides, in the first place, retard the growth and development of bacteria without killing them, that is, they carry out a bacteriostatic effect, but their antiprotozoal and antiviral effects are less pronounced than in volatile compounds. Modern research has confirmed the high antibacterial activity of essential oils. The most effective are essential oils of lemon, lavender, coriander, pine, fir, eucalyptus, thyme, mint, rosemary, etc. Essential oils and natural antibiotics, for example, in St. John's wort (imanin), immortelle (arenanin), salvia medicinal (salvin), celandine, and others, only act on the representatives of the world of microbes, and on higher organisms do not have a negative effect. The aggressiveness of essential oils against the pathogenic combined with their almost completely harmless to the human body. Immunological reactivity decreases with prolonged antibiotic therapy, there is an allergy to medicines, dysbiosis, the formation of antibiotic resistance of microorganisms. Importantly, the ability of antiseptic essential oils is not reduced over time, and the microorganisms to which practically does not develop resistance. This is due to the fact that the antimicrobial effect of essential oils is caused by destruction of cytoplasmic membrane and decrease the activity of aerobic respiration, which reduces the energy required for the synthesis of various organic compounds. Thus, modifying the ecological environment, essential oils do not allow microorganisms to create mechanisms to protect their own and adapt to the aggressive agent; it is important that this does not happen any changes the genetic apparatus of microorganisms that essential oils are not mutagenic properties. This enables their widespread use in infections of various etiologies.

SYNERGISTIC EFFECT OF ALTANUM WITH ERYTHROMYCIN AGAINST SKIN STRAINS OF STAPHYLOCOCCI WITH CONSTITUTIVE AND INDUCIBLE MECHANISMS OF MLS-RESISTANCE. Yurchyshyn O.I., Rusko H.V., Kutsyk R.V. Ivano-Frankivsk National Medical University, Ivano-Frankivsk, Ukraine.

One of the main ways to control microorganisms' resistance to antibiotics is to find substances that are able to overcome it and potentiate antibiotics action, in particular to neutralize the antibiotic-inactivating enzymes (Orhan I.E. etc., 2011; Goswami S. etc., 2012) and block the active efflux of antibiotic from microbial cells (Fankam A.G. etc., 2011). Every year there is a growing interest in the therapeutic potential of herbals active compounds as modifiers of antibiotic resistance and to MLS-resistance (macrolide-lincosamide-streptoramin B) (An J. etc., 2011; Ochi T. etc., 2005). Summarizing the results of scientific literature analysis, it should be emphasized that a number of biologically active substances of plant origin can potentiate antimicrobial activity of erythromycin (ERY) against staphylococci MLS-resistant strains. *Altanum* is purified extract of *Alnus glutinosa (L.)* and *Alnus incana (L.)* fruits and its main components are polyphenolic substances. It exhibited a strong antimicrobial activity against *Staphylococcus aureus*, *Salmonella enteridis*, *Enterobacter aerogenes*, *Citrobacter diversus* by the presence in the medicine hydrosoluble tannins (polymers of ellagic and gallic acid) (Yakovleva L.V., etc., 1998). Hydrosoluble tannins are also known for their ability to enhance the sensitivity of MRSA to β-lactam antibiotics (Yam TS etc., 1998; Shimizu M. etc., 2001) and tetracyclines (Roccaro AS etc., 2004; Novy P. etc., 2013). The aim of our study was to investigate synergistic effect of *Altanum* bioactive substances with erythromycin (ERY) against skin isolates of *S. epidermidis* and *S. aureus* with constitutive (MIC ERY 2-250 μg/ml) and inducible phenotypes of MLS-resistance (MIC ERY 500-4000 μg/ml). In previous investigations we found a synergistic interaction of *Altanum* with ERY by agar diffusion and microdilution broth susceptibility assay (Yurchyshyn O.I. etc., 2016) against MLS-resistant strains of *S. aureus* and *S. epidermidis.* Effective antimicrobial concentrations of *Altanum* and ERY were determined by two-fold serial dilution in nutrient agar. Combinatory effects between *Altanum* and ERY were assessed using the checkerboard assay against tested strains to evaluate culture growth in the presence of two antimicrobials with different

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concentrations. Fractional inhibitory concentration index (FICI) was used to evaluate the interaction of *Altanum* with ERY (Santos A. etc., 2015). The results of our investigation determine that the combination of *Altanum* and ERY have a synergistic interaction against 85% tested strains (FICI <0.5). Average FICI against strains with inducible phenotype of MLS-resistance is 0.26 and the constitutive phenotype of MLS-resistance - 0.18 (p <0,005). As to two isolates of staphylococci with constitutive phenotype of MLS-resistance *Altanum* demonstrated non-interactive effect with ERY (1 <FICI <4). The results of our investigation determine that the active components of *Altanum* potentiate the antimicrobial activity of antibiotics and are able to influence on different mechanisms of MLS-resistance. Experimental data indicate the feasibility of *Altanum* and macrolides combination in therapeutic regimens, particularly for the treatment of pyoderma.

INFLUENCE OF GENTAMICIN AND GENTAMICIN WITH PENETRATOR ON THE VIABILITY OF ENTEROCOCCI IN THE BIOFILM. L.G. Myronenko, Peretyatko O.G., Iagniuk J.A., Martynov A.V. Mechnikov Institute of Microbiology and Immunology National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine

Today medical science is receiving more and more evidence on bacteria in biofilms acquiring features of increased resistance to antibiotics, disinfectants and other aggressive environmental factors, complicating the course of infectious disease and playing an important role in its chronicity. Despite a large number of publications on the high enterococci biofilm formation potential, the effect of antibiotics and other antimicrobial agents on the viability of enterococci in the biofilm has not been sufficiently studied. Analysis of scientific literature has shown the prospects of searching for the compounds-penetrators that enhance the biocides penetration into the microbial biofilm. The aim of the study was to explore the impact of gentamicin and gentamicin in combination with a penetrator (polyethylene glycol) on the viability of enterococci in the biofilm. The objects of the study included 3 strains of bacteria genus *Enterococcus*, obtained from the bacteria museum of the Mechnikov Institute of Microbiology and Immunology National Academy of Medical Sciences of Ukraine: *E. faecalis* ATCC 29212, *E. faecalis* IMI (X) 49 p, *E. faecium* IMI (X) 80. Our previous studies have shown that these strains are characterized by high biofilm formation capability. While conducting the research, gentamicin, 4% solution for injections, produced by Darnitsa Ukraine; polyethylene glycol (PEG), produced by Himstatus Ukraine, were used. Biofilm modeling and study of the impact of gentamicin and gentamicin with a penetrator on biofilms were performed using sterile plastic 4-section Petri dishes (Myronenko L.G. et al., 2015). To determine the impact of the investigated compounds on the viability of enterococci in the biofilm, microbial suspension obtained after biofilms destruction was seeded on 0,1 ml of Enterococcus Agar from tenfold dilutions (from 10^{-1} to 10^{-9}). After 48-hour incubation of seeding at 37 ° C, counting of the number of colony forming units (CFU) in 1,0 ml of microbial suspension was performed. To determine the impact of the investigated compounds on the viability of enterococci in the biofilm, Bacteria Survival Index (BSI) was calculated (Athanassiadis B. et al., 2010). The impact on the viability of enterococci in the biofilm was investigated for the gentamicin with 64 mcg/ml, 32 mcg/ml, 16 mcg/ml, 4 mcg/ml concentrations and gentamicin with similar concentrations in combination with a penetrator with a volume fraction of 1,0%. It was found that while applying gentamicin in concentration of 8 mcg/ml and 16 mcg/ml, the average enterococci CFU number amounted to (lg 2,66±0,06) and (lg 2,51±0,08) respectively, which was significantly different from the control value (without gentamicin adding) – (lg 7,52±0,03) (p<0,05), while for 32 mcg/ml and 64 mcg/ml concentrations the enterococci growth was not observed. Bacteria Survival Index (BSI) for gentamicin in concentration of 16 mcg/ml equaled (-3), in concentration of 8 mcg/ml – (-2,67), indicating significant inhibition of enterococci viability in the biofilm. When applying gentamicin in concentrations of 8 mcg/ml and 16 mcg/ml with 1% PEG, the average CFU value amounted to (lg 2,66±0,04), for concentration of 32 mcg/ml – (lg 2,45 ± 0,08), for concentration of 64 mcg/ml – (lg 2,29±0,04), which was statistically different from the control value (p<0,05). Due to significant inhibiting impact of gentamicin with PEG on enterococci viability in the biofilm, the BSI value was negative. Thereby, it was found that gentamicin in concentrations of 64 mcg/ml, 32 mcg/ml, 16 mcg/ml, 4 mcg/ml and gentamicin in similar concentrations in combination with polyethylene glycol with a volume fraction of 1,0% inhibit the viability of enterococci in the biofilm.

AN ESTIMATION OF THE BACTERIAL LOADING OF WOUND AT APPLICATION OF VACUUM ASSISTED THERAPY. Terletskyi[1] I., Orel[2] U., Verchola[1] M., Tymchuk[2] I., Korniichuk[2] O. 1. Lviv Regional Clinacal Hospital, Lviv, Chernigivska str 7, www.hospital.lviv.ua. 2. Danylo Halytskyi Lviv Nacional Medical University, Lviv, Pekarska str 69, www.meduniv.lviv.ua

Vacuum assisted therapy is widely used in the holiatry of running sore, in particular at a diabetes mellitus. At creation of negative pressure on all wound surface there is the permanent moving away of products of disintegration of fabrics, wound exudate and bacteria. It is clinically proven that therapy of negative pressure stimulates cicatrization of wounds, the situation is more difficult with microorganisms as bacteria form a biological tape on the surface of a wound that densely fits closely to fabric. That is why a question appears: is there influence of negative pressure on microorganisms that form a biofilm? For today, the changes of the bacterial loading of wound are not enough investigated, using vacuum assisted therapy without application of anti-infectives. The aim of our research was establishment of influence of vacuum assisted therapy on the bacterial loading of wound. Materials and methods. 10 patients with the chronic diabetic wounds of foot participated in the research. They were not appointed any system antibacterial and antiseptic preparations for

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external application at the moment of the research realization. Biopsy material from a wound was taken away before the beginning of vacuum assisted therapy and in 3 days after the removal of a vacuum bandage. Wound was washed with sterile diluent and drained with a sterile gauze tampon before the implementation of biopsy. The self-weighted pieces of fabric were ground down in a sterile mortar with nourishing clear soup. The tenfold breeding was sowed on a blood agar, environment of Endo, ZHSA, Saburo and tioglycolic clear soup for the selection of anaerobes. As a result of undertaken studies it was set that the bacterial loading of wounds before the beginning of application of a vacuum bandage hesitated from $8,4\times10^4$ KUO/g to $4,5\times10^7$ KUO/g. The average bacterial loading of wounds in a group was a 6,15±0,27 lgKUO/g that is considerably higher than the critical level of bacterial semination of wounds. In three days after the removal of a vacuum bandage there was an increase of the bacterial loading of wounds in a group ($p<0,05$). There was a gain of population level of microorganisms in 8 (80%) patients, and it remained without changes in 2 (20%) of them. Indexes hesitated in limits from $2,3\times10^5$ KUO/g to $1,2\times10^9$ KUO/g.. 8,11±0,44 lgKUO/g was the average bacterial loading of wounds in a group after the removal of bandage. Conclusion. Therapy of wounds by negative pressure that was used for treatment of wounds for patients with a diabetic foot, does not diminish the bacterial loading in a wound and vice versa, assists its increase. It is necessary to undertake further studies for establishment of influence of system antibiotics therapy on the microbial loading of wound for patients with diabetic ulcers.

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