2015 № 4

ЗМІСТ
(Contents)

ОГЛЯДИ (REVIEWS)

Lisnyak Yu. V.

Introduction. Emergence of nosocomial bacterial pathogens (especially Gram-negative bacteria) with multiple resistance against almost all available antibiotics is a growing medical problem. No novel drugs targeting multidrug-resistant Gram-negative bacteria have been developed in recent years. In this context, there has been greatly renewed interest to cyclic lipodecapeptides polymyxins. Polymyxins exhibit rapid bactericidal activity, they are specific and highly potent against Gram-negative bacteria, but have potential nephrotoxic side effects. So polymyxins are attractive lead compounds to develop analogues with improved microbiological, pharmacological and toxicological properties. A detailed knowledge of the molecular mechanisms of polymyxin interactions with its cell targets is a prerequisite for the purposeful improvement of its therapeutic properties. The primary cell target of a polymyxin is a lipopolysaccharide (LPS) in the outer membrane of Gram-negative bacteria. The binding site of polymyxin on LPS has been supposed to be Kdo2-lipid A fragment. **Methods.** For all molecular modeling and molecular dynamics simulation experiments the YASARA suite of programs was used. Complex of antimicrobial peptide polymyxin B_3 (PmB_3) with Kdo2-lipid A portion of E. coli lipopolysaccharide was constructed by rigid docking with flexible side chains of the peptide. By alanine scanning of polymyxin B_3 bound to LPS followed by simulated annealing minimization of the complexes in explicit water environment, the molecular aspects of PmB_3-LPS binding have been studied by 20 ns molecular dynamics simulations at 298 K and pH 7.0. The AMBER03 force field was used with a 1.05 nm force cutoff. To treat long range electrostatic interactions the Particle Mesh Ewald algorithm was used. **Results.** Ala-mutations of polymyxin's residues Dab1, Dab3, Dab5, Dab8 and Dab9 in the PmB_3-LPS complex caused sustained structural changes resulting in the notable loss in stability of LPS complexes with Ala-mutants of PmB_3. The mutations disturbed the characteristic hydrogen-bond network of PmB_3-LPS complex. Ala-mutations of Dab1, Dab8 and Dab9 amino acid residues of PmB_3 destabilized PmB_3-LPS complex to a greater extent: the values of binding energy for these mutants showed increase and large-amplitude irregular fluctuations.
Conclusions. Hydrogen bonding of polymyxin B with the lipopolysaccharide is an important factor of the stability of PmB_3-LPS complex. Detailed knowledge of the peculiarities of molecular interactions of polymyxins with its primary target on the outer membrane of Gram-negative bacteria is a prerequisite of a purposeful design of novel polymyxin-like lipopeptides.
Keywords: polymyxin, lipopolysaccharide, lipid A, docking, molecular modeling.

Рубан Е. А., Колиснык Т. Е., Слипченко Г. Д.

PROSPECTS FOR DEVELOPMENT OF ANTIDIABETIC POLYPHENOL-BASED DRUGS: MECHANISMS OF HYPOGLYCEMIC ACTION AND PHARMACOKINETICS

Ruban E. A., Kolisnyk T. Ye., Slipchenko G. D.

Introduction. Diabetes mellitus is one of the most serious chronic diseases and considered to be non-infectious epidemic worldwide. Persistent hyperglycemia is a major hallmark of diabetes and risk factor for the development of its complications. Therefore, the main therapeutic goal in the treatment of diabetes is to reduce the elevated blood glucose level. Unfortunately, management of diabetes without any side effects is still a challenge to the modern medicine and pharmacy. Among potential alternatives to synthetic antidiabetic drugs plant polyphenols are very promising. However, polyphenol efficiency in diabetes is determined by their chemical structure and hence the affinity to a certain molecular targets in body tissues. Moreover, the bioavailability and other pharmacokinetic parameters of different individual substances may also vary significantly. In this context the present paper is devoted to the analysis of the available data on the hypoglycemic mechanisms and pharmacokinetics of various individual polyphenolic compounds in order to provide the necessary biopharmaceutical requirements in the development of a new blood glucose-lowering drug**. Materials and methods**. A systematic literature search of Pubmed, EMBASE and other databases with no language restrictions was performed until to the end of August 2015. The following terms were used: polyphenols, diabetes mellitus, hypoglycemic action, pharmacokinetics and bioavailability of polyphenols**. Results and discussion**. According to available experimental data various polyphenols may influence carbohydrate metabolism at many levels. The mechanisms by which plant polyphenols exert their hypoglycemic action are mediated primarily by their ability to directly bind to target proteins (or peptides) and include inhibition of carbohydrate digestion and glucose absorption in the intestine, stimulation of insulin secretion from the pancreatic β-cells, modulation of glucose release from the liver, activation of insulin receptors and glucose uptake in the insulin-sensitive tissues. On the other hand, most polyphenols are characterized by low bioavailability mostly due to intensive metabolism. Thus absorption of such polyphenols as anthocyanins, phenolcarboxylic acids and some others appears low, but it is supposed that it could have been underestimated because not all metabolites might have been considered. Besides the absorption rate of these compounds is very rapid and may take place already in stomach. In contrary, rutin and other quercetin glycosides are absorbed only after release of the aglycones by the intestinal microflora. The elimination half-lives of most polyphenols tend to be short, especially in the case of anthocyanins. However, some polyphenolic compounds such as quercetin glycosides may have longer half-lives, and even accumulate in plasma with repeated ingestion. **Conclusions**. Polyphenols have unique therapeutic potential in the treatment of diabetes mellitus. Nevertheless, the possibility to use polyphenols as hypoglycemic agents in clinical practice is limited by their low bioavailability. Taking into account information reported in the literature on the hypoglycemic mechanisms and pharmacokinetics of polyphenols, promising method of increasing their bioavailability is the development of

prolonged-release dosage forms based on polyphenol substances. This approach would extend residence time of polyphenols in the small intestine – the main site of hypoglycemic action in their intact, non-metabolized form, and will help maintain a constant concentration of active substances in the blood plasma, the target organs and tissues.
Key words: polyphenolic compounds, diabetes mellitus, hypoglycemic action, pharmacokinetics, bioavailability

FEATURES OF THE IMMUNE RESPONSE DURING INFECTION AND PROSPECTS FOR THE VACCINES CREATION
Davidova T.V.
The influenza virus belongs to the family Orthomyxoviridae and is a major cause of respiratory infections in humans. Each year, influenza viruses cause, according to experts, 3-5 million severe course of the disease and 250 000-500 000 deaths. Influenza A viruses are divided into serotypes based on their surface glycoproteins - known currently 17 subtypes of HA and NA subtypes ten. Upon infection with an influenza virus, both innate and adaptive immune responses are inducing. In recent years the annual seasonal epidemics were causing strains of the virus A (H1N1 and H3N2) and virus B. This may be due to their ability to be unrecognizable virus specific antibodies due to antigenic drift (Figure 1). Seasonal flu vaccine, to be effective, must be updated almost annually, according to new epidemic strains. In this work will discuss various strategies used by influenza viruses to evade innate immune responses and recognition by components of the humoral and cellular immune response, which consequently may result in reduced clearing of the virus and virus-infected cells.The primary targets for influenza viruses are the epithelial cells that line the respiratory tract and which initiate an antiviral immune response upon detection of the virus. The first line of defense is formed by the innate immune system, which is quick but lacks specificity and memory. Innate immunity is formed by physical barriers and innate cellular immune responses. Here, we outline several of the innate defense mechanisms directed against influenza infections. During homeostasis, alveolar macrophages exhibit a relatively quiescent state, producing only low levels of cytokines, and suppress the induction of innate and adaptive immunity. Activated macrophages enhance their pro-inflammatory cytokine response, including IL-6 and TNF-α. Alveolar macrophages have a direct role in limiting viral spread by phagocytosis of apoptotic infected cells and by phagocyte-mediated opsonophagocytosis of influenza virus particles. They are also involved in regulating the adaptive immune response. The second line of defense against influenza is the adaptive immune response. This highly specific response is relatively slow upon first encounter with a pathogen. The adaptive immune response consists of humoral (virus-specific antibodies) and cellular (virus-specific CD4+ and CD8+ T cells) immunity. Influenza virus infection induces the production of influenza virus-specific antibodies by B cells. Antibodies directed to the viral HA and NA correlate with protective immunity.Immune pressure on influenza viruses forces them to adopt strategies to evade immunity.Various mechanisms contribute to immune evasion of influenza viruses from the humoral immune response. Due to the lack of proofreading activity, the transcription of viral RNA by the viral RNA polymerase is error prone and results in mis-incorporation of nucleotides. Under the selective pressure of antibodies that are present in the human population, induced after influenza virus infections and/or vaccination, variants are positively selected from the quasi species that have accumulated amino acid substitutions in the antigenic sites of HA that are recognized by virus-neutralizing antibodies. This phenomenon is known as antigenic drift. Introduction of influenza viruses of a novel antigenically distinct subtype into the human population is known as antigenic shift and may cause a pandemic outbreak, since neutralizing antibodies against the new virus strain are absent in the population at large.Introduction of antigenically distinct viruses can occur after zoonotic transmission. However, in most cases, pandemics were caused by viruses that had exchanged gene segments between human and avian or swine influenza viruses. Currently used seasonal influenza vaccines are predominantly inactivated vaccine preparations. Development of vaccines that induce broad range of antibodies and preferably long heterosubtypic CTL response is desirable. Yes viral proteins such as the NP and M1 highly conservative, they are likely targets for the induction of cross-reactive T cells. This requires effective delivery of viral proteins in the cytosol. Several vaccine candidates cytosolic delivery is currently being investigated, including DNA vaccines, recombinant viral vectors, Iscoms and virosomal. They have already passed clinical trials. In addition, the induction of cross-reactive antibodies has attracted attention in recent years, antibodies directed against conserved regions of molecules on the stem are of particular interest. Unlike subtype specific antibodies induced against the main round of the AB, these stem HA-specific antibodies capable of neutralizing a broad activity against a large number of subtypes of influenza virus. In addition, ectodomen M2 highly conserved protein and antibodies induced against this region are able to create protection against infection. Thus, vaccines that induce both humoral and cell-mediated immune responses aimed at conserved areas of virus, in addition to the strain-specific antibodies can afford. Protective immunity to many different flu viruses, including new variants and subtypes drift. Knowing the complexity of the interaction between the immune system and variable pathogen such as influenza virus, has increased significantly in recent years. This can help reduce both morbidity and mortality, through the creation of effective seasonal vaccine, but there are still gaps in understanding, providing opportunities for improvement and developing a more widely-protecting vaccines. Induction STL-reactions with the same epitope can be a way to create fully protecting vaccines. Current research also focuses on the responses of cross antibodies directed to a more conservative regions of the surface proteins. Together, these will create new ways to confront the changing nature of influenza virus, and subsequently be able to protect even the emergence of new pandemic strains.

Key words: influenza; evasion; innate immunity; adaptive immunity

ЕКСПЕРИМЕНТАЛЬНІ РОБОТИ
Experimental papers

STATUS OF THE IMMUNITY OF PATIENTS WITH CHRONIC STAPHYLOCOCCUS'S PHARYNGITIS
Ognivenko E.V., Popov N. N.
Immunomodulatory and immunostimulatory drugs present the greatest interest in treating such patients and the rehabilitation of their immune system. Today, a wide clinical application has Polioksidonium (Petrovax Pharm), which has a wide range of influence on the immune system. There are studies proving the effectiveness of Polioksidonium treatment of inflammatory diseases of the nasal cavity and paranasal sinuses, chronic inflammatory process in pharyngeal plexus. **Material and methods**. We observed 62 patients on chronic staphylococcus's pharyngitis in age from 21 to 45 years, who were treated in the communal health institution "Kharkiv city hospital №

6". The first group (basic group) amounted to 32 patients, together with anti-inflammatory therapy (topical Decatilen 1 tablet 3 times daily for 7 days, physiotherapy for 5 days, was obtained Polioksidonium (12 mg every 24 hours per os for 10 days). The second group (control group) consisted of 30 patients who received similar therapy without Polioksidonium. Clinical, microbiological, immunological studies were performed before the treatment, at 7 and 30 days after the end of the therapy. As indicators of standards the results of 30 healthy individuals were used. Immunological studies included the determination of the phagocytic activity of neutrophils, their biocidity, opsonizing properties serum titers of antibodies to the causative infectious agents, concentrations of the major classes of immunoglobulins in saliva and serum. **Results and discussion**. Before the treatment the patients showed complaints to pain and irritation in a throat, feeling of a foreign matter in a throat, dry cough and low-grade fever. Microbiological examination of oropharyngeal secretions ChFh patients revealed a 34 % S. pneumonia, at 24 % - S.aureus. Microbial associations were sown in 45 % of the cases. Immunological studies have shown that patients with chronic staphylococcus's pharyngitis of increasing concentrations of IgG and mIgA and reducing values sIgA and lysozyme in oropharyngeal secretions. It has also been found that digesting and absorbing capability of bacterial particles neutrophils peripheral blood of patients with ChPh lower than that of healthy individuals. Low phagocytic ability of cell for patients with HF was observed in respect of opsonized autoserum bacteria. In all patients of the main group and the comparison group revealed a significant increase in antibody titer to bacterial etiological factors and common antigenic determinative (CAD) bacteria. High antibody titers were detected for almost all microbes studied. The clinical observations have shown that under the influence of Polioksidonium patients with chronic staphylococcus's pharyngitis on the 7th day after the treatment has shown a marked decrease or complete disappearance of the major clinical symptoms. All patients receiving Polioksidonium markedly improved overall health. The instrumental examination the 65% of the patients of the main group and the 70% of comparison group on the 7th day after the end of treatment were observed with swelling and hypertrophy of the mucous membrane of the posterior pharyngeal wall. On the 30th day after the end of treatment, 71.8% of the study group patients were without complaints (in the comparison group - 30 % of patients), and their clinical status was characterized by the norm. Pharyngoscope at 22 % of the patients of the main group and at 66% of the patients of the comparison group experienced a slight hypertrophy of the mucous membrane of the posterior pharyngeal wall. Microbiological examination of the main group found in 15,7 % of cases the present of pathogens, marked decrease in microbial associations without the appearance of fungal flora and 68% of the pathogenic microflora. In the control group half of the patients (52 %) was sown pathogenic flora, a slight decrease in the amount of microbial associations. Under the effect of Polioksidonium the increase of the secretory IgA and serum immunoglobulins, and lysozyme occurred in the content of oropharyngeal secretions. On the 7th day after the treatment the patients receiving Polioksidonium, had a significant increase in the phagocytic activity of neutrophils and biocide effect, and increase serum opsonizing properties. The autoserum increased both in the absorption capacity of neutrophils and their biocidal effect. Full restoration of the functional activity of phagocytic cells in these patients occurred by 30 days after treatment. To compare the group of patients we have studied that the properties of cells and serum opsonizing properties recovering very slowly and by 30 days were significantly different from the norm. On the 7th and 30th days after the end of the treatment the patients who received Polioksidonium, had an increase in antibody titer to infectious etiologic pathogens and IgG antibodies to CAD bacteria. The patients who did not receive Polioksidonium, such dynamic improvements in humoral immunity was observed. By 30th days after the treatment the patients in a comparison group the antibody titer to infectious etiologic pathogens and their affinity were not significantly changed compared to their values before treatment. The monitoring of patients during the year showed that the main group was not observed recurrence ChFh. They are much less likely than the comparison group was ill patients with acute respiratory infections, which are mild and not accompanied by complications. In the study group acute respiratory infections 2-3 times a year have been reported in 17 % of patients. Patients with ChFh comparison group relapses occurred in 40% of cases, of which 25% of patients - 2-3 times a year, 70% of patients 2-3 times a year suffered acute respiratory illness, which in 23,8% of cases complicated by acute bronchitis, 15% - by acute sinusitis. **Conclusions:** 1. Polioksidonium stimulates the increase of phagocytic and biocidal activity of white blood cells, the production of high affinity antibodies antimicrobial, increased serum opsonin properties. 2. Using polyoxidonium decrease the manifestations of pain and intoxication. 3. Polioksidonium has a positive effect both on the clinical course of chronic pharyngitis and prevention of its recurrence.

Key words: Chronic pharyngitis, Polioksidonium, local immunity, oropharyngeal secretions.

ІМУННІ ПОРУШЕННЯ У ПАЦІЄНТІВ З ГЕРПЕТИЧНОЮ ІНФЕКЦІЄЮ РОТОГЛОТКИ ТА ЇХ КОРЕКЦІЯ

Макаревич В.А., Коляда Т.І., Тупотілов О.В., Коляда О.М.

IMMUNE DISORDERS AND THEIR CORRECTION IN PATIENTS WITH HERPES INFECTION OF THE OROPHARYNX

Makarevich V.A., Kolyada T.I. Tupotilov O.V. Kolyada O.M.

Recurrent herpes infection of the oropharynx caused by herpes simplex virus type I and II occupies an important place among the infectious diseases of the oral cavity. The mechanisms which lead to the development of recurrence of the disease are studied insufficiently, and this limits the clinical possibilities of prophylactics. The frequency of the manifestations of herpetic infection and their intensity depend on the state of the immune system, in particular, the nature and level of pathogenic disorders of immune response. The immunotherapy requires a personalized approach taking into account the variability of "sensitivity" of immune index of the patient for potential therapeutic effects. The aim of the study was to justify the treatment of immune disorders and timeous prevention of recurrence, and also complications that occur when infection activates during the long-term viral persistence, based on definition of the characteristics of immune disorders in patients with moderate and high recurrence rate of the disease. **Materials and methods**. The study involved 86 patients aged 18 to 49 years with herpesviral gingivostomatitis and pharyngotonsillitis and herpetic vesicular dermatitis. The control group consisted of 19 healthy people of comparable age. Patients with recurrent HSV infection were divided into two groups. Group I was formed of patients with moderate rates of relapse less than 4 times per year (n = 51), and group II represented patients with high rates of relapse not less than 4 times a year (n=35). Lymphocyte subsets were defined by fluorescent microscopy method using FITC-labeled monoclonal antibodies against surface antigens CD3, CD4, CD8, CD16, CD22. Evaluation of functional lymphocyte reactivity was performed by setting 5 mg/ml PHA-stimulated RBTL. Phagocytic activity was defined by latex method. The NBT-test was used to evaluate the metabolic capacity of phagocytes. The CIC in serum were defined by method of selective 3.5% PEG precipitation of antigen complexes. Complementary activity of blood serum was determined by 50% hemolysis. The content of IFN-α and IFN-γ in supernatants was determined by ELISA after 24 hours of PBMC incubation. **Results and discussion**. The level of immunodeficiency disorders expression by herpes infection depended on the frequency of relapses during the year. A decrease of white blood cells number and relative content of lymphocytes of about 1.6 times as compared to the control group was observed in patients with a high relapse rate of recurrent HSV. Herewith, the relative content of CD8 + lymphocytes was 1.4 times lower than the control and 1.5 times lower than the same index in patients with moderate recurrent HSV relapse rate, and reduction of RBTL stimulation index was expressed stronger as compared with the control group. Levels of serum IgA and IgG were increased 2.1 times and 1.7 times respectively relative to the control group. Concentration of CIC in serum of patients in both groups exceeded the control which points to the failure of elimination function. A significant decrease in phagocytic activity in both groups in patients with recurrent HSV was more expressed in the group with high frequency of relapses. Also the decrease metabolic reserves were found in both groups of patients which points to the phagocytic function disorder. Elevated level of B-lymphocytes and increased level of immunoglobulins points to the

activation of humoral immunity. Activity of complement in patients with recurrent HSV was significantly higher than controls (1.4 times) in the group with high frequency of relapses. Expressed deficiency of IFN-α compared with controls and patients with moderate frequency of relapses were observed in the group of patients with a high relapse rate. The level of spontaneous production of IFN-α was elevated 1.6 times compared to control in patients with moderate frequency of recurrent HSV relapses, and the level of spontaneous production of IFN-γ was elevated 1.3 times compared to control group. In our previous studies we have determined that the content of perforin-positive cytotoxic lymphocytes in patients with a high frequency of disease relapses was reduced 2 times relative to healthy donors. It was shown that HSV-inactivated vaccine was able to elevate the content of perforin-positive cytotoxic lymphocytes in patients with moderate and high recurrence rate; herewith the largest index of influence of HSV-antigen was defined in patients with a high frequency of relapses. HSV-induced production of IFN-α increased 3 times in patients with moderate frequency of relapses and it had no significant difference from the control group, and in patients with a high relapse rate - 2.3 times. Reserve ability to synthesize IFN-γ in patients with moderate frequency of HSV relapses remained at the level of index of almost healthy donors, while the expressed reduction of stimulating action of HSV antigen was observed in patients with a high relapse rate. We have previously shown that the high recurrence rate of herpes infection accompanies by reduction of levels of TNF-α, by increase of spontaneous and induced production of IL-10 (in 76% patients), IL-12 and IL-1β by monocyte cells (in 85% of cases). Herewith 67% of patients with a high frequency of disease relapses had an imbalance of IL-12p70/IL-12p40, and 43% of patients had increased production of IL-1 receptor antagonist.It was determined that incubation of PBMCs with the addition of recombinant IFN-α causes a significant increase of the production of IFN-γ in patients with moderate relapse rate and also in the control group (stimulation index 1.3). The level of interferon-induced IFN-γ had no significant difference from the basal level in patients with a high relapse rate. Regulatory effect of IFN-α manifested also as increase of production of IL-1β, herewith the increase of the ratio IL-1β/IL-1RA was noted in patients with a high relapse rate. Stimulation of IFN-α in patients with a high relapse rate leads to 1.4 times increase of induced production of IL-10 by cells of monocyte fractions of MNC. The influence of IFN-α on the relative content of perforin-positive lymphocytes in patients with recurrence HSV was less expressed as compared to HSV-vaccine. So the stimulation index in patients with moderate relapse rate was 1.4, while patients with high relapse rate had stimulation index 1.2. Thereby, the choice of immunotherapeutic strategy of treatment of recurrent herpes infection of the oropharynx requires the immunological test to clarify the HSV pathogenesis type.

Keywords: recurrent herpes simplex infection, immunodeficiency, interferons, cytokines, cytotoxic lymphocytes, immunocorrection

ЗМІНИ МІКРОБІОТИ ПОРОЖНИНИ ТОВСТОГО КИШЕЧНИКУ У ХВОРИХ НА ВІЛ-ІНФЕКЦІЮ

Савінова О.М., Горобченко К.М., Ніколаєва Л.Г. , Большакова Г.М. , Майстат Т.В., Д'яченко А.Г.

THE CHANGES OF LARGE INTESTINE CAVITY'S MICROBIOTA IN PATIENTS WITH HIV INFECTION

Savinova O.M., Gorobchenko K.M., Nikolaeva L.G., Bolshakova G.M., Majstat T.V., Djachenko A.G.

Introduction. Infections of the gastrointestinal tract are caused by a wide range of fungi, viruses and bacteria. The great value has the ratio of microorganisms. There are certain regularities in microecological system of intestinal microflora. Thus, bifidous bacteria should be more than lactobacterium; enterobacteria – more than enterococcus; E.faecalis more than E.faecium. However, these differences should be at least one or two orders of magnitude. An important indicator is the ratio of enterobacteria and enterococcus.

Material & methods. In the paper were used following materials and methods: bacteriological and statistical. The conditions of intestinal microbiocenosis were evaluated according to the methodical instructions about researches of fecal masses on dysbiosis and modern methods of correction of intestinal dysbiosis that included identifying of anaerobic and facultative anaerobic microorganisms, staphylococci, enterococci, opportunistic enterobacteria, Proteus spp., Klebsiella spp., P.aeruginosa, C.albicans. Bacterial cultures were identified by standard techniques. Statistical analysis of the results was performed by the standard method of determining the average value and its standard deviation (M + m) and Student's t-test. The reliability of the difference was evaluated at the level of probability $p < 0.05$. The experiments' data were processed using software applications Microsoft Excel 2003 and «Biostat-6".

Results & discussion. We studied the species and quantitative composition of intestinal microflora of patients with HIV infection. All studied patients had disrupted quantitative and qualitative composition of intestinal flora. The changes were identified both anaerobic and aerobic microorganisms. Abnormality in the components of microbiota was manifested by reduction in the number of microbiota in the absence of conditionally pathogenic microflora. In the first place by deficit of microorganisms were bifidus bacteria. According to our research in 94.1+4.01% of cases bifidus bacteria were found in the amount of <106 CFU/grams and in 5.9+4.04 % of cases they were founded in the amount of 107 CFU/grams. The second place by importance is occupied by lactobacillus. In comparison with the norm patients with HIV infection had this indicator reduced and amounts to 88,2+5,53% in ≤105 CFU/grams and 11.8+5.53% in 106–107 CFU/grams. Bacteroides from the group of anaerobic bacteria was not found in any patient. Among the group of aerobic bacteria leading representative was E.coli, which belongs to the group of obligate microflora. 19 patients had E.coli in the amount of ≤106 CFU/grams, which made up to 56% while the norm is 108 CFU/grams of faeces. 56% of patients with the 3rd clinical stage of HIV had simultaneous shortage of bifidus bacteria, lactobacillus and Escherichia. Hemolytic E.coli were detected in small amounts of 2.9 + 2.93%. The results of microbiological studies of fecal on dysbacteriosis shown that despite the decrease of bifidus bacteria over 40 times in patients with the 2–3rd clinical stage of HIV infection conditionally pathogenic microflora appeared in small amounts, such as hemolytic isolates of E. coli 2.9 + 2.93%, S.aureus in amount of >104 CFU/grams in 11,8 + 5,53%, S.epidermidis in amount of > 105 CFU/grams in 32,4 + 8,03%, C.albicans in amount of > 104 CFU/grams in 11,1 + 6,59% and 1 patient had Clostridium in amount > 103 CFU/grams, which was 3 + 2,93%. These data show that patients with HIV infection is detected at the same time reducing number of anaerobic microflora (bifidus bacteria and lactobacilli) and aerobic microflora, a leading representative of which is intestinal E.coli irrespective of the clinical stage of the disease. Association of these microorganisms is 56%. To this attach indicators of reduction E.faecalis and E.faecium. Taking into account the features of obligate microfloras' functions (bifidus bacteria, lactobacillus, E.coli), its lack has a negative impact on microecological system of the human body and reduces immunomodulatory effect on humoral and cellular immunity. So one of the issues which will have a positive impact on the health of patients with HIV infection is a normalization of obligate microflora deficit and reducing of opportunistic microflora. The conducted researches point to the need of microbiological analysis of fecal on dysbiosis for the patients with HIV infection and depending on the revealed dysbiotic changes making correction of microflora by biological agents. To correct the number of anaerobic bacteria (bifidus bacteria, lactobacillus) use of bacterial preparations is not enough for only one month. It is necessary to continue taking of medicine for at least one month under the control of microbiological studies. The positive dynamics of the microflora of the large intestine points to changes that may be found in the immune system of the person that takes biological preparations. The close interaction between the microbiota of intestinal canal and the immune system leads to the formation of non–specific resistance of the organism. In this regard, the big importance has a modulating effect of intestinal microflora on products of cytokines, which are characterized by a wide range of biological effects.

Conclusion. 1. Patients with HIV infection irrespective of the clinical stage of the disease have deficit both anaerobic (bifidobacteria and lactobacilli) and facultative anaerobic microorganisms. 2. E.coli is the leading microorganism among the facultative anaerobic intestinal microflora, its amount of has been reduced to levels <106 CFU / mL at 56% at the patients. 3. Correction of patients' microflora by bacterial agents showed that the number of E.coli already in a month have reached the normal level in 100% of cases.

Key words: dysbiosis, HIV infection, intestinal discharge.

EXPERIMENTAL STUDY OF BIOFILM-FORMING ABILITY TO METHICILLIN-RESISTANT AND METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS STRAINS.
Voronkina I.A., Derkach S.A., Krilova I.A., Gabysheva L.S.,

In medicine there are many methods for studying of formation of biofilms. Cultivation in dynamic systems allows to create the conditions as much as possible close to that exist in the macroorganism. The majority of experimental methods are based on building of static culture conditions of microorganisms, most often for this purpose use 96-well plastic microplates in various modifications. Using microplates even one manufacturer leads to different results of the study, which is due to physical and chemical characteristics. In addition, the formation of biofilms using this method affects the composition of culture media (micronutrient and electrolyte) and aeration degree.To quantify biofilm formation in microplates researchers use the various wavelengths of the photometer: 450 nm, 540 nm, 562 nm, 630 nm, 650 nm, etc. Thus, this method is quite common, but its basic lack is that there are no standards that would allow it to unify all laboratories.The aim of this study was to optimize the test parameters to detect the ability of film formation MRSA and MSSA strains. **Materials and methods.** We used staphylococcus strains: S.aureus ATCC 25923, strains from the laboratory of the museum with a certain in previous studies of methicillin-sensitive and recently received S.aureus strains from patients with purulent-inflammatory diseases of different localization. Defining the properties of a biofilm forming staphylococcus culture plates was performed by D. Christensen. **Results and discussion.** In this experiment nutrient broth (HiMedia, India) was used with different volume fractions ingredients: 2 % glucose, 6 and 7 % NaCl. Microplates were incubated 4, 24, 48 and 72 hours at 35 ˚C. Optical density of formed biofilm evaluated by the color intensity of spirit on a photometer (StatFax 303 Plus). This method was studied biofilm-forming properties of staphylococcus obtained from all 36 patients with community-acquired methicillin-resistant (MRSA) (n = 16) and methicillin-susceptible (MSSA) (n = 20) strains. It is defined that from 16 strains MRSA of 12,5 % had high ability to biofilms formation of (OD 0,25-0,4 units), 3 strains of 18,75 % - an average (OD 0,12-0, 24 units), - have found 43,75 % weak ability to formation of biofilms (OD <0,12 units), 25,0 % - a biofilm did not create in general (an authentic difference in comparison with the control well it is not revealed). It was defined that among 16 strains of MRSA 12.5 % had a high ability to form biofilms (OD 0,25-0,4 units.), 18.75 % - average (OD 0,12-0, 24 units), 43.75 % - found weak ability to form biofilms (OD <0.12 units.) and 25.0% - do not create biofilm (significant difference compared with control wells not detected). MSSA strains also differ in their ability to form biofilms. 30.0 % of the isolates were referred to the fact that not form a biofilm, 40.0 % - to strains with weak ability to form a biofilm, 20.0 % - with the average, 10.0 % are highly active biofilm formation. **Conclusions.** 1. The optimal parameters for the experimental determination of the ability of biofilm formation of staphylococcus strains are: use of nutrient broth with the bulk part of the 2 % glucose, incubating the plates for 24-48 hours at 35 °C. The measurement of the optical density (OD) of the resulting biofilms should be performed at wavelength of 630nm. 2. Experimental confirmation of a high ability to form biofilm in the studied strains of staphylococci occurred in 10.0 % MSSA and 12.5 % - MRSA. 25.0 - 30.0 % of the strains were classified as not forming a biofilm, and the rest - to the cultures with weak or medium activity. 3. As a result of a comparative study of the ability to form biofilms of circulating strains of community-acquired staphylococcus significant difference between MRSA with methicillin-resistant phenotype and MSSA strains not detected ($\chi 2 > 0.05$).
Key words: staphylococcus, biofilm, the method of biofilm formation.

ANTIMICROBIAL ACTIVITY OF ESSENTIAL OILS OF PLANTS BELONGING TO LAMIACEAE JUSS. FAMILY
Shanayda M.I., Pokryshko O.V.

Introduction. One of the important sources of therapeutic and prophylactic agents of modern medicines are essential oils of medicinal plants. Essential oils are the main group of biologically active substances of a number of plants belonging to Lamiaceae Juss. Family. Antibacterial activity of medicinal plants belonging to Lamiaceae Family many scientists associated with containing of essential oils. In this regard, considerable interest presents the comparative analysis of the antimicrobial properties of essential oils of Lamiaceae Family representatives. **Material and methods**.The antimicrobial activity of essential oils of investigated plants was studied with using in vitro condition. The essential oils derived from the aerial parts of cultivated plants of Ocimum, Hyssopus, Dracocephalum, Lophanthus, Monarda and Satureja genus harvested during flowering period (in terms of Ternopil region). The antimicrobial activity of essential oils studied plants was studied by serial dilution method and disk diffusion assay. It has been applied on standard microorganism test strains: Bacillus subtilis ATCC 6633, Escherichia coli ATCC 25922, Staphylococcus aureus ATCC 6538, Pseudomonas aeruginosa ATCC 9027 and Candida albicans ATCC 885-653. **Results and discussion.** It was conducted a comparative study of the influence of some essential oils of cultivated plants belonging to Lamiaceae family on microorganisms in conditions in vitro. It was found that essential oils of the studied plants were most effective in the maximum concentration (1:10). Gram-positive cocci S. aureus and yeast C. albicans were the most sensitive to influence of investigated essential oils. It was analyzed the relationship of the biological activity with the component composition of essential oils of plants. Essential oils of L. anisatus, M. fistulosa and S. hortensis characterized by the dominance of aromatic compounds and had shown stronger antimicrobial activity than essential oils of other species. Therefore, essential oils of these species are very promising source of antibacterial and antifungal drugs, especially in the treatment and prevention of skin diseases, upper respiratory tract inflammations and vaginitis. **Conclusion**. Obtained results indicate promising further study of antibacterial properties of essential oils of plants species L. anisatus, M. fistulosa and S. hortensis (Lamiaceae family). It was discovered that Gram-positive cocci, including S. aureus, and yeast Candida were the most sensitive to these oils. Along with the prospect of creating antimicrobial drugs which include essential oils of studied plants these oils can be recommended as active ingredients of preservatives in the composition of cosmetic products or dietary supplements also.
Key words: Lamiaceae, essential oils, antimicrobial activity

INVESTIGATION OF ECOLOGICAL FEATURES OF ACUTE DIARRHEAL INFECTION PATHOGENS
Malysh N.G., Holodilo E.N., Chemych N.D.

Introduction. Microbiocenosis of human body also differs in extreme multicomponents and diverse content of microflora representatives forming its part. According to the biotype of bacterial contamination certain inter-bacterial relations are formed, which is reflected in the qualitative and quantitative characteristics of appropriate microbial landscape. Analysis of numerous microbial association manifestations allows evaluating changes in the pathogen properties influenced by associative microbiota. Work objective - based on the study ecological features of microorganisms isolated from intestine of patients with acute intestinal infections and apparently healthy people, identify potential risk factors for diarrheal infections. **Materials & methods**. A retrospective epidemiological analysis of acute diarrheal infections incidence was conducted during 2004-2013, using the statistics of the Main Department of the State Sanitary and Epidemiological Service of Ukraine in Sumy region. The intestinal microflora of 93 patients with acute diarrheal infections and 60 persons of the control group (apparently healthy people). As the result 130 bacterial cultures were allocated. Permanence rate was used to estimate biocenosis. Relationships between microbiocenosis members were investigated by determining degree of bond conjunction in associations, using Jaccard coefficient (g). **Results & discussion**. In 2005-2014 acute diarrheal infection incidence rates of Sumy region population were within 163.7 - 193.6 per 100 people without tendency to decrease. Acute intestinal infections and food toxicoinfections caused by opportunistic pathogens and viruses ($p<0.05$) dominated in nosological structure. In 35.5 % of cases diarrheal infections were of polyetiological nature. Noroviruses in associations with Candida bacteriaand fungi most often occurred ($p<0.05$) in the intestinal biotypes. Permanence rate of K. pneumonia, noroviruses, S. aureus, C. albicans was the highest and was accordinly 23.6; 21.5; 19.4 and 19.4 %. C. albicans (88.9 %), noroviruses (80 %), S. thyphimurium (80 %), P. aeruginosae (75 %), E. cloacae (75 %), S. aureus (72.2 %), K. pneumonia (68.2 %), rotaviruses (66.7 %) had average and high associativity coefficient values. The most part of associated causative agents ($p<0.05$) had antagonistic relations. Stable bacterial associations were formed between noroviruses and K. pneumonia, noroviruses and S. typhimurium, noroviruses and P. aeruginosae (g respectively 36.4; 40.0; 40.0 %). C. albicans, K. pneumoniae, S. aureus, E. cloacae were isolated from healthy people feces in diagnostically significant degree of contamination 43.3 % of cases. The permanence coefficient rated respectively 26.7; 20.0; 20.0; 3.3 %, as well as the associativity coefficient was 90.0; 50.0; 83.3; 100 %. K. pneumonie and S. aureus (g=42.9 %), S. aureus and C. albicans (g=33.3 %) cultures showed the greatest strength of microbial relations. **Conclusion**. In the process of microorganism co-existence different kinds of relations are formed between them - competitive or cooperative, and as the result the specific microsymbiocenosis is formed according to them. Having established universal common factors of this microsymbiocenosis, you can find ways to protect body from infection.
Key words: acute diarrheal infections, microorganism association, ecological features.

СИНТЕЗ, ФІЗИКО-ХІМІЧНІ ВЛАСТИВОСТІ ТА ПРОГНОЗ БІОЛОГІЧНОЇ АКТИВНОСТІ НОВИХ ПОХІДНИХ 2-R^1-N-(5-R)-1,3,4-ТІАДІАЗОЛ-2-ІЛ- БЕНЗОЛСУЛЬФОНАМІДІВ 75-81

Сич І.В., Перехода Л.О., Єрьоміна З.Г.

NEW DERIVATIVES OF 2-R^1-N-(5-R)-1,3,4-THIADIAZOL-2-YL-BENZOLSULFONAMIDES: SYNTHESIS, PHYSICOCHEMICAL PROPERTIES AND BIOLOGICAL ACTIVITY PREDICTION

Sych I.V., Perekhoda L.O., Ieremina Z.G.

Introduction: The analysis of modern literature, including overseas one, showed that a lot of the scientific researches is devoted to finding and creating biologically active compounds on base 1,3,4-thiadiazole. Derivatives of 1,3,4-thiadiazole are the large group of heterocyclic compounds with high rates of antimicrobial, antituberculosis, antidiabetic, antineoplastic and anticonvulsant activity. **Material and methods:** The purpose of this study was the expansion of sulfone derivatives substituted nitrogen-containing heterocyclic systems through the synthesis of 2-R^1-N (5-R)-1,3,4-thiadiazol-2-ilbenzolsulfonamides and prediction their pharmacological activity for future planning pharmacological screening. Synthesis of semi-products 2-amino-5-R-1,3,4-thiadiazoles was carried out by cyclization thiosemicarbazide and substituted derivatives of carboxylic acids in the presence of concentrated sulfuric acid. The synthesis of target compounds 2-R^1-N(5-R)-1,3,4-thiadiazol-2-ylbenzolsulfon-amides was carried out by N-acylation of 2-amino-5R-1,3,4-thiadiazole substituted benzolsul-fochlorides in the presence of anhydrous pyridine. The reaction proceeds by the classic S_N^2-mechanism. The resulting compounds are white crystalline substances, soluble in alcohol, chloroform and acetone, difficult to dissolve in water. Yields of obtained compounds was satisfactory (76-84%). The purity of the obtained compounds was determined by TLC. The structure of the obtained compounds was proved by elemental analysis, IR methods and ^{1}H NMR spectroscopy. NMR ^{1}H spectra were recorded at Bruker WM spectrometer (200 MHz); solvent DMSO-d_6; chemical shifts were in ppm, internal standard (TMS (tetramethylsilane)) was used. The prognosis of biological activity for obtained compounds were carried out using the program PASS (Prediction of Activity Spectra for Substances) in order to plan the further pharmacological screening. The program PASS predicts more than 500 kinds of biological activity using the chemical structural formula and helps to narrow the limits of experimental screening to identify compounds-leaders. This program is used just to assess the affinity of new compounds with known drugs, that is, to characterize their «drug likeness». The calculation was conducted with the help of Internet service that offers the software package of processing of listed structures and calculation of properties. **Results and discussion:** Synthesis of new potential biological active substances 2-R^1-N (5-R)-1,3,4-thiadiazol-2-ilbenzolsulfonamides has been carried out. Finished products have been obtained by the interaction of 2-amino-5-(R)-1,3,4-thiadiazoles with corresponding substituted benzolsulfochlorides in the presence of anhydrous pyridine. Target products have been obtained with satisfactory yields. All semi-products have two-proton signal of aminogroup in the area from 2.5 to 2.82 ppm in NMR^{1}H spectra. Signals of protons substituents in the second position of the heterocycle (methyl, propyl, i-propyl, butyl, sec-butyl) on corresponding areas of spectra is present in NMR^{1}H spectra of the all initial compounds aswell. In contrast to the spectrums of initial compounds signals of amino groups at the spectra of the finished compounds are absent. All spectra of the target products have the secondary amino group signal at 6.81 and 6.71 ppm areas. The purity of the obtained compounds determined by TLC. Prediction of biological activity derived substances was conducted using a computer program PASS. **Conclusion.** The group of 2-R^1-N-(5-R)-1,3,4-thiadiazol-2-ylbenzolsulfonamides has been synthesized by acylation of the corresponding 2-amino-5 -(R)-1,3,4-thiadiazoles. The structures of the synthesized compounds have been proved by elemental analysis, IR and ^{1}H NMR spectroscopy data. All substances for which the PASS program prognosis was carried out can show themselves as potential antidiabetic and antimycobacterial drugs.
Key words: 1,3,4-thiadiazole, synthesis, IR and ^{1}H NMR spectroscopy, prognosis of biological activity.

ВІДНОВЛЕННЯ *IN VIVO* НЕКУЛЬТУРАБЕЛЬНОЇ СУБПОПУЛЯЦІЇ *SALMONELLA ENTERICA* 82-85

Юдін І. П.

RECOVERY *IN VIVO* OF NONCULTURABLE SUBPOPULATION OF *SALMONELLA ENTERICA*

Yudin IP

Introduction. As one of mesophilic, easily cultivated species of pathogenic bacteria, *Salmonella enterica* transformed into viable but nonculturable (VNC) state in response to environmental stresses, including action of biocides. The cells in this state, preserve the integrity of membranes and metabolism of some, but not detected by conventional methods of cultivation. Some researchers suggest that the evolutionary significance of this phenomenon is part of an adaptive response aimed at long-term survival of bacteria in adverse

conditions; others argue that it is the result of stochastic cellular damage, in which nonculturable cells are in a state of gradual death. In any case, the phenomenon of existence VNC pathogens if they retain the ability to restore its growth *in vivo* is a significant problem in medicine, pharmaceutical, veterinary, food industry. VNC subpopulation of *S. enterica* was obtained under action of ethanol. In this paper was investigated *in vivo* resuscitation VNC *S. enterica* using intraperitoneal injection of mice. **Materials and methods.** Obtaining of stressful *S. enterica* populations. Bacteria were grown to exponential phase in broth Luria–Bertani (LB). To 1.0 ml sample suspension diluted to 1.5×10^6 cells/ml was added 1.0 ml of ethanol at a concentration of 40 % (v/v). After exposure of 10 to 600 minutes in the suspension were added 8.0 ml of phosphate buffered saline (FBS), washed by centrifugation (4500 g for 5 minutes) and serially diluted at a ratio of 1:10 (v/v) samples were stained with LIVE/DEAD BacLight (produced by "Invitrogen", USA), filtrated on membrane filters for fluorescence microscopy and parallel plated on LB agar cup to determine colony-forming units (CFU) per ml. *In vivo* resuscitation VNC *S. enterica* was made following way. Three groups of animals were inoculated by intraperitoneal injection: 1) 10^3 culturable cells (0.1 ml suspension containing 10^4 CFU / ml); 2) 10^3 VNC cells (0.1 ml suspension containing 10^4 cells / ml of nonculturable population); 3) 10^3 inactivated cells (pasteurization at 60 °C in 70 % ethanol, 30 min). Mice were observed daily for 14 days to register the death and extraction of internal organs. Liver and spleen of dead mice were removed and homogenized in 1.0 ml of FBS to detect restored *Salmonella* cells by seeding on selective medium bismuth sulfite agar (BSA). **Results and discussion.** In this study *S. enterica* cells in the exponential growth phase, exposed to ethanol (final concentration 20 %) lost culturability within 60 minutes. After 50 minutes of exposure with ethanol culturability of bacterial suspensions was outside evaluation cup method. At the same time, the integrity of cell membranes was determined at 4 $\log_{10}$ cells/ml. Bacteria that become VNC state can restore culturability. Thus, the state is reversible. Importantly, the resuscitation of VNC *in vitro*, which is achieved by simply eliminating or VNC induction factor (increasing the growth temperature, availability of nutrients) or more complex conditions such as a combination of environmental and chemical stimuli, does not reveal the full pathogenic potential of resuscitated bacteria. Therefore, the process of *Salmonella* resuscitation *in vivo*, we studied on infection model in mice. In experiments *in vivo S. enterica* resuscitation death of test animals was observed in 13.3% ($p < 0.05$) during the observation period, with 100% mortality in the group of animals infected with a suspension of living culturable cells *Salmonella* and 100% survival of the animals in the control group (who received injections of inactivated bacteria). From the dead mice from homogenates of internal organs plated recovered salmonella, which was confirmed by their growth on BSA. **Conclusions.** Under conditions *in vivo* recovery process VNC *S. enterica* cells can occur, but with low intensity in healthy mice (at 13.3%, $p < 0.05$). However, these cells retain pathogenic potential and can represent a danger if their underestimation. We can assume that the bacteria lose their virulence in part, but manifest it in individuals with a weak immune response.

Key words: VNC, *Salmonella*, resuscitation.

ДОСЛІДЖЕННЯ АНТИБАКТЕРІАЛЬНОЇ АКТИВНОСТІ КОМБІНОВАНИХ ПРЕПАРАТІВ НА КЛІНІЧНІ ШТАМИ МІКРООРГАНІЗМІВ, ВИДІЛЕНИХ ВІД ХВОРИХ З БАКТЕРІАЛЬНИМ ВАГІНІТОМ

Асланян М.А., Бобрицька Л.О., Солонина Н. Л., Осолодченко Т. П., Кучма І. Ю.

INVESTIGATION OF ANTIMICROBIAL ACTIVITY COMBINED PREPARATIONS FOR CLINICAL STRAINS OF MICROORGANISMS ISOLATED FROM PATIENTS WITH BACTERIAL VAGINIT

Aslanian M. A., Bobritskaya L. O., Solonina N. L., Osolodchenko . T. P., Kuchma I. Y.

The problem of bacterial vaginit in some cases the cause of severe infectious diseases genitalia of the fetus and newborn, which can impair the health of future generations. It is noted that the treatment of antibacterial agents observed numerous negative side effects-reducing the biochemical activity of the intestinal microflora, abuse microbiota, leading to the development of dysbiosis, increasing the number of resistant strains of pathogens, the risk of allergic reaction sand immunological disorders. A study was conducted towards finding effective combinations of drugs from different pharmacological groups means to create a combination of drugs. The **aim of the study** was to develop and explore and Flamini combination of miramistin combined medicines to treat bacterial vaginit. As a **result of studies** in patients with bacterial vaginit pathological material was isolated and identified 72 strains of microorganisms (*Staphylococcus spp, Streptococcus spp, Enterococcus spp, Escherichia coli, Haemophillu sssp, Candida albican* sand various strains of anaerobic microorganisms. For the combined treatment of infectious and in flammatory diseases (mixed infections) in humans the combined drugin tablet form. All clinical strains of microorganisms isolated from patients with bacterial vaginit were tested for sensitivity to the combined preparation in tablet form with Flamini and miramistin. The greatest sensitivity to the drugs found clinical strains of microorganisms: *Staphylococcu saureus, Staphylococcus epidermidis, Peptococcus niger* (diameter zone growth retardation is 25,5-23,5 mm). composition tablets number 1 (0.05 g Flamini, miramistini 0.02 g), which was selected for further study shows bacteriostatic effect against a wide range of microorganisms and fungi Rod *Candida*. IPC for *Staphylococcus sp* was 20-25 pg / mL for *Streptococcus sp* 35,0-40,0 mg / ml, for intestinal group 35,0-40,0 for fungi 30,0 mg / ml unlike pills number 2 and number 3, where the IPC was higher and amounted to 40,0 -55,0 mg / ml. Summing upthe results of experimental studies capsules combined with the composition Flamini and miramistin becon cluded that the most effective eagainst the different clinical strains of microorganism sand fungi is a combination Flamini 0,05g, miramistin 0,02 (tablets number1), giving opportunity to develop drug combinations for use in bacterial vaginit.

Key words: vaginitis, clinical isolates, miproorganisms, activity, antimicrobial drugs.

ANTAGONISM OF *A. VIRIDANS* TO CONDITIONALLY - PATHOGENIC MICROFLORA OF THE NOSE AND OROPHARYNX OF CHILDREN WITH CARDIAC PATOLOGY

Stepansky D.O.

Introduction. Search for harmless and simultaneously effective probiotics, which could be successfully used for treatment and prevention of infectious deseases, is currently important. *A. viridans i*s of particular interest, as it is representative of the normal microflora of human with broad spectrum of antibacterial action. The use of this microorganism has a number of advantages: the absence of side effects on the body; high adhesive abilities; resistance to lysozyme in saliva; the ability of use in patients, sensitized to antibiotics and chemotherapeutic drugs; stimulation effects on the human immune system. **Material and methods.** The purpose of the study was to investigate the antagonism of *A. viridans № 167* and autostrains of aerococcuses, isolated at patients, to conditionally - pathogenic microflora of the nose and oropharynx of children with cardiac patology. At the first stage of the study the microflora of the of the nose and oropharynx of 2 investigated categories was examined – 40 children 4-14 years with cardiac patology and 40 healthy children 4-5 years old. The second stage of work was to study the effect of A. viridans on the explored strains. **Results and discussion.** *A. viridans*

manifests the antagonism to all studied strains of gram-positive and gram-negative microorganisms, except *C. albisans*. *A. viridans* antagonistic activity to staphylococci (10 + 3 mm) and streptococci (10 + 2mm) is at the approximately same level. It is interesting to compare the antagonism of aerococcuses to clinical isolates of *S. pyogenes* and similar strains from carriers (healthy children category). Impact of aerococcuses on *P. mirabilis* strain appeared at the highest level. Autosimbionts of *A. viridans*, isolated from healthy children, are more antagonistic to CPM strains, isolated from these children, than autostrains of *A. viridans*, isolated from children with with cardiac patology, and higher than the museum strain of *A. viridans № 167* antagonism, and do not affect the growth of microorganisms of *Candida* kind. Severe antagonistic activity of the *A. viridans № 167* strain and autostrains of *A. viridans* to isolated conditionally patogenetic strains was discovered: *S. pyogenes*, *S. pneumoniae*, *S. aureus*, *K. pneumoniae*, *P. mirabilis*. Antagonism of *A. viridans № 167* to *C. albicans* was not found. **Conclusion.** The recieved data can serve as a basis for further study of the strain of *A. viridans № 167* and aerococcuses' autostrains usage for correction of fauces and nasopharynx microbiocenosis and also for the complex treatment and preventive actions in case of cardiac pathology.
Key words*:* Aerococcus viridans, probiotics, autostrains of aerococcuses, children.