

## 2017 № 2

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## Reviews

### STRUCTURES AND BIOLOGICAL ACTIVITY OF CUPROPHYLLINS

**Martynov A.V., Bomko T.V., Nosalskaya T.N., Kabluchko-Baruah T.V.**

Chlorophylls (a, b) are the porphyrin compounds and most common chemical in the plant's world. In fact, these compounds are an obligatory intermediate product both in energy metabolism and in plant catabolism. At the same time, currently there are few pharmaceutical preparations on the pharmaceutical market based on chlorophylls. Dyes based on hydrolyzed chlorophyll are successfully used in the food industry. Commercial chlorophylline is a copper complex of hydrolyzed chlorophylls. As shown earlier in TLC, the chlorophyllin mixture contains a large number of different compounds. It is like water-soluble saponified derivatives in the form of sodium-magnesium complexes, and similar structures in the form of a complex with copper. The latter are more brightly colored, soluble in water and widely used as coloring agents in cooking. In this case, if the initial chlorophyll was not found to have a pronounced biological activity, the substituted derivatives in the form of copper complexes possessed a number of new unique biological properties. Non-hydrolyzed hydrophobic cuprophylline obtained from eucalyptus leaves possessed high antimicrobial activity to most strains of staphylococci, inclusion resistant to antimicrobials and multiresistant strains. This drug is called Chlorophyllipt, it is allowed to be used as a medicinal product and is one of the oldest antibacterial drugs from plants on the market. It is marketed as ethanoic and oily solutions for topical use, and as an alcohol solution for intravenous injections. Its main purpose is the fight against staphylococcal infections. Recently, found that the oral administration of chlorophyllipt activates cellular immunity and indirectly exhibits antiviral activity. Another compound of cuprophyllin is water-soluble chlorophyllin. Some authors show the variability of the structure and biological activity of cuprophyllins. Different derivatives of chlorophyll have different biological activity. Hydrophilic cuprophyllin chlorophyllin very good studied and have good profile of toxicity and uses in cooking as colorant. Chlorophyllin have such biological effects: antiatherosclerotic, antiviral, antimicrobial, immunomodulating, antimutagenic and anticancerogenic, antioxidant. Most of the studies were carried out as in vitro and in vivo with statistically trustworthy results. Derivatives of chlorophyll are very perspective candidates for fight with multiresistant strains of microorganisms and viral infections. Derivatives of chlorophyll must be more studied for using as active pharmaceutical ingredients for development a new drugs in the form of injection, tablets, ointments.

**Keywords:** cuprophyllins, chlorophyllin, chlorophyllipt, biological activity, chemical structure

## Experimental papers

### ANTIGENS BRONCHOPULMONARY SYSTEM AND THEIR ROLE IN THE DIAGNOSIS OF AUTOIMMUNE PROCESSES IN BRONCHIAL ASTHMA IN CHILDREN

**Chernusky V.G., Popov N.N., Govalenkova O.L., Letyago A.V.,**

**Kashina-Yarmak V.L., Evdokimova T.V.**

Introduction. One of the promising directions of improvement of immunodiagnostic BA recently recognized the creation of tissue antigens of the respiratory system structures and their use in diagnostic assays to detect subtle disturbances in the structure of the respiratory system in the development of this disease. Each of the body tissue has an extremely wide range of proteins that characterize its species and organ specificity of the individual. It follows that satisfactory diagnostic results can be obtained only if the isolation of individual proteins characteristic lesion of certain components of the trachea, bronchus and lung tissue. Materials&methods. The results of studies using the blood serum of children with asthma during exacerbations, showed that the resulting diagnostic tools are characterized by mild pretsipitogennymi properties, in consequence of which they can not be used in the passive hemagglutination (PHA) response for diagnostic purposes, since there is a low the percentage of positive reacting sera from children with asthma (23.7% - 58.1%). Established that were significantly higher than in children patients with asthma for two of the four test diagnostics (nuclear antigen substance and mitochondria) cells of the bronchial mucosa frequency of positive results with serum of healthy children of the control group (63.0 - 100%). It is emphasized that except diagnosticum constituting supernatants mitochondria and bronchial mucosa cells, all other antigens differed in TPHA antigenic activity is extremely low, providing a positive result (1: 0,87 - 1: 1,38), which eliminates them diagnostic significance. It is found that the diagnostic tools derived from the cells of the bronchial mucosa, chemically presented protein components did not significantly differ among themselves antigenic activity in children with asthma, which also negatively affects the possibility of their intended use. On the supernatant antigens and mitochondria of cells in bronchial mucosa RPGA with sera of children with asthma autoantibodies determined in the following credits: supernatants - 1:75,4-1:108,2; mitochondria - 1: 58,9-1: 82,4. These results indicate that the test protein as diagnostics antigens bronchial mucosa cells are not able to stimulate development of bronchopulmonary autoantibodies involved in autoimmune manifestations component in children with asthma. Low diagnostic ability of the tested antigens of bronchial mucosa cells in PHA, obviously, is connected with the fact that asthma in children is a chronic non-specific inflammatory process, which is based on the initial changes in the interstitial stroma bronchopulmonary system. Features of asthma development in children can be identified by the use of immunologically relevant tests in tissue antigens, derived from the interstitial connective tissue stroma of bronchopulmonary system. We have tested antigens trachea, bronchi, lung tissue derived from connective tissue interstitial pulmonary system data structures. Antigens were presented lipopolysaccharide. Proteins are composed of antigenic preparations were absent, the peptides were determined only in trace amounts. This diagnostic kit used in the reaction aggregates quantitation immune serum of children with asthma. Immunological examination showed that lipopolysaccharide antigens of the trachea, bronchus and lung tissue, as opposed to protein antigens of cell structures of the bronchial mucosa, possessed high antigenic activity and the ability to detect differential diagnostic differences of clinical forms and degrees of severity of the disease. Thus, the main range of immunological and immunopathological reactions in asthma in children has a clear dependence on the antigen-activated interstitial stroma inflammatory bronchopulmonary system. Conclusions. 1. Antigens derived sectional proteinaceous material bronchopulmonary systems can not be obtained industrially, as they are not standardized to protein have not sterile, which greatly limits their use, and reduces the diagnostic value. 2. Multi-antigenic composition of protein homogenates derived from cell-

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tissue structures of the respiratory system, does not allow to clearly identify the nature of morphological changes in bronchial asthma in children. 3. Lipopolysaccharide antigens from bronchopulmonary structures contain protein in their composition may be prepared industrially under sterile conditions and stored in a lyophilized state for more than two years, which allows to use them widely in the forms and immunodiagnoses clinical severity of asthma in children.

**Keywords:** bronchial asthma, children, protein antigens, lipopolysaccharide antigens, autoimmune process.

## IN VITRO STUDY OF ANTI-INFLUENZA ACTIVITY OF PARA-AMINOBENZOIC ACID AND PROSPECTS OF NASAL DRUG DEVELOPMENT ON ITS BASE

20-22

**Nefedova L., Boyko N., Starosila D., Rybalko S., Zhilyakova E., Novikov O., Zhukovina O., Sagaydak-Nikitjuk R., Iurchenko I.**

One of the promising molecules having antiviral activity is a vitamin-like substance, para-aminobenzoic acid (PABA). The aim of this work is to study antiviral activity of para-aminobenzoic acid,  $\epsilon$ -aminocaproic acid, and their mixture against influenza virus, to evaluate their cytotoxic effect and to calculate their selectivity index by in vitro methods. Materials and Methods. For evaluation of cytotoxic concentration (CC50) of the substance tested, we used MDCK cell culture. For determination of anti-influenza activity of PABA,  $\epsilon$ -ACA, and their mixture under conditions of in vitro experiment, we used 24-hour passaged MDCK culture cells of dog's kidney, influenza virus strain A/FM/1/47 (H1N1), infected titer of which in MDCK culture cells of was between 3.0 and 9.0 lgID50. Results. As a result of our studies, we have determined that PABA in the concentration range studied from 10 to 1,000  $\mu$ g/ml did not have any cytopathic effect in MDCK culture cells. We calculated selectivity index (SI) for PABA, that was equal SI=128205, this fact confirm high level of therapeutic safety of this substance. The result of our experiments demonstrate that anti-influenza activity of PABA solution is almost 100 times higher than that of "ACA", furthermore in our in vitro experiment the mixture of PABA and  $\epsilon$ -aminocaproic acid (in ratio 1:100) demonstrates a synergetic effect. In addition, for combination of PABA and  $\epsilon$ AKK (1:100) we calculated fractional inhibitory coefficient FIC=0.79, that indicates to moderate synergetic effect of these substances. Conclusions. As a result of our in vitro studies, we have determined a high-level antiviral activity of para-aminobenzoic acid against influenza virus, and in combination with  $\epsilon$ -aminocaproic acid it demonstrated a synergetic effect. We have determined that PABA does not exhibit any cytotoxic effect on MDCK culture cells in the concentration range studied and demonstrates high level of therapeutic safety.

**Keywords:** para-aminobenzoic acid, antiviral activity, influenza virus.

## A STUDY OF ANTIMICROBIAL ACTIVITY OF FOAM-WASHING AGENT SPECIMENS AT 23-27 ACIDIC pH VALUES

**Strilets O. P., Petrovska L. S., Baranova I.I., Bospala Yu. O.**

Introduction. It is well-known that any parapharmaceutical substance, in particular, foam-washing agents comprising water in combination with detergents, extracts, water-soluble vitamins, viscosity regulators, pH, etc., is the ideal environment for microbial growth. Therefore, it is indispensable to use preservatives to protect any foam-washing agent from possible contamination by microorganisms. Their main advantages are: presence of a single antimicrobial and antifungal effect, expanded range of effects, decrease in the risk of resistance of microorganisms and decrease in the toxicity and concentration of the preserving mixture. In this regard, the shelf life of parapharmaceutical substances is not provided through the use of large quantities of preservatives, but thanks to their rational combination. Materials and Methods. For this study, we have made a number of samples of foam washing bases with a number of preservatives, which are often used in developing foam-washing agents with acidic pH value, namely: sample number 1 – foam washing base + sodium benzoate; sample number 2 – foam washing base + «Euxyl K300» (phenoxyethanol, methylparaben, butylparaben, ethylparaben, propylparaben, isobutylparaben); sample number 3 – foam washing base + «Germaben II» (polypropylene glycol, diazolum dinomovine, methylparaben, propylparaben); sample number 4 – foam washing base + «Nipaquard CMB» (benzyl alcohol, triethylene glycol, chloromethylisothiazoline, methylisothiazoline). The concentration of preservative in each sample was 0.1% (average concentration that is recommended for developing foam-washing agents). The antimicrobial activity of prototype gels was studied in vitro by diffusion in agar ("wells" method). The antimicrobial activity was measured immediately after sample preparation. All the studies were performed in aseptic conditions using a laminar box (biological safety cabinet AS2-4E1 "Esco" Indonesia). Results. According to the study, it was found that among the selected preservatives "Nipaquard CMB" was just the most active. When studying the antimicrobial activity of foam-washing agent samples with different concentrations of the preservative "Nipaquard CMB", it was found that namely the sample with the concentration of "Nipaquard CMB" of 0.1% showed satisfactory results due to its antimicrobial activity against all cultures such as bacteria and fungi. Conclusions. On the basis of microbiological studies it has been demonstrated that all the selected preservatives such as sodium benzoate, "Euxyl K300", "Germaben II" and "Nipaquard CMB" at a concentration of 0.1% have a broad spectrum of antimicrobial action and antimicrobial activity against all test strains used. We just chose «Nipaquard CMB» as a preservative at a concentration of 0.1% according to the results of experimental research, because it had the best results and a very high antimicrobial activity both against the bacterial cultures - *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pr. Vulgaris* and in relation to the effect on fungal cultures – *Candida albicans*, *Aspergillus brasiliensis*. **Keywords:** biological researches, preservative, antimicrobial activity, foam- washing agent, pH value.

## SUBSTANTIATION OF OVERCOMING OF ANTIBIOTIC RESISTANCE IN ACINETOBACTER BAUMANNII CLINICAL STRAINS BY USAGE OF DECAMETHOXINUM®

28-33

**Nazarchuk O. A., Paliy D. V.**

Introduction. Non-fermenting Gram-negative bacilli are known as one of the most frequent causative agents of hospital-acquired infections. *Acinetobacter baumannii*, as causative agent of infection complications of different localization, has obtained recently high resistance to antibiotics and has belonged to ESKAPE group of pathogens. Antimicrobials, recommended for the prophylaxis ant therapy of hospital-acquired infections, have been failing in their effectiveness and lead to selection of antibiotic resistant strains of *A. baumannii*. The aim of this research was to substantiate the way of overcoming of resistance in clinical strains of *A. baumannii*, by means of synergetic antimicrobial activity of antibiotics and antiseptic decamethoxinum®. Material and methods. The research was carried out on 190 clinical strains of *A. baumannii*, isolated from patients with burn disease in 2011-2015 years. The sensitivity of clinical strains of *A. baumannii* was determined to such antibiotics as ampicillin/sulbactam, cefoperazone, cefoperazone/sulbactam, meropenem, imipenem, amikacin, ciprofloxacin, gatifloxacin and antiseptic decamethoxinum® (DCM; Registration certificate № UA/14444/01/01 since 24.06.2015. Order of Ministry of Health of Ukraine № 373). The sensitivity of *A. baumannii* to antibiotics and DCM were done by means of disc-diffusion method and serial dilution one (Order of Ministry of Health of Ukraine №167 since 05.04.2007 year; EUCAST Expert rules). The research of the influence of antiseptic DCM on the sensitivity of acinetobacteria to antibiotics was studied on 35 clinical strains of *A. baumannii*, drafted from the general number of isolates enrolled in the research. For this, the sensitivity of *A. baumannii* to antibiotics in the presence of subminimal inhibitory concentrations (subMIC) of DCM was identified. The received experimental data were analyzed by «Statistica 6.0». Results and discussion. The changes of antibiotic sensitivity profile of *A. baumannii* during five years were shown. The sensitivity of *A. baumannii* to majority of antibiotics, selected for study, was found to decrease significantly. But the only ampicillin/sulbactam was found to have vice versa tendency.

We found the rising quantity of antibiotic resistant strains of *A.baumannii*. At the same time, high resistance of acinetobacteria in 2015 year was found to fluoroquinolones (ciprofloxacin – 96,1%; gatifloxacin – 95,8%). The in vitro research of combined activity of antiseptic remedy DCM and early mentioned antibiotics against clinical strains of *A.baumannii* demonstrated the reveal antibiotic effectiveness. As follows, minimal inhibitory concentrations of antibiotics decreased in 1,5-4 times in the mediums, had contained subMIC of DCM. Especially vividly this tendency was found in resistant clinical strains. Conclusion. Under selective influence of antibiotic use of protected by inhibitors  $\beta$ -lactams, carbapenems, fluoroquinolones, aminoglycosides the antibiotic resistance increases in *A.baumannii*, causative agents of infectious complications in patients with burn disease. The antiseptic remedy decamethoxinum® helps to improve antibiotic sensitivity in resistant *A.baumannii*.

**Keywords:** antibiotics, acinetobacteria, decamethoxinum, resistance.

## **METABOLIC PECULIARITIES AT EXPERIMENTAL GENERALIZED PROCESS CAUSED BY PSEUDOMONAS AERUGINOSA**

**34-38**

**Popov M.M., Malanchuck S.G., Mishina M.M.**

System of free radical oxidation is a non-specific link of most of pathologic processes formation in organism. Enzymological studies allowing the definition of both organospecific violations and the state of biological membranes are of great interest in complex approach to the estimation of structural and metabolic peculiarities of organism in conditions of inflammatory pathology. Thus the purpose of the given study is the definition of metabolic state peculiarities at experimental generalized process caused by *Pseudomonas aeruginosa*. According to the results of the carried out studies the activation of lipids peroxidation in myocardium of infected animals rises: the content of MDA and DC is increased in comparison with intact animals while SH-groups content and catalase activity are decreased, i.e. the oxidative stress takes place in myocardium of infected animals which leads to energy-hungry state process which is also proved by AF – enzyme activity increase which implements hydrolysis of monophosphoric esteris and LDH – enzyme of anaerobic glycolysis. Activity of AsAT, ALAT and  $\gamma$ -GTP is reliably higher which proves about the activation of protein biosynthesis into tissues which is connected with accelerated enzyme synthesis under the influence of inflammation mediators, i.e. compensatory reaction activation takes place. The similar picture is found in kidneys and liver: LPO under insufficiency of AOS, power-hungry state. The level of MCB – integrated indicator of intoxication as well as LPO products grows in blood of infected experimental animals which proves about high level of inflammatory process and organism intoxication. Increasing of protein concentration of acute phase – haptoglobulin – also proves about high level of inflammatory process. High activity of LDG (cytoplasmatic enzyme) proves about cytoplasmic membranes injury. The decrease of catalase activity and level of SH-groups of blood are found in organisms of experimented animals which proves that the content of thiol compounds in organism decreases due to oxidative modification to disulfide. Thus AOS enzymatic link becomes insufficient, as a result of which the oxidative stress is developing which harms tissues. The results of metabolic processes study at experimental generalized process caused by *Pseudomonas aeruginosa* allowed determining the activation of LPO processes which destroyed the structure of biological membranes modulating the development of free radical pathology in organism. Lingering stimulation of LPO leads to the exhaustion of AOS, inhibition of the processes of bioenergetics and biosynthesis which are specifying in the formation of biologic mechanisms of AOS suppression under the influence of MSM, acute phase proteins and the misbalance in fermentative link work.

**Key words:** metabolic state, experimental study, *Pseudomonas aeruginosa*, LPO level and AOS activity indices.

## **EVALUATION AND PREDICTIVE METHODS OF EPIDEMICAL SITUATION IN THE AREA OF ACUTE ENTERIC INFECTIONS**

**39-44**

**Malys N.G., Podavalenko A.P.**

**Introduction.** Despite the fact, that nowadays acute intestinal infections (AII) sick rate is decreasing, the aggravation of the epidemical situation is always there. Increased attention to AII caused by unpredictable epidemical rises of the AII diseases, which cannot be prevented without assessing the epidemical situation of these infections and forecasting of the levels of sick rate. However, developed mathematical methods of forecasting in most cases do not take into account the risk factors, also they are time-consuming and it is difficult to calculate them; and developed special computer programs, which predict infectious sick rates, are often in the lack in the institutions of sanitary-epidemiological service. An urgent problem for today is establishing of the most influential social and environmental factors, which can make a contribution to the spread of AII. The aim of this work was to improve the method of assessment and prediction of epidemic situation of AII by identifying the influence of climatic and demographic factors. Materials and methods. In order to determine the influence of meteorological and demographic factors on the epidemic process of acute intestinal infections the official reports of the State Sanitary and Epidemiological Service of Ukraine in Sumy region, the Department of Statistics, Sumy Regional Center for Hydrometeorology and Environmental Monitoring have been studied. Results and discussion. The work on the evaluation of the epidemical situation of the AII begins from collecting data, according to the AII sick rate. The main source of this information is the logbook of infectious diseases, which recorded all sick people that were found in the area. It is necessary to gather the initial information, calculate the sick rate and monthly distribution of AII cases on investigated area and evaluate the tendency. At the same time with accounting of AII cases on investigated territory, takes place a monitoring of air temperature, humidity and rainfall. Simultaneously, should be gathered the information about the population on the investigated area, its density (for 1 km<sup>2</sup>), natural and migratory movement. When the information is gathered, begins the stage of analytical research. At first, determines the long-term tendency of the sick rate. If the average time of growth of the sick rate ranges from 0 to 1.0% - the epidemical situation of this nosology is good, ranges from 1.1% to 5.0% - unstable, more than 5.0% - bad. The probability of the influence of natural and social "risk factors" (X) on the AII sick rate (Y) calculates according to this formula:  $R_{xy} = \frac{\sum dx \cdot dy}{\sqrt{\sum dx^2 \cdot \sum dy^2}}$ , where  $R_{xy}$  - correlation coefficient; dx - departure from the arithmetical average of levels of natural or social factors; dy - departure from the arithmetical average of the annual sick rate or seasonal distribution. If it was founded an authentic correlation ( $p < 0.05$ ) between the average monthly rates of air temperature, humidity, rainfall, number and density of population (per 1 km<sup>2</sup>), natural and migratory movements, and the sick rate of the AII nosological entities, the AII epidemical situation, in a case of increasing of the indicators of abovementioned "risk factors", will be also considered as unstable, which requires immediate elaboration and implementation of the targeted preventive steps. a result, the study found, that in current conditions in Sumy region the epidemical situation of shigellosis, AIIIDA and AIIUE is good, according to  $T_{red.av.} = -10.7\%$  for shigellosis, and  $T_{gr.av.} = +0.6\%$  for acute intestinal infection, caused by other determined agents (AIIIDA) and acute intestinal infections of unknown etiology (AIIUE); epidemical situation of salmonellosis is unstable, because:  $T_{gr.av.} = +2.3\%$ . It was found, that the number and density of population (1 km<sup>2</sup>). Similar relationships were also found between the levels of salmonellosis sick rate and net migration rate and natural population movement. On the seasonal distribution of salmonellosis sick rate affected temperature and rainfall. From the average daily temperature levels, to some extent, depended a frequency of cases, in which people with AIIIDA asked for medical service. Thus, despite the fact, that in the current conditions of Sumy region, epidemical situation of shigellosis and AIIIDA is considered as good, accordingly:  $T_{red.av.} = -10.7\%$  i  $T_{gr.av.} = +0.6\%$ , increasing of number and density of population and average daily temperature in this region can cause increase the sick rates of shigellosis and acute intestinal infection, caused by other determined agents. The epidemical situation of salmonellosis at the time of research was unstable ( $T_{gr.av.} = 2.3\%$ ), but if the indicators of the natural and migratory movement of population are increasing, the situation will be worse. Although, climatic factors haven't got a direct relation to the transmission of salmonellosis agents, and not directly related to it, but they influence on the dynamics of this disease. Conclusion. So, in a case of growth of number and density of population, can exist the favourable

conditions for increasing of shigellosis epidemical process; rising of natural and migratory movements and levels of daily average temperature and rainfall promote the probability of salmonellosis; rising of environmental temperature promotes the probability of AIDA. To avoid the aggravation of the AII epidemical situation, when the levels of natural and social "risk factors" are growing up, it is necessary to organize and take the prophylactic measures immediately. This method can be used by Hygienic and Epidemiological Center in conducting of epidemiological surveillances of intestinal infections for optimizing of preventive measures.

Key words: acute intestinal infections, epidemical situation, risk factors.

## **IDENTIFICATION OF SALMONELLA SEROVARS ISOLATED DURING 2009-2016 IN TERNOPIL REGION, UKRAINE** 45-46

**Pokryshko O.V., Barna T.B., Klymnyuk S.I.**

Introduction. Salmonellosis is registered in all regions of the world. Relevance of salmonellosis is due its global distribution, increasing incidence, even in developed countries, frequent outbreaks. The most reports in different countries demonstrated that one of the common Salmonella serotypes isolated from food and environmental samples had been serovars Salmonella Enterica, Typhimurium. In Ukraine 7.3% of all acute diarrheal infections have been cases of salmonellosis. Although large Salmonella outbreaks usually attract media attention, 60–80% of all salmonellosis cases are not recognized as part of a known outbreak and are classified as sporadic cases, or are not diagnosed as such at all. Material & methods. The samples from cultured stool, bile samples, food and environment were inoculated in the Tryptic Soya Broth (TSB) for the enrichment and detection of the bacteria. After 24 hours incubation, microorganisms were cultured on the MacConkey agar plates. Then biochemical and serological tests were performed to identify the serovars of the isolated Salmonella in Ternopil regional laboratory center, Ukraine. Results & discussion. Over the past 8 years the incidence of salmonellosis has varied between 8.41–3.3 cases per 100 thousand of population (35–90 cases). During this period, the lowest rate recorded in 2015 (3.3 cases per 100 thousand of population), the highest – in 2014. Analysis of morbidity has been shown that elevated levels of infection were due to outbreaks registered in 2011 (the number of infected people was 23), in 2013 (53 infected people), in 2014 (67 infected people) and in 2016 (16 infected people). In Ternopil region the dominant serovar of Salmonella spp. isolated from patients are *S. enteritidis* (56.8–93.5% of all cases of diseases) and *S. typhimurium* (7.8–43.8%) in last 8 years. Among the carriers circulate *S. enteritidis*, *S. typhimurium* – mainly (64.8% and 35.2% respectively). Not typical for Ternopil region serotypes, such as: *S. soncord* (in 2009), *S. vraenderup* (in 2015) were isolated from sick persons' samples; *S. soncord* and *S. wippra* (in 2009), *S. give* (in 2010), *S. braenderup* (in 2015), *S. haifa* (in 2016) – from carriers' samples. Serotypes *S. enteritidis*, *S. typhimurium* were isolated from food products (meat, culinary and confectionery, dairy products, eggs) – 72.4% of taken samples, from drinking water – 6.9% of samples, from environmental samples – 18.9%. Serotype *S. isangi* which is not typical for Ternopil region was isolated from the soil in 2010. Conclusion. Stabilization of the salmonellosis morbidity in the region supported by the absence of improvements epidemiological conditions. To prevent of outbreaks of salmonellosis among the population, the monitor the environment, of food raw materials and active conduction of the sanitary educational work among the population are required.

Keywords: Salmonella infection, serotype.

## **INFUENCE OF GENE POLIMORPHISM ON THE COURSE OF EPSTEIN-BARR VIRUS** 47-52

**Sorokina O.G.**

Introduction. Currently, infectious diseases occupy a dominant place in human pathology. The relevance of the Epstein-Barr virus infection (VEB) is due to a high degree of infection of the population around the world, as well as specific antibodies to this virus, detected in almost 95% of the adult population. Material and methods. We have examined 96 patients with chronic VEB infection, the main clinical manifestations of which were various immunopathological and immunodeficiency states, as well as 10 patients who had undergone a history of VEB without any complaints at the moment. The comparison group consisted of 10 clinically healthy people who had no record of infectious mononucleosis. Polymorphism of the genes was determined using the RFLP method (polymorphism of the length of restriction fragments) and the real-time PCR method using the Corbett Research Rotor-Gene-3000 and the DNA-detecting DT-96 amplifier. To detect the polymorphisms under study, amplification of certain sections of the corresponding genes was carried out. To determine the allelic variation of the IL28B gene, a commercial DNA-technology test system was used. SNP 39743165T>G (rs8099917) and SNP 39738787C>T (rs 2979860) of the IL-28B gene were used to detect point mutations using polymerase chain reaction and polymorphism of restriction fragment lengths. As a material for the study, DNA obtained from leukocytes was used with commercial reagents to extract DNA from the clinical material "Cytolysin" by AmpliSens (Russia). Statistical processing of the results of the study was carried out in accordance with the recommendations for statistical processing of biomedical data. The statistical software package STATISTICA 10.0 was used. Results and discussion. A group of patients with a record of VEB who do not currently have any complaints, and also in the comparison group for the IL-28B gene, found the CC genotype at the locus rs12979860, and the TT genotype at the locus rs8099917. This suggests that in patients with chronic VEB infection, when the genotype of the CC genotype in the locus rs12979860 and the TT genotype at the locus rs8099917 are detected in the IL-28B gene, a more favorable course. In the analysis of single nucleotide substitutions in the regulatory regions rs8099917 and rs12979860 of the gene IL28B, statistically significant evidence was obtained of a non-random combination of allele pairs CC and TT in individuals with a more favorable course of EBV infection was also obtained, and the number of episodes of exacerbation during the year is significantly less. Conclusion. The data suggest that the IL-28B genotype is a significant factor influencing the favorable course of the VEB infection, the frequency and severity of episodes of exacerbation throughout the year, and even the probability of transition or non-transition of the disease to a chronic form, and is an important factor in the prognosis. A more favorable course of EBV infection was noted in patients with CC genotype at the locus rs12979860 and TT genotype at the locus rs8099917 compared with the genotypes of CT and TT in the locus rs12979860 and the genotypes GT and GG at the locus rs8099917. Thus, the study of the genotype of IL-28B is an urgent issue and requires further study. Keywords: infectious mononucleosis, Epstein-Barr virus infection, genotype, cytokine, interleukin-28, the polymorphism of genes.

## **HYDROGEN PEROXIDE PRODUCTION ACTIVITY AND ADHESIVE PROPERTIES OF AEROCOCCI, ISOLATED IN WOMEN** 53-56

**Stepanskyi D.O., Kremenchutsky G.M., Chuyko V.I., Koshova I.P., Khomiak O.V., Krushynska T.Y.**

Introduction. Antagonistic activity of probiotic microorganisms against other species of bacteria is an important mechanism of their ecology and it is widely used in practice. This activity is inherent in many heme-deficient bacteria, which include aerococci, and can be composed of several components: the production of organic acids, antibiotics, lysozyme, hydrogen peroxide and others. Ability to produce hydrogen peroxide under aerobic conditions and in a state of relative anaerobiosis was established in aerococci. They were divided into strong and weak producers, depending on the amount of peroxides. Lack of data about peroxide-productive ability of aerococci, isolated from the lower genital tract of women, as well as a proven mechanism of hydrogen peroxide excretion in the oxidation of lactic acid, led to need in studying the aerococci hydrogen peroxide production level, to create autobacterial drugs, based on aerococci symbiont strains for sanitation of birth canal. Colonization resistance of the vaginal mucous and normal microflora value depends largely on the degree of adhesion of microbial cells to the mucosal surface. Along with numerous studies of lactobacilli adhesive properties to the vaginal epithelium, there are no data on the adsorption capacity of aerococci to the vaginal epithelial cells. Material and methods. 18 aerococci resident strains and 1 museum strain

were explored in total. Presence and quantity of autotrophic aerococci content in different parts of the birth tract (cervical canal, vagina, external genitalia skin (EGS) and perineum) was studied in 44 healthy women. Isolation and identification of aerococci from the women body was conducted by the method, taking into account growth on selective indicator medium, growth and biochemical activity in environments with selenium and tellurium salts, lactate oxidase and superoxide dismutase activity. Hydrogen peroxide was determined by iodometric method. Hydrogen peroxide production in 19 strains of aerococci (museum strain - *Aerococcus viridans* 167 and 18 strains of autotrophic aerococci) was investigated. The level of hydrogen peroxide production was compared with aerococci adhesive activity to cells of vaginal epithelium. Autotrophic strains were used to evaluate the aerococci adhesion on vaginal epitheliocytes. 18 aerococci resident strains and 1 museum strain were explored in total. Results and discussion. Comparison of hydrogen peroxide production levels between the museum and symbiotic *Aerococcus viridans* strains showed a lower level (from  $p < 0,05$  to  $p < 0,001$ ) in strains isolated from vaginal microbiocenosis, cervix and lower genital skin. Despite approximately the same number of multiplied cells, the amount of hydrogen peroxide produced by aerococci varied in a fairly large range. Thus, 8 *Aerococcus viridans* strains (167, 2V, 9V, 10V, 4S, 13S, 18S, 39 S) during reproduction in the number lg 8,9 - 9,1 SUN / ml, extracted considerable amount of hydrogen peroxide in the range 0, 34-0,79 mg / ml. However, 11 autotrophic aerococci strains, with identical number of multiplied cells produced hydrogen peroxide in much smaller amounts - within 0,07-0,24 mg / ml. The foregoing results allowed to divide aerococci cultures into two groups: strong and weak peroxide producers. Comparative evaluation of aerococci strains isolated from the birth canal activity, showed the predominance of weak producers of hydrogen peroxide (7 - 61.1% of cases) under strong (11 - 38.9%). Aerococci strains isolated from microbiocenosis of EGS skin showed the maximal activity compared with strains isolated from other parts of the birth path - 4 out of 5 cases (80.0%) compared with 3 of 13 (23.1%) cases ( $p < 0,05$ ). The aerococcal ability to adhere varied in a wide range (AA from 3.25 to 10.24). 3 strains were isolated from all aerococcal strains with low adhesion (15.8%), with average degree - 12 (63.2%) and 4 highly adhesive aerococcal strains were identified (21.0%). Analysis of the aerococci symbiont strains ability to adhere (tab. 2) showed that highly adhesive strains were observed only in the vagina, while autotrophic strains isolated from the skin of the genital organs had usually low or medium level of adhesion to epithelial cells. The average index of adhesion (AA) for all strains isolated from the vagina, equaled  $7,87 \pm 0,12$ , for the cervical canal strains -  $6,30 \pm 0,09$ , for strains from the skin of EGS -  $4,89 \pm 0,11$  ( $p < 0,001$  in all comparisons). Conclusion. 1. *Aerococcus viridans* autotrophic strains are a component of normal flora of the female genital organs. 2. Aerococci autotrophic cultures isolated from the birth canal, are mainly weak hydrogen peroxide producers (61.1%) and have medium adhesive (61.1%) and high adhesive (22.2%) properties on vaginal epithelium. 3. Strains isolated from vagina possessed higher adhesive ability ( $p < 0,001$ ). 4. *Aerococcus viridans* museum strain 167 was the strongest hydrogen peroxide producer (from  $p < 0,05$  to  $p < 0,001$ ).

#### ANTIMICROBIAL ACTIVITY OF EXTRACTS OF IRIS HUNGARICA AND IRIS SIBIRICA

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Introduction. Referring to the latest data, infectious diseases command a large part of among the total number of pathologies in the world and are an important problem in medicine. The leading role in prevention and treatment of diseases of microbial origin belongs to antibacterial chemotherapeutic agents. Advantages of antibiotics of synthetic origin are the high activity compared to phytochemical drugs. But it is known that microorganisms can release the resistance to synthetic antibiotics, so the use of drugs based on the plant materials is appropriate: phytochemical drugs more rarely induce the formation of resistance of the strains of microorganisms, they have a gentle action, can be used for a long-term, have the low cost. Therefore, it is appropriate to examine the drug plants with the aim of determination their antibacterial activity. *Iris hungarica* Waldst et Kit. and *Iris sibirica* L. are the representatives of the family Iridaceae, genus *Iris* and they have a wide spectrum of the pharmacological activity. Biologically active substances that were recovered from plants of the genus *Iris* (tectoridin, iristectorigenin B, nigracin, kaempferol, quercetin, etc.) exhibited an antitumor, antimicrobial, estrogenic, insecticidal, antiplasmodial, anticholinesterase action, they were the inhibitors of enzymes and exhibited the immunomodulatory properties, which made these plants perspective for the research study. Raw materials *Irises* are constituent components of more than 9 medicines. Materials and Methods. The objects of the study were the leaves and rhizomes of *Iris hungarica* and *Iris sibirica* that were prepared during the growing season in 2014 in the M.M. Gryshko National botanical garden (Kiev, Ukraine). The dry and lipophilic extracts from the leaves and rhizomes of *Irises* were used to establish the antimicrobial activity. For the study of extracts antimicrobial activity was used agar well diffusion method. According to the WHO recommendations the following test-strains were used: *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Bacillus subtilis* ATCC 6633, *Proteus vulgaris* ATCC 4636, *Candida albicans* ATCC 885/653. The 18 to 24-hour culture of microorganisms was used for the test. Mueller-Hinton agar was used for bacteria. The strains of *Candida albicans* were cultivated using Sabouraud agar. Method of serial dilutions was used for the examination of antibacterial properties of selected extracts. The concentration of substances was 1) 1000 µg/ml; 2) 500 µg/ml; 3) 250 µg/ml; 4) 125 µg/ml; 5) 62.5 µg/ml. To each test tube was added of 0.1 ml 109 microbial cells test strains. Examined preparations represented the alcohol and aqueous solutions of the dry and lipophilic extracts of *Irises* in the different concentrations. Water is the solvent for the dry extracts of *Iris hungarica*, for the lipophilic – is 70% ethyl alcohol. For dissolution of the dry extracts of *Iris sibirica* was used water, 70% and 96% ethyl alcohol, for lipophilic extracts – was used 70%, 96% ethyl alcohol. The concentration of the substances was 1.0 % in all experiments. In the capacity of the comparative drug was selected an alcohol solution of chlorophyllipt in the dose of 10 µg/ml («Chlorophyllipt alcohol solution 1%» 100 ml, «GNCLS» Pilot Plant). Results and discussions. The dry extract of the leaves of *Iris hungarica* at the concentration 1% has a more pronounced antibacterial activity than the extract of the rhizomes and is the most susceptible to gram-negative bacteria – *Escherichia coli*, *Proteus vulgaris*, *Pseudomonas aeruginosa*. At that time, as the dry extract of the rhizomes of *Iris hungarica* at the concentration 1% is more susceptible to gram-positive bacteria. The lipophilic extracts of the leaves and rhizomes were more susceptibility to gram-positive bacteria. The dry extracts of the leaves and rhizomes of *Iris sibirica* in aqueous and alcohol solutions have a more pronounced antimicrobial activity against gram-negative bacteria and fungi. The lipophilic extracts of *Iris sibirica* were more susceptible to gram-negative bacteria. In summary of the results of the examinations "technique of wells" by definition the diameters of growth zones, the antibacterial properties were presented in the lipophilic extracts of the leaves and rhizomes of *Iris hungarica* and the dry extracts of the leaves and rhizomes of *Iris sibirica*. The lipophilic extracts of the leaves and rhizomes of *Iris hungarica* and the dry extracts of the leaves and rhizomes of *Iris sibirica* exhibit a bacteriostatic activity against a wide range of test strains of microorganisms and *Candida*. Conclusions. Antibacterial properties have been examined of the dry and lipophilic extracts of the leaves and rhizomes of *Iris hungarica* and *Iris sibirica*. It has been established that the dry ethanolic extracts and lipophilic extracts from leaves and rhizomes of *Iris hungarica* and *Iris sibirica* exhibit an antimicrobial activity against the test strains of microorganisms of the different taxonomic groups. Thus, this examination offers an opportunity to use *Iris hungarica* and *Iris sibirica* as a raw material to produce the substances with antibacterial pharmacological effect for the further development of antimicrobial action.

Keywords: *Iris hungarica*, *Iris sibirica*, leaves, rhizomes, extracts antimicrobial activity.

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