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course of the disease lymphoproliferative disorders like T or NK cell lymphomas may arise. The determined pattern of latent gene expression during CAEBV is latency type II. In this review we sum up the existing data linking EBV with rheumatoid arthritis and systemic erythematous lupus. SLE patients have abnormally high expression of several viral mRNAs coding for BZLF1, gp350, viral IL10, LMP1, LMP2 and EBNA1. So during this pathology EBV persists in litic and in latent phases. Also it has been demonstrated the humoral response to both latent and lytic EBV antigens in both sera and synovial fluids from patients with rheumatoid arthritis. Chronic Fatigue Syndrome (CFS) is characterized by severe fatigue with typical, cognitive dysfunctions and flu-like symptoms. Numerous studies find evidence for an association of CFS with EBV. In a subset of patients CFS begins with infectious mononucleosis. Elevated antibodies against EBV dUTPase and DNA polymerase has been found in CFS patients but not in controls Consistent with these data, elevated titers antibodies to ZEBRA detected in CFS patients. These data suggest that during CFS virus reactivate and enter in lytic replication. But according to other reports EBV virus in CFS patients replicates only latently. So, in the articles we summarized the data which reveal the connection between the disease development, phase of persistence and the program of gene expression.

Key words: Epstein-Barr virus, persistence, virus lytic replication, phase of latency, chronic active EBV infection.

СУЧАСНИЙ ПОГЛЯД НА ЕТІОЛОГІЮ І ЛІКУВАННЯ ТАЗОВОГО БОЛЮ ПРИ ЗАПАЛЕННІ ГЕНІТАЛІЙ У МОЛОДИХ ЖІНОК

Чернякова Г.М., Косілова О.Ю., Добровольська Л.А.

THE MODERN VIEW OF THE ETIOLOGY AND TREATMENT OF PELVIC PAIN IN YOUNG WOMEN WITH GENITALS INFLAMMATION

Chernyakova A. M., Kosilova O. Yu, Dobrovol'skaya L. A.

Sensitive issue of modern gynecology can be considered widespread and substantial "rejuvenation" of inflammatory diseases of the pelvic organs in women of reproductive age.Ascending path of infection prevails in the pathogenesis of inflammatory diseases of the internal genital organs. Invasion of microbes in the internal genital organs may occur during the various manipulations, different pelvic operations and in the postpartum period. The degree of colonization of microorganisms of the vagina and cervix plays an important role in the development of the infectious process. In obstetrics and gynecology inflammatory diseases can be caused by pathogenic and non- pathogenic (opportunistic) microorganisms. Among the pathogens causing the defeat of the female genital organs, most often found N. gonorrhea, C. trachomatis, T. vaginalis. Opportunistic pathogens, part of the normal flora of the genital tract, in certain circumstances, can become agents of post-partum, post-abortion, post-operative complications and inflammatory diseases of the female genital organs. Among the opportunistic pathogens that are part of the normal microflora of the female genital organs, found hemolytic and non-hemolytic streptococci (the most important are streptococci groups A, B, D), coagulase-negative staphylococci and micrococci (allocated 60% and 35% of healthy women, respectively). They can cause secondary infectious processes of the urinary system, inflammatory diseases of the genital organs of pregnant women and mothers with immunosuppression. These microorganisms are often the agents of inflammatory diseases in the newborn, especially with low weight and malnutrition children. Gram-negative opportunistic bacteria that are isolated from the genital tract, can also be agents of inflammatory processes of various localization. Escherichia coli is the most frequently obtain and cause urinary tract infection in pregnant and postpartum women. It is also causative agent of postpartum sepsis and postoperative peritonitis. Among other gram-negative bacteria should be noted genus Klebsiella. Therefore, therapy of inflammatory diseases of the pelvic organs high demands due to the risk that represents this state to the reproductive function of patients. The mixed nature of the infection, the increasing rates of resistance of pathogens to antibiotics creates difficulties in selecting antimicrobial therapy, which remains the empirical till now. The inclusion of specific bacteriophages and plant antiseptics in therapeutic regimens for local treatment of inflammatory diseases of the vagina associated with an excessive colonization of the vaginal mucosa by aerobic opportunistic bacteria justified and can serve as an alternative to the traditional antibiotic therapy. All this determines the necessity for further studying the etiology and pathogenesis of infectious and inflammatory complications, the development of new highly effective methods of prevention and treatment.

Key words: inflammatory diseases, antimicrobial treatment, harmons, women reproductive system, dismenorrhea.

ЕКСПЕРИМЕНТАЛЬНІ РОБОТИ (EXPERIMENTAL STUDY)
ФАРМАЦІЯ (PHARMACY)

ANTIMICROBIAL ACTIVITY OF [1,2,4]TRIAZOLO[4,3-a]PYRAZIN-8(7H)-ONE DERIVATIVES

Kulikovska K. Yu., Kovalenko S. S., Drushlyak O. G., Zhuravel I. O., Kovalenko S. M.

Today the problem of microbial resistance to antibacterial agents becomes the global one. Antimicrobial drugs that are in the pharmaceutical market do not satisfy the needs of modern treatment regimens, particularly Hospital-acquired infections. Therefore, the search for new and effective means of this pharmacological group is an important task of medical chemistry. From the literature it is known that derivatives of [1,2,4]triazolo[4,3-*a*]pyrazine show a wide range of biological actions, including antimicrobial and fungicidal. This makes it relevant microbiological study of primary derivatives of [1,2,4]triazolo[4,3-*a*]pyrazine for identifying promising compounds of the series and then study it in biological experiment.Using the PASS C&T (Prediction Activity Spectra for Substances: Complex & Training) program and based on published data, we have generated virtual library of derivatives of [1,2,4]triazolo[4,3-*a*]pyrazine. As a result, we have received 35 new synthetic compounds of 7 series that were not previously described in the literature.

Materials and methods

The research of antimicrobial and fungicidal activity of the synthesized compounds was carried out in the laboratory of antimicrobial agents GA "Mechnikov Institute of microbiology and immunology" under the leadership of PhD, senior scientist V.V.Kazmirchuka. The activity of the synthesized compounds were studied by conventional method of the two-fold serial dilutions in liquid and solid nutrient medium. For primary screening we have used a set of clinical and reference strains of microorganism: *Escherichia coli* ATCC 25922 (F-50), *Staphylococcus aureus* ATCC 25923 (F-49), *Bacillus anthracoides* ATCC 1312, *Pseudomonas aeruginosa* ATCC 27853, *Candida albicans* ATCC 885-653. As the reference preparations were chosen Palin - modern antimicrobial agent of class of fluoroquinolones, Nevigramon - nalidixic acid derivative and Fluconazole - modern antifungal agent. Activity of substances determined by the minimum bacteriostatic ($MB_{st}K$) and minimal bactericidal (MB_cK) concentrations. All experiments were accompanied by appropriate controls.

Results and Discussion

As a result of microbiological screening of 35 compounds we have allowed to identify a number of derivatives of [1,2,4]triazolo[4,3-

a]pyrazine-8(7H)-one with antimicrobial and antifungal activity. The most pronounced effect showed compounds that contains in their structure aryl moiety with halogen atom, or N-arylatsetamide group in position 3 or 2 of the heterocycle. Principal condition for the demonstration of antifungal activity is presence of Sulfur atom in the triazole cycle.

Conclusions

The substance of the series N^7-aryl/benzyl-3-thioxo-[1,2,4]triazolo[4,3-*a*]pyrazin-8(7*H*)-ones showed the best antimicrobial and antifungal activity of all synthesized compounds. Compound 7-(3-chloro-2-methyl-phenyl)-3-thioxo-[1,2,4]triazolo[4,3-a]pyrazin-8(7*H*)-one **4***{4}* showed high values of antimicrobial activity against gram-negative microorganisms ($MB_{st}K$ – 12.5-25.0 mkg/ml, MB_cK – 25.0-50.0 mkg/ml) and was the most promising for further development.

Key words: [1,2,4]triazolo[4,3-*a*]pyrazin-8(7*H*)-one derivatives, antimicrobial activity, antifungal activity.

КІЛЬКІСНЕ ВИЗНАЧЕННЯ ОСНОВНИХ ГРУП РЕЧОВИН В ГРАНУЛАХ НА ОСНОВІ ЛІКАРСЬКОЇ РОСЛИННОЇ СИРОВИНИ ДЛЯ ЛІКУВАННЯ ЗАХВОРЮВАНЬ ШЛУНКОВО-КИШКОВОГО ТРАКТУ

Спиридонов С.В., Котов А.Г.

QUANTITATIVE DETERMINATION OF MAIN GROUPS OF SUBSTANCES IN GRANULES ON THE BASIS OF MEDICINAL VEGETABLE RAW MATERIAL FOR TREATING GASTROINTESTINAL DISEASES

Spiridonov S.V., Kotov A.G.

In the last time a significant increasing of gastrointestinal tract diseases has been observed. The poor quality and irrational feeding, environmental pollution, psychological and other factors is the causes of this. Very often the gastrointestinal tract has a multifactorial pathological effects, also affecting the hepatosphere organs and urogenital system. Also a great importance have accompanying disorders of the central nervous system. Thus we must to require a comprehensive approach to the creation of drugs for use in gastroenterology, the assortment range of which should be expanded. Advantageous position in this case takes a phytotherapy using drugs based on medicinal plant raw material, which acting on the main areas of the pathological process. For this purpose the scientists from the National University of Pharmacy (Kharkov, Ukraine) was created a complex herbal drug in the form of granules under the code name "Poligerbagastrin", includes the following types of medicinal plant raw material powders: helichrysum arenarium flowers, corn stigmas, horsetail grass, knotweed grass, horse chestnut seeds, licorice roots and wheat bran.

Materials and methods

To determine the quantity of biologically active substances the method of spectrophotometry in the visible and UV spectral region was used. This method is well studied and available, equipped with high-precision hardware. He also described in the Ukrainian normative documents and contained in the world's leading pharmacopoeias. For determination was used the unifieds methods, which shown in pharmacopoeia monographs and other reference literature. Determination was carried out with a spectrophotometer HP 8543 UV-VIZ of «Hewlett Packard» company, USA.

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Results and discussion

For the quantitative determination of flavonoids was used a methodology, which based on the complexation reaction of isolated by acid hydrolysis and extraction with ethylacetate hydrolysis products with aluminum chloride in methanol - ethyl acetate - acetic acid environment and calculation of flavonoid content as hyperoside recalculating. For the quantitative determination of polyphenols was used the methods of State Pharmacopoeia of Ukraine "Determination of tannins in herbal drugs" or European Pharmacopoeia «Determination of tannins in herbal drugs». The method is based on the color reaction of polyphenolic substances, which including in the plant raw material, with phosphomolybdic-tungsten reagent and measuring the optical density of the resulting solution at the wavelength of 760 nm. The content of total polyphenols in the drug was determined as pyrogallol recalculating.

Conclusions

1. The determination of quantitative content of biologically active substances in granules based on medicinal plant raw material for the treatment of gastrointestinal tract diseases is carried out.
2. In the studied sample of granules contents of flavonoids, calculated as hyperoside, which equal to 0.43% and the polyphenols, calculated as pyrogallol, which equal to 0.44% has been established.
3. The data obtained can be used to develop the normative and technical documentation.

Keywords: gastrointestinal tract diseases, medicinal plants raw material, granules, spectrophotometry, quantitative determination.

ИССЛЕДОВАНИЕ ВКЛАДОВ БОКОВЫХ АМИНОКИСЛОТНЫХ ОСТАТКОВ ПОЛИМИКСИНА B_3 В ЕГО СВЯЗЫВАНИЕ С ЛИПОПОЛИСАХАРИДОМ ВНЕШЕЙ МЕМБРАНЫ *E.COLI* МЕТОДАМИ МОЛЕКУЛЯРНОГО МОДЕЛИРОВАНИЯ

Лисняк Ю. В.

MOLECULAR MODELING STUDY OF THE CONTRIBUTIONS OF SIDE AMINO ACID RESIDUES OF POLYMYXIN B_3 TO ITS BINDING WITH *E.COLI* OUTER MEMBRANE LIPOPOLYSACCHARIDE

Lisnyak Yu. V.

Introduction

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Last decades, antimicrobial peptides (AMPs) are the subject of intense investigations aimed to develop effective drugs against extremely resistant nosocomial bacterial pathogens (especially Gram-negative bacteria). In particular, there has been greatly renewed interest to polymyxins, the representatives of AMPs which are specific and highly potent against Gram-negative bacteria, but have potential nephrotoxic side effect. A prerequisite of purposeful enhancement of therapeutic properties of polymyxins is a detailed knowledge of the molecular mechanisms of their interactions with cell targets. Lipopolysaccharide (LPS), the main component of the outer leaflet of outer membrane of gram-negative bacteria, is a primary cell target of polymyxins. The aim of the paper was to study the peculiarities of molecular interactions of polymyxin B_3 with lipopolysaccharide of the outer membrane of gram-negative bacterium.

Materials and methods

The complexes of polymyxin B_3 (PmB_3) and its alanine-derivatives with *E. coli* outer membrane lipopolysaccharide were built and studied by molecular modeling methods (minimization, simulated annealing, docking). Atom coordinates of polymyxin B_3 and LPS structures were taken from nuclear magnetic resonance and X-ray crystallography experiments, respectively. The AMBER03 force field was used with a 1.05 nm force cutoff. Longrange electrostatic interactions were treated by the Particle Mesh Ewald method.

Results and discussion
Alanine scanning of PmB_3 molecule has been carried out and the role of its side amino acid residues in the formation of complex with lipopolysaccharide has been investigated. It has been shown that substitutions of polymyxin's Dab residues in positions 1, 3, 5, 8 and 9 for alanine markedly reduce the binding energy of PmB_3-LPS complex, where as the similar substitutions of residues in positions 2, 6, 7 and 10 leave the binding energy virtually unchanged. Structural aspects of antimicrobial action of polymyxins have been analyzed. Changes of minimal inhibitory concentrations (MIC) of alanine-derivatives of polymyxin and binding energies in dependence on the alanine substituent position were parallel, except Ala2- PmB_3 mutant.
Conclusions
Polymyxin's side Dab residues, especially Dab1, Dab5, Dab 8 and Dab9, essentially contribute to the energy of polymyxin B_3 binding with LPS of the outer membrane. Contribution of the others polymyxin's side residues to the binding energy of the complex of polymyxin B_3 with LPS was insignificant.
Key words: polymyxin, lipopolysaccharide, alanine scanning, binding energy

ВИКОРИСТАННЯ КОМП'ЮТЕРНОЇ ПРОГРАМИ PASS ТА МОЛЕКУЛЯРНОГО ДОКІНГУ ДЛЯ ПОШУКУ НОВИХ АНТИКОНВУЛЬСАНТІВ

Перехода Л.О.

THE APPLICATION OF PASS-COMPUTER PROGRAMME AND MOLECULAR DOCKING FOR THE SEARCH OF NEW ANTICONVULSANTS

Perekhoda L.O.

Introduction. Currently the priority goal of designing drugs is the integration of the methods of organic chemistry and pharmacology. The application of computer programmes which can predict interaction of potential drugs with molecules of biological targets makes possible to decrease the number of experiments on laboratory animals. Thereby the economic efficiency of production of new medicines increases. Models of the research the anticonvulsant activity (in particular, korazol, thiosemikarbazid, strychnine, etc.) are the most rigid experimental models of pharmacological screening, which basically entails the pains of laboratory animals or their death. The application of computer programmes in the research of potential anticonvulsants has economic and social desirability and high level of importance for the pharmaceutical science and health care. The most perspective methods of research are the virtual screening, molecular docking. These methods allow to evaluate the affinity of a substance to a specific biological target, i.e. to identify an inhibitor of a particular enzyme or protein.
Material and methods. We have carried out the construction of 50 groups substances (507 hypothetical structures). We have chosen the five-membered di(three)azaheterocycle as basic pharmacophores to form virtual structures because firstly their structure is similar to cyclic conformation of neurotransmitter and secondly according to the literature perspective anticonvulsants had already found among these derivatives. Computer prediction of pharmacological activity for all compounds of virtual database was performed using the PASS (Prediction of Activity Spectra for Substances) computer programme. Results obtained by PASS-computer programme showed prospects of search the anticonvulsants among 10 groups of derivatives di(three)azaheterocycles (probable activity (Pa) of substances of these groups are from 0.5 to 0.84). In order to determine the potential anticonvulsant activity of 1,2,3(1,2,4)triazole, 1,3,4-oxa(thia)diazole we investigated the mechanisms of action that involve the interaction of the ligand NMDA-, $GAMK_A$- or glutamate receptors and GABA-AT ligand-enzyme. We have perfomed docking research for our structures and for known anticonvulsants using the Fast Dock method, in which both protein and ligand are rigid (Software SCIGRESS; Fujitsu, Fukuoka, Japan). We have evaluated affinity of the investigated structures with molecules biotargets: $GABA_A$ receptor protein (PDB code 1GNU), glutamate receptor protein Glu-1 (PDB code 1EWK), GluN1 NMDA receptor protein (PDB code 3Q41) and protein enzyme GABA-AT (PDB code 1OHW). **55-60**
Results and discussion. As a result, we have obtained the values of scoring functions Consensus, which enabled to evaluate affinity compounds and biological anticonvulsant targets and identify 11 perspective groups of compounds (number of compounds 190) that can selectively inhibit NMDA, a GABA - or glutamate receptors and GABA aminotransferase enzyme in comparison with known anticonvulsant drugs. The number of active groups of the results PASS prediction according to the obtained results is 10 (the number of compounds 168). It should be noted that result of docking research coincided with the results of PASS prediction for eight groups of compounds.
Conclusion
1. Eleven groups of compounds derivatives of 1,2,3(1,2,4) -triazols, 1,3,4-oxadiazoles and 1,3,4- thiadiazoles was selected for further screening as perspective anticonvulsants;
2. GABA-ergic mode of action for 8 groups of derivatives and glutamatergic mode of action for 3 groups of derivatives five-membered di(three)azaheterocycle was predicted.
Keywords: docking, anticonvulsant activity, PASS computer program, di (three) azaheterocycle.

ПРОТИМІКРОБНІ, ФІЗИКО-ХІМІЧНІ ВЛАСТИВОСТІ ЛІКАРСЬКИХ АНТИСЕПТИЧНИХ ПРЕПАРАТІВ

Палій Д. В., Назарчук О. А., Береза Б. М.

ANTIMICROBIAL, PHYSICAL AND CHEMICAL QUALITIES OF MEDICINAL ANTISEPTIC DRUGS

Paliy D. V., Nazarchuk O. A., Bereza B. N.

In our research results of the study of antimicrobial, physical and chemical qualities of antiseptic medicines of decamethoxin (DCM). Antimicrobial activity of DCM, palisan, decasan, deseptol against srains of *S.aureus* (n 56), *S.epidermidis* (n 26), *E.coli* (n 24), *P.mirabilis* (n 11), *P.vulgaris* (n 8) was studied by means of method of serial dilutions. Obtained data of mass spectrometry study of antimicrobial compositions with constant concentrations of DCM have shown that medicinal forms of DCM are complex physical and chemical systems, because of different origin and number of adjuvant ingredients used during their fabrication. Among synthetic quaternary ammonium agents there have been found the substance (commercial name of medicine is decamethoxin) to have high antimicrobial activity against strains of gram-positive and gram-negative microorganisms, an also *C.albicans*. There was found that antimicrobial activity of antiseptic palisan had been higher comparably to DCM in equivalent concentration. The composition and concentrations of acting agents and the methodology of preparation of palisan have been substantiated on the basis of microbiological, mass spectrometry characteristics of antiseptics DCM, palisan. **61-66**
Key words: antiseptics, decamethoxin, decasan, palisan, mass spectrometry.

СКРИНИНГ АНТИМИКРОБНЫХ СВОЙСТВ СПИРТОВОДНЫХ ВЫТЯЖЕК ИЗ НЕКОТОРЫХ ВИДОВ РАСТИТЕЛЬНОГО СЫРЬЯ СОДЕРЖАЩЕГО ХИНОНПРОИЗВОДНЫЕ

Бойко Н. Н., Зайцев А. И. , Осолодченко Т. П.

SCREENING OF ANTIMICROBIAL PROPERTIES OF ETHANOLIC EXTRACTS FROM SOME KINDS OF RAW MATERIALS WITH QUINONEDERIVATIVES

Boyko N.N., Zaytsev A.I., Osolodchenko T.P.

This paper presents data on screening of antimicrobial properties of extracts from some kinds of raw materials (18 plants) with hydroquinone, naphtoquinone or anthraquinone derivatives. Some technological parameters of extracts (density and concentration of extraneous substances) have been determined. The most appropriate microbiological method of studying antimicrobial properties of extracts, diffusion method of "well", has been applied; special mathematic method of comparison of antimicrobial properties of extracts vector analysis has been applied in order to study and to compare antimicrobial properties of extracts. Indexes of antimicrobial properties of extracts have been determined: a complex index of medicinal product antimicrobial activity for quantitative estimation of antimicrobial effect - A, and square of correlation coefficient - r^2, which demonstrates the spectrum of antimicrobial activity of the extracts (degree of similarity to the standard). The most active extracts have been selected; they have antimicrobial properties of medium strength: from the herb of chimaphila umbellata A=2.20; the fruits of rhamnus cathartica A=2.12; the root of rubia tinctorum A=2.11; the bark of frangula alnus A=2.05; the root of rumex confertus A=2.04; the leaf of pyrola rotundifolia A=2.00; and leaf of arctostaphylos uva-ursi A=2.08 (but extract from uva-ursi did not affected on 2 strains of microorganisms r^2=0.64). Low levels of antimicrobial activity have been demonstrated by the extract obtained from the leaf of urtica dioica A=0.72, r^2=0.34. The mean result of the complex index of antimicrobial activity for the most of extracts from plants containing quinonederivatives is A = 1.77 (on 70% vol. ethanol at a ratio of raw material : extracting agent – 1:7 wt. : vol.) and may range from 0.68 to 2.85. The mean result of the correlation coefficient is r = 0.93 and may range from 0.59 to 0.99. The mean result of the concentration of extractives in extracts is C = 0.0386 g/g extract and may range from 0.0017 to 0.0755 g/g extract. The mean result of the extract density is ρ = 0.897 g/cm³ and may range from 0.877 to 0.917 g/cm³. It is noted antimicrobial properties of the solution of alizarin 0.1% m / m in 70% vol. ethanol, which in studies showed moderate strength antimicrobial properties: A = 1.60 and inhibited the growth of all tested strains of microorganisms r=0.99. This potentially allows to predict the antimicrobial properties of extracts from plants containing derivatives of alizarin on its concentration in them. Study data show significant antimicrobial properties of numerous kinds of raw materials that contain of hydroquinones, naphtoquinones, anthraquinones and high possibility of their use in complex phytochemical medicinal products as antimicrobial component.

Keywords: antimicrobial properties, raw material, extracts, hydroquinones, naphtoquinones, anthraquinones.

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МЕДИЦИНА (MEDICINE)

ЗАСТОСУВАННЯ ПРЕПАРАТІВ НА ОСНОВІ БАКТЕРІАЛЬНИХ ЛІЗАТІВ У ТЕРАПІЇ ХРОНІЧНОГО ТОНЗИЛІТУ У ПАЦІЄНТІВ З РЕВМАТОЇДНИМ АРТРИТОМ

Коляда Т.І., Тупотілов О.В., Вдовіченко Н.І., Літвиненко О.Ю.

THE USE OF PREPARATIONS BASED ON BACTERIAL LYSATES IN THE TREATMENT OF CHRONIC TONSILLITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Kolyada T.I., Tupotilov A.V., Vdovichenko N.I., Litvinenko O.Y.

In the therapy of decompensated form of chronic tonsillitis (CT) were used as immunomodulatory agents IRS and Ismigen. These bacterial lysates differ in the bacterial setting, the method of preparation (chemical, mechanical) and the method of application.Rheumatoid arthritis (RA) is one of the important factors that could significantly complicate the therapy of chronic tonsillitis. RA is a chronic immune inflammatory disease that progressively affects connective tissue mostly of the peripheral joints and it has a wide range of extra-articular manifestations. The aim of our study was to explore the dynamics of immunologic indicators during the active disease and treatments in patients with decompensate form of chronic tonsillitis, including tonsillitis complicated with RA.

Materials and methods.

33 patients with decompensate form of chronic tonsillitis in active period of disease observed during the study. Patients were divided into the following groups: 24 persons with the decompensate form of CT, 9 persons with the rheumatoid arthritis and 9 persons with the decompensate form of CT complicated with RA in remission stage. The control group consisted of 15 apparently healthy persons. Concentrations of serum IgA, IgM, IgG were determined by the method of radial immune diffusion by Manchini. Levels of sIgA, IFN – γ and rheumatoid factor in the blood serum of patients were evaluated using ELISA test systems of "Vector-best". Patients of group CTD (with decompensate form of chronic tonsillitis) were divided into subgroups CTD1 and CTD2, depending on the applied treatment. Both subgroups treated with standard therapy for two weeks and received Derynat during 1 month by 2 drops in each nostril twice a day. After 30 days of the standard therapy beginning the subgroup CTD1 patients received IRS 19 during two weeks, one intranasal inhalation in each nostril 3 times a day. Patients subgroup CTD2 and CTD+RA instead IRS 19 received Ismigen after 30 days of the beginning of the standard therapy, during 10 days, sublingually 1 per day.Patients with RA were at the stage of clinical remission and do not receive basic disease-modifying drugs for at least 6 months after the last course of therapy. The effectiveness of the treatment was assessed by the general state of the patients according to oropharyngoscopy, concentration of IgA, IgM, IgG and IFN-γ in serum and sIgA in pharynx secret after 45 days of observation.Antibodies to microbial antigens (antistreptolysin O-hemolytic streptococci) were determined before treatment and after 45 days using passive hemagglutination reaction.Statistical analysis of the results was performed using the Mann-Whitney U test. According to the accepted level of reliability index value between the groups (p), which constituted or were less than 0.05.

Results and discussion

1. In all groups before treatment was determined deficiency of humoral immunity. The level of sIgA was significantly reduced relative to controls as in patients with exacerbation of decompensate form of chronic tonsillitis with RA (CTD + RA group) and in the group with chronic tonsillitis without RA (CTD group). The level of IgG before treatment group CTD + RA was significantly elevated relative CTD group, the comparison group (patients with RA without tonsillitis) and the control group.2. Preparations Ismigen and IRS 19 demonstrated high efficacy as immune modulatory agents in the treatment of decompensate form of chronic tonsillitis in the acute stage. Combined with Derynat use of these drugs after standard therapy allowed to normalize humoral

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immunity. In the subgroup of patients which received Ismigen level of sIgA after 45 days was significantly higher with respect to the subgroup that received IRS 19. These differences may be related both to the various quantitative and qualitative antigenic composition of the drug, and the difference in the method and circuit their application and in accordance with the bioavailability of the components of bacterial lysates.3. Patients at CTD + RA before treatment is characterized by elevated levels of ASO for the group CTD. ASO level was significantly higher than normal level in CTD and CTD + RA groups.4. Application of bacterial lysates containing antigens of hemolytic streptococci, such as Ismigen or IRS 19, does not cause increase level of ASO and rheumatoid factor in all groups of patients, indicating an insufficient level of immunogenicity of these drugs to influence the course of RA in the inactive phase of the disease.

Keywords: immunity, chronic tonsillitis, rheumatoid arthritis, immunoglobulins, bacterial lyzates.

ДОСЛІДЖЕННЯ ПРОТИМІКРОБНОЇ АКТИВНОСТІ КОМБІНАЦІЙ ФОСФОМІЦИНУ З ЦЕФЕПІМОМ ТА ФОСФОМІЦИНУ З ТІЄНАМОМ ЩОДО ПОЛІАНТИБІОТИКОРЕЗИСТЕНТНИХ ШТАМІВ СИНЬОГНІЙНОЇ ПАЛИЧКИ

Дяченко В.Ф., Ягнюк Ю.А., Марющенко А.М., Куцай Н.М.

THE STUDY OF ANTIMICROBIAL ACTIVITY OF COMBINATIONS OF FOSFOMYCIN WITH CEFEPIME AND FOSFOMYCIN WITH TIENAME IN RESPECT POLYANTIBIOTIC-RESISTANT STRAINS OF *PSEUDOMONAS AERUGINOSA*

Dyachenko V.F. , Yagniuk Yu.A., Mariushchenko A.M., Kutsay N.M.

The rapid decrease in sensitivity of pathogens septic infections to antimicrobial agents has led to significant difficulties in the fight against antibiotic-resistant infections even in developed countries. One solution to this problem is a method of combining antimicrobial different pharmacological groups. The most promising for combination drugs are derivatives of phosphonic acids, which are able to deeply penetrate biological film and microbial cells and enhance the antibacterial action of other antibiotics. A study of the effectiveness of combination antibiotic fosfomycin with cefepime and fosfomycin with tiename on polyantibiotic-resistant strains Pseudomonas aeruginosa. Set the antibiotic used in the experiments performed by *P.aeruginosa* strains of "serial dilutions" and the disco-diffusion method. The efficacy of combinations of antibiotics was carried out by determining the minimum inhibitory concentrations routine method in vitro method "checkerboard". The results of experimental studies the combination of cefepime on multiresistant strains Fosfomycin on *Pseudomonas aeruginosa* show a significant decrease in the MIC of cefepime in combination on ten of the thirteen strains. MIC Fosfomycin significantly decreased relative to the nine strains. In calculating the index FIX appears that a synergistic effect of the combination of antibiotics studied (FIX ≤ 0,5) was observed on 69.2% of the subjects strains of *P.aeruginosa.* In experiments on three strains observed effect summation antimicrobial antibiotics specified combinations (FIX> 0,5, ≤ 1,0), one strain - indifferent effect (FIX> 1.0). You can also combined fosfomycin with tiename significant (greater than 2-fold) reduction in MIC these antibiotics was observed only for 2 subjects cultures *P. aeruginosa.* Calculation of the FIX showed that combined use of fosfomycin with tiename created largely indifferent effect refers to the strains of *P. aeruginosa*. Thus, studies have shown a high degree of synergy combination of fosfomycin with cefepime on polyantibiotic-resistant strains strains of *P. aeruginosa*.

Keywords: combinations of the antibiotics, polyantibiotic-resistant strains, checkerboard method.

ІСТОРІЯ МЕДИЦИНИ

К 150-ЛЕТИЮ СО ДНЯ РОЖДЕНИЯ ПЕРВООТКРЫВАТЕЛЯ ВИРУСОВ ДМИТРИЯ ИОСИФОВИЧА ИВАНОВСКОГО

Панченко Л.А., Попова Н.Г., Звягольская И.Н., Васина С.И.

150th ANNIVERSARY OF VIRUSES DISCOVERER DMITRI IOSIFOVICH IVANOVSKY

Panchenko L.A., Popova N.G., Zvyagolskaya I.N., Vasina S.I.

The article is devoted to the 150th anniversary of the birth day of Dmitri Iosifovich Ivanovsky. On the example of tobacco mosaic disease, he first proved the existence of a new type of pathogens – viruses.

Dmitri Ivanovsky is considered as founder of a new, independent science - Virology.

Keywords: D.I.Ivanovsky, discoverer of viruses, tobacco mosaic virus disease, the founder of Virology.

ПАМЯТИ БОНДАРЕНКО ВИКТОРА МИХАЙЛОВИЧА (1940-2014)

Інформаційні листи

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