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attacks) in 46 infants. In a randomized controlled trial, tyndallized *L. acidophilus* HA122 with chamomile and *melissa* extracts significantly reduced the mean daily infant crying time compared to simethicone. Heat-killed *L. acidophilus* LB significantly reduced clinical symptoms in patients with chronic diarrhea, and the effect was superior to that of live lactobacilli. In a placebo-controlled study in children with acute diarrhea caused by rotavirus, lyophilized, heat-killed *L. acidophilus* LB significantly reduced the number of children with loose stools and significantly reduced the duration of diarrhea. In a randomized, double-blind, placebo-controlled clinical trial in children with persistent non-rotavirus diarrhea, the use of lyophilized, heat-killed bacteria *L. acidophilus* LB reduced the recovery time of normal stool. In a multicenter, randomized, double-blind, controlled study, the use of formula containing heat-killed *B. breve* C50 and *S. thermophilus* 065 in children at high risk of atopy reduced the incidence of digestive and respiratory allergic events. Recently, products containing various tyndallized probiotics strains have appeared on the market. These are *L. reuteri*, *B. breve* and xyloglucan for the treatment of colic in adults and children, *L. acidophilus* HA122 with extracts of chamomile and lemon balm for the treatment of colic in children, a complex of tyndalized lacto- and bifidobacteria with gelatinate tanat for the treatment of intestinal dysbacteriosis associated with diarrhea. **Conclusion.** Heat-killed probiotics are no less effective than live bacteria and have benefits such as greater safety, ease of standardization, transportation, and storage. They are an alternative to live probiotics and open up the possibility of using them to treat various diseases and conditions.
Keywords: stress-factors, probiotics, metabiotics, heat-killed probiotics, review

Ivermectin - molecular mechanisms of antivirus and antiparasitic effects **15-24**
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Specific highly affinity recognition of imports is crucial for the viral proteins nuclear localization. One of the drugs that affects the viral nuclear localization signal is ivermectin. It is shown that the addition of 5 mcM ivermectin to Vero-hSLAM cells 2 hours after the SARS-COV-2 infection led to a decrease in the viral RNA load by 99.98% after 48 hours. Ivermectin for treatment SARS-COV-2 people have already approved in a number of states and countries, including Peru and the Northeastern region of Beni in Bolivia. It is important to note that about 70 tests around the world are currently checking the clinical efficacy of ivermectin for the treatment or prevention of SARS-COV-2; They include variations in dosing modes, combined therapy and prophylactic protocols. Scientists suggested that this drug can reduce viral load in infected patients with potential influence on the progression and dissemination of the disease. Possible directions for the further study of the recruitment of Ivermectin for the treatment of SARS-COV-2 may be in the development of an inhalation preparation for the effective delivery of high local concentration into the lungs with minimal systemic exposure and estimating the synergistic effects of ivermectin with other connections that also inhibit SARS-COV-2 replication.
Keywords: ivermectin, SARS-COV-2, nuclear signal localization inhibitor, cells culture, pilot clinical trials

Experimental works

Formulation and evaluation of the nanosilver gel using bioreductor ethanol extract of Katuk leaf *(Sauropus androgynus (l)* Merr) as antibacterial **25-31**
Nurfadilah, Yunahara Farida, Faizatun
Introduction: The current type of nanoparticle that attracts a lot of attention in the pharmaceutical field is Nanosilver. Nanosilver can be acted as an antimicrobial. The aim of this study is to obtain the Nanosilver gel preparation from katuk leaf extract, which is effective as an antibacterial agent against acne. **Materials and Methods:** Katuk leaf extract remains as a reducing agent in the synthesis of Nanosilver using a green synthesis method. Nanosilver characterization was performed using PSA, FTIR and TEM. **Results and Discussions:** Particle size of Nanosilver (Katuk leaf extract concentration 0.16% with a silver nitrate volume of 10 mM is 1: 9) of 164.40 nm, Nanosilver (Katuk leaf extract Concentration 0.32% with silver nitrate volume 10 mM is 1: 9) of 176.47 nm and Nanosilver (0.48% katuk leaf extract concentration with a volume of 10 mm silver nitrate of 1: 9) of 194.95 nm. Antibacterial activity using the Well method was shown that the nanosilver gel from Katuk leaf extract had an inhibitory effect on *P. acnes* bacteria with an inhibition zone of 26 mm classified as very strong, and 12 mm was strongly categorized against *S. aureus* bacteria, namely in Formula 1. **Conclusion:** A variation in the concentration of katuk leaf extract influences the size of the particles formed. The Nanosilver of katuk leaf extract has an antibacterial cause for acne with a very strong category.
Keywords: Acne; Nanosilver gel; Antibacterial; Katuk leaf.

Comparative analysis of the antibiotic sensitivity level of Escherichia coli strains of different isolation periods **32-35**
Peretyatko O. G., Yagnyuk Yu. A., Sklyar N. I., Bolshakova G. M., Kholodna T. V.
Introduction. The problem of the spreading of the microorganisms resistance to antimicrobial drugs is so acute nowadays, that the XXI century can rightly be called the "era of antibiotic resistance". In our opinion, to study the mechanisms of antibiotic resistance in the population of microorganisms, it is important to analyze the antibiotic

sensitivity of microorganisms isolated during different periods of antibiotics use in clinical practice. The aim of the study was to compare antibiotic sensitivity profiles of *E. coli* strains isolated in the preantibiotic, metaantibiotic and modern periods. **Material & methods.** Objects of the study: 41 *E. coli* museum strains from the collection of the Museum of microorganisms stored in a lyophilized state for 44-73 years, and 55 circulating *E. coli* strains. Determination of the sensitivity of microbial cultures to antibiotics was performed using disco-diffusion method, serial broth dilution method and serial agar dilution method. Statistical data processing was performed using computer programs Microsoft Excel 2007, STATISTICA 6.0. **Results & discussion.** A comparative analysis of the results of the study of antibiotic sensitivity of *E. coli* of different isolation periods demonstrated significant decrease in activity of the antibiotics of aminopenicillin group (ampicillin, ampicillin-sulbactam), generation I-III cephalosporins, tetracycline, chloramphenicol against modern clinical *E. coli* strains. In contrast to the museum strains, the circulating population of *E. coli* showed resistance to carboxy- and ureidopenicillins, generation IV cephalosporins, carbapenems, aminoglycosides, doxycycline, fluoroquinolones, and cotrimoxazole. The vast majority (70,0%) of the antibiotic-resistant museum strains showed resistance to 1–3 antibiotics groups, while 52,2% of the modern strains showed resistance to antibiotics of the 4–7 chemical groups. **Conclusion.** Comparative analysis of the antibiotic sensitivity profiles of *E. coli* isolated during different historical periods showed an increase in the proportion of resistant strains among circulating *E. coli* and an expansion of the range of antibiotics groups for which resistance was identified.

Key words: *E. coli* strains isolated during different historical periods, antibiotics, antibiotic sensitivity.

Introduction: Bacteria that treated with antibiotics has ability to adapt or mutate due to form a defend mechanism. OXA-48 produces isolate that have ability as a resistance to drugs and all β-lactam, including *cephalosporin*, *cephamycin*, *monobactone*, and *carbapenem*. This study aims to identify the availability of OXA-48 gene as *Carbapenem* resistance in *Klebsiella pneumonia (K.pneumoniae)* and *Escherichia coli (E.coli)* from patient in Dr. Mohammad Hosein Hospital in Palembang, Indonesia. **Method:** The isolate bacteria from patients in Dr. Mohammad Hosein Hospital who infected with *K.pneumoniae and E.coli* in September until November 2017 were identified using Vitek 2 Compact. Polymerase Chain Reaction (PCR) used to detect the presence of bla OXA-48 to compare the pattern of antibiotic resistance. **Result:** The result showed that from 24 samples, there was 1 sample (4.7%) who positive with OXA-48 gene from *K.pneumoniae* bacteria and no positive gene found in *E.coli* bacteria. While the rest of the samples (95.3%) had negative OXA-48 gene. **Conclusion:** Therefore, the OXA-48 gene was only identified in *K.pneumoniae*.

Keywords: Klebsiella pneumonia, Escherichia coli, OXA-48, Carbapenem resistance, PCR.

Introduction: This research is about formulation and activity test of seaweed extract (Sargassum binderi) and sunflower oil kenaga (Cananga oil) as lip moisturizer. The purpose of this study was to utilize natural ingredients and determine the evaluation of lipbalm from seaweed and cananga flower oil which has a function to increase the moisture level of lip. **Methods:** The formulation of lipbalm was made by three concentrations, formulation 1, formulation 2 and formulation 3. Evaluation was done to test the skin irritation, skin hydration and hedonic test. The method of skin hydration helps to enhancer and moisture the skin by TEWL (transepodermal water loss) tool of derma lab combo. **Results:** The result of this research showed that all the formulas does not irritate the skin, moisturize and preferred by the panelists. In the third formula, it has a result to increase the humidity of skin within the high significant differences among the three formulas. **Conclusion:** Therefore, the lip balm formulation increase humidity of skin within the high significant differences among the three formulas.

Keywords: Seaweed; Ylang flower oil; Lipbalm formula; Moisture.

Introduction. One of the main pathogens of purulent and inflammatory diseases, including multi-different serum groups specificity, remains a *P. aeruginosa*. The pathogen has a wide serogroup landscape, has polyresistance to antibiotics, high resistance to disinfectants, aseptives, external factors. Clear progress in the treatment of this infection is not observed. In a very actual problem of antibiotic resistance, an urgent necessity is the creation of vaccine preparations for the prevention and treatment of pseudomonosis. The search for new approaches to the creation of immune drugs continues in different countries of the world. In Ukraine, vaccine preparations for the prevention and treatment of pseudomonosis infection are absent, so their development and domestic production is promising, relevant and socially grounded. One of the modern directions of research of scientists from different countries is the use of bacteria decontamination technologies and obtaining immunogens from its by inactivating the original microbial producer with a photodynamic method. We have developed and a patented method for obtaining a synogogeneous vaccine by using bacteriophages adapted to specific freshly used P. aeruginosa strains, use as photosensitizers - vikasol and riboflavin followed by irradiation by light. **Materials and methods**. For the

production of vaccine samples, cultures of freshly branched from various biotopes of patients with purulent inflammatory diseases of *P. aeruginosa* strains, specific adapted bacteriophages, 0.1% solution of riboflavin and 1.0% vikasol. The irradiation was carried out using a photopolymer lamp "Luxior" and ultraviolet bactericidal lamp in laminar box. The protective properties of vaccine drugs were studied in an experiment on non-inbred mice by determining animal survival rates after control infection with homologous and heterogeneous *P. aeruginosa* strains. The protective activity of vaccine samples was evaluated in comparison with the control (non-vaccinated) group of infected animals. Statistical methods determined the reliability of the difference in indicators (X2). **Results and discussions**. In laboratory conditions, 3 series of monovaccines and 2 series of multistrain vaccines (out of 5 strains were obtained *P. aeruginosa*). The comparative study results of the vaccine monopeparates series received from strains with different baseline characteristics have shown that all of them provided approximately the same protective effect of infection with homologous strains. The high efficiency of vaccination of experimental mice is shown, as a result of which the mortality in the infestation by auto-strain due to different periods after immunization, starting from 3 days, was insignificant (10%) and compared with non-vaccinated - reliably less ($P < 0.01$). Number of animals surviving after infection with heterogeneous strains *P. aeruginosa* in all experiments was also significantly smaller than in the control (non-vaccinated) group ($P < 0.05$). Taking into account the wide serogroup landscape *P. aeruginosa*, the main task was to develop a method for obtaining a phagolysate multistrains pseudomonosis vaccine based on the application of the method of photodynamic inactivation of *P. aeruginosa* candidate strains and determined experimentally with its protective properties. Infection of experimental animals was carried out as strains involved in obtaining a multi-strains vaccine and other heterogeneous strains. In all cases there is a significant difference in comparing survival rates in vaccinated and non-vaccinated animals ($p < 0.01$). The multistrain vaccine protected immunized mice from infection both by autostrain and from heterogeneous strains *P. aeruginosa*, which were not included in the vaccine. **Conclusion**. The resulting phagolisis multistrain vaccine has protective properties as relative to homologous and heterogeneous *P. aeruginosa* strains, was non-toxic and non-reactive. The survival rate of vaccinated mice in infection with a homologous strain has 28.9%, heterogeneous - 78.6%. It is important to emphasize that the strain composition of the developed immunufacturer may vary, supplemented with new, relevant for a particular region or, even, clinical department, etc.

Keywords: pseudomonas infection, photodynamic inactivation of bacteria, vaccine, protective properties of the vaccine.

Features of microbiocenosis of female genital organs and immune factors in patients with adenomiosis **50-55**

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Endometriosis is one of the most enigmatic gynecological diseases. An analysis of modern concepts of etiology and mechanisms of endometriosis development, published in PubMed, UpToDate, eLibrary databases over the past 10 years, indicates the theory of bacterial contamination as one of the factors of endometriosis. **The purpose of the study.** To study the state of microbiocinosis of women's genital organs and immune factors in patients with adenomiosis. **Materials and methods.** A survey of 65 women of reproductive age was conducted. Based on the clinical course of the disease, the data of genital status are formed by 2 groups: I group amounted to 35 (53.8%) patients with adenomiosis and degree of distribution. Group II (control) amounted to 30 (46.2%) gynecologically healthy women. In order to assess the content of microorganisms in the secrets of the genital organs of women, the material was taken from the cervical channel and the posterior vault of the vagina and subjected to a bacteriological study. In the detection of infections of the urogenital sphere, a polymerase chain reaction (PCR) and ELISA was used. **Research results.** By studying the microscopic characteristic of the vaginal biocenosis in women with adenomiosis prevailing the II-III degree of purity of the vagina with the “intermediate” type of biocenosis (43.3%), which is characterized by a reduced content of lactobacillus, the presence of various types of morphotypes of gram-positive and gram-negative rods and cocci and “dysbiosis” (50.0%) when mixed bacterial microflora prevails. Microbiological researches of vaginal allocation showed the presence of dysbiosis in all examined women, which was manifested by a significant decrease in the number of lactobacillus or their absence and increasing the content of conditionally pathogenic microbes. In 17 (48.6%) patients, *Staphylococcus aureus* was isolated at a concentration of $10^2 – 10^3$ cfu/ml, y 12 (34,3%) – *enterococcus*: *Enterococcus faecalis y* 7 (20,0%) in an amount of 10^2 cfu/ml; *Enterococcus faecium* in 2 (5,7%) in an amount of 10^3 cfu/ml; *Enterococcus* sp in 3 (8,5%) in an amount of 10^3 cfu/ml; in 9 (25,7%) withdrawn *Escherichia coli* 10^3 cfu/ml, in 2 (5,7%) patients – *Klebsiella spp* 10^2 cfu/ml, in 4 (11,4%) *Proteus spp* in the amount of 10^2 cfu/ml; in 16 (45,7%) – *Mobiluncus* in the amount of $10^3 – 10^4$ cfu/ml; in 5 (14,3%) *Peptococcus sp.* in the amount of 10^3 cfu/ml; in 13 (37,1%) patients were isolated *Candida albicans*, $10^4 – 10^5$ cfu/ml, in 15 (42,8%) – *Gardnerella vaginalis* (CFUs were not determined, fixed the presence of "key cells" and a change in the pH of discharge). In 9 (25,7%) patients were isolated asporogenic anaerobic bacteria: *Bacteroides spp* – 6 (17,1%). The PCR diagnosis of the material of the cervical channel revealed: *Cytomegalovirus* in 4 (11,4%) patients of I group , *Virus herpes simplex* in 5 (14,3%), *Virus papilloma hominis* – 5 (14,3%). In women of the control group, the positive definition of *Cytomegalovirus* and *Virus Herpes Simplex* amounted to 3.3% of observations. The conducted studies have shown mixed infection in all patients of I group. The obtained data indicate that adenomiosis proceeds against the background of disturbed microbiocenosis of genitalia. Detected microbial associations are able to lead to changes in physico-chemical properties and pH of the secretions of the urogenital sphere, followed by possible penetration into the cavity of the uterus. In peripheral blood, patients with adenomiosis showed a reduced level LL-37 – 21,4±1,3 pg/ml (in the

control group LL-37 – 23,4±2,5 pg/ml respectively). With grade I adenomyosis, a typical inflammatory reaction occurs with a decrease in the level of antimicrobial peptides in the vaginal and cervical secretions, which indicates their possible role in the pathogenesis of the disease.
Key words: adenomyosis, vaginal microbiocenosis, antimicrobial peptides.

Case Report

Arantrinita, Lukisiari Agustini

Background: Optic neuritis is an inflammatory disease that results in demyelination of the optic nerve. Isolated Optic Neuritis in Acute Disseminated Encephalomyelitis is a rare case, this disease attacks the central nervous system. It is monophasic, and make various clinical manifestations. Early diagnosis of Isolated Optic Neuritis due to Acute Disseminated Encephalomyelitis is based on clinical manifestations accompanied by laboratory and radiological investigations. In Acute Disseminated Encephalomyelitis patient, radiological examination can shows normal result in the acute stage. This is a challenge in establishing the diagnosis of the disease. **Materials and Methods:** This is a case study in post-vaccine patient. Seven-year-old girl with complaints and typical clinical manifestations includes high fever, sudden decrease in vision accompanied by pain in the movement of the eyeball. Optic nerve papillary examination shows hyperemic color with firm borders, according to the results of optical coherence tomography examination. Laboratory examination showed an increase in white blood cell count and C-reactive protein value, and multiple hyperintense lesions in the subcortical temporo-parietal characteristic of Acute Disseminated Encephalomyelitis on Magnetic Resonance Imaging. **Results&Discussion :** Management guided by the Optic Neuritis Treatment Trial protocol accompanied by close observation showed significant clinical improvement. **Conclusion:** Optic neuritis in Acute Disseminated Encephalomyelitis is an acute and monophasic disease. The most common cause is inflammatory reaction to viral and molecular mimicry reactions of the vaccine component. Early diagnosis and proper management give good results and can prevent recurrence.
Keywords: Isolated Bilateral Optic Neuritis, Acute Disseminated Encephalomyelitis, central nervous system, vaccine.