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EPIDEMIOLOGICAL EVALUATION OF BACTERIOPHAGES AS FACTORS OF EVOLUTION OF HOSPITAL STRAINS AND MEANS OF CONTROL WITH HOSPITAL-ACQUIRED INFECTIONS

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Relevance. The investigation of the problem of infections, especially hospital-acquired infections (HAIs), is closely related with the studying of the biological properties of pathogens in the evolution of hospital strains. Bacteriophages play an important role in the development of bacteria and in the realization of their pathogenic potential. The phenomenon of phage transduction is accompanied by the acquisition by bacteria of genes for resistance to antibacterial drugs and by increase in epidemiological spread. In such circumstances, the situation in the fight against infectious diseases may soon become the same as it was before the discovery of antibiotics. Accordingly, one of the effective components in the fight against bacterial infections, including those caused by antibiotic-resistant strains, is the use of bacteriophages.

Aims. Estimation of the role of bacteriophages in the evolution of HAIs pathogens and anti-epidemic potential of bacteriophages.

Materials and methods. A retrospective analysis of the literature of scientific databases Web of Science, Scopus, Pub Med and studies conducted in a number of treatment and prevention organizations of various profiles and patients in the out-hospital population.

Results. Control bacteriological exam of the material after phage therapy showed the absence of *Staphylococcus aureus* in the material. Against the background of the use of staphylococcal bacteriophage, the frequency of infection decreased to zero. Therefore, complete elimination of *S. aureus* was observed after phage therapy. Mono- or combined drugs of phages were used. After analyzing the statistics, we were able to conclude that the use of bacteriophage was an effective method of eliminating the outbreak caused by *S. aureus*. The epidemiological effect of phage use against methicillin-resistant strain of *S. aureus* was also demonstrated.

Conclusion. The results of this studying convincingly indicate the high anti-epidemic efficacy of bacteriophages in outbreaks of HAIs. A number of properties that phages have, in particular high specificity for specific pathogens, give them an advantage over other antibacterial agents.

PROSPECTS FOR THE USE OF NANOCRYSTALLINE CERIUM DIOXIDE AS A PREBIOTIC FOR MICROBIOME CORRECTION

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Microbiome modulation is a pillar intervention to treat metabolic syndrome and cascade of related pathologies such as atherosclerosis, among others. *Lactobacillus* and *Bifidobacterium* probiotic strains demonstrate efficacy to reduce obesity, dyslipidemia, and improve metabolic health. Novel prebiotic substances composed with known probiotics may strongly synergize health benefits to the host. The aim of this study was to evaluate beneficial effects of *Lactobacillus* and *Bifidobacterium* strains if composed with nanoceria (potential prebiotic) to reduce cholesterol levels and restore gut microbiota in obese mice.

Two lines of mice were used in the study: BALB/c mice (6 – 8 weeks, 18 – 24 g) and CBA mice (11 – 12 months, 20 – 26 g); experimental animals were fed by fat-enriched diet 3 weeks before the evaluation. Animals were divided into groups to test probiotic strains and nanoceria. All groups received probiotic strains orally and cerium dioxide orally or intravenously in various composition. A group of untreated animals was used as a control. Cholesterol level and gut microbiota of mice were studied.

Cerium dioxide nanoparticles, probiotic strain *L. casei* IMV B-7280, and composition *B. animalis* VKB/*B. animalis* VKL applied separately and in different combinations all reduced at different levels free and bound cholesterol in blood serum of mice fed by fat-enriched diet. The combination of 0.01 M nanoceria and probiotic strain *L. casei* IMV B-7280 resulted in the fastest cholesterol level decrease in both young and mature animals. Oral administration of CeO_2 applied alone reduced the number of microscopic fungi in the gut of mice and Gram-positive cocci (staphylococci and/or streptococci). Application of *L. casei* IMV B-7280 as a probiotic strain increased most significantly the number of lactobacilli and bifidobacteria in the gut of mice. The most significant normalization of gut microbiota was observed after oral administration of alternatively either *L. casei* IMV B-7280 + 0.1 M CeO_2 or *L. casei* IMV B-7280 + 0.01 M CeO_2.

The presented results provide novel insights into mechanisms behind nutritional supplements and open new perspectives for application of probiotics combined with substances demonstrating prebiotic qualities benefiting, therefore, the host health. If validated in a large-scale clinical study, this approach might be instrumental for primary and secondary prevention in obese individual and patients diagnosed with diabetes. To this end, individualized prediction and treatments tailored to the person are strongly recommended to benefit the health condition of affected individuals.

COMPARATIVE ANALYSIS OF SKIN MICROBIOCENOSIS OF PATIENTS WITH ATOPIC DERMATITIS AND PSORIASIS

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According to WHO the frequency of Atopic dermatitis (AD) makes up 2 - 5%, psoriasis - up to 11.4%. The change of skin barrier properties in AD leads to impoverishment of the specific composition of commensals as well as colonization of *Staphylococcus aureus*. As of now, the role of microorganisms in pathogenesis of psoriasis has not been studied completely.

Purpose of the research: a comparative study of the microbiocenosis state of patients' skin lesions in psoriasis and AD.

The study included 100 patients hospitalized in the Department of Dermatology in the GA "Institute of Dermatology and Venereology, NAMS of Ukraine" in 2017-2021. The group of AD patients consisted of 34 people (average age 28.5±1.9), the group with psoriasis included 66 people (average age 43.1±2.8). The methods of classical bacteriology were applied for the study of bacteriological material from the patients' affected skin.

In the group of AD patients, 55 bacterial strains were isolated that were attributed to 4 genera: *Staphylococcus*, *Micrococcus*, *Streptococcus* and *Corynebacterium* (87.3%, 5.7%, 1.9% and 1.9%, respectively). Among the staphylococci *S. aureus* (41.7%), *S. epidermidis* (25.0%), *S. haemolyticus* (20.8%) were dominating, the share of other species made up 12.5%. Particular attention is being drawn to the identification of associations of *S. aureus* with CN (catalase-negative) *Staphylococcus* spp. (20.6%).

During the study of skin lesion microbiocenoses in patients with psoriasis, 109 bacterial strains were isolated and attributed to 5 genera: *Staphylococcus*, *Micrococcus*, *Corynebacterium*, *Streptococcus* and *Klebsiella* (82.6%, 13.8%, 1.8%, 1.0% and 1.0%, respectively). As in patients with AD the dominant position was held by representatives of the genus *Staphylococcus*: *S. haemolyticus* (22.9%), *S. epidermidis* (15.6%) and *S. cohnii* (11.1%) while a share *S. aureus* accounted for 8.3%. As in AD patients in this group of patients the associations were found – 54.5%. In general associations of the CN *Staphylococcus* spp. were observed among themselves – at the level of 79.0%, the associations of *S. aureus* with CN *Staphylococcus* spp. – 21.5%.

As a result of the studies of microbiocenoses of skin lesions, microorganisms of the genus *Staphylococcus* were found to be a dominant group in both AD and psoriasis. In the case of AD a high percentage of *S. aureus* detection indicates a significant influence of the microorganism on both maintaining of inflammatory process in skin and aggravating the course of dermatosis.

BIOTECHNOLOGY OF MULTICOMPONENT ORGANIC WASTE DEGRADATION WITH THE USE OF GMP-BIOREACTOR

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One of the global problems of mankind is the accumulation of solid organic waste in landfills, the degradation of which occurs for a long time. Some farms use bioseptics to process such waste, but they have a number of disadvantages. Therefore, the aim of our work was to develop and test a new bioreactor for the degradation of multicomponent household organic waste.

GMP-Bioreactor is a plastic container with a capacity of 300 L. It contains a mixing pump, a heat exchanger for heating the culture fluid and a thermocouple to control and maintain a stable temperature. Control and regulation of temperature and mass transfer is carried out by the electronic control unit outside the bioreactor. The previously developed universal granular microbial preparation (GMP) was used for efficient degradation of organic waste.

The main distinguishing feature of bioreactor is the pulse mode of the technological cycle, which is cyclic change of anaerobic and aerobic conditions. The advantages of the pulse mode are as follows. The first stage of degradation of solid food waste (polymers) occurs due to anaerobic microorganisms with the accumulation of hydrolysis products: fatty acids and alcohols. When switching the bioreactor to aerobic mode is the complete oxidation of fatty acids and alcohols to CO_2 and H_2O. The end result is the complete degradation of solid food waste and the reduction of dissolved organic compounds on total carbon from 466 ppm to up to 24 ppm.

To determine the optimal mode, several variants of the ratio of pause and mixing time were investigated. The main studied parameters were pH, Eh, the concentration of dissolved organic compounds on total carbon and the concentration of ammonium nitrogen in the culture fluid. It is determined that the most effective mode of the technological cycle is 5 minutes of mixing and 30 minutes of pause. Under such conditions, the duration of fermentation **T** was 39 hours, and the degradation coefficient for total carbon **Kd** = 20. The **pH** values were in the range 7 – 7.4, and **Eh** – +274 - +300 mV.

Thus, the bioreactor developed by us provides fast and effective degradation of solid and liquid mixed organic waste to obtain water suitable for watering vegetables. This installation is offered for use in cottage townships. In the future, we plan to scale the bioreactor, increasing its working volume from 300 to 1000 liters and improving biotechnology, which is a prospect for its large-scale implementation in industry.

BIOLOGICAL AND FUNCTIONAL ACTIVITY OF *AZOSPIRILLUM BRASILENSE* LIPOPOLYSACCHARIDES

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Introduction. *Azospirillum brasilense* is a Gram-negative, nitrogen-fixing bacterium that colonizes the rhizosphere of various grasses and cereals. Azospirils can stimulate plant growth, its productivity and organic nitrogen content under certain environmental and soil conditions. Lipopolysaccharides (LPS) are a class of complex glycolipids present in the cell membrane of Gram-negative bacteria that mediate plant-bacteria interactions. Although the effects of LPS of pathogenic plant bacteria in the induction of plant defense mechanisms have been characterized, the role of LPS of beneficial rhizobacteria on plant growth is less clear. Therefore, a very important point is the study of the chemical characteristics, biological and functional activities of *A. brasilense* LPS, which was the **aim** of this work. **Methods.** *A. brasilense* LPS were isolated from dry bacterial mass by phenol-water method. The carbohydrates were analyzed by Dubois method, nucleic acids - by Spirin, protein content - by Lowry and 2-keto-3-deoxyoctonic acid (KDO) - by Osborn. Pyrogenicity of LPS were tested observing the rules of bioethics in mice and rabbits. Serological studies were performed by Ouchterlony method. The identification of monosaccharides and fatty acids in LPS preparations was carried out on an Agilent 6890N/5973 inert chromatography-mass spectrometry system. **Results and discussions.** LPS of 3 strains of *A. brasilense* were isolated from dry bacterial mass and purified from nucleic acids by ultracentrifugation. The purified LPS were characterized by different relative yields from 2.44% to 4.75%, which is slightly higher than in other strains of the *A. brasilense* species (1-3%). The studied preparations were characterized by a rather high content of carbohydrates from 50.1% to 72.1% in comparison with the literature data for other strains of *A. brasilense* (21% - 53%). The protein content ranged from 3% to 9.39%; nucleic acids - from 3.52 to 4.34%. All LPS molecules contained up to 0.17% KDO, which is a specific component of the LPS of gram-negative bacteria. Heptoses were not detected. Analysis of the monosaccharide composition indicates that the LPSs of the studied *A. brasilense* strains turned out to be heterogeneous. All three strains had differences in the monosaccharide composition of LPS. At the same time, such monosaccharides as mannose, galactose, glucose and heptose were recorded in LPS of all studied strains. The study of the fatty acid composition of LPS showed the presence of fatty acids containing from 14 to 18 carbon atoms. Hydroxylated, saturated, monounsaturated acids and their cis isomers were found. Typical for most *A. brasilense* strains is the presence of such fatty acids as 14:0(3-OH), 16:0 and 16:0(3-OH). In the studied LPS, the dominant fatty acids were 16:0, 18:1, 14:0(3-OH), and 16:0(3-OH), which coincides with the literature data. The study of the pyrogenic effect of LPS of *A. brasilense* strains showed that LPS solutions are not pyrogenic, since no temperature rise above the physiological norm of healthy animals was observed. The double immunodiffusion reaction in Ouchterlon agar showed that all tested LPS in homologous systems exhibited antigenic activity. Serological cross-reactions can be used as an approach in classifying bacteria. Thus, we found that antisera to *A. brasilense* 18-2 and 61 react with all LPS molecules of the studied strains. That may indicate the presence of common antigenic determinants in the strains and allows us to assign them to the same serogroup. **Conclusions.** The results received during biological-functional studies of three strains of *A. brasilense* LPS contribute to the biological characteristics of this species.

BIOAUGMENTATION EFFECT OF *COMAMONAS TESTOSTERONI* IN HCB-LOADING SOIL

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Due to safety, economy and prolonged effect bioremediation of pesticide-polluted soil ecosystems by the microorganisms - xenobiotic potential destructors has significant advantages compared to chemical and physical methods. It is important to study the effect of *Comamonas testosteroni* strains as potentially hexachlorobenzene (HCB) degrading agents on plant development and their resistance to biotic factors. The aim of the present study was to determine the effectiveness of the introduced *C. testosteroni* strains on the developing tomato plants and their resistance to phytopathogens under cultivating conditions in HCB-polluted gray podzolic soil.

Methods. The experiment was performed in the laboratory. The experiment was carried out in the following variants: 1 - uncontaminated soil; 2, 3 - introducing the *C. testosteroni* UCM B-400 and B-401 liquid culture into the unpolluted soil; 4, 5 – HCB-polluted soil at doses of 30 and 100 mg/kg; 6, 7 – HCB-polluted soil at 30 and 100 mg/kg doses, which was inoculated by *C. testosteroni* UCM B-400 liquid culture, 8 and 9 - HCB polluted soil at 30 and 100 mg/kg doses, which was inoculated by *C. testosteroni* UCM B-401 liquid culture. Tomato plants of the cultivar "Lagidniy" were used in all experimental variants. Biometric parameters (plant length, root length, root mass, and plant mass) were determined at the 3-4 leaf formation stage. Resistance to phytopathogens was studied by the Kreitzburg-Eggert method under artificial infection conditions of leaf plates with micromycete *Alternaria alternata* and bacteria *Clavibacter michiganensis* UCM B-629.

The obtained **results** demonstrate that introduction of studied strains in polluted soil exert the phytostimulating effect on plants, which is confirmed by the increasing of all biometric parameters, especially plant mass: by 17.5 and 20%, respectively for strains B-400 and B-401. In plants grown in HCB-polluted soil, growth inhibition was observed, and it was most pronounced in the variants with 100 mg/kg HCB: the plant mass decreased by 46% compared to control plants. The *C. testosteroni* liquid culture introducing into the contaminated soil reduced the negative impact of the pesticide load. Thus, compared to plants grown in polluted soil (30 and 100 mg/kg HCB) without bacterial inoculation, root mass of plants grown in soil after *C. testosteroni* UCM B-400 treatment increased by 24 and 19%, respectively. The treatment of polluted soil by liquid culture of *C. testosteroni* UCM B-401 strain resulted in the increasing of root mass up to 14.6% and 24.4% in the variants with 30 mg/kg and 100 mg/kg HCB respectively. Nevertheless all biometric indicators of these plants were 7.5 - 23% lower than in tomatoes grown in unpolluted soil. At the same time the gain of plant resistance to phytopathogens after inoculation of bacterial cultures into polluted soil was observed.

Conclusions. Introduction of *C. testosteroni* UCM B-400 and B-401 strains into the HCB-polluted soil improves conditions for plant development, has a phytostimulating and protective effects on tomatoes of cultivar “Lagidniy”.

FEATURES OF THE COLON MICROBIOME IN PATIENTS WITH OBESITY WITH DIFFERENT PHENOTYPES

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Microbiome is a set of bacteria, fungi, viruses inside a person and on the surface of their skin. It is distributed unevenly in our body, its localization distinguishes the microbiome of the skin, mouth, intestines, etc. At present, the concept of heterogeneity in obesity is being developed, because not all obese patients are prone to the development of metabolic dysfunction. The urgency of the work lies in the need to understand and determine the dependence of obesity development on the colon microbiome composition.

The aim of the study is the features of the microbiome of the colon by metagenomic analysis in patients with different phenotypes of obesity and in healthy people.

Materials and methods. Bacteriological research by the method of metagenomic analysis was carried out on the basis of the department of microbiology of DMU. 150 people (50 men and 100 women, mean age 35.1±4 years) were combined into clinical groups: healthy people with normal body weight (n=70); obese patients (n=80), including metabolically healthy (n=35) and metabolically unhealthy (n=45). High-quality and quantitative assessment of the intestinal microbiome was performed by metagenomic analysis. Total DNA was isolated from fecal samples and sequencing of the variable region of the variable v3-v4 region of the 16S rRNA gene was performed.

Results and discussion. There were statistically significant ($p<0.05$) differences in quantitative and qualitative indicators of the studied microorganisms of the colon in healthy people without obesity and in patients with different phenotypes of obesity. In healthy patients, the quantitative characteristics are slightly increased for *Bacteroidetes* and decreased for *Firmicutes* compared to patients with metabolically healthy obesity. In patients with metabolically healthy obesity, in the microbiome of the colon there is an increase in the number of *Firmicutes* and a decrease in *Bacteroidetes* compared with those in metabolically unhealthy obesity. In healthy patients, the quantitative characteristics are slightly increased for *Bacteroidetes* and decreased - for *Firmicutes* compared to patients with metabolically healthy obesity.

Conclusions. In obese patients, increased amounts of *Proteobacteria, Bacteroidetes* and decreased amounts of *Actinobacteria, Firmicutes*. Healthy adults and obese patients in the intestinal microbiome in 100% of cases register 4 phylotypes of microbiomes (*Actinobacteria*, *Bacteroidetes, Firmicutes, Proteobacteria*). The data obtained in patients with different phenotypes of obesity indicate a change in the microbiome of the colon.

CHARACTERIZATION OF THE BACTERIOPHAGE ACTIVE AGAINST *PROTEUS* GENUS BACTERIA

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Proteus genus harbors the causative agents of serious diseases such as urinary tract infections (UTI) in urinary catheter patients, gastrointestinal, respiratory system, skin and eye infections. Because of a wide variety of adaptational mechanisms exhibited by the bacteria, including biofilm formation, transition to swarmer state, etc. antibiotic treatment hasn't been proven to be largely successful. This situation calls for development of novel therapeutical methods with the use of phages (or phage-derived products) being among the most promising. Some of the benefits of phage therapy include specific host targeting, unique activity mechanisms, cost efficiency and a comparative easiness of development. Isolation and characterization of broad-host-range phages are of specific interest.

Recently a *Proteus mirabilis* strain (assigned according to the biochemical identification) was isolated from tomato plants (Kharina, 2015). A phage, able to cause productive infection, was isolated after application of the sewage water on the bacterial lawn. The aim of the present work was to characterize the bacteriophage and perform the molecular-genetic identification of the isolated bacterial strain to prove its species assignment.

The morphology of the phage and its interaction with the host were studied by TEM of the sample obtained directly from the plaque. Detected phage particles featured B1 morphology (*Siphoviridae*), with icosahedral capsid (Dmax of nearly 50 nm) and a long non-contractile tail. Along with it, highly flagellated bacterial cells at different stages of lysis were observed. The intact phage tails were difficult to detect, the ones detected on the microphotographs reached a length of 119 to 278 nm. It has been noted that the tails have a transverse arrangement of subunits. We detected the presence of bacteriocins of poly-sheath type with a length from 422 to 529 nm as well. It was also established that some phage particles or individual tails were attached to the flagellum, which may indicate the probable flagellotropic nature of a phage. In order to characterize the host range of the phage, *P. vulgaris* UCM B-905T, as well as *E. coli* C600 and *Erwinia* sp. 60 were used along with the host. The bacterial virus was able to develop plaques on the lawn of *P. mirabilis* and *P. vulgaris* strains, while the bacteria of other genera were not infected.

With respect to current guidelines on species assignment, partial 16S rRNA gene sequencing was used to prove the identification of *P. mirabilis*. Using a specific set of primers (a forward 27F-5'-GAGTTTGATCMTGGCTCAG-3' and a reverse 803R-5'-CTACCRGGGTATCTAATCC-3') we obtained amplicons of approximately 800 bp that contained variable regions V1, V2, V3 and V4. Sanger sequencing of the amplicon resulted in obtaining 708 bp fragment. Comparative analysis has shown that our sequence shares significant similarities with *P. mirabilis* strain MPE4069 – with 0 mismatch count, but as well with *P. vulgaris* JCM 20013 – with 0 mismatches, *P. vulgaris* strain P190036 – with 1 mismatch.

Thus, the ability of the phage to overcome the species barriers, while proved up to biochemical and morphological studies of the hosts, remains unproved on molecular genetic level, as the 16S rRNA comparison appears to be poorly informative for within-genus discrimination for *Proteus*. Usage of other phylogenetic markers or approaches is planned.

TAXONOMIC POSITION OF COPPER-RESISTANT MICROORGANISMS OF THE EXTREME ECOSYSTEMS

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Contamination of ecosystems with metal compounds is a common environmental problem. Isolation of new metal-resistant microbial strains and development of environmental biotechnologies is a promising approach. The inefficiency of existing physicochemical and biological methods is caused by the lack of a distinct theoretical approach. Therefore, the aim of the work was to theoretically substantiate and experimentally confirm the possibility of copper resistant microorganism's isolation from extreme ecosystems and to determine their taxonomic position. The thermodynamic prognosis allows substantiating the existence of microorganisms in the presence of Cu^{2+} at super-high concentrations up to 1 M/L, as well as the pathways of its transformation by microorganisms. Microorganisms were grown in NA and NB media (HiMedia Laboratories Pvt. Ltd., India) in the concentration gradient of Cu^{2+} ions (100-63 546 ppm). Determination of the taxonomic position of microorganisms was performed based on their morphological-cultural and physiological-biochemical properties, as well as by the method of phylogenetic analysis of the nucleotide sequence of the 16S rRNA gene. The growth of microorganisms is possible if the redox potential of the system formed by the metal-oxidizer and its reduced form is contained in the zone of thermodynamic stability of water (+814…-414 mV). It was confirmed by 10 strains (9 bacterial and 1 yeast) of copper-resistant microorganisms isolation at 1 M/L Cu^{2+}. Isolate UKR1 from Kyiv region was identified as *Pseudomonas lactis*, isolate UKR2 from Kyiv region belonged to the *P. panacis* species, and two isolates from the Svalbard archipelago in Arctic and Galindez Island in Antarctica (UKR3 and UKR4) belonged to the *P. veronii* species. Bacterial isolate Cop101 («Atlantida» cave, clay, Ukraine) belonged to the species *Pantoea agglomerans*, and bacterial isolates Cop41 (copper contaminated soil, Ukraine), Cop99 («Optymistychna» cave, clay, Ukraine) and Cop102 (Ecuador, soil) were identified as *Bacillus velezensis*, *B. megaterium*, *B. mycoides* respectively. Isolate Cop98 (Dead Sea, sand) was identified as *Staphylococcus succinus.* Isolate UKR5 was isolated from the volcanic ash of Antarctica (Deception Island), which was able to grow at 63 546 ppm Cu^{2+} and belonged to *Rhodotorula mucilaginosa* species. All isolated strains were not only resistant to Cu^{2+} at super-high concentrations, but were able to interact with it (accumulate, immobilize and mobilize).

Thus, a wide biodiversity of copper-resistant microorganisms in the extreme ecosystems was shown. Thermodynamic positions about the possibility of the existence of microorganisms at super-high concentrations of Cu^{2+}, and the permissible pathways of their interaction with copper were experimentally confirmed. The industrially promising strains that can be used for the development of environmental biotechnologies were isolated.

PSEUDOMONAS PHAGE UANTARCTICA – A NOVEL LYTIC VIRUS ISOLATED FROM ANTARCTIC SOIL

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The Antarctic continent is considered the coldest and driest place on earth with simple ecosystems, devoid of higher plants. Biotopes in the ice-free regions of Antarctica are known to harbor a wide range of microorganisms from primary producers to grazers, yet their ecology and particularly the role of viruses is poorly understood.

In this study, we present biological characteristics and a complete genome analysis of *Pseudomonas* phage UAntarctica isolated from low-temperature terrestrial environments Antarctic samples collected in 2019 at the Ukrainian Antarctic Station 'Academician Vernadskiy', Argentina Islands.

Bacteriophage was isolated from soil and the dsDNA was extracted and sequenced using the MinION sequencing. Annotation of the UAntarctica genome was performed using the BLASTp, ExPASy and CD-search tools. The genome sequence of UAntarctica was deposited in GenBank under the accession number MZ605292.

TEM analysis revealed that phage UAntarctica has siphovirus morphology. Phage is characterized by an 48±2 nm isometric head and an apparently non-contractile flexible tail 156±5 nm in length. UAntarctica produces plaques surrounded by a constantly growing transparent zones on the *Pseudomonas fluorescens* FCKU 533 strain. After three days of incubation at 18°C, the plaques formed by UAntarctica are up to 1±0.1 mm in diameter, after five days - 0.15±0.05 in diameter. The phage plaques stop increasing in diameter after the fifth day of incubation. The 81.1 kbp genome of UAntarctica has a GC content of 58.4% and contains 119 putative protein encoding genes and 3 genes for $tRNA^{Gln}$, $tRNA^{His}$ and $tRNA^{Met}$.

A comparative sequence analysis allowed for a putative functional annotation of 23 genes, including those coding for the proteins responsible for virion morphogenesis, phage-host interactions, and DNA metabolism. The closest relatives of UAntarctica are *Pseudomonas* phages PMBT3 (NC_047902) and Lana (NC_048166). The overall nucleotide sequence similarity calculated using VIRIDIC indicates low identity that ranges from 37.4% (UAntarctica vs PMBT3) to 35.8% (UAntarctica vs Lana). Their genomes share several regions of nucleotide similarity that cover the essential structural and virion morphogenesis protein-encoding genes, as well as genes related to DNA metabolism and modification. To determine the evolutionary relationship between UAntarctica and other bacterial viruses, the phylogenetic tree was constructed on the base of the alignment of the large terminase subunit proteins. The obtained dendrogram shows that UAntarctica represents a distinct branch and has no close relatives among studied phages.

In conclusion, our results indicate that UAntarctica is substantially different from the previously described phages and may be considered as a representative of a novel genus within the *Siphoviridae* family.

SIMULTANEOUS TREATMENT OF SOLID AND LIQUID ORGANIC WASTE VIA SPATIAL SUCCESSION OF MICROBIAL COMMUNITIES

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The microbial treatment of organic waste is one of the most promising as well as challenging approaches. Existing technologies do not provide effective degradation of solid organic waste that causes the increase in the amount of landfills and toxic filtrate. The goal was to investigate spatial microbial succession during the degradation of solid and liquid organics with fuel obtaining.

The process was carried out consistently in the direct flow system consisting of anaerobic bioreactor, aeration tank and aquarium. For solid waste degradation, 240 L anaerobic bioreactor was used. Liquid organics removal was conducted in the 10 L aeration tank. The aquarium was used for purification of the filtrate. Spatial succession, i.e. gradual change of the physiological groups of microorganisms in space functioning simultaneously was applied to accelerate the process.

The accelerated fermentation of solid waste took place in the 240 L anaerobic bioreactor due to the spatial stratification of the redox zones. Aerobic microorganisms provided first stage of waste degradation in the high potential surface zone. After decrease in the oxygen concentration and redox potential anaerobic microorganisms provided effective synthesis of hydrogen in low potential zone up to 50 - 60 L/kg of waste during 3 days. Anaerobic degradation provided 80-90 fold reduction of solid waste weight. However, it produced filtrate with the concentration of soluble organics up to 500 mg/L. Its removal was carried out in the direct flow 10 L aeration tank during 24 hrs. Here, spatial succession of microorganisms was observed. Among 10 sections of the installation, 4 were anaerobic with the domination of copiotrophic microorganisms. The following 6 sections contained less organics and demonstrated the decrease in the amount of copiotrophs increasing the number of oligotrophic ones. The purified filtrate was removed to the aquarium evidencing complete purification of the solution.

Thus, the approach based on the spatial succession of microbial communities is promising for the further optimization and industrial implementation to accelerate the process of solid and liquid organic waste degradation and hydrogen production.

INFLUENCE OF ADAMANTANE DERIVATIVE KVM-97 ON *cidA* GENE EXPRESSION IN *STAPHYLOCOCCUS AUREUS*

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Introduction. Biofilm formation is the preferred lifestyle for many microorganisms, including human bacterial and fungal pathogens (Santos ALSD et al., 2018). Biofilm bacteria are enclosed in a self-produced extracellular matrix composed of extracellular DNA (eDNA), proteins, lipids and exopolysaccharides. Extracellular DNA (eDNA) is a key structural component of biofilms that protects resident bacteria from the host's immune system and antimicrobial agents. DNA is adsorbed on the cell surface and spreads away from it, promoting adhesion to abiotic surfaces due to acid-base interactions. Cell lysis and eDNA release are regulated by the *cidA* gene. Inhibition of *cidA* expression reduces the ability of *Staphylococcus aureus* to form biofilms *in vitro* and *in vivo* biofilm growth models (Kelly C. Rice et. Al., 2007).

The aim of the study was to determine the expression of gene that regulate the production of eDNA in *S. aureus* under the action of an adamantane derivative 1-[4-(1-adamantyl)phenoxy]-3-(N-benzyl,N-dimethylamino)-2-propanolchloride.

Materials and methods. In this study bacterial strain *S. aureus* 222, resistant to oxacillin, chloramphenicol, ciprofloxacin, erythromycin, tetracycline, tobramycin was used. A derivative of adamantane KVM-97, used in the experiments, was investigated in concentration 0.5 × minimum inhibitory concentration (MIC). The effect of the compound on expression of *cidA* gene was determined using real-time PCR. The relative gene expression level was calculated with $2^{-\Delta\Delta Ct}$ method (Livak K. J., Schmittgen T. D., 2001). The expression of 16S rRNA gene was considered as an internal control. The data obtained were compared by Newman-Keuls test ($p<0.05$) (program «StatSoft «Statistica 6.0»).

Results. In previous studies, it was found that the compound KVM-97 exhibits antimicrobial activity against planktonic cells of *S. aureus* 222 and biofilms (N.O. Vrynchanu, N.I. Hrynchuk et. al., 2021). The KVM-97 treatment at a concentration of 0.5 MIC led to the considerable inhibition of the expression of *cidA* gene. The quantitative real-time PCR experiments demonstrated that the transcriptional activity of *cidA* gene was 7-fold less in *S. aureus* exposed to KVM-97 relative to control ($p<0.05$).

Conclusions. The obtained data suggest that adamantane derivative KVM-97 exhibited anti-biofilm activity and reduced transcriptional activity of *cidA* gene in *S. aureus* 222 at sub-inhibitory concentration.

METABOLIC AND GENOMIC DISSIMILARITIES OF *PRIESTIA ENDOPHYTICA* STRAINS, FLUORESCENT PIGMENT PRODUCERS

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Bacteria within a single species may contain populations that have significant phenotypic variations even under the same culture conditions, and this is determined by genetic polymorphism. However, such genetic variability for certain species may be high (e.g., *Bacillus subtilis*) or low (e.g., *Mycobacterium bovis*). In previous works, we isolated 11 strains of aerobic spore-forming bacteria from different ecological niches and geographical areas. According to their physiological and biochemical characteristics and the ability to synthesize pink fluorescent pigments, they were similar to the 3 strains of *Priestia endophytica* (*Bacillus endophyticus*) from the Ukrainian Collection of Microorganisms of D.K. Zabolotny Institute of Microbiology and Virology of the NAS of Ukraine. This study aimed to determine metabolic and genetic dissimilarities between *Priestia endophytica* strains.

In our research, we used a number of classical and modern research methods: microbiological and biochemical methods, gas chromatography with mass detection, molecular genetic methods, and statistical data analysis. We found that the total fatty acid composition of all strains was almost identical, which indicated a high probability of them belonging to one species. Molecular genetic analysis of 16S rRNA gene fragments of *P. endophytica* UCM B-5715 typical strain and CHAES 2/3 strain showed that their sequences were identical. Nevertheless, we revealed quite a significant variability in colonies morphology between strains grown on one of the nutrient media (King A and LB). Moreover, the same strain expressed colonies of varying morphology on different media. Examining metabolic profiles, we noticed significant differences in the quantitative composition of metabolites. Furthermore, we observed a significant metabolic shift in different media for each strain. Orthogonal partial least squares analysis demonstrated that the metabolic dissimilarities between strains are partially due to the ecological niches from which they were isolated. To confirm the genome polymorphism of these strains, we performed ISSR-PCR analysis. According to the results, we found that only 1 of the 8 primers used gave a product that contained differences between strains. This outcome indicates a low level of strains' genetic variability. In respect of the results obtained, we hypothesize that significant differences in colony morphology, pigment synthesis, and metabolic profiles between strains are likely to stem from epigenetic mechanisms rather than genome polymorphism.

THERMODYNAMIC FORECAST OF THE INTERACTION OF MICROORGANISMS WITH NICKEL

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The treatment of artificial metal containing rivers - products of mining enterprises, is a global problem. None of the existing technologies ensures the proper level of cleaning of artificial metal-containing rivers. It is obvious that in order to solve this problem, it is necessary to search for new methodological solutions.

We used the thermodynamic prediction method to theoretically substantiate the extraction of metals from aqueous solutions using the example of soluble Ni compounds. Pourbaix diagrams of the stability of Ni compounds in the coordinates "pH-Eh" were used for prediction.

Hence, it follows that the reactions of Ni^{3+} reduction to Ni^{2+} ions are inaccessible to microorganisms, since the potential of this reaction is above the upper limit of water stability. The reduction reaction of Ni^{2+} to metallic Ni is also impossible, since its potential is below the limit of water stability. Let us consider examples of using forecasting to achieve the desired effect: at pH≥9 take place the soluble Ni^{2+} transformation into insoluble $Ni(OH)_2$. It follows that to remove Ni^{2+} ions from the solution, it is necessary to increase the pH with the help of certain microbial metabolic pathways. This is possible through microbial denitrification and ammonification. Finally, in the zone of thermodynamic stability of water, there is insoluble nickel sulfide NiS, which is stable in a wide range of pH values. Obvious that precipitation with biogenic hydrogen sulfide provides a more reliable environmental effect in comparison with the formation of $Ni(OH)_2$. Contrariwise, the transformation of insoluble $Ni(OH)_2$ to soluble Ni^{2+} is achieved by decrease of the pH of the medium due to anaerobic hydrolysis of plant polymers and the accumulation of organic acids.

Thus, the thermodynamic forecast made it possible to determine the necessary conditions and pathways of microbial metabolism for both the mobilization and immobilization of metals. The most effective metabolic pathway for removing nickel from wastewater is biogenic sulfidogenesis.

CASE OF *SERRATIA MARCESCENS* DETECTION IN SEALED QUATERNARY AMMONIUM COMPOUND-BASED DISINFECTANT

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Serratia marcescens is a Gram-negative bacteria, known as an opportunistic pathogen of the respiratory and urinary systems and a common cause of hospital-acquired infections. Besides the growing number of multi-drug resistant (MDR) isolates reported, *S. marcescens* is also known to gain resistance against surface disinfectant cleaners, such as chlorhexidine, triclosan, and quaternary ammonium compounds (QAC) solutions. The proper monitoring of disinfectants contaminations in the healthcare-associated facilities and in domestic use is needed to prevent MDR strains from uncontrolled spreading.

The pathogen was isolated from QAC-based disinfectant using the Bacteriological Culture Method and cultivated on Mueller-Hinton agar for 24 hours under 37°C. Identification was performed using the MIKRO-LA-TEST ENTERO kit (ErbaLachema) in five technical repetitions, and confirmed on MALDI Biotyper (Bruker Daltonics).

The presence of bacteria was detected during efficacy testing of commonly-available hand-sanitizers of the Ukrainian market. It is important to highlight that the bottle of studied sanitizer was never opened before and unsealed directly in the laboratory. The disinfectant specimen had N,N-dimethyl-N-Alkyl-(C6-18)-benzolmethane ammonium chloride as an active compound and was bought in a grocery store. It was effective against both reference strains and clinical isolates of Gram-negative bacteria and Fungi (*Escherichia coli* ATCC 25922; *Pseudomonas aeruginosa* ATCC 27853, *E. coli* №5; *Citrobacter sedlakii* №37; *P. aeruginosa* №13; *Candida albicans* ATCC 885/653, *C. albicans* №60), but ineffective against Gram-positive bacteria (*Staphylococcus aureus* ATCC 26923, *S. lentus* №19; *Enterococcus* spp. №161*; Aerococcus viridans* №26). At the studied bacteria growth inhibition zones, the secondary culture's growth, later identified as *Serratia marcescens*, was detected (ID score 2.20, very good identification).

This research shows that contamination risk exists not only while direct use of disinfectant but also on stages of its production, transportation, and/or storage. This point at the necessity of the reinforcement of the contamination prevention procedures by adding pre-use bacteriological expertise stage to already existing monitoring protocols.

SCREENING OF LACTIC ACID BACTERIA BY ITS ABILITY OF RYE FLOUR FERMENTATION

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Bread is considered to be the leading staple food around the world. Rye bread is typically consumed in Central, Eastern, and Northern Europe, since rye is a local cereal whose flour is commonly used in these countries. Traditional baking process and novel modifications rely on the metabolic activities of lactic acid bacteria (LAB) in the sourdough. Along with organic acids production, biosynthesis of acetoin by LAB could be beneficial to achieve pleasant organoleptic properties and amylolytic activity of strains during flour fermentation can improve digestibility of the final product. In order to evaluate the eligibility of using LAB in food production, LAB strains should be tested negative for biogenic amines biosynthesis which are toxic for digestion.

The aim of our work was to conduct screening of LAB strains by its ability for acidification of rye flour, amylolytic activity, ability to produce acetoin and biogenic amines.

Materials and methods. 56 LAB strains belong to genera *Lactobacillus* (36 strains), *Leuconostoc* (19 strains) and *Enterococcus* (1 strain) were used. Bacteria were cultured in the MRS medium at 30°C for 24 hours. 20 g of rye flour with 30 ml water was inoculated with 1 mL of 24h LAB culture and control sample was not inoculated, to form sourdoughs that were stored at 30°C. Titratable acidity of sourdough was evaluated after 8 hours and 24 hours using 0.1 N NaOH solution according to the Association of Official Analytical Chemists (AOAC) method no. 947.05. All strains were examined for ability to synthesize acetoin (Kvasnikov, 1975), ability to produce biogenic amines (Bover-Cid, 1999). To evaluate amylolytic activity, modified MRS agar without glucose was used with 0.2% starch as a main carbon source. Statistical analysis was performed in Statistica Software version 12.0.

Results and discussion. According to obtained results of titratable acidity of rye sourdough 56 LAB strains were divided into 4 groups: the first group contains a control sample and 11 test-strains that are weak acidificators in rye flour, the second group was formed of 22 LAB strains that produce moderate amount of acid after 8 hours as well as during next 16 hours of fermentation, the third group includes 16 strains of fast acidificators that reach 6.3-10.4°T of acidity within 8 hours. But accumulation of acids slows down significantly to maximum of 4.5 °T gain next 16 hours, and the fourth group is represented by 7 strains that accumulate acids gradually and cross the threshold of 12°T of acidity after 24 hours of fermentation. 5 strains can synthesize acetoin in high amounts, 2 strains in moderate amounts and 6 strains are weak producers. 6 strains possess amylolytic activity. Screened strains have either amylolytic activity or ability to produce acetoin. 7 LAB strains showed ability to produce tyramine – biogenic amine that possesses toxicological effect, so these strains are eliminated because they don't meet the requirements for starters.

Conclusion. Totally 26 LAB strains were selected for further investigation aimed to develop effective rye sourdough for baking industry as a main starter and 14 strains could be considered as supporting second strain in sourdough.

POLYENE ANTIBIOTICS AND PHYTOHORMONES BIOSYNTHESIS BY *STREPTOMYCES NETROPSIS* IMV AC-5025 UNDER THE COMPLEX ACTION OF EXOGENOUS INDOLE-3-CARBINOL AND β-SITOSTEROL

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Streptomyces genus are active producers of a wide spectrum of biologically active substances (BAS) that provide antagonism against phytopathogenes and parasitic nematodes, determines the regulation of plant growth, and induction of their resistance. *Streptomyces netropsis* IMV Ac-5025 was isolated by the researchers from the Institute of Microbiology and Virology, NAS of Ukraine. It produces a wide spectrum of BAS, such as polyene antibiotics, phytohormones, sterols, etc. Sterols play an important role in the vital activity of cells serving as structural elements of membranes. Indole-3-carbinol (IC) is a phytohormone that has an effect on the biosynthesis of other metabolites. To date, the biosynthesis of polyene antibiotics under the complex effects of BAS in soil streptomycetes hasn't been studied.

The aim of the work was to research the effect of the exogenous IC and β-sitosterol complex action on the polyene antibiotics and phytohormones biosynthesis by *S. netropsis* IMV Ac-5025.

The strain was cultivated in synthetic nutrient medium by in-depth method. Concentrations of exogenous substances were the following: 1. Control variant without the addition of exogenous BAS; 2. IC 25 μg/mL; 3. β-sitosterol 10 μg/mL; 4. IC 50 μg/mL; 5. β-sitosterol 20 μg/mL; 6. IC 12.5 μg/mL + β-sitosterol 5 μg/mL; 7. IC 5 μg/mL + β-sitosterol 2 μg/mL; 8. IC 0.5 μg/mL + β-sitosterol 10 μg/mL. The biomass accumulation was determined by the gravimetric method and expressed in grams of absolutely dry biomass (ADB) per 1 liter of the nutrient medium, polyene antibiotics and phytohormones biosynthesis were determined by the thin layer spectrodensitometric chromatography method. The results were analyzed by using Statistica v.10.0 program.

In the culture liquid, the sum of polyene antibiotics ranged from 30.295 to 170.56 μg/mL and was the highest under the action of IC 12.5 μg/mL + β-sitosterol 5 μg/mL (151% of the control value). The lowest amount of polyenes was accumulated under the action of 50 μg/mL of IC (26.8% of the control value). In producer biomass, the sum of polyene antibiotics ranged from 517.6 to 5859.38 μg/g ADB and was the highest under the action of IC 12.5 μg/mL + β-sitosterol 5 μg/mL (240% of the control value). The lowest sum of polyenes was accumulated under the action of 50 μg/mL of IC, also as in the culture liquid. In this case, the biosynthesis of the strain characteristic pigment was blocked. The amount of biomass was ranged from 4.9 to 5.8 g/L, exogenous compounds didn't have a significant effect on it. The auxins sum was ranged from 20.17 to 107.64 μg/g ADB and increased 5.3-fold under the action of IC 0.5 μg/mL + β-sitosterol 10 μg/mL and 4.8-fold – 50 μg/mL of IC. The cytokinins sum was ranged from 3.15 to 107.1 μg/g ADB and was the highest under the action of 50 μg/mL of IC (11.6-fold higher of the control variant). The ABA content was increased 3.6-fold under the action of IC 0.5 μg/mL + β-sitosterol 10 μg/mL.

The results of the work are fundamental for understanding the possible interrelationships of biologically active substances in the biosynthesis by soil streptomycetes and for the possibilities of regulating the accumulation of beneficial metabolites in the biotechnological process.

BIOSYNTHESIS OF PHYTOHORMONES BY STRAIN OF *MESORHIZOBIUM CICERI* ND-64

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In the cultivation of legumes, microbial preparations based on beneficial soil microorganisms are becoming increasingly important. Due to the mechanisms of biological fixation of molecular nitrogen and its conversion into a form accessible to plants, nodule bacteria are able to meet significantly the needs of crops in this element. This helps to increase plant productivity and soil fertility. Cultivating chickpeas in different soil and climatic zones, especially in new areas, involves the inclusion of such an agricultural measure as pre-sowing bacterization of seeds by active and highly efficient strains of *Mesorhizobium ciceri* in the technology of cultivation. This will contribute to the implementation of the symbiotic potential of plants, increase their resistance to adverse soil and climatic conditions and increase yields.

The objective of our work was to study the ability to produce phytohormones substances with new effective strain of chickpea nodule bacteria *M. ciceri* ND-64. The ability of chickpea rhizobia to produce biologically active substances was studied using biotests according to methodological recommendations and methods for determining phytohormones, growth inhibitors, defoliants, and herbicides. The analysis of the quantitative content of extracellular phytohormones synthesized by *M. ciceri* microorganisms was carried out using the method of high performance liquid chromatography.

A new strain of *M. ciceri* ND-64 was selected, which is able to form an effective symbiosis with such chickpea varieties of Ukrainian selection. It was shown that the use of inoculation of seeds of these varieties using bacterial suspension of *M. ciceri* ND-64 contributed to an increase in the number (by 5–89%), weight of nodules (by 10–190%) and their nitrogenase activity (by 26–290%) compared with positive control (inoculation *M. ciceri* H-12), as well as structural parameters of chickpea yield: number of beans (by 5–34%), seeds from the plant (by 7–27%), weight of seeds from the plant (by 8–26%) and yield (by 4–19%) compared to the positive control in the zones of the Steppe and Polissia of Ukraine.

The ability of nodule bacteria *M. ciceri* ND-64 of intensive synthesis of phytohormones and the formation of highly effective symbiosis with chickpea plants of different varieties provided a complementary interaction of rhizobia with plants and a significant increase in crop yield.

It was found that *M. ciceri* ND-64 with high nitrogen-fixing activity is characterized by the ability to synthesize phytohormone-like substances: auxins, cytokinins and gibberellins. For example, when wheat coleoptiles were treated with a suspension of *M. ciceri* ND-64, the highest increase in their length was registered at a dilution of 1:1000 (20%), the highest increase in cucumber cotyledons weight at the same dilution – by 50%, and gain in the length of corn mesocotyles was 23% at a concentration of 1:500. High-performance liquid chromatography in the culture fluid of *M.ciceri* ND-64 revealed a high content of auxin substance with a total concentration of 29.6 μg/g absolutely dry biomass.

M. ciceri ND-64 are capable of active synthesis of substances of phytohormonal nature, which contributes to the effective interaction between rhizobia and chickpea plants.

THE EFFECT OF ANTISEPTICS ON *STAPHYLOCOCCUS EPIDERMIDIS* SKIN ISOLATES

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Nowadays bacterial skin infections are some of the most common infectious diseases. Treatment of skin infections usually include application of the topical antimicrobials, which may be an antibiotic (such as macrolides) or an antiseptic. However, there are some concerns that indiscriminate usage of antiseptics can potentially promote developing of antibiotic resistance. In our research we studied the effect of most common antiseptics on skin isolates of staphylococci, which have different susceptibility to MLS-group antibiotics (macrolides, lincosamides, and streptogramin B).

The aim was to determine susceptibility of MLS-resistant strains of *Staphylococcus epidermidis* to antiseptics.

In our experiment we used 6 strains of *S. epidermidis:* 3 – with MLS-resistance (MIC of erythromycin 250-4000 μg/mL), 3 – with intermediate susceptibility to macrolides (MIC of erythromycin 125 μg/mL). All microbial strains were isolated from patients with recurrent purulent skin infections. As antiseptics we took those, which are frequently used in treatment of pyoderma: decametoxinum (0.2 mg/mL), chlorhexidine bigluconate (5 mg/mL), myramistin (0.1 mg/mL), povidone-iodine (10 mg/mL), extractum chlorophyllipti spissum (2.5 mg/mL), salicylic acid (20 mg/mL). The antibacterial activity of antiseptics was determined by serial two-fold dilution assay in Muller-Hinton broth. After incubation for 24 hours at 37°C, inhibition of bacterial growth was evaluated based on the increasing in optical density (OD), which was recorded at a wavelength 495 nm using a spectrophotometer Synergy^{TM}HTX S1LFTA (BioTek Instruments, Inc., USA). Gene5 and Microsoft Office Excel 2016 software were used for statistical processing of the results.

Decametoxinum showed the best antimicrobial activity against all *S. epidermidis* strains (0.625-1.25 μg/mL). Myramistin and chlorhexidine bigluconate were active against all tested staphylococci in concentration 0.3-10 μg/mL and 15.6-31.25 μg/mL. Povidone-iodine was active in concentation 125 μg/mL against all microorganisms. Extractum chlorophyllipti spissum inhibits the growth of all examined microorganisms in concentation 62.5-250 μg/mL. Salicylic acid showed low antimicrobial activity (1000 μg/mL) against all microbial samples.

To sum up, such antiseptics like decametoxinum, myramistin, chlorhexidine bigluconate showed pronounced antimicrobial effect against investigated strains of staphylococci. Antimicrobial activity of povidone-iodine and extractum chlorophyllipti spissum are characterized by moderate action. Salicylic acid manifested low antimicrobial activity. Consequently, acquired MLS-resistance of *S. epidermidis* does not affect the level of their sensitivity to antiseptics.

PECULIARITIES OF VAGINAL MICROBIOTA AND INDICATORS OF IMMUNE FACTORS IN BACTERIAL VAGINOSIS

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Relevance: Facultative - anaerobic and obligate - anaerobic opportunistic pathogens, components of the resident microbiota of the urogenital tract, under the action of certain exo - and endogenous risk factors may exhibit pathogenic properties and become microorganisms which are a part of etiological structure of infectious - inflammatory process.

The aim of the study is to evaluate the clinical and microbiological efficiency and safety of "Dialak" for women with intermediate type of bacterial vaginosis (BV) and its effect on humoral immunity.

Materials and methods. 30 women of reproductive age were examined: 20 women with intermediate type of BV, and 10 with normocenosis. The content of immunoglobulins M, G, A, E and complement components C3 and C4 in the serum ware examined using electrochemiluminescence analysis (ECLIA).

Results. In analysis of indicators, the concentration of **IgA** before treatment was (2.15±1.13) g/L and after (2.05±1.06) g/L, **IgM-c** (1.32±0.62) g/L before (1.23±0.64) g/L, respectively; **IgG** (11.22±1.99) g/L and after (11.37±2.28) g/L; and **IgE** from (76.04±87.90) to (69.62±89.03). The complement index of C3C before treatment was (1.04±0.20) g/L and after (1.04±0.19) g/L, C4 complement before treatment (0.21±0.05)) g/L and after (0.20±0.05) g/L. When comparing the results of women with normocenosis IgA (2.07±0.65) g/L, IgM (1.67± 0.82) g/L, IgG (12.02±1.73) g/L, IgE (41.34±39.80) and components of the complement system C3C (1.09±0.21) g/L and C4 (0.20±0.04) g/L indicators of humoral immunity did not change significantly. The established changes in the humoral part of the immune system were regarded as a compensatory response of the immune system to dysbiotic changes in the microflora of the vagina.

Conclusion. Patients with intermediate type of vaginosis did not develop inflammation at the systemic level, which is confirmed by the normal level of serum C3 and C4 component of complement. Opsonization of objects of phagocytosis by components of complement is not violated.

ANTI-CORROSIVE PROPERTIES OF THE GUANIDINE-CONTAINING OLIGOMER WITH ALKYL RADICAL

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Recently, corrosion, especially microbiologically influenced corrosion (biocorrosion), is one of the problem in building construction and oil and gas industry. Annual losses from corrosion reach 3-6% of Gross Domestic Product (GDP) of countries. This problem demand the search of effective methods of protection and use of new inhibitors which are one of the promising and economically preferable. Guanidinium oligomers are a poorly studied class of organic compounds that attract attention due to their antimicrobial properties. Such compounds are perspective for use as a microbial corrosion inhibitor.

To study anticorrosive properties of newly-synthesized guanidinium oligomer DEG-2 with $C_{10}H_{21}Br_2$ alkyl radical (compound was obtained at the Institute of Macromolecular Chemistry, NAS of Ukraine) collection SRB cultures *Desulfovibrio* sp. 10, *D. desulfuricans* DSM642, *D. vulgaris* DSM644 from UCM of D.K. Zabolotny Institute of Microbiology and Virology NAS of Ukraine were used. To evaluate the efficacy of the studied compound, such inhibitors as DPC (N-decyl pyridinium chloride – quaternary ammonium compound (National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute", Ukraine) and Armohib CI-28 (Diamine Ethoxylate) (Akzonobel, Holland) were used for comparance. In liquid Postgate "B" nutrient media inoculated with SRB cultures previously treated steel coupons and inhibitors in concentrations - DPC (1 g/L), Armohib CI-28 (5 mL/L) and guanidinium oligomer (5 g/L) were added. As a control Postgate "B" media with coupons and inoculated with SRB as well as sterile media without inhibitors were used. Exposure period was 30 days at 28°C. The inhibitor's efficacy was estimated according to such indicators as bacterial titer change, the corrosion rate and degree of metal protection (Z).

The titer of three strains of SRB in control variants without inhibitors was in range $1 \cdot 10^7$ - $4 \cdot 10^8$ cells/mL. During the cultivation of bacteria with DPC bacterial amount of *D. desulfuricans* DSM642 strain was decreased to dozens cells per mL, and no growth for other two stains was observed. The adding of Armohib CI-28 led to decreasing of SRB titers to $3.4 \cdot 10^6$ – $3.7 \cdot 10^7$ cells/mL (by 1-2 orders). Similarly to DPC, in the presence of the guanidinium oligomer with alkyl radical only dozens of cells were observed. Thus, efficacy of biocidic properties of DPC, Armohib CI-28 and newly-synthesized guanidinium oligomer were 99.99-100%, 63.0-95.89% and 99.99%, respectively. The determined rate of steel corrosion in control variants with SRB and without inhibitors were 0.21 – 0.35 mg/cm^2·hour. The adding of DPC decreased corrosion rate to 0.032 – 0.046 mg/cm^2·hour for all three SRB strains and adding of Armohib CI-28 decreased corrosion rate to 0.027 – 0.039 mg/cm^2·hour. The rate of steel corrosion with guanidinium oligomer for three SRB strains were 0.075-0.079 mg/cm^2·hour. According to weight loss of steel coupons the degree of metal protection (Z) were for DPC- 84.54 – 90.46%, for Armohib CI-28 – 75.96 – 92.0%, and for guanidinium oligomer were lower (60.15-63.17%).

The data shows that newly synthesized guanidinium oligomer with alkyl radical possess not only biocide properties, but anticorrosive as well. This compound is new-promising for usage as anticorrosive agent to fight with microbiologically influenced corrosion.

METABOLOMICS-ASSISTED DRAFT METABOLIC NETWORK RECONSTRUCTION OF *PRIESTIA ENDOPHYTICA* UCM B-5715

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Priestia endophytica UCM B-5715 synthesizes a variety of biologically active compounds, such as pigments, substances with anticancer activity, and plant hormone precursors, which makes it a promising industrial strain. However, biotechnologically relevant metabolic pathways and biochemical reaction cascades of this bacterium remain undiscovered.

The information regarding its primary and secondary metabolism, gene regulation, and protein-protein interactions is scattered. This study aimed to gain an insight into the metabolic network interconnections of *P. endophytica* UCM B-5715 and construct a knowledgebase merging genomic, proteomic, and metabolomic data on this microorganism. To conduct metabolomic profiling, the strain *P. endophytica* UCM B-5715 was grown on beef-extract agar for 24 hours. Exo- and endometabolites were extracted following standard protocol and separated by gas chromatography-mass spectrometry. The results were imported into MetaboAnalyst5.0 for evaluation. The strain's whole genome annotated assembly was obtained from the GenBank database (GCA_900115845.1) and manually reannotated via ebi-blastp search against the uniprotkb_bacteria database. Merlin software was used for metabolic network reconstruction. Gene-Protein-Reaction associations and gap-fill analysis were introduced manually into the model based on genome annotation, experimental data, and literature evaluation. We obtained 101 metabolites that were categorized into 7 categories. The majority of metabolites were clustered into the organic acids, carbohydrates, and fatty acyls RefMet super-classes, which comprised 28%, 25%, and 25% of the total number of compounds, respectively. Over Representation Analysis indicated that 25 pathways were significantly associated with the metabolic profile obtained, Protein biosynthesis, Aspartate metabolism, and Glutathione metabolism showing the largest enrichment ratio. Manual genome reannotation showed that 2016 genes out of 5144 had an enzyme-coding function. According to gene content analysis, 40% of genes in the network code for amino acid metabolism enzymes. Both nucleotide metabolism genes and genes involved in cofactor biosynthesis represent 18% of the enzyme-encoding genome. The pathways of terpenoids and polyketides biosynthesis, indole alkaloid biosynthesis, cyanoamino acid biosynthesis, and xenobiotic degradation are reported in the strain *P. endophytica* UCM B-5715 for the first time. The model contains 73 KEGG pathways featuring 1559 reactions. There are 5750 reactants and 7023 products in *P. endophytica* UCM B-5715 metabolic network in total. Thus, with the help of metabolomic profiling and genome reannotation, we developed a draft metabolic network reconstruction of *P. endophytica* UCM B-5715, which deepens the current knowledge of its metabolism and sheds light on the previously unexplored biotechnologically important traits.

NEUROLOGICAL MANIFESTATIONS OF COVID-19

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The relevance of the topic is due to the extensive spread of coronavirus infection (COVID-19) as a pandemic disease around the world. Although SARS-CoV-2 mainly manifests with respiratory symptoms, it has already been found out and reported of the virus' effects systemically, including that of the nervous system. This thesis is intended to provide a comprehensive overview of the neurological manifestations of COVID-19 and to discuss potential pathogenic mechanisms of damage to the central nervous system (CNS). Clinicians and, in particular, therapists, neurologists and infectious disease specialists should be aware of these symptoms and be able to identify them at an early stage.

The aim of the study is related to a retrospective analysis of the main neurological manifestations of coronavirus infection in humans.

The materials and methods of the study included a systematic review of clinical studies of cases of neurological manifestations, complications and disorders associated with COVID-19 throughout the entire period of the pandemic. Data search was carried out in electronic databases PubMed, Scopus, Embase and LILACS. As the new epidemic is still ongoing, there is insufficient documentation of the neurological manifestations of SARS-CoV-2. Patients with COVID-19 may initially present with nonspecific neurological symptoms, including headache and dizziness. Others may develop more specific symptoms such as seizures and cardiovascular disease. There is also evidence that the more severe the infection, the greater is the likelihood of developing neurological symptoms, especially cardiovascular diseases and changes in the patient's mental status. Human coronaviruses are already recognized as neuroinvasive and neurotropic ones. In particular, SARS-CoV is proved to cause various neurological diseases such as polyneuropathy, encephalitis, and ischemic aortic stroke. In addition, its RNA was detected in the cerebrospinal fluid of a patient with severe acute respiratory syndrome (SARS), while autopsy samples from eight SARS patients revealed the presence of SARS-CoV in brain samples using immunohistochemistry, electron microscopy, and real life studies. The new coronavirus can potentially enter the central nervous system using the same pathophysiological mechanisms as other coronaviruses. In spite of the fact that the exact pathophysiological mechanisms are not fully researched, two possible theories have been proposed so far: hematogenous spread and retrograde neuronal spread. The olfactory nerves and the olfactory bulb in the nasal cavity can act as a connecting channel between the nasal cavity and the central nervous system. The latter scenario is further supported by the fact that many COVID-19 patients experience anosmia or hyposmia. Moreover, removal of the olfactory bulb in mice resulted in limited penetration of CoV into the central nervous system. As a result of data analysis and literature review, the conclusion is made that COVID-19 is a common pathology able to affect various organs, including the central and peripheral nervous system. The neurological symptoms caused by CoV are similar and can occur in any age group. Continuous documentation of neurological symptoms, complications and disorders, timely testing of cerebrospinal fluid, EEG and autopsy in surviving COVID-19 patients can help us in better understanding of the new coronavirus neurological manifestations, as well as the pathophysiological mechanisms of CNS damage.

BIOLOGICAL PROPERTIES OF ACTINOBACTERIA ISOLATED FROM THE BLACK SEA MUSSELS

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Today, among various marine microorganisms, marine actinobacteria are one of the most promising groups due to their ability to produce secondary metabolites with various types of biological activity, including antimicrobial and antitumor action.

The study aimed to isolate actinobacteria from mussels of the Black Sea, to characterize some of their biological properties and to carry out primary identification by fatty acid composition.

The study was based on deep-sea samples of Black Sea mussels. Isolation was performed on oat agar with sea salt, Gause №1 and Gause №2. During the study, 14 isolates of marine actinobacteria were obtained. The morphology of colonies and cells was studied according to generally accepted methods. Identification of strains by fatty acid composition was performed by gas chromatography using an automatic system for the identification of microorganisms MIDI Sherlock, antibiotic sensitivity was evaluated by disc-diffusion method.

Microscopy of the slides stained with Pfeiffer's magenta detected short rods located alone, in chains, V-shaped or chaotic in the cultures of most actinobacteria. In addition, filamentous cells were found in the preparations along with short rods. The cells of some of the studied strains were represented by coccal forms. The ability of strains Myt 2, Myt 6, Myt 7b to produce melanoid pigment was detected on ISP-6 and ISP-7 media. The study of the fatty acid spectrum of selected strains of actinobacteria revealed that they belong to *Streptomyces* genus. For actinobacteria of the *Streptomyces* genus, fatty acids 15:0 anteiso (from 36.05% to 33.05%), 16:0 iso (15.05% - 12.75%), 14:0 iso (4.13% - 1.87%), 17:0 anteiso (10.41% - 7.75%), 15:0 iso (14.89% - 6.64%). Evaluation of antibiotic susceptibility of isolated actinobacteria to 13 antimicrobials showed that strains were sensitive to streptomycin, kanamycin, tetracycline, gentamicin, amikacin, chloramphenicol and neomycin; resistant to penicillin, oleandomycin and nystatin. Sensitivity to amicillin, erythromycin and rifamycin was variable and strain-specific.

Primary identification of 14 cultures of marine actinobacteria isolated from deep-sea mussels of the Black Sea by fatty acid profile allowed classifying them as representatives of the *Streptomyces* genus. The strains were characterized by typical morphological and culture properties and showed variable susceptibility to antibiotics. According to the literature data, the *Streptomyces* genus alone can produce a wide spectrum of bioactive molecules. Therefore, isolation of actinobacteria from marine environments and study of their metabolite profiles is promising for the subsequent search for new antimicrobial compounds.

RELATIONSHIP BETWEEN RHEUMATOID ARTHRITIS AND *MYCOPLASMA PNEUMONIA*

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Mycoplasmas are the smallest self-replicating, pleotrophic bacteria that lack cell walls. The largest group of the Mollicutes class is divided into more than 100 *Mycoplasma* species. Mycoplasmas are often found as extracellular parasites attached to the external surfaces of host cells, but some species invade host tissues and cells, and replicate intracellularly. These microorganisms can produce a variety of effects on host cells and tissues. Besides affecting cell growth and morphology, mycoplasmas are able to alter metabolic, immunological and biochemical functions. Rheumatoid arthritis (RA) has a complex and multifactorial etiology. Infectious agents could start this disease. The majority of the characteristics of this infirmity can be observed in chronic arthritis produced by mycoplasmas in animals. In this study, the association between *Mycoplasma pneumoniae* and RA has been evaluated.

Patients with *Mycoplasma pneumonia* (MP) infection have an increased risk of rheumatoid arthritis (RA) developing. The results indicated that this risk is more pronounced in the first 2 years of MP and for patients aged ≤19 and ≥65 years. To determine the incidence of mycoplasmas in human arthritis new direct methods such as the polymerase chain reaction and a known human mycoplasma isolates should be used. Cooperation on an international level would be valuable. The presence of antibodies against *M. pneumoniae* was associated with RA (odds ratio=2.34, $p<0.001$).

The results suggest that *M. pneumoniae* could be a cofactor in the pathogenesis of RA; however, more studies need to be done.

PURIFICATION OF TOXIC LEACHATE BY METHANOGENIC MICROORGANISMS

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The problem of accumulation of liquid organic waste is urgent for countries of all over the world. Toxic leachate is formed in municipal landfills as a result of microbial fermentation of solid organic waste. It has caused catastrophic pollution of groundwater and natural ecosystems. The leachate contains toxic soluble organic acids and alcohols in high concentrations. Currently, there are no effective technologies for liquid organic waste purification. The application of microbial technologies is a promising method for solving this environmental problem.

The aim of the work was to determine the effectiveness of the leachate purification by metanogenic microorganisms.

The anaerobic bioreactor (50 L) was used for leachate purification. Fermented methane tank sludge was used as inoculum. The concentration of soluble organic substances was determined by the permanganate method. Determination of pH and Eh was performed using an ionometer universal EZODO MP-103. Gas holders connected to methane tank were used to determine the volume of gas. The composition of the gas phase was determined by standard methods on a gas chromatograph.

Effective purification of the leachate by methanogenic microorganisms was shown. The concentration of soluble organic compounds decreased from 280 to 20.8 mg/L during 56 days of fermentation. However, the concentration of organic compounds increased from 208 mg/L to 520 mg/L on 33 days of fermentation. This indicated the hydrolysis of unfermented food waste particles by diversified microbial community of methane tank sludge. The concentration of CH4 in the gas phase of the anaerobic bioreactor increased and ranged from 40% to 72% (from 12 to 56 days).

Thus, the high efficiency of toxic filtrate purification indicates the possibility of using methanogens for the development of environmental biotechnologies for filtrate purification in landfills with the simultaneous obtaining of high-energy fuel – biomethane.

ASSESSION OF INTERFERONS AS THE THERAPEUTIC DRUGS

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Interferons are proteins that consist of 146-166 amino acid residues organized in the polypeptide chain. They are synthesized by mammalian cells in response to viral infection and provide nonspecific antiviral immunity. Their biosynthesis in response to the penetration of a viral infection is one of the fastest organism's reactions. Interferons are the first line of defense against a viral attack. Besides, interferons are the family of cytokines regulating innate and adapted immunity. This is the reason for using these molecules as an attractive target for immunomodulation therapy.

The aim of the present study was to perform a comparative analysis of interferon-containing drugs on the Ukrainian market. Results of the performed comparison showed that on the Ukrainian market there are three main classes of interferons drugs - alpha, beta, and gamma -which are differing by their amino acid sequences, physicochemical properties, and induction by different agents such as viruses, bacteria, bacterial products, polymers, low molecular weight compounds. Major players in the world interferons market are Roche, Merck, Novartis AG, Pfizer Inc, Nanoge, and others. In Ukraine, interferon-containing drugs are produced by BioPharma, Valartin pharma and etc. The pharmaceuticals are presented mostly as the recombinant human interferon-alfa or interferon-beta and used as antiviral medicines. Interferon-gamma is also presented as a recombinant molecule with antiviral, immunomodulating, and antitumor activity. Using interferon-containing drugs as crucial elements of cellular defense mechanisms in humans has revealed their clinical effectiveness against viral infections, cancer, and neurodegenerative diseases by inhibiting virus replication, decreasing tumor cell mass, or controlling disease symptoms, and prolonging survival.

All these data suggest the global increase of the interferon drugs market in the nearest future due to growing numbers of incidence of various virus diseases, including respiratory viruses: coronaviruses, flu, and diseases as cancer, and multiple sclerosis. Thus, it is considered using interferon in combination with other drugs as the perspective direction of therapeutics.

IDENTIFICATION OF *PLECTOSPHAERELLA MELONIS* ISOLATED FROM CUCUMBER PLANTS IN UKRAINE

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In the last ten years, many countries around the world recorded the cases of a new disease of the Cucurbits family group plants, the agent of which was identified as *Plectosphaerella melonis* (syn. *Acremonium cucurbitacearum*) (Garsia-Jimenez *et al*., 1994; Bruton *et al*., 1995; Gubler *et al*., 1996; Alfaro-Garsia *et al*., 1996; Cluck *et al*., 1997; Armengol, 1997; Armengol *et al*., 1998; Bruton, 1998; Bruton *et al*., 1999; Bruton *et al*., 2000a,b; Aergeten *et al*., 2000; Martinez-Culebras *et al*., 2004; Chilosi *et al*., 2008). The spectrum of host plants of *P. melonis* is limited. The fungus is pathogenic only for plants of the Cucurbitaceae family.

In 2012 *P. melonis* 502 strain as a probable pathogen was isolated from the affected cucumber plants grown indoors. The aim of our work was to identify the isolate on the basis of morphological-cultural and molecular-genetic characteristics and to confirm the pathogenicity of the isolate based on Koch's postulates.

The results of the research of the ability of the *P. melonis* fungus to cause a disease of cucumber plants are presented further. *P. melonis* 502 isolate was isolated from the highly affected plants grown in glass block greenhouses. The morphological and cultural characteristics of the fungus *P. melonis* 502 were described that allowed to classify it as the *P. melonis* species.

For DNA isolation, parts of fungus colonies grown on BMA were processed using the AmpliSens DNA-sorb-B kit. The necessary quantity of DNA solution obtainment was carried out in appliance to described methods (Birnboim & Doly, 1979; Chowdhury & Akaike, 2005; Chi et al., 2009; Sika et al., 2015). For sequencing, obtained DNA solution polymerase chain reaction was carried out using ITS1 and ITS4 primers (White et al., 1990). The amplification reaction was conducted within Applied Biosystems equipment following prescribed methods (Watts & MacBeath, 2001; Garrido et al., 2009). Analysis of resulting 5.8S rDNA sequences were compared with GenBank database sequences using BLAST analyses (http://www.ncbi.nlm.nih.gov/blast).

Using PCR method, the amplicon was obtained, with the length of 317 bp and phylogenetic analysis was performed. BLASTn searches at GenBank showed that the sequence of *P. melonis* 502 had 99% similarity with 14 isolates of *A. cucurbitacearum* and *Plectosphaerella melonis*. In addition, 99% of similarity with a typical strain of *A. cucurbitacearum* A-419 was established, that made it possible to attribute the strain 502 to *P. melonis* species. The Koch triad was reproduced in the work, namely the pathogenicity of *P. melonis* 502 on cucumber plants was confirmed, the pathogen was reisolated into a pure culture and the symptoms of the disease were described. The most sensitive to *P. melonis* 502 were young seedlings in 14 days after sowing the seeds in the soil, with the death of the lateral roots observed and the brown main root. After 28 days of cultivation, lesions of the root cervix were observed.

The present results are the first to show pathogenicity of *P. melonis* on cucumber plants in Ukraine. This study has confirmed the pathogenicity of this fungus to cucumber, and has shown that young cucumber seedlings were very susceptible to this pathogen.

INFLUENCE OF CULTIVATION CONDITION FOR ORGANIC ACIDS PRODUCTION BY *LACTOBACILLUS PLANTARUM*

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Phytopathogenic bacteria cause many different plant diseases and do harm to agriculture. The use of pesticides and chemical fungicides is the main method of control for phytopathogenic microorganisms. One of the alternative trends in biological plant protection is the development and use of biological products based on bacterial antagonists, which synthesize a wide spectrum of metabolites active against bacteria and fungi that cause plant diseases in agriculture. Lactic acid bacteria show a strong antagonistic effect against phytopathogenic bacteria due to organic acids, hydrogen peroxide, bacteriocins, short-chain fatty acids synthesized by them. The production of metabolites depends not only on the individual characteristics of the strain-producer, but also on the cultivation conditions - the pH and composition of the medium, temperature and duration of cultivation**. The aim of the study** was to investigate the effect of cultivation conditions on the synthesis of organic acids by *L. plantarum* strains and their effect on the antagonistic activity against phytopathogenic microorganisms. **Materials and methods.** Quantitative composition of organic acids of cell-free supernatant of *L. plantarum* strains was investigated by high-performance liquid chromatography (HPLC). The influence of different physical parameters of cultivation on *L. plantarum* antagonistic action (pH of medium, temperature and duration) was tested. Role of organic acids in the manifestation of antagonistic activity of four *L. plantarum* strains was determined by measuring of diameter of inhibition zone around the discs with cell-free culture supernatants (CFS). **Results.** The content of organic acids in the culture fluid of 4 strains of *L. plantarum* was studied. It was found that all strains synthesized four organic acids - lactic, acetic, citric and succinic acids in quantities from 0.1 to 1.3 mg/mL. All studied *L. plantarum* strains synthesized the most amount of succinic acid (0.8 - 1.3 mg/mL), while the amounts of citric acid was produce less - from 0.1 to 0.13 mg/mL. *L. plantarum* 1112 fs strain synthesized almost equal amounts of acetic and succinic acids (0.8 - 0.9 mg/mL). 12 experiments with a combination of variables were performed to examine the combined effect of temperature, pH, and duration of cultivation on the synthesis of organic acids and antimicrobial activity of each *L. plantarum* strain against phytopathogenic bacteria. It was found that antagonistic activity of *L. plantarum* 13c strain against phytopathogenic bacteria during 48 hours of cultivation was highest at pH 7.8 and 23°C and pH 6.8, and 30°C. Under these conditions zones of growth inhibition of indicator strains were 17.25±0.5mm and 16.88±0.5mm, respectively. The highest antagonistic activity against phytopathogenic bacteria *L. plantarum* strains showed at 72 hours of cultivation and 23°C then zones of growth inhibition of the indicator strains reached 18.62±0.5mm. Parameters of cultivation (duration, temperature and pH of the medium) were affected the synthesis of lactic and acetic acids. It can be assumed that *L. plantarum* 13c would synthesize the largest amount of acetic acid under following conditions of cultivation: pH 7.8, at 72 hours and 23°C. **Conclusions.** Among organic acids all studied *L. plantarum* strains synthesized the largest amounts of succinic acid (0.8 - 1.3 mg/mL). The highest antagonistic activity of the strains *L. plantarum* against phytopathogenic bacteria was highest at time 72 hours and 23°C and zones of growth inhibition of the indicator strains was 18.62±0.5mm. Optimum parameters for acetic acid production by *L. plantarum* 13c were following: pH of medium – 7.8, temperature - 23°C and duration of cultivation - 72 hours.

PRODUCTION OF EXOPOLYSACCHARIDES BY MEDICINAL MUSHROOM *GRIFOLA FRONDOSA* IN SUBMERGED CULTURE

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Various nutritional, medicinal and prophylactic properties of basidiomycete *Grifola frondosa* (maitake) promote an interest in investigations of that fungus. Pharmacological activity of products obtained from these fungi is conditioned of polysaccharides - beta-glucans having immunomodulation, antitumor, antiviral, antimicrobial and others effects. However, preferably maitake is cultivated on solid plant substrates and thus produce fruiting bodies from which endopolysaccharides are obtained and used. At the same time, these species in the conditions of submerged cultivation is less studied. There are also insufficient data on the peculiarities of exopolysaccharides *G. frondosa* biosynthesis. Therefore, investigation of *G. frondosa* in the cultivation of this fungus in the submerged culture is currently important.

This work is devoted to studying the production of biomass and exopolysaccharides by two strains of *Grifola frondosa* (Dick.) Gray in condition of cultivation in the liquid nutrient media with different pH.

Cultivation was carried in flasks on the shaker (120 rpm) at +28°C, 15 days, in liquid medium: NH_4NO_3 – 3 g/L; KH_2PO_4 - 1 g/L; K_2HPO_4 - 1 g/L; $MgSO_4 \cdot 7H_2O$ – 0,4 g/L, glucose - 20 g/L and molasses - 10 g/L (Linovytska, Bukhalo, 2007). The most favorable pH values for the accumulation of biomass and exopolysaccharides by *G. frondosa* strains were determined in the above synthetic medium, in which by changing the concentration of KH_2PO_4 and K_2HPO_4, solutions with different pH values from 4.7 to 8.1 were obtained. Acidity was determined by potentiometric method using a pH meter. Determination of the concentration of exopolysaccharides was performed by the phenol-sulfur method (Varbanets, 2006). Determination of biomasses production was weighing method.

Under the conditions of cultivation on the liquid nutrient media, favorable for the mycelial growth pH values were determined: for strain 1790 — pH=6.0, and for strain 1794 pH 5.4. The acidity of the nutrient media that promotes the biosynthesis of exopolysaccharides was determined: pH 6.0 for strain 1790 and pH 5.8 for strain 1794. The dynamic of biomass production was similar for two strains *G. frondosa* – the highest importance were registered on the 6-7 days of cultivations. The maximal level of exopolysaccharides biosynthesis was on the 10-11 day. The highest level of biomass accumulation was found on media with molasses for strain *G. frondosa* 1790 - 5.1 g/L and for strain *G. frondosa* 1794 – 4.2 g/L.

The highest concentration of exopolysaccharides was 2.8 g/L in strain *G.frondosa* 1790 and 1.3 g/L in strain *G.frondosa* 1794.

Thus, for the promising for biotechnological application strain *G. frondosa* 1790, the duration and conditions of submerged cultivation were determined to obtain the target products - biomass and exopolysaccharides.

A BROAD-HOST-RANGE LYTIC ERWINIA PHAGE KEY WITH EXOPOLYSACCHARIDE DEGRADING PROPERTIES

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Fire blight, a plant disease caused by *Erwinia amylovora*, leads to significant economic losses in the cultivation of fruit and ornamental trees. Currently, a promising approach for *E. amylovora* biocontrol is usage of phages and phage-based products, such as phage exopolysaccharide depolymerases (EPSDs). Phage EPSDs can target amylovoran and levan, specific capsular polysaccharides of the pathogen, making cells accessible to bactericidal treatment. The aims of this work were comparative genome analysis of *Erwinia* phage Key, identification and characteristics of its genes associated with EPSD activity.

Phage DNA was isolated by the phenol-chloroform extraction method and sequenced using the Illumina HiSeq 2500 platform. The contig was assembled with DNASTAR's SeqMan NGen12 software. The Key genome was scanned for potential genes using Glimmer and GeneMark.hmm. Functional annotation was conducted by the BLASTp, ExPASy and HHpred tools based on homology search. Phylogenetic analysis was performed using the maximum likelihood method after alignment with Clustal W implemented in MEGA XI with 500 bootstraps.

Bacteriophage Key is a lytic siphovirus that was originally isolated from quince with symptoms of fire blight. The host range analysis identified that Key is able to infect the *E. amylovora*, *P. agglomerans* and *E. horticola* strains. On the lawns of the sensitive bacteria Key forms 1-2 mm turbid plaques. But when plated with the *P. agglomerans* g157 or *E. horticola* 60-3m cultures, the large halo zones around plaques increasing over time of incubation are observed. This indicates an EPSD activity of KEY associated with phage virions.

The dsDNA genome of Key is 115,651 bp long with a GC ratio of 39.03%. It contains 182 putative genes and 27 tRNA genes. In total, 57 functionally annotated genes involve in DNA replication, recombination, repair, and packaging, virion morphogenesis, nucleotide metabolism, lysis, phage-host interaction and others. Gp 141 was identified as a potential EPSD that has homologues in many phages *Erwinia*-specific phages and can be responsible for the halo formation observed around the phage Key plaques. Due to the revealed genome synteny as well as protein similarity to T5-like phages, phage Key together with its closest relative, *Pantoea* phage AAS21, are suggested to represent a novel genus within the *Demerecviridae* family.

Broad host-range together with EPSD activity makes phage Key as an attractive candidate for biological control of fire blight. Further experimental studies are needed to test this assumption.