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Introduction. The gut microbiome significantly affects the functioning of the body: it participates in the protection of the body against pathogenic microorganisms, in the processes of metabolism, inhibition of inflammatory responses, in the formation of innate and adaptive immune response in the intestinal mucosa. One of the reasons for changing the microbiota is the use of antibiotics. Therefore, the processes of interaction of antibiotics, *Salmonella enteritidis* and *Salmonella typhimurium* with representatives of normal intestinal microflora are of particular interest. **Materials and methods.** The quantitative and qualitative composition of the wall microbiota in rats by bacteriological method, the statistical analysis of data using the program StatSoft Statistica v12 were conducted. **Results & discussion.** With the introduction of vancomycin and *S. enteritidis, S. typhimurium* in groups II, III, IV there was a decrease in *E. coli* quantitative content by 10, 7 and 110 times, respectively ($p \leq 0.05$). The number of *P. aeruginosa* decreased significantly only in the third group ($p \leq 0.05$). The number of representatives of *Bacteroides spp.* significantly decreased by several thousand times (group II) and by 70 and 87 times (groups III and IV) ($p \leq 0.05$). The content of *E. faecalis* and *E. faecium* decreased by 861,6 and several thousand times (groups II, III, IV) ($p \leq 0.05$). The number of *Proteus spp.* significantly decreased in group II by 27 times and increased rapidly in group IV ($p \leq 0.05$). Group III showed a sharp decrease in the content of representatives of *Enterobacter spp.* and *Klebsiella spp.* in 847 and 150 times, and in group II there is an increase in their number by 7 and 46 times, respectively ($p \leq 0.05$). The number of *Staphylococcus spp.* decreased by 9.8 times only in II group. The quantitative content of *Clostridium spp.* decreased by several thousand times (group II) and by 5.5 times (group IV) ($p \leq 0.05$). The number of *Lactobacillus spp.* decreased by several thousand times (group II). The number of representatives of *Bifidobacterium spp.* significantly decreased by 10.9 times and by several thousand times (groups III, IV). The quantitative content of *Peptostreptococcus anaerobius* decreased significantly in all three study groups ($p \leq 0.05$). The content of *Salmonella spp.* increased in group II by 49 times and significant increase was observed in groups III and IV ($p \leq 0.05$). The introduction of salmonella, against the background of vancomycin pre-treatment, causes a dramatic change in the composition of the microbiota in groups V and VI, namely: an increase in the number of *E. coli* 65 and 105 times, a significant increase in the content of *P. aeruginosa* in the V group, and in the VI, 3 times. Also, in these groups there is a decrease in the number of *Bacteroides spp.* 9 and 10 times ($p \leq 0.05$). The content of *E. faecalis* and *E. faecium* decreased significantly only in the fifth group ($p \leq 0.05$). The number of *Proteus spp.* decreases 17 times in group V and also a significant decrease was observed in group VI ($p \leq 0.05$). A sharp increase in the content of representatives of *Enterobacter spp.* and *Klebsiella spp.* was observed in the V and VI groups ($p \leq 0.05$). However, representatives of *Peptostreptococcus anaerobius* in V and VI groups decreased 20 and 9 times, respectively ($p \leq 0.05$). The number of *Salmonella spp*. decreased only in group V 7 times ($p \leq 0,05$). With the introduction of experimental animals B. fragilis treated with *S. enteritidis, S. typhimurium* on the background of vancomycin pre-treatment, a significant decrease in the level of *E. coli* in group VII, and in VIII - by 538 times ($p \leq 0.05$). The number of *P. aeruginosa* in groups VII and VIII decreased significantly and the number of representatives of *Bacteroides spp.* naturally increases ($p \leq 0.05$). The content of *Lactobacillus spp.* decrease by 10.3 times only in VI group. The content of *E. faecalis* and *E. faecium* increased by 10 and 19 times in the seventh and eighth groups respectively, and the number of *Proteus spp.* decreases only in group VII 322 times ($p \leq 0.05$). Also, in VII and VIII groups there is a sharp decrease in the content of representatives of *Enterobacter spp.* and *Klebsiella spp.* ($p \leq 0.05$). The level of representatives of *Peptostreptococcus anaerobius* and *Lactobacillus spp.* increased significantly 7, 12 times and several thousand and 40 times (groups VII and VIII, respectively) ($p \leq 0.05$). The number of *S. enteritidis* and *S. typhimurium* in the VII and VIII groups decreased intensively ($p \leq 0.05$). **Conclusions.** The introduction of *B. fragilis* can be used in the treatment of inflammatory bowel diseases or diseases with impaired barrier function of the intestine.
Keywords: parietal microflora, microbiome, vancomycin, salmonella, bacteroids.

Introduction. Precursor directed biosynthesis is one of the promising approaches to finding new antimicrobial agents and creating next-generation probiotics. *L. reuteri* is capable to convert triatomic polyol glycerol into reuterine, a broad-spectrum antimicrobial substance. There are no data on the use of other polyols as precursors. The aim of the research was to investigate the effect of cell-free supernatants obtained by culturing *L. reuteri* DSM 17938 in its own disintegrate, supplemented with polyols (xylitol, sorbitol, mannitol and glycerol & glucose) on the daily biomass growth of opportunistic microorganisms. **Material & methods.** Reference strains *Staphylococcus aureus* ATCC 25923; *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* clinical isolate were used as a test cultures. The effect of the lactobacillus supernatant on the daily biomass growth of the test cultures was investigated by spectrophotometry using a 96-well polystyrene microtiter plates and a «LisaScanEM» spectrophotometer («ErbaLachemas.r.o.», Czech Republic). The final concentration of supernatants in the incubation medium was 30%, and the final concentration of bacterial cells was ~10^6 CFU/ml. Inhibition (II) or stimulation (SI) indices of the daily biomass growth of test cultures by formula were calculated. **Results & discussion.** Supplementation of culture medium with glycerol & glucose during *L. reuteri* cultivation resulted in the *S. aureus* (II = 70.7%), *Escherichia coli* (II = 72.2%) and P. aeruginosa (II = 74.7%) daily biomass growth inhibition. As a result of *L. reuteri* cultivation in its own disintegrate supplemented with mannitol, the supernatant acquired growth-promoting properties with respect to *S. aureus* (SI = 45.5%), *E. coli* (SI = 19.1%) and *P. aeruginosa* (SI = 19, 9%). The supernatant obtained after *L. reuteri* cultivation in disintegrate supplemented with sorbitol had no significant effect on the *S. aureus* and *Escherichia coli* daily biomass growth, but significantly stimulated the growth of *P. aeruginosa* (SI = 29.4%). The supernatant of *L. reuteri*, cultured in disintegrate supplemented with xylitol had no effect on staphylococcus growth, inhibited of *E. coli* (II = 16.5%) growth and increased of *P. aeruginosa* (SI = 19.1%) daily biomass growth. The data obtained for glycerol, the introduction of which into the culture medium of *L. reuteri* led to the appearance of inhibitory activity of the supernatant against all test cultures, were expected. They coincide with the results of studies by other authors and are associated with the ability of this type of lactobacilli to convert glycerol into a broad-spectrum antimicrobial substance reuterin. The results of the study confirm that xylitol, sorbitol and mannitol do not undergo fermentation with the formation of acidic end products during the cultivation of *L. reuteri*. These polyols remain either unchanged or undergo slight modification in the composition of the supernatant and have different effects on the daily biomass growth of test cultures. **Conclusion.** The results of the study showed that the use of xylitol, sorbitol and mannitol as precursors, and *L. reuteri* DSM 17938 as a biotransformer system in the development of new antimicrobials using a precursor-directed biosynthesis strategy is ineffective. They also confirmed that the supernatant obtained after cultivation of *L. reuteri* DSM 17938 in its own disintegrate supplemented with glycerol & glucose, has a pronounced inhibitory activity against the investigated opportunistic microorganisms.
Keywords: polyols, Lactobacillus reuteri, cell-free, supernats

Introduction. Troches are very popular in children due to their high compliance, pleasing organoleptic characteristics and easiness of administration. Nevertheless, the expanding range of drugs in this dosage form still lack anthelmintic products. In order to introduce the new anthelminthic drug in the form of chewable troches under the conditional name “Albenpast”, there were conducted the studies over selection the optimal gel-forming agent and flavorings as correctors of taste characteristics. The purpose of this work is to develop the technology of chewable troches under the conditional name “Albenpast” and to establish the critical points of the production process. **Materials &**

methods. As the objects of research the pure substances (albendazole, gelatin, glycerol, purified water, glucose syrup, fructose, citric acid, fruit flavoring, food coloring) and samples of troches on their basis were used. The research methods used are reflected in the State pharmacopoeia of Ukraine. **Results & discussion.** Research was conducted against the chewable troches "Albenpast" to the composition of the components of which the patent is claimed. Compositions of troches 1 and 2 differ in the type of sweetness flavoring: 1 contains glucose syrup, 2 contains fructose. Composition 2 is offered for the use in children who need to control the level of glucose. The production process offered includes 9 stages with critical points in 2, 3, 4, 5 and 7. Additionally, for each stage the possible types of quality control are described. The further quality control of the obtained by the offered technology samples of chewable troches showed their full correspondence with the requirements of SPhU. **Conclusion.** The technological process of production of chewable troches is offered and the technological scheme of their production is given. Critical parameters of the production process and their values are identified and described. The results of the quality evaluation of obtained chewable troches according to the main quality indicators in accordance with the requirements of SPhU are presented.
Keywords: oromucosal drug, production, helminthiases, children

Molecular dynamics study of the structural role of metal atoms in the urease active site 36-48
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Introduction. Urease is a representative of a small group of enzymes that can bind different alternative metals to execute the same catalytic function. The experimental X-ray studies conclude that a urease activity critically depends on the precise positions of amino acid ligands at a metallocenter, the bound solvent molecules and the type of metal, and very subtle changes of metallocenter structure can essentially influence the urease activity. Are these conclusions valid in the case of the urease structures in the solution? By molecular dynamics simulations, we studied these aspects for urease derivatives with alternative metals in solution under physiological pH and temperatures. **Methods.** Molecular dynamics (MD) simulations were carried out for the following systems: Ni-containing *Sporosarcina pasteurii* urease both native (PDB code 2ubp) and in complex with competitive inhibitor acetohydroxamic acid, AHA (PDB code 4ubp); *Klebsiella aerogenes* urease both Ni- and Mn-containing (PDB codes 1fwj and 1ef2, respectively); Fe-containing *Helicobacter mustelae* urease (PDB code 3qga) (table 1). As well, there was studied an apoenzyme of Ni-containing urease: the structure of the complex of competitive inhibitor AHA with *Sporosarcina pasteurii* urease (4ubp) from which there were removed Ni atoms. The systems studied (α subunits or its complex with competitive inhibitor) were placed in a cubic periodic cell filled with TIP3P water molecules. The simulation cell was 1 nm larger than the molecular system studied along all three axes. Na^+ and Cl^- counterions were added to neutralize the system and to reach ion mass fraction 0.9% NaCl. Before simulations the systems were energy-minimized. After a short steepest descent minimization, the the procedure continued by simulated annealing minimization. AMBER14ipq force field was used. To treat long-range electrostatic interactions the Particle Mesh Ewald algorithm was used. The equations of the movement were integrated by 2.5 fs step. To speed up the calculations the non-bounded van der Waals and electrostatic forces were evaluated only each second step and added with the scaling factor 2. The molecular dynamics simulations were run in NPT ensemble at pH 7.4 and two temperatures (298 K and 310 K). Trajectories were computed for 50 ns, the data were saved each 25 ps. Models building, structure refinement, molecular dynamics simulations, and analysis as well as the result presentation by using molecular graphics were performed by using the molecular modeling program YASARA Structure. **Results and discussion.** After equilibration the RMSD values for different systems are close to each other and change insignificantly (except Fe-containing *Helicobacter mustelae* urease), evidencing that their global structure is quite stable and that no significant conformational transformations occur within these systems, whereas *H. mustelae* urease structure revealed instability during the simulations. The presence of the competitive inhibitor in the active site did not change the Ni (1) and Ni (2) coordination numbers. There were observed no essential deformations of the geometry of the ions binding with the active site ligands as well. A similar situation was observed in the case of Mn-containing *K. aerogenes* urease too. In the case of *S. pasteurii* urease apoenzyme, there were observed the insignificant shifts of the active site residues. The root mean square deviation of the residues of the active site of apoenzyme relative to holoenzyme was 0.65 Å. In the absence of Ni ions in apoenzyme, the position of the inhibitor AHA within the active site is unstable and it gradually drifts and leaves the active site. For all ureases, the temperature increase from 298 K to 310 K had a little effect on the average distances "metal-ligand". The temperature increase from 298 K to 310 K had an insignificant effect on the distances "metal-water" in the active site of the Ni-containing ureases *S. pasteurii* and *K. aerogenes* and a little influence on these distances in the Mn-containing *K. aerogenes* urease. The metallocentre structures in the Mn- and Ni-containing *K. aerogenes* ureases are very similar. **Conclusions.** There have been studied the structural role of the nickel ions in a urease active site, the influence of the temperature and the ion type on the structure of the urease active site. It have been shown that binding of the competitive inhibitor (acetohydroxamic acid, AHA) did not change the Ni ions coordination in the urease active site and did not essentially effect the geometry of the active site near the nickel ions. The main factor of the inhibitor binding are the nickel ions. It have been shown that the active site structures of the Ni- and Mn-containing ureases *Klebsiella aerogenes* and *Sporosarcina pasteurii* are approximately identical. It have been shown that the metallocentre structure of these ureases are in general stable regardless of the urease source, the ion type and the temperature.
Keywords: urease metallocentre, Ni-, Mn- and Fe-containing urease, molecular dynamics.

Standardization of a method for identification of elecampane sesquiterpene lactones 49-53
Kotova E., Kotov S., Kotov A.

Introduction A wide use of elecampane, *Inula helenium* L. (*Asteraceae*), in both, folk and formal medicine, is explained by variety of its chemical composition. Rhizomes and roots of elecampane contain an essential oil, the content of which reaches 4%; the composition of the oil includes a mixture of sesquiterpene lactones. The main components of this mixture are alantolactone (0.5-2.0%), isoalantolactone (1.0-2.7%), and their hydrogenated derivatives: dihydroalantolactone, dihydroisoalantolactone, tetrahydroalantolactone, etc. These compounds seem to be responsible for pharmacological action of elecampane-based preparations. Herbal drug (HD) from elecampane is rhizomes and roots. There is no monograph on this type of HD in the State Pharmacopoeia of Ukraine (SPhU), therefore research related to its development is relevant. The mandatory identification test for HDs by the thin-layer chromatography (TLC) method in accordance with the requirements of SPhU is absent in the article GF XI "Rhizomes and roots of elecampane", therefore it is necessary to develop a procedure for identification of the main biological active substances (BAS) of elecampane by TLC-method. **Materials and Methods.** The rhizomes and roots of *Inula helenium* L. (Asteraceae) were obtained from various pharmaceutical enterprises of Ukraine during 2016-2018. The following equipment was used: Silica gel 60 F_{254} TLC plates (20x20 cm^2, 0.25 mm), Merck (Germany); Ultrasonic bath SUPER RK100H «Bandelin», (Germany); Glass vertical chamber; Automatic spraying device ChromaJet DS20. As standard substances have been used alantolactone, isoalantolactone and dihydroisoalantolactone (<95%) - **pharmacopoeial reference standards of the State Pharmacopoeia of Ukraine. Results and discussion.** A procedure for identification of elecampane by TLC method for the national monograph of the SPhU "Elecampane roots and rhizomes" has been developed.. The identification method is based on the ability of silver ions to react with unsaturated C-C bonds in the molecules of the isomers at the position of double bonds, which are alantolactone and isoalantolactone. The development of a procedure for identification was carried out in conjunction with its validation in accordance with the requirements of SphU according to the following scheme: 1) the choice of stationary phase (examination of plates with a thin layer of silica gel treated with 1, 3, 5, 7% (m/v) solutions of silver nitrate); 2) the choice of mobile phase (review of unified phases for chromatography of terpenoids); 3) the choice of concentration for markers-substances (study of 0.05, 0.1, 0.2% methanol solutions of alantolactone, iso-alantolactone, dihydroiso-alantolactone and SQTL mixture for preparation of the reference solution); 4) the choice of the method for test solution preparation (study of

extraction of herbal material with methanol, followed by concentration of the extract to the ratio of HD-test solution 1: 2, 1: 5, 1: 8); the choice of application volume of the test solution ; 5) the choice of the detection method (review of unified reagents and/or solutions for derivatization of chromatograms). Following conditions for identification have been chosen: the test solutions of HD (1: 5 in methanol), standard solution *CRS SPhU* alantholactone and isoalantholactone (0.1% solutions in methanol), TLC plates with a thin layer of silica gel treated with 5% silver nitrate solution, a solvent system toluene-ethyl acetate (9: 1), detection is carried out after treatment the plate with anise aldehyde solution and followed by heating. **Conclusion.** A procedure for identification of elecampane by for the national monograph of the SPhU "Elecampane roots and rhizomes" has been developed. It allows to identify such biologically active substances of the elecampane, as sesquiterpene lactones, which are markers of this species The developed chromatographic conditions allow to reliably chromatographically identify HD of elecampane in the presence on chromatograms of 3 zones of lactones – alantolactone, isoalantolactone and dihydroisoalantolactone.

Keywords. Elecampane roots and rhizomes, sesquiterpene lactones, monograph of the SPhU, TLC method, alantolactone, isoalantolactone and dihydroisoalantolactone.

Research of antimicrobic activity of foaming products samples with octopirox 54-57

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Introduction. Seborrheic dermatitis (SD) - chronic recurrent skin disease, which is associated with increased cutaneous fatty secretion, change in its qualitative composition and is characterized by localization in the areas of accumulation of sebaceous glands on the scalp, face, upper torso. Therefore, the choice of tactics for the treatment of patients with SD depends on the degree of clinical manifestations, duration of the disease, information about the effectiveness of previously conducted therapy. Particular attention is paid to the choice of antifungal medicines in the treatment of SD. Traditionally, local remedies in the form of ointments or creams are used to treat SD of the scalp, they cause many inconveniences when used. In this respect, foaming products, in particular shampoos, which include active substances that have certain therapeutic potential regarding the main mechanisms of SD treatment, having self-regulating, anti-inflammatory, antifungal, antibacterial, reparative, moisturizing properties, etc. are very appropriate. One of the main factors in the development of this disease is the yeastlike fungus of Malassézia fúrfur genus (or Pityrósporum ovále), which is present in the skin of each person. Octopirox®, which has strong fungicidal (antifungal) and antibacterial actions, was chosen among a number of modern products in this field. Therefore, the main purpose of our experiment was to study the antimicrobial activity of developed samples of foaming agents with octopirox to justify the rational concentration. **Materials and methods.** For this study, we produced a number of experimental samples of foaming bases with octopirox and α-lipoic acid at different concentrations: sample № 1 - foaming base; sample № 2 – foaming base + α-lipoic acid; sample № 3 – foaming base + octopirox (0,25 %); sample № 4 – foaming base + octopirox (0,5 %); sample № 5 – foaming base + octopirox (0,75 %); sample № 6 – foaming base + octopirox (1,0 %). The antimicrobial activity of prototype gels was studied in vitro by diffusion in agar ("wells" method). This method is based on the ability of active substances to diffuse in the agar medium, which was previously inoculated by bacterial crops. The results of the studies make it possible to characterize both the antimicrobial activity of the samples and the release of antimicrobial substances from the base, because the growth inhibition zones of microorganisms are formed as a result of the diffusion of these substances into a dense nutrient medium. **Results.** Based on the experimental data, in the development of the foaming product composition with octopirox AFI concentration of 0.5% is optimal and further increase it to 0.75% (sample No. 5) and 1.0% (sample No. 6) is impractical. It should be noted that the studies showed that foaming samples had high antifungal activity and moderate effect on gram-negative bacteria, so in the development of the optimal composition of the tool and its long-term storage and use, it is necessary to consider the introduction of preservatives and conduct appropriate research. **Conclusion.** Thus, the results of the experiments showed that the test samples No. 1 and No. 2 did not have any antimicrobial action pertaining to gram-positive, gram-negative bacterial cultures and antifungal activity. Samples No. 3, No. 4, No. 5 and No. 6 of the foaming product with octopirox at concentrations of 0.25%, 0.5%, 0.75% and 1.0% have a broad spectrum of antimicrobial action pertaining to gram-positive (*Staphylococcus aureus* ATSC 25293 and spore cultures of *Bacillus subtilis* ATSS 6633), gram-negative (*Escherichia coli* ATSS 25922 and *Pseudomonas aeruginosa* ATCC 27853) bacterial cultures, as well as in relation to the cultures of *Candida albicans fungi* ATSS 885-653 and *Aspergillus niger fungus* ATCC 16404. However, the experimental results showed that sample No 4 (octopirox concentration of 0.5%) was the most promising for further work on the development of antimicrobial activity of the foaming product.

Key words: seborrheic dermatitis, antimicrobial activity, octopirox, foaming product, product for men.