



Biomedical Sciences

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HEART PATHOLOGY IN ACUTE AFRICAN SWINE FEVER

INTRODUCTION. African swine fever (ASF) virus causes a disease of varying mortality which depends on its particular isolate in domestic pigs. A common clinical presentation in Eurasian region is peracute or acute hemorrhagic fever with almost 100% case fatality rate. The aim of our research was the study of heart pathology in acute form of ASF induced by virus genotype II (Georgia 2007).

METHODS USED. Infections were carried out using ASFV (genotype II). The titre of ASFV for each intramuscular injection was 10^4 50% hemadsorbing doses (HAD₅₀)/ml.

Eight healthy pigs of the same age and weight were infected by intramuscular injection. Animal care and euthanasia were done according to the AVMA Guidelines on Euthanasia, and local guideline for animal care and use (Institutional Review Board/ Independent Ethics Committee of the Institute of Molecular Biology of NAS, IRB00004079).

Clinical signs of infection were recorded daily. Pathological and anatomical characteristics were observed during routine post-mortem examinations.

RESULTS AND DISCUSSION. Experimental infection was characterized by early viraemia from 1-2 days post infection (dpi). Viraemia peaked on 5 dpi (virus titres were 5.0-5.25 log₁₀ HAD₅₀/ml). The high titres of ASF virus were determined in all pigs until 7 dpi. Incubation period of acute ASF induced by intramuscular injection of the virus varied between 18 to 24 h. The first clinical signs were observed after 20-36 h post infection when all infected pigs demonstrated loss of appetite and slight diarrhoea. Some pigs manifested dyspnoea, vomiting, incoordination, and prostration. A post-mortem examination was performed on all eight pigs, which died or were killed during the course of infection. Gross pathology of the heart in postmortal studies of animals revealed cardiac enlargement, intramural myocardial haemorrhages (in 5 pigs out of 8) and hyperaemia, and one of the pigs showed massive haemorrhages with over 30% of the tissue being involved in pathological process. Hydropericardial and epi- to endocardial haemorrhages were described in majority of cases. The pericardial cavities often were filled with yellowish, red or dark-red fluid, the volume usually exceeding 50-100 ml.

Heart pathology in acute ASF is described very rare. Myocardial haemorrhages are described for the first time in this study. Although in acute forms of ASF severe vascular disorders and haemorrhages in various organs (intramural haemorrhages present in more than 50% cases) are characteristic.

CONCLUSION. ASFV-induced heart pathology in acute form of infection is expressed in cardiac enlargement, intramural myocardial haemorrhages and hyperaemia, as well as hydro- and hemopericardium. However, there is no any correlation between severity of clinical manifestation, course of disease before death and intensity/localisation of myocardial haemorrhages.



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KEYWORDS:

*African swine fever virus,
Acute infection,
Heart pathology*



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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heart failure,
parathyroid hormone,
vitamin D₃,
thyrocalcitonin,
calcium

CALCIUM-PHOSPHATE REGULATING HORMONAL SYSTEM STATUS IN CHRONIC HEART FAILURE

INTRODUCTION. The importance of ionized calcium for the functional activity of heart is illustrated by its essential role in the synchronized cellular depolarization, pacemaker activity and subsequent activation of contractile proteins, i.e. in the cardiac excitation–contraction coupling. Therefore calcium-regulating hormonal system is important for the functional activity of myocardium. The regulation of calcium homeostasis is not limited exclusively to the major calcium-phosphate regulator parathyroid hormone (PTH) signaling. Accumulated evidence suggests that thyrocalcitonin (TKT) and vitamin D₃ can ensure regulation of calcium levels by including into integrated calcium-phosphate regulating hormonal system. However, little is known about the role of this system in the pathogenesis of cardiovascular diseases. On the other hand, some studies demonstrate that cardiovascular diseases of different origin may have gender-dependent variations [2, 3].

The aim of the investigation is the evaluation of calcium-phosphate regulating hormonal system status in female and male patients with chronic heart failure (CHF), caused by ischaemic (coronary artery) disease.

METHODS USED. Blood serum samples from the patients with CHF and individuals from control group were used to analyze the levels of ionized calcium, inorganic phosphate spectrophotometrically, using kits from Biosystems (India). Calcium-phosphate regulating hormones were detected by ELIZA: PTH with the help of enzyme immunoassay kit from DRG International (USA); and TKT, vitamin D₃, estradiol and testosterone -by enzyme immunoassay kit from Roche (Switzerland).

RESULTS AND DISCUSSION. Alteration of investigated parameters was found in patients, which is expressed by decrease of calcium, TKT and vitamin D₃, whereas the levels of PTH and phosphate increased.

The extent of these changes was found more pronounced in the female patients, in blood of which estradiol concentration sharply decreased, but in the male patients the blood testosterone concentration was not changed.

PTH increasing and declining levels of ionized calcium seem to be inconsistent at the first glance. However, it is known that the low concentrations of calcium may stimulate the synthesis and release of PTH by a negative feedback mechanism in order to restore the level of calcium that is needed for the normal activity of all organs, including heart. Comparing our data with the studies indicating less frequent occurrence and less severe consequences of heart failure in females, better overall survival after myocardial infarction [1] it can be speculated that the potential cardioprotective features of PTH might contribute to the better cardiac remodeling of female organism and a greater resistance to myocardiocyte apoptosis. At the same time, it is not excluded, that insufficiency of female sex hormone estradiol in female patients' blood can be one of the important reasons of CHF development.

CONCLUSION. It is suggested, that calcium regulating hormonal system is involved in the pathogenesis of ischemic heart disease and consequently CHF development; however the increase of PTH level may play a compensatory role in maintaining the heart function.

This work was supported by State Committee Science MES RA, in frame of the research project № SCS 15T-3A074.

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TRANSLOCATION OF ESCHERICHIA COLI IN SIGMOID COLON ADENOCARCINOMA

INTRODUCTION. The problem of carcinogenesis is one of the most important in modern medicine. Associated infections in cancer patients cause partial resorption of the tumor, and in such patients, enterobacteria are most often sown from the blood. Escherichia obligate representatives of enterobacteria in human microbiota. A typical biotope for these bacteria is the large intestine. The interest in these bacteria is due to their importance in the normal life of the macroorganism (activation of the immune system, participation in digestion processes, metabolic reactions associated with metabolic processes and vitamin synthesis, detoxification of endogenous and exogenous biologically active substances) and the role in the development of a number of infectious-inflammatory sick of a person.

The possibility of penetrating the escherichia beyond the intestine is determined not so much by the invasive characteristics of bacteria as by defects in the colonization resistance system of the host, increased intestinal mucosa and a violation of the immune status of the macroorganism.

MATERIAL USED. We examined more than twenty patients with sigmoid adenocarcinoma. Bacteriological study was carried out according to methodological instructions for microbiological diagnosis of diseases caused by enterobacteria. For ultrastructural studies, methods adopted in electron microscopy for studying microbes were used. Viewing and survey were carried out using an electron microscope BS 613 from Tesla.

RESULTS AND DISCUSSION. Our research has shown that the intestinal rod was mainly sown, both lactose negative and lactose of positive forms. As for the extra-colonial population of E. coli, at the time of the operation, its quantity was the maximum, on the second day it decreased and was restored again for 3-4 days after the operation. Ultrathin sections of E. coli, obtained from the stool of patients with adenocarcinoma of sigmoid colon show some bacteria, which changes are observed in the form of cytoplasm on the tip of the rod and its detachment from the cell wall along with the cytoplasmic membrane, and the cytoplasmic membrane invaginates into the cytoplasm. A group of bacteria with plasmolysis was found. Circulating in the patient's blood, intestinal rods on ultrathin sections are basically similar to control ones, sometimes fuzzy contours of the bacterial wall are visible. In some bacteria, at one of the two ends, a focal extension of the periplasmic space is visible.

CONCLUSION. The translocation of opportunistic microbes of E. coli in adenocarcinoma of the sigmoid colon was studied. Obtained electron microscopic data, which showed that if the intestine where changes occur with the microbe, sometimes irreversible, is a favorable environment for E. coli, the blood, and especially the tumor, is the most favorable conditions for its existence.


Science week
CONFERENCE ABSTRACTS
 NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

*translocation,
E. coli,
adenocarcinoma of sigmoid colon,
microbiota*



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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antibacterials,
essential medicines,
access to medicines

AVAILABILITY AND AFFORDABILITY OF ESSENTIAL AN- TIBACTERIALS IN ARMENIA

INTRODUCTION. Anti-infective medicines save lives and have an important place in clinical medicine. Access to these pharmaceuticals is essential for providing appropriate treatment; however, they are not always available and affordable in low- and low-middle income countries [1,2]. The aim of this work was to evaluate prices, availability and affordability of antibacterials in Armenia, as well as to assess inclusion of essential medicines recommended by the World Health Organization (WHO) in the Armenian medicines supply system.

METHODS. USED. The Armenian Essential Medicines Lists (AEML) of 2013 was analyzed to calculate the percentage of medicines from the World Health Organization Model Essential Medicines List (WHO EML) which are included in the current AEML. Data on availability and prices of 8 antibacterials for systemic use selected from AEML were collected in 60 pharmacy outlets from all the Marzes (regions) of Armenia including Yerevan in May-June 2015. Affordability of medicines was calculated using methodology developed by World Health Organization and Health Action International: assessing the number of days for worker with the minimal salary to work in order to pay for one course of treatment with a particular medicine.

RESULTS. 28 (96.6%) of 29 names of antibacterials listed in WHO EML were included in AEML; however only 53 (77.4%) of 41 pharmaceutical forms and 55 (74.3%) of 74 strengths presented in WHO EML for 29 antibacterials are covered by AEML. In addition to 28 essential antibacterials recommended by WHO, AEML includes 4 other antibacterials. 8 selected antibacterials for systemic use were available at the great majority (more than 90 %) of all the community pharmacies studied. Originator brands (OB) were found for 3 (Ceftriaxone, Clarithromycin and Amoxicillin + Clavulanic Acid) of 8 pharmaceuticals, generics - for all 8 medicines. OBs for 2 of these 3 medicines were much higher priced than lowest-priced generics (LPGs); however for the 3rd anti-infective medicine (Amoxicillin + Clavulanic Acid) price of OB was the same as price of highest priced generics (HPGs). Using matched medicine pairs (OBs:LPGs ratio), OBs were from 3.7 to 22 times the price of LPGs. One medicine (Amoxicillin + Clavulanic Acid) was affordable (both OB and generics). OBs for Ceftriaxone and Clarithromycin were unaffordable; generic products of Ceftriaxone and Clarithromycin were affordable only if prescribed at low doses, and unaffordable at higher doses. Generic products of Amoxicillin, Azithromycin, Ciprofloxacin and Doxycycline were affordable.

CONCLUSION. Some pharmaceutical forms and strengths of antibacterials recommended by the WHO are not covered by AEML. Antibacterials for systemic use are mainly available at pharmacy outlets in Armenia. There is a large difference in prices of OBs and LPGs. Some of generic products are unaffordable when prescribed at high doses. Due to high prices many patients who pay for medicines out-of-pocket, will be not able to cover a cost of treatment of infection diseases. A new policy on medicines reimbursement system could improve the situation.

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THE ROLE OF POLYAMINES AS A POTENTIAL DIAGNOSTIC AND PREDICTIVE MARKERS IN THE FIELD OF STUDY OF SOME SOMATIC DISEASES

INTRODUCTION: Changes of polyamines can occur in a variety of disorders of the nervous system. It is known that, cranial injuries are serious public health problems among the military and civilian population. Cranial injuries are often associated with brain secondary traumas: such as hemorrhage, edema, oxidative stress, ischemia, cerebral vascular dysfunction (vasospasm, hyperemia) or thrombosis. The level of polyamines in patients who suffer from cancer can be changed. In particular, when studying the correlation between the number of polyamines in the reproductive organs; such as uterus, cervix, sperm and mammary gland and increasing their levels, was shown that, spermidine, spermine, and cadaverine can be used both as cancer markers and diagnostic indicators. Metabolism disorders of polyamines have been of particular interest over the last 15-20 years in case of acute ischemic and ischemic reperfusion disorders. Data in which observed the role of polyamines in the treatment of chronic cardiovascular diseases, especially in acute chronic cardiac insufficiency are rare. In modern research results hasn't been implemented an assessment for a group of polyamines, such as potassium, spermidine, spermine, cadaverine, agmatine, and histamine, but they have preferred to observe only one to three target groups of polyamines, which does not completely reveal the role of polyamines in the pathogenesis of the disease .

MATERIAL AND METHODS: Using high-performance liquid chromatography (HPLC) method in 100 patients' plasma and erythrocytes with women prematurely given birth , congenital heart disease, cranial injuries, cardiovascular insufficiency were studied the quantity of Putrescine, spermidine, spermine, cadaverine, agmatine, and histamine.

DATA: With the help of the high-performance liquid chromatography the polyamines and the derivatives formed from each of the biological fluids , one can get the idea and distinguish a group of polyamines for the given pathology.

CONCLUSION: As a result of qualitative research of chromatograms, one can confidently state that in the complete range of polyamines can distinguish a particular group of polyamines that do not have simultaneous research data, when these studies will give a complete picture of the metabolic processes in healthy and pathological polyamines ,as well as will implement the target prediction and diagnosis.



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KEYWORDS:

polyamine,
 HPLC,
 erythrocytes,
 brain injury
 cardiovascular insufficiency



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NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

Synucleine,
Putrescine
Neurodegeneration
Parkinson' diseases,
Cancer

**SYNUCLEINS AND POLYAMINES: MODERN APPROACHES
IN THE DEVELOPMENT OF PATHOGENESIS, DIAGNOSIS
AND PROGNOSIS OF A NUMBER OF SOMATIC DISEASES.**

Parkinson's disease is a neurodegenerative disease, clinical manifestation of which are most strikingly pronounced from the age of 60. At the same time, it should be noted that the first symptoms of the disease appear much earlier- 20 to 30 days after the onset of the disease, i.e. in a period, when a significant part of the dopaminergic neurons degenerate. In the initial stages of this process proceeds without pronounced clinical manifestations. The early symptoms appear in patients only after degeneration 50-60% of dopaminergic neurons localized in the black substance and a decrease in 70 - 80% of dopaminergic neurons in the corpus striatum.

At present, according to a number of authors, both in the familial and sporadic forms of Parkinson's disease, dystrophic changes occur in the dopaminergic neurons, with progressive nature, and a large group of neurons eventually die. The death of dopaminergic neurons is accompanied by a significant increase of α -synuclein in the content, protein misfolding in Lewy bodies, up to the appearance of large aggregates.

Such large intra-neuronal cytoplasmic inclusions are now considered to be the main pathomorphological feature of Parkinson's disease. In this case, intermediate forms of α -synuclein-in the form of oligomers possess pronounced neurotoxicity. It has been long established that aliphatic polyamines (putrescine, spermine, spermidine) are given an important role in biochemical processes that are selectively directed towards the activation of the neuronal function of various parts of the brain (5-10). At the same time, very informative publications appeared in the last 15 years in which the role of polyamines in the pathogenesis of Parkinson's disease was discussed.

As a rule, in all studies aimed at revealing the role of polyamines in the pathogenesis of Parkinson's disease, one important circumstance is pointed out: in all studied bio-objects, in the given disease, relatively high rates of polyamine-putrescine, spermine, spermidine were recorded. Moreover, some authors believe that in the mechanisms of induction of degenerative processes in Parkinson's disease, even the physiological concentrations of the above-mentioned aliphatic polyamines can be involved.

In a number of studies, an attempt was made to establish the functional-structural dependence between shear in the content of polyamines and the processes of increasing destruction of neurons associated with the accumulation of α -synuclein in Lewy bodies.

Thus, in particular Antony T. et al. (2003), in experiments in vitro, it was established that in the presence of polyamines, the kinetic parameters of α -synuclein was significantly changed, i.e., transition of protein from non-aggregated to highly aggregated state. Thus, according to the author, in the presence of polyamines of α -synuclein fibril in the final stage, with the increased aggregation, began to form large aggregate structures condensed exclusively in Lewy bodies. At the same time, there are also literary sources in which, in Parkinson's disease, the involvement of polyamines in the processes of excessive accumulation of α -synucleins in Lewy bodies is in question. So, in particular, based on research conducted to study the levels of (putrescine, spermine, spermidine) polyamines in blood erythrocytes, with Parkinson's disease, amyotrophic lateral sclerosis and in healthy cohort of individuals (control group), the authors came to a conclusion according to which the processes of aggregation of α synuclein in Lewy bodies don't depend on high levels of polyamines in dopaminergic neurons.

Moreover, the high levels of spermidine and spermine and low levels of putrescine should according to the authors, with Parkinson's disease, they detected be regarded as a compensatory protective reaction, or manifestation of the disease.

**THE DOCKING ANALYSIS OF SOME CYCLOBUTANE-
AND CYCLOPROPANE CARBOXYLIC ACIDS
DERIVATIVES AND SOME SYNTHETIC, NON PROTEIN
AMINO ACIDS CONTAINING PEPTIDES
INTERACTION WITH COLLAGENASE**

INTRODUCTION. According to wide range of modern research, there's a well known fact, that the activity of matrix metalloproteases (MMP's) is one of the main biochemical markers of different fast metastasizing types of cancer. And there is a definite correlation between high level of activity of matrix metalloproteases and ability of tumor to generate secondary neoplastic grows. And in terms of worldwide enlarging of cancer spreading negative tendency, with the significant growth of patients quantity, the search of new highly effective and relatively safe MMP's specific, inhibitors as well as the investigation of new anticancer technics is the one of perspective directions of modern drugs design.

This research is being devoted to docking analysis of interaction of two classes of synthetic compounds and their containing peptides, in aspects of their potentially effectiveness for antimetastatic therapy.

METHODS USED. For potential activity screening of 92 non-protein heterocyclic amino acids, produced at SPC "Armbiotechnology" NAS RA, cyclobutane carboxylic and cyclopropane carboxylic acids Cl- and NH₂- derivatives, synthesized at the NPUA laboratory of new agrochemical creation and the quality control, and dipeptides containing of their fragments was modeled *in silico*. And by the help of Autodock VINA molecular docking and virtual screening program, ChemBio3D, ChemBio-Draw Ultra 12.0 Software and PDB Protein data Bank there were epitomized the series of molecular docking experiments with registration of Gibbs free energy (ΔG) of mentioned above ligands with collagenase models.

RESULTS AND DISCUSSION. Among the all 92 tested *in silico* substances, approximately 75% of ligand compound demonstrated several affinity to enzyme and 5 compounds: (1R)-1-(3-(4-allyl-3-(pyridine-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-aminopropanamido)-2-phenylcyclopropanecarboxylic acid; (R)-3-(4-allyl-3-(pyridin-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-((1S-2S)-1-amino-2-phenylcyclopropanecarboxamido)propanoic acid; (R)-3-(4-allyl-3-(pyridine-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-((1R-2R)-1-amino-2-phenylcyclopropanecarboxamido)propanoic acid; (2R)-3-(4-allyl-3-(pyridin-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-((1R)-1-chloro-2-phenylcyclopropanecarboxamido)propanoic acid; (S)-3-(4-allyl-3-(pyridin-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-((1S-2S)-1-amino-2-phenylcyclopropanecarboxamido)propanoic acid have demonstrated the high value of Gibbs free energy (ΔG). For these compounds $\Delta G = -8,4-8,9$ kcal/mol. The minimal value of Gibbs free energy and appropriate maximal affinity to collagenase had been registered for (S)-3-(4-allyl-3-(pyridin-3-yl)-5-thioxo-4-5-dihydro-1H-1-2-4-triazol-1-yl)-2-((1S-2S)-1-amino-2-phenylcyclopropanecarboxamido)propanoic acid and it was $\Delta G = -8,9$ kcal/mol.

In case of regio-stereo specifically synthesized Cl- and NH₂-substituted cyclobutane- and cyclopropane carboxylic acids trans- isomers and the mentioned non-protein amino acids containing peptides interaction with the collagenase, during the research there were registered the values of ΔG , significantly higher than in both pre-components with the appropriate significant up-regulation of binding ability while the docking experiments with Collagenase enzyme molecule models (PDB-ID 1NQD, 1NQJ).

CONCLUSION. As a result of collecting research data, it might be hypothesized that the majority of described synthetic compounds can be potentially effective and from them it might be selected a group of substances with the maximal specificity and affinity to selected enzyme, for further more detailed *in vitro* and *in vivo* research aimed to target oriented drug design and antimetastatic therapy methods development, what is especially actual for Armenia, in terms of high percentage cancer occurrence.



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KEYWORDS:

cyclobutane,
cyclopropane,
non-protein amino acid,
collagenase



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KEYWORDS:

neuronal activity,
amigdala,
immobilization stress,
taurine

STUDY OF NEURONAL ACTIVITY AMIGDALA OF RAT'S AFTER IMMOBILIZATION STRESS AND UNDER THE INFLUENCE OF TAURINE

INTRODUCTION. The cause of stress can be various adverse factors of daily life associated with the emergence of negative emotions. Stress leads to changes in many indicators that characterize the functional state of the organism at all its structural levels. The amigdala is actively involved in the processes of neuronal rearrangements during stressful actions. It seems relevant to study the nature of the changes in the parameters of the background impulse activity of neurons of the amygdala of the brain after immobilization stress. In stressful situations, there is a deficiency of taurine in the organism, and to improve the nervous activity it is necessary to use it, which probably has a modulating effect on the functional state of the organism and contributes to the stabilization of the activity of the nervous system.

The goal of the studies was an electrophysiological study of the effect of taurine on the parameters of the background impulse activity of rat brain neurons of amigdala after immobilization stress. In semichronic studies in rats, a change in the ratio of excitatory and depressant post-stimulatory manifestations of amygdala activity to tetanic stimulation of the hippocampus was studied in norm, in dynamics after acute immobilization stress and under taurine protection (for 7 days).

METHOD USED. Microelectrophysiological experiments with extracellular recording of single neurons of amygdala were performed in rats in 3 groups. Acute immobilization stress was caused by fixing the animal on its back for two hours. An aqueous solution of taurine (50 mg / kg) was injected directly to the animals immediately after the stress for 7 days.

RESULTS AND DISCUSSION. Immobilization stress leads to a significant change in the parameters of activity of neurons of amygdala. In neurons of amygdala, in comparatively with the norm, after strengthening above the norm of post-stimulus excitation by 1 day, its sharp decrease by 90 days is shown, and its significant increase when combined with taurine. In the amygdala after 1 day of testing, there was a more drastic decrease in depression, and on the 90th day, on the contrary, increased depression, but the same sharp decrease when combined with taurine. In amygdala, in comparatively with the norm, an increase in tetanic excitatory effects on day 7 after stress in combination with taurine and a powerful increase in tetanic depressor effects on day 90 after stress. In comparatively with the norm, under the influence of taurine to the 7th day after stress, the excitation sharply increases and the depression sharply decreases, which indicates the ability of taurine to promote the tendency of restoring the ratio of multidirectional post-stimulus effects. Histochemical data were obtained confirming the neuroprotective effect of taurine.

CONCLUSION. The analysis of electrophysiological data allows us to conclude that taurine has a neuroprotective effect on the neurons of the amygdala on the 7th day already with the systematic introduction of taurine immediately after stress, since under the influence of taurine in neurons of the amygdala is an increase in excitatory and a sharp weakening of inhibitory effects, in comparatively with immobilization.

VALPROIC ACID MULTIPLE INJECTIONS IN THE EARLY POSTNATAL PERIOD AS A NEW MODEL OF ASD

INTRODUCTION. Autism Spectrum Disorders (ASD) are complex neurodevelopmental disorders characterized by repetitive behavior, impaired verbal and nonverbal communication. Valproic acid (VPA) is known as an antiepileptic drug with teratogenic effect and is used for animal models of ASD. Recent studies show that VPA exposure causes increasing of neonate's GABA concentration in the brain. GABA demonstrates excitatory effect at the late embryonic and early postnatal stages of life, thus regulates a variety of different neurodevelopmental processes [3]. Thus dysfunction of the GABAergic signaling on perinatal period may lead to an excitatory/inhibitory imbalance in neuronal circuits, which can manifest through behavioral alterations like observed in ASD patients. The aim of the present study was to observe the neurobehavioral development of newborn rats treated with VPA.

METHODS USED. Pups received intraperitoneal (i.p.) injections of NaVPA 200 mg/kg and saline vehicle at postnatal days 5-12 (P5-12). On P25-30 period different behavioral tests were carried out respectively each day. Anxiety-related behavior was examined in the standard elevated X maze by measuring of two parameters: 1) ratio of time spent in open arms to total time spent in the maze (5 min); 2) ratio of entries' number into open arms to total entries' number. Sensitivity to thermal nociception was determined by measuring the latency of response to the thermal stimulus ($50 \pm 0.5^\circ\text{C}$) during 60 s on a hot plate analgesia meter. Locomotor activity of rats was tested in an open field (5 min), where arena was divided into center and peripheral zones, we quantified time spent in each zone and total passed distance. For social interaction test previously isolated animals were placed in the test cage for 15 min, and the duration of the following parameters were scored: self grooming, sniffing, following, playing.

RESULTS AND DISCUSSION. To examine pup's normal physical development we monitored eye opening time and body weight between control and VPA treated groups during the first 20 days of life. There are no significant differences in eye opening days. Analysis of pups body weight data revealed a significant increase, VPA treated pups have higher body weights than controls during the development period P5-20, on P21, 22 the body weight of both of the groups was equal ($p < 0.001$). An elevated plus-maze test was performed to assess anxiety-related behavior. The ratio of time spent in open arms to total time spent in the maze was increased in the VPA exposed animals than the control group ($M = 0.25$, $SD \pm 0.1$, $M = 0.44$, $SD \pm 0.1$, $p < 0.001$ for CNR and VPA treated groups respectively). VPA treated pups exhibited significantly higher latency to lick hind paw than control ($M = 21.7$, $SD \pm 9.3$, $M = 30.2$, $SD \pm 7.7$, $p < 0.05$). There were no significant differences between treated and control group in open field test. For validation of impairments in social interaction, we evaluated how pairs of VPA-treated or control rats interact during 15 min in Plexiglas box, which were previously isolated for 3 hours. Results revealed that treated animals exhibited less play behavior than control group ($M = 26.85$, $SD \pm 7.02$, $M = 11.13$, $SD \pm 6.7$, $p < 0.001$), at the same time had more self grooming behavior ($M = 49.35$, $SD \pm 22.78$, $M = 74.17$, $SD \pm 34.9$, $p < 0.05$).

CONCLUSION. Summarizing our study we can conclude that valproic acid induced model does mimic some of the features seen in individuals with ASD.

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KEYWORDS:

Autism Spectrum Disorders,
Valproic acid,
Behavioral characteristic



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KEYWORDS:

Porphyrins,
antitumor,
photodynamic therapy,
photosensitizer,
HeLa,
cationic porphyrins

**NEW AMPHIPHILICPORPHYRINS AND
 THEIR ANTITUMOR ACTIVITY**

INTRODUCTION. Porphyrins have been evaluated in the context of photodynamic therapy PDT since they strongly absorb light and convert to energy in illuminated areas, which generate reactive oxygen species and conduct free-radical cell damage. Porphyrins' unique properties open wide perspectives to researchers and practical medicine for creation of new remedies. During years we have implemented numerous studies to understand the cellular mechanisms of porphyrins' PDT (photodynamic therapy) activity on various cell lines (HeLa, KCL-22, 3T3 etc.).

The purpose of the study was determining the relations between PDT activity, dark toxicity, cell uptake and incubation duration of meso-substituted porphyrins.

METHODS USED. The porphyrins were synthesized by the method of Rothermund and Adler-Longo. The purification was implemented by column chromatography.

Then was observed the loss of cell viability (HeLa cell line) in different ways of application of porphyrins different durations of preincubation of cells with PS (photosensitizer-porphyrin), 15 minutes of cell illumination, different durations of incubation of cells in dark (after illumination) followed by MTT assay. Also was performed observation of dark toxicity of PSs. Cells were incubated 24 h with PSs in the dark and MTT assay was performed without illumination.

RESULTS AND DISCUSSION. Results point to substantial differences in PDT efficiency among PSs with different structures and symmetry. Our previous investigations revealed that shapes, size and charges are the main factors which determine cellular uptake and subcellular distribution of PSs. The observed differences in the PDT efficiency therefore might reflect cellular accumulation of the PSs.

Asymmetric PSs with specific arrangement of the substituents at the periphery of the tetrapyrrole ring display PDT efficiency higher than the symmetric cationic ZnPs.

Illumination at low fluency and in the presence of low concentrations of PSs triggers reactions that continue in the dark and cause irreversible cell damage and cell death. Once initiated, such processes cannot be stopped by cellular defenses and cells cannot be rescued.

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A STEP CLOSER TO MEASURING “BRAIN POWER” UNDER MICROSCOPE

INTRODUCTION. The question which structures of brain are most responsible for human intelligence will be relevant for a long time. It is known that many parts of the brain participate in the formation of intellect. Numerous researchers continue to emphasize their research on one of the most important structure of the brain, even with the use of quantitative morphological methods. But such approach reveals only certain aspects of this complex phenomenon. Trying to operate with a large number of parameters of several brain structures, the researcher finds himself at a dead end, because it becomes impossible to process the heaped digital material. The methodical approach developed by us and called the “Quantitative Functional Morphology” (QMF), allowed us to answer to similar question for other organs, in particular for the heart muscle, skeletal muscles, lungs, liver, placenta.

A question has aroused. Would be possible measuring the functional power of the brain morphologically using principles of QFM? At the beginning, this seemed impossible to us because of diversity and complexity of the structural and functional organization of the brain. The moment came when the desire to develop such a method became the goal of this study.

METHODS USED. For the brain of experimental animals is more suitable the term of brain power. The brain of 15 white healthy male rats were used. Frozen sections of 40 μm thickness were cut from 5 brains and stained by A. Chilingaryan’s methods on neurons and by the method of I.B. Meliksetyan on the capillaries. From cerebral hemispheres of 10 brains the transverse tissue layer were cut out and embedded with paraffin. Histological sections were stained with hematoxylin-eosin and Nissle method. Morphometric measurements were carried out on standard areas of the cerebral cortex under a microscope with an ocular net designed by T.H. Ghevondyan. The stereometric parameters of the number, surface and volume of cortex neurons, capillaries and glia were calculated.

RESULTS AND DISCUSSION. A trigger for this study was the choice of system-forming factor for the cerebral cortex which is the value of the electrical potential developed in a unite volume of cortex per unit time. The system-forming factor allowed selection the most important structural and functional parameters, which take part in the generating of electrical potential. As a next important step a mathematical model was developed for the calculation of the integrative index equivalent to electric potential. The basic model has a modular construction and in its simplest version includes 6 stereological parameters and 6 rates of dynamic processes.

CONCLUSION. The choice of the backbone factor and the compilation of the mathematical model brought clarity to the prospect of this research. Now the questions of reproducibility of the research data, representativeness of selected brain areas for the entire cortex, precise choice of cortical fields, the number of fields, the standardization of tissue material processing obtain actuality. Step-by-step solution of these tasks lies in the near future.



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KEYWORDS:

*measurement of brain
power, quantitative
functional morphology*



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KEYWORDS:

Bulbous-rooted chervil,
ash,
volatile oil,
flavonoids, tannins

THE PHYTOCHEMICAL ANALYSIS OF BULBOUS-ROOTED CHERVIL'S HERB (CHAEROPHYLLUMBULBOUSUM L.) GROWING WILDLY IN DIFFERENT REGIONS OF ARMENIA

INTRODUCTION. There are 40 species of bulbous-rooted chervil, and only 2 of them are met in Armenia: *Chaerophyllum bulbosum* and *Chaerophyllum aureum*. Bulbous-rooted chervil is a much useful plant. It is appetizing, assist the digestion. The juice produces mild diarrhetic and soft diuretic effects. The goal of this work is phytochemical analysis of bulbous rooted chervil's herb growing wildly in RA flora, as a source of biologically active compounds.

METHODS USED. As a material for the research served the overground part of bulbous-rooted chervil- the herb, picked up on may-june, 2010, from different regions of RA.

The phytochemical analysis of the raw materials was carried according to the XI SPh. The essential oil content was defined by the Ginsburg method. The sum of flavanoids was defined by spectroscopy. The amount of tannins was defined by gravimetric method. Volatile oil analysis was carried out by the gas chromatography- mass spectrometry (GC-MS) method. The content of minerals was defined by thermal emission method.

RESULTS AND DISCUSSION. The results of phytochemical research of the bulbous-rooted chervil herb harvested from Kapan, Eghegnadzor and Aparan regions showed, that the contents of general ash are 19.8%, 18.8% and 15.5% and extracted substances- 20.3%, 39.5%, 30.0% respectively. The amounts of rutin in Kapan and Eghegnadzor are 2%, 1.6% and quercetin- 0.24%, 0.12% respectively. In Aparan region the sum of flavonoids is 0.5%. Tannins are 2.6% in Kapan and 3% in Eghegnadzor regions. The amount of essential oil obtained from Aparan region sample was 0.13%.

The analysis of the volatile fraction of *Chaerophyllum bulbosum* L. growing wildly in Aparan, by capillary GC-MS method, demonstrated the presence of at least 36 constituents and the amounts of only 15 components exceed 1%. The following major components were found β -Caryophyllene epoxide (21.9%), 6-[91E0-1,3-Dimethyl-1,3-butadienyl]-1,5,5-trimethyl-7-oxabicyclo[4.1.0]hept-2-ene (12.9%), Pulegone (10.3%), 3-Methyl-5-propylonane (8%), Eucalyptol (6.8%), β -cis-Caryophyllene (5.1%), 1-Menthone (5%), Dodecane (5%), Spathulenol (3.35%), (+)-valeranone (2.9%), Heptaethylene glycol monododecyl ether (2.3%) etc. From 33 components only 9 of them are of terpenoid structure.

From sesquiterpenes β -caryophyllene epoxide, β -cis-caryophyllene, spathulenol, (+)-valeranone, α -humulene epoxide II and from monoterpenes pulegone, eucalyptol, 1-menthone predominate. The analysis of general ash showed, that bulbous rooted chervil's herb harvested from all 3 regions contains 11-15 elements, from which 5 (Si, Na, Ca, Mg, P) are macroelements, 6 microelements (Cu, Pb, Cr, Mn, Fe, Al) and 4 ultramicroelements (V, Ti, Ni, Zr):

The amount of some heavy metals (Al, Fe, Ti, V, Ni, Cr, Pb) exceed the maximal permissible density in Aparan sample.

These results represent the first report regard chemical composition of Bulbous-rooted chervil's herb. This experiment has provided scientific foundation for further utilization of Bulbous-rooted chervil's herb.

COMPARATIVE DOCKING OF MESEDINE AND BEDITINE WITH HOMOLGY MODEL OF ALPHA2A-ADRENERGIC RECEPTOR

INTRODUCTION. Alpha2a-adrenergic receptors are attractive targets for the treatment of several general afflictions like hypertension, pain, depression, anxiety, and obesity, thus their specific agonists and antagonists would have important medical applications. AutoDock vina4 is a suite of free open-source software for the computational docking and virtual screening of small molecules to macromolecular receptors. This computer modeling program has been applied in our studies to analyze the similarities and differences between ligands binding sites and to detecting of new synthetic ligands potential activity like Mesedine and Beditin with alpha2a-adrenergic receptor subtype.

METHODS USED. The absence of crystal structure of α_2 -adrenergic receptor subtypes creates a major hindrance in the drug design efforts. We used Swiss-Model software (<https://swissmodel.expasy.org/>) for homology modelling of the Human α_{2A} -adrenergic receptor (α_{2A} -AR), GenBank accession code: AF284095.1 [1, 2]. The **2ycw_m** pdb file was created on the base of homology to the turkey beta1 adrenergic receptor (pdb: **2ycw**), with 40.56 % sequence identity, 39 % sequence similarity and 64 % coverage of amino acid sequences [3]. Ligands were built using a packet ChemOffice Ultra and converted into pdbqt format. Seven ligands, clonidine, norepinephrine, epinephrine, idazoxane, anapriline, beditine, mesedine were automatically docked to homology model (**2ycw_m**) of α_2 -adrenergic receptor. But for us more important ligands were Mesedine and Beditine, because the main goal of this docked detecting binding sites of represented ligands and to estimate their agonist or antagonist influence.

For each ligand – protein interaction we received 9 different conformations with different ΔG kcal/mol values, in each set with the lowest value of the objective function, which describes the degree of fit of the model to the input structural data used in its construction, derived by the program MODELLER. Thus, we have combined the docking results from Autodock to choose the representative pose for each of these ligands.

RESULTS AND DISCUSSION. It was revealed, that ligand – receptor complex formation with ALA78, PHE387, PHE403 aminoacids residues of macromolecule takes place both with Mesedine ($\Delta G = -6.7$ kcal/mol) and Adrenaline ($\Delta G = -5.8$ kcal/mol). Mesedine – receptor interactions binding-sites with high affinity ($\Delta G = -6.7$ kcal/mol) are six poses with corresponding aminoacids residues ALA78, LYS80, ALA81, ARG383, ARG386, PHE387. Beditine best conformation ($\Delta G = -7.2$ kcal/mol) shows higher affinity to selected part of protein than Mesedine. Mesedine which bound at 6 poses with ALA78, LYS80, ALA81, ARG383, ARG386, PHE387 ($\Delta G = -6.7$ kcal/mol), Beditine forms 9 bound poses with macromolecule at positions LEU125, ASP125, VAL129, CYS132, LYS189, ASP207, PHE403, PHE405, PHE427. Both Mesedine, Beditine and Adrenaline bound at the same poses of adrenoceptor homology model with corresponding amino acids residues ARG383, PHE387, LYS424, PHE427.

CONCLUSION. We have identified residues through our modelling and docking studies, which would be crucial in giving subtype specificity and also analyzed binding site volume, and the residue variations which may play important role in ligand binding.

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KEYWORDS:

α_2 adrenergic receptors;
homology modeling;
docking analysis;
beditine;
mesedine.



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physical destruction,
chronic low grade inflammation,
allostasis

BEHAVIORAL RESPONSES TO LIMITATION OF PHYSICAL ACTIVITY: BEHAVIORAL ALLOSTASIS?

INTRODUCTION. Sedentary lifestyle is considered as one of the most common risk factors for a host of common diseases of civilized world, including ischemic heart disease, stroke, type II diabetes, etc. The problem of limited physical activity is further emphasized due to its association with obesity and metabolic syndrome. More recently, it was shown, that hypokinesia induces a state of chronic low grade inflammation which is considered as a culprit of developing slow vicious cycles, which eventually disturb homeostasis leading to multiple derangements. During last decade our research group has focused on behavioral shifts in rats exposed to hypokinetic conditions. We assume that behavioral changes are at the top of an iceberg which is downstream of molecular changes underlying the complex of physical inactivity related shifts. We have previously reported some effects of chronic hypokinetic stress exposure on rats behavior. Importantly, not all the behavioral and cognitive indices deteriorate. In this study we aimed to delineate the compensatory vs. maladaptive shifts induced by experimental hypokinesia.

METHODS USED. 16 white male non-linear rats were included in the study. Animals were assigned into 2 groups: control and hypokinetic groups. Experimental hypokinesia was induced by placing rats in special narrow individual cages (22 hours per day) for 70 days. During the 70 day period specially designed behavioral battery was applied to measure cognitive and locomotor skills. The battery of tests included open field, novel object recognition, modified bridge walking and social interaction test. AnyMaze software was used for analysis of the behavior.

RESULTS AND DISCUSSION. The behavioral performance of the rats significantly depended on the duration of exposure. In the early terms of hypokinesia (2-15 days) rats express enhanced memory function in Y maze and at least normal novel object recognition. Locomotor activity in most of the tests was also intact. Nevertheless, the altered grooming pattern, recorded in hypokinetic animals indicates exposure to a chronic stressor. At the late stages of restricted physical activity, an increase in aggression indices in social interaction tests was observed along with some decrease in memory tasks. Hypokinetic rats also exhibit decreased rate of motor learning in rotarod running trials. In terms of general locomotion hypokinetic rats exhibit better adaptations in behavioral responses especially in the 45-70 days of hypokinesia. Comparison with control rats also indicates a paradigm shift in the memory formation. More specifically, the behavioral encoding moves towards egocentric (vs. allocentric) pathway, allowing some adaptation to the restricted conditions.

CONCLUSION. Limitation of physical activity causes complex behavioral adaptations in rats, in some aspects with different strategies of memory formation. We consider the observed changes in the context of allostasis where the animal behavior is pushed from the steady state towards an alternative state of homeostasis – an allostasis, which allows some beneficial adaptations, but at the expense of allostatic load, including the deleterious effects of chronic low grade inflammation.

**THE SCANNING ELECTRON MICROSCOPIC AND
CELLULAR - BACTERIOSCOPIC CHARACTERISTICS
OF LYMPHOMACROPHAGAL INTERRELATION
ON THE SURFACE OF PALATINE TONSILS
AT THE CHRONIC TONSILLITIS**

INTRODUCTION. Chronic tonsillitis, as a clinical manifestation of focal streptococcal infection, is an inflammatory disease and affects the lymphoid structures that are associated with the pharyngeal mucosa. In the mechanisms of development of the inflammatory process, the persistent microbial foci and the violation of barriers on the path of infection are of great importance. But the importance of surface structures is also great, since sometimes the mucosal epithelial cell barrier can allow the inflammatory process to affect the entire mucous throat. Therefore, to obtain additional information on the state of local protective reactions of the pharyngeal mucosa, the cell population and the microbial landscape of palatine tonsils should also be studied.

Therefore, along with the cyto-bacterioscopic method of verifying the focal infection of the throat, we carried out the raster-electron microscope study of the epithelial surface of the tonsils.

METHODS USED. The palatine tonsils removed from the patients suffering from decompensated chronic tonsillitis have been subjected to the scanning electron microscopy research.

We have studied the surface of palatine tonsils with the cellular-bacterioscopic and the electron microscopic methods to define the composition of cellular population, microbial population and the inflammatory process activity.

SEM research was carried out on preparations-sections of the surface layer of palatine tonsils, prepared after their preliminary fixation. The samples were dehydrated in the ascending dilutions of ethanol, subjected to sputtering, and examined by the SEM Vega Tescan microscope.

RESULTS AND DISCUSSION. It appeared that in the immune subsystem of local antimicrobial protection of the surface of the pharynx mucous membrane the lymphatic immunity mechanisms were of essential importance. The received data show, that between the lymphocytes and macrophages, containing intracytoplasmatic cationized and non cationized microbes, there is intercellular interaction on the surface of epithelial coverage. On the prickly surface of the epithelial cover of the tonsils, a large number of microbes were found. Herein, at the gates of mucosal infection, there were the langerhans cells have had contacts with microbes and small lymphocytes. It could be assumed that they thus participate in the immunization process: collecting antigens and delivering them to the lymphoid tissue.

On the tonsils surface there were also found a large number of macrophages surrounded by several lymphocytes. In the SEM study, multiple bridges were defined between the cells in a form of thin processes.

This fact is the morphological documentation of an intercellular interaction between the cells of the immune system on the tonsils surface. It allows us to conclude that the mechanisms of lymphocytic immunity with the participation of lymphocytes in the function of the mycular recognition are already included starting from the surface of the mucous membrane of the pharynx infested with a huge number of avirulent and virulent microorganisms.

The above-described should be considered one of the mechanisms that provide the initial pre-immune physiological reaction of resistance of organism to infections.

The results of the conducted work complete the existing ideas upon the antimicrobial resistance of organism and the barrier role of the pharynx mucous membrane.



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KEYWORDS:

*chronic tonsillitis,
palatine tonsils,
lymphomacrophagal
interrelations*



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KEYWORDS:

brain
ischemic
stroke,
DNM1L,
DIABLO,
aging

ESTIMATION OF DNM1L AND DIABLO GENE EXPRESSIONS DURING AGING AND BRAIN ISCHEMIC STROKE

INTRODUCTION. Brain ischemic stroke (BIS) is characterized with high level of fatal outcome and disability. One of post-BIS consequences is immunosuppression which is one of the main causes of fatal outcome. Aging is also characterized with immunosuppression. From this point of view we were interested in immune cells apoptosis as one of the potential sources of post-BIS and aging-dependent immunosuppression. Mitochondria are critical for apoptosis because they control release of apoptogenic proteins cytochrome c and DIABLO into cytoplasm. Coming from cytoplasm into mitochondria, DNM1L provokes an impairment of the mitochondrial electron transport chain, resulting in dissipation of mitochondrial transmembrane potential and reactive oxygen species generation. Also, deficiency of DNM1L delays the release of cytochrome c and subsequent apoptosis.

The aim of our study was the estimation of DIABLO and DNM1L genes expression in leucocytes during aging and BIS as apoptotic factors.

METHODS USED. Studied groups were three: 48 healthy young (mean age±SE; min/max age: 37.6±1.1; 20/54), 20 healthy aged (mean age±SE: 66.7±1.5; min/max age: 57/85) and 38 patients with brain ischemic stroke (BIS) (mean age±SE: 71.8±1.6; min/max age: 56/89). All of them had Armenian origin. RNA was isolated from peripheral blood leukocytes. Estimation of selected genes expression was done by RT-PCR. p<0.05 was considered as statistically significant.

RESULTS AND DISCUSSION. According our results the expression level of DNM1L was increased in aged group compared with young ones (0.058), also is significantly higher compared with BIS patients results (P<0.0001). There were no changes in the DIABLO gene expression level. DNM1L has influence only on cytochrome c release into cytoplasm, but not on DIABLO release. So, the release of the cytochrome c increases during aging, at the same time it is suppressed in BIS patients of same age. From our results we can conclude that the level of apoptosis and impairment of mitochondria of leukocytes increase during aging and promote immunosuppression, while the immune cell apoptosis in BIS patients is suppressed.

THE FORMALIN TEST MODIFICATION AS A TOOL
TO INVESTIGATE THE PROPERTIES OF “PAIN MEMORY”
FORMATION AND MAINTENANCE IN DIFFERENT
REGIONS OF CENTRAL NERVOUS SYSTEM

INTRODUCTION. Pain is a complex experience encompassing sensory-discriminative, affective-motivational and cognitive-emotional components. Different regions of central nervous system play important roles in pain modulation, formation and maintenance of painful memories and analgesia. The hard and multicomponent pathway of nociception starts with primary afferent neurons from periphery and ends in cerebral cortex including a large brain network, which is activated during the acute pain experience and is called the “pain matrix”.

The prefrontal cortex is associated with high-order cognitive and emotional functions including attention, decision making, goal-directed behavior, and working memory.

According to data available, different subregions of the prefrontal cortex have a role in acute pain. Peripheral tissue damage or nerve injury often leads to development of pathological pain processes, such as spontaneous pain, hyperalgesia and allodynia that persist for years or decades after all possible tissue healing has occurred.

METHODS USED. In our experiments we have used the modification of classic formalin test with two subsequent injections of formalin with five days interval. This modification can be useful to investigate the central mechanisms of “pain memory” and to evaluate the effect of different analgesic drugs on ascending and descending pain pathways. For our experiments we have used four groups of analgesics: a local anaesthetic-lidocaine, NSAID - diclofenac, a mu-opioid receptor agonist-DAMGO, anticonvulsant with chronic pain-relieving action - gabapentin. As a pain marker the c-Fos protein is defined by Western blotting.

RESULTS AND DISCUSSION. The results of our experiments let us to consider, that the painful information evoked by application of stimuli with different intensity are transferred to different brain regions, particularly, prefrontal cortex receives it in unchanged form, whereas hippocampus receives it in “milder” form. It is most likely a result for protective mechanism formation, which is, taking into account the emotional component, is to protect organism from negative effects. The results of analgesic drugs investigation indicate, that some drugs, i.e. opioids affect both, first and second phases, others, i.e. gabapentin, have no effect on first phase, but significantly reduces the second one.

During the experiments in the conditions of repetitive noxious stimulation the second injection reveals the “mirror pain” phenomenon, which is a pain response in previously injected but unaffected in second injection paw. Some analgesics, i.e. gabapentin, substantially relieve the “mirror pain”, whereas lidocain has no significant effect on it. The investigations performed let us to partially explain why painful memories are stored and to take steps in processing new, more effective analgesic drugs.

CONCLUSION. A new chronic pain model is tested, which is the modification of widely used formalin test. Duplication of formalin test allows revealing behavioral changes after second noxious stimulation, which corresponds to long-lasting plasticity changes taking place during pain chronization, so called “pain memory”.

Such two consecutive noxious stimulations of contralateral hind paws cause behavioral changes which can be explained by different phenomena: convergence of noxious stimuli (i.e. increase in first phase duration), as well as divergence (i.e. mirror pain), sensitization and desensitization (i.e. opposite changes in first and second phase durations).



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*pain memory,
analgesia,
nociception,
mirror pain,
central nervous system*



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KEYWORDS:

chromatin,
gangliosympathectomy,
phosphoinositides,
fatty acids,
histones

WHITE RAT BRAIN CELLS CHROMATIN PHOSPHOINOSITIDE COMPOSITION CHANGES AND INTERACTION WITH HISTONE MODIFICATIONS AT UNILATERAL GANGLIOSYMPATHECTOMY

INTRODUCTION. Phosphoinositide cycle plays critical role in signal transduction, various intracellular processes as well as gene expression, regulation of Ca²⁺ ion homeostasis and so on. Intracellular messengers and signal transduction agents regulate various processes so disruption in any level of signal transduction chain will lead either to development of disease or to pathological state. In this respect, the role of vegetative nervous system and L.A. Orbeli's conception in regulation of subcellular structures and development of organism homeostasis is extremely important. Purpose of current research is to investigate quantitative and qualitative changes of white rat's brain cells chromatin phospholipids and phosphoinositides, their fatty acids and interaction with histones modifications after unilateral gangliosympathectomy (UGSE) as modelling of extreme state.

Phosphoinositides are key components of cell signal transduction chain. In both pathological and normal state, they modulate cellular activity and compensatory functions in pathological state. Parallel work with phosphatidylcholine cycle amplifies the activity and cellular protective properties of phosphoinositides. In this respect, the changes of phospholipids and phosphoinositides as well as histone fractions in white rat's brain cells chromatin after UGSE were administered.

METHODS USED. Experiments were carried out on mongrel white male rats, fed on general ration. The right UCSG was removed under a slight ether anesthesia. The isolation of brain cells nuclei and chromatin carried out by Dingman and Sporn method, phospholipids and phosphoinositides by Folch method in Karageuzyan's modifications. Methyl ethers of nuclear phospholipids fatty acids obtained by Stoffel method. From isolated chromatin, histones were extracted by methods of J. Bonner et al. Separation of histones were done by electrophoretic method.

RESULTS AND DISCUSSION. The experiments show the quantitative and qualitative changes of phospholipids and histones in rat brain chromatin at UGSE. During the experiments, changes in both types of phospholipids were noticed. The changes show increased concentration of LPC (more than two times). Curiously, the decrease of SM, and MPI (38%), DPI (31%), TPI (32.5%) were noticed, which leads to the chromatin structural and functional damage. From the other hand the increase of LPC shows the activation of PLA₂ and DNA/Histone structural composition changes, besides, the changes in content of LPC can lead to the decrease of activity of ATP-dependent Topoisomerase, which has both enzymatic and structural function. The changes of total histones (besides decreases) leads to conclusion that the removal of histones from chromatin depends from unsaturated fatty acid levels in cells especially arachidonic acid levels.

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THE CHANGES OF CALCINEURIN ACTIVITY IN PATHOPHYSIOLOGY OF GASTRIC CANCER DEPEND ON TISSUE DIFFERENTIATION AND STAGE OF DISEASE

INTRODUCTION. Calcineurin is a unique calcium activated protein, serine/threonine phosphatase contributing to immune response, cell differentiation, and inflammation via dephosphorylation and activation of the nuclear factor of activated T cells (NFAT) transcription factors. Several studies from different laboratories indicate on involvement of calcineurin-NFAT signaling pathways in pathophysiology of cancer. Moreover, calcineurin demonstrates bifunctional activity depending on different physiological and pathophysiological conditions of the organism. We have suggested that the bifunctional activity of calcineurin in cancer pathophysiology may depend on the stage of disease, tumor bearing organ as well as the other factors. Indeed, recently, we have found that changes in calcineurin activity in the pathophysiology of breast, ovary, uterine and cervical cancer depend on the stage of disease and are also organ-specific. In the present study we have investigated the regulation of calcineurin activity in pathophysiology of gastric cancer as well, which is one of the most common gastrointestinal malignancies in the world.

METHODS USED. Enzyme activity has been determined by the spectrofluorimetric assay in plasma and tissue samples of the untreated oncologic patients (30 individuals with the range of age 50-80) with different stages (I-IV) of primary gastric cancer. Histological differentiation of samples has been determined by the Laboratory of Clinical Pathomorphology of the National Center of Oncology after V. A. Fanarjyan (Ministry of Healthcare, RA). The plasma of healthy donors and histologically checked healthy parts of remote tissue were used as a control.

RESULTS AND DISCUSSION. Data obtained demonstrated that calcineurin activity was shown to increase continuously ($p < 0.05$) in the plasma of patients depending on the stage of disease (I-IV) compared with control ($n=6$). In comparison with control ($n=10$) calcineurin activity was shown to increase continuously ($p < 0.05$) in tumor tissue of patients with the I, II, III stages as well and decreased significantly in the IV stage of disease. Moreover, depending on tissue differentiation (moderately and poorly differentiated), calcineurin activity was shown to increase significantly ($p < 0.05$) in the plasma and decrease in tumor tissue of patients with gastric cancer. It was expected since the advanced stages of cancer are characterized mainly by poorly differentiated cells.

CONCLUSION. These findings highlight the involvement of calcineurin in pathophysiology of gastric cancer and demonstrate that the changes in calcineurin activity depend on stage of disease and tissue differentiation.



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KEYWORDS:

*gastric cancer,
inflammation,
calcineurin*



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KEYWORDS:

Zovuni,
Aparan,
Valerian officinalis,
Valerian cardiola.

THE PHARMACOGNOSTIC RESEARCH OF VALERIAN OFFICINALIS AND VALERIANA CARDIOLA RHIZOMES AND ROOTS CULTIVATING IN DIFFERENT REGIONS OF ARMENIA

INTRODUCTION. The preparations of valerian don't lose their actuality and use as a classical sedatives till nowadays.

First time cultivation, enlargement of raw material resources, phytochemical analysis and standartization of valerian species was carried out.

METHODS USED. As a material served the rhizomes with roots of valerian species cultivating in Zovuni and Aparan regions, which were harvested in second half of September annually. The processing was carried out according to WHO guidelines. Resourcological analysis was carried out according to experimental fields estimation method.

The chemical composition of volatile oil, derived from valerian species was carried out by GC-MS method.

The total ash content was determined in the tested samples according to WHO guideliens. Determination of the macro- and micro-elements was performed in the Institute of Geological Sciences of NAS of RA, with the help of DPS-8 device through thermo-emission photometric analysis method.

The sum of flavonoids was determined according to myricetine (silufol Rf= 0,64, 2-butanol-acetic acid-water 4:1:6 solvent mixtures) [3]. The sum of tannies was determined by gallic acid (by the method which is processed and modified by us).

RESULTS AND DISCUSSION. The resourcological analysis showed, that valerian species cultivated in Zovuni and Aparan are stand out by high fruitfulness, specially Valerian cardiola (exceeds almost 2 time Valerian officinalis). The fruitfulness for 1m² is 135±2,3g/m² for Valerian officinalis (Zovuni), 156±3,3g/m² Valerian cardiola (Zovuni), Valerian officinalis (Aparan) 256±4,2g/m², 275±4,4g/m² Valerian cardiola (Aparan) respectively.

The volatile oil analysis showed, that in Valerian officinalis cultivated in Zovuni 21 compound were determined, from which 6 were identified. In Valerian officinalis cultivated in Aparan region 5 compounds were identified, in Valerian cardiola cultivated in Aparan 7 compounds were identified. In all 3 samples 9 compound were investigated, in which bornyl acetate predominats (in Valerian officinalis of Aparan sample 55,2%, in Valerian cardiola of Aparan sample 51,8%, in Valerian officinalis of Zovuni sample 21,2%).

Raw materials derived from the both types of valerian cultivating in these regions have the high content of flavonoids.

According to the investigation results the total ash content in the samples of raw material harvested from different regions of Armenia did not exceed admissible limits noted in the SPh, which were not more than 14% .

In ash content of raw materials of the both types of valerian harvested from Zovuni and Aparan regions the mentioned heavy metals amounts, especially of lead (Pb) did not exceed the admissible terminal limits (SanRN RF 2.3.2. 1078-01).

The highest content of tannins was found in Valerian cardiola cultivating in Zovuni and Aparan, which exceeds 7 times the content of tannins in Valerian officinalis cultivating in the same regions.

Such a variety of content is due to the specificity of the species.

MORPHOLOGICAL SPECTRUM OF RENAL PATHOLOGY AND ITS CORRELATION TO CLINICAL FEATURES IN PIGS WITH ACUTE FORM OF AFRICAN SWINE FEVER (GENOTYPE II, GEORGIA 2007): A STUDY OF AUTOPSY CASES

INTRODUCTION. The occurrence of african swine fever (asf) virus in new areas after 2007 has placed further emphasis on the permanent threat this disease represents to the world pig industry. Although clinical and post-mortem characteristics of laboratorial and natural infections are a little bit different. We analysed specialties of clinical, and post-mortem characteristics of kidney pathology during the asf which is induced by intramuscular injection of asfv (genotype II, georgia2007).

METHODS USED. Infections were carried out using asfv (genotype II) distributed in the republic of armenia and the republic of georgia [Rowlands et al, 2008]. The titre of asfv for each intramuscular injection was 10^4 50% hemadsorbing doses (had50)/ml [Enjuanes et al, 1977].

Eight healthy pigs of the same age and weight were infected by intramuscular injection. Animal care and euthanasia were done according to the avma guidelines on euthanasia, and local guideline for animal care and use (institutional review board/ independent ethics committee of the institute of molecular biology of nas, irb00004079).

Clinical signs of infection were recorded every day. Pathological and anatomical characteristics were observed during routine post-mortem examinations.

RESULTS AND DISCUSSION. The first clinical signs were observed at 2-3 day post infection (dpi) when all infected pigs demonstrated loss of appetite and depression. From 2 to 4 dpi, infected animals displayed hyperthermia with body temperature more than of 40°C. Simultaneously, decreased activity in behavior, difficulties in breathing and reddening of the skin were detected. Blood diarrhea and lethargy were seen at 5-6 dpi.

Kidneys enlarged, the sub-capsular surface of the kidney and the mucosa of the urinary bladder were petechiated at the late stages of asfv infection. Sometimes were observed confluent haemorrhages in kidneys. Kidney with confluent haemorrhages became bigger and dark-red coloured. Patoanatomical observations identified developed glomerulonephritis after 3-4 dpi.

Renal pathology at autopsy in pigs at the late stages of asfv infection, produced by the another genotypes of *asfarviridae*, is well described in previous studies [hervas et al, 1996]. However postmortem examinations of pigs infected by asf virus genotype II investigated first time. Our data revealed the coincidence of patanatomic changes in the kidneys of pigs with initial clinical manifestations of the disease.

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KEYWORDS:

African swine fever,
kidney pathoanatomy,
haemorrhage



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KEYWORDS:

triflusal,
aspirin,
cerebral ischemia

PREVENTION OF CEREBRAL ISCHEMIC DISORDERS' CONSEQUENCES BY TRIFLUSAL

INTRODUCTION. Antiplatelet therapy is the main approach in complex treatment and secondary prevention of stroke [1]. Clinical data evident, that antiplatelet drug triflusal appears competitive effectiveness in preventive therapy of thrombovascular events with less incidence of bleeding and gastrointestinal events compare with aspirin [2]. As a promising agent for secondary stroke prevention [3] it was interesting to evaluate the effects of triflusal on neurobehavioral consequences and microcirculatory changes of cerebral ischemic disorders.

METHODS USED. Adult male white albino rats weighing 170–220 g were used. Acute disturbance of cerebral circulation was caused by ligation of the right common carotid artery (rcca) and triflusal as well as aspirin was administrated by intraperitoneal injection at the dose of 30mg/kg. A continuous laser-doppler-flowmeter was used to monitor the lcbf in the right hemisphere. Brain slices were obtained from cerebral cortex of rats, which were decapitated 60 minute after the injection of proper drugs or 0.9% saline solution for the control group animals. The microcirculation was observed by ca²⁺-adenosine triphosphate method. The mean diameter of capillaries, quantity of functioning capillary and distribution by luminal diameters were calculated.

Focal cerebral ischemia was induced by permanent occlusion of the middle cerebral artery (mcao). 24 hours after mcao 2,3,5-triphenyltetrazolium chloride (ttc) staining was used to determine ischemic damage [4]. Stroke volume measurements were done by imagej software. Neurobehavioral consequences of stroke were evaluated by assessment of anxiety and loco-motor activity in elevated plus maze test on 3rd and 6th day after mcao [5]. Drugs were administered orally 1 hour after mcao and continued once daily for three days at a dose of 30mg/kg. Data analysis was done by any-maze software.

RESULTS AND DISCUSSION. The data obtained have shown that ip injection of aspirin decreased lcbf in the right hemisphere aggravating ischemic process. The maximum reduction of cbf was noticed at 30 minute after injection up to 16.39±5.42% compared with occlusion level. Ip injection of triflusal in spite of aspirin did not cause any significant changes in lcbf. Moreover, for triflusal-treated group it was registered significant increase in mean diameter of all and functioning capillaries compared with both vehicle-treated and aspirin-treated animal groups. It was detected increase of functioning capillaries and decrease of constricted capillaries quantity leading their ratio near to intact condition.

It was determined that oral administration of triflusal and aspirin significantly reduce average stroke size by 44.26% and 25.19% compared to vehicle control, respectively. It means that triflusal prevents infarct size 1.8 times more than aspirin. As a result triflusal treatment relieved stroke-induced anxiety and motor dysfunction of alchemized rats on the 3rd and 6th days after mcao more significantly than aspirin.

CONCLUSION. Thus, our investigation allowed to reveal the property of triflusal to stimulate the microcirculation of cerebral tissue, reduce the infarct size in experimental model of stroke, and provide evidence that this is accompanied by improved neurobehavioral outcomes.

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THE EFFECT OF THE GLOBUS PALLIDUS ON THE SUBSTANTIA NIGRA NEURONS

INTRODUCTION. The Globus Pallidus (GP) is one of the principal output structures of basal ganglion (BG). In the present time, researchers are encouraged to focus on motor functions BG, concentrated in cognitive and motivational roles. It has been confirmed pallido-nigral projection in dopamine (DA) cells of substantia nigra pars compacta (SNc). In turn, GPe and GPi segments take the projection of SNc. Disturbances in interaction of SNc with others structures of the BG, including the GP, lead to the following manifestations: rigidity, bradykinesia, tremor and postural instability, characteristic of Parkinson's disease (PD).

GP is in the unique position on the process of motor information, thanks to its wide spread projection to BG nuclei and its roles in coding of movements and associated pathologies, confirming the central location of GPe in motor function and dysfunction. Unless the critical role of the motor function regulation, GP's functional organization stays not enough studied, that prevent us from understanding the role of GP in Parkinson's disease.

The present study is aimed at determining the ratio of depressor and excitatory effects in neurons SNc to high-frequency stimulation (HFS) of GP.

METHODS USED. 4 intact Albino rats, 300 g. Urethane (40 mg / kg). Recording of evoked spike activity of single SNc neurons on HFS(100 Hz for 1 sec, rectangular shocks of current 0.05 msec and 0.18 mA.) of GP. Stereotaxically oriented stimulating electrode was implanted in an ipsilateral GP, a glass recording microelectrode with 2M NaCl solution was immersed in SNc. 191 SNc neurons were recorded for HFS GP. The analysis of single spike activity was performed by using the average frequency of spikes for the selected compared groups of spiking of neuronal activity. Summarized and averaged peristimular, cumulative histograms and frequency histograms were constructed. It was used by Student's t-test, as well as the Mann-Whitney and z-test. Statistically significant change with the level of significance of 0.05.

RESULTS AND DISCUSSION. In SNc neurons, in response to GPHFS in TD PTD and TD PTP was determined to be in the order of 4.63 and 5.43 times the understatement of activity, respectively. TP PTP and TP PTD was detected within 1.50 and 3.32-fold excess of activity, respectively. That is, the manifestations of inhibitory activity are much higher than the manifestations of the excitatory activity. This is recorded in both unidirectional manifestations and in multidirections.

CONCLUSIONS. Preliminary studies have found that GP neurons can have special patterns of bursting activity in different time phases of motion or motor sequence, i.e. are thought for the collectively represented fragmentation of the motor sequence. GP can play a role in canceling reactive action or suppressing planned actions. Despite the clinical importance, information regarding its organization is limited. In experiments, the prevalence of depressor effects over excitatory effects in uni- and multidirectional sequences was revealed, especially expressed in that of unidirectional (of the order of 3.08-fold), versus 1.63-fold in multidirectional sequences. This effect is expected, since GP activity is regulated by GABAergic inhibition.



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KEYWORDS:

*substantia nigra,
globus pallidus,
single neuronal activity*



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

chromatin,
gangliosympathectomy,
phospholipids,
fatty acids,
non-histones

THE CHANGES IN WHITE RATS BRAIN CELLS CHROMATIN PHOSPHOLIPIDS AND THEIR FATTY ACIDS COMBINED WITH CHANGES OF NON-HISTONE PROTEINS AT UNILATERAL GANGLIOSYMPATHECTOMY

INTRODUCTION. The changes of white rat's brain cells chromatin phospholipids, their fatty acids and also non-histone proteins are associated with regulation of various functions, as well as regulation of chromatin matrix activity, gene stability, transcription regulation, protection of chromatin from various damaging agents, such as increase of oxygen toxic derivatives, oxidative stress mediated damage and so on. In this case significant changes of fatty acids have compensatory role but their continuous decrease and also non-histone protein content lead to development of pathological state or disease. In organismal level regulation of functions and homeostasis of subcellular structures by vegetative nervous system is extremely important.

Purpose of current investigation was the revealing of quantitative and qualitative changes of white rat's brain cells chromatin phospholipids and their fatty acids, combined with changes of non-histone proteins after unilateral gangliosympathectomy (removal of right upper cervical ganglion). According to Orbeli's conception about adaptational-trophical and compensatory role of vegetative nervous system current process in molecular level via changes of chromatin phospholipids, their fatty acids and non-histone protein content were described.

METHODS USED. Experiments were carried out on mongrel white male rats, fed on general ration. The right UCSG was removed under a slight ether anesthesia. The isolation of brain cells nuclei and chromatin were carried out by Dingman and Sporn method and phospholipids by Folch method in Karageuzyan's modifications. Methyl ethers of nuclear phospholipids fatty acids was obtained by Stoffel method. Electrophoretic separation of brain chromatin non-histone proteins were carried out by Teng and Allfrey method.

RESULTS AND DISCUSSION. Changes of fatty acids correlated with changes of non-histone proteins testify significant disorders in signal transduction processes and serious disruption in whole signal transduction system. The sum of neutral phospholipids decreased in both hemispheres of chromatin (for about 13% and 24% respectively), while the sum of acidic phospholipids decreased in ganglioectomated and decreased in the intact hemispheres (for about 27% and 22% respectively). The increase of saturated fatty acids in ganglioectomated hemispheres chromatin phospholipids is very interesting. From the other hand, the decrease of non-histone proteins fractions as well as decrease of C¹⁴-lysine including intensity also testifies disorders in structural organization and functional activity of ectomated hemisphere chromatin. The changes of polyenic fatty acids is of another character: decrease in ganglioectomated and slight increase in intact hemispheres chromatins (6.3% and 2% respectively), which testify to compensatory perturbations in chromatin of intact – left hemisphere.

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LEVEL OF SPERMINE IN BLOOD PLASMA IN PATIENTS WITH PARKINSON'S DISEASE

INTRODUCTION. Parkinson's disease (PD) is one of the most common neurodegenerative, chronic systemic, multifactorial diseases. 200 years have passed since the description of "trembling paralysis" by the English physician D. Parkinson, which later received his name and is currently considered as a Parkinson's disease. PD is a progressive neurodegenerative disorder affecting more than 6 million people over 60 years of age. Given the increase in the life expectancy of people, many neurologists reasonably predict an increase in the PD by 2030. The clinical picture of PD is characterized by movement disorder: bradykinesia, muscle rigidity, rest-less tremor, postural disorders. On the basis of the PD is the irreversible damage and death of nigrostriatal dopamine-synthesizing neurons, leading to a deficiency of dopamine in the striatum. With Parkinson's disease, not only nigrostriatal degeneration with movement dysfunction is observed, but a significant proportion of PD patients suffer from non-motor symptoms, including anosmia, constipation, depression and cognitive dysfunction. Cognitive symptoms contribute significantly to disability in PD. Spermidine is a polyamine containing 3 amino groups. It plays an important role in some mechanisms, including cellular proliferation and differentiation, gene transcription and translation, modulation of ion channel function, cellular signal macromolecular synthesis and so on. Spermidine act as a free radical scavenger, a biologically important antioxidant *in vitro*.

The aim of this work was to study the level of spermidine in the blood plasma of PD patients at different stages of the disease.

METHODS USED. Patients with PD were examined, ranging in age from 36 to 73 years 1 to 4-stage functional scale, Hoehn Yahr. The clinical diagnosis of PD was established in accordance with the criteria of "inclusion-exclusion" based on UK Brain Bank Criteria.

The severity of movement disorders was assessed according to international rating scale UPDRS. Blood sampling was performed in the morning on an empty stomach-the 1st-day patient's admission to the hospital in heparinization of the tube, then, the resulting blood plasma after centrifugation was stored at -80°C.

Spermidine determination was carried out by HPLC (PerkinElmer) in column Lichrospher RP18 (250x4,6), benzoyl derivatives of polyamine to identify in the UV at 229 nm. The spermidine content in the blood plasma was expressed in nmol of polyamine per ml of plasma.

The results are presented as M±m. Mathematical processing of data was performed using the program "Statistica 6.0". To assess the reliability of detected changes used the Student test (comparison of two independent groups of data).

RESULTS AND DISCUSSION. The results of the studies are shown in the table.

Table. Spermidine contents in patients' plasma with Parkinson's disease

Learned indicators	Donors (n=12)	Stages of development with Parkinson's disease			
		I (n=10)	II (n=10)	III (n=10)	IV (n=8)
Spermidine (nmol/ml)	6.8±4,7	24.22±4,9	19±6.2	2.5±1.7	1.33±0.5
	n=21	p≤0.0001	P=0.715	p≤0.05	p≤0.05
		n=13	n=15	n=10	n=14

As can be seen from the table, in the 1-st stage of PD in patients' plasma spermidine content increased 3.5 times in comparison with donors. In the 2nd phase of PD spermidine content significantly higher than the control value, which, was statistically not significant.

In the 3rd stage of PD was observed a decrease in the spermidine content by 63% in comparison with donors. All PD patients with the 3rd stage included in this group, except for pronounced bilateral motor manifestations, cognitive impairment had been marked (MMSE=12). On the 4th stage of PD decrease in the spermidine content was 80% compared to donors.



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Parkinson's disease
Spermidine
HPLC



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Autism,
amygdala,
behavior

BEHAVIORAL CHANGES AFTER EARLY POSTNATAL DAMAGE OF RATS' AMYGDALAE

INTRODUCTION. Autistic disorder is the most severe of a group of life-long neurodevelopmental disorders, referred to as autism spectrum disorders (ASDs), and is characterized by a triad of impairments in social skills, verbal communication, and stereotypic (repetitive) behavior or a narrow range of interests, as well as symptoms emerging early in childhood. Several theories have been proposed to account for the atypical pattern of socio-emotional behavior in ASDs. The most influential are the Theory of Mind, the Socio-emotional theory, the Social Motivation theory, and the Fast-track modulator model. All these theories are compatible with a core deficit of the so-called “social brain” in which the amygdala is the key component. That’s why It is not surprising that amygdala must be involved in the etiopathogenesis of such symptoms manifestation.

METHODS USED. On postnatal day 7 (PND7) pups’ were anesthetized by induction of hypothermia placing on ice package. After that pups were fixed on stereotaxic apparatus and amygdala were damaged by bilateral injection of ibotenic acid in concentration 3µg/0.3µl and NaCl solution respectively for control group. The coordinates for the amygdala lesions were 3.8 mm lateral to the midline, 1.0 mm posterior to bregma and 6.0 mm below the surface of the skull at an angle of 4°. The offspring were weaned on PND30 and rats were housed four per cage. During the PND 30-35 the following behavioral test were carried out: novel object recognition (NOR), hot plate, social interaction, elevated plus-maze and Y maze.

RESULTS AND DISCUSSION. As a parameter of social behavior were scored duration of sniffing, crawling, pinning and following. Ibotenic acid lesioned rats were significantly less involved in active behavior than controls (M=145.5, SEM±21.2, M=106.9, SEM±6.4, p<0.05 for control and lesioned groups respectively). Sensitivity to thermal nociception was determined on a hot plate analgesia meter by a measuring the latency of response to the thermal stimulus (50±0.5°C) during 60s. Ibotenic acid treated rats expressed significantly higher latency to lick hind paw than control (M=23.1, SEM±2.8, M=45.1, SD±3.2, p<0.01). The novel object recognition test was evaluated by the differences in the exploration time of novel and familiar objects as well as total exploration time. Our findings showed that ibotenic acid treated rats spent more time for process of familiar object’s exploration (M=29.5, SEM±6, M=46.4, SEM±5, p<0.05), as well as total time needed for exploration of both objects in comparison with control ones (M=52.3, SEM±8.9, M=77.3, SEM±9, p<0.05). Meanwhile, ibotenic-treated rats showed no statistically significant differences in novel object exploration time period in comparison to control. There were no significant differences between treated and control groups in elevated plus-maze and Y maze.

CONCLUSION. Summarizing our study we can conclude that ibotenic acid induced damage of amygdala may mimic some of the behavioral changes seen in individuals with ASD.

**THE INVESTIGATION OF MERCHANDISING,
PHYTOCHEMICAL AND BIOLOGICAL ACTIVITY OF HERB
OREGANO ORDINARY (HERBA ORIGANI VULGARIS L.)
WILDLY GROWING IN FLORA OF ARMENIA**

INTRODUCTION. Oregano ordinary (herba *Origani vulgaris* L.) grows in Western and Eastern Europe, In Japan, In India, in Russia, in Asia etc, as well as in different regions of Armenia. The plant is a perspective raw material possessing high biological activity (antibacterial, antiradical, antioxidant).

The aim of the investigation is the pharmacognostic research of herb Oregano ordinary wildly growing in different regions of Armenia (Kotayk, Tavush, Lori, Gegharkunik), during its vegetation period (pre-blossoming, blossoming, fruiting).

METHODS USED. The sample of Oregano ordinary herb harvested from different regions of Armenia (Kotayk, Tavush, Lori, Gegharkunik) during vegetative period (pre-blossoming, blossoming, fruiting) from May to August in 2011-2015 served as a material for investigation are registered with ERE 192245, ERE 192247, ERE 192246, ERE 191395 serial numbers.

RESULTS AND DISCUSSION. The morphological anatomical diagnostic features have been found in merchandising analysis warty cuticle oil glands, glandular trichoms, simple trichoms, diacid type of stomats.

The quality indexes defining good quality of herbal raw materials which meet the requirements of WHO, have been determined in prestandartization.

The study of the dynamics of the extracted substances has shown that the maximal outcome is observed in the period of blossoming in Kotayk region, with the content of several low molecular substances (catechol, phtalic acid, stearic acid, isomenton, hydroquinone, lidocaine, palmitic acid, angelicin etc.). The analysis of climatic factor confirmed in different fractions (aqueous, benzol, chloroform, ethyl acetate) of raw material alcohol extract the presence of the secondary metabolits of the plant (flavons: apigenin, lyuteolin, cosmosiine). It was found out the presence of flavonoids and tannins. Their quantatitive content (the greatest content was found in the region of Kotayk (22.29 %, 3.84 % respectively)) compared to the region of Gegharkunik (18.03 %, 3.41 % respectively)). It was worked out a mechanism of Oregano herb's standardization according to extractive substances.

Issuing the presence of catechins in raw material and the quantitative content of flavonoids in ethanol extract according to the evaluation of catehin ($3,9 \% \pm 0,7 \% w/w$ CE), studied the antiradical activity of Oregano ordinary essential oil and ethanol extract. The results of the assay indicated that the scavenging effect (IC_{50} value) of ethanol extract, *O. vulgare* essential oil and standart was in the following order: catechin ($IC_{50} 12 \pm 0,9 \mu g/mL^{-1}$), ethanol extract ($IC_{50} 18,2 \pm 1,4 \mu g/mL^{-1}$) and essential oil ($IC_{50} 1311,4 \pm 20,6 \mu g/mL^{-1}$). It was confirmed that the antiradical activity of *O. vulgare* wildly growing in Armenian flora is not due to phenolic substances, but due to the sum of biologically active substances (organic acids, carotoids, vitamins). The investigation of the dynamics gathering of essential oil in different phonological stages confirmed the IV chemorass belonging of *O. vulgare*. The major compound of essential oil is β -Caryophyllene.

It was confirmed that the essential oil and the ethanol extract possess antibacterial activity towards Gram negative (*S. Typhimurium* TA 100, *E. coli* VKPM M-17) and Gram positive (*B. subtilis* AIWT2, *P. aeruginosa* GRP3, *S. aureus* WDCM 5233) bacteria.



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KEYWORDS:

*herb Oregano ordinary,
merchandising analysis,
phytochemical analysis.*



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KEYWORDS:

FMF,
 F-actin,
 phagocytosis,
 fMLP

SOME MANIFESTATIONS OF INCREASED PRO-INFLAMMATORY ACTIVITY OF INNATE IMMUNE CELLS IN FMF PATIENTS

INTRODUCTION. Familial Mediterranean Fever (FMF) is the most common autoinflammatory disease among Armenians: carrier rate is 1:5, and disease rate is 1:500. It is caused by MEFV gene mutation that leads to impairment of pyrin functions. Pyrin is an intracellular regulator of pro-inflammatory activity of innate immune cells. Among other functions, it interacts with actin-binding proteins and, correspondingly, regulates actin-dependent processes including phagocytosis. The mechanisms of attacks, their resolution and periodicity are not fully clear, despite of many researches. Innate immunity of FMF patients shows hyperactive pro-inflammatory response not only during attacks, but also subclinical inflammatory activity in attack-free periods. And the periodicity of attacks suggests that there are periodic changes in cellular level too. Taking into consideration above mentioned, we hypothesized that the content and time-dependent dynamics of F-actin of FMF patients neutrophils differ from the same parameters in normal donors (NDs). Assuming, that FMF attacks can be provoked by yet unclear trigger, we used chemotactic peptide as an activator of cytoskeleton. At the same time, to strengthen the results, we examined phagocytic activity of neutrophils as an actin-dependent process.

METHODS USED. Peripheral blood samples were obtained from 20 normal donors (NDs) and 37 attack-free patients with FMF, diagnosed according to the Tel-Hashomer criteria and genetic testing. Blood samples were divided into 5 parts. Chemotactic peptide fMLP (N-formyl-methionyl-leucyl-phenylalanine) was added to all parts. One part was left on ice during the whole experiment, that showed baseline. Others were incubated in a water bath at 37°C for 1, 3, 5, 10 min respectively. Intracellular F actin was stained by fluorescein isothiocyanate (FITC)-conjugated phalloidin and phagocytic activity was visualized by adding latex beads with fluorescence activity. Both F-actin and phagocytosis were measured by flow cytometry relative fluorescence intensities (expressed as a mean channel number - MCN).

RESULTS AND DISCUSSION. We observed that both unstimulated neutrophils F-actin content and intensity of phagocytic uptake of latex beads in FMF patients were significantly higher ($P_w < 0.01$), than in ND. The period of fMLP-induced neutrophil F-actin oscillation was 4.66 ± 0.11 min in FMF patients and 3.58 ± 0.17 min for NDs, starting from higher baseline in FMF patients vs NDs. And fMLP stimulated neutrophils phagocytosis oscillation period was 6.03 ± 0.05 min in FMF patients, whereas linear time-dependence in NDs, starting from higher baseline in FMF patients than in NDs.

Increased level of F-actin and intensive phagocytosis of neutrophils show high reactivity of this cells in attack-free periods, and is supposed to be one of the manifestations/mechanisms of subclinical inflammation in FMF patients. The results of chemotactic activation show that the behavior of neutrophils of FMF patient differs from NDs. High period of oscillation (compared with NDs) of F-actin of FMF patients stimulated neutrophils can indicate impaired plasticity of their cytoskeleton and activation-deactivation program. Chemoattractant-stimulated phagocytosis oscillation in FMF patients is also different than in NDs. Concluding, we can assume that mutations in MEFV cause alterations in neutrophil F-actin and phagocytosis dynamics and impairment of cellular adaptation to chemoattractant stimuli.

USAGE OF GUMMI ARMENIACA AS AN EXCIPIENT FOR DEVELOPMENT OF PARACETAMOL TABLETS

INTRODUCTION. Pharmaceutical formulation development involves various components in addition to the active pharmaceutical ingredients. Nowadays the interest in natural excipients is increased considering a number of advantages natural excipients (cheap and easily available,

lack of toxicity and multifunctional action)[1]. In view of this Gummi Armeniaca is one of the promising sources of natural excipients. The chemical composition and application of Gummi Armeniaca are similar to Gummi Arabica, which is widely used as excipient in pharmaceutical and food industry. Thus, the aim of this study was assessment of the bioequivalence paracetamol 50 mg tablets containing Gummi Armeniaca or synthetic origin PVP (polyvinylpyrrolidone) by biowaiver method.

METHODS USED. The paracetamol 50 mg tablets containing Gummi Armeniaca or PVP as a bonding agents were prepared by liquid granulation methods. Bioequivalence study was carried out according to WHO Guidance (75 rpm, $37\pm 0.5^\circ\text{C}$, dissolution media volume was 900 mL) [3]. All dissolution studies were performed using USP Apparatus 2 (Erweka DT 60, Germany). Dissolution media were buffer solutions: hydrochloric acid solution (pH 1.2), acetate buffer solution (pH 4.5) and phosphate buffer solution (pH 6.8). All three media have been prepared according to USP XXX (USP-NF 25) [2]. Buffers pH has been detected by pH meter (PH/MV BENCH METER HANNA, GERMANY). The sampling was carried out at 5, 10, 15, 20, 30 and 45 min for the dissolution profile. Quantitative detection has been performed by spectrophotometric method using UV-Vis spectrophotometer at 243 nm. Twelve tablets of each preparation were studied to obtain statistically significant results. Statistical analysis was carried out using Microsoft Excel software.

RESULTS AND DISCUSSION. The obtained data indicate that PVP and Gummi Armeniaca containing paracetamol 50 mg tablets were rapidly dissolved ($\geq 85\%$ of the labeled amount of drug in 30 minutes) in all three dissolution media. The percent relative standard deviation (% RSD) for all time points fulfills all requirements ($\leq 20\%$ for 15 min, $\leq 10\%$ for other time points), so results are valid. Moreover, both tablets (PVP or Gummi Armeniaca containing) have high solubility but in all dissolution media solubility of Gummi Armeniaca containing tablets exceeds the PVP containing tablets.

CONCLUSION. The calculation of similarity factor (f_2) shows that PVP and Gummi Armeniaca containing tablets dissolution profiles are not similar. Moreover Gummi Armeniaca containing tablets exhibit higher solubility than PVP containing tablets in all dissolution media. Thus, Gummi Armeniaca increases drug substances release from the tablet and could be recommended for further studies as bonding excipient for paracetamol tablets development.

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KEYWORDS:

Gummi Armeniaca,
PVP,
biowaiver,
paracetamol tablets



CONFERENCE ABSTRACTS

NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

electrostatic field,
 hippocampus,
 DNA,
 protein

THE CHANGES OF TOTAL PROTEIN/DNA RATIO OF RAT HIPPOCAMPAL CELLS AS A RESPONSE TO THE INFLUENCE OF HIGH VOLTAGE ELECTROSTATIC FIELD

INTRODUCTION. The functional activity of neuronal cells largely depends on the difference of potentials generated on membrane, which is a result of internal electrostatic interactions and, it is logically to suggest that the superposition of external and internal fields can change the existing “balance”. Actually, there are a lot of studies testifying about the direct effect of ESF on neurons. Particularly, it was shown that rat hippocampal neurons respond to applied ESF with directional migration, which, in authors’ opinion, may be used as a cue to direct neuronal migration in novel strategies to repair the CNS. Thus, it can be said that external electrostatic fields (ESF), in all probability, can affect the functional state of hippocampal cells.

To characterize the effect of short term (1 hour) and fractional (6 days, 6 hour for day) influences of 200kV/m ESF on the cells of rat hippocampus, we conducted measurements of DNA and cell protein fractions to characterize the changes of cell number and cell size after the field influence.

METHODS USED. The hippocampus of 120-150g male outbred rats were used as an object of investigations. ESF was created using the condenser type device with controlling parameters of the field. Each tissue was homogenized and aliquots of the homogenate were withdrawn for measurement of DNA and total protein. DNA was assessed with a fluorescent dye-binding method using Hoechst 33258. Samples were read in a spectofluorometer ($\lambda_{ex} = 356 \text{ nm}$; $\lambda_{em} = 458 \text{ nm}$) and were quantified using standards of purified DNA. The total concentration of tissue proteins was assayed spectrophotometrically.

RESULTS AND DISCUSSION. In accordance with data obtained (Tab. 1) any changes in DNA concentration were not observed after the field influences, while after the fractional influence of ESF the concentration of total protein significantly decreased by 68%.

TABLE. 1.

Quantitative analysis of DNA and total protein of rat hippocampal cells after the influence of 200 kV/m ESF

	Control	One hour influence of ESF	Fractional influence of ESF
DNA ($\mu\text{g/ml}$)	1.00 \pm 0.17	1.05 \pm 0.09	0.955 \pm 0.05
Protein (mg/ml)	0.25 \pm 0.04	0.27 \pm 0.08	0.17* \pm 0.04
Total protein/DNA	0.25	0.26	0.18

p < 0.1

Taking into account that the DNA content reflects the total number of cells; and the falling of total protein/DNA ratio indicates decrease of cell size, we can suggest that the ESF influence did not affect the cell amount in rat hippocampus. But after the fractional influence of field the total protein/DNA index reduced by 1.4 fold compared with control, which indicates the decrease of cell size.

CONCLUSION. The results obtained indicate that the studied field exposures do not alter the cell nucleus. The quantitative change in the total protein due to fractional exposure of ESF indicates a metabolic component of the cellular response to the field influence. At this stage of research it is not possible to identify the mechanisms underlying observed changes, but it is possible to assert about the shifts in the functional state of hippocampal cells.

CRITERIA USED BY COMMUNITY PHARMACISTS FOR SELECTING RESOURCES OF MEDICINES INFORMATION

INTRODUCTION. Pharmacists and pharmacy assistants working at the community pharmacies play an important role in ensuring safe and effective use of medicines by patients [1]. To provide appropriate services these professionals need objective and up-to-date information on pharmaceuticals [2]. However, not all the resources of medicines information provide reliable data. The aim of this study was to identify criteria which pharmacy professionals working at community pharmacies in Armenia use for selecting the sources of medicines information used by, as well as resources used by them.

METHODS USED. Pharmacists and pharmacy assistants working at randomly selected community pharmacies were interviewed. The sample (n=348) included professionals from all the regions of Armenia including Yerevan. Previously developed questionnaire was used for interviewing respondents. A survey was conducted in 2012. The results were analysed using SPSS statistical software, version 22.0.

RESULTS AND DISCUSSION. The most of professionals consider as important and very important the following criteria for selecting sources of medicines information: accessibility (98.8% of respondents), recency (97.4%), comprehensibility (96.9%), reliability (94.3%), completeness (88.2%) and labour intensity (85.7%). All respondents use one or more sources of information. The great majority (88.2%) of respondents reported that they always and often look for information in Patient Package Inserts. Many professionals mentioned using certain reference books: 66.7% seek information in the Reference book "Medicines" by M. D. Mashkovski; 44.8% - in the Reference book "Vidal". Only 27.6% of responders seek information in the Armenian National Formulary (ANF). The number of professionals who always and often use ANF among those who completed continuing education courses is significantly higher than among those who have not completed ($p<0.001$). Also, there are more community pharmacists and assistants who use ANF among those working in Yerevan than among those who are employed in regions ($p<0.001$). 59.5% of participants look for information on the Internet. Another popular source is medical representatives of pharmaceutical companies; 51.4% of respondents reported use of information provided by them. Some resources are less used: 24.1% of respondents noted that they seek information in professional journals and newspapers, 13.3% - at congresses and conferences, 6.9% use data received from clinical trials and 3.7% - from the Cochrane Library. 37.1% of participants noted that they would like to have an access to references with up-to-date information.

CONCLUSION. Although the great majority of professionals consider the main criteria, necessary for correctly selecting sources of information, as important, few of them still do not understand value of using reliable, up-to-dated and comprehensive information. Pharmacy professionals use different sources of medicines information, both printed and electronic. The most frequently used resource is Patient Package Inserts. References in Russian are used by a lesser number of professionals. The most reliable resource, ANF of 2008 (the last edition) is not used by the majority of professionals. There is an urgent need in publishing a new Reference book in Armenian that would include objective and up-to-date information on all the authorized medicines in Armenia, as well as in improving knowledge of pharmacy professionals on medicines information.

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KEYWORDS:

medicines information,
community pharmacists,
sources of medicines
information



CONFERENCE ABSTRACTS

NOVEMBER 27th – DECEMBER 1st

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Pharmacy,
student,
employed,
pharmacist,
faculty.

PROFESSIONAL FEATURES FOR EMPLOYED PHARMACY FACULTY STUDENTS' IN GEORGIA

INTRODUCTION. Educational focus of professional programs are increasingly recognized the need for an opportunity to apply what they have learned in the classroom through laboratory simulations or experiential learning, which requires different types of faculty and staff positions to meet these educational needs. Innovative types of faculty and staff positions with great attention to training or practice and less responsibility for traditional research appeared in Pharm degree programs and should encourage graduates pharmacies carry these roles [1]. At the same time, should encourage graduates to conduct Pharm degree degrees in masters or doctoral level philosophy .or providing the basis for and research in biomedical, pharmaceutical, clinical and administrative sciences in pharmacy programs. Pharmacy educators need to become more actively involved in the development of special educational opportunities to prepare a new generation of faculty and staff and to review the types and nature of faculty and staff positions in our institutions in order to attract graduates to participate in the academy[2]. Pharmacy graduates should be encouraged to explore the potential role of other medical and scientific educational programs, given the increased attention to inter-professional teams in health professions education is essential for high-quality patient care [3].

Aim and objects was to study and analyze professional features for employed pharmacy faculty students' in Georgia.

METHODS USED. The study was quantitative investigation by using survey.222 employed pharmacy faculty students were interviewed in Georgia. The survey was conducted on 09.09.2016. - 30.04.2017.

RESULTS AND DISCUSSIONS. 222 employed pharmacy faculty students were interviewed in Georgia. Respondents 81.5 % was working with specialty. Respondents-97.7% was satisfies with their professional choice. In respondents-45.0% reasons for your employment was payment for studies, In respondents 57.7% reasons for your employment was lack of financial (material) resources in the family, In respondents 43.2% reasons for your employment was post graduate recruitment; Respondents' 41.9% thinks that work has not impeded in their studies , respondents' 21.6% thinks that work has partly impeded in their studies . Respondents' 55.9% practically have no missed their classes, respondents' 12.6% have missed approximately half of their classes; Respondents' 20.3% work Two-three days per week, respondents' 23% works three-four days per week , respondents' 23.0% works- four or five days per week, respondents' 21.2% works 5 Five-six days per week. Respondents' 15.8 % thinks, that work is more important, respondents' 84.2% thinks, that studies are more important. Respondents 19.8% started learning better and respondents' 37.4 % started learning worse. Respondents 82.0% thinks that government should make the certification of pharmacists.

CONCLUSION. Near the half of pharmacy faculty students the most attractive areas (spheres) of activities are- pharmacy- drugstore. The vast majority of pharmacy faculty students consider that education should not be ceased. Pharmacy faculty students' more than a third was working by specialty. Employed pharmacy faculty students' vast majority consider that the government should make the certification of pharmacists.

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ELECTROPHYSIOLOGICAL ANALYZE OF THE POTENTIALS OF MEDIAL RETICULAR FORMATION NEURONS' TO STIMULATION OF THE CEREBELLAR AURICULAR LOBE IN FROG

INTRODUCTION. The reticulo-spinal tract is the most ancient system of supra-segmental control of body movement control. In amphibians, reticulo-spinal neurons are located in the medial zones of the reticular formation (RF) medulla oblongata. Along with the vestibular, reticulo-spinal neurons are also important in the regulation of body movements.

Thus, it is interesting to investigate the effect of the auricular lobe of the cerebellum on the reticular neurons, which was the goal of this work.

METHODS USED. The experiments were performed on frogs (*Rana ridibunda*) of both sexes using the isolated perfused brain method. The animals were anesthetized with MS-222 solution. A computer analysis of the data was carried out.

RESULT AND DISCUSSION. It was registered intracellular activity of 175 reticular neurons that were identified on the basis of EPSP, which arise in response to stimulation of the ipsilateral vestibular nerve and synaptic inhibition of the same neurons to stimulation of the auricular lobe of the cerebellum. Only 30% of the MRF neurons responded to the stimulation of the cerebellum. The stimulation of the auricular lobe caused inhibitory postsynaptic potentials (IPSP). On the basis of the temporal characteristics of the studied responses, we conditionally divided the recorded IPSP into short and long-latency ones. The first group included 56 neurons, the latency of which was up to 3.0 ms. The temporal characteristics of these IPSPs at varying intensity of stimulation of the cerebellar cortex practically did not change. The above mentioned gave grounds for considering the IPSP data as monosynaptic and they were generated by direct activation of the axons of Purkinje cells projected into the MRF.

The second group includes 119 reticular neurons, in which the stimulation of the auricular cortex caused IPSP with a longer and more unstable latency of 3.04-6.0 ms. With an increase in stimulation intensity, was observed a clear shortening of the temporal characteristics of the IPSP. The dependence of registered IPSP on intensity of stimulation and their temporal characteristics indicate di- and polysynaptic origin. The IPSP data indirectly activated Purkinje cells through parallel fibers.

The latency of IPSP neurons depends not only on the stimulation intensity, but also on the localization of the stimulating electrode. The frequency of appearance of marked IPSP decreased as the stimulating electrode was moved closer to the middle line of the cerebellum. Taking into registered account the IPSPs, we can assume that the mechanism described above also exists in relation to the cerebellar-reticular relations.

CONCLUSION. Based on the results obtained, one can judge the great similarity of the functional correlation of the vestibular input with the vestibulo-spinal system in the frog and higher vertebrates, like mammals. Active participation and interaction of reticulo- and vestibulo-spinal systems in the motor spino-bulbar reflex are shown. Thus, RF, like Deiter's nucleus, is an important relay in the organization of motor control. The cerebellum plays an important role in regulating the posture and movement of a very different nature, cooperating in addition to the vestibulo-spinal cord as well as the reticulo-spinal system of the brainstem.



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KEYWORDS:

*vestibular nerve,
medial reticular formation,
cerebellum*



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

neurodegeneration,
proline-rich
polypeptide-1 (PRP-1),
enzyme linked immunosorbent
assay (ELISA)

MORPHO-FUNCTIONAL INVESTIGATION OF BRAIN PLASTICITY ON THE DIFFERENT NEURODEGENERATIVE MODELS

INTRODUCTION. Our multiyear field of studies was the investigation of the action of the various compounds on the brain plasticity in rats with different neurodegenerative models [spinal cord (SC) hemisection; intraventricular injection of beta-A peptide (Alzheimer's disease model); vestibular nuclei injury by vibration and unilateral labyrinthectomy; immobilization stress (IMO stress)]. A new type of cytokines, the proline-rich polypeptides, isolated by prof. Galoyan and coworkers from bovine neurohypophysis neurosecretory granules, was synthesized in the form of a common precursor protein (neurophysin-vasopressin associated glycoprotein). PRP-1 consisting of 15 amino acid residues (AGAPEPAEPAQPGVY) is one of these peptides. PRP-1 has been shown to possess neuroprotective (1), immunoregulatory, hematopoietic, and angiogenic effects through its involvement in the neuro-immuno-haematopoietic interaction. Our results obtained in the applied models of the central nervous system injury indicated that PRP-1 therapy might protect against the neurodegeneration through different mechanisms – by enhancing the survival of the damaged neurons, by neurogenesis, and by angiogenesis. Indeed, PRP-1 participation in the production of new neurons in the brain of 45-75-day old rats exposed to prenatal IMO stress was immunohistochemically demonstrated using GFAP-, Nestin-, and PRP-1-antisera (3). Neuroprotective action of NOX snake venom (2) was also demonstrated in rats with the SC hemisection. PRP-1 participation in the regeneration of brain nerve structures was immunohistochemically demonstrated in the trauma-injured rats with SC hemisection in result of NOX snake venom administration (2).

METHODS USED. Histochemical method on detection of Ca²⁺-dependent acid phosphatase activity, enzyme linked immunosorbent assay (ELISA), and ABC immunohistochemical method were applied.

RESULTS AND DISCUSSION. Neuronal injuries have been suggested to promote PRP-1 synthesis and its release – as a messenger that modulates signaling cascades, thus contributing to protection, regeneration, and repair of the neurons. Our immunohistochemical data regarding the detection of PRP-1 in the cell nuclei of the labyrinthectomized rats indicate that PRP-1 can control the DNA transcription and function as a transcription factor similar to c-fos. To confirm this assumption, application of *in situ hybridization* histological method is needed. Nevertheless, PRP-1 was detected and quantified in human and rat blood serum samples under the normal and pathophysiological conditions using ELISA developed by us for PRP-1 quantification. Recently, PRP-1 was immunohistochemically detected in the immune system cells in bone marrow of rats with IMO stress. Using flow cytometry, we succeeded to reveal PRP-1 biosynthesis *in vitro* in the intact lymphocytes in result of the action of various activators. This also confirmed our suggestion about the putative stress-induced PRP-1 biosynthesis in the immune system cells *in vivo* under the action of the several cytokines.

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DEVELOPMENT METHOD OF ZIZIPHORA CLINOPODIOIDES RAW MATERIAL STANDARDIZATION BY FLAVONOIDS

INTRODUCTION. The research for the new flavonoid-containing plant-derived sources, have showed that the main biological active substances of extracts of the herb *Ziziphora clinopodioides* are phenolic and flavonoid compounds.

The aim of this work is to develop the method of quantifying the amount of the flavonoids in the extracts obtained from the grass *Ziziphora clinopodioides* by the help of spectrophotometric method.

METHODS USED. In order to determine the sum of the flavonoids in the extracts of herbs *Ziziphora clinopodioides*, there were collections from the aerial part of natural populations of wild species *Ziziphora clinopodioides* plants in the flowering stage (i.e. in the phase of greatest accumulation of flavonoids) in June – July, 2013 from the mountain villages of Armenia and Arsach, as well as the grass grown up in the conditions of soils and of hydroponics. To quantify the sum of flavonoids in the grass *Ziziphora clinopodioides*, the modified method was used. Using the standard (the standard sample) - flavonoid 7-methyl sudahitin, by spectrophotometry absorption, the specific absorption coefficient was determined at the analytical wavelength (207 nm) 920. Spectrophotometric method of the sum of flavonoids determination without prior separation of the components is based on the property of absorbance values additives (optical density) of the components of the mixture at the same wavelength $\lambda = 207$ nm.

In the formula for calculating the value of the specific absorption coefficient for the flavonoid 7-methyl sudahitin was incorporated.

The percentage of the flavonoids amount in absolutely dry raw material in terms of the 7-methyl sudahitin is calculated by the formula:

$$\chi = \frac{D_z \cdot 250 \cdot 50}{920 \cdot 2m}$$

where m – the mass of the sample materials, - an optical density of the test solution at $\lambda = 207$ nm; 250 - a solution volume (ml); 50- the aliquots volume is taken from solution (ml); 920 - the specific absorption coefficient flavonoid 7-methyl sudahitin at $\lambda = 207$ nm.

RESULTS AND AISCUSION. The development method was tested on the samples of the raw materials from the different climatic zones, as well as different growth conditions (in the conditions of the soil and hydroponics). These results lead to the conclusion that the content of the sum of flavonoids in the grass *Ziziphora clinopodioides* ranges from 2.57 to 4.18%.

Thus, the modified development method for calculating the amount of flavonoids, can be used to assess the quality of grass *Ziziphora clinopodioides* by the content of the basic group of biological active compounds, flavonoids. Our results indicate that all the samples of extracts both the qualitative composition and the quantitative content of the total flavonoids are close. Differences in the quantitative content of the certain components are not only the climatic factors, as well as the growth conditions.

CONCLUSIONS.

at first the specific absorption coefficient was given to flavonoid 7-methyl sudahitin by the spectrophotometric method

a modified method for the quantitative determination of the sum of flavonoids in raw *Ziziphora clinopodioides* in terms of flavonoid 7-methyl sudahitin was done by the spectrophotometry method.



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KEYWORDS:

Ziziphora clinopodioides,
flavonoid,
spectrophotometric method



CONFERENCE ABSTRACTS

NOVEMBER 27th – DECEMBER 1st

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PRESCRIBING RECOMMENDATIONS FOR PEDIATRIC MEDICINES USE IN REFERENCE-BOOKS

INTRODUCTION. Rational pediatric prescribing depends on availability of reliable, evidence-based data including the dosing recommendations, contraindications and so on. However, information on medicines use in children can be absent or unclear especially in low- and middle-income countries[2]. The objective of this work was assessing availability of prescribing recommendations for pediatric medicines use in reference books in the Republic of Armenia (RA).

METHODS USED. Availability of information was assessed for 377 randomly selected medicines. Two reference books (the last version of Armenian National Formulary [1] and Vidal [3]) were selected based on the results of our previous study on identifying the main sources of information for family physicians and pediatricians working at primary health care facilities. In addition to a printed version of Vidal, an electronic version of this source of information available on-line was also included in this study. Availability of articles on medicines selected and content of these articles in the reference-books were analyzed for assessing availability of recommendations on use of each of selected medicines in children. The study was conducted in 2012.

Articles for medicines selected were only partly available in reference-books. In the printed version of Vidal articles containing information on 197 (52.3%) of 377 medicines studied were founded, in the electronic version of Vidal – on 337 (89.4%), in Armenian National Formulary (ANF) - on 103 (27.3%). The percentage of selected pharmaceuticals, articles about which were available and included any information about use in children, of the number of medicines, articles about which were available, in the printed version of Vidal was 61.4% (121of 197), in the electronic version of Vidal – 80.1% (270 of 337), in ANF - 75.7% (78 of 103). In 10.2% of articles from the printed version of Vidal and in 23.3% of articles from ANF in which at least some information on use in children has been available, age of children was not specified. Information on the use of medicines in neonates and children up to one year was very limited. The percentage of selected pharmaceuticals, articles about which include any information on use in children, of the total number of medicines studied was low: 32.1% (121of 377) in the printed version of Vidal and 20.7% (78 of 377) in ANF.

CONCLUSION. There is a limited access to reliable recommendations on medicines use in children in reference books mainly used by family physicians and pediatricians in Armenia. As lack of information is a challenge for appropriate medicines prescribing there is a need in improving access of local physicians to appropriate evidence-based, accurate and up-to-date data including dosing information for children of various age. Publishing a pediatric national formulary in Armenian or providing on-line version of necessary information would be a very effective strategy for improving the situation.

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KEYWORDS:

reference books,
children,
rational medicines use,
medicines information

METABOLIC ALTERATIONS IN RATS FED HIGH FAT DIET IN CONDITIONS OF RESTRICTED PHYSICAL ACTIVITY

INTRODUCTION. Obesity has become a serious challenge for the modern medicine due to wide spread and association with different life threatening disorders i.e. cardiovascular disorders, type 2 diabetes, cancer, dementia etc. The main risk factors for obesity are high calorie intake and sedentary lifestyle. They have synergistic action on main pathological consequences of visceral obesity i.e. chronic inflammation and insulin resistance. Multiple different approaches were proposed for modeling obesity in experimental animals. High fat diet-induced models of obesity are often used to study polygenic causes of obesity. We consider that involvement of modulation of physical activity in experiment will help to evaluate the role of low physical activity in development of obesity and will contribute to more representative/valid model. The main aim of this study was to evaluate the metabolic alterations in rats fed high fat diet in conditions of restricted physical activity.

METHODS USED. Male albino rats (10 weeks old) were housed in a controlled environment with free access to food and water. Low-fat diet contains 4g fat/100g food, high-fat diet contains 24 g of fat/100g food. Narrow cages have size 20x7x7 cm and restrict the movement of animals in all directions. Animals were randomly assigned into 4 groups:

1. Rats fed high fat diet and housed in narrow cages.
2. Rats fed low-fat diet and housed in narrow cages.
3. Rats fed high fat diet and housed in usual cages.
4. Control group fed low-fat diet and housed in usual cages.

All the animals were monitored by weighing 2 times weekly. On the 70th day the animals were euthanized after an 8 h period of fasting. Epididymal adipose tissue was dissected, fixed and stained by hematoxylin and eosin. Size of adipocytes was measured. The plasma concentration of total blood cholesterol was measured.

RESULTS AND DISCUSSION. Weight gain in animals fed high fat diet (housed both in usual and narrow cages) were significantly higher than in animals fed low fat diet (housed both in usual and narrow cages) by 45% ($p<0.01$). Weight gain and total blood cholesterol levels in animals fed high fat diet and housed in narrow cages were significantly higher than in animals fed low fat diet and housed in narrow cages (by 57%, $p<0.01$ and 22%, $p<0.05$, respectively). These facts demonstrate that chosen high fat diet was effective to model obesity in rats. Somewhat unexpectedly, weight gain in animals housed in usual cages was significantly higher than in animals housed in narrow cages by 34.5%, $p<0.05$, that may be related to less food intake noted in the latter group. Adipocytes of hypokinetic rats fed low-fat diet and housed in narrow cages were larger than adipocytes in control group that indicates adipocyte hypertrophy in conditions of restricted physical activity.

Conclusion. Above-mentioned metabolic alterations in rats show that combination of high fat diet and restricted physical activity provides valid model of obesity. This model can be useful for investigation of role of low physical activity in development of obesity and other aspects of obesity.

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KEYWORDS:

*obesity model,
high fat diet,
restricted physical activity,
weight dynamics,
cholesterol levels*



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NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

Alzheimer's disease,
bone marrow,
Sox family,
Wnt

POTENTIAL OF ENDOGENOUS HYPOTHALAMIC AGENT IN
MANAGEMENT OF BONE-MARROW NEURONAL LINAGE
ACTIVATION IF IT PROCEEDS

INTRODUCTION. In case of Alzheimer's disease (AD) the wide spectrum of different pharmacological treatments have limited efficacy and only provides symptomatic relief. Therefore, there is an exigent need to develop new and workable medications for AD which provide long-term cure. One of possible and effective directions to handle neurodegenerative diseases in the field is stem cell-based therapy. On the other hand, it has been found that *in vitro* bone marrow mesenchymal stem cells can differentiate not only into the osteocytes, chondrocytes, adipocytes, but also neurons. The mechanisms support these processes are still unknown, but it is clear that agents support the proliferation and differentiation of the cells are of special interest. Therefore, the current study aimed to explore the possible role of hypothalamic proline rich polypeptide in creating an "environment" for bone marrow.

METHODS USED. Experiments were performed on 30 mature white Sprague-Dawley male rats. The experiments were carried out in accordance with the European Communities Council Directive (86/609/EEC) on care and use of animals for experimental procedures; protocol was approved by the Institutional Animal Care and Ethics Committee.

In case of the study the animals were divided into 3 groups: the control group consisted of vehicle-treated animals; the 1st experimental group was intracerebroventricularly (i.c.v.) injected with aggregated A β 1-42 (experimental model of AD); the 2nd experimental group was intramuscularly (i.m.) administered with PRP-1 on the 31st day after amyloid injection. Markers of dividing cells (Wnt), and Sox's family transcriptional factors, responsible for stem cells maintenance (Sox2), differentiation of glial (Sox14) and neuronal (Sox10) lineage, were determined in bone marrow of rats' on the 90th day from i.c.v. injection of A β by flow cytometric detection and immunohistochemistry.

RESULTS AND DISCUSSION. As a result of the preliminary analysis, it has become clear that the bone marrow neurogenetic markers change was not detected by the methods chosen by us: both flow cytometry as well as immunohistochemistry did not detect any changes in Wnt and Sox family markers. However, *i.m.* injection of PRP-1 doubled the content of bone marrow Sox10-positive cells compared to control and amyloid groups by FACS flow. The latter is a guiding factor for glial cells differentiation, which indicates the activation of the myeloid tract in bone marrow. This can serve as a basis for the bone marrow through the proliferative polypeptide on the occurrence of glycolysis and possible penetration of the brain. In fact, PRP-1 activates the myeloid growth in bone marrow.

CONCLUSION. This research aims to shed light on the real existence of the brain and bone marrow connection and the intermediate regulation. If really proves that bone marrow involves in brain damage, and it directs the differentiation of its stem cells to neurons at neurodegeneration, it will be a new approach in the prevention and treatment of neurodegeneration.

REGIONAL ENDOCRINE-IMMUNE ASSOCIATIONS IN THE INTEGRATIVE ACTIVITY OF THE ORGANISM

Over the past 50 years, fundamental researches conducted in many countries was the subject of extensive discussion, in which with great conviction was shown that not only the central structures of the brain serves as the source for the synthesis of a number of “ancient” hormones but also some peripheral secretion glands, immunocompetent cells, APUD system cells. Thus, in particular, melatonin, is produced not only in the epiphysis but also in the periphery: in the adrenal glands, pancreas, intestinal tract, eosinophilic leukocytes, tissue basophils (mast cells). Apparently, the function of extrapineal melatonin implemented within those organs that act as the source of its synthesis. Thus, melatonin produced in tissue basophils provides the exchange of transcapillary functions, melatonin produced in the gut mucosa-the maintenance of bacterial homeostasis and preventing the process of bacterial translocation, melatonin is produced by the secretory cells of the endocrine unit-are actively involved in the process of synthesis of insulin. Produced in the islets apparatus somatostatin takes an active part in the processes of modulation of the incremental function of the pancreas.

Extrahypophisar ACTH is synthesized in the cells of leukocyte-lymphocytic series tissue basophils. In our view Extrahypophisar ACTH, takes an active part not only in the processes of steroidogenesis of the adrenal glands but also in the activation processes of the endocrine function of the pancreas.

Based on the analysis of literature data and our own conducted research, we propose a hypothesis that the biological effects of a number of “ancient” hormones on the periphery are not only the results of synthesis of the brain neurosecretory cells, but also the results of internal secretion in peripheral glands, immunogenesis organs, APUD cells –Systems.

In this particular case, above mentioned all these hormones and their biological effects implement the theory in situ short-distance mechanism, as a result of evolutionarily worked out vertical connections.



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KEYWORDS:

*melatonin,
somatostatin,
ACTH,
APUD-system,
pancreas,
intestinal tract,
bacterial translocation.*



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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KEYWORDS:

adrenocorticotrop hormone,
pancreas,
modulation,
acini, lipase

EFFECT OF ACTH ON LIPASE ACTIVITY IN ACINAR APPARATUS OF THE PANCREATIC GLAND

Introduction. Numerous studies in this direction have served as a prerequisite, according to which many neurohormones, in addition to their main (long established function), also have “side”, additional functions, the effects of which extend to almost all integrative systems of the body.

Over the past half century, it has been established that adrenocorticotrop hormone (ACTH) not only plays a dominant role in regulating the corticoid function of the adrenal glands, but also modulates many processes both in the central nervous system and in the periphery. At the periphery it increases lipase activity in adipose tissue. It is possible that ACTH has a modulating effect on the excretory apparatus of the pancreas, whose acini have a pronounced lipase activity.

Purpose of the study We set ourselves the task of revealing the modulating effect of ACTH on the processes of lipase excretion in acinar cells of the pancreas.

Materials and methods. The experiments were performed on 32 white male rats, 130-150 g. The animals were subdivided into a control and case groups. The animals of the experimental group received a single intraperitoneal injection of a therapeutic dose of ACTH, at a rate of 0.005 U / 100 g of animal mass. In the experiment we used the commercial synthetic drug ACTG “Synacthe” manufactured by “Sigma-tau” Munich (Germany). Animals were sacrificed 30 minutes after drug administration, i.e. in the period of complete disintegration of the hormone in the serum. Morphological analysis of pancreatic tissue was carried out to reveal the peculiarities of cytoarchitectonics of the excretory and endocrine gland apparatus. Simultaneously, lipase activity was determined both in serum and in the pancreas of the animals of the experimental and control groups. A biochemical analysis was also performed using the commercial kit “Rendox Laboratories Limited” (UK).

Results of the study. As the results of a morphological study in the endocrine apparatus of the pancreas showed under the conditions of administration of a therapeutic dose to the laboratory animals, signs of hypersecretion of insulinocytes localized mainly in the central parts of the islets of Langerhans were observed. The structure of the excretory apparatus was retained. Acinar cells everywhere were characterized by a clear localization on the inner surface of the basement membrane. In the vast majority of acinar cells, there were signs of mild hypertrophy. When carrying out biochemical studies it was found that the introduction of a synthetic analog of ACTH to experimental animals was accompanied by a sharp decrease in lipase activity (more than 2 times) in the blood serum (270.0 ± 22.3 U / l) against 552.7 ± 31.3 U / l in the control, $p < 0.0005$. Significantly lipase activity decreased also in the pancreas itself (181.3 ± 12.4 U / l versus 374.7 ± 45.2 U / l).

Conclusion. Synthetic analog of ACTH in a therapeutic dose has a pronounced inhibitory effect on the specific function of the excretory apparatus of the pancreas - synthesis and excretion of lipase. It is possible that ACTH, in addition to its main function in the mammalian organism, is also involved in the excretory processes of the pancreatic acinar apparatus.

“ARMENICUM” PASTE AS AN EFFECTIVE DRUG FOR PATHOGENETIC THERAPY OF PURULENT WOUNDS.

INTRODUCTION. The problem of wound infection even today stays in the focus of comprehensive study. Due to the permanently increasing resistance of wound microorganisms to antibacterial drugs, search for new effective drugs of pathogenetic and symptomatic therapy of purulent wounds, is a very actual direction in modern medicine.

Relevance. Armenian preparation “Armenicum” has pleiotropic spectrum of action, effects of which apply to a number of organs and “bacterial homeostasis” of organism. At the same time, it should be noted, that the latter is not yet referred to as an effective drug for purulent wound treatment.

AIM. Definition of the role of fibronectin in the pathogenesis of aerobic purulent wound, under topical application of “Armenicum” Paste.

METHODS USED. Experiments were carried on 120 white male rats weighing 130-150 gram. The animals were divided into two groups: control and experimental. The model of a purulent wound was induced in the animals of both groups. “Armenicum” paste was applied to the wound surface in experimental group animals, on the basis of 150 mg per 100 gram of animal body weight. The animals of both groups were removed from the experiment on the 3rd, 5th and 9th days of the regional inflammatory process. Cryostat sections were prepared, which were stained with hematoxylin-eosin and azur II-eosin. From fresh frozen slices of the wound, cryostat sections were prepared, which then were subjected to immunofluorescence analysis for fibronectin determination using serum against fibronectin (“Sigma”, USA) and FITC-labeled serum against rabbit IgG (“Sigma”, USA).

RESULTS. The treatment of the wound with “Armenicum” paste on the very early stages of the regional inflammatory process was accompanied by stimulation of fibronectin synthesis processes by macrophage-leukocyte and fibroblastic lineage cells, which, in its turn resulted in activation of reparative-proliferative processes by subsequent wound healing by substitution.

CONCLUSION. Previously uninvestigated fibronectin-dependent mechanisms of “Armenicum” paste stimulating effect on the course of the wound inflammatory processes have been specified, which allow using it in the pathogenetic therapy of aerobic purulent wounds.



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KEYWORDS:

antibacterial drugs
Armenicum
fibronectin
bacterial homeostasis



CONFERENCE ABSTRACTS
NOVEMBER 27th – DECEMBER 1st

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INFLUENCE OF THE THYMIC MEDIATOR-THYMALIN ON THE MORPHOFUNCTIONAL STATE OF TISSUE BASOPHILS

INTRODUCTION. The biological role of tissue basophils is still a subject for extensive discussion to this day. This circumstance is due to the fact that over the past 30 years, has appeared very informative data, according to which hormonal, mediator and protein nature various endogenously active factors act as stimulants that provide the synthesis processes in the histamine, serotonin, melatonin tissue basophils.

Purpose of the study. In the present study, we asked whether the low-molecular peptide fraction of thymic mediator-thymalin influences the processes of tissue basophil degranulation.

MATERIAL AND METHODS. In the experiment, 32 white male rats were examined, which were divided into two groups: control and experimental. The animals of the experimental group received a single intramuscular injection of a therapeutic dose of thymalin at a rate of 0.01 ml per 100 g of animal mass.

Animals of both groups were killed one hour after thymalin injection.

Preparations made from rat mesentery were stained with toluidine blue and azur II-eosin. Structural bonds in tissue basophils were determined by the degree of their degranulation, using a histiosteometric grid.

RESULTS. As shown by the results of the morphological analysis, only the tissue basophils dominated in the connective tissue base of the mesentery, with no signs of degranulation or with partial degranulation.

Thus, in comparison with the control group, the content of tissue basophils without signs of degranulation increased by 2.1 times (50.1 ± 10.7 vs. 24.3 ± 3.6 in the control, $p < 0.025$). Against this background, the content of tissue basophils that characterize a high degree of degranulation (5.4 ± 1.7 vs. 16.3 ± 2.9 in the control, $p < 0.005$) was markedly reduced.

CONCLUSION. Administered therapeutic dose of thymaline to experimental animals was accompanied by a marked inhibition of the secretory process of tissue basophils, which was manifested by a marked decrease in their degranulated forms, against a background of a significant increase in tissue basophils without signs of degranulation. It is not excluded that the low molecular weight thymus-thymalin mediator fractions in mammals have a direct and / or indirect modulating effect on the functional state of the tissue basophils of one of the components of the APUD system.

KEYWORDS:

tissue basophils,
thymalin,
stimulation,
degranulation.



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