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D. M. Botbaeyev[1,2], A. M. Belkozhaev[1,2], A. K. Khanseitova[2], A. Zh. Borbayeva[3], N. A. Aitkhozhina[2]

[1]Aitkhozhin Institute of Molecular Biology and Biochemistry KS MES;
[2]Al-Farabi Kazakh National University, Almaty, Kazakhstan;
[3]Satbayev University, Almaty, Kazakhstan.
E-mail: Daur_92_05@bk.ru, ayaz_jarkent@mail.ru, akhanseiova@mail.ru

POLYMORPHISMS IN THE GENES OF REPARATIONS AMONG EMPLOYEES OF THE ATOMIC INDUSTRY OF KAZAKHSTAN

Abstract. Single nucleotide polymorphisms (SNPs) are the most convenient marker and the widespread subject of polymorphism testing. To identify the presence or absence of the effects of chronic low-dose radiation on nuclear industry personnel, the occurrence of single-nucleotide substitutions at the polymorphic sites of the genes of the repair system 3 and 6 of the introns of the APC gene P53.11 gene, in positions -2549 of the VEGF gene, XPD gene rs313181 (Lys751Gln) and rs25487 of the XRCC gene (Arg399Gln) were compared. Analysis of allele frequencies and distribution of genotypes in the variable regions of the tested genes was performed by the method of polymerase chain reaction (PCR), followed by determination of restriction fragment length polymorphism (RFLP). When comparing the frequencies of alleles and the distribution of genotypes between the second group of miners (11–20 years' experience) and control, differences in the distribution of genotypes in the rs25487 XRCC plot ($\chi 2 = 7.11$, $p = 0.028$) were revealed. These differences satisfy the criterion $p < 0.05$ and, accordingly, are statistically significant.

Key words: polymorphism, genes, a nuclear industry.

Introduction. The development of the nuclear industry and the emergence of all new radiation objects allows a large number of researchers to study the effect of systematic exposure under prolonged exposure. There are a large number of works devoted to this subject, both domestic and foreign authors, however, the issue of inducing cancer with "small" doses of radiationremains open. Genotyping of persons employed in the nuclear industry (mining and processing) and other industries related to potential genotoxicity seems to be a promising direction in the world, aimed at early detection of mutations and taking preventive measures before the development of diseases, including cancer. The personnel of the nuclear industry is exposed to radiation more than the general population, and, accordingly, has a greater risk of radio-induced DNA damage. Population genetic studies of uranium mineworkers in the United States, Canada, and Czechoslovakia showed an increase in the incidence of cancer in the studied cohorts [1, 2]. The problem of the occurrence of genetic defects due to radiation recurrence occurs in the Republic of Kazakhstan due to the increasing scale of uranium mining and the consequences of tests at the Semipalatinsk nuclear test site where somatic mutations in AML1 genes (acutemyeloideleukemiya) [3] and Glycophorin A [4] were found in the adjacent population areas. The genes responsible for the DNA repair process are vital for the normal functioning of the body, as they prevent the processes of malignant transformation of cells, which can be PCR and restriction products were separated by electrophoresis in

8% polyacrylamide gel (PAAG) and a current of 60 mA and a voltage of 300 V for 2-3 hours. Taq DNA polymerase used in PCR, deoxyribonucleoside triphosphates, and restriction endonucleases were manufactured by SibEnzyme (Novosibirsk, Russia).

Materials and methods. The study included 187 DNA samples isolated from whole venous blood of male workers of Russian nationality of the Balkashinsky uranium deposit, the village of Shantobe, Akmola region, 160 DNA samples isolated from the venous blood of practically healthy male donors of Russian nationality provided by the City Blood Center, Almaty, as a control group. The workers of the uranium mining industry were divided into 2 groups depending on the duration of radiation exposure in low doses: group I - 1-10 years (n = 89) and II - 11-20 years (n = 98). The study was conducted in compliance with the anonymity, awareness and voluntary participation of nuclear industry workers, confirmed in writing during the survey. The biomaterial was collected on a voluntary basis after receiving a written consent, observing anonymity and informing about the research objectives.

DNA isolation was performed using a Qiagen reagent kit (USA) according to the manufacturer's protocol. The determination of the allelic variant in the polymorphic sites of the tested genes was carried out by the method of polymerase chain reaction (PCR), followed by analysis of the restriction fragment polymorphism (RFLP). The matched restriction endonucleases were used. The sequences of primers complementary to the test site were compiled using the Primer-Express program [5], according to data obtained from the Ensembledate PCR and restriction products were separated by electrophoresis in 8% polyacrylamide gel (PAAG) and a current of 60 mA and a voltage of 300 V for 2-3 hours. Taq DNA polymerase used in PCR, deoxyribonucleoside triphosphates, and restriction endonucleases were manufactured by SibEnzyme (Novosibirsk, Russia).

Used primers and amplification conditions

Genes, sites	Primers :forward – F, reserve - R	Conditions of amplification
Intron 3 gene *P53*	F: 5'GGGACTGACTTTCTGCTCTT3' R: 5'TCAAATCATCCATTGCTTGG3'	95^0C - 10 min, 95^0C- 1 min , 55^0C – 1 min, 72^0C - 1 min (40 cycles), 72^0 C - 5 min
Intron 6 gene *P53*	F:5'TGGCCATCTACAAGCAGTCA3' R: 5'TTGCACATCTCATGGGGTTA3'	94^0C – 1 min, 10 cycles 30 sec - 94^0C, 30 sec- 60^0C, 30 sec - 72^0C, 10 cycles 30 sec- 94^0C, 30 sec - 58^0C, 30 sec - 72^0C, 10 cycles 30 sec - 94^0C, 30 sec - 56^0C, 30 sec - 72^0C, 10 – min - 72^0C.
Exon 11 gene *APC*	F:5'GGACTACAGGCCATTGCAGAA3' R: 5'GGCTACTCTCCAAAAGTCAA-3'	95^0 C - 6 min, 58^0 C - 2 min, 72^0 C – 2 min, 35 cycles 1 min 95^0 C, 30 sec - 58^o C, 72^0 C - 30 sec, 72^0C - 5 min.
-2549 gene *VEGF*	F:5'GCTGAGAGTGGGGCTGACTAGGTA3′ R:5′GTTTCTGACCTGGCTATTTCCAGG3′	95º C- 6 min, 94ºC- 1min, 57ºC- 1.5 min, 2min -35 cycles 2 min 72ºC 72ºC -10 min.
XPD, rs313181	F: 5'ATCCTGTCCCTACTGGCCATTC3' R: 5'TGTGGACGTGACAGTGACAAAT3'	95°C-5 min, 94°C-30 sec 64°C-30 sec, 72°C-30 sec (35 cycles), 72°C-3 min
XRCC, rs25487	F: 5'TTGTGCTTTCTCTGTGTCCA3' R: 5'TTCTCCAGCCTTTTCTGATA3'	94°C-4 min, 94°C-30 sec, 63°C-30 sec, 72°C–30 sec (35 cycles), 72°C - 2 min

PCR and restriction products were separated by electrophoresis in 8% polyacrylamide gel (PAAG) and a current of 60 mA and a voltage of 300 V for 2-3 hours. Taq DNA polymerase used in PCR, deoxyribonucleoside triphosphates, and restriction endonucleases were manufactured by SibEnzyme (Novosibirsk, Russia).

Statistical analysis was performed using STATISTICA, v. 5.0, "Statsoft", (USA). When comparing the frequencies of alleles and genotypes, the standard Pearson compliance criterion - $\chi 2$ was used. To reject the null hypothesis (no differences), the level of statistical significance was assumed to be $p < 0.05$. The criteria are the odds ratio (oddsratio - OR) and confidence within the 95% interval (confidence interval - 95% CI). DNA polymorphism can occur as a result of point mutations, microdeletions, and insertions, as well as large deletions and insertions, transversions, translocations, transpositions of mobile genetic elements and other changes in the nucleotide sequence.

Results. DNA polymorphism can occur point mutations, microdeletions, and insertions, as well as large deletions and insertions, transversions, translocations, transpositions of mobile genetic elements and other changes in the nucleotide sequence.

The distribution of genotypes and allele frequencies in the polymorphic sites of the p53 (3 intron, 6 intron), APC (11 exon), VEGF (2549), XPD (rs313181) and XRCC (rs25487) genes was analyzed in the Russian ethnic group of the miners of the uranium mine Balkashinskoe deposit, town of Shantobe and in the control group. To assess the duration of the influence of low doses of radiation, the workers of the industry were divided into 2 groups depending on the length of service: the first group of miners has been working in the nuclear industry for 1-10 years, the experience of the second group ranges from 11-20 years.

When comparing the first group (work experience in the nuclear industry for 1-10 years) with control, there are no statistically significant differences in allele frequencies and genotype distribution.

An earlier experiment in Russia of the association of polymorphisms of the p53 gene with the risk of developing malignant neoplasms among workers associated with radiation exposure did not detect such a relationship [7]. A review of the linkage of mutagenesis in the p53 gene with the systematic exposure to radon [8] also does not provide unambiguous answers to the existing questions.

When comparing the frequencies of alleles and the distribution of genotypes between the second group of miners (11–20 years' experience) and control, differences in the distribution of genotypes in the rs25487 XRCC ($\chi 2 = 7.11$, $p = 0.028$) were revealed. These differences satisfy the criterion $p < 0.05$ and, accordingly, are statistically significant.

The data collected as a result of summarizing the results of five studies conducted among workers of uranium mines showed an increase in their mortality rate associated with cancer. A survey of former miners of uranium mines at WISMUT, East Germany, revealed a significant increase in lung cancer among those workers whose total cumulative radiation dose exceeded 800 monthly norms.

The data we obtained earlier that describe differences in allele frequencies and the distribution of genotypes in the RAD51, XPD, and XRCC1 genes among nuclear industry workers [9], in combination with those obtained in this study results may indicate the presence of a certain effect of small doses radiation to the human genetic apparatus.

Scientific opinion differs on the issue of the influence of natural background radiation on humans. There is a need for additional research to identify effects arising from the action of natural radiation background [10],

Conclusion. Ionizing radiation is considered a factor of occupational hazards for workers engaged in production associated with radiation exposure. One of the possible consequences of its action is an increase in the mutational load among the personnel of radiation-hazardous industries and the population living next to them, which can be a factor that increases the risk of developing cancer.The preliminary result presented may be the basis for expanding the scope of research with an increase in the sample size and the coverage of the categories of persons exposed, due to professional activity or places of residence, to the chronic effects of low doses of radiation.

Д. М. Ботбаев[1,2], А. М. Белкожаев[1,2],
А. К. Хансеитова[1], А. Ж. Бөрібаева[3], Н. А. Айтхожина[1]

[1]РМК «М. Ә. Айтқожин атындағы молекулалық биология
және биохимия институты» ҚР БҒМ ҒК, Алматы, Қазақстан;
[2]әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан;
[3]Satbayev University, Алматы, Қазақстан

ҚАЗАҚСТАН АТОМ ӨНДІРІСІНДЕГІ ЖҰМЫСШЫЛАРДЫҢ РЕПАРАЦИЯ ГЕНДЕРІНІҢ ПОЛИМОРФИЗМДЕРІ

Аннотация. Жыл өткен сайын адамзат баласына иондаушы сәулелердің кері әсері артып келеді. Сонымен қатар көптеген тездеткіштер бақыланып, атом бомбалары, тағы да басқа сол сияқты зиянды заттар атылып жатыр. Ол заттардан қаншама зиянды радиоактивті сәулелер бөлініп, адам ағзасының бірқатар ауруларға ұшырауына алып келеді.

Ғалымдар осы күнге дейін «аз мөлшерлі» деп аталатын төмен интенсивті радиациялық сәулелер әсерінің дозасын біршама талқылап, зерттегенімен, ол тақырып әлі де өте аз зерттелген өзекті мәселелердің бірі болып отыр.

БҰҰ атомдық сәулеленулердің әсері жөнінде ғылыми комитеттің анықтамасы бойынша, аз дозалы болып келетін радиацияға 200 $м^3$-қа дейінгі дозаның жиналуы, төмен интенсивті сәулеленулердің күші 10^{-4} Гр/мин-нен аз болмауы қажет. Атомдық сәулеленулердің биологиялық эффектісі жөніндегі халықаралық комиттетке (АСБЭЖХК) 1990 жылы аз мөлшерлі радиацияның дозалық мөлшері ретінде 1 $м^3$/жыл өлшемі қабылданды және бұл көрсеткіш табиғи радиациялық фондардың мөлшеріне тең болып келеді.

Созылмалы аз болатын, біркелкі мөлшердегі радиацияның әсері және оның кері зардаптары жекеше түрдегі деңгейінде өзгеріс табады. Сондықтан да ИС-нің зардаптары созылмалы кері әсерге ұшыраған адам ағзасын қайта өз қалпына келтіруі және жеке адам баласына бағытталған диагностикаларды талап етеді. Генетикалық тұтас құрамдас бөліктер барлық бөліктегі мультифакторлы аурулардың дамуында айтарлықтай маңызды рөл атқарады. Мысалы, қатерлі ісік ауруының тұқым қуалаушы факторынан пайда болу мүмкіндігі орташа есеппен 30 %-ға, ал аутоиммунды зерттеу бұзылыстарда бұл көрсеткіштер 50-60%-ға дейінгі аралыққа жетеді. Генетикалық полиморфизмдердің гендік қатарлардың негізгі маркерлерімен байланысып отырған онкологиялық аурулардың дамуында басты объект болып пайдаланылатын және канцерогендермен ассоциацияланатын клетканың бөлінуін реттейтін гендердің зерттеуі қазіргі кезде болашағы мол, жоғары және өте маңызды мәселе болып отыр. Канцерогенез және гендермен байланысты гендік объектілер ретінде пайдаланылатын қатерлі ісік ауруларының дамуына қатысатын бірқатар гендердің генетикалық полиморфизмді негізгі маркерлерге (соматикалық мутациялардың) қатысты зерттеу – бұл келешегі бар және өзекті бағыт болып табылады.

Қазақстан Республикасы үшін генетикалық ақаулардың, соматикалық мутациялардың, уран өндірісінің ауқымы үнемі өсіп келе жатқандығымен байланысты радиациялық патологиялардың пайда болу мүмкіндігін анықтау маңызы және өздерінің ядролық энергетикасын дамыту перспективалары есебінен артуда.

Атом өнеркәсібінде (тау-кен өндіру және өңдеу) және басқа да өндірістік салаларда жұмыс істейтін адамдардың генотиптілігі, мутацияны ертерек анықтауға және ауруларды, оның ішінде онкологиялық ауруларды дамытуға қарсы профилактикалық іс-шараларды жүргізуге бағытталған әлемдегі перспективалық бағыт болып саналады. Созылмалы аз мөлшерлі радиацияның атом өнеркәсібі жұмысшыларына әсерін анықтау үшін репарация жуйесінің *P53генінің* 3 және 6 интроноы, *APC генінің* 11 экзоны, *VEGF* генінің - 2549 позициясы*, XPD* (Lys751Gln) гені rs313181 және *XRCC* (Arg399Gln) гені, rs25487 бірнуклеотидті ауысымдардың кездесу жиіліктері салыстырмалы түрде зерттелді. Зерттеу материалы ретінде ДНҚ қолданылады, сондай-ақ Ақмола облысының Балкашинское уран өңдейтін кәсіпорнының жұмысшыларынан ДНҚ қан үлгілерінен (172 орыс ұлты) алынған зерттеулер пайдаланылды. ДНҚ бақылау ретінде қолданылды, іс жүзінде сау донорлардан құрылған топтан алынған (160 орыс) үлгілер іріктелді.

Аллель жиілігін талдау және сыналған гендердің айнымалы аймақтарындағы генотиптерді бөлу полимеразды тізбекті реакция (ПТР) кейіннен шектеу фрагменттерінің полиморфизмі арқылы анықтайды. Әртүрлі аймақтағы сыналатын гендердің аллельдерінің жиілік сараптамасы мен генотиптерінің таралуы бойынша рестрикциялық фрагменттің ұзындығы полиморфизмнің (ПҰРФ) келесі анықтамасы полиморфты тізбекті реакция (ПТР) әдісімен жүргізілді. Бақылау тобымен атом өнеркәсібі жұмысшыларының аллельдер жиілігі мен генотиптердің таралуын салыстырмалы зерттегенде, rs25487 *XRCC* (χ^2 = 7,11, p = 0,028) генінің ауданында маңызды статистикалық айырмалық анықталды.

Түйін сөздер: полиморфизм, гендер, атом өнеркәсібі.

Д. М. Ботбаев [1,2], А. М. Белкожаев[1,2],
А. К. Ханнсеитова[1], А. Ж. Борибаева[3], Н. А. Айтхожина[1]

[1]РГП «Институт молекулярной биологии и биохимии им. М.А. Айтхожина» КН МОН РК, Алматы, Казахстан;
[2]Казахский национальный университет им. аль-Фараби, Алматы, Казахстан;
[3]Satbayev University, Алматы, Казахстан

ПОЛИМОРФИЗМЫ В ГЕНАХ РЕПАРАЦИЙ СРЕДИ РАБОТНИКОВ АТОМНОЙ ПРОМЫШЛЕННОСТИ КАЗАХСТАНА

Аннотация. Действие ионизирующей радиации (ИР) высокой интенсивности в больших дозах на организм человека подробно исследовано в результате изучения последствий военного применения радиоактив-

ных материалов (Хиросима, Нагасаки) и последствий техногенных катастроф на ураноперерабатывающих предприятиях и атомных электростанциях

Влияние ИР низкой интенсивности в так называемых «малых дозах», пороговая величина которых продолжает оставаться предметом обсуждения, изучено в значительно меньшей степени. Существуют различные, вплоть до диаметрально противоположных точек зрения и данных, связанных с возможностью наследования приобретенных радиоиндуцированных мутаций.

По определению НКДАР (Научный комитет по действию атомной радиации) ООН – наиболее компетентного международного органа – к малым дозам относятся накопленные дозы до 200 $м^3$ и к низкоинтенсивному излучению – мощность доз менее 10-4 Гр/мин. Международным Комитетом по биологическим эффектам атомной радиации (UNSCEAR) в 1990 году в качестве единицы малых доз принята величина 1 миллиЗиверт/год и для населения допустимая доза находится в пределах естественного радиоактивного фона (1 $м^3$/год) .

Установлено, что при хроническом радиационном воздействии невысокой мощности реакция тканей на одинаковые дозы радиации, а также тяжесть негативных последствий облучения варьируют на индивидуальном уровне. В связи с этим, востребована разработка новых методов к снижению неблагоприятных воздействий радиоактивного облучения на организм человека и реабилитации хронически облучённых людей с использованием индивидуальных подходов к диагностике, оценке радиационных рисков и коррекции выявляемых нарушений. Генетическая составляющая играет важную роль в развитии всех мультифакторных заболеваний. Так, например, возникновение злокачественных новообразований (ЗНО) в среднем на 30% обусловлено влиянием наследуемых факторов, а в случае с аутоиммунными нарушениями этот показатель достигает 50-60%. Это позволяет предположить влияние генотипа на риск возникновения негативных эффектов облучения, прежде всего, онкопатологий, тем более, что популяционно-генетические исследования рабочих урановых рудников в США, Канаде и Чехословакии показали рост встречаемости онкологических заболеваний в изученных популяциях.

Изучение генетического полиморфизма ряда генов по основным маркерам (соматических мутаций), связанным с развитием онкологических заболеваний с использованием в качестве объектов генов, ассоциированных с канцерогенезом и генов – регуляторов клеточного деления является перспективным и актуальным направлением.

Для Республики Казахстан значимость проблемы определения вероятности возникновения генетических дефектов, соматических мутаций, радиационных патологий возрастает в связи с постоянно растущими масштабами добычи урана и перспективами развития собственной атомной энергетики.

Генотипирование лиц, занятых в атомной промышленности (добывающей и перерабатывающей) и других производствах, связанных с потенциальной генотоксичностью, представляется в мире перспективным направлением, нацеленным на раннее обнаружение мутаций и проведения профилактических мероприятий до развития заболеваний, включая онкологические. Для выявления наличия или отсутствия влияния хронического воздействия малых доз радиации на персонал работников атомной промышленности проведено сравнение встречаемости однонуклеотидных замен в полиморфных сайтах генов системы репарации 3 и 6 интронов гена *P53,*11экзона гена *APC*, в позиции -2549 гена *VEGF,* rs313181 гена *XPD*(Lys751Gln) и rs25487 гена *XRCC* (Arg399Gln). В качестве материала исследования использована ДНК, выделенная из образцов крови ДНК работников (172 русской национальности) ураноперерабатывающего предприятия Балкашинское. В качестве контроля использована ДНК, выделенная из образцов, полученных от группы (160 русских), сформированной из практически здоровых доноров.

Анализ частот аллелей и распределения генотипов в вариабельных участках тестируемых генов проведен методом полимеразной цепной реакции (ПЦР) с последующим определением полиморфизма длин рестрикционных фрагментов (ПДРФ). При сравнении частот аллелей и распределения генотипов между второй группой шахтеров (стаж работы 11-20 лет) и контролем выявлены различия в распределении генотипов в участке rs25487*XRCC* (χ^2 = 7,11, p = 0,028). Данные различия удовлетворяют критерию $p < 0,05$ и, соответственно, являются статистически значимыми.

Ключевые слова: полиморфизм, гены, атомная промышленность.

Information about authors:

Botbayev D.M., junior scientist at Aitkhozhin Institute of Molecular Biology and Biochemistry KS MES, Almaty; daur_92_05@bk.ru; https://orcid.org/0000-0002-3161-5468

Belkozhaev A., junior scientist at Aitkhozhin Institute of Molecular Biology and Biochemistry KS MES, Almaty, Phd student at Al-Farabi Kazakh National University; ayaz_jarkent@mail.ru

Khanseitova A., c.b.s., Chief Researcher at Aitkhozhin Institute of Molecular Biology and Biochemistry KS MES, Almaty; akhanseiova@mail.ru; https://orcid.org/0000-0002-33161-5589

Borbayeva A.Zh., student at Satbayev University

Aitkhozhina N., academician RK NAS, Chief Researcher at Aitkhozhin Institute of Molecular Biology and Biochemistry KS MES, Almaty; aitkhozhinaimbb@mail.ru; https://orcid.org/0000-0003-4198-4730

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Kunzhan S. Adekenova[1], O. V. Maslova[2], E. G. Tolokonnikov[1]

[1]LLP «Karaganda Pharmaceutical Plant», Kazakhstan, Karaganda;
[2]LLP «Center of Phytotherapy», Kazakhstan, Karaganda.
E-mail: o.morozova@phyto.kz, etolokonnikov@krgpharm.kz, kadekenova@krgpharm.kz

PHARMACOECONOMIC ANALYSIS OF ANTIPARASITIC DRUGS FOR THE TREATMENT OF GIARDIASIS IN ADULT PATIENTS

Abstract. This article presents the pharmacoeconomic rationale for the treatment of giardiasis in adult patients. Giardia is one of the most common pathogenic eukaryotic microorganisms and the most common cause of diarrhea in the world. Currently, there are a number of drugs recommended for the treatment of giardiasis that differ in terms of effectiveness and safety, as well as the cost of therapy. Therefore, it is necessary to conduct a clinical and economic analysis in order to comparatively assess the quality of drug therapy for giardiasis.

The use of treatment regimens for giardiasis using the domestic drug "Sausalin" is economically feasible given the high level of eradication and the safety profile of the new drug. When conducting a repeated course of therapy for one patient with the drug "Sausalin", the savings is up to 25% in comparison with the "Ornisid".

The effectiveness of the original drug "Sausalin" is discussed.

Key words: Giardiasis, Sausalin, Ornidazole, Albendazole, pharmacoeconomics.

Introduction. Currently, infectious and parasitic diseases remain one of the most common causes of human disease in the world. Many of them are oligosymptomatic, but there are those that can cause significant harm to health, even death. According to the data of the Ministry of Health of the Republic of Kazakhstan, in 2017 year, 2,175 cases per 100,000 people of infectious and parasitic diseases were registered [1].

Parasitic diseases are a group of diseases of various etiologies, the common feature of which is that they are caused by the presence of parasites inside the body or on its surface. Three types of diseases are distinguished: protozoal - caused by unicellular microorganisms (protozoa) (dysenteric amoeba, malaria parasite, giardia); helminthiases - caused by helminths (roundworms, pinworms, schistosomes, trichinella); ectoparasites - caused by parasites that live on the surface of the host (lice and fleas). According to the WHO data, every third person in the world suffers from helminth infections, 1.4 billion and 600 million people, respectively, suffer from malaria and parasitic diseases [1].

The most significant parasitic invasion is giardiasis. Giardiasis is considered an independent, widespread protozoal disease with various clinical manifestations, ranging from subclinical to severe.

The pharmaceutical market has a large assortment of antiparasitic drugs, but all of them, except for a large number of side effects and contraindications have a fairly narrow spectrum of action, that is, they are intended only to kill one or more parasites. Therefore, expanding the market for antiparasitic drugs with a high safety profile for eradicating a wide range of pathogens is an important aspect of improving the

quality of medical services. Currently, the main pharmaceutical antiparasitic drugs under the international non-proprietary names - metronidazole, ornidazole and albendazole are presented on the pharmaceutical market of Kazakhstan. The use of metronidazole in peroral form is limited due to frequently reported side effects from the gastrointestinal tract. In clinical practice, the most widely used drugs are under the trade names "Ornisid" (Ornidazole), "Albezole" (Albendazole) [2].

It should be noted that JSC "International Research and Production Holding "Phytochemistry" and LLP "Karaganda Pharmaceutical Plant" are engaged in the development and production of a pilot batch of the dosage form of the new drug "Sausalin" based on the biologically active terpenoids of *Saussurea salsa* (Pall.) Spreng for clinical studies.

The original antiparasitic drug "Sausalin" of plant origin was developed on the basis of pharmacologically active sesquiterpene lactones from *Saussurea salsa* (Pall.) Spreng and is an antiparasitic, antibacterial agent [3]. They are used for parasitoses of the intestines and hepatobiliary system (acute and chronic giardiasis, opisthorchiasis), non-specific (bacterial) and specific (trichomonas) acute diseases in women. Due to its plant origin, the drug has no pronounced side effects and contraindications.

According to the results of studies, it was shown that the "Sausalin" drug is comparable or even superior in effectiveness to the above reference drugs in pharmacological action [3-6].

Aim of the study: To conduct a pharmacoeconomic analysis of the use of the drugs “Ornisid”, “Albezole” and “Sausalin” using the analysis of “cost of disease” and “cost-effectiveness”.

Materials and methods:

The research methodology involved a search for scientific publications on the results of clinical studies, meta-analyzes and systematic reviews of the use of antiparasitic drugs in patients with giardiasis. The search was conducted in international and national databases, registers of clinical studies results. The keywords were: «Sausalin», «Ornidazole», «Albendazole», «Giardiasis», «Lamblia».

The target population was patients over 18 years old with chronic giardiasis.

When selecting publications for analysis during pharmacoeconomic studies, the following exclusion criteria were used:

– lack of access to the full text;

– duplication of publication;

– the absence of microscopic methods for confirming the eradication of the pathogen.

When analyzing the "cost of the disease" the following calculation formula was used: COI=DC+IC, where COI – disease cost indicator, DC – direct costs, IC – indirect costs. As part of our study, only direct costs for the treatment of giardiasis were recorded, namely, the cost of therapy with "Ornisid", "Albezole" and "Sausalin". The cost of drugs “Ornisid” and “Albezole” was calculated at the market price according to the price lists of pharmaceutical market entities presented in the database of the Center for Medical and Pharmaceutical Information [7]. Calculation of the cost of the preparation "Sausalin" was carried out taking into account the previously planned cost of the drug according to the information of the developer and manufacturer JSC "International Research and Production "Phytochemistry" and LLP "Karaganda Pharmaceutical Plant".

Indirect costs were also not estimated, since the published results of the study of the effectiveness of drugs did not evaluate delayed outcomes, such as survival, disability, periods of disability.

When conducting the "cost-effectiveness" analysis, the calculation was carried out according to the formula: CEA= DC/EF, where CEA- "cost-effectiveness" ratio, DC - direct costs, EF - treatment effectiveness. The level of parasite eradication according to the results of a clinical study was considered as criteria for the effectiveness of treatment of giardiasis.

Taking into account the results obtained, an indicator of increment of cost effectiveness (achievement of one additional unit of efficiency) was estimated by the formula: ICEA= (DC1-DC2)/(EF1-EF2), where DC1- direct costs when using the first method, DC2 - direct costs when using the second method, EF1 and EF2 - treatment effects when using the first and second methods.

Research results. According to the results of the search, publications were found evaluating the effectiveness of "Sausalin" in comparison with "Ornidazole" in adult patients with giardiasis [6]. The analysis also included the results of the internal report on the clinical study “The study of the clinical efficacy and safety of the drug "Sausalin" as an anti-giardia agent”, conducted in 2015 on the basis of Karaganda Medical University and "International Research and Production Holding "Phytochemistry". This report was presented under the program of the Russian-Kazakhstan scientific seminar "Pharma-

cological and clinical studies of the antiparasitic drug "Sausalin" in 2016 [8]. According to the results of this study, a total of 250 patients with giardiasis invasion with age from 18 to 60 years were examined on the basis of the Karaganda State Medical University (average age – 38,5±1,2 years). Of the men examined, there were 130 (52%), women - 120 (48%). The first group consisted of 125 patients with a diagnosis of "intestinal giardiasis chronic course in the acute stage", in the treatment of which was used the drug of plant origin "Sausalin" in a dose of 240 mg (2 tablets, 3 times a day) for 10 days. In the second group, 125 patients used the antiparasitic drug "Ornidazole" (500 mg) manufactured by Abdi Ibrahim (Turkey), 1 tablet 2 times a day for 7 days. The dosing regimen was established on the basis of clinical studies and instructions for medical use. The effectiveness of treatment in the group of patients treated with drug "Sausalin" (the first group) was 85.71%, in the group taking drug "Ornidazole" (the second group) only 42.19%. In 57.81% of patients of the second group, re-allocation of lamblia cysts was noted 1-3 months after rehabilitation, in the first group only 14.29%. The elimination percentage of giardia cysts in the first group is 4 times higher than in the control group, which indicates the high efficiency of the new drug "Sausalin".

The results of qualitative clinical studies comparing the effectiveness of "Sausalin" and "Albendazole" have not been established. At the same time, an analysis of the "cost of the disease" for this drug was carried out, since this drug is widely used in clinical practice and is included in the National Clinical Protocol "Giardiasis" [9]. The drug of Kazakhstan production "Albezole" (Albendazole) (JSC "Nobel") is used in the treatment of giardiasis in a dosage of 400 mg, 1 tablet 1 time per day for 5-7 days.

Table 1 presents the results of the cost of drug therapy for a patient with giardiasis with "Ornisid" (Ornidazole), "Albezole" (Albendazole) and "Sausalin" drugs.

Table 1 – Results of cost analysis for “Ornisid”, “Albezole” and “Sausalin” in the treatment of giardiasis per 1 patient

Tradename	Ornisid	Sausalin	Albezole
Dosage	500 mg	120 mg	400 mg
Method of application	peroral	peroral	peroral
Frequency of use per day	2	6	1
Frequency of application per course	14	60	7
The number of doses in the package	10	12	1
Number of packages per course	2	3	7
Price for 1 package, tenge	2 235	3 000	1 470
Costs for 1 course, tenge	4 470	9 000	10 290

Thus, the direct costs for the treatment of giardiasis are - 4470 tenge for "Ornisid", 9000 tenge for "Sausalin", 10290 tenge for "Albezole".

However, the data obtained allow us to estimate direct economic damage without taking into account qualitative assessments of the results achieved. To compare alternative medical interventions, accounting and the ratio of both costs and drug efficacy, a "cost-effectiveness" analysis was used. The calculation of "cost-effectiveness" indicators (direct costs) for patients with giardiasis during treatment with drugs "Ornisid" and "Sausalin" are presented in table 2.

Table 2 – Comparative indicators of "cost-effectiveness" in the treatment of giardiasis with drugs "Ornisid" and "Sausalin"

Therapy regimen	Direct costs (DC), tenge	Effectiveness (EF)	The "cost-effectiveness" indicator (CEA)
Sausalin	9 000	85,71	105,00
Ornisid	4 470	42,19	105,94

It should be noted that from the point of view of the "cost-effectiveness" pharmacoeconomic analysis, the methods for treating giardiasis using "Sausalin" and "Ornisid" are indifferent, that is, despite the fact that the direct costs of "Sausalin" therapy are relatively high, its use is costly effective.

Given the lower effectiveness when using the drug "Ornidazole", patients require a second treatment, which also incurs additional costs. Therefore, the increment of cost effectiveness was estimated taking

into account the need for an additional course of therapy in patients with ineffective primary therapy. The indicator of increment of costs effectiveness, that is, the price of the achieved higher effect was: ICEA= (9000-4470)/(85,71-42,19) =104 tenge. This cost is additional and must be paid to prevent one case of ineffective eradication of the pathogen. According to the study, 72 patients from the group receiving "Ornisid" and 18 patients from the group receiving "Sausalin" needed a second course of treatment [6]. The calculation of the costs of additional treatment for patients with re-identified giardiasis during therapy with "Ornisid" and "Sausalin" are presented in table 3.

Table 3 – Comparative indicators of additional costs
in the treatment of giardiasis with drugs "Ornisid" and "Sausalin"

Therapy regimen	The number of patients receiving primary therapy, person	Effec-tiveness, %	The number of patients requiring repeated eradication therapy, person	Indicator of costs effectiveness increment, tenge	Additional costs for pharmacotherapy, tenge
Sausalin	125	85,71	18	104	1872
Ornisid	125	42,19	72	104	7488

Thus, the use of the drug "Sausalin" in comparison with the drug "Ornisid" allows saving 5616 tenge during a repeated course of therapy per patient.

Conclusions. The use of treatment regimens for giardiasis using the domestic medicinal product "Sausalin" is economically feasible given the high level of eradication and the safety profile of the new drug.

Күнжан С. Әдекенова[1], О. В. Маслова[2], Е. Г. Толоконников[1]

[1]«Қарағанды фармацевтикалық зауыты» ЖШС, Қарағанды, Қазақстан;
[2]«Фитотерапия орталығы» ЖШС, Қарағанды, Қазақстан

ЕРЕСЕК ЕМДЕЛУШІЛЕРДЕ ЛЯМБЛИОЗДЫ ЕМДЕУГЕ АРНАЛҒАН ПАРАЗИТТЕРГЕ ҚАРСЫ ПРЕПАРАТТАРДЫ ФАРМАКОЭКОНОМИКАЛЫҚ ТАЛДАУ

Аннотация. Мақалада ересек емделушілерде лямблиоз терапиясының фармакоэкономикалық негіздемесі ұсынылған. «Саусалин» бірегей дәрілік препаратын қолдану тиімділігі талқыланады.

Лямблиялар – әлемдегі ең көп жайылған патогенді эукариотикалық микроорганизмдердің бірі және диареяның ең көп таралуының себепшісі. Қазіргі уақытта тиімділік пен қауіпсіздік көрсеткіштерімен, сондай-ақ терапия құнымен ерекшеленетін, лямблиозды емдеу үшін ұсынылған бірқатар препараттар бар. Сондықтан лямблиоздың дәрілік терапиясының сапасын салыстырмалы бағалау мақсатында клиникалық-экономикалық талдау жүргізу қажет.

Өсімдік текті «Саусалин» – паразиттерге қарсы бірегей препараты *Saussurea salsa* (Pall.) Spreng (сортаң шұбаршөп) терпеноидтарының фармакологиялық белсенді қосылыстары негізінде жасалған және паразиттер мен бактерияларға қарсы құрал. Ішектің және гепатобилиарлық жүйенің паразитоздары (жіті және созылмалы лямблиоз, описторхоз), әйелдердің спецификалық емес (бактериялық) және спецификалық (трихомонадты) жіті аурулары кезінде қолданылады. Шығу тегі өсімдік болуына байланысты, препараттың жанама әсерлері мен қарсы көрсетілімдері жоқ.

«Саусалинмен» ем алған науқастар тобындағы (бірінші топ) емдеу тиімділігі 85,71 %-ды, «Орнидазол» қабылдаған науқастар тобы (екінші топ) небәрі 42,19 %-ды құрады. Екінші топтағы науқастардың 57,81 %-ында санациядан 1-3 айдан кейін лямблия цисталарының қайта бөлінуі байқалады, ал бірінші топта тек 14,29 %-да ғана. Бірінші топта лямблия цисталарының жойылу пайызы бақылау тобына қарағанда 4 есе жоғары, бұл жаңа «Саусалин» препаратының жоғары тиімділігін көрсетеді.

Фармакоэкономикалық талдау тұрғысынан, лямблиозды «Саусалинді» және «Орнисидті» пайдалана отырып емдеу әдістемесінің «шығындар-тиімділігі» индифферентті болатынын атап көрсеткен жөн, яғни «Саусалинмен» емдеуге жұмсалатын тікелей шығындардың салыстырмалы түрде жоғары болуына қарамастан, оны пайдалану шығыны тиімді болып саналады.

Зерттеу нәтижелеріне сәйкес, фармакологиялық әсері бойынша «Саусалин» препараты тиімділігі жағынан жоғарыда көрсетілген референс-препараттармен бірдей немесе олардан жоғары.

«Орнидазол» препаратын қолданған кездегі төмен тиімділікті ескере отырып, емделушілерге қайта емдеуді тағайындауға тура келеді және бұл қосымша шығындарды талап етеді. Сондықтан бастапқы тиімсіз

терапияны алған емделушілерде қосымша терапия курсын жүргізу қажеттілігін ескере отырып, шығындар тиімділігінің өсу көрсеткіші бағаланды. Шығын тиімділігінің өсу көрсеткіші, яғни қол жеткізілген жоғары әсердің бағасы: ICEA = (9000-4470)/(85,71-42,19) = 104 теңгені құрады. Бұл –қосымша құн, сондай-ақ оны қоздырғыштың тиімсіз эрадикациясының бір жағдайын болдырмау үшін төлеу қажет. Зерттеу мәліметтеріне сәйкес, қайта емдеу курсы «Орнисид» препаратын алған топтың 72 емделушісіне және «Саусалин» препаратын алған топтың 18 емделушісіне қажет болды.

Отандық «Саусалин» дәрілік препаратын пайдалана отырып, лямблиозды емдеу тәсімдерін қолдану – жаңа препараттың қауіпсіздік профилі мен эрадикацияның жоғары деңгейін ескергенде, экономикалық тұрғыдан орынды. «Саусалин» препаратымен бір емделушіге қайта емдеу курсын жүргізген кезде, «Орнисид» препаратымен салыстырғанда, үнемдеу көрсеткіші 25 %-ға дейін жетті.

Түйін сөздер: лямблиоз, саусалин, орнидазол, альбендазол, фармакоэкономика.

Кунжан С. Адекенова[1], О. В. Маслова[2], Е. Г. Толоконников[1]

[1]ТОО «Карагандинский фармацевтический завод», Караганда, Казахстан;
[2]ТОО «Центр фитотерапии», Караганда, Казахстан

ФАРМАКОЭКОНОМИЧЕСКИЙ АНАЛИЗ ПРОТИВОПАРАЗИТАРНЫХ ПРЕПАРАТОВ ДЛЯ ЛЕЧЕНИЯ ЛЯМБЛИОЗА У ВЗРОСЛЫХ ПАЦИЕНТОВ

Аннотация. В статье представлено фармакоэкономическое обоснование терапии лямблиоза у взрослых пациентов. Обсуждается эффективность применения оригинального лекарственного препарата «Саусалин».

Лямблии являются одними из наиболее распространенных патогенных эукариотических микроорганизмов и самой распространенной причиной диареи во всем мире. В настоящее время имеется ряд препаратов, рекомендованных для лечения лямблиоза, отличающихся показателями эффективности и безопасности, а также стоимостью терапии. Поэтому необходимо проведение клинико-экономического анализа с целью сравнительной оценки качества лекарственной терапии лямблиоза.

Оригинальный противопаразитарный препарат «Саусалин» – растительного происхождения, разработан на основе фармакологически активных соединений терпеноидов *Saussurea salsa* (Pall.) Spreng. (соссюрея солончаковая) и является противопаразитарным, антибактериальным средством. Применяют при паразитозах кишечника и гепатобилиарной системы (острый и хронический лямблиоз, описторхоз), неспецифические (бактериальные) и специфические (трихомонадные) острые заболевания у женщин. Благодаря своему растительному происхождению, препарат не имеет выраженных побочных эффектов и противопоказаний.

Эффективность лечения в группе больных, получавших лечение «Саусалином» (первая группа), составила 85,71%, в группе принимавших «Орнидазол» (вторая группа – всего 42,19%. У 57,81% больных второй группы отмечено повторное выделение цист лямблий через 1-3 месяца после санации, в первой группе – только у 14,29 %. Процент элиминации цист лямблий в первой группе выше в 4 раза, чем в группе контроля, что свидетельствует о высокой эффективности нового препарата «Саусалин».

Следует отметить, что с точки зрения фармакоэкономического анализа «затраты-эффективность» методики лечения лямблиоза с использованием «Саусалина» и «Орнисида» индифферентны, то есть несмотря на то, что прямые затраты на терапию «Саусалином» сравнительно высокие, его использование является затратно-эффективным.

По результатам исследований было показано, что препарат «Саусалин» по фармакологическому действию сопоставим или даже превосходит по эффективности вышеуказанные референс- препараты.

С учетом более низкой эффективности при использовании препарата «Орнидазол» пациентам требуется назначение повторного лечения, что также несет дополнительные расходы. Поэтому был оценен показатель приращения эффективности затрат с учетом необходимости проведения дополнительного курса терапии у пациентов с неэффективной первичной терапией. Показатель приращения эффективности затрат, то есть цена достигнутого более высокого эффекта составила: ICEA = (9000-4470)/(85,71-42,19) = 104 тенге. Данная стоимость является дополнительной и её необходимо заплатить для предотвращения одного случая неэффективной эрадикации возбудителя. Согласно данным исследования, повторный курс лечения потребовался 72 пациентам из группы, получавших препарат «Орнисид» и 18 пациентам из группы, получавших препарат «Саусалин».

Применение схем лечения лямблиоза с использованием отечественного лекарственного препарата «Саусалин» является экономически целесообразным с учетом высокого уровня эрадикации и профиля безопасности нового препарата. При проведении повторного курса терапии на одного пациента препаратом «Саусалин» экономия составляет до 25% в сравнении с препаратом «Орнисид».

Применение схем лечения лямблиоза с использованием отечественного лекарственного препарата «Саусалин» является экономически целесообразным с учетом высокого уровня эрадикации и профиля безопасности нового препарата.

Ключевые слова: лямблиоз, саусалин, орнидазол, альбендазол, фармакоэкономика.

Information about authors:

Adekenova Kunzhan S., LLP «Karaganda Pharmaceutical Plant», Republic of Kazakhstan, Karaganda; kadekenova@krgpharm.kz; https://orcid.org/0000-0001-5707-5255

Maslova O.V., LLP «Center of Phytotherapy», Republic of Kazakhstan, Karaganda; o.morozova@phyto.kz; https://orcid.org/0000-0001-8601-0098

Tolokonnikov E.G., [1]LLP «Karaganda Pharmaceutical Plant», Republic of Kazakhstan, Karaganda; etolokonnikov@krgpharm.kz; https://orcid.org/0000-0002-0098-6098

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R. O. Salimbaeva, A. A. Tagay, A. Bulambaev, K. Meyrambek

University of Almaty, Almaty, Kazakhstan.
E-mail: Rsalimbaeva@mail.ru; atagayev_01@mail.ru; k.r.asavchik@mail.ru; Karla1987@bk.ru

FORMATION AND IMPLEMENTATION OF COMPETITIVE STRATEGIES IN PHARMACEUTICAL COMPANIES

Abstract. The aim of the article is to study the features of the formation and implementation of competitive strategies in pharmaceutical companies based on the assessment and organization of a competitiveness management system. The paper substantiates the significance of the problems of competitiveness, pricing and marketing policy of distribution companies in the pharmaceutical market. The authors of the article adhere to a systematic method of research and consider the competitiveness management of pharmaceutical enterprises as a system. The object of the study was the global pharmaceutical distribution companies present in the Kazakhstan market. By studying their competitive strategies, the authors revealed the features of their functioning on the Kazakhstan market, as well as identified the risks associated with changing and managing the pricing policy of the studied companies. The specific features of the functioning of the enterprises under investigation revealed in the work made it possible to identify the main components of the analysis of the external environment of the distribution company. The authors describe the stages of developing a competitive strategy for a pharmaceutical distribution company and develop measures to further operate and adjust the strategy to take into account new conditions.

Key words: pharmaceutical market, distribution industry, pharmaceuticals, competitive strategy.

Introduction. The contemporary state of Kazakhstan pharmaceutical market imposes on its participants tough requirements on elaborating a behavior strategy that would ensure stable development of a certain enterprise under the conditions of constantly changing competitive environment, enhancement of pharmaceutical companies competitiveness, enlargement of its capabilities to operate under stiff competition.

Despite the availability of enough number of researches that contributed significantly to the development of theory and practice of enterprises management, the peculiarities of competitive strategies elaboration for pharmaceutical enterprises are underexplored. In addition, new market conditions, the volume of activity types implemented by pharmaceutical enterprises, specifics of the pharmaceutical drugs variety require more detailed investigation and elaboration of competitive strategies able for flexible reaction on internal and external environment changes, and achievement of high level of competitiveness in short- and long-term perspective.

Methodology of investigation. During the implementation of the work the methods of system analysis, abstract and logical method, the method of monograph research, the method of comparative analysis, and organizational and structural modeling were used; this allowed achieving necessary profoundness of the research results and conclusion soundness.

The main body. The companies that manufacture the pharmaceutical drugs, medical goods, health and hygiene items, galenicals etc. often apply the strategies of differentiated, undifferentiated, concentrated marketing [1, p.66]. Down to the beginning of XX century, there was no urgency to manage the promotion of pharmaceutical goods and other items used in medical practice and manufactured at the pharmaceutical market. To manufacture the distribution products it was enough to have a patent allowing for pharmaceutical drugs advertising and selling. The initiator of marketing application in the medicine was a professor of the pharmaceutical college of Texas University, R.A. Gosselin who in 1962 made a proposal, and in 1966 the “Certified Medical Representation (CMR) Institute, Inc.” started the training of

pharmaceutical sales agents [2, p.45]. During the period of the distribution products promotion to the market a lot of pharmaceutical companies forming its sales policy due to the trade channels that include distributers and dealers, or focused on dealers only without creation of the own sales network were established. The dealer companies investigate the market of manufacturers and consumers to reveal free niches for the development of new types of services. The drugs and items promotion activity manufactured by the enterprises of distributor industry enlarge the market offer of the manufactured goods due to the active operation of dependent and independent companies specializing on rendering of various trade and mediation services (wholesale supply, small-scale wholesale etc.) [2, p.45].

The opportunities for the development of new tendencies in the trade and mediation activity on promoting drugs and items manufactured by enterprises of distribution industry became possible due to the current strengthening of participants interests confrontation within the format: "manufacture – distribution – exchange – consumption" of the distributed products.

All corporations engaged in the manufacture are aimed at reimbursing of expenses spent on research and development, and therefore strive for high profit allowing for further research works and creation of new pharmaceutical medicines. Under the conditions of the strongest pressure on the side of companies that copying them during the promotion the various instruments are used. The expensive promotion causes high cost of pharmaceutical drugs and negative reaction on the side of the State that, due to this, has to constantly increase the budget of the healthcare programs. From time to time there are corrupt trials, these are the cases when the patients' health incurred grievous harm as a result of new pharmaceutical drugs intake, and this, for sure, influences on the reputation of this or that company, and on the actions of the regulatory system that is responsible for the content of the game rules in the pharmaceutical products market [3, p.41].

The foreign pharmaceutical companies during several recent decades applied a model allowing, at common increase of demand on pharmaceutical products, profiting insignificant margin comparing to the companies-originators. Among these companies, the leading is the world distributor company Teva that exists in Kazakhstan market, and in the market of distributor companies of other CIS countries.

The results of the investigation on forming process and implementation of the competitive strategy of Teva distributor company showed that under the conditions of continuing forming of pharmaceutical market in Kazakhstan the strategy of concentrated or target marketing is less reasonable than previous. In opinion of Reikhart D.V. the pharmaceutical companies try to avoid it as this excludes completely an opportunity of any diversification [3, p.41]. The high level of pharmaceutical companies' infrastructure the Head offices of which are located in the economically developed countries, plus financial stability of these companies allow applying different options of the marketing strategies. For example, the undifferentiated marketing is applied by such leaders of the world pharmaceutical business as Pfizer company (USA) the stock of which has innovative antibiotics, anti-inflammatory medicines, psychotherapeutic medicines, cardiovascular medicines, diabetic treatment medicines etc.; Austrian company R. Bittner GmbH; Johnson & Johnson (USA) company that promotes the pharmaceutical medicines, diagnostics means, medical equipment [4, p.15].

The high-tech products include the manufacture of medical equipment, healing remedies, and these are not necessarily the medicines aimed at treatment of cancer or AIDS [5].

The development of the distributor sector in the field of high technologies is not only due to the manufacture of pharmaceutical medicines used for treatment of cancer diseases, heart diseases and other new medicines applied for treatment of the currently rare and fatal diseases. And this is proved by the results of WHO data analysis on the structure of medications consumption. This analysis testifies that the largest volume of purchases falls on painkillers, medicines taken against diseases connected with different infections, etc. Therefore, the development of high-tech manufactures of medicals for all spectrums of action is still topical. However, the development of new manufactures as well as production of new medicals under the formed distributor competitive medium is connected with high risks at the consumer market.

Despite the high risks in the distributor activity the creation and support of this kind of manufactures is one of the ways on ensuring the national safety the same as the national policy on medicals issuing to persons having grave health problems and registered for medical reasons.

This approach to the national policy in Kazakhstan narrows the frames of retail sales market and leads to strengthening of competition in promoting the pharmaceutical products that in most cases cannot

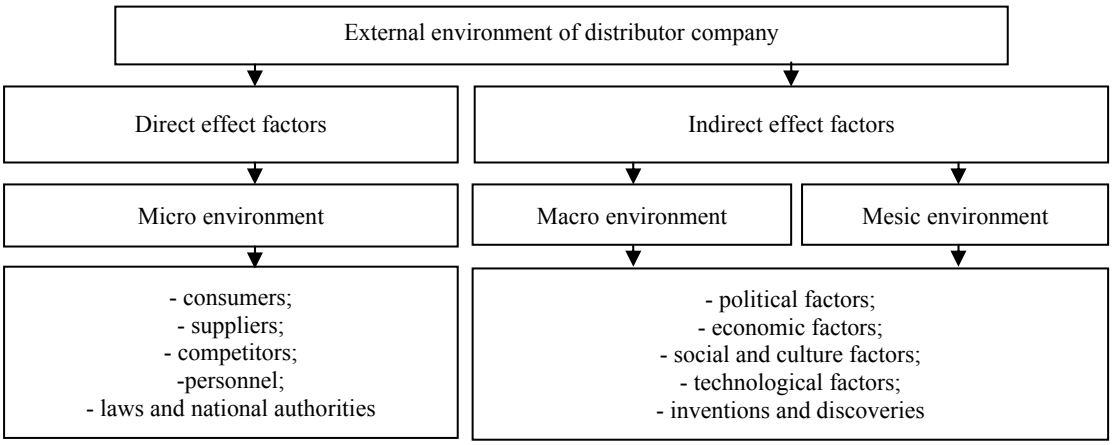
be implemented by the companies itself due to high costs, but that is an integral component of the common corporate strategy.

The selling specifics of pharmaceutical companies items, due to peculiarity of products created by them, is reflected in the mechanism of the business entity strategy development, it does not exclude the general principles of its forming, but strengthens the significance of the effective competitive strategy elaboration that includes the integrity of definite actions of a company in the market covering the elements of marketing together with market and volume characteristics, and are implemented under the general corporate strategy.

Focusing on the significance of the competitive strategy for business entities in the field of distributor activity, the motivation of this focus is that in the contemporary practice, independently on the trend and field of activity, the competitive strategy is a weighty instrument as its implementation influences on solving of a wide range of problems urgent for the business entity [6, p.11].

Thus, the elaborated competitive strategy of a distributor company includes, first of all, finding of resources becoming clear during the implementation of successful projects. The successful implementation of projects reveals the possible resources also that cannot be foreseen quite accurately, therefore while elaborating the competitive strategy the generalized phrasing of results is used.

The market tendency in the field of distributor activity shows that the traditional fields of macro- and micro medium analysis should also include the analysis of mesic environment as the scale of competitors activity is beyond the frame of influence at macro- and micro levels, and globalizes the significance of companies' activity [7]. To show the analysis components of business entity external environment in the field of distributor sector it is necessary to construct in figure the specifics of external environment investigation objects content.



Components of external environment analysis of business entity in the field of distributor sector.
Note: compiled by the author basing on reference [8]

The specifics of pharmaceutical manufacture is that it produces the original medicals and analogues or generics that have not been investigated completely so far. However, the price of generics makes them of primary demand and production due to impossibility or unavailability to purchase the originals. By strengthening the competitive strength at separate segments of pharmaceutical market this segment of business environment of companies requires flexible strategic policy, and thus implies the introduction of efficiency estimation procedures of the selected and earlier developed strategy of the pharmaceutical market entity. Therefore, while developing a strategy it is necessary to analyze the results achieved by a company, to correct its behavior at the given niche of the selected market segment. Thus, to elaborate a strategy it is necessary to assess already introduced strategy for its total change or correction; it means that for the active distributor company it includes 8 main stages:

1. Mission and corporate-wide strategy of a company development.
2. Setting of tasks to struggle against competitors.
3. Acquisition and analysis of data on the state of external and internal environment of the company.
4. Selection of the best strategy in view of the competition.
5. Analysis of the selected strategy.

6. Implementation of the competitive strategy basing on the strategic plan.

7. Analysis of results.

8. Correction of the existing strategy or development of a new one that will be more successful for implementation of tasks on achieving a company goal [9, p.187].

In general view, the activity of companies focused on the medicals promotion in the market or trade and mediatory activity requires knowing the manufacturers of pharmaceutical medicines needed to a consumer. If a company-manufacturer investigates the market demands to adjust the production and starts it only when it is sure in its competitiveness, the independent dealer company also estimates the market demand, but considering its saturation with goods – originals and analogues proposed by its direct competitors manufacturers, and the share of definite preferences to activate the process. Therefore, the development of the competitive strategy of companies focused on medicals and other pharmaceutical items promotion has its own specifics and does not exclude the base that is the strategic analysis.

The strategy of differentiated marketing is applied, for example, by GlaxoSmithKline Company (USA) providing the innovative prescribed and not prescribed medications, products for hygiene and disease prevention, vitamin energy drinks. The pharmaceutical markets of many world countries accept positively such medicaments of the company as Panadol, Coldrex in in different modifications. The strategy of concentrated marketing is usually applied by companies that produce the medicals for definite category of consumers. An example of this tendency is the distributor company Novo Nordisc – the leading manufacturer of insulin [2, p.43].

The development of pharmaceutical market led to the strong holding of positions by the companies from the USA, France, China, India, and other world countries. During the recent five years and in 2018 the leading position belonged to Pfizer Company (USA) with sales volume on the level of 47.6 billion dollars. Its main competitors are Swiss companies Novartis with sales volume 42.8 billion dollars, and Roche with sales of 42.4 billion dollars. The following companies improved its position and kept the competitiveness: Johnson & Johnson with sales at the level of 39.9 billion dollars, French Company Sanofi with sales volume 38.2 billion dollars, and after that Merck&Co Company (beyond the USA – MSD), GlaxoSmithKline, AbbVie, Gilead, and Bayer. Teva [2, p.43].

If we consider the effectiveness of the selected behavior reflected in the corporate strategies of companies, it is necessary to note that if the prediction of Pfizer and Novartis Companies leading position was fulfilled and the companies kept its positions until the end of 2018, and despite that Roche Company is ranked third, its activity is not as operative as predicted.

Numerous unpopular management solutions lead to the fact that a range of companies, while keeping its positions at the pharmaceutical market lost its positions by individual competitive advantages. For example, the Israeli Company Teva experienced significant financial difficulties in 2018 to solve which it used such unpopular measures as reduction of staff and closing of plants.

Thus, under the stiff competition at the pharmaceutical market the unpopular and ineffective strategic managerial decisions lead to the loss of competitive advantages and positions of a distributor company at the given market. The stiff competition at the pharmaceutical market aggravates due to appearance of new participants producing innovative medicals using less expensive and more progressive technologies of production.

Considering the corporative strategy of the French Company Sanofi it should be noted that its competitive advantages are constructed on the base of managerial decisions focused on reduction of expenses, and distributor products suggestions to consumers at acceptable prices. Sanofi Company should resolve all these issues and create effective barriers to protect its competitive advantage.

The key issue of the competitive policy is confrontation to threat of new participants' appearance in the market. The managerial board the Sanofi Company renews constantly the range of products and extends the services provided to a consumer. At the same time, the managerial board assumes that due to the development of new products and services, the company attracts new consumers and increases the share of permanent consumers of its products that have a chance to choose necessary medicals among a variety of items produced namely by this company. Despite that the enlargement of production can lead to the scale effect, the company managers assumes to avoid it by decreasing the fixed price.

The building of capacity at simultaneous decrease of expenses on research and development will allow the company to optimize the prices. Consequently, in opinion of the company managers, new participants less likely will enter the dynamic industry of distributor sector already having the permanent

players such as Sanofi and other companies. This decreases significantly the window of extraordinary profit for new companies putting off new players in the sector [10, p.102].

One of the instruments of the competitive strategy implementation in Sanofi Company ensuring its leading position in the market is a work with permanent suppliers that are also leading in their segment of the market and are able to decrease the margin that Sanofi can earn in the market. The large suppliers in the field of healthcare use its negotiation capabilities for obtaining higher prices from the manufacturers of medicals of the main field. The general effect of higher negotiation position of suppliers is that it decreases the common profitability of large manufacturers. To optimize the prices for delivery of items and raw materials for medical production, Sanofi Company constructs an effective scheme of supplies with large number of suppliers that provides an opportunity for maneuver and selection of counterparts with price proposals beneficial for it. The company has developed the sales policy that includes suppliers focused on arrangement of business the only goal of which is promotion of medicals and other products of manufacture used by the treatment practice, and specific suppliers whose business depends on the company. One of the lessons the Sanofi can learn from Walmart and Nike is that these companies developed the outsourced manufacturers whose business depends on them only by creating a scenario when these outsourced manufacturers have significantly less negotiation strength comparing to Walmart and Nike [10, p.102].

As one of the main instruments of competitive positions protection and forming of the competitive strategy, Sanofi Company uses the model of five competitive forces by M. Porter that allows obtaining the complete pattern of the things influencing on the profitability of the organization at medical manufacturers of large sector. The analysis allows determining the tendencies of the status change and estimate the competitive positions at early stage; it also allows the quick response on negative changes to use all instruments of management to minimize the economic losses.

The effective application of the competitive strategy allows “STADA” Arzneimittel AG keeping its position at the pharmaceutical market for more than hundred years. Despite the long activity it continues to be the main trender for all who is engaged in producing of generics. The company, in the German manner, is conservative and accurate, but open for innovations, that provides STADA an opportunity to remain stable and achieve the set tasks at every issue. The main competitive advantages of the company that it keeps to the present day are the quality and wide range of products that counts more than hundred items that allowed the company taking the award “Global Generics & Biosimilars Awards -2018” in 2018. It should be noted that the foreign pharmaceutical manufacturers has no specific arrangement of the sale due to the features of this market segment regulation. However, this is especially important for the product promotion produced by medical companies as the implementation of the competitive strategy assumes that the market capacity and other indicators estimating the prospectivity of the distributor company activity will be fulfilled [11].

The features of the competitive strategies of pharmaceutical companies

Strategy components	Компании			
	«STADA» Arzneimittel AG.	Sanofi	Teva	GlaxoSmithKline (USA), Novo Nordisc
Work with permanent suppliers; Wide range; Innovations	The main trender for generics. Strategy – the quality and wide range of products that counts more than hundred items.	The large suppliers in the field of healthcare use its negotiation capabilities for obtaining higher prices from the manufacturers of medicals. Strategy – price advantage	Reduction of staff and closing of plants. Strategy – optimization of staff of produc-tion capacity	Provides the innovative prescribed and not prescribed medications, pro-ducts for hygiene and disease preven-tion, vitamin energy drinks. The phar-maceutical markets of many world countries accept positively such medi-caments of the company as Panadol, Coldrex in in different modifications. Strategy – differentiated marketing
Note: compiled by the author.				

Considering the experience of forming and implementing of the competitive strategy it is obvious (table) that it can be applied for development and establishment of pharmaceutical companies in Kazakhstan, and it also provides an opportunity to form the activity of the business entities on promoting

the products produced by the leading pharmaceutical dealers making important that namely independent dealer company is an object of investigation.

Indeed for companies carrying out the independent trade and mediatory activity the development of the competitive strategy is a special aspect of the strategic planning. This is mostly due to the fact that independent trade and mediatory companies are more sensitive to the appearance of new products in the market, to fluctuation of manufacture prices, and to the lack of long-term connections or impossibility of its operation with the manufacture companies due to regulatory barriers or even as a result of irrational forms of supplies and its scale etc. It is clear that companies promoting the distributor products are focused on acceptable conditions of manufacturers' sales policy [12, p.3].

Conclusion. The construction of the effective system on managing the competitiveness of pharmaceutical enterprises requires efforts on solving the strategic and tactic tasks of competitiveness management aimed at ensuring the sustainable competitive position at the pharmaceutical market. Therefore, while developing the competitive strategy it is reasonable to apply a system approach assuming the integration of managing, managed, target, provision and functional subsystems able to fit the external environment conditions.

All data that can be acquired and structured in the process of the competitive strategy development provide an opportunity to the top management of the company and to those who will implement the strategy directly to see clearly the market situation, company position in it, and really imagine the ability to achieve the set goals. After that the competitive strategy acts as an executive document that concentrates all resources necessary to follow the strategic points. At the same time, on the base of the conducted analysis on the past activity, a company can constantly improve and enlarge its sphere of activity, response to the market changes, strengthen its positions and become a possessor of new markets and niches.

Р. О. Сәлімбаева, А. А. Тағай, А. Бұламбаев, К. Мейрамбек

«Алматы» университеті, Алматы, Қазақстан

ФАРМАЦЕВТИКАЛЫҚ КОМПАНИЯЛАРДЫҢ БӘСЕКЕЛІК СТРАТЕГИЯЛАРЫН ҚАЛЫПТАСТЫРУ ЖӘНЕ ЖҮЗЕГЕ АСЫРУ

Аннотация. Зерттеу тақырыбының өзектілігі фармацевтикалық кәсіпорындардың ішкі және сыртқы ортаның өзгерістеріне икемделе алатын, қысқа және ұзақ мерзімді келешекте бәсекеге қабілеттіліктің жоғарғы деңгейін қамтамасыз ете алатын бәсекелік стратегияларды әзірлеу үшін, олардың қызмет етуінің нарықтық шарттары мен ерекшеліктерін толық саралау қажеттілігінде жатыр.

Мақаланың мақсаты – фармацевтикалық компаниялардың бәсекеге қабілеттілікті басқару және ұйымдастыру жүйесін бағалау негізінде, олардың бәсекелік стратегияларын қалыптастыру және іске асыру ерекшеліктерін зерттеу. Зерттеу нысаны – Қазақстан нарығында қызмет ететін жаһандық фармацевтикалық дистрибьюторлық компаниялар. Мақала авторлары жүйелі зерттеу әдісін ұстанады және фармацевтикалық кәсіпорындардың бәсекеге қабілеттілігін басқаруды жүйе ретінде қарастырады. Одан басқа, жұмысты орындау барысында абстрактылық-логикалық әдіс, монографиялық зерттеу әдісі, салыстырмалы талдау және ұйымдық-құрылымдық үлгілеу әдістері қолданылды, бұл зерттеу нәтижелерінің қажетті тереңдігі мен жасалған қорытындылардың негізділігін қамтамасыз етуге мүмкіндік берді.

Мақалада фармацевтика нарығындағы дистрибьюторлық компаниялардың бәсекеге қабілеттілік, баға қалыптастыру және өткізу саясаты мәселелерінің маңыздылығы негізделген. Зерттелетін компаниялардың бәсекелестік стратегияларын зерттей отырып, авторлар олардың Қазақстан нарығындағы жұмыс істеу ерекшеліктерін анықтаған. Қазақстан аумағында қызмет ететін дистрибьюторлық фармацевтикалық компаниялардың бағалық саясатын талдау нәтижелері авторларға баға саясатын өзгертуді басқарумен байланысты тәуекелдерді анықтауға мүмкіндік берді.

Жұмыста анықталған зерттелетін кәсіпорындардың қызмет ету ерекшеліктері дистрибьюторлық компанияның сыртқы ортасын талдаудың негізгі компоненттерін анықтауға мүмкіндік берді, ал оның негізі ретінде стратегиялық талдау әдістемесі қолданылды. Сонымен қатар мақалада дистрибьюторлық фармацевтикалық компанияның бәсекелестік стратегиясын әзірлеу үрдісі сипатталған, оны жасаудың 8 кезеңі ұсынылған, олар енгізілген стратегияны бағалауды және түбегейлі өзгертуді қамтиды. Оған қоса, жаңа шарттарды ескере отырып, әзірленген стратегияны ары қарай қолдану және түзету бойынша шаралар әзірленген.

Мақалада стратегиялық басқару шешімдерін дұрыс қабылдау мәселелеріне баса назар аударылған, олардың тиімсіздігі дистрибьюторлық компанияның осы нарықтағы орны мен бәсекелік артықшылық-

тарынан айрылуына әкелетіндігі негізделген. Фармацевтикалық нарықтағы қатаң бәсекелестік күресті авторлар өндірістің анағұрлым жаңа, аз шығынды қажет ететін, ілгерілемелі технологияларын қолдану арқылы инновациялық препараттар өндірісін құратын жаңа нарық қатысушыларының үнемі пайда болып отыруымен байланыстырады.

Фармацевтикалық кәсіпорынның бәсекеге қабілеттілігін басқарудың тиімді жүйесін құру үшін, фармацевтикалық нарықтағы оның тұрақты бәсекелік жағдайын қамтамасыз етуге бағытталған, басқарудың стратегиялық және тактикалық міндеттерін шешу бойынша шаралар ұсынылған. Сонымен қатар бәсекелік стратегияны әзірлеу барысында, авторлар жүйелік тәсілді қолдануды ұсынады, ол сыртқы ортаның шарттарына үйлесе алатын, жүйенің басқарушылық, мақсатты, қамтамасыз етуші және функционалдық құрамдастарын ықпалдастыруды білдіреді.

Авторлар ұсынған әдістеме бойынша әзірленген бәсекелік стратегияны ұйымдық-жарлық құжат ретінде қолдануға болады, онда стратегиялық бағдарларды ұстану үшін барлық қажетті ресурстар шоғырланады. Одан басқа, бәсекелік стратегияны әзірлеу барысында алынуы және құрылымдануы мүмкін деректер компанияның топ-менеджментіне де, сондай-ақ стратегияны орындаушыларға да нарықтағы жағдайды, ондағы компанияның орнын нақты көруге, сонымен қатар қойылған мақсаттардың қол жетімділік деңгейін бағалауға мүмкіндік береді. Стратегияда компанияның өткен кезеңдегі қызметіне талдау жүргізіледі, оның нәтижелері негізінде компания қызметін жақсартуға және қызмет ету салаларын кеңейтуге, нарықтағы өзгерістерге икемделуге, нарықтағы орнын нығайтуға және нарықтағы жаңа орындарға ие болуға байланысты шаралар жасалады.

Р. О. Салимбаева, А. А. Тагай, А. Буламбаев, К. Мейрамбек

Университет «Алматы», Алматы, Казахстан

ФОРМИРОВАНИЕ И РЕАЛИЗАЦИЯ КОНКУРЕНТНЫХ СТРАТЕГИЙ ФАРМАЦЕВТИЧЕСКИХ КОМПАНИЙ

Аннотация. Актуальность исследования состоит в необходимости тщательного изучения рыночных условий, специфики деятельности фармацевтических предприятий для выработки их конкурентных стратегий, которые могут более гибко реагировать на изменения внутренней и внешней среды и обеспечить достижение высокого уровня конкурентоспособности в краткосрочной и долгосрочной перспективе.

Целью статьи является исследование особенностей формирования и реализации конкурентных стратегий фармацевтических компаний на основе оценки и организации системы управления конкурентоспособностью. Объектом исследования выступили глобальные дистрибьюторские фармацевтические компании, присутствующие на рынке Казахстана.

Авторы статьи придерживаются системного метода исследования и рассматривают управление конкурентоспособностью фармацевтических предприятий как систему. Кроме того, в ходе выполнения работы были использованы абстрактно-логический метод, метод монографического исследования, метод сравнительного анализа и организационно-структурное моделирование, что позволило обеспечить необходимую глубину результатов исследования и обоснованность выводов.

В работе обоснована значимость проблем конкурентоспособности, ценообразования и сбытовой политики дистрибьюторских компаний на рынке фармацевтики. Посредством изучения их конкурентных стратегий авторы раскрыли особенности их фунционирования на рынке Казахстана. Результаты анализа ценовой политики глобальных дистрибьюторских фармацевтических компаний, функционирующих на территории Казахстана, позволили авторам выявить риски, связанные с изменением и управлением их ценовой политикой.

Выявленные в работе специфические особенности функционирования исследуемых фармацевтических предприятий позволили выделить основные компоненты анализа внешней среды дистрибьюторской компании, при этом в качестве базиса была использована методика стратегического анализа. Описан процесс разработки конкурентной стратегии фармацевтической дистрибьютерской компании, состоящий из 8 основных этапов, предполагающих оценку уже внедренной стратегии и ее тотальное изменение. Кроме того, выработаны меры по дальнейшей эксплуатации и корректировки разработанной стратегии с учетом новых условий.

В статье основное внимание уделено вопросам адекватности принятия стратегических управленческих решений, непопулярность и неэффективность которых может привести к потере конкурентных преимуществ и позиций дистрибьюторской компании на данном рынке. Жесткую конкурентную борьбу на фармацевтическом рынке авторы объясняют периодическим появлением новых участников, создающих производство

инновационных препаратов, используя новые, менее затратные и более прогрессивные технологии производства.

Для построения эффективной системы управления конкурентоспособностью фармацевтического предприятия предложены меры по решению стратегических и тактических задач управления, направленных на обеспечение устойчивого конкурентного положения на фармацевтическом рынке. При этом при разработке конкурентной стратегии авторы рекомендуют использование системного подхода, предполагающего интегрирование совокупности управляющей, управляемой, целевой, обеспечивающей и функциональной подсистем, способных в единстве адаптироваться под условия внешней среды.

Разработанная конкурентная стратегия по предложенной авторами методике может использоваться как организационно-распорядительный документ, в котором происходит концентрация всех необходимых ресурсов для следования стратегическим ориентирам. Кроме того, все данные, которые могут быть получены и структурированы в процессе разработки конкурентной стратегии, дают возможность как топ-менеджменту компании, так и тем, кто непосредственно будет данную стратегию исполнять, ясно видеть ситуацию на рынке, место на нем компании, а также реально представлять, насколько поставленные цели достижимы. На основании проведенного анализа своей деятельности в прошлом компания может постоянно улучшать и расширять свою сферу деятельности, отвечать на изменения на рынке, усиливать свои позиции и становиться обладателем новых рынков и ниш.

Information about the authors:

Salimbaeva Raushan Ongarbaevna, candidate of economic sciences, Almaty University, Almaty, Kazakhstan; Rsalimbaeva@mail.ru; https://orcid.org/0000-0001-7543-8208

Tagay Akhozha Asanuli, candidate of Technical Sciences, Almaty University, Almaty, Kazakhstan; atagayev_01@mail.ru; https://orcid.org/0000-0003-4049-5282

Bulambaev Almas, Master of MBI Almaty University, Almaty, Kazakhstan; k.r.asavchik@mail.ru; https://orcid.org/0000-0001-7748-6086

Meirambek Karlygash, Master, Almaty University, Almaty, Kazakhstan; Karla1987@bk.ru; https://orcid.org/0000-0003-2726-560X

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A. M. Belkozhayev, R. Ye. Niyazova

Al-Farabi Kazakh National University, Almaty, Kazakhstan.
E-mail: ayaz_jarkent@mail.ru, raygul.nyiyazova@kaznu.kz

THE INTERACTION OF miR-4258, miR-3960, miR-211-3p AND miR-3155b WITH mRNAs GENES OF NON-POLYGLUTAMINE TRINUCLEOTIDE DISORDERS

Abstract. Trinucleotide repeat expansion disorders constitute a group of dominantly inherited neurological diseases that are incurable and ultimately fatal. In the present work, miRNA binding sites were predicted by the MirTarget program. It was given characteristics of miRNAs binding sites in 5' and 3' UTR mRNAs genes of non-polyglutamine trinucleotide disorders with CGG, GCC, CUG repeats. Binding sites of 2567 miRNAs with mRNAs of 17494 human genes were determined. 206 genes with nucleotide repeats, mRNAs of which are bind with miRNA in the 5'UTR and 3'UTR, were observed. From thus, 2668 miRNAs binding sites are located in the 5'UTR, 3853 – in the 3'UTR with ΔG/ΔGm values equal to 85 % and more. It was found that 34 gene's mRNA having trinucleotide (CGG\GCC\CUG) repeats were targets for miR-4258, miR-3960 miR-211-3p and miR-3155b. miR-4258 binds to mRNA of *ADARB1, C11orf87* and *CBFB* genes with free binding energy - 93 kJ/mole and ΔG/ΔGm 91%, to mRNA of *ARHGEF7, BCR, BRSK2* and *C9orf91* genes with free binding energy - 91 kJ/mole and ΔG/ΔGm 89%. miR-3960 binds in GCC repeats to mRNA of *ABCC1* and *BLMH* genes with free binding energy - 116 kJ/mole. miR-211-3p and miR-3155b interact with mRNA of *ACACA* and *ANKRD13D* genes in 5'-3'untranslated regions. Studying binding characteristics of miRNA and genes will help identify association of miRNAs with genes with trinucleotide repeats for recommending for the diagnosis of nucleotide repeat expansion disorders.

Key words: miRNA, mRNA, binding site, trinucleotide repeat expansion.

Introduction. Trinucleotide repeats are sets of three nucleotides present in succession in various copy numbers throughout the human genome [1]. Repetitive sequences of genetic code are quite common. However, when these sequences grow beyond the scope of what would be considered normal, they cause disease. While the human genome has mechanisms to protect against these expansions, patients present with what can be severe neuromuscular and neurodegenerative disorders. There have been many diseases discovered by TNR (trinucleotide repeat) expansions, but the most prominent are spinocerebellar ataxia, Huntington disease, Fragile X syndrome, myotonic dystrophy, and Friedrich ataxia [2].

Small regulatory RNAs, particularly miRNAs, are known to be dynamically regulated in neurogenesis and brain development. Some recent studies have suggested that the alterations in small regulatory RNAs could contribute to the pathogenesis of several neurodevelopmental disorders [3,4]. miRNA refers to a small non-coding, single stranded RNA molecule comprising of around 22 nucleotides. By base pairing to messenger RNA (mRNA) and triggering translation repression, the miRNAs control gene

expression [5]. The use of miRNA as biomarkers to help diagnose neurodegenerative disorders offers several advantages. As the expression of miRNAs are commonly altered during disease, they have gained much attention for their potential use as biomarkers [6]. With better understanding of the role of miRNAs in neurodegenerative diseases, scientists and researchers may create effective new drugs to treat these devastating human illnesses. However, the biological function of most miRNAs remains to be uncovered [7, 8]. It is therefore important to provide characteristics of miRNA interaction with mRNA genes associated with non-polyglutamine trinucleotide disorders**.**

Materials and methods. The nucleotide sequences of mRNAs of human genes were downloaded from NCBI (http://www.ncbi.nlm.nih.gov). The nucleotide sequences of human miRNAs were downloaded from the miRBase database (http://mirbase.org). The miRNAs binding sites in mRNAs of several genes were predicted using the MirTarget program [9]. This program defines the following features of miRNA binding to mRNA: a) the start of the initiation of miRNA binding to mRNAs; b) the localization of miRNA BS in 5′UTRs, CDSs and 3′UTRs of the mRNAs; c) the free energy of interaction miRNA and the mRNA (ΔG, kJ/mole); d) the schemes of nucleotide interactions between miRNAs and mRNAs. For analyzing and formatting sequences of genes, we used the sequence manipulation suite program (https:// bioinformatics.org/sms). To prediction the secondary structure of RNA, the software RNA fold was used (http://rna.tbi.univie. ac.at) [10].

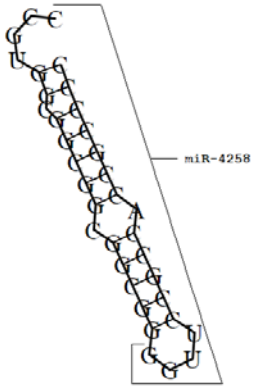
Results and discussion. Using the MirTarget program, the binding sites of 2567 miRNA with the mRNA of 17494 human genes were determined. 206 genes with nucleotide repeats, the mRNAs of which are bind with miRNA in the 5'UTR and 3'UTR, were observed. 2668 miRNAs binding sites are located in the 5'UTR, 3853 – in the 3'UTR with ΔG/ΔGm values equal to 85 % and more. Only miR-4258, miR-3960 miR-211-3p and miR-3155b bind with 34 gene's mRNA having trinucleotide CGG, GCC, CUG repeats causing non - polyglutamine disorders. In table 1-3 are shown characteristics of miRNA binding with mRNA genes having trinucleotide repeats in 5'-UTR and 3'-UTR. The mRNA of *ABL2, ACVR1B, ADARB1, ADRBK1, APBA1, ARHGEF7, FMR1, B4GALT2, BCL11B, BCR, BRSK2, BRWD1, BTBD7, C11orf87, C9orf91, CACNA1A, CADM4, CAMK4, CARM1, CBFB, CBL* and *CCDC93* genes having trinucleotide repeats interact with miR-4258 in 5'-UTR in regions with CGG repeat. The binding sites of miR-3960 in mRNA of*ABCC1, ABCD3, AFF2, ANKH, ANKRD13D, BCL11A, BCL2L11, BLMH, C4orf19* and *CA10* genes are located in 5'-UTR in regions with GCC repeat. mRNA of *ACACA* and *ANKRD13D* genes interact with miR-211-3p and miR-3155b in 5'-UTR / 3'-UTR in regions with CUG repeat.

Table 1 – Characteristics of miR-4258 binding sites
in the 5'-UTR mRNA genes having CGG trinucleotide repeat

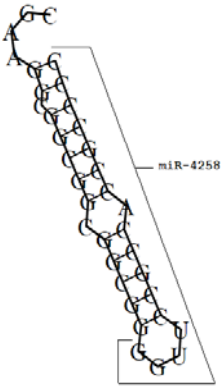
Gene	Beginning of binding site	ΔG, kJ/mole	ΔG/ΔGm, %	Scheme of miRNA binding with mRNA genes
ABL2	21	-89	87	5' - CGGCGGCGGUGGCGGCGG - 3' || |||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
ACVR1B	46	-89	87	5' - CGGCGGCGGUGGCGGCGG - 3' || |||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
ADARB1	18	-93	91	5' - CCGUGG**CGGCGGCGGCGG** - 3' ||| ||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
ADRBK1	7	-87	85	5' - CGCGGG**CGGCGGCGGCGG** - 3' | |||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
APBA1	50	-87	85	5' - UCC**CGGCGGCGGCGGCGG** - 3' || ||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
ARHGEF7	155	-91	89	5' - GCGAGG**CGGCGGCGGCGG** - 3' |||||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'

FMR1	98	-87	85	5' - GCG**CGGCGGCGGCGGCGG** - 3' || |||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
B4GALT2	133	-87	85	5' - CCCG**CGGCGGCGGCGG**CG - 3' ||	|||||||||||| | 3' - GGUU-CCGCCACCGCCCC - 5'
BCL11B	150	-87	85	5' - **CGGCGGCGGCGGCGGCGG** - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
BCR	200	-91	89	5' - CCGAGGAGG**CGGCGGCGG** - 3' |||||| |||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
BRSK2	100	-91	89	5' - CCU**CGGCGGCGGCGGCGG** - 3' || |||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
BRWD1	175	-87	85	5' - **CGGCGGCGGCGGCGGCGG** - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
BTBD7	87	-87	85	5' - **CGGCGGCGGCGGCGG**UGG - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
C11orf87	11	-93	91	5' - CGAAGG**CGGCGGCGGCGG** - 3' | |||||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
C9orf91	10)	-91	89	5' - CCGGGGUGG**CGGCGGCGG** - 3' |||||||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
CACNA1A	158	-87	85	5' - UCAG**CGGCGGCGGCGG**CG - 3' |||| |||||||||||| | 3' - GGUU-CCGCCACCGCCCC - 5'
CADM4	27	-87	85	5' - **CGGCGGCGGCGGCGGCGG** - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
CAMK4	90	-87	85	5' - CGCGGG**CGGCGGCGG**UGG - 3' | |||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
CARM1	12	-87	85	5' - CAG**CGGCGGCGGCGGCGG** - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
CBFB	39	-93	91	5' - CUGAGG**CGGCGGCGGCGG** - 3' |||||||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'
CBL	14	-89	87	5' - CCGG**CGGCGGCGGCGG**CG - 3' |||| |||||||||||| | 3' - GGUU-CCGCCACCGCCCC - 5'
CCDC93	33	-87	85	5' - **CGGCGGCGGCGGCGGCGG** - 3' |	|||||||||||| || 3' - GGUUCCGCCACCGCC-CC - 5'

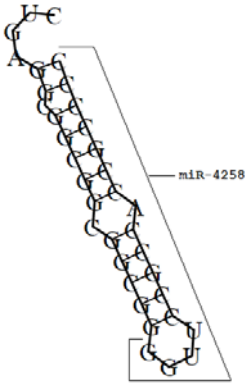
According to the table 1 only mRNA of *ADARB1, C11orf87* and *CBFB* genes have miR-4258 binding sites with free binding energy – 93 kJ/mole with the ΔG/ΔGm values equal to 91%. miR-4258 binds to CGG repeats of *ADARB1* gene in repeat nucleotide sequences CGG_{10}. The binding sites are located between 15 and 62 repeat nucleotide sequences with start in 18 nt. The binding sites of miR-4258 in mRNA of *C11orf87* and *CBFB* genes are located in repeat nucleotide sequences CGG_{10} /CGG_8 between 5-40 and 36-65 with start in 11 and 39 nt, respectively free binding energy equal to – 93 kJ/mole (figure 1). The secondary structures given in the figure clearly show the preferential formation of bonds with miR-4258.



A- mir-4258 binding site
in mRNA *ADARB* gene



B - mir-4258 binding site
in mRNA *C11orf87*gene



C -mir-4258 binding site
in mRNA *CBFB*gene

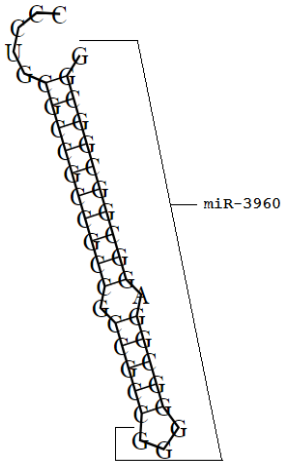
Figure 1 – Secondary structures of location of mir-4258 binding sites in 5' UTR mRNA of *ADARB, C11orf87* and *CBFB* genes

It was known that *ADARB1* gene encodes an RNA editing enzyme, expressed mainly in the central nervous system (CNS), which is involved in the downstream regulation of neuro transmitters. *ADARB1* (also known as *ADAR2*) spans a genomic region of 25 kb on chromosome 21q22.3 and comprises 16 exons and regulates its own expression through self-editing [11]. It was demonstrated that mRNA of *ARHGEF7, BCR, BRSK2* and *C9orf91* genes interact with miR-4258 with free binding energy – 91 kJ/mole and ΔG/ΔGm values equal to 89%.

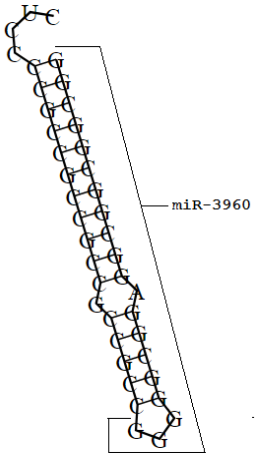
Table 2 – Characteristics of miR-3960 binding sites in the 5'-UTR mRNA genes having GCC trinucleotide repeat

Gene	Beginning of binding site	ΔG, kJ/mole	ΔG/ΔGm, %	Scheme of miRNA binding with mRNA genes
ABCC1	31	-116	93	5' - CCCUGC**GCCGCCGCCGCCGCC** - 3' |||| |||| |||||||||| 3' - GGGG-GCGGAGGCGGCGGCGG - 5'
ABCD3	46	-114	91	5' - **GCCGCCGCCGCCGCCGCCGCC** - 3' || ||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'
AFF2	14	-110	88	5' - GCCGCU**GCCGCCGCCGCCGCC** - 3' || ||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'
ANKH	34	-112	89	5' - CCUUCU**GCCGCCGCCGCCGCC** - 3' ||| ||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'
ANKRD13D	19	-108	86	5' - CCU**GCCGCCC**GCGCU**GCCGCC** - 3' ||| |||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'
BCL11A	177	-112	89	5' - CGUCCGCCC**GCCGCCGCCGCC** - 3' | ||||||| |||||||||| 3' - GGGGGCGGA-GGCGGCGGCGG - 5'
BCL2L11	61	-110	88	5' - GCCGCU**GCCGCCGCCGCCGCC** - 3' || ||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'
BLMH	182	-116	93	5' - CUCCCC**GCCGCCGCCGCCGCC** - 3' ||||| ||| |||||||||| 3' - GGGGG-CGGAGGCGGCGGCGG - 5'
C4orf19	73	-108	86	5' - GACCCC**GCCGCCGCCGCCGCC** - 3' ||| ||| |||||||||| 3' - GGGGG-CGGAGGCGGCGGCGG - 5'
CA10	772	-110	88	5' - GCUGCC**GCCGCCGCCGCCGCC** - 3' || ||||| |||||||||| 3' - GGG-GGCGGAGGCGGCGGCGG - 5'

It can be seen from the table 2 that the free energy of the interaction of the miR-3960 with mRNA of *ABCC1, ABCD3, AFF2, ANKH, ANKRD13D, BCL11A, BCL2L11, BLMH, C4orf19* and *CA10* genes are constituted more than - 108 kJ/mole with ΔG/ΔGm values equal to 86 -91%. Among mRNA genes having nucleotide GCC repeats only *ABCC1* and *BLMH* genes bind with high free energy - 116 kJ/mole with miR-3960. miR-3960 binding sites are located in region with GCC_7 and GCC_8 repeats between 31 (beginning of binding sites) – 57 and 182 (beginning of binding sites) – 211 nt (figure 2). The secondary structures given in the figure clearly show the preferential formation of bonds with miR-3960. The mRNA gene of *ABCD3* interact with miR-3960 with full GCC_7 repeat. However, the binding sites of miR-3960 and mRNA genes of *ANKH (*GCC_5*), ANKRD13D* (GCC_4) and *BCL11A* (GCC_4) have only four and five GCC repeat.



A - mir-3960 binding site in mRNA *ABCC1* gene



B - mir-3960 binding site in mRNA *BLMH* gene

Figure 2 – Secondary structures of location of miR-3960 binding sites in 5'UTR mRNA of *ABCC1* and *BLMH* genes

ABCC1 (*MRP1*) is well known for its role in rendering cancer cells resistant to chemotherapy. ABCC1 is expressed in brain capillaries on the abluminal surface between the luminal membrane (CD31) and astrocytic end-feet (GFAP). Moreover, the free energy of miR-3960 interaction with mRNA gene of *ABCD3* indicate –114kJ/mole with ΔG/ΔGm values equal to 91%. *ABCD3* is one of the most abundant peroxisomal membrane proteins, at least in hepatocytes, and has been reported to be involved in the transport of various fatty acids. Mutation in *ABCD3* have been found in two individuals affected by Zellweger syndrome.

Table 3 – Characteristics of miR-211-3p, miR-3155b binding sites in 5'-UTR and 3'-UTR mRNA genes having CUG trinucleotide repeat

Gene	miRNA	Region	Beginning of binding site	ΔG, kJ/mole	ΔG/ΔGm, %	Scheme of miRNA binding with mRNA genes
ACACA	miR-211-3p	5'UTR	61	-101	85	5' - GCGCGC**CUGCUGCUG**UCCCCGU - 3' |||| ||| |||||||||||| 3' - CGUGGGGA-AACGACAGGGACG - 5'
ANKRD 13D	miR-3155b	3'UTR	2056	-87	85	5' - UCU**CUGCUGCUG**AGCUUGG - 3' |||| ||||| |||||||| 3' - AGGG-UGACGUCUCGGACC - 5'

From the table 3 obtained data indicate that miR-211-3p and miR-3155b interact with mRNA of *ACACA* and *ANKRD13D* genes in 5'-3'untranslated regions. miR-211-3p binding site in the 5'UTR mRNA of *ACACA* gene is located from 61 to 82 nt with $(CUG)_3$ repeat. miR-211-3p interact with high free energy -101 kJ/mole mRNA of *ACACA* gene.

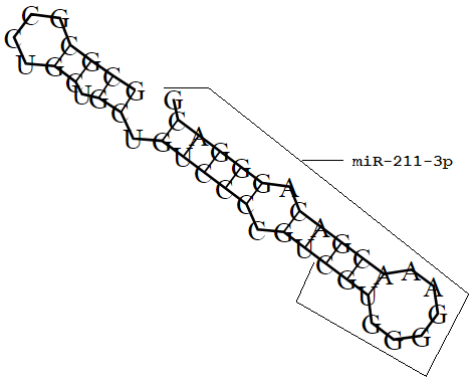


Figure 3 –
Secondary structures
of miR-211-3p binding sites
location in 5'UTR mRNA
of *ACACA* gene

Thus, the obtained results show that the greater number of genes are targets for miR-4258. miR-4258 binds to mRNA of 22 genes (*ABL2, ACVR1B, ADARB1, ADRBK1, APBA1, ARHGEF7, FMR1, B4GALT2, BCL11B, BCR, BRSK2, BRWD1, BTBD7, C11orf87, C9orf91, CACNA1A, CADM4, CAMK4, CARM1, CBFB, CBL* and *CCDC93*) with free binding energy -89 kJ/mole -(-93 kJ/mole) and ΔG/ΔGm value from 85% to 91%. Moreover, the binding sites of miR-3960 in mRNAs of *ABCC1, ABCD3, AFF2, ANKH, ANKRD13D, BCL11A, BCL2L11, BLMH, C4orf19* and *CA10* genes have highest free binding energy from -108 kJ/mole to -116 kJ/mole and ΔG/ΔGm value from 86% to 93%. The maximum free energy of miR-3960 binding to mRNA is -116 kJ/mole. miR-3960 plays an important role in osteogenic transdifferentiation of vascular smooth muscle cells (VSMCs) and contributes to vascular calcification [12]. miR-3960 has 1100 binding sites on 375 target mRNAs with $\Delta G/\Delta G_m$ values of 90% or more and belong to a group of unique miRNAs [13].

Conclusion. In this paper, we have presented characteristics of predicted binding sites of miRNAs with mRNA genes of non - polyglutamine trinucleotide disorders. The most interesting data concern the analysis of target genes of miR-4258, miR-3960 miR-211-3p and miR-3155b. The identified associations of these miRNAs and target genes can be used to develop molecular methods for the neurological disease diagnosis. Also to date, there is a limited researches on nucleotide repeats. Therefore, further analysis using interaction of miRNAs with mRNA genes of all nucleotide repeats (di-, tri-, tetra-, penta-) including CDS region may be very useful to obtain advances knowledge.

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А. М. Белкожаев, Р. Е. Ниязова

Әл-Фараби атындағы Қазақ ұлттық университеті, Алматы, Қазақстан

ПОЛИГЛУТАМИНДІ ЕМЕС ТРИНУКЛЕОТИДТІК БҰЗЫЛЫСТЫ ГЕНДЕРДІҢ Mrna-МЕН miR-4258, miR-3960, miR-211-3P ЖӘНЕ miR-3155b-ЛАРДЫҢ ӨЗАРА ӘРЕКЕТТЕСУІ

Аннотация. Тринуклеотидтік қайталанымды экспансия бұзылыстары емделмейтін, ақыр соңында өлімге әкеліп соғатын неврологиялық тұқым қуалайтын аурулар тобын құрайды. Жұмыс барысында miRNA-дың байланысатын сайттары MirTarget бағдарламасы арқылы болжанды. Бұл бағдарлама келесілерді анықтайды: miRNA-ның mRNA-мен байланыстыратын сайттарының басталуын; 5'UTR, CDS және 3'UTR-де mRNA сайттарының орналасуы; бос байланысу энергиясы (ΔG, кДж/моль) және miRNA-ның нуклеотидтерінің mRNA-мен әрекеттесу схемалары. Әр аймақ үшін ΔG/ΔGm қатынасы (%) есептелді, мұндағы ΔGm нуклеотидтердің толық тізбегі бар miRNA-ның бос байланыс энергиясына тең. Гендердің барлық нуклеотидтік тізбегі GenBank-тан алынды (http://www.ncbi.nlm.nih.gov). miRNA нуклеотидтер тізбегі miRBase мәліметтер базасынан алынды (http://www.mirbase.org). miRNA-гендік экспрессияны транскрипциядан кейінгі реттеуде маңызды рөл атқаратын, кодталмаған РНҚ-ның үлкен тобы. CGG, GCC, CUG қайталанатын полиглутаминдік емес тринуклеотидті бұзылыстардың 5' және 3' UTR-де гендердің mRNA-мен miRNA-дың байланысатын сайттарына сипаттама берілді. 2567 miRNA-дың 17494 адам гендерінің mRNA-мен байланысатын

сайттары анықталды. 5'UTR және 3'UTR-де mRNA-лары miRNA-мен байланысқан нуклеотидтердің қайталануы бар 206 ген байқалды. Осылайша, 5'UTR-де 2668, 3'UTR-де 3853 miRNA-мен байланысатын сайттар 85 % және одан да көп ΔG / ΔGm мәндерде орналасқан. Тринуклеотидтік CGG, GCC, CUG қайталануы бар 34 геннің mRNA-лары miR-4258, miR-3960 miR-211-3p және miR-3155b-ларына нысан екендігі анықталды. *ADARB1, C11orf87* және *CBFB* гендердің mRNA-ларының бос энергиясы ΔG/ΔGm 91 % мәнінде – 93 кДж/моль-ға тең, сонымен қатар *ARHGEF7, BCR, BRSK2* және *C9orf91* гендердің mRNA-ларының бос байланысатын энергиясы ΔG/ΔGm 89 % мәнінде – 91 кДж / моль-ға тең, miR-4258-бен байланысады. *ABCC1* және *BLMH* гендерінің mRNA-ларының GCC қайталанымдары бос байланысатын энергиясы – 116 kJ/mole болатын miR-3960-бен байланысады. miR-3960 байланыстыру сайттары GCC_7 және GCC_8 қайталанатын 31 аймақта орналасқан (байланыстыру сайттарының басталуы) – 57 және 182 (байланыстыру сайттарының басталуы) – 211 nt. GCC_7-қайталымның толық қайталануымен, *ABCD3* генінің mRNA-сы miR-3960-пен өзара әрекеттеседі. Дегенмен miR-3960 және *ANKH* (GCC_5), *ANKRD13D* (GCC_4) және *BCL11A* (GCC_4) гендерінің байланысу сайттарында тек төрт және бес GCC қайталануы бар. miR-3960-375 гендердің mRNA нысандарында ΔG/ΔGm 90 % үлесінде 1100 сайтпен байланысады немесе одан жоғары нысандарға арналған байланысу сайттары бар және ерекше miRNA тобына жатады. 5’ және 3’'UTR-де *ACACA* және *ANKRD13D* гендерінің mRNA-лары miR-211-3p және miR-3155b-мен өзара әрекеттеседі. *ACACA* гендерінің mRNA-лары 5'UTR-де miR-211-3p-пен байланысуы 61-ден 82 нт аралығында $(CUG)_3$ қайталануымен орналасқан. miR-211-3p жоғары бос энергиямен mRNA-да – 101 кДж/моль есебімен *ACACA* генімен әрекеттеседі. miRNA-лармен гендердің байланысу сипаттарын зерттеу нуклеотидтік қайталанатын экспансиялық бұзылыстарды диагностикалауда miRNA-мен ассоциациясын анықтауға көмектеседі.

Түйін сөздер: miRNA, mRNA, байланысатын сайт, тринуклеотидті қайталанатын экспансия.

А. М. Белкожаев, Р. Е. Ниязова

Казахский национальный университет им. аль-Фараби, Алматы, Казахстан

ВЗАЙМОДЕЙСТВИЕ miR-4258, miR-3960, miR-211-3P И miR-3155b С mRNA ГЕНОВ НЕПОЛИГЛУТАМИНОВЫХ ТРИНУКЛЕОТИДНЫХ РАССТРОЙСТВ

Аннотация. Расстройства экспансии тринуклеотидных повторов представляют собой группу доминантно-наследуемых неврологических заболеваний, которые неизлечимы и в конечном итоге приводят к летальному исходу. Изменение экспрессии miRNA считается отличительным признаком многих заболеваний, включая нарушения экспансии тринуклеотидных повторов. В настоящей работе сайты связывания miRNA были предсказаны программой MirTarget. Программа определяет: начало сайтов связывания miRNA с mRNA; расположение сайтов в 5'UTR, в CDS и в 3'UTR mRNA; свободную энергию гибридизации (ΔG, kJ/mole) и схемы взаимодействия нуклеотидов miRNA с mRNA. Для каждого сайта рассчитывали отношение ΔG/ΔGm (%), где ΔGm равна свободной энергии связывания miRNA с полностью комплементарной нуклеотидной последовательностью. Все нуклеотидные последовательности mRNA генов заимствовали из GenBank (http://www.ncbi.nlm.nih.gov). Нуклеотидные последовательности miRNA получены из базы miRBase (http://www.mirbase.org). miRNA представляет собой большое семейство консервативных некодирующих РНК, играющих ключевую роль в посттранскрипционной регуляции экспрессии генов. Приведены характеристики сайтов связывания miRNA в 5'UTR и 3'UTR mRNA генов неполиглутаминовых тринуклеотидных расстройств с повторами CGG, GCC, CUG. Были определены сайты связывания 2567 miRNA с mRNA 17494 генов человека. Было обнаружено 206 генов с нуклеотидными повторами, mRNA которых связывались с miRNA в 5'UTR и 3'UTR. Таким образом, 2668 сайта связывания miRNAs расположены в 5'UTR, 3853 - в 3'UTR со значениями ΔG/ΔGm, равными 85% и более. Было обнаружено, что mRNA 34 генов, имеющих тринуклеотидные CGG, GCC, CUG повторы, были мишенью для miR-4258, miR-3960 miR-211-3p и miR-3155b. miR-4258 связывается с mRNA генов *ADARB1, C11orf87* и *CBFB* со свободной энергией взаимодействия - 93 кДж/моль и ΔG/ΔGm 91%, с mRNA генов *ARHGEF7, BCR, BRSK2* и *C9orf91* со свободной энергией взаимодействия - 91 кДж/моль и ΔG/ΔGm 89%. miR-3960 связывается в повторах GCC с mRNA генов *ABCC1* и *BLMH* со свободной энергией взаимодействия - 116 кДж/моль. Сайты связывания miR-3960 расположены в области с повторами GCC_7 и GCC_8 между 31 (начало сайтов связывания) - 57 и 182 (начало сайтов связывания) - 211 нт. mRNA гена *ABCD3* взаимодействует с miR-3960 с полным повтором GCC_7. Однако сайты связывания генов miR-3960 и mRNA генов *ANKH* (GCC_5), *ANKRD13D* (GCC_4) и *BCL11A* (GCC_4) имеют только четыре и пять повторов GCC. miR-3960 имеет 1100 сайтов связывания на 375 mRNA - мишенях со значениями ΔG / ΔGm 90% и более и относятся к группе уникальных miRNA. miR-211-3p и

miR-3155b взаимодействуют с mRNA генов *ACACA* и *ANKRD13D* в 5'-3'-нетранслируемых областях. Сайт связывания miR-211-3p в 5'UTR mRNA генов *ACACA* расположен от 61 до 82 нт с повторением $(CUG)_3$. miR-211-3p взаимодействует с mRNA высокой свободной энергии -101 кДж / моль гена *ACACA*. Изучение характеристик связывания miRNA и генов поможет выявить связь miRNA с генами с тринуклеотидными повторами для рекомендации для диагностики нарушений экспансии нуклеотидных повторов.

Ключевые слова: miRNA, mRNA, сайт связывания, экспансия тринуклеотидных повторов.

Information about authors:

Belkozhayev A.M., PhD-student, al-Farabi Kazakh National University, Almaty, Kazakhstan; ayaz_jarkent@mail.ru; https://orcid.org/0000-0001-7429-4994

Niyazova R.Ye., c.b.s. professor; al-Farabi Kazakh National University, Scientific research institute of biology and biotechnology problems, Almaty, Kazakhstan; raygul.nyiyazova@kaznu.kz; https://orcid.org/0000-0002-7946-1189

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A. K. Yedilova, Z. A. Inelova

Al-Farabi Kazakh National University, MES RK, Almaty, Kazakhstan.
E-mail: edil_aigul@mail.ru, z.inelova2015@gmail.com

FEATURES OF THE STRUCTURE OF NATURAL POPULATIONS *HUMULUS LUPULUS* L. (REVIEW)

Abstract. The article provides an overview of the structural features of the natural populations of *Humulus lupulus* L. in the world and in Kazakhstan. Currently, the use in medicine of natural products, medicines and biologically active substances of plant origin is increasing. Significant parts of the medicinal raw materials are wild plants. The need for medicinal plant raw materials (medicinal plants) is not decreasing; the technology of its procurement and reproduction in natural conditions wants significant perfection. It is known that they have a milder, more complex effect on the human body and are used in the treatment of many chronic diseases. The growing anthropogenic impact on populations of valuable medicinal plants is decreasing their stocks of raw materials. In this regard, the study of biological characteristics and the development of scientifically based agricultural techniques for the cultivation of many medicinal plants are becoming relevant. *Humulus lupulus* L. (common hop) is a valuable medicinal plant. They are used as painkillers, sedatives, hypnotics for increased nervous irritability, sleep disturbances, neuralgia, vegetovascular dystonia, mild coronary spasms, tachycardia, and in the early stages of hypertension. According to the classification of medicinal plant resources, *Humulus lupulus* L. is a plant with a wide range, but with a limited supply of raw materials. In places of growth of *Humulus lupulus* L. does not form large thickets [1].

Recently, a comprehensive approach has been applied in the study of natural plant populations, including ontomorphological and population-ecological studies. This makes it possible to objectively assess the state of the species in the cenosis and predict its future behavior. In this regard, a comprehensive study of the natural populations of *Humulus lupulus* L. is of great relevance.

Hops (*Humulus lupulus* L.) is an important crop worldwide, known as the main flavor ingredient in beer. A diversified brewing industry requires a variety of flavors, superior technological properties and sustainable agronomy, which are the center of advanced molecular breeding efforts in hops. Hop breeders have been limited in their ability to create strains with desirable traits, however, due to unusual and unpredictable inheritance patterns and the associated non-Mendelian segregation of genetic markers [2].

The use of hops has recently been undergoing a new change, driven by a growing international preference for more intensely flavored beer, supported by the craft-brewing sector. This movement led to the introduction of much more hops at various stages of beer production and to an ever-growing search for new flavors. Some hop varieties have thus received particular attention, including several older typical hops mostly used to date, although an intensive search for new varieties dubbed "Green Gold" has also taken place. A large number of new exquisite varieties have been described and are increasingly appreciated in the market. Global hop growing areas have increased over the past 5 years, although total world beer production has declined over the same period, confirming the trend of using more hops per liter of beer. In addition, a wide range of pharmacological properties have been described for hops and its derivatives, namely antioxidant, anti-inflammatory and antitumor properties, which are of great importance for the pharmaceutical industry. The bioactivity of beer can depend on the use of hops, which can become an important tool for brewers aiming to develop functional products.

Taken together, the compounds isolated from *Humulus lupulus* L. have a wide range of biological activity, such as anti-inflammatory action, antimicrobial action, antioxidant action, antiproliferative effects, cytochrome P450 effects, glucose metabolism effects, hormonal effects, lipid effects and sedative / hypnotic effects.

Therefore, the purpose of this Chapter is to describe the importance of hops in this new direction of beer production, market overview of hops, varieties, forms and methods of use, composition, value in bioactivity of beer and new discoveries in research hops [3].

Key words: *Humulus lupulus* L., essential oils, phenolic compounds, lupuluin.

Introduction. The generic name of hops "humulus" comes from the Latin word "humus" – land, soil and indicates that it creeps on the ground. The species name "lupulus" translates as "wolf", indicating that the plant wraps around the tree like a predator. In ancient times, it was believed that hops is a parasite of trees and sucks juices from them, from which the trees dry up. However, in fact, the plant uses the trunk and crown of trees only for support.

Previously, scientists attributed ordinary hops to the family of mulberry (Moraceae). Since 1972, most systematic botanists, based on embryonic and chemotaxonomic studies, have come to the conclusion that creeping hop's and other plants of the hops genus (Humulus) belong to the Cannabaceae family, which is part of the Urticales order, and consider that hops has more typical features characteristic of the hemp family.

However, even now, in some publications on botany and pharmacognosy, as well as in popular scientific literature, hops belong a statement to the mulberry family.

In addition, some botanists believe that four species belong to the genus hops: common hops, heart-shaped hops-*Humulussordifolius*, American hops-*Humulusamericanus* R., climbing hops-*Humulus scandens* (Lour.) Merr., which is known as the Japanese hop-*Humulus japonicus*Sieb. et.Zucc. Since the first three species are very similar to each other and do not have significant distinguishing features from the climbing hops, most botanists do not consider them separate species, but refer to varieties or races of this species. Therefore, because of modern Botanical research to the genus hops include two species: common hops-*Humulus lupulus* L. and climbing hops-*Humulus scandens* (Lour.) Merr.

History of hops. Hops were known as a wild plant already during ancient times. Historical findings allow us to conclude that their origin was in Asia, more precisely in fertile Mesopotamia, the lowlands of the Caucasus and southern Siberia [4]. Botanically, however, the hop plant is believed to have originated in China because China is the only country in the world where all three-hop species (H. Lupulus, H. Japonicus, and H.Yunnanensis) occur naturally [5-7]. Hops have been cultivated since the beginning of our era. Records showing that hops were used for seasoning and canning beer by Slavic tribes date back to at least 1500-1000 BC. Other people began using hops for brewing from the 13th century (ad). Until the 12th century (ad), however, hops were probably obtained only by harvesting wild plants [8].

Over time, people discovered the healing effects of hops, which then found its place in folk medicine. Hops were used, according to the ancient herbarium, to treat various diseases, such as unpleasant foot odor, liver disease of bitter and aromatic properties. In addition, hops are used in the cosmetic and pharmaceutical industries, especially for their antimicrobial and antiviral effects. The fact that hops were originally used and added to beer for its antimicrobial activity as a preservative classifies this plant as a natural source of compounds with biological action.

An increasing number of pathogenic strains of bacteria (and viruses) resistant to various types of antimicrobials pose a serious medical problem. Secondary metabolites of hops have been described for constipation, sleep disorders and for blood purification [9,10]. Records from the 7th and 9th centuries' ad show that the earliest predecessors of hop gardens were founded under the monastic administration, where hops were grown for their medicinal properties along with other herbs [11]. Even at that time, hops extracts were recognized for their anti-inflammatory and antiseptic effects, as decoctions made from hops were used to treat poorly healing wounds.

Another example of this treatment is the use of heated hops as a poultice [12] for pneumonia or the treatment of fever using hops decoctions [13]. Alcohol extracts of hops have also been used in Chinese medicine to treat pulmonary tuberculosis or acute bacterial dysentery, and have been part of Ayurvedic procedures [14]. Some recent studies have shown that alcohol extracts from hops have a strong antispasmodic effect on smooth muscles and are therefore effective in conditions characterized by tension of visceral smooth muscles, including nervous colitis, nervous dyspepsia, palpitations, nervous or irritable cough and asthma [15,16].

Phytogeography and botany of hops. Wild hops, which grows in humid areas near rivers, are widespread in vast areas of Europe, Asia and North America [17].

Today, cultivated hop production is concentrated in areas with a humid, temperate climate, with most of the global production coming from the Middle East.

Hop yards are an integral part of the countryside around Europe, North and South America, South Africa, Australia and New Zealand. Varietal plants are grown, as a rule, on large flat areas with acidic soil. Currently, the largest hop producers are Germany, the USA, China and the Czech Republic (production in 2014 amounted to 25 338, 38 499, 6 887 and 6 202 tons, respectively) [18].

Some botanists believe that climbing hops come from the Mediterranean region. However, reliable data that would confirm such an origin are absent in the literature on botany. M. I. Vavilov attributed hops to the Mediterranean focus of the origin of cultivated plants, the range of which extends far to the north, where, obviously, it was first introduced into the culture. V. Linke considers the homeland of hops Northern and Central Europe. According to L. Venta, the primary geobotanical region of hop distribution is the fertile valleys and foothills of the Caucasus, as well as the Black Sea coast. Hence, during the resettlement of the Slavs in the II-V century AD hops spread throughout Europe. As a wild plant, climbing hops are widely distributed in the forest zone of the temperate climate of Eurasia: it grows throughout Europe (reaching the Arctic belt), the Caucasus, Western Siberia, Altai, the Far East, and Central Asia. Wild hops are distributed throughout the forest and forest-steppe zones of Ukraine, where they grow in humid broad-leaved forests, along the banks of rivers and marshes, in ravines, on the edges, among shrubs, near roads and fences.

Hops have long been widely cultivated for the needs of the food industry as a technical culture in many countries, in particular in France, England, the Czech Republic, southern Germany, North-east China, South Africa, the USA, Argentina, Chile, Brazil, Australia and New Zealand. In Ukraine, specialized hop cultivation farms are located mainly in the northern regions (more than 60% of all Ukrainian hoppers).

It grows in river valleys, ravines, shrubbery, forest edges, and is bred in gardens and kitchen gardens. Found in Tobyl-Esil, Irtysh, Semey, Kokshetau, Aktobe, Western and Eastern small hills, Altai, Tarbagatai, Dzhungarsky Alatau, ZailiyskyKungei Alatau, Karatal. The general distribution is South Europe, the Caucasus, Western Siberia, Western Europe, the Mediterranean, Asia Minor, and North America [19].

In the Russian Far East, common hops used to be known only in culture. However, later botanists in some areas of revealed insignificant thickets of feral and introduced hops. Since ordinary hops are widely cultivated in many regions of the world, in some places, it becomes an alien and feral species; it is sometimes quite difficult to establish clear boundaries of its natural range.

When discussing the technological aspects or medical effects of products derived from hops, it should be noted that these products are obtained only from cones from female plants. *Humulus lupulus* L. is a dioecious climbing perennial creeper from the Cannabis family [20], which also includes the genera Cannabis (hemp) and Celtis (blackberry). The leaves are located on the stem in the opposite way on stems from seven to 12 cm long and have roughly jagged edges in the shape of a heart. Female flowers (often bumps) are made up of short green spikelets (called hop cones, seed cones or strobiles) and secrete a fine yellow resinous powder from structures called lupulin glands. Lupulin glands synthesize resins and essential oils [21,22], which characterize the bitter taste and aroma of beer, but also stabilize the foam and the final product [23]. Special vacuoles of the external system of lupulin glands are rich brewing tanks and pharmacologically important substances, which are often called secondary metabolic products.

Male plants are characterized by small yellow flowers and are important for breeding new varieties! Otherwise, male plants are removed from hop fields to prevent fertilization of female plants and seed production [24].

Medicinal raw material. For medical needs use inflorescences hops ordinary, which mistakenly call soplodiyami-women's "cones" (StrobuliHumulilupuli, or StrobuliLupuli), and glands hops (Glandulae Lupuli), or lupulin (Lupulinum). Lupulin-glands in the form of a bright yellow coarse-grained powder called hop flour. Lupulin is derived from the dried cones of the knocking in the city. The finished product has the form of a heterogeneous coarse-grained adhesive substance of a greenish-yellow color, which gradually acquires a reddish hue in the air. For the needs of the pharmaceutical industry, the inflorescences of hops are harvested in mid-August, when they acquire a greenish-yellow color (later they become brownish, dry and after drying, they easily crumble), tear them off with their hands together with the pedicels. The collected raw materials are quickly dried in the shade in the fresh air, spreading a thin layer on paper or fabric. It is better to store cones in non-ground form, since they lose activity when crushed [25].

Ordinary hops and its medicinal raw materials - "hop cones" - are official in Ukraine and Russia, as well as in Germany, France, Spain, Portugal, Greece, Romania, Mexico, and the United States. Lupulin entered the Pharmacopoeia of Germany, Portugal, Switzerland, Italy, Austria, Holland, Brazil, and USA.

The inflorescence of the hop plant, *Humulus lupulus* L., contains unique compounds used primarily for beer production, but also contain compounds with bioactive properties, with the potential to improve human health. Hops are bitter soft resins and aromatic oils derived from their lupulin glands are essential for beer. The third component in lupulin is solid resins, which are undesirable in beer but contain biologically active polyphenols that have been shown to reduce the risk of disease in humans and animals. Extracts of hard hop resins are rich in antioxidants and estrogenic prenyl flavonoids and are used today as food additives, especially to relieve menopausal discomfort. However, the bioavailability of prenylflavonoids depends on their metabolism by the intestinal microbiota. This review focuses on women's use of prenyl flavonoid-rich hop extracts to alleviate complaints during menopause with the added benefit of reducing the risk of diseases including metabolic syndrome and cancer. The role of the gut microbiota and bioavailability of prenyl flavonoids will also be discussed [26].

Biologically active substance. The main biologically active substances that determine the pharmacological activity of hop cones are bitterness and polyphenolic compounds, as well as essential oil. These are the most important compounds of hops; they are of particular importance in pharmaceutical production and in scientific and practical medicine. Hop cones contain 0.2-1.8% essential oil, 2-5% polyphenolic compounds and 5 to 26% water.

Lupulin contains 1-3% essential oil, about 5% bitterness, 50-70% resinous substances, as well as waxes, yellow pigment, choline, hypoxanthin, adenine, ceratinic and isopropylacrylic acids, as well as Humulin (hopein) - alkaloid-like substance with narcotic effect [27].

Bitterness of hops, related to polyketide allforgiving type, are a mixture of acidic and resinous substances. According to J. Kuroiwe and E. Kukubo (1973), more than 90 chemical compounds were isolated in the analysis of hop bitterness. According to the international nomenclature, they are called "common resins". They are soluble in cold methanol and diethyl ether. According to the classification, there are hard and soft resins. Solid resins are a fraction of common resins insoluble in paraffin hydrocarbons, hexane, and petroleum ether with a low boiling point. Soft resins-fraction of General resins, soluble in paraffin hydrocarbons with low boiling point, consisting of α-and β-acids, α - and β-soft resins. Uncoated soft resins are a mixture of α-and β-soft resins-oxidation products of α-and β-acids, respectively. The composition of hop resins is shown in the diagram.

Phenolic compounds contained in plant raw materials are of interest to science and industry, because their chemical structure causes the manifestation of different physiological activity.

One of the sources of phenolic compounds is common hops-an important technical crop, which is widely used both in medicine and in the brewing industry. The importance of phenolic compounds of hops for brewing is their participation in slowing down oxidative processes, thereby increasing the shelf life of beer. Nevertheless, on the other hand, it is believed that the interaction of some polyphenols with proteins leads to colloidal turbidity of the drink [28].

Currently, the industry uses mainly hop products (up to 80% of hop raw materials). They are extremely complex mixtures of chemical compounds, and the technology of production, and, consequently, the composition of individual species is dramatically different. Despite the fact that hops have been subjected to quite a thorough study, phenolic compounds of hop products from a chemical point of view have not been studied enough.

Among the phenolic compounds contained in hop raw materials, the Central place is occupied by prenylated chalcons, which exhibit high antitumor, antioxidant, phytoestragenic, anti-inflammatory and antiviral activity. Many laboratories around the world are developing methods for isolating these compounds. However, due to the multicomponency and complexity of the composition of hop products, the existing schemes do not allow obtaining compounds of a high degree of purity, and are quite complex in hardware design. Therefore, a promising direction is the development of schemes for the isolation of prenylated chalcons, devoid of these shortcomings, and the actual task is to study the chemical composition of phenolic compounds of hop products [29].

The cultivation of hops for this purpose has been traced back to Germany, 736 ad. for hops, despite its long successful history of domestication, modern breeding practice is fraught with a number of

problems. For example, although hops are usually cultivated vegetatively using rhizomes, sexual crosses are necessary to breed new disease-resistant and chemically desirable varieties. The long history of cultivation includes colchicine-induced polyploidization and introgression of genetically distinct wild populations. Recent genetic, genomic, and quantitative character analyses have shown that the hop genome is complex and structurally diverse. Violations in the genetics of hop transmission are reflected in the non-Mendelian distortion of segregation and displacement of the ratio [30].

Hops (*Humulus lupulus*, Cannabinaceae) - is a source of a number of biologically active compounds, such as essential oils, bitterness and flavonoids. One of the most interesting from a pharmacological point of view are the flavonoids of hops, represented by flavonol glycosides and prenylated flavonoids [31]. While flavonol glycosides are ubiquitous in green plants, the prevalence of prenylated flavonoids is limited to a small number of species, primarily the order urticaceae, the mulberry Mogaseae family, and the hemp Cannabinaceae (the latter family includes the hop plant). Hops are almost the only significant source of prenylated flavonoids such as xanthohumol and isoxanthohumol.

Interest in natural flavonoids is associated with their pronounced antioxidant properties, a number of types of flavonoids have anti-allergic, anti-inflammatory, antiviral, antibacterial properties and other types of biological activity. In addition, xanthohumol and isoxanthohumol of hops exhibit antiproliferative and anticancerogenic properties [32]. According to experimental data of many scientists, the presence of isoprenoid chains leads to various modifications of biological activity, which is mainly associated with a pronounced affinity with biological membranes and more pronounced interactions with proteins.

Hops are part of a number of well-known drugs and many registered dietary supplements (BAA) to food.

Humulus lupulus - it is a specialized crop with potential for new uses beyond its most common use in the brewing industry. As a medicinal plant already used in the food industry, hops are a compelling candidate for further scientific research, especially biochemical and molecular genetic studies. However, since hops are a niche crop, crop improvement studies should have superior cost-effectiveness [33].

In brewing practice, the use of appropriate hops is important for the production of stable and high-quality beer. However, batches of hops of the same variety cultivated in different geographical regions can exhibit significant biochemical differences, leading to specific taste and aroma characteristics of the beer. Genetic studies illustrate the complementarity of genetic and biochemical fingerprinting methods for the complete characterization of hop batches. Using genotyping by sequencing (GBS), a set of 1,830 polymorphic single nucleotide polymorphism markers (SNP) yields 48 unique genetic imprints for a collection of 56 commercial hop varieties. Three groups of varieties consisting of somaclonal variants could not be further differentiated using this set of markers. Biochemical marker information provides additional value for the characteristics of hop samples of this variety grown in different geographical locations [34].

Humulus lupulus L. (Cannabaceae), commonly called hops, is widely grown worldwide for its use in the brewing industry. Its female inflorescences (hops) are especially prized by brewers because they produce some secondary metabolites that give the beer bitterness, flavor and antiseptic properties. These metabolites exhibit numerous biological activities, including antimicrobial, sedative, and estrogenic properties. This review presents a list of chemical properties of hops with an emphasis on secondary metabolites and their biological activity. These compounds, of biological interest, are mainly formed in female inflorescences, while other parts of the plant synthesize them only in small quantities [35].

Hops ordinary (*Humulus Lupulus* L.) - root herbaceous plant. The length of the stem of hops 3-5 m, sometimes more, has a faceted, sloping, on the hair with low-rounded spines. The bottom of the leaves is a heart-shaped opening, at the edges-toothed, mouth. Leaf satellites of Lancet. The flowers of the males are collected on the tips of the stem and branches as tassels. Females are located in the saddle, on the upper leaf scaffolds. The nut is round. In June – July bloom, fruits ripen in July-August. In medicine, the use melnichnye bottles. Vitamin C is found in the leaves. On the Kazakh land, it is found in the Northern part of the West Kazakhstan region, along Tobolsk, Irtysh, Ishim, Mugalzhar, Aktobe,Kokshetau [36].

Summing up, undoubtedly, due to the increased anthropogenic impact on the environment, as well as the weakening of the adaptation of nature, there is a need for actions to ensure the restoration of natural resources now.

In addition, the best knowledge can be used in the hope of breeding programs that allow the targeted enrichment of new varieties in the right compounds.

Given the key role of hops, there is great scientific interest in the use of hops extract to create for the taste of beer and study the molecular and biochemical basis of hops.

In world practice, the use of natural products, medicines and biologically active substances of plant origin in medicine is currently increasing. Significant parts of the medicinal raw materials are wild plants. The need for medicinal plant raw materials (medicinal plants) is not reduced; the technology of its preparation and reproduction in natural conditions requires significant perfection.

А. К. Едилова, З. А. Инелова

Әл-Фарабиатындағы Қазақ ұлттықуниверситеті, Алматы, Қазақстан

ТАБИҒИ ПОПУЛЯЦИЯЛАР ҚҰРЫЛЫМЫНЫҢ ЕРЕКШЕЛІКТЕРІ *HUMULUS LUPULUS* L. (ШОЛУ)

Аннотация. Мақалада әлемдегі және Қазақстандағы *Humulus lupulus* L. табиғи популяциялар құрылымының ерекшеліктері көрсетілген. Қазіргі уақытта медицинада табиғи өнімдерді, дәрі-дәрмектерді және өсімдік тектес биологиялық белсенді заттарды пайдалану ұлғайып келеді. Жабайы өсімдіктер дәрілік шикізаттың елеулі бөлігін құрайды. Дәрілік өсімдік шикізатына (дәрілік өсімдіктерге) қажеттілік азаймайды, оны дайындау және табиғи жағдайларда қайта өндіру технологиясы айтарлықтай жетілдіруді қажет етеді. Олар адам ағзасына кешенді әсер етеді және көптеген созылмалы ауруларды емдеуде қолданылады. Антропогендік әсердің артып отыруы салдарынанбағалы дәрілік өсімдіктер популяциясындағы шикізат қорларын азаяды. Осыған байланысты биологиялық ерекшеліктерді зерттеу және көптеген дәрілік өсімдіктерді өсірудің ғылыми негізделген агротехникасын әзірлеу өзекті болып отыр. *Humulus lupulus* L. (кәдімгі құлмақ) – бағалы дәрілік өсімдік. Олар жоғары жүйке қоздырғыштығы, ұйқының бұзылуы, невралгия, вегето-тамыр дистониясы, коронарлық тамырлардың айқын көрінбейтін спазмалары, тахикардия кезіндегі, гипертониялық аурудың ерте сатыларындағы ауырсыну кезінде, седативті, ұйықтататын дәрі ретінде қолданылады. *Humulus lupulus* L. дәрілік өсімдіктер ресурстарын жіктеу бойынша,*Humulus lupulus* L. өсетін жерлер қарастырылады [1].

Соңғы уақытта, өсімдіктердің табиғи популяцияларын зерттеуде, онтоморфологиялық және популяциялық-экологиялық зерттеулерді қамтитын кешенді тәсіл қолданылып келеді. Бұл ценоздағы түрдің жай-күйін объективті бағалауға және болашақта оның мінез-құлқын болжауға мүмкіндік береді. Осыған байланысты *Humulus lupulus* L. табиғи популяцияларын кешенді зерттеу үлкен маңызға ие.

Құлмақ (*Humulus lupulus* L.) сырадағы негізгі дәм – ингредиент ретінде белгілі, бүкіл әлемдегі маңызды мәдениет. Әртараптандырылған сыра қайнату өнеркәсібі құлмақ алдыңғы қатарлы молекулалық селекциялық күш-жігердің орталығы болып табылатын дәмдердің, тамаша технологиялық қасиеттердің және тұрақты агрономияның әртүрлілігін талап етеді. Құлмақ селекционерлері қалаған белгілері бар штаммдар жасау қабілетіне шектеулі болды, алайда тұқым қуалаудың ерекше және болжанбаған модельдеріне және генетикалық маркерлердің Менделевтік сегрегациясына байланысты [2].

Соңғы уақытта құлмақ пайдалану қолөнер сыра қайнату секторы қолдайтын неғұрлым қарқынды хош иістендірілген сыраны халықаралық деңгейде өсіп келе жатқан артықшылық тудырған жаңа өзгерісті бастан кешуде. Бұл қозғалыс сыра өндірісінің әртүрлі кезеңдерінде құлмақтың көп мөлшерін енгізуге және ұдайы өсіп отыратын жаңа талғамды іздеуге алып келді. Осылайша, құлмақтың кейбір сорттары – негізінен қазіргі уақытқа дейін пайдаланылып келген ескі типтегі сорттар, бірақ, соның ішінде "жасыл алтын" деп аталатын жаңа сорттарды қарқынды түрде іздеу жұмыстары ерекше назар аудартады. Таңдаулы жаңа сорттардың көптеген саны анықталып, сипатталған және нарықта көбірек бағаланады. Құлмақ өсірудің жаһандық алаңдары соңғы 5 жылда ұлғайды, бірақ сыраның жалпы әлемдік өндірісі сол кезеңде қысқарды.Бұл жайт сыраның бір литріне құлмақтың көп мөлшерін пайдалану үрдісін растайды. Бұдан басқа, құлмақ және оның туындылары үшін фармакологиялық қасиеттердің кең спектрі, атап айтқанда, фармацевтикалық өнеркәсіп үшін үлкен маңызы бар антиоксиданттық, қабынуға қарсы және ісікке қарсы қасиеттері сипатталған. Сыраның биоактивтілігі құлмақ пайдалануға байланысты болуы мүмкін, сондай-ақ ол функционалдық өнімдерді әзірлеуге бағытталған сыра қайнатқыштары үшін маңызды құрал болуы мүмкін.

Қабынуға қарсы әрекет, микробқа қарсы әрекет, антиоксидантты әрекет, антипролиферативті әсерлер, P450 цитохромының әсерлері, глюкоза метаболизмнің әсерлері, гормональды әсерлер, липидті әсерлер және седативті / гипнотикалық әсерлер сияқты биологиялық белсенділіктің кең спектріне ие.

Сондықтан осы тараудың мақсаты сыраны өндірудің осы жаңа бағытындағы құлмақ мәнін сипаттау, құлмақ нарығына, сорттарға, формаларға және пайдалану әдістеріне, құрамына, сыраның биобелсенділігіне және құлмақ зерттеулеріндегі жаңа жаңалықтарға шолу жасау болып табылады [3].

Түйін сөздер:*Humulus lupulus* L.,эфир майлары, фенолды қосылыстар, лупулуин.

А. К. Едилова, З. А. Инелова

Казахский национальный университет им. аль-Фараби, Алматы, Казахстан

ОСОБЕННОСТИ СТРУКТУРЫ ПРИРОДНЫХ ПОПУЛЯЦИЙ *Humulus lupulus* L. (ОБЗОР)

Аннотация. В статье представлен обзор особенностей структуры природных популяций *Humulus lupulus* L. в мире и в Казахстане. В настоящее время увеличивается использование в медицине натуральной продукции, лекарств и биологически активных веществ растительного происхождения. Существенную часть лекарственного сырья составляют дикорастущие растения. Потребность в лекарственном растительном сырье (лекарственных растениях) не уменьшается, технология его заготовки и воспроизводства в природных условиях желает значительного совершенства. Известно, что они оказывают более мягкое, комплексное действие на организм человека и используются при лечении многих хронических заболеваний. Растущее антропогенное воздействие на популяции ценных лекарственных растений сокращает запасы их сырья. В связи с этим актуальными становятся изучение биологических особенностей и разработка научно обоснованной агротехники возделывания многих лекарственных растений. *Humulus lupulus* L. (хмель обыкновенный) – ценное лекарственное растение. Их используют как болеутоляющее, седативное, снотворное средство при повышенной нервной возбудимости, нарушениях сна, невралгии, вегетососудистой дистонии, нерезко выраженных спазмах коронарных сосудов, тахикардии, при ранних стадиях гипертонической болезни. По классификации ресурсов лекарственных растений *Humulus lupulus* L. – растение с широким ареалом, но с ограниченным запасом сырья. В местах произрастания *Humulus lupulus* L. не образует крупных зарослей [1].

В последнее время в изучении природных популяций растений применяется комплексный подход, включающий онтоморфологические и популяционно-экологические исследования. Это дает возможность объективно оценить состояние вида в ценозе и прогнозировать его поведение в будущем. В связи с этим, комплексное изучение природных популяций *Humu luslupulus* L. имеет большую актуальность.

Хмель (*Humulus lupulus* L.) является важной культурой во всем мире, известной как основной вкусовой ингредиент в пиве. Диверсифицированная пивоваренная промышленность требует разнообразия вкусов, превосходных технологических свойств и устойчивой агрономии, которые являются центром передовых молекулярных селекционных усилий в хмеле. Селекционеры хмеля были ограничены в своей способности создавать штаммы с желательными признаками, однако из-за необычных и непредсказуемых моделей наследования и связанной с ними неменделевской сегрегации генетических маркеров [2].

В последнее время использование хмеля переживает новое изменение, вызванное растущим на международном уровне предпочтением более интенсивно ароматизированного пива, поддерживаемого сектором ремесленного пивоварения. Это движение привело к введению гораздо большего количества хмеля на различных этапах производства пива и к постоянно растущему поиску новых вкусов. Некоторые сорта хмеля, таким образом, получили особое внимание, в том числе несколько старых типичных хмелей, в основном используемых до настоящего времени, хотя интенсивный поиск новых сортов, получивших название “Зеленое золото”, также имел место. Большое количество новых изысканных сортов было описано и все больше ценится на рынке. Глобальные площади выращивания хмеля увеличились за последние 5 лет, хотя общее мировое производство пива сократилось за тот же период, что подтверждает тенденцию использования большего количества хмеля на литр пива. Кроме того, для хмеля и его производных описан широкий спектр фармакологических свойств, а именно антиоксидантные, противовоспалительные и противоопухолевые свойства, которые имеют большое значение для фармацевтической промышленности. Биоактивность пива может зависеть от использования хмеля, который может стать важным инструментом для пивоваров, нацеленных на разработку функциональных продуктов.

Взятые вместе, соединения, выделенные из *Humulus lupulus* L., обладают широким спектром биологической активности, таким как: противовоспалительное действие, противомикробное действие, антиоксидантное действие, антипролиферативное эффекты, эффекты цитохрома P450, глюкоза эффекты метаболизма, гормональные эффекты, липидные эффекты и седативные / гипнотические эффекты.

Поэтому целью настоящей статьи является описание значения хмеля в этом новом направлении производства пива, обзор рынка хмеля, сортов, форм и методов использования, состава, значения в биоактивности пива и новых открытий в исследованиях хмеля [3].

Ключевые слова: *Humulus lupulus* L., эфирные масла, фенольные соединения, лупулуин.

Information about authors:

Yedilova A.K., PhD student, “Al-Farabi Kazakh National University”, MES RK, Almaty, Kazakhstan; https://orcid.org/0000-0002-6733-0878

Inelova Z.A., Deputy Dean for teaching and educational work, candidate of biological sciences, associate Professor, “Al-Farabi Kazakh National University”, MES RK, Almaty, Kazakhstan; https://orcid.org/0000-0001-8778-5848

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D. Sh. Akimzhanov[1], P. A. Esenbekova[2], B. K. Yelikbayev[1]

[1]Kazakh National Agrarian university, Almaty, Kazakhstan;
[2]Zoology institute, CS MES RK, Almaty, Kazakhstan.
E-mail: darhan-14@mail.ru, esenbekova_periz@mail.ru, bek29@bk.ru

MATERIALS FOR THE HEMIPTERA FAUNA (HETEROPTERA) OF ALTYN EMEL STATE NATIONAL NATURE PARK

Abstract. As a result of research performed at Altyn-Emel SNPP, we noted 19 species of hemiptera (true bugs), belonging to 3 families. By nutrition links the identified true bugs are: polyphytophages - 3 species (16%), wide oligophytophages - 5 species (26%), narrow oligophytophages - 8 species (42%), zoophytophages - 3 species (16%). By the number of generations per year, the hemipteraofSNPP Altyn-Emel are divided into 3 groups: monovoltaic - 6 species (37%), bivoltaic - 10 species (53%), polyvoltaic - 3 species (10%). By confinement to the habitats, the hemiptera of SNPP Altyn-Emel are divided into several groups: hortobionts (12 species, 63%), herpeto-hortobionts (4 species, 21%), herpetobionts (3 species, 16%). The following ecological groups of species were distinguished: meso-xerophiles (13 species, 68%), xerophiles (2 species, 11%), mesophiles (4 species, 21%). Fauna's zoogeographic spectrum is represented by 7 groups: transpalearctic (4 species, 21%), west palaearctic (3 species, 16%), trans-eurasian (1 species, 5%), west eurasian (7 species, 37%), middle asian (2 species, 11%), mediterranean-black sea-european (1 species, 5%), mediterranean-european-euro-siberian-kazakhstani (1 species, 5%).

Key words: true bugs (Hemiptera), Heteroptera, Altyn-Emel National Nature Park, South-East Kazakhstan.

Introduction. The landscapes of Altyn-Emel nature park were formed within four types: meadow-steppe, steppe, semi-desert and desert. The value of invertebrates in nature and in human life is truly enormous, and the role they perform is extremely diverse. Unfortunately, invertebrates at Altyn-Emel SNNP territory are still a poorly studied group and information on fauna, biology, ecology is not available in all taxa. The fauna of the park is characterized by rich diversity and endemism.

Hemiptera, or the Bugs (Heteroptera) are the largest unit of incomplete insects that inhabit a wide variety of biotopes and play an important role in biological processes in biogeocenoses. Among the bugs are many predatory or mixed-feeding species, but herbivorous forms predominate; they feed on the juices of plants, mainly their generative organs and seeds, multiplying periodically in large quantities, causing significant damage to crops (cereals, fodder, vegetables, fruits), as well as pastures and forests.

The purpose of the study is to identify the biodiversity of semi-winged insects inhabiting the study area, to study the ecological, biological features and distribution of species of semi-winged insects at territory of Altyn-Emel SNNP.

Methods of research. The study of fauna and ecology of true bugs was carried out by means of route surveys and stationary observations. Different methods were used for collecting bugs: mowing with an entomological net, collecting by exhauster, catching on light, etc [1-5].

Research results. The material for writing this article was obtained from collections and observations by the authors, performed in 2018-2019 at different biotopes of Altyn-Emel SNNP.

Below is an annotated list of identified species. Collection points, summary information on distribution, biology, and ecology are provided for each species.

Piesmatidae family. *Parapiesma atriplicis* (Frey-Gessner, 1863). Almaty oblast, Kerbulakraion, AltynEmel SNNP, Kizylauiz gorge. 17.06.2018. 2♀, 3♂; 05.07.2018. 3♀, 2♂; 24.08.2018, 2♀, 2♂; Taygak gorge, 21.06.2018, 3♀, 2♂; Shygan border, interzonal biotope. 04.07.2018. 3♀, 2♂; Minbulak border, 06.07.2018. 3♀, 2♂; 23.08.2019, 1♀, 2♂; floodplain of the river Ili. 06.07.2019 4♀, 3♂. Hortobiont; mesophyll (ditches around gardens, forests' edges); narrow oligophytophagus (at Atriplex); 2-3 generations per year; wintered imago [6, 7]. West Eurasian species

Parapiesmakochiae(Becker, 1867). Almaty oblast, Kerbulakraion, AltynEmel SNNP,Uzynbulak border Konakbaisai, 03.07.2018, 2♀, 3♂; Shigan border, introsonal biotope. 04.07.2018 3♀, 2♂; 23.08.2019 1♀, 2♂; Border Shigan, 08.07.2019, 1♀, 2♂; Zhantogai border, floodplain of Ili river, 10.07.2019, 2♀, 1♂. Hortobiont; meso-xerophyll (on alluvial sands, forest edges, mostly on saline soils of ponds, in deserted places and on open slopes of foothills [7]; narrow oligophytophagus (on *Kochia protrata, Echinopsilon (Chenopodiaceae)*;2-3 generations per year; wintered imago.Western Eurasian species.

Parapiesma kolenatii Fieber, 1861. Almaty oblast, Kerbulakraion, AltynEmel SNNP,Koyandytau, canyon Uzynbulak, 27.07.2018, 3♀, 2♂; Shygan border, 08.07.2018, 3♀, 2♂; Zhantogay border, floodplain of Ili river, 10.07.2019, 2♀, 2♂; Ch. Valikhanov spring. 08.07.2018, 1♀, 2♂; Katutau mountains - Aktau. 04.07.2018. 1♀, 2♂; 23.08.2019. 3♀, 2♂. Hortobiont; meso-xerophile; narrow oligophytophage (at *Atriplex cana, A.verrucifera* [7]; 2-3 generations per year; adults wintered. Middle-Tetian species.

Parapiesma quadratum (Fieber, 1844).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Kyzylauyz gorge. 17.06.2018. 3♀, 2♂; 24.08.2018, 2♀, 2♂; Taigak plains, 21.06.2018, 3♀, 2♂; Zhantogay border, floodplain of Ili river, 10.07.2019, 2♀, 1♂;.23.08.2019, 3♀, 2♂. Hortobiont; Meso-xerophile (on saline soils at banks of water bodies, in desertified places, solonetzes, solonchaks); polyphytophage (mainly on the cynopods: *Chenopodium, Atriplex, Salsolae*, etc.); 2 generations per year; adults wintered [7]. Trans-Palaearctic species.

Parapiesma salsolae (Becker, 1867). Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Minbulak border, 09.08.2009, 1♀, 2♂; Kizilauiz gorge. 17.06.2018. 3♀, 2♂; Uzunbulak gorge, Konakbaisay gorge, 22.08.2019. 2♀, 2♂; Aktau mountains. 04.07.2018, 1♀, 2♂; Shygan borders, interzonal biotope 08.07.2018. 3♀, 2♂.Hortobiont; Meso-xerophilus (sea coast, on river and coastal sands, especially saline, characteristic for *Salsola* and similar species of cynopods (*Chenopodiaceae*); narrow oligophytophage (on *Salsola, Corispermum*); bivoltine; wintering imago [8]. Transeurasioan species ubiquitous in Kazakhstan.

Parapiesma silenes (Horvath, 1888).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,кордон Мынбулак, 06.07.2018. 3♀, 2♂; 23.08.2019, 1♀, 2♂; пойма р. Или. 06.07.2019. 4♀, 3♂. Hortobiont; meso-xerophile (salt marsh steppes); narrow oligophytophage - on *Silene parviflora, Otites*, etc. [7]; bivoltine; winter adults. Mediterranean-Black Sea-European view.

Parapiesma variabile (Fieber, 1844).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Minbulak border, 06.07.2018. 3♀, 2♂; 23.08.2019, 2♀, 2♂; Katutaumountins. 04.07.2018. 1♀, 2♂; 23.08.2019. 2♀, 2♂ Hortobiont; meso-xerophile; narrow oligophytophage (on cloves *Caryophyllacaea, Herniaria spp., Atriplexcana*, etc.); bivoltine; adults wintered [9]. Mediterranean-European-Euro-Siberian-Kazakh species.

Piesma capitatum (Wolff, 1804).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Kizylauiz gorge. 17.06.2018. 3♀, 3♂; 05.07.2018. 3♀, 2♂; 24.08.2018, 2♀, 3♂; Taigak gorge, 21.06.2018, 2♀, 2♂; Shigan border, interzonal biotop. 04.07.2018. 3♀, 3♂; Minbulak border, 06.07.2018. 3♀, 2♂; 23.08.2019, 3♀, 2♂; floodplain of Ili river. 06.07.2019. 4♀, 3♂. Hortobiont; mesophile (roadsides, along ditches near gardens and forest belts, along forest edges and other similar places; in lowered plains); narrow oligophytophagous (on wild-growing goosefoots: *Chenopodium, Atriplex*, etc.); 2 generations per year [8]; wintering adults. Transpalearctic species

Piesma maculatum (Laporte, 1833).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Shigan border, 08.07.2018, 3♀, 2♂; Zhantogay border, floodplain of Ili river, 10.07.2019, 2♀, 3♂;Ch. Valikhanov's spring.08.07.2018, 4♀, 2♂;12.07.2019, 3♀, 3♂.Herpeto-hortobiont; mesophile (roadsides, along ditches near gardens and forest belts, along forest edges and other similar places; in depressions, in rather humid, almost wet places; on plants and among detritus); wide oligophytophagous (on goosefoots: *Chenopodium, Atriplex*); 2-3 generations per year [10]; wintering adults. Trans-Palaearctic species.

Berytidae family. *Neides afghanus* Seidenstucker, 1968.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Minbulak border, 06.07.2018, 2♂, 2♀; Koyanditau mountains, Uzinbulak border, Konkbasay gorge, 18.07.2019, 2♀, 1♂; Uzinbulak gorge, Tulkily and Kaiyndi, 28-30.07.2019, 3♀, 4♂. Herpeto-hortobiont; Meso-xerophilus (in dry places, under stones and on the soil under grasses, flies over shrubs and high grains in warm weather [7]; wide oligophytophage (most often on cereals); monovoltine; wintering adults.Middle Tetian kind.

Neides tipularius (Linnaeus, 1758).Almaty oblast, Kerbulak raion, Altyn Emel SNNP, Minbulak border, 16.06.2018, 1♀, 2♂; 06.07.2018, 1♂, 2♀; Uzinbulak border, Konkbasay gorge, 10.07.2018, 1♀, 2♂; 18.08.2019, 3♀, 2♂; Katutau mountains. 04.07.2018. 1♀, 2♂; 23.08.2019. 2♀, 1♂ Hortobiont; meso-xerophile (in dry places, forest edges and forest glades, both in the lowland and in the mountains up to 3000 m above sea level); wide oligophytophage (most often on cereals, mainly on Cerastium u Arenaria, but sometimes on other herbaceous plants); monovoltine; wintering adults [7]. West Eurasian kind.

Berytinusgeniculatus Horvath, 1885**.**Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Shygan border, 06.07.2018, 3♀, 2♂; Minbulak border, 08.07.2018, 2♂, 2♀; Zhantogay border, Ili floodplain, 10.07.2019, 2♀, 3♂. Hortobiont; meso-xerophile (on solonetzes and solonchaks in the desert and in floodplains); wide oligophytophage (on legumes, sometimes on alfalfa crops); monovoltine; wintering adults [7]. West Palaearctic species.

Berytinussignoreti Fieber, 1859.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Singing barkhan, 09.06.2018, 3♀, 2♂; 06.07.2018, 2♂, 2♀;18.08.2019, 3♀, 2♂;10.07.2019, 2♀, 3♂.Hortobiont; xerophile (lives on sandy soils, dune sands); wide oligophytophage (on *Lotus, Ononis, Hippocrepis*, etc.); monovoltine; adults are wintering [11]. West Eurasian kind.

Gampsocoris culicinus culicinus Seidenstucker, 1948.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Koyanditau ridge Uzinbulak gorge, Tulkily and Kaiyndi, 28-30.07.2018, 2♀, 2♂; 24.06.2019, 2♀, 3♂;18.08.2019, 3♀, 2♂.Herpeto-hortobiont; meso-xerophile (habitats - from the dry rocky slopes of hills and mountains, well warmed by the sun, to moist shady); polyphytophage (herbaceous plants of many families: lipaceae, rosaceae, borage, chickweed, legumes, asteraceae and others); up to 2 generations per year; wintering imago [7, 11]. West Palaearctic species

Gampsocoris punctipes punctipes (Germar, 1822).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Koyanditau, Konakbasay gorge, 30.07.2018, 2♀, 2♂; 24.06.2019, 2♀, 3♂; 18.08.2019, 3♀, 2♂.Herpeto-hortobiont; xerophile (dry rocky slopes of hills and mountains, well warmed by the sun, clearings, in sandy meadows and coastal dunes); polyphytophage (herbaceous plants of many families: lipaceae, rosaceae, borage, chickweed, legumes, asteraceae and others); monovoltine; wintering imago [7, 11]. West Palaearctic species.

Metacanthus meridionalis Costa, 1847.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Katutau mountains. 04.07.2018. 1♀, 2♂; 23.08.2019. 2♀, 1♂;Aktau mountains. 04.07.2018, 2♀, 2♂; 03.08.2019, 2♀, 2♂.Hortobiont; meso-xerophile (semi-desert, in dry stations in the mountains); narrow oligophytophage (on *Epilobium hirsutum*); monovoltine; wintering imago [12]. West Eurasian species.

Pyrrhocoridae family. *Pyrrhocorismarginatus* Kolenati, 1845.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Koyanditau ridge Uzinbulak gorge, Tulkily and Kaiyndi, 28-30.07.2018, 4♀, 3♂; 24.06.2019, 3♀, 3♂;15.07.2019, 3♀, 4♂; 18.08.2019, 3♀, 2♂;Katutau mountains. 04.07.2018. 3♀, 2♂; 23.08.2019. 2♀, 3♂. Herpetobiont (on the upper layers of the soil at the roots of herbaceous plants and under stones); Meso-xerophile (in the steppe and semi-desert, in the middle zone of mountains, dry places, hillsides, areas of the virgin steppe, edges and glades of forests, forest belts, parks, gravitates to lowlands); zoophytophagus (feeds on plant seeds, prefers mallow, *Tilia, Robinia*, as well as on insect eggs, dead insects [7]; up to 2 generations per year; wintering imago (under stones, in plant litter). West Eurasian species.

Pyrrhocoris apterus (Linnaeus, 1758).Almaty oblast, Kerbulak raion, Altyn Emel SNNP,Kizilauiz gorge. 17.06.2018. 5♀, 6♂; 05.07.2018. 7♀, 5♂; 12.08.2019, 7♀, 6♂; Taigak gorge, 21.06.2018, 4♀, 5♂; Shigan gorge, 06.07.2018, 8♀, 7♂; Minbulak gorge, 08.07.2018, 8♂, 9♀; Zhantogay gorge, Ili floodplain, 10.07.2019, 10♀, 8♂. Herpetobiont; mesophile (forest edges and clearings, forest belts, parks, protective

afforestation and other mesophilic biotopes; among detritus; often feed on plants, on the ground, in sunny places, often large colonies; zoophitophagous (feeds on small insects and ticks, also on dead insects, fallen seeds and juices of green parts of plants (*Malva neglecta, Alcea rosea, Lavatera thuringiaca, Caragana arborescens*); up to 2 generations per year; wintering adults in groups among plant residues [7, 13, 14]. Trans-Palaearctic species.

Scantius aegyptius rossii Carapezza, Kerzhner & Rieger, 1998.Almaty oblast, Kerbulak raion, Altyn Emel SNNP,ущ. Кызылауыз. 17.06.2018. 2♀, 3♂; 05.07.2018. 3♀, 2♂; 12.08.2019, 2♀, 2♂; Taigak gorge, 21.06.2018, 3♀, 2♂; Shigan gorge, 06.07.2018, 3♀, 2♂; Minbulak gorge, 08.07.2018, 2♂, 2♀; Zhantogay goge, Ili floodplain, 10.07.2019, 2♀, 3♂. Herpetobiont (lives in the soil, among the remains of dried plants); meso-xerophile (steppe, edges and glades of forests, rocky mountainsides with sparse vegetation); zoophytophage (small insects and fallen seeds of malva, *Compositae*, cruciferous and some other families); up to 2 generations per year [7]; wintering adults. West Eurasian species.

Taxonomic composition of AltynEmel SNNP Hemiptera

Family	Species	# of kinds	%
Piesmatidae	*Parapiesma atriplicis* (Frey-Gessner, 1863)	9	47
	Parapiesmakochiae(Becker, 1867)		
	Parapiesma kolenatii Fieber, 1861		
	Parapiesma quadratum (Fieber, 1844)		
	Parapiesma salsolae (Becker, 1867)		
	Parapiesmasilenes(Horvath, 1888)		
	Parapiesma variabile (Fieber, 1844)		
	Piesma capitatum (Wolff, 1804)		
	Piesma maculatum (Laporte, 1833)		
Berytidae	*Neides afghanus* Seidenstucker, 1968	7	37
	Neides tipularius (Linnaeus, 1758)		
	Berytinusgeniculatus Horvath, 1885		
	Berytinussignoreti Fieber, 1859		
	Gampsocoris culicinus Seidenstucker, 1948		
	Gampsocoris punctipes (Germar, 1822)		
	Metacanthus meridionalis Costa, 1847		
Pyrrhocoridae	*Pyrrhocorismarginatus* Kolenati, 1845	3	16
	Pyrrhocoris apterus (Linnaeus, 1758)		
	Scantius aegyptius rossii Carapezza, Kerzhner & Rieger, 1998		
Total		19	100

As can be seen from the data presented in Table 1, as a result of studying 3 families, 19 species of Hemoptera were identified, the species diversity of the identified bugs was dominated by representatives of the Piesmatidae family - 9 species (47%), Berytidae - 7 species (37%) . Pyrrhocoridae has only 3 species (16%).

Conclusion. As a result of the analysis of field and laboratory studies, taxonomic structure of Hemipteraspecies diversity at Altyn-Emel SNNP was determined. The vast majority of species are typical representatives of desert fauna, distributed throughout the desert zone of Palearctic or in most of it. As a result of studying 3 families, 19 species of Hemoptera were identified. By the number of generations per year, the Hemiptera of Altyn-Emel SNNP are divided into 3 groups: monovoltaic - 6 species, bivoltine - 10 species, polyvoltaic - 3 species. According to nutritional links of the identified true bugs:

polyphytophages - 3 species (16%), wide oligophytophages - 5 species (26%), narrow oligophytophages - 8 species (42%), zoophytophages - 3 species (16%). By confinement to the habitats, the Hemiptera of Altyn-Emel SNNP are divided into several groups: hortobionts (12 species), herpeto-hortobionts (4 species), herpetobionts (3 species).

Different species of Hemiptera have different requirements for the habitat's degree of moisture. Based on this feature, the following ecological groups of species were identified: meso-xerophiles (13 species), xerophiles (2), mesophiles (4 species).

The zoogeographic spectrum of the fauna is represented by 7 groups: transpalearctic (4 species), West Palaearctic (3 species), Trans-Eurasian (1 species), West Eurasian (7 species), Middle Tetian (2 species), Mediterranean-Black Sea-European (1 species), Mediterranean-European-European -Euro-Siberian-Kazakhstani (1 species).

Д. Ш. Акимжанов[1], П. А. Есенбекова[2], Б. К. Еликбаев[1]

[1]Қазақ Ұлттық аграрлық университеті, Алматы, Қазақстан,
[2]ҚР БҒМ ҒК «Зоология институты», Алматы, Қазақстан

«АЛТЫНЕМЕЛ» МЕМЛЕКЕТТІК ҰЛТТЫҚ ТАБИҒИ ПАРКІ ЖАРТЫЛАЙ ҚАТТЫҚАНАТТЫЛАР (HETEROPTERA) ФАУНАСЫНА МАТЕРИАЛДАР

Аннотация. «Алтынемел»табиғи паркінің ландшафттары төрт түрге бөлінді: шалғынды-дала, дала, шөлейт және шөл. Табиғаттағы және адам өміріндегі омыртқасыздардың маңызы өте зор, сондай-ақ олардың атқаратын рөлі де сан алуан болып келеді. Ал өкініштісі, фауна, биология, экология туралы ақпараттан тыс барлық таксон бойынша, «Алтынемел»МТҰП аумағында омыртқасыздар аз зерттелген топ болып қала береді. Парктің фаунасы сан алуан түрлілігімен және эндемизммен ерекшеленеді.

Жартылай қатты қанаттылар немесе қандала тәрізділер (Heteroptera) – әртүрлі биотоптарды мекендейтін және биогеоценоздардағы биологиялық процестерде маңызды рөл атқаратын, толық емес өзгеруі бар жәндіктердің ең үлкен отряды. Бұталардың арасында жыртқыштар немесе әртүрлі жолмен қоректенетін көптеген түрлер бар, бірақ шөп қоректі түрлер басым; олар өсімдік шырындарымен, негізінен олардың генеративті бөліктерімен және тұқымдарымен қоректенеді, мерзімді массалық түрде көбейеді; олар ауылшаруашылық дақылдарға (дәнді дақылдар, жемшөп, көкөністер, жемістер), сондай-ақ жайылымдар мен ормандарға айтарлықтай зиян келтіреді.

Зерттеу мақсаты – зерттелетін аймақта тұратын жартылай қатты қанатты жәндіктердің биологиялық алуан түрлілігін анықтау, «Алтынемел»МТҰП аумағында жартылай қатты қанатты жәндіктер түрлерінің экологиялық, биологиялық ерекшеліктері мен таралуын зерттеу.

Бұл мақаланы жазу үшін 2018-2019 жылдары «Алтынемел»МҰТП-нің әртүрлі биотоптарында зерттеу жүргізген авторлардың материалжинақтары мен бақылаулау нәтижелері пайдаланылды.

Далалық және зертханалық зерттеулерді талдау нәтижесінде «Алтынемел»жартылай қатты қанатты МТҰП түрлерінің алуан түрлілігінің таксономиялық құрылымы анықталды. Түрлердің басым көпшілігі Палеарктиканың шөлді аймағында немесе оның көп бөлігінде таралған шөл фаунасының типтік өкілдері болып табылады.

Мақалада анықталған түрлердің аннотацияланған тізімі берілген. Әрбір түр үшін, жинау пункттері, таралуы, биология және экология туралы қысқаша ақпарат берілген.

«Алтынемел» МҰТП территориясында жүргізілген зерттеулер нәтижесінде жартылай қаттықанаттылардың 3 тұқымдасына жататын 19 түр анықталды. Табылған жартылай қаттықанаттылар қоректік жағынан байланысты, олар:полифитофагтар – 3 түр (16%), кең олигофитофагтар – 5 түр (26%), тар олигофитофагтар – 8 түр (42%), зоофитофагтар – 3 түр (16%).«Алтынемел» МҰТП жартылай қаттықанаттылары жылына ұрпақ қалдыруы жағынан 3 топқа бөлінеді:моновольтинді – 6 түр (37%), бивольтинді – 10 түр (53%), поливольтинді – 3 түр (10%).«Алтынемел» МҰТП жартылай қаттықанаттылар тіршілік ету ортасына байланысты бірнеше топқа бөлінеді: хортобионттар (12 түр, 63%), герпето-хортобионттар (4 түр, 21%), герпетобионттар (3 түр, 16%). Зерттеу аймағынан табылған жартылай қаттықанаттылар келесідей экологиялық топтарға бөлінеді: мезо-ксерофилдер (13 түр, 68%), ксерофилдер (2 түр, 11%), мезофилдер (4 түр, 21%). Жартылай қаттықанаттылар фаунасы зоогеографиялық таралу аймағының 7 тобына жатады: транспалеарктикалық (4 түр, 21%), батыспалеарктикалық (3 түр, 16%), трансеуразиялық (1 түр, 5%), батысеуразиялық (7 түр, 37%), ортатетийлік (2 түр, 11%), жеротатеңізі-қаратеңіз-еуропалық (1 түр, 5%), жеротатеңізі-еуропалық-еуросібір-қазақстандық (1 түр, 5%).

Ключевые слова: жартылай қаттықанаттылар, Heteroptera,«Алтынемел»ұлттық табиғи паркі,Оңтүстік-Шығыс Қазақстан.

Д. Ш.Акимжанов[1], П. А. Есенбекова[2], Б. К. Еликбаев [1]

[1]Казахский Национальный аграрный университет, Алматы, Казахстан
[2]Институт зоологии КН МОН РК, Алматы, Казахстан

МАТЕРИАЛЫ К ФАУНЕ ПОЛУЖЕСТКОКРЫЛЫХ (HETEROPTERA) ГОСУДАРСТВЕННОГО НАЦИОНАЛЬНОГО ПРИРОДНОГО ПАРКА «АЛТЫН-ЭМЕЛЬ»

Аннотация. Ландшафты природного парка «Алтын-Эмель»сформировались в пределах четырех типов: лугово-степного, степного, полупустынного и пустынного. Значение беспозвоночных в природе и в жизни человека поистине огромно, а роль, которую они выполняют, крайне разнообразна.К сожалению, беспозвоночные животные на территории ГНПП «Алтын-Эмель» остаются еще слабоизученной группой и сведения по фауне, биологии, экологии имеются далеко не по всем таксонам. Фауна парка характеризуется богатым разнообразием и эндемизмом.

Полужесткокрылые, или Клопы (Heteroptera) представляют самый крупный отряд насекомых с неполным превращением, заселяющих самые разнообразные биотопы,играющих важную роль в биологических процессах в биогеоценозах. Среди клопов много видов хищных или со смешанным питанием, но преобладают растительноядные формы; они питаются соками растений, главным образом,их генеративных органов и семян.Периодически размножаясь в массовом количестве, они наносят существенный вред сельскохозяйственным культурам (зерновым, кормовым, овощным, плодовым), а также пастбищам и лесам.

Цельданного исследования – выявление биоразнообразия полужесткокрылыхнасекомых, населяющих территорию исследования, изучить экологические, биологические особенности и распространение видов полужесткокрылыхнасекомых на территории ГНПП «Алтын-Эмель».

Материалом для написания настоящей статьи послужили сборы и наблюдения авторов, проведенные в 2018-2019 гг. в различных биотопах ГНПП «Алтын-Эмель».

В результате анализа, проведенных полевых и лабораторных исследований определена таксономическая структура видового разнообразия полужесткокрылых ГНПП «Алтын-Эмель». Подавляющее большинство видов являются типичными представителями пустынной фауны, распространенными по всей пустынной зоне Палеарктике или на большей ее части.

В статье приводится аннотированный список выявленных видов. Для каждого вида приведены точки сборов, краткие сведения по распространению, биологии и экологии.

В результате проведенных исследований в ГНПП «Алтын-Эмель» нами было отмечено 19 видов полужесткокрылых, относящихся к 3 семействам.По пищевым связям из выявленных полужесткокрылых: полифитофаги – 3 вида (16%), широкие олигофитофаги – 5 видов (26%), узкие олигофитофаги – 8 видов (42%), зоофитофаги – 3 вида (16%). По числу поколений в год полужесткокрылые ГНПП «Алтын-Эмель» разделяются на 3 группы:моновольтинные – 6 видов (37%), бивольтинные – 10 видов (53%), поливольтинные – 3 вида (10%). По приуроченности к местам обитания полужесткокрылые ГНПП «Алтын-Эмель» подразделяются на несколько групп: хортобионты (12 видов, 63%), герпето-хортобионты (4 видов, 21%), герпетобионты (3 вида, 16%). Выделены следующие экологические группы видов: мезо-ксерофилы (13 видов, 68%), ксерофилы (2 вида, 11%), мезофилы (4 вида, 21%). Зоогеографический спектр фауны представлен 7 группами: транспалеарктическая (4 вида, 21%), западнопалеарктическая (3 вида, 16%), трансевразиатская (1 вид, 5%), западноевразиатская (7 видов, 37%), среднететийская (2 вида, 11%), средиземноморско-причерноморско-европейская (1 вид, 5%), средиземноморско-европейско-евросибирско-казахстанская (1 вид, 5%).

Ключевые слова:полужесткокрылые, Heteroptera, «Алтын-Эмель», национальный природный парк, юго-восток Казахстана.

Information about authors:

Akimzhanov Darhan Shoganbekovich, PhDdoctorate, Kazakh National Agrarian University, Almaty, Kazakhstan; darhan-14@mail.ru; orcid.org/0000-0002-1365-7250

Esenbekova Perizat Abdykairovna, leading scientific worker of RSE “Zoology institute” of CS MES RK, Candidate of Biology Science, Almaty, Kazakhstan; esenbekova_periz@mail.ru; orcid.org/0000-0002-5947-8514

Yelikbayev Bakhytzhan Koshkinbayevich, Kazakh National Agrarian University,Doctor of Biology Science, Professor, Almaty, Kazakhstan; bek29@bk.ru; orcid.org/0000-0002-1262-6524

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ХУДАЙБЕРГЕНОВ
ЭНВЕРБЕК БЕКОВИЧ

(22.07.1924 – 26.07.2019)

26 июля 2019 года на 95 году жизни скончался заслуженный работник Института ботаники и фитоинтродукции, ветеран труда Худайбергенов Энвербек Бекович.

Худайбергенов Энвербек Бекович родился в 1924 году, окончил биологический факультет Казахского государственного университета им. С.М. Кирова.

С 1958 года Энвербек Бекович начал работать в отделе растительных ресурсов, созданном в 1956 году по инициативе д.б.н. Валентины Павловны Михайловой – ученицы Н.В. Павлова.

В отделе растительных ресурсов, где он проработал 13 лет, Энвербек Бекович вместе с зав. отделом В.П. Михайловой занимался изучением распространения и запасов различных видов солодки в Казахстане, а также культурой этого рода на юге Казахстана. Эти исследования (исполнители В.П. Михайлова, Э.Б. Худайбергенов), ставшие частью всесоюзного изучения и использования солодки в народном хозяйстве СССР, изложены в отчетах и напечатаны в научных трудах Института ботаники АН КазССР.

В 1970 году он защитил диссертацию на тему «Солодка голая и уральская на юго-востоке Казахстана». Им опубликовано свыше 100 работ, в том числе 2 монографии, посвященные солодке.

В монографии «Солодки Казахстана» (1979) рассматриваются ареалы, запасы, экология, биология, фитоценология, формовое разнообразие солодки и других полезных растений, освещены результаты опытов по культуре различных видов солодки в условиях Казахстана, даны рекомендации по охране и использованию перспективных растений Казахстана. В 1990 году была опубликованы вторая монография «Биологическая и хозяйственная характеристика видов солодки Казахстана».

В 1975 году Энвербек Бекович был командирован в Иран, где руководил работой по исследованию флоры и растительности пастбищных угодий северной части этой страны. На основании этих материалов им составлен отчет и разработано технико-экономическое обоснование по улучшению естественных и организации культурных пастбищ и сенокосов.

С 1976 года продолжил трудовую деятельность в Главном ботаническом саду АН КазССР, где по заданию Государственного комитета по науке и технике Совета Министров СССР выполнял научно-исследовательскую работу «Оценка состояния растительных ресурсов Аральского региона» (1976–1979 гг.). Отчет и проработка к заданию ГКНТ были переданы в Институт географии АН КазССР.

С 1980 г. руководил исследованиями по теме «Испытание хозяйственно ценных видов растений на опустынивающихся территориях Приаралья, обусловленное снижением уровня Аральского моря» и являлся руководителем обширной темы «Совершенствование приемов репродукции интродуцентов».

Будучи заведующим отдела репродукции и защиты интродуцентов Главного ботанического сада, он выполнял плановые работы по разработке эффективных методов семенного и вегетативного размножения интродуцентов, прошедших первичное испытание в отделах и лабораториях сада; проводил опытно-промышленную проверку и разрабатывал способы массового размножения наиболее перспективных декоративных растений, рекомендуемых для внедрения.

Кроме того, продолжал заниматься интродукцией солодок и разработкой вопросов их охраны и рационального использования, уделяя большое внимание и разработке программы и методических вопросов по интродукции растений, вопросам внедрения.

Им был подготовлен ассортимент деревьев и кустарников по освоению освободившихся земель в дельте реки Сырдарьи. Большое внимание Энвербек Бекович уделял вопросам озеленения и реконструкции сада. Руководимый им отдел репродукции и защиты интродуцентов ГБС в 1977–1978 годы занимал призовые места по итогам соцсоревнования.

Худайбергенов Э.Б. являлся постоянным участником ВДНХ СССР и Казахской ССР, а в 1979 г. за достигнутые успехи в развитии народного хозяйства СССР был награжден Бронзовой медалью ВДНХ СССР и Дипломом второй степени ВДНХ Казахской ССР.

Худайбергенов Э.Б. всегда принимал активное участие в научно-производственной и общественной жизни сада, являлся членом Ученого совета и проблемного Совета ГБС, членом Всесоюзного ботанического общества, неоднократно избирался председателем местного комитета ГБС, пользовался заслуженным авторитетом и уважением у коллег и сотрудников.

Э.Б. Худайбергенов за заслуги в области изучения и использования солодки в народном хозяйстве СССР был награжден почетной грамотой Всесоюзного объединения «Союзлакрица», а его монографии, посвященные солодке, не утратили своей актуальности и в настоящее время.

Находясь на заслуженном отдыхе, Э.Б. Худайбергенов не переставал интересоваться деятельностью и жизнью Ботанического сада, всегда активно участвовал во всех юбилейных мероприятиях института, был непременным участником встреч сотрудников с ветеранами Великой Отечественной войны и трудового фронта накануне дня Победы.

Награжден юбилейными медалями: «50 лет Победы в Великой Отечественной войне 1941–1945 гг.», «60 лет Победы в Великой Отечественной войне 1941–1945 гг.», «65 лет Победы в Великой Отечественной войне 1941–1945 гг.» и «70 лет Победы в Великой Отечественной войне 1941–1945 гг.», а также нагрудным знаком «Ветеран войны 1941–1945».

Энвербек Бекович – любящий муж и отец, воспитавший одного сына и двух дочерей, заботливый дедушка и прадедушка, пользовался в семье исключительным уважением и любовью. Стойкий, закаленный судьбой человек, немногословный и вдумчивый, привыкший открыто говорить правду, а если разочаровывался в людях, не осуждал, отходил и прекращал общаться. Независимый и никогда не жалующийся, щедрый и всегда готовый помочь, ценивший истинную дружбу и обладающий чувством юмора. Таким он останется в нашей памяти…

Последний раз встреча с нашими ветеранами состоялась 4 мая 2019 года, во время которой коллеги навестили Энвербека Бековича в домашней обстановке и поздравили с наступающим Днем Победы.

Светлая память о заслуженном сотруднике, ученом, преданном выбранному пути, ветеране, энергичном и жизнерадостном человеке сохранится в наших сердцах.

Ситпаева Г.Т., генеральный директор РГП
на ПХВ «Институт ботаники и фитоинтродукции» КН МОН РК,
Ученый совет института

ЧЕКАЛИН СЕРГЕЙ ВЛАДИМИРОВИЧ

(14.05.1954 – 24.08.2019)

24 августа 2019 года ушел из жизни замечательный человек, учёный, теоретик в области интродукционных исследований, один из авторов экосистемного подхода в изучении интродукции растений, заведующий лабораторией дендрологии, кандидат биологических наук Сергей Владимирович Чекалин.

Чекалин Сергей Владимирович родился 14 мая 1954 года в г. Алма-Ате.

В 1971–1976 годы учился на биологическом факультете Казахского государственного университета им С.М. Кирова.

После окончания университета с 1977 года начал свою трудовую биографию в Главном ботаническом саду АН КазССР (ныне РГП на ПХВ «Институт ботаники и фитоинтродукции» КН МОН РК) и прошел все ступени научного роста от инженера до заведующего лабораторией дендрологии.

В 1982 году успешно защитил диссертацию: «Водный режим и адаптация лиственных древесных растений к засухе южного типа» на соискание ученой степени кандидата биологических наук по специальности «ботаника».

В 1990-1994 годы работал заместителем директора Главного ботанического сада по научной работе.

С 1995 года до последних дней жизни руководил лабораторией дендрологии, обеспечивающей сохранение и развитие коллекционных фондов древесных растений Главного ботанического сада, которые в настоящее время насчитывают свыше 900 таксонов, а общее число древесных растений открытого грунта превышает 25 тыс. экземпляров.

Сергей Владимирович Чекалин являлся одним из главных теоретиков интродукционного направления в Казахстане. В 1987 году им опубликована монография: «Водный баланс и состояние растений», по материалам которой было получено авторское свидетельство СССР на «Способ определения физиологического состояния тканей листьев растений».

В 1992 году в соавторстве с академиком НАН РК И.О. Байтулиным и доктором биологических наук М. А. Проскуряковым вышла в свет монография «Системно-экологический подход к интродукции растений в Казахстане», в которой впервые изложены теоретические и методические основы системной деятельности ботанических садов республики.

В 2010 году совместно с Т.М. Нурмуратулы опубликована «Национальная методология оценки и сохранения диких плодовых лесов Казахстана».

В 2012 году издана книга С.В. Чекалина, Г.Т. Ситпаевой и В.А. Масаловой «Расселения и холодоустойчивость древесных растений Евразии (субтропические, умеренные и субполярные

территории)», в которой представлены концепция расселения растений под влиянием циклических макроклиматических изменений и принципиально новый системно-ареалогический метод интродукционного прогнозирования.

В 2017 году были опубликованы 3 научных труда:

«Ассортимент и каталог древесных растений, рекомендованных для озеленения города Алматы» с коллективом авторов;

«Барбарисы юго-восточного и южного Казахстана» в соавторстве с А.С. Пожарским, А.Н. Ишаевой, где обобщены результаты исследований барбарисов в таксономическом, морфологическом и ботанико-географическом аспектах;

«Эпигенетическая гомологическая изменчивость формы плодов растений» (монография), в которой С.В. Чекалин на материалах исследований яблони и барбариса показывает объективность и эпигенетическую обусловленность системной изменчивости формы плодов растений, раскрывая некоторые закономерности такой изменчивости.

С.В. Чекалин являлся научным руководителем 3-х грантовых проектов и ответственным исполнителем научно-технических программ.

Автор более 100 научных статей и тезисов, из которых 10 опубликованы за рубежом.

Участник международных научных проектов в рамках «Программы развития ООН», «Глобального экологического фонда» и др.

Бессменный член редколлегии 14 опубликованных сборников международных научных конференций, посвященных изучению растительного мира Казахстана (2001 –2017 гг.).

Он всегда активно участвовал в общественной жизни института и города, будучи членом Общественного экологического совета города Алматы. Его имя и интервью по актуальным проблемам ботанического сада, озеленения города, сохранения биоразнообразия можно найти в средствах массовой информации.

За плодотворный многолетний труд и научные достижения в области ботаники Сергей Владимирович награжден благодарственной грамотой «Алғыс» МОН РК (2016) и нагрудным знаком «Еңбек ардагері» (2017).

Коллектив института, в котором он трудился 42 года, потерял друга, единомышленника, соратника, наставника и известного ученого-ботаника, безгранично преданного своей профессии и избранному пути, замечательного руководителя, отзывчивого и внимательного к своим сотрудникам, приветливого, неравнодушного и чуткого коллегу, душевного человека, а семья – заботливого отца и любящего дедушку.

Сергей Владимирович прожил яркую жизнь, всегда отличался активной позицией, высоким профессионализмом, человечностью, интеллигентностью, жизнелюбием и оптимизмом.

Светлая память о Сергее Владимировиче сохранится в наших сердцах, а его имя – в истории нашего института и города!

Ситпаева Г.Т., генеральный директор РГП
на ПХВ «Институт ботаники и фитоинтродукции» КН МОН РК,
Ученый совет института

МАЗМҰНЫ

Генетика

Фармакология

Биоинформатика

Биологически активные вещества

Флора и фауна

Ғалымдарды еске алу

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