

## Brief information about the project

Name of the project	AP19177815 «Phytochemical Profiles and Pharmacological Activity of <i>Lepidium sativum</i> L. Seeds»
Relevance	The present project main focused is to make use of the medicinal plants' resources to investigate natural bioactive components, determine phychemical profiles, and isolate of unique natural product leads via using modern chemical, physico-chemical methods. This will follow by studying their structure and bioactivity relationships. The project for natural drug research from the <i>Lepidium sativum</i> L. seeds will be engaged in cutting edge fundamental and translational research on phytochemical compositions and pharmacological activities of the medicinal plants for developing safe and effective phytomedicines to defense against diabetes and several human health threatened disease.
Purpose	The project focused on phytochemical and pharmacological studies of <i>L. sativum</i> seeds, to isolate new bioactive compounds, develop technological isolation schemes, determine, and evaluate their structures and bioactivities towards antidiabetic, antioxidation properties to create safe botanical oral supplement that used in the prevention and treatment of diabetes, inflammatory, cancer, heart and liver disease.
Objectives	<p><b>Specific Aim 1</b></p> <p>(A) Conduct a complete literature review on the uses of <i>Lepidium sativum</i>.L seeds in traditional and scientific natural medicine, and study of their active chemical compositions.</p> <p>(B) Collect of medicinal plants, and run initial preparation (cleaning, drying, grinding) of the raw materials in sufficient quantities for scientific research.</p> <p>(C) Study the chemical profiling of the collected plant materials and perform the required qualitative and quantitative analysis of their main bioactive compositions based on the guidance of Pharmacopoeia of Kazakhstan.</p> <p>(D) Carry out extractions from <i>Lepidium sativum</i>.L seeds and partitioning the crude extract with the different solvent system; Develop principal isolation block scheme for obtaining the biological active complexes (BAC); Optimize of the needed quality control methods associated with the biologically active constituents and run the needed pharmacological studies for the active complexes produced at the initial phase.</p> <p><b>Specific Aim 2</b></p> <p>A) Search and design purification methods suitable for dealing with the bioactive complexes and compounds.</p> <p>B) Identification and isolation of the bioactive compounds by using state of art chromatographic and physical and chemical methods as Column Chromatography (CC), High Performance Liquid Chromatography (HPLC), Gas Chromatography-Mass spectrometry (GC-Mass), Preparative HPLC, Liquid Chromatography-Mass Spectrometry (LC-MS), Electrospray ionization mass spectrometry (ESI MS) from medicinal plants.</p>

	<p>C) Structure elucidation of the main biologically active compounds by using modern chemical and physical methods as High-Resolution Mass Spectroscopies (MS), One Dimensional and Two-Dimensional Nuclear Magnetic Resonance Spectroscopy (1D and 2D NMR).</p> <p>D) Evaluate isolated components of <i>Lepidium sativum</i> L seeds against anti-diabetic and anti-oxidation activities; Study the Structure Activity Relationships (SAR); Investigate potential synergy among the active constituents.</p> <p>The results of scientific research will be issued and registered in the form of interim and final reports. All project members will actively participate in national and international conferences. The research results will also be published in leading national journals and in peer-reviewed scientific publications indexed by international databases Web of Science and (or) Scopus.</p>
Expected and achieved results	<p><i>1) Publication of articles in peer-reviewed foreign scientific journals</i></p> <p>- at least 2 (two) articles and (or) reviews in peer-reviewed scientific publications on the scientific direction of the existing project, that indexed in Science Citation Index Expanded and, included in 3<sup>rd</sup> quartiles according to the impact factor in the Web of Science database and (or) at least 50 (fifty) percentiles according to CiteScore in the Scopus database.</p> <p><i>2) Dissemination of the results to potential users, the scientific community and the General public</i> – Research results of the project will be presented and published in national/international conferences and peer-reviewed scientific journals.</p> <p><i>3) Other measurable results in accordance with the requirements of the tender documentation and the specifics of the project. Additionally, the section specifies:</i></p> <p><i>A) The scope and target users of each of the expected results</i> - the new gained knowledge will be applied in medicinal application, technology of processing plant raw materials, and cosmetology. Target consumers are research institutes, pharmaceutical, food, and cosmetic companies.</p> <p><i>B) The impact of expected results on the development of the main scientific direction and related fields of science and technology</i> – <u>the results are applicable in bioorganic chemistry, the chemistry of natural products, chemical technology of organic substances, and medicinal chemistry.</u></p> <p><i>C) Applicability and the (or) possibility of commercialization of the obtained scientific results</i>–Plants are important not only for food but also for medicine. Understanding the taxonomy, ecology and conservation of herbs, as well as the associated secondary metabolites, their biological properties and pathways of their synthesis is important for drug development. Investing in research into ethnobotany, traditional medicine, phytochemistry, plant medicinal chemistry, pharmacognosy, and plant ecology will be vital for a healthy society and protect the global population from current and future pandemics and other</p>

	<p>human diseases. Results of the project are possible further commercialization in the production of health care products, medicines and cosmetics.</p> <p><i>D) Social, economic, environmental, scientific and technical, multiplicative and (or) other effects of the project results with justification.</i></p> <p>Plant resources of Kazakhstan are enormous; they are of great importance to the economy of the country. <i>Lepidium sativum</i> L. are an important edible and medicinal source used in traditional medicine for the treatment of various diseases. The seeds also used in the treatment of diabetes, high blood pressure, cough, bronchitis, respiratory disturbances, skin diseases caused by impurities and toxins in blood, rheumatologic, cardiovascular, metabolic, and gastrointestinal disorders. <b>The economic point</b> realization of the project will highlight the new bioactive natural leads needed to obtain drugs with a further introduction to medicine and will contribute to accelerated innovation development of the economy of the Republic of Kazakhstan</p> <p><b>Social effect.</b> The developed technology will open new businesses and jobs, improve profitability and the economic effect of existing enterprises. Young Scientists participation in the project will allow improving the quality of education and training of highly qualified specialists that in the future will increase their ability for a better career development.</p> <p><i>4) Other direct and indirect results of the project, indicating their qualitative and quantitative characteristics.</i></p> <p>Develop natural product leads from plant resources, particularly for health care products, medicine, food and cosmetic industries.</p>
<p>Research team members with their identifiers (Scopus Author ID, Researcher ID, ORCID, if available) and links to relevant profiles</p>	<p>The <b>PI</b> of the project, Shybyray Yergazy - citizen of the RK, was a PhD student of XTIPC (2018-2024), University of Chinese Academy of Sciences. He works as as a senior researcher at Research Institute of Natural Products &amp; Technologies since July 2022. Same time, He has been participated the research projects at the Research Center for Medicinal Plants of the Al-Farabi Kazakh National University (KazNU)since anuary 2021.</p> <p><b>Project Supervisors :</b></p> <p><b>Jenis Janar (Ph.D.)</b>, Professor, Director of the Research Center for Medicinal Plants of Al-Farabi KazNU. Dr. Jenis is a leading scientist in the field of chemistry and technology of natural compounds. Scientific interests are related to the study of developing of new smart molecules, which isolate from Kazakh medicinal plants by using methods spectroscopic and analytical techniques. Biological evaluation and modification of the drug lead natural products. She studies chemical compositions of various medicinal and edible plants. Jenis J. is a member of the American Society of Pharmacognosy (ASP), and the Asian natural products Association (ASNP). Dr. Janar has experience in the field of chemistry of natural compounds for more than 23 years. Dr. Janar Jenis serves as <b>Co-PI</b> of the project, will be responsible for the overall intellectual direction. She will supervise all the research works in this proposal, review protocols and data, and supervise and</p>

	<p>train all other personnel. She will maintain constant communication with internal and external collaborators to address scientific issues, progress and evaluate results. The <i>h</i>-index is 8.  Link to the profile: <a href="https://orcid.org/0000-0002-7148-7253">https://orcid.org/0000-0002-7148-7253</a></p> <p><b>Hajiakber Aisa</b> – Ph.D., Professor, Chinese Distinguished Young Scholar, Academic Deputy Director of Xinjiang Technical Institute of Physics &amp; Chemistry (XTIPC), CAS, concurrently a member of Chinese Pharmacopoeia Commission, guest professor in Al-Farabi KazNU. He obtained his Ph.D. degree in organic chemistry in Shanghai Institute of Materia Medica (SIMM), Chinese Academy of Sciences (CAS) in 1999. His research works is concentrated on Traditional Chinese Medicine. He has published more than 500 SCI papers; 136 invention patents have been authorized; 3 new Traditional Chinese Medicine have obtained clinical approval in China, 2 of which have been transferred to enterprise and the Phase II clinical trials are underway; 3 drugs have obtained registration certificate in Uzbekistan; 3 first prizes and 3 second prizes of Xinjiang Science and Technology Progress Awards have been awarded. Prof. Hajiakber <u>will serve as scientific consultant of the project.</u> And will be responsible for the conduct of all the studies in this proposal.</p>
<p>List of publications with links to them</p>	<p><b>Scientific publications of a postdoctoral student.</b></p> <ol style="list-style-type: none"> <li>1. Yergazy Shybyray1, Janar Jenis1,2* , Haji A. Aisa 1,2*. Studies on chemical constituents of the Seeds of <i>Lepidium sativum</i> L. // The eighth International Mediterranean Symposium on Medicinal and Aromatic Plants, 20-22 October, 2022, Izmir, Turkey.</li> <li>2. Y.Shybyrai, A.Erkin, L. Kusepova. THE PEDAGOGICAL ISSUES OF ORGANIZING INDEPENDENT WORK ON IMPROVING STUDENTS COGNITIVE QUALITY. No 2(2), vol, October 2015, International Scientific and Practical Conference “WORLD SCIENCE” ISSN 2413-1032.</li> <li>3. Е. Шыбырай, Кусепова Л. А. Химияны оқыту барысында студенттердің таным сапасын ұжымдық үдерісі арқылы жетілдіру. Proceedings of XI International Scientific Conference for students and young scholars &lt;&lt;SCIENCE AND EDUCATION-2016&gt;&gt;. (2016) 1041-1044.</li> </ol> <p><b>Main publications of <u>Janar Jenis (PI)</u>:</b></p> <ol style="list-style-type: none"> <li>1. <u>Nurlybekova A.K., Kudaibergen A.A., Kazymbetova A., Amangeldi M., Baiseitova A., Ospanov M., Haji Akber Aisa, Yang Ye, Mohamed Ali Ibrahim, Jenis J.*</u> «Traditional Use, Phytochemical Profiles and Pharmacological Properties of <i>Artemisia</i> Genus from Central Asia» // <i>Molecules</i> 2022, 27, 5128. <a href="https://doi.org/10.3390/molecules27165128">https://doi.org/10.3390/molecules27165128</a>. (Q2, Percentile 83).</li> <li>2. Sailike B., Omarova Zh., <b>Jenis J.</b>, Adilbayev A., Akbay B., Askarova S., WeiLin Jin, Tokay T. «Neuroprotective and Anti-Epileptic Potentials of Genus <i>Artemisia</i> L.» // <i>Frontiers in Pharmacology</i>. DOI: 10.3389/fphar.2022.1021501. (Q1, Percentile 81).</li> </ol>

3. Peng Xu, Zhentao Zhang, Xueyuan Peng, Junling Yang, Xiaoqiong Li, Tiejian Yuan, Xiaohan Jia, Yaoyang Liu, Olim Abdullaev, **Janar Jenis**. Study on vacuum drying kinetics and processing of the *Lonicera japonica* Thunb. aqueous extracts // LWT - Food Science and Technology 2022, 167, 113868. <https://doi.org/10.1016/j.lwt.2022.113868> (Q1, Percentile 87).
4. Ospanov, M., León, F., **Jenis, J.**, Khan I. A., Ibrahim, M.A. Challenges and future directions of potential natural products leads against 2019-nCoV outbreak // Current Plant Biology. – 2020. – 24. – P. 100180. DOI: 10.1016/j.cpb.2020.100157 (Q1, Percentile 71).
5. **J. Jenis**, A. Baiseitova, S. H. Yoon, Ch. Park, J. Y. Kim, Z. P. Li, K. W. Lee, K. H. Park, Competitive a-glucosidase inhibitors, dihydrobenzoxanthenes, from the barks of *Artocarpus elasticus*. Journal of Enzyme Inhibition and Medicinal Chemistry, 2019, 34 (1), P.1623-1632. DOI: 10.1080/14756366.2019.1660653. (Q1, Percentile 81)
6. Abilova Zh., Yaun J., **Jenis J.**, Tang Ch., Ye Y. Monomeric and Dimeric Sesquiterpene Lactones from *Artemisia heptapotamica* // Chinese Journal of Natural Medicines, 2019, 17(10), P. 785-791. DOI: 10.1016/S1875-5364(19)30095-0. (Q2, Q3, Percentile 85)
7. Zhu, N., Tang, Ch., Xu, Ch.-H., Ke, Ch.-Q., Lin, G., **Jenis, J.**, Yao, Sh., Liu, H. Ch., Ye, Y.. Cytotoxic Germacrane-type Sesquiterpene Lactones from the Whole Plant of *Carpesium lipskyi* // Journal of Natural Products, 2019 Apr 26; 82 (4), P. 919-927, doi: 10.1021/acs.jnatprod.8b01004. (Q1, Percentile 94)
8. J. Y. Kim, Y. W., Z. Uddin, Y. H. Song, Z. P. Li, **J. Jenis**, K. H. Park. Competitive neutrophil elastase inhibitory isoflavones from the roots of *Flemingia philippinensis* // Bioorganic Chemistry 2018, 78, P.249-257. DOI:10.1016/j.bioorg.2018.03.024. (Q1, Percentile 85)
9. M.A. Dyusebaeva, A.K. Kurmanbaeva, A.K. Nurlybekova, H.A. Aisa, **J. Jenis\***. Amino-acid and fatty-acid compositions of two *Artemisia* species // Chemistry of Natural Compounds, 2018, 54 (6), P.1208-1210. DOI: 10.1007/s10600-018-2599-1. (Q4, Percentile 34)
10. **J. Jenis**, J. Y. Kim, Z. Uddin, Y. H. Song, H.-H. Lee, K. H. Park. Phytochemical Profiles and Angiotensin-I Converting Enzyme (ACE) Inhibitory Activity of *Limonium michelsonii* Lincz. // Journal of Natural Medicine, 2017, 75(4), P. 650-658. doi:10.1007/s11418-017-1095-4. (Q3, Percentile 79, 57)
11. A. Baiseitova, **J. Jenis**, J. Y. Kim, Z. P. Li, K. H. Park. Phytochemical analysis of aerial part of *Ikonnikovia kaufmanniana* and their protection of DNA damage // Natural product research, 2019, May 14, P. 1-4. DOI: 10.1080/14786419.2019.1607858. (Q2, Q3, Percentile 71).
12. Zh.Zh., Akzhigitova, M.A. Dyusebaeva, T. Tursonjan, A. Idyrys, Xuan Lijiang, **J. Jenis\***. Phytochemical Study of *Bergenia crassifolia* // Chemistry of Natural Compounds, 2020,

56(5), p. 912-914. (Q4, Percentile 34) DOI 10.1007/s10600-020-03184-y

13. L. Rakhymbay, A. Turak, **J. Jenis**, and H.A. Aisa. Phenolic Compounds from *Vernonia anthelmintica* Seeds // Chemistry of Natural compounds, 2019, 55(4), P.732-733. DOI 10.1007/s10600-019-02874-6. (Q4, Percentile 34)

14. M.S. Muratova, G.A. Zou, **J. Jenis**, and H.A. Aisa. Chemical Constituents of *Alhagi sparsifolia* // Chemistry of Natural compounds, 2019, 55(5), P. 932-933. DOI 10.1007/s10600-019-02850-0. (Q4, Percentile 34)

15. H. M. Choi, J. Y. Kim, Z. Peng Li, **J. Jenis**, A. Baiseitova, K. H. Park. Effectiveness of Prenyl Group on Flavonoids from *Epimedium koreanum* Nakai on Bacterial Neuraminidase Inhibition // Molecules, 2019, 16(24) P. 317-330. DOI:10.3390 / molecules 24020317. (Q2, Percentile 82)

16. J. Y. Kim, J. Y. Kim, **J. Jenis**, Z. P. Li, Y. J. Ban, A. Baiseitova, K. H. Park. Tyrosinase inhibitory study of flavonolignans from the seeds of *Silybum marianum* (Milk thistle) // Bioorganic & Medicinal Chemistry, 2019, 27(12), P. 2499-2507. doi.org/10.1016/j.bmc. 2019.03.013. (Q2, Percentile 77)

#### **Published Books:**

1. Medicinal plants, phytochemical profile, biological significance: monography // **Jenis J.**

- Almaty: Kazakh University, 2020. - 160 P.

2. **J. Jenis**. Bioactive Natural Products from Medicinal Plants // Publishing House of Kazakh National University, 2020, 160 pages (in English)

3. Chemistry of natural compounds: educational and methodical manual // **Jenis J.**, Almaty: Kazakh University, 2020. - 208 P.. (in three languages).

4. **J. Jenis**, R. S. Iminova. Study Guide and Practice Tests for Organic Chemistry (Organic Compounds of Aliphatic Series) // *Educational-Methodical Handbook*, Publishing House of Kazakh National University 2017, 108 pages (in English).

5. **J. Jenis**, Chemistry of Natural Compounds // Educational manual, Publishing House of Kazakh National University, 2016, ISBN 978-601-04-1691-8, 114 pages (in English).

6. X. Xu, B. Konirhan, B. Zakaria An X.G. Jin, A. Yili, **J. Jenis**, et al. The Kazakh Herbal Medicine // Ethnic publishing house, Beijing 2009. ISBN 978-7-105-10066-8, 477 pages (in Kazakh and Chinese).

#### **Patents:**

1. Patent for the invention "Method for obtaining a biologically active complex with antidiabetic action", applicant DGP Scientific Research of New Chemical Technologies and Materials; application. No 2018/0725.1, 10.10.18, No. 34841, 15.01.2021, byul. No. 2, **Haji Akbar Aisa**, Dyusebaeva M. A., **Nurlybekova A. K.**, **Jenis J.**

2. Patent for a useful model "Method for obtaining a vasodilator", applicant **Jenis J.**; No. 5835, application 23.10.2020,

29.10.2021, Jenis J., Dyusebaeva M. A., Nurlybekova A. K., Kudaibergen A. A.

3. The useful model patent for " Method for obtaining an antioxidant agent", the applicant Jenis J.; No. 5792, Appl. 19.10.2020, 22.10.2020, Jenis J., Dusebaeva M. A., Nurlybekova A. K., Kudaibergen A. A., A. M. Baiseitova.

4. The useful model patent for "Method of obtaining antidiabetic active complex", the applicant Jenis J.; No. 5963, Appl. Jenis J. 07.01.2021, 02.04.2021, G. J., Dusebaeva M. A., Nurlybekova A. K., Baiseitova A. M., Haji Akbar Aisa.

5. The useful model patent for "Way of developing a virus-inhibiting agent of plant origin", applicant Jenis J., No. 7367, Appl. 07/04/2022, 08/19/2022, Jenis J., Nurlybekova A.K.

***Main publications of Prof. Hajiakber Aisa (Scientific Consultant):***

1) Khamidulla Kamoldinov, Jun Li, Komila Eshbakova, Shamansur Sagdullaev, Gaoya Xu, Yubo Zhou, Jia Li, Haji Akber Aisa\*, *Phytochemistry* 187 (2021) 112705. DOI: 10.1016/j.phytochem.2021.112705

2) Yuanchao Xie, Tianwen Hu, Yan Zhang, Daibao Wei, Wei Zheng, Fuqiang Zhu, Guanghui Tian, Haji A. Aisa\* and Jingshan Shen\*, *J. Org. Chem.* 2021, 86, 5065–5072.

3) Dilireba Shataer, Jun Li, Xiao-Mei Duan, Liu Liu, Xue-Lei Xin, and Haji Akber Aisa\*, *J. Agric. Food Chem.* 2021, 69, 4111–4119. DOI 10.1021/acs.jafc.1c00297

4) Cun Zhang, Bianlin Wang, Paruke Aibibula, Jiangyu Zhao and Haji Akber Aisa\*, *Org. Biomol. Chem.*, 2021, 19, 7081. DOI 10.1039/d1ob01299a

5) Guangying Sun, Munire Abuduaini, Guliqire Adili, Yongxin Zhao, Haji Akber Aisa\*, *Journal of Chromatography A* 1651 (2021) 462281. DOI 10.1016/j.chroma.2021.462281

6) Daibao Wei, Tianwen Hu, Yumin Zhang, Wei Zheng, Haitao Xue, Jingshan Shen, Yuanchao Xie\*, Haji A. Aisa,\* *Bioorg. Med. Chem.* 46 (2021) 116364.

7) Hequn Yang, Aytilla Mamatjan, Dan Tang, Haji Akber Aisa,\* *Boorganic Chemistry* 112 (2021) 104989. DOI 10.1016/j.bioorg.2021.104989

8) Ablajan N, Zhao B, Zhao JY, Wang BL, Sagdullaev S, Aisa HA\*. *Phytochemistry*, 2021, 181: 112567.

9) Tuohongerbieke A, Li J, Sabir G, Xin XL, Hu M, Duan XM, Liu L, Tang D, Zhu J, Aisa HA\*. *Phytochemistry*, 2021, 184: 112648. DOI 10.1016/j.phytochem.2020.112648

10) Adili G, Sun GY, Abuduaini M, Zhao YX, Abdulla R, Aisa HA\*. *J. Chromatogr. A*, 2020, 1622: 461129. DOI 10.1016/j.chroma.2020.461129

11) Gong XD, Sun CL, Abame MA, Shi WQ, Xie YC, Xu XB, Zhu FQ, Zhang Y, Shen JS\* and Aisa HA\*. *J. Org. Chem.*, 2020, 85: 2704-2715.

12) Ma Y, Li J, Tong F, Xin XL\*, Aisa HA\*. *Ind. Crop Prod.*, 2020, 153: 112592. DOI 10.1016/j.indcrop.2020.112592

13) Aisa HA\*, Xin XL and Tang D. *Chinese Herbal*

	<p><i>Medicines</i>, 2020, 12: 224-236. DOI 10.1016/j.chmed.2020.05.001</p> <p>14) Turghun C, Bakri M, Abdulla R, Ma QL, <u>Aisa HA*</u>. <i>J. Ethnopharmacol.</i>, 2020, 261: 113019. DOI 10.1016/j.jep.2020.113019</p> <p>15) Zhang X, Yang J, Wang C, Sun YK, Liu ZS, Huang YP*, <u>Aisa HA*</u>. <i>Microchem. J.</i>, 2020, 158:105140. DOI 10.1016/j.microc.2020.105140</p> <p>16) Hasan A, Liu GY, Hu R, <u>Aisa HA*</u>. <i>J Nat. Prod.</i>, 2019, 82: 724-734.</p> <p>17) Niu C, Lu XY, <u>Aisa HA*</u>. <i>RSC Advances</i>, 2019, 9: 1671-1678. DOI 10.1039/c8ra09755k</p> <p>18) Li G, Obul M, Zhao JY, Liu GY, Lu W*, <u>Aisa HA*</u>. <i>Bioorg. Med. Chem. Lett.</i>, 2019, 29: 126605. DOI 10.1016/j.bmcl.2019.08.009</p> <p>19) Bozorov K, Zhao JY, <u>Aisa HA*</u>. <i>Bioorg. Med. Chem.</i>, 2019, 27: 3511-3531.</p> <p>20) Reheman A, Gao ZY, Tursun X, Pu XP, Wu T, He F, Zhao X, <u>Aisa HA*</u>. <i>Sci. Rep.-UK</i> 2019, 9: 4626. DOI 10.1038/s41598-019-41006-6.</p>
Patents	