DOI: https://doi.org/10.5281/zenodo.14498444

SIBUTRAMINE USE IN OBESITY PATIENTS WITH ARTERIAL HYPERTENSION

Scientific adviser: **Daminov Abdurasul Takhirovich**
Assistant of the Department of Endocrinology,
Samarkand State Medical University

[1]Toshtemirov Mehroj Oybek o'gli
[2]Shodiyorova Charos Qilich qizi
[3]Raxmatullayeva Nigina Umidjon qizi
[4]Kamolova Shaxzoda Ziyodulla qizi
[5]Davirova Sabina Xasanovna
[1-5]Students of the Samarkand state Medical University

Relevance. *Obesity is a metabolic disorder that is becoming an epidemic. The World Health Organization (WHO) has declared obesity one of the most common chronic diseases among the adult population, which is no longer just a problem associated with poor nutrition. In 2014, 1.9 billion people over 18 years of age worldwide were overweight, of which 600 million were obese. According to WHO, in Europe in 2015, obesity was detected in 21.5% of men and 24.5% of women. It is expected that the number of obese people by 2030 will be 1.1 billion [1]. According to the ESSE-RF epidemiological study, an increase in the prevalence of obesity, diagnosed both by body mass index (BMI) and waist circumference (WC), is noted in Uzbekistan. It has been established that 26.6% of men and 24.5% of women aged 35–44 years are obese, 31.7% of men and 40.9% of women aged 45–54 years, and 35.7% of men and 52.1% of women aged 55–64 years [2]. Obesity, especially its visceral form, increases the risk of developing arterial hypertension (AH), type 2 diabetes mellitus, dyslipidemia, coronary heart disease (CHD), stroke, cholelithiasis, osteoarthritis, obstructive sleep apnea syndrome, and some oncological diseases. Visceral obesity is also associated with an increased risk of cardiovascular and overall mortality [3]. The results of recent studies show that visceral obesity and its consequences are based on an imbalance of the body's neurohumoral systems, a deficiency of functional forms of natriuretic peptides, and the development of selective insulin, leptin, and adiponectin resistance. Given the heterogeneity of patients with obesity, it is considered appropriate to distinguish phenotypes of the disease, such as metabolically healthy and metabolically active obesity.*

KEYWORDS: *visceral obesity; arterial hypertension; epicardial fat; sibutramine.*

Introduction. The majority of obese patients (60–90%) belong to the metabolically active phenotype. They are characterized by visceral (abdominal) distribution of adipose tissue, the presence of metabolic disorders and associated diseases [4, 5]. The pathogenesis of obesity-associated diseases is based on chronic inflammation, which causes insulin resistance, endothelial dysfunction with increased vascular tone, diastolic dysfunction of the left ventricle (LV) and myocardial fibrosis [6]. The epicardial visceral fat depot has been the most studied in terms of the relationship with cardiovascular diseases. A number of studies have demonstrated an association of epicardial fat (EF) with myocardial hypertrophy and fibrosis, preclinical decrease in diastolic and systolic function of the LV [7]. In this regard, the main goal of obesity treatment is not only weight loss, but also a reduction in the risk of developing concomitant diseases and an increase in life expectancy. Currently, the safest and at the same time most effective method is considered to be gradual (0.5-1.0 kg per week) weight loss for 6 months or more, with 5-10% of the initial body weight lost, mainly due to fat tissue, and not due to the loss of muscle mass or fluid. Drug and non-drug therapy is used for weight loss, including diet, regular exercise and changes in eating behavior. One of the drugs for the treatment of obesity, approved in the Russian Federation, is a serotonin and norepinephrine reuptake inhibitor - sibutramine. Due to this double effect, a feeling of satiety is achieved and the amount of food consumed is reduced, energy expenditure increases as a result of increased thermogenesis [8]. A number of studies, in particular in the PrimaVera program, have shown good efficacy and safety of the drug with long-term use in patients with obesity [9]. According to the instructions for use, sibutramine is prescribed to patients with hypertension with special caution due to a possible increase in blood pressure (BP). Considering that hypertension often develops in patients with visceral obesity, the aim of our study was to evaluate the efficacy and safety of sibutramine in patients with combined pathology during antihypertensive therapy, as well as to study the effect of the drug on epicardial fat depot during long-term use. etdy individuals and study design The study included 57 patients with hypertension and obesity (BMI≥30 kg/m²) aged 35–60 years. All patients initially and after 7 months of observation underwent a comprehensive clinical, instrumental and laboratory examination, including a general examination with anthropometric measurements, electrocardiography (ECG), office blood pressure measurement, 24-hour blood pressure monitoring with aortic stiffness analysis, and echocardiography (EchoCG). The study included patients with controlled hypertension undergoing antihypertensive therapy with office blood pressure <140/90 mm Hg.During the 1st month of observation, all patients were recommended a diet with limited caloric content of food to 1500 kcal/day for women and 1800 kcal/day for men, regular physical activity up to 30 minutes per day, changes in eating behavior

(reducing portion sizes, limiting food consumption in the evening and at night, regularly eating small amounts of food frequently). At the end of the 1st month, sibutramine (Reduxin, manufactured by Promomed, Russia) at a dose of 10 mg per day was added to non-drug therapy. Control visits to assess the efficacy and safety were carried out after 1 and 6 months of taking the drug. Anthropometric measurements Height, weight were measured, body mass index (BMI) was calculated, waist circumference (WC), hip circumference (HC) were determined, the WC/HC and WC/height ratios were calculated. All measurements are necessary for the diagnosis of obesity, identification of the type of distribution of adipose tissue and assessment of the dynamics of weight loss. Measurement methods All patients underwent office blood pressure measurement at each visit. The procedure was performed three times in a sitting position, after a 15-minute rest, the first measurement was excluded from the analysis. The average value of 2 consecutive measurements taken with a 5-minute interval was calculated. Between visits, patients performed self-monitoring of blood pressure in the morning and evening hours using an automatic brachial tonometer. All patients underwent 24-hour blood pressure monitoring using the BPLab system (Russia) before treatment and after 7 months of observation. Average daily, daytime and nighttime values of systolic blood pressure (SBP) and diastolic blood pressure (DBP) were analyzed, the degree of nighttime decrease, variability and morning dynamics of blood pressure were assessed. Echocardiography EchoCG was performed with an S4 transducer in the second harmonic mode with a frequency range of 1.8–3.6 MHz on a VIVID 7 device by General Electric (USA) in accordance with the recommendations of the Nomenclature and Standardization Committee of the American Association of Echocardiography (ASE). All studies were performed in M- and B-modes using standard positions. The LV examination included measurement of end-diastolic (EDS, cm) and end-systolic (ESR, cm) sizes, interventricular septum thickness in systole and diastole (IVST, cm) and posterior wall thickness in systole and diastole (PWS, cm) from the parasternal position along the long axis. The LV myocardial mass was calculated using the formula: LVM = 1.08 × (1.04 × [(EDR + PVD + ISPd)3 - EDR3]) + 0.6 g; where LVM is the LV myocardial mass, ISPd is the interventricular septum thickness in diastole, PVD is the posterior wall thickness in diastole, and LVM is the end-diastolic dimension in diastole. LV hypertrophy was diagnosed if the LVM index (iLVMI) exceeded 95 g/m2 in women and 115 g/m2 in men. Evaluation of epicardial fat depot The thickness of the epicardial fat depot was measured initially and after 7 months of observation during echocardiography.The echo-negative space between the myocardium and the visceral leaflet of the pericardium behind the free wall of the right ventricle in the parasternal position along the long axis was estimated. The measurement was performed at the end of systole,

with the ultrasound beam directed perpendicular to the aortic ring used as an anatomical landmark. The mean value of 3 consecutive measurements was calculated. Ethical review The study was approved by the Local Ethics Committee at A.I. Evdokimov Moscow State Medical University. Upon inclusion in the study, all patients signed an informed consent form in 2 copies. One of the copies was given to the patient. Statistical analysis Statistical processing of the material was performed using the licensed software package Stastica 10.0 Statsoft (USA). When choosing the method for comparing data, the normality of the distribution of the feature in subgroups was taken into account, taking into account the Shapiro-Wilk criterion. With a normal distribution, the mean value and standard deviation were calculated. The null hypothesis when comparing groups was rejected at a significance level of less than 0.05. Delta (Δ) was calculated as the difference between repeated and initial measurements. For multiple comparisons, one-way ANOVA was used. The relationship between two features was assessed using the Pearson correlation coefficient.

Results. The general characteristics of the patients included in the study are presented in Table 1. Women predominated among the study participants. All patients had visceral obesity confirmed by anthropometric data: BMI ≥30 kg/m², WC >102 cm in men and >88 cm in women, WC/HR >0.9 in men and >0.85 in women, WC/height ≥0.5. At inclusion in the study, the patients were on effective antihypertensive therapy, which was confirmed by the results of office BP measurement. According to echocardiography, most patients had impaired LV geometry by the type of concentric remodeling or concentric hypertrophy, which is typical of obesity and hypertension. An increase in one of the main parameters of aortic stiffness, pulse wave velocity (PWV), determined as part of daily BP monitoring, was also revealed. Approximately one third of patients had carbohydrate metabolism disorders, in particular, impaired glucose tolerance or type 2 diabetes mellitus. Almost all patients had dyslipidemia, manifested by an increase in total cholesterol (6.5±1.0 mmol/l), low-density lipoprotein (LDL) (3.7±1.1 mmol/l) and triglyceride (2.4±0.9 mmol/l) concentrations, and a decrease in high-density lipoprotein (HDL) concentrations (1.0±0.09 mmol/l in men, 1.2±0.07 mmol/l in women). During the first month of observation, patients were recommended to follow a diet and general weight loss recommendations. At the end of this period, insignificant dynamics of weight and other anthropometric indicators were revealed (Table 2). On average, patients lost 2 kg, which was less than 2% of the initial weight. With sibutramine intake at a daily dose of 10 mg for 1 month, a more significant weight loss was observed, by an average of 3.7 kg, which was more than 2% of the initial body weight. Subsequently, the rate of weight loss slowed down and by the end of the observation period (6 months of sibutramine intake) it averaged 8.6

kg (6.2% of the initial). With sibutramine intake, a reliable decrease in WC and WC/height was noted, more pronounced in women. No significant dynamics of WC/HC were found, since the hip volume (HV) decreased proportionally to the change in WC. When analyzing the dynamics of echocardiography indicators (Table 3), a tendency towards a decrease in iLVM was revealed, more pronounced in women. According to the latest data, indexing LVM to body surface area (BSA) in obese patients may be inaccurate, especially during weight loss. In this regard, it is recommended to index LVM to height2.7. When analyzing the dynamics of this indicator, a more significant decrease was found, which became reliable in women. The number of patients with impaired LV geometry decreased slightly (from 74 to 63%). Against the background of long-term therapy with sibutramine, a slight decrease in the EF thickness was noted (from 0.79 to 0.71 cm). A more detailed analysis revealed that in women, the dynamics of this indicator was significantly more pronounced than in men.Taking into account more significant dynamics of weight and other anthropometric parameters, it can be said that in our study women lost weight better than men. During the observation period, side effects of sibutramine were detected in 26.3% of the study participants (Table 4). The most common complaints of patients were constipation (12.3%) and dry mouth (10.6%). The severity of symptoms persisted during the first month of sibutramine therapy and then decreased. No drug discontinuation or additional prescriptions were required. Complaints of palpitations occurred in 2 patients (3.5%), while no tachycardia was detected during the general examination or according to ECG data. The average HR according to ECG data was 71.5±8.2 bpm before treatment and 70.5±12.8 bpm after treatment. The study included patients with controlled hypertension. At all scheduled visits, office BP measurements were performed, between visits, patients measured BP at home and filled in a corresponding diary, and 24-hour BP monitoring (ABPM) was performed before and after sibutramine therapy. No episodes of clinically significant BP increase were detected during 6 months of sibutramine therapy. The average daily SBP and DBP in the study group before treatment was 126.3±8.9 mmHg and 81.2±9.1 mmHg, respectively, and after treatment – 127.6±9.3 mmHg and 80.7±7.3 mmHg, respectively. Discussion The rate of obesity spread in all countries is comparable to an epidemic, and the choice of drugs for treating the disease is limited. One of the few drugs approved in Russia for the treatment of obesity is sibutramine. A number of studies have proven the efficacy and safety of the drug during long-term use. Thus, about 70 thousand patients with obesity participated in the All-Russian observational program "PrimaVera". Most of them were prescribed sibutramine in a daily dose of 10-15 mg for a period of 3 months to 1 year. According to the study results, about 65% of patients achieved clinically significant weight loss of 10% or more after 6-12 months

of taking the drug. At the same time, adverse events were registered in only 4.1% of program participants [9]. In our study, the dynamics of weight loss was less pronounced (about 6%), and the frequency of adverse events reached 26.3%, which is possibly due to the more common visceral form of obesity and the presence of metabolic disorders in those included in our study. The PrimaVera program involved 6.5% of patients with controlled hypertension. During the observation period, episodes of clinically significant increases in blood pressure (more than 10 mm Hg over 2 consecutive visits) were recorded in 26% of patients, but this did not lead to discontinuation of sibutramine [10]. In our study, no episodes of clinically significant increases in blood pressure were detected, which was confirmed by self-monitoring data, office and daily blood pressure measurements. Similar results were obtained in the observational program "Vesna", also conducted in Russia. About 35 thousand people participated in it.patients with alimentary obesity aged 18 to 60 years [11]. All patients were prescribed sibutramine (Reduxin) at a daily dose of 10–15 mg. The observation period was 6 months. During sibutramine therapy, there was an average weight loss of 14.3%, WC decreased by an average of 11 cm. In our study, WC decreased more significantly in women – by an average of 7 cm, which was accompanied by a reliable decrease in the thickness of the uterine cavity and could indicate regression of visceral obesity in these patients. Adverse events were recorded in 2.8% of patients. The most common complaints of patients in our study were dry mouth and constipation. Study Limitations The main limitation of this study is the small number of included patients. Also, given the presence of concomitant pathology and metabolic disorders, patients were prescribed sibutramine at a daily dose of 10 mg. Further dose titration was not performed. Conclusion The prevalence of obesity and associated diseases is steadily increasing. Drug therapy for obesity promotes more effective weight loss, affects the nature of the distribution of adipose tissue, and slows down the development of concomitant pathology. The drug sibutramine (reduksin), approved in Russia, in a daily dose of 10 mg is an effective and safe drug that can be used in patients with visceral obesity in combination with controlled hypertension.

References:

1. Ахматов А, Ахматова ЮА. БЕЛКОВЫЙ МЕТАБОЛИЗМ И ПАТОГЕНЕТИЧЕСКАЯ РОЛЬ ЭНДОГЕННОЙ ИНТОКСИКАЦИИ ПРИ ХРОНИЧЕСКОМ ТУБУЛОИНТЕРСТИЦИАЛЬНОМ НЕФРИТЕ У ДЕТЕЙ. *Educational Research in Universal Sciences*. 2024;3(4 SPECIAL):603-612.
2. Собирова ДШ, Закирова ЗШ кизи, Гаффорова ЧЕ кизи, Нормаматова ДФ, Эркинова НШ кизи. ГЕСТАЦИОННЫЙ САХАРНЫЙ ДИАБЕТ. *World of Scientific news in Science*. 2024;2(1):607-618.

3. Шухратовна НГ, Суратзода ЗМУХТЗ угли СМ, Шухратовна СД. ГОРМОНАЛЬНАЯ РЕГУЛЯЦИЯ. *Multidisciplinary and Multidimensional Journal*. 2024;3(2):9-18.
4. А.х С, И.б М, Б.п Н, М.э Б. ДИАГНОСТИКА И ЛЕЧЕНИЕ ТЕРМОИНГАЛЯЦИОННОЙ ТРАВМЫ. *Research Focus*. 2024;3(3):120-129.
5. Гульмухамедов ПБ, Ризаев ЖА, Хабилов НЛ, Бобоев КТ. ИЗУЧЕНИЕ УЧАСТИЯ ПОЛИМОРФНОГО ВАРИАНТА ГЕНА MTR (A2756G) В МЕХАНИЗМАХ РАЗВИТИЯ ВРОЖДЕННЫХ ПОРОКОВ ЧЕЛЮСТНО-ЛИЦЕВОЙ ОБЛАСТИ. *INTELLECTUAL EDUCATION TECHNOLOGICAL SOLUTIONS AND INNOVATIVE DIGITAL TOOLS*. 2024;3(31):64-68.
6. А.к Х, С.б Ш, С.д К, И.б М. НЕРЕШЕННЫЕ ПРОБЛЕМЫ ЛЕЧЕНИЕ БОЛЬНЫХ С ИНГАЛЯЦИОННЫМИ ТРАВМАМИ. *Boffin Academy*. 2024;2(1):64-74.
7. А.к Х, С.б Ш, Н.к С, И.б М. ОПТИМИЗАЦИЯ СОВРЕМЕННЫХ МЕТОДОВ ИНТЕНСИВНОЙ ТЕРАПИИ ПРИ ОЖОГОВОМ ШОКЕ. *JTCOS*. 2024;6(1):27-39.
8. А.к Х, С.б Ш, И.а Т, И.б М. ПОВРЕЖДЕНИЯ КИШЕЧНИКА ПРИ СОЧЕТАННОЙ ТРАВМЕ ЖИВОТА (Обзор литературы). *Science and innovation*. 2024;4(1):24-35.
9. Гульмухамедов ПБ, Ризаев ЖА, Бобоев КТ, Хабилов НЛ. ПОЛИМОРФИЗМ ГЕНА MTHFR (A1298C) И ВРОЖДЕННЫЕ ПОРОКИ ЧЕЛЮСТНО-ЛИЦЕВОЙ ОБЛАСТИ. *INTELLECTUAL EDUCATION TECHNOLOGICAL SOLUTIONS AND INNOVATIVE DIGITAL TOOLS*. 2024;3(31):69-73.
10. Алиярович ХА, Бойназарович МИ. ПРИЧИНЫ ПАРАПРОТЕЗНЫХ РЕЦИДИВНЫХ ВЕНТРАЛЬНЫХ ГРЫЖ И ВЫБОР СПОСОБА ХИРУРГИЧЕСКОГО ЛЕЧЕНИЯ. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*. 2024;4(11):161-168.
11. Бойназарович МИ, Алиярович ХА. ПРИЧИНЫ РЕЦИДИВА ГРЫЖИ ПОСЛЕ ГЕРНИОАЛЛОПЛАСТИКИ. *EUROPEAN JOURNAL OF MODERN MEDICINE AND PRACTICE*. 2024;4(11):156-160.
12. Ахматов А, Ахматова ЮА. СОВРЕМЕННЫЕ ПОДХОДЫ К ДИАГНОСТИКЕ И ЛЕЧЕНИЯ ХРОНИЧЕСКОГО ТУБУЛОИНТЕРСТИЦИАЛЬНОГО НЕФРИТА У ДЕТЕЙ. *Центральноазиатский журнал междисциплинарных исследований и исследований в области управления*. 2024;1(9):65-77.
13. Аблакуловна АЮ, Аблокул А. СОСТОЯНИЕ БЕЛКОВГО ОБМЕНА И ПАТОГЕНЕТИЧЕСКОЕ ЗНАЧЕНИЕ ЭНДОГЕННОЙ ИНТОКСИКАЦИИ У ДЕТЕЙ С ХРОНИЧЕСКИМ ТУБУЛОИНТЕРСТИЦИАЛЬНЫМ НЕФРИТОМ. *Eurasian Journal of Medical and Natural Sciences*. 2024;4(5-2):97-107.
14. Hsu CY, Rizaev JA, Pallathadka H, et al. A review of new emerging biosensors based on bacteria-imprinted polymers towards pathogenic bacteria: Promising new tools for selective detection. *Microchemical Journal*. 2024;207:111918. doi:10.1016/j.microc.2024.111918

15. Rizaev JA, Sattorov BB ugli, Nazarova NS. ANALYSIS OF THE SCIENTIFIC BASIS FOR ORGANIZING DENTAL CARE FOR WORKERS IN CONTACT WITH EPOXY RESIN. *Журнал гуманитарных и естественных наук*. 2024;(15):280-283.
16. Sobirdjanovna KN, Abdumaruf A, Tolib B, Shavkat I, Dilorom O. Assessment of the Level of Knowledge of Residents of Samarkand Region about Osteoporosis. *JSML*. 2024;2(4):45-49.
17. Siddikovna TG, Davranovna A, Shuxratovna NG. Basic Mechanisms of Development, Diagnosis and Treatment of Acromegaly. *International Journal of Alternative and Contemporary Therapy*. 2024;2(4):26-29.
18. А.х С, И.б М, Б.п Н, М.э Б, Ж.а Р, Б.а Я. СОВРЕМЕННЫЕ ТЕХНОЛОГИИ В ХИРУРГИЧЕСКОМ ЛЕЧЕНИИ ОСТРОГО КАЛЬКУЛЕЗНОГО ХОЛЕЦИСТИТА. *Research Focus*. 2024;3(3):130-138.
19. Sabirdjanovna KN, O‘g‘li VSA, Baxtiyorovich MB, O‘g‘li MBG, O‘g‘li PLU, Dilorom O. Development of Sarcoidosis after Successful Treatment of Itsenko–Cushing‘s Disease. *JSML*. 2024;2(5):91-98.
20. Aramovna DZ, Samariddin A, Bobir A, Abbos B, Ravza D. DIAGNOSIS AND INTENSIVE TREATMENT OF TYPE 2 DIABETES TO ACHIEVE THE TARGET LEVEL OF GLYCED HEMOGLOBIN AND REDUCE THE RISK OF VASCULAR COMPLICATIONS. *Research and Implementation*. 2024;2(4):26-35.
21. K.z A, J.a R, Sh.T A. DIAGNOSTIC AND PROGNOSTIC SIGNIFICANCE OF GINGIVAL FLUID CYTOKINES IN THE DEVELOPMENT OF INFLAMMATORY PERIODONTAL DISEASES. *TAJMSPR*. 2024;6(07):12-18. doi:10.37547/TAJMSPR/Volume06Issue07-03
22. Aramovna DZ, Suhrob R, Zuhraxon O, Dilovar Z, Muxlisa X, Dilorom O. DIAGNOSTIC AND TREATMENT METHODS OF HYPERPARATHYROIDIS. *FAN, TA’LIM, MADANIYAT VA INNOVATSIYA JURNALI | JOURNAL OF SCIENCE, EDUCATION, CULTURE AND INNOVATION*. 2024;3(6):1-9.
23. Sabirdjanovna KN, O‘g‘li RST, O‘g‘li XHA, Qizi QMM, O‘g‘li XBU, Qizi TSR. Diagnostic Aspects and Comparative Diagnostics of Thyroid Disease. *JSML*. 2024;2(5):99-106.
24. Rodrigues P, Rizaev JA, Hjazi A, et al. Dual role of microRNA-31 in human cancers; focusing on cancer pathogenesis and signaling pathways. *Experimental Cell Research*. 2024;442(2):114236. doi:10.1016/j.yexcr.2024.114236
25. Daminov AT, Abilov SB ugli, Akhadov AA ugli, Yangabayev SG ugli, Kuchkarova MZ kizi. EFFECT OF NON-STEROID ANTI-INFLAMMATORY DRUGS IN THE TREATMENT OF RHEUMATOID ARTHRITIS. *FAN, TA’LIM, MADANIYAT VA INNOVATSIYA*. 2024;3(8):36-40.
26. Saadh MJ, Khalifehsoltani A, Hussein AHA, et al. Exosomal microRNAs in cancer metastasis: A bridge between tumor micro and macroenvironment. *Pathology - Research and Practice*. 2024;263:155666. doi:10.1016/j.prp.2024.155666
27. Sobirdjanovna KN, Yusufbek J, Suhrob O, Jamshid O, Dilorom O. Features of Use

of Combined Glow-Lowing Therapy in Patients with Type 2 Diabetes and IHD. *JSML*. 2024;2(4):40-44.
28. Rizaev JA, Nazarova NS, Vohidov ER. HOMILADOR AYOLLARDA PARODONT KASALLIKLARI RIVOJLANISHINING PATOGENETIK JIHATLARI. *Журнал гуманитарных и естественных наук*. 2024;(11 [2]):104-107.
29. Djurayeva ZA, Rajabov L rustam o‘g‘li, Ibragimov A akmal o‘g‘li, Toshpulatov A yusuf o‘g‘li, Shomurodov L akobir o‘g‘li. HOMILADOR AYOLLARNING YENGIL YOD TANQISLIGI VA QALQONSIMON BEZ HOLATINI TAHLIL QILISH. *Analysis of world scientific views International Scientific Journal*. 2023;1(8):159-173.
30. Farrux E, Nurmuxammad X, Bekzod N, A DZ. Indicators of Renal Filtration Function in Elderly Patients with Arterial Hypertension in Association with Type 2 Diabetes Mellitus. *EUROPEAN JOURNAL OF INNOVATION IN NONFORMAL EDUCATION*. 2023;3(9):128-130.
31. Aramovna DZ, Diyorbek K, Diyorjon S, Akrom E, Feruz E, Dilorom O. IODINE DEFICIENCY CONDITIONS. *PEDAGOGIKA, PSIXOLOGIYA VA IJTIMOIY TADQIQOTLAR| JOURNAL OF PEDAGOGY, PSYCHOLOGY AND SOCIAL RESEARCH*. 2024;3(5):296-306.
32. Shukhratovna SD, O‘g‘li OUS, O‘g‘li SJG, Qizi RRO, Qizi MMB. MECHANISM OF SARCOIDOSIS AFTER CUSHING‘S DISEASE. *JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH*. 2024;3(3):134-140.
33. Aramovna DZ, Sevinch U, Nigina S, Umidjon M, Maqsud I, Dilorom O. MODERN APPROACH TO THE TREATMENT OF TYPE 2 DIABETES MELLITUS. *PEDAGOGIKA, PSIXOLOGIYA VA IJTIMOIY TADQIQOTLAR | JOURNAL OF PEDAGOGY, PSYCHOLOGY AND SOCIAL RESEARCH*. 2024;3(5):307-317.
34. Shukhratovna SD, Qizi TAS, O‘g‘li OII, Hamzayevich NM, Qizi ODO. MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE ADRENAL CORTEX DURING POISONING. *JOURNAL OF HEALTHCARE AND LIFE-SCIENCE RESEARCH*. 2024;3(3):148-153.
35. Pallathadka H, Khaleel AQ, Zwamel AH, et al. Multi-Drug Resistance and Breast Cancer Progression via Toll-Like Receptors (TLRs) Signaling. *Cell Biochem Biophys*. 2024;82(4):3015-3030. doi:10.1007/s12013-024-01418-2
36. N.k I, I.b M, M.e B, Z.a J. NEW METHODS COMPARISON OF COST EFFICIENCY OF TISSUE EXTRACTION TECHNIQUES IN LAPAROSCOPIC SURGERY. *Boffin Academy*. 2023;1(1):303-313.
37. Sobirdjanovna KN, Mirkomil T, Siyovush S, Zoyirjon T, Dilorom O. Pros and Cons of Using a Combination of Glow-Lowing Drugs, In Particular Dpp-4 Inhibitors and Metformin in Patients with Type 2 Diabetes and Overweight. *JSML*. 2024;2(4):50-53.
38. Taxirovich DA, Jamshidbek E, Javohir O, Ravshan E, Feruz J, Jahongir Q. ROLE OF INFLAMMATORY CYTOKINES IN DIABETIC NEPHROPATHIES IN PREGNANT WOMEN WITH TYPE 1 DIABETES MELLITUS. *PEDAGOGIKA*,

PSIXOLOGIYA VA IJTIMOIY TADQIQOTLAR | JOURNAL OF PEDAGOGY, PSYCHOLOGY AND SOCIAL RESEARCH. 2024;3(5):555-565.

39. Aramovna DZ, Islom I, Azizbek A, Zaxriddin S, Shohruh S, Dilorom O. ROLE OF VITAMIN D IN HYPERPARATHYROIDIS. *FAN, TA'LIM, MADANIYAT VA INNOVATSIYA JURNALI | JOURNAL OF SCIENCE, EDUCATION, CULTURE AND INNOVATION*. 2024;3(6):10-17.
40. Khaleel AQ, Alshahrani MY, Rizaev JA, et al. siRNA-based strategies to combat drug resistance in gastric cancer. *Med Oncol*. 2024;41(11):293. doi:10.1007/s12032-024-02528-w
41. Daminov AT, Kuchkorova MZ, xadov AA o'g'li, Yangabayev SG o'g'li, Abilov SB o'g'li. Sporadich Goitter. *International Multi-disciplinary Journal of Education*. 2024;2(8):112-120.
42. Daminov AT, Abilov SB ugl, Akhadov AA ugli, Yangabayev SG ugl, Kuchkarova MZ kizi. STUDYING THE CLINICAL AND LABORATORY COURSE OF NON-ALCOHOLIC FATTY LIVER DISEASE. *FAN, TA'LIM, MADANIYAT VA INNOVATSIYA*. 2024;3(8):41-46.
43. Daminov AT, Kuchkorova MZ, Axadov AA o'g'li, Yangabayev SG o'g'li, Abilov SB o'g'li. Subacute Thyroiditis. *International Multi-disciplinary Journal of Education*. 2024;2(8):121-129.
44. Mei S, Roopashree R, Altalbawy FMA, et al. Synthesis, characterization, and applications of starch-based nano drug delivery systems for breast cancer therapy: A review. *International Journal of Biological Macromolecules*. 2024;280:136058. doi:10.1016/j.ijbiomac.2024.136058
45. Obaidur Rab S, Altalbawy FMA, Chandra M, et al. Targeting the lung tumor microenvironment by phytochemicals and their nanoformulations. *Pathology - Research and Practice*. 2024;264:155679. doi:10.1016/j.prp.2024.155679
46. Eshnazarovna MS, Aramovna DZ, Ishnazarovich BS, Oromjonovna OS. The Development of the Economy in the Field of Tourism in Uzbekistan. *EUROPEAN JOURNAL OF BUSINESS STARTUPS AND OPEN SOCIETY*. 2023;3(2):71-73.
47. M F, E T, D K, Kurbanova NS. THE IMPACT OF NEW APPROACHES TO THE DIAGNOSIS AND TREATMENT OF GESTATIONAL DIABETES MELLITUS (GDM). *Western European Journal of Modern Experiments and Scientific Methods*. 2024;2(4):96-99.
48. Rizaev JA, Vohidov ER, Nazarova NS. THE IMPORTANCE OF THE CLINICAL PICTURE AND DEVELOPMENT OF THE CONDITION OF PERIODONT TISSUE DISEASES IN PREGNANT WOMEN. *Central Asian Journal of Medicine*. 2024;(2):85-90.
49. A RJ, A HF. The Relationship between Somatic and Dental Diseases. *International Journal of Integrative and Modern Medicine*. 2024;2(6):609-611.