The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS)
ISSN: 2791-8033

The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS), 2024

Volume 15, Pages 1-8

ICVALS 2024: International Conference on Veterinary, Agriculture and Life Sciences

Biochemical Parameters Studying in Experimental Diabetes

Oralbek Ilderbayev
L.N. Gumilyov Eurasian National University

Gulmira Zharmakhanova
West Kazakhstan Marat Ospanov Medical University

Darkhan Uzbekov
L.N. Gumilyov Eurasian National University

Gulzhan Ilderbayeva
L.N. Gumilyov Eurasian National University

Ainur Zhanilova
L.N. Gumilyov Eurasian National University

Abstract: Objective of study was biochemical parameters studying in experimental modeling of 2nd type diabetes in animals. To achieve the goal 2nd type induced diabetes was modeled in white male rats weighing on average 200.0±20.0 gr. Streptozotocin (MP Biomedicals, USA) administered intraperitoneally at 30 mg/kg dose was used as β-cytotoxin in modeling diabetes. After injection in experimental animals glucose concentration increased by 1.2 times ($p<0.05$), glycated hemoglobin level increased by 1.4 times ($p<0.05$). Lipid peroxidation outputs and antioxidant preservation enzymes in blood lymphocytes were studied: diene conjugates, malondialdehyde content, glutathione reductase, glutathione peroxidase, catalase activities. Studies have shown that in diabetes peripheral blood lymphocytes DC concentration increases by 20.68% ($p<0.05$), whereas MDA also increases by 23.07% ($p<0.05$). Antioxidant system enzymes underwent the following changes in diabetes: GlR activity in the blood decreased by 21.38% ($p<0.05$), catalase by 18.26% ($p<0.05$), whereas GlP activity was observed to decrease ($p>0.05$). Results show decrease in antioxidant system activation against the background of oxidative stress activation. AOP state studying seems crucial from the point of view of correctional therapy methods and determining pathological and adaptive alteration origin in the body. Conclusions. In diabetes mellitus oxidation process of chain lipids free radicals is activated entailing undesirable outputs accumulation in tissues having extremely harmful effects leading to cell membranes changes at different levels. Diabetes formation is accompanied by decrease in antioxidant system activation confirming by decrease in GlR, GlP, Kt expression against oxidative stress expression background.

Keywords: Diabetes, Lipid peroxidation, Antioxidant system

Introduction

It is clear that diabetes mellitus constitutes a complex metabolic disorder induced by a multifactorial etiology, mainly characterized by chronic hyperglycemia, a popular belief that is one of the most common diseases at present, occurring in approximately 8-9% of the world's population (Shimizu & Oniki, 2019; Roglic, 2016). R. Sherwin maintains (Sherwin & Jastreboff, 2012) that both the incidence and prevalence of diabetes continue to grow with the approaching tsunami force. Constantly the IDF (International Diabetes Federation) updates data, the number of people suffering diabetes rises.

Over the past 28 years, the number of patients bearing diabetes in the world has increased more than 12 times: from 30 million patients having diabetes in 1985 to 387 million in 2014, mainly as a result of patients suffering the 2nd type diabetes mellitus (DM II). It should be noted that the real rate of peak in incidence is tremendously ahead of even such disappointing forecasts of experts from the World Health Organization (WHO). According to IDF experts, in the number of patients bearing diabetes (in 2013 and 2014, respectively), China leads (98.4 million and 96.3 million), followed by India (65.1 million and 66.8 million), then USA (24.4 million and 25.779 million) (IDF, 2013; 2015). The number of patients suffering diabetes is constantly increasing due to the growth prevalence of obesity and sedentary lifestyle. Currently, it can be noted that diabetes is becoming sharply younger (an increase in the number of cases of DM II in children, adolescents and young adults) (Zimmet et al., 2014). The total quantity of patients having diabetes in Kazakhstan is growing steadily. Over the past 10 years, a progressive increase in the incidence of diabetes has been observed in Kazakhstan (an increase of 1.6 times). The number of sufferers tends to further increase, primarily in age groups over 40 years. Every 10-15 years, the number of human suffering diabetes doubles.

In accordance to IDF experts, the quantity of diabetes diseased in Kazakhstan in 2013 reached 526,000 people (IDF, 2013), in 2014 – 536,400 people (IDF, 2015). The significance of the medical and social problem of DM II is due not only to its high prevalence and the continuing trend towards an rise in the number of ailing, however also to high disability, mortality of sufferers owing to the development of micro- and macroangiopathies, additionally the need to organize a system of specialized care for patients. The development of chronic diabetic complications is the main problem of the 2nd type diabetes. Currently, there is convincing evidence of the direct involvement of hyperglycemia in the initiation of vascular complications of diabetes, while oxidative stress associated with increased generation of ROS plays a decisive role in their pathogenesis (Chandra et al., 2019).

Excessive production of ROS in β-cells can entail alterations in the shape, volume and function of mitochondria contributing to the breakdown of ATP-dependent K+ channels and impaired insulin secretion (Wang, 2017). These processes may be due to the fact that the content of antioxidant enzymes in β-cells is 10-20 times lower than in the cells of the liver, kidneys, heart, brain and other organs (Ceriello et al., 2016). Oxidative damage to β-cells caused by ROS as a result of hyperglycemia affects the quantity and quality of secreted insulin. There is evidence that β-cell dysfunction (impaired secretory capacity and increased insulin resistance) induced by oxidative stress plays a pivotal role in the pathogenesis of DM I and DM II. ROS can activate several other pathways, which, in turn, leads to one of the main complications of diabetes, namely endothelial dysfunction (Ighodaro, 2018).

Nowadays, the quality of the patients' life with diabetes is determined by the development and progression of chronic complications of this disease, caused by microangiopathies (injury to capillaries, arterioles and venules) and macroangiopathies (injury to medium and large vessels). Clinical manifestations of microangiopathies are diabetic retinopathy, nephropathy and neuropathy. Macroangiopathies result in myocardial infarction, stroke and gangrene of the lower extremities. The main culprit of disability and mortality in patients suffering diabetes are cardiovascular complications that develop as a result of progressive atherosclerotic vascular deterioration (Gracheva et al., 2012). The risk of developing coronary heart disease (CHD) is 2-4 times higher in the 2nd type diabetes sufferers compared to individuals out of diabetes (Wannamethee et al., 2011). In patients having DM II, diabetic nephropathy constitutes the second leading cause of death after CVD (Dedov, 2010). The culprit of the development and progression of vascular complications of diabetes is chronic hyperglycemia (American Diabetes Association, 2007). Numerous studies have confirmed the hypothesis of a causal association between hyperglycemia and oxidative stress (OS) (Esposito et al., 2002; Ikebuchi et al., 2010; Fiorentino et al., 2013).

In hyperglycemia, due to increased accumulation of advanced glycation end owtputs (advanced glycation end products - AGEs), pronounced changes are observed in the cytoplasm, nuclear structures and components of the extracellular matrix (Ramasamy et al., 2011). AGEs, by binding to their specific receptors (RAGE), are able to activate nicotinamide dinucleotide phosphate-NAD(P)H oxidase (NADPH) and elevate the oxygen free radicals production. Subsequently, by activating the transcription factor NF-kB (Nuclear Factor kappaB), they induce the production of vascular endothelial growth factor (VEGF) in monocytes/macrophages, epithelial cells, vascular smooth muscle cells and microvascular wall cells (Devi & Sudhakaran, 2011; Piarulli et al., 2013).

Study Objectives

Study of biochemical parameters in experimental modeling of the 2nd type diabetes in animals.

Methods

To achieve this goal, we modeled induced the 2nd type diabetes in experimental white male rats weighing on average 200.0±20.0 grams. All experimental procedures were carried out in accordance with the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes, 2005; Position of the Council at first reading with a view to the adoption of a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes, 2010) and "Rules for Conducting Biomedical Experiments, Preclinical (Non-Clinical) and Clinical Research, as well as Requirements for preclinical and clinical bases" Order of the Minister of Health of the Republic of Kazakhstan dated April 2, 2018 No. 142. Before the start of the study, laboratory animals were kept for 14 days to adapt to group housing in cages. At the time of this period, the animals were monitored for clinical status by visual inspection every day. Laboratory animals with abnormalities detected during the examination were not included in the experimental groups. Before the start of the study, laboratory animals meet the criteria for inclusion in the experiment.

To induce diabetes in rats, the Mansor L.S. model was used (Mansor, 2013). When modeling diabetes, low doses of streptozotocin (CAT NO.100557, CAS NO. 18883-66-4. MP Biomedicals, USA) were used as a β-cytotoxin. The cytotoxin streptozotocin, characterized by increased tropism for β-endocrinocytes, is administered intraperitoneally to animals of group II on the 8th day of the experiment at a dose of 30 mg/kg in a solution (0.1 M) of citrate buffer (pH=4.4). A dose of 30 mg/kg of animal weight was chosen due to the fact that administration of a higher dose of streptozotocin to animals (>50 mg/kg) leads to injury to the vast majority of β-cells, simulating the 1st type diabetes (Srinivasan et al., 2005). A dose of 30 mg/kg of animal weight minimizes the detrimental effect of the cytotoxin. The administration of streptozotocin entails disruption of insulin signaling, contributing to disruption of carbohydrate metabolism. The intact group rats were intraperitoneally injected with a citrate buffer solution in the same volume as the diabetic groups. We combine the induction of diabetes using a diet associated a high fat content (food containing 61% saturated fatty acids, i.e. fats of animal origin) for 5 weeks.

The experimental model of DM II, induced by low doses of streptozotocin in combination with a high fat content, at the pathogenetic level most closely corresponds to the development of DM II in humans. This model of DM II, on the one hand, sufficiently imitates the stages of development of the disease, as well as the metabolic features of DM II in humans, on the other hand, it is less expensive, easily reproducible and suitable for research. In order to confirm the established experimental diabetes, 2 weeks after the injection of streptozotocin, fasting glucose levels were measured in order to identify animals that did not correspond to the model of diabetes. Blood for the study was taken from the tail vein. The main criteria for including animals in groups having experimental diabetes: the fasting glucose level was more than 7.0 mmol/l. Animals are removed from the experiment in accordance with ethical standards and recommendations for the humanization of work with laboratory animals.

Laboratory research. Determination of glucose concentration was carried out usage the express method using a glucometer. Blood for the study was taken from the tail vein.

Determination of HbA1c. The concentration of HbA1c, an indicator of chronic, stable hyperglycemia, was analyzed by enzyme immunoassay using the CEA190Ra ELISA Kit For Glycated Hemoglobin A1c (HbA1c), 96T, Cloud-Clone, Corp. (Weykamp et al., 2008).

Determination of C-peptide. C-peptide determinations were carried out using test kits, enzyme immunoassay using CEA447Ra ELISA Kit For C-Peptide (CP), 96T, Cloud-Clone, Corp.

Determination of insulin. To assess the degree of insulin resistance and functional activity of β-cells, the determination of immunoreactive insulin is used. Determination of insulin concentration was carried out by ELISA using test kits CEA448Ra ELISA Kit For Insulin (INS), Cloud-Clone Corp.

Determination of 1,5-anhydroglucitol. The concentration of 1,5-AG, an indicator of glycemic status, was analyzed by enzyme immunoassay using CEB046Ge ELISA Kit For 1,5-Anhydroglucitol (1,5-AG), 96T, Cloud-Clone, Corp.

Determination of lipid peroxidation products. The content of diene conjugates (DC) in lymphocytes was determined according to the method of Gavrilov and Mishkorudnaya (1983) and the content of malondialdehyde (MDA) was determined according to the method of Konyukhova et al. (1989).

Determination of the activity of enzymes of the antioxidant system. The activity of the enzyme glutathione reductase (GrR) and glutathione peroxidase (GlP) was determined according to the method of S.N. Vlasova (Vlasova, Shabunina & Pereslegina, 1990) and the activity of the enzyme catalase (CT) was determined according to the method Korolyuk et al. (1988).

The obtained research results were processed using the "STATISTICA 8.0" software package from StatSoft, Inc. USA. The arithmetic mean values of quantitative indicators presented in the text as M±SD were calculated, where M is the arithmetic mean, SD is the standard deviation. In all statistical analysis procedures, the significance level was assumed to be $p \leq 0.05$.

Results and Discussion

Metabolic Status

Changes in biochemical parameters under conditions of experimental diabetes mellitus were studied. At this stage, indicators of metabolic status were studied and the validity of the experimental model of the 2nd type diabetes was confirmed. The results of the metabolic status study in experimental rats of group II linked to the 2nd type diabetes demonstrated an increase in fasting glycemia, glycated hemoglobin, concentrations of 1,5-AG and C-peptide, insulin concentrations, relative to the intact group. It was found that the glucose concentration in experimental animals having the 2nd type diabetes mellitus increased 1.2 times ($p<0.05$), the glycated hemoglobin level rised from 2.85±0.22 to 3.91±0.23 ($p<0.05$). In comparing the concentration of C-peptide with the intact control group, a significant increase in this indicator was found in diabetic animals: in the control group - 2.01±0.2 ng/ml, whereas in the experimental group comes to 3.12±0.27 ng/ml ($p <0.05$).

1,5-anhydroglucitol (1,5-AG) is a medium-term indicator of glycemic status, reflecting fluctuations in the hyperglycemic range over a 2-week period. At normal glucose levels, the concentration of 1,5-AG in the blood plasma is maintained by a balance between dietary intake and renal excretion. Under conditions of hyperglycemia, when the renal threshold for glucose is exceeded, the plasma concentration of 1,5-AG falls owing to competitive inhibition of its reabsorption by glucose. The advantages of 1,5-AG as a marker of glycemic status are stability and lack of dependence on the physiological state at the time of blood sampling. When studying the hyperglycemia marker - 1.5-AG, a result was obtained showing constant hyperglycemia in experimental animals, which revealed a significant decrease: in the intact group - 24.21 ± 3.8 ng/ml, in the experimental group - 11.27 ± 3, 11 ng/ml ($p<0.05$).

When comparing the insulin concentration with the intact control group, a significant increase in this indicator was found in diabetic animals: in the intact group - 0.64±0.09 ng/ml, in the experimental group - 1.33±0.19 ng/ml ($p<0 .05$). Thus, summarizing the results of the metabolic status, we state that a model has been created that characterizes the typical pattern of established the 2nd type diabetes mellitus with a pronounced disturbance of the metabolic status.

Biochemical Status

Lipid peroxidation. Numerous studies in recent years indicate pivotal role of reactive oxygen species (ROS) in the development of pathological deviation caused by tissue factors (Johnson, 1981). Excessive production of ROS can lead to injury to one's own cells and damage to nuclear structures owing to oxidative modification of proteins, lipids and nucleic acids (Vladimirov, 1991; Dubinina & Shugaley, 1993). Activation of phagocytes tends to spontaneously increase, and a vicious circle of inflammation can form in inflammatory realm. Essential manifestations of the detrimental effects of free radicals in living systems are the mutagenic effect and disruption of the structural and functional state of cells through the initiation of lipid peroxidation processes (Soodaeva et al., 1982). Under physiological conditions, LPO is limited by antioxidant protection, which can be disrupted when exposed to harmful factors. Considering the importance of this above mentioned system in the formation of the pathological process, its lability, high sensitivity, as well as significant consequences when it is injured, we observed its manner in the formation of the pathological process in animals having the 2nd type diabetes interesting.

As studies have shown in experimental diabetes mellitus, the concentration of diene conjugates (Figure 1) significantly increases in peripheral blood lymphocytes from 0.29±0.02 to 0.35±0.02 ($p<0.05$) and the concentration of malondialdehydes also significantly increases in peripheral blood lymphocytes from 0.13±0.01 to 0.16±0.01 ($p<0.05$). The data obtained show that in diabetes mellitus, the process of chain free radical oxidation of lipids is activated leading to the accumulation of undesirable outputs in tissues having a very harmful effect, causing alterations in cell membranes at different levels.

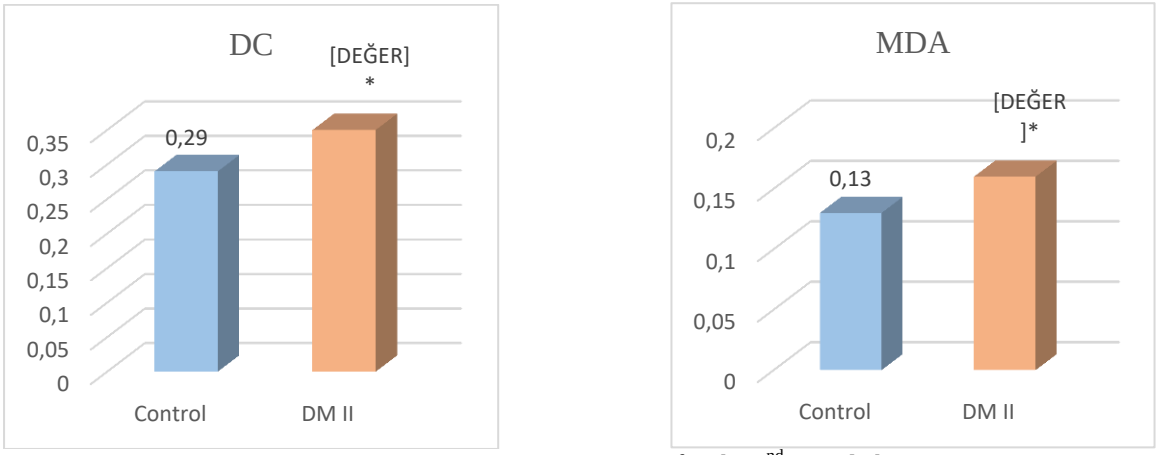
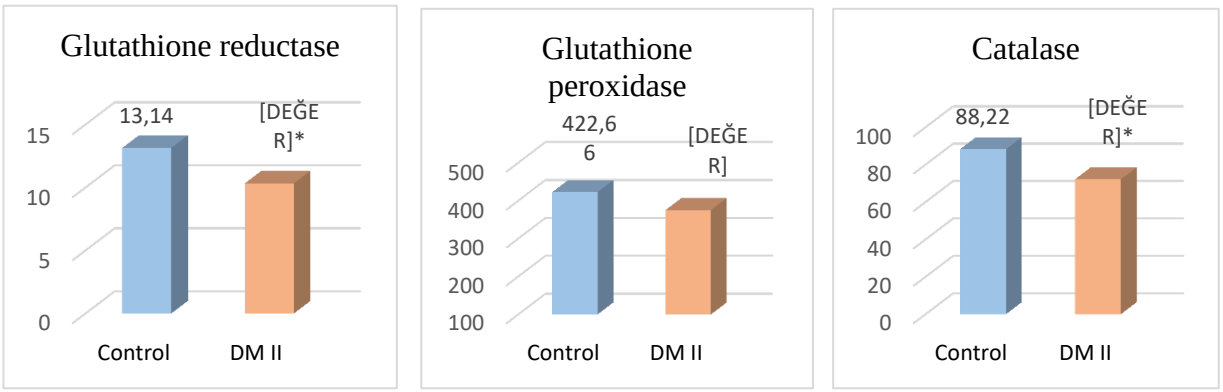


Figure 1. Deviations in LPO outputs for the 2nd type diabetes
Note: the difference is significant compared to the control group * - $p<0,05$.

The study conducted by Mrowicka M. (2005), Marjani A. (2010), Javed A, et al. (2023) found results consistent with the current study regarding MDA levels. Once again we are convinced that 2nd type diabetes is associated with increased lipid peroxidation. The latter is rised in the 2nd type diabetes mellitus and plays pivotal role in the pathogenesis and complications of diabetes. Antioxidants are known to prevent the progression and occurrence of diabetes. Free radical production can be reduced by preventing high blood glucose levels and controlling blood glucose instability. Patients suffering the 2nd type diabetes mellitus may have very high physiological requirements for antioxidants (Marjani, 2010; Mrowicka, 2005; Javed, 2023).

Findings from other researchers supported evidence that patients bearing diabetes were susceptible to oxidative stress, and higher blood glucose levels were associated with free radical lipid peroxidation. High levels of MDA in DM II indicate that oxidative stress plays an important role in the pathogenesis of cardiovascular complications. There is an imbalance between the oxidant and antioxidant systems in DM II (Davì et al., 2005; Likidlilid et al., 2010).

Antioxidant protection system. The research results obtained are reflected in Figure 2. Analysis of the research results indicates that the activity of the GlR enzyme in peripheral blood was significantly reduced from 13.14±0.97 to 10.33±0.81 ($p<0.05$). GlP activity in experimental animals changed slightly, this indicator was within the range of 375.39±28.34 in experimental animals, and in the control group 422.66±30.42 ($p>0.05$). Simultaneously, catalase activity was also significantly reduced from 88.22±6.27 to 72.11±4.37 ($p<0.05$).



Note: the difference is significant compared to the control group * - $p<0,05$.
Figure 2. Deviations in AOS enzyme activity in the 2nd type diabetes

Thus, the results of the studies indicate a decline in the antioxidant system activation against the background of oxidative stress activation in experimental DM II. Diabetes depletes the cellular antioxidant defense system and is associated with increased free radicals production. Oxidative stress can result from several pathways. Some of them are inextricably linked to substrate-mediated overproduction of reactive oxygen species in mitochondria, accelerated formation of advanced glycation end products, glucose autoxidation, and depletion of micronutrients and cellular elements with antioxidant properties. The gap between the robust experimental evidence for the pathogenetic role of increased oxidative load in diabetes mellitus and the overwhelming failure of antioxidants to demonstrate any health benefits can be described as the "antioxidant paradox" (Sheikh-Ali et al., 2011). High levels of free radicals and a simultaneous decrease in antioxidant defense mechanisms leading to injury to cellular organelles and enzymes increased lipid peroxidation and the development of insulin resistance. These oxidative stress effects may provoke the diabetes complications (Maritim et al., 2003).

Conclusion

1. In diabetes the oxidation of chain free radicals of lipids is activated leading to the accumulation of undesirable outputs in tissues having an extremely harmful effect entailing alterations in cell membranes at different levels

2. The development of diabetes is accompanied by a decrease in the activation of the antioxidant system confirming by a decrease in the expression of GlR, GlP, Ct against the background of the oxidative stress expression (impaired LPO-AOP processes).

Scientific Ethics Declaration

* The authors declare that the scientific ethical and legal responsibility of this article published in EPHELS Journal belongs to the authors.

* The authors declare no conflict of interest.

Acknowledgements or Notes

* This article was presented as a poster presentation at International Conference on Veterinary, Agriculture and Life Sciences (www.icvals.net) held in Antalya/Turkey on November 14-17, 2024.

* This research was funded by the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan, grant No. AP19677010.

References

American Diabetes Association. (2007). Standards of medical care in diabetes. *Diabetes Care, 30*, 4-41.

Ceriello, A., Testa, R., & Genovese, S. (2016). Clinical implications of oxidative stress and potential role of natural antioxidants in diabetic vascular complications. *Nutrition, Metabolism & Cardiovascular Diseases*, *26*(4), 285-292.

Chandra, K., Singh, P., Dwivedi, S., & Jain, S.K. (2019). Diabetes mellitus and oxidative stress: A co-relative and therapeutic approach. *Journal of Clinical and Diagnostic Research, 13*(5), BE07-BE12.

Davì, G., Falco, A., & Patrono, C. (2005). Lipid peroxidation in diabetes mellitus. *Antioxid Redox Signal,* 7(1-2), 256-268.

Dedov, I. I. (2010). Diabetes mellitus: development of technologies in diagnostics, treatment and prevention. *Diabetes Mellitus*, *13*(3), 6-13.

Counsil of Europe. (1986). *European convention for the protection of vertebrate animals used for experimental and other scientific purposes.* Retrieved from https://rm.coe.int/168007a67b

Devi, M. S., & Sudhakaran, P. R. (2011). Differential modulation of angiogenesis by advanced glycation end products. *Experimental Biology and Medicine*, *236*(1), 52-61.

Dubinina E.E., & Shugaley, I.V. (1993). Oxidative modification of proteins. *The Successes of Modern Biology. 113*, 71-81.

Esposito, K., Nappo, F., Marfella, R., Giugliano, G., Giugliano, F., Ciotola, M., ... & Giugliano, D. (2002). Inflammatory cytokine concentrations are acutely increased by hyperglycemia in humans: role of oxidative stress. *Circulation*, *106*(16), 2067-2072.

Gavrilov, V. B., & Mishkorudnaya, M. I. (1983). Spectrophotometric determination of the content of lipid hydroperoxides in blood plasma. *Laboratory Work*, *3*, 33-36.

Gracheva, S. A., Klefortova, I. I., & Shamkhalova, M. S. (2012). Prevalence of combined atherosclerotic vascular lesions in patients with diabetes mellitus. *Diabetes Mellitus*, *15*(1), 49-55.

International Diabetes Federation. (2013). *IDF diabetes atlas* (6th ed.). Retrieved from www.idf.org/diabetesatlas.

International Diabetes Federation. (2015). *IDF diabetes atlas* (7th ed.). Retrieved from www.idf.org/diabetesatlas.

Ighodaro O.M. (2018). Molecular pathways associated with oxidative stress in diabetes mellitus. *Biomedicine and Pharmacotherapy*, *108*, 656-662.

Ikebuchi, M., Nishio, Y., Maegawa, H., & Kashiwagi, A. (2010). Effects of hyperglycemia on oxidative stress and antioxidant potential in patients with type 2 diabetes. *Diabetology International*, *1*(2), 72-77.

Javed, A., Mehboob, K., Rashid, A., Majid, A., Khan, S., & Baig, Z. A. (2023). Oxidative stress and lipid peroxidation in NAFLD with and without type 2 diabetes mellitus. *Journal of the College of Physicians and Surgeons--Pakistan: JCPSP*, *33*(11), 1254-1258.

Johnson, K. J., Fantone, J. C., Kaplan, J.., & Ward, P. A. (1981). In vivo damage of rat lungs by oxygen metabolites. *The Journal of Clinical Investigation*, *67*(4), 983-993.

Konyukhova S.G., Markin S.G., Konyukhova A.A., & Fedorova T.N. (1989). Lipid peroxidation and methods for determining lipoperoxidation products in biological media. *Laboratornoe Delo, 9*, 40-46.

Korolyuk M.A., Ivanova L.I., Mayorova N.O., & Tokarev, V.E. (1988). Method for determining catalase activity. *Laboratornoe Delo*, *1*, 16-19.

Likidlilid, A., Patchanans, N., Peerapatdit, T., & Sriratanasathavorn, C. (2010). Lipid peroxidation and antioxidant enzyme activities in erythrocytes of type 2 diabetic patients. *J Med Assoc Thai*, *93*(6), 682-693.

Mansor, L. S., Gonzalez, E. R., Cole, M. A., Tyler, D. J., Beeson, J. H., Clarke, K., ... & Heather, L. C. (2013). Cardiac metabolism in a new rat model of type 2 diabetes using high-fat diet with low dose streptozotocin. *Cardiovascular Diabetology*, *12*, 1-10.

Maritim, A. C., Sanders, A., & Watkins, I. J. B. (2003). Diabetes, oxidative stress, and antioxidants: A review. *Journal of Biochemical and Molecular Toxicology*, *17*(1), 24-38.

Marjani, A. (2010). Lipid peroxidation alterations in type 2 diabetic patients. *Pakistan Journal of Biological Sciences: PJBS*, *13*(15), 723-730.

Mrowicka M. (2005). Procesy wolnorodnikowe W cukrzcy [Free-radical reactions in diabetes mellitus]. *Pol Merkur Lekarski. 9*(112), 571- 576.

Piarulli, F., Sartore, G., & Lapolla, A. (2013). Glyco-oxidation and cardiovascular complications in type 2 diabetes: A clinical update. *Acta Diabetologica*, *50*, 101-110.

Ramasamy, R., Yan, S. F., & Schmidt, A. M. (2011). Receptor for AGE (RAGE): Signaling mechanisms in the pathogenesis of diabetes and its complications. *Annals of the New York Academy of Sciences*, *1243*(1), 88-102.

Roglic, G. (2016). *Global report on diabetes.* Geneva, Switzerland: World Health Organization.

Sheikh-Ali, M., Chehade, J. M., & Mooradian, A. D. (2011). The antioxidant paradox in diabetes mellitus. *American Journal of Therapeutics*, *18*(3), 266-278.

Sherwin, R., & Jastreboff, A. M. (2012). Year in diabetes 2012: the diabetes tsunami. *The Journal of Clinical Endocrinology & Metabolism*, *97*(12), 4293-4301.

Shimizu, K., & Onik, I K. (2019). Development of a novel method for the treatment and prevention of diabetes mellitus. *Yakugaku Zasshi*, *139*(1), 39.

Soodaeva, S. K., Skotzelias, E. D., Zhukov, A. A., & Archakov, A. I. (1982). Comparative studies of superoxide generation in microsomes and reconstituted monooxygonose systems. *Cytochrome P-450. Biochemistry, Biophysies and Environmental Implications*, 615-618.

Srinivasan, K., Viswanad, B., Asrat, L., Kaul, C. L., & Ramarao, P. J. P. R. (2005). Combination of high-fat diet-fed and low-dose streptozotocin-treated rat: A model for type 2 diabetes and pharmacological screening. *Pharmacological Research*, *52*(4), 313-320.

Vanessa Fiorentino, T., Prioletta, A., Zuo, P., & Folli, F. (2013). Hyperglycemia-induced oxidative stress and its role in diabetes mellitus related cardiovascular diseases. *Current Pharmaceutical Design*, *19*(32), 5695-5703.

Vladimirov, Y.A., & Azizova, O.A. (1991). Free radicals in living systems the results of science and technology. *Biophysics Series*, *29*, 251.

Vlasova, S. N., Shabunina, E. I., & Pereslegina, I. A. (1990). The activity of the glutathione-dependent enzymes of erythrocytes in chronic liver diseases in children. *Laboratornoe Delo*, (8), 19-22.

Wang, J., & Wang, H. (2017). Oxidative stress in pancreatic beta cell regeneration. *Oxidative Medicine and Cellular Longevity*, *2017*(1), 1930261.

Wannamethee, S. G., Shaper, A. G., Whincup, P. H., Lennon, L., & Sattar, N. (2011). Impact of diabetes on cardiovascular disease risk and all-cause mortality in older men: Influence of age at onset, diabetes duration, and established and novel risk factors. *Archives of Internal Medicine*, *171*(5), 404-410.

Weykamp, C., John, W. G., Mosca, A., Hoshino, T., Little, R., Jeppsson, J. O., ... & Siebelder, C. (2008). The IFCC reference measurement system for HbA1c: A 6-year progress report. *Clinical Chemistry*, *54*(2), 240-248.

Zimmet, P. Z., Magliano, D. J., Herman, W. H., & Shaw, J. E. (2014). Diabetes: A 21st century challenge. *The Lancet Diabetes & Endocrinology*, *2*(1), 56-64.

Author Information

Oralbek Ilderbayev
L.N. Gumilyov Eurasian National University
010008, Astana, Satpayev 2, Republic of Kazakhstan
Contact e-mail: *oiz5@yandex.ru*

Gulmira Zharmakhanova
West Kazakhstan Marat Ospanov Medical University
030019, Astana, Maresyev Street 68. Republic of Kazakhstan

Darkhan Uzbekov
L.N. Gumilyov Eurasian National University
010008, Astana, Satpayev 2, Republic of Kazakhstan

Gulzhan Ilderbayeva
L.N. Gumilyov Eurasian National University
010008, Astana, Satpayev 2, Republic of Kazakhstan

Ainur Zhanilova
L.N. Gumilyov Eurasian National University
010008, Astana, Satpayev 2, Republic of Kazakhstan

To cite this article:

Ilderbayev, O., Zharmakhanova, G., Uzbekov, D., Ilderbayeva, G., & Zhanilova, A. (2024). Biochemical parameters studying in experimental diabetes. *The Eurasia Proceedings of Health, Environment and Life Sciences (EPHELS), 15*, 1-8.