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Hemato-biochemical status of laboratory mice with a GM corn based diet

E S Krasnikova¹, Y S Karmeeva², M M Aledo¹, A V Krasnikov¹ and S A Kalganov¹

¹ Department of Microbiology, Biotechnology and Chemistry, FSBEI HE "Saratov State Agrarian University", 1 Teatralnaya square, Saratov, Russia

² Scientific Training Laboratory of food and agricultural products quality, FSBEI HE "Saratov State Agrarian University", 1 Teatralnaya square, Saratov, Russia

E-mail: krasnikovaes77@yandex.ru

Abstract. GM analogues have about 30 plant species, and main share from GM crops belong to soybean and corn. According to the literature data, the introduction of GM fodder in the diet of laboratory mice and rats was accompanied by negative consequences for the health of experimental animals and their offspring. Corn is a component of animal feed and popular product among people, especially sweet canned corn. The lack of experimental data regarding effects of canned sweet GM corn on an organism was the drive behind our research subject. The objective of the research was a comparative analysis of hematological and biochemical parameters of laboratory mice with a conserved GM corn based diet and without it. Clinical blood analysis indicated the development of hyperchromic anemia, leukocytosis due to an increase in the fraction of medium blood cells and thrombocytosis in experimental group mice. Biochemical studies of these mice blood revealed signs of renal and liver pathology, myocardial damage and hyperproteinemia. A comparative analysis of the hemato-biochemical status of laboratory mice indicated the development of signs of anemia, intoxication and allergy in the group of mice with a conserved GM corn based diet as compared to intact mice of the control groups.

Genetically modified organisms (GMOs) are plants that animals or microorganisms whose genetic material (DNA) was modified by artificial means without the natural recombination but the means of genetic engineering. This allows the transmitted individual genes between unrelated species. Products created as a result of genetic modification are referred to as genetically modified (GM) products. Tobacco was the first crop to be genetically modified with the introduction of antibacterial resistant genes by, Michael Bevan in 1983 [1].

Currently, GM analogues have about 30 plant species, including crops the human and animal consumption, the widest spread being, GM soybeans, corn, canola and cotton make up about 99%. Main share from all GM crops belong to soybean (49%) and corn (33%) [2].

The introduction of genetically modified corn to the mice diet in a laboratory setting did not go without any consequences: the experiment revealed a dysfunction of homeostasis, characterized by a decrease in the total number of erythrocytes and leukocytes and an increase in stab and reduction of segmented neutrophils, a decrease in neutrophil phagocytic activity, phagocytic number, bactericidal and lysozyme activity of blood serum, total lymphocytes. At the same time in the intestinal contents of



animals increases number of conditionally pathogenic microbes *K. oxytoca*, *P. Vulgaris*, *E. coli*, *S. marcescens*, *E. cloacae*, *E. faecalis*, *C. coli*, *H. pylori*, *L. interrogans*, and the proportion useful automicroflora *L. delbrueckii* and *B. bifidum* is low [3].

Scientists of the food safety laboratory of the Kazakh Scientific Research Veterinary Institute found that with the introduction of GM into the diet of laboratory mice, the animals observed a decrease in size, asymmetry and hypoplasia of the uterus, the absence or reducing the number of fruits change in consistency parenchymal organs. The study of the offspring of rats, for three generations have used GM-feed, revealed the immaturity of the internal organs, the absence of one of the three sheets (ecto-, endoderm), hydropic and granular dystrophy of cartilage cells, fragmentation and hypoplasia myocytes, partial desquamation of ectoderm cells in their offspring [4].

Every year there are more and more reports of the dangers of GMOs for animals, humans and the environment. In the review of I.V. Ermakova (2013) it is reported that experimental animals develop sterility, oncology and identical pathological changes in the internal organs with the introduction of various GM components into their feed [5].

There is another opinion. Studies to assess the GMO toxicity were conducted at the Federal research center for nutrition, biotechnology and food safety (Moscow). Analysis of damages of DNA and structural chromosome aberrations, assessment of the allergenic potential and immunoreactive properties has not confirmed any genotoxic, allergenic embryotoxic, immunotoxic and teratogenic effect of soybean event MON 89788 and maize event MIR604 [6].

Some researchers even suggest using GM plants for cleaning the environment from pollution of anthropogenic origin and to improve the human environment [7].

Despite the contradictory data, it is obvious that the danger of GMOs may be due to a number of reasons, in which there is an introduction a new gene with possible pleiotropic action and new substances resulting from their expressions, the content in the GM products may be toxic and cause allergenic reactions.

In the Russian Federation, from January 2019, the use of GMOs for food or in animal feed is prohibited; however, checks regularly detect GM-ingredients in feed and feed additives imported from abroad [8].

Corn is a component of animal feed and poultry, and popular product on the table of people, especially sweet canned corn. This fact, as well as the lack of experimental data on investigating the effects of canned sweet GM corn was the drive behind our research subject.

The objective of the research was analysis of hematological and biochemical parameters of laboratory mice with a conserved GM corn based diet. The study was to observe the differences between mice that have had an introduction of GM sweet corn and those that had all natural sweet corn and without it.

The objects of the study were 60 Balb / C mice, which (were divided into 3 groups according to the principle of analogues. At the rate of two to three females per male. The control group I received only extruded rodent feed. "Happy Jungle" universal (Russia). The control group II received along with feed sweet canned corn "Kormilitca" 50% of the diet while the experimental group III received, along with food, sweet canned corn «American garden» (USA) in the amount of 50% of animal diet.

The experiment lasted 2 months, then the animals were euthanasia by displacement of the cervical vertebrae, the blood was collected in vacuum tubes with stabilizer K3 EDTA for the general analysis of blood and in test tubes with clot activator (PUTH, Russia) for biochemical studies. The study of the morphological composition of the blood of mice was carried out on hematology analyser of automatic type PCE-90VET (USA). Blood biochemical parameters were investigated on an automatic analyser Stat Fax 3300 (USA) using biochemical research kits blood sera of Diakon-DS JSC (Russia).

The results of the comparative analysis of hematological parameters of the laboratory mice are presented in table 1.

Table 1. The comparative analysis of the hematological parameters of the mice.

Indicator	Group of animals		
	Group 1 (universal feed)	Group 2 (universal + non GM feed)	Group 3 (universal + GM feed)
RBC, $10^{12}/L$	6.6±0.6	8.0±0.7	4.4±0.4 ^a
HGB, g/l	102.7±8.6	106.0±9.3	81.0±7.8 ^a
MCHC, g/l	268.0±24.5	265.0±25.7	305.0±28.0 ^{a1}
RDWc, %	16.2±1.6	16.4±1.5	16.3±1.4
MCV, fl	53.6±5.2	55.6±5.3	60.4±5.8 ^a
WBC, $10^9/L$	7.7±0.7	8.2±0.7	14.1±1.3 ^a
LYM, %	31.3±3.0	32.1±3.1	33.1±1.1
MID, %	3.4±0.2	4.1±0.3	9.4±0.3 ^a
GRA, %	65.3±5.4	63.8±5.8	57.5±5.1 ^a
PLT, $10^9/L$	129.0±11.9	136.0±12.4	164.0±14.9 ^a
MPV, fL	8.1±0.6	7.9±0.6	6.5±0.6 ^a

Note: ^a The difference of the experimental group III from the control groups, $p < 0.05$.

The data of the clinical blood analysis indicates the development of hyperchromic anemia in group III mice, which is characterized by a combination of a high index of the average hemoglobin content in one erythrocyte with a low content of hemoglobin as a whole. Since the number of erythrocytes in mice in this group is reduced by 1.5-1.8 times in comparison to the mice of the control groups, an increased destruction of erythrocytes in the bloodstream in this group mice can be assumed. This is observed in case of poisoning with hemolytic poisons, such as the roundup herbicide (glyphosate) when it enters the body in large quantities. Confirms our assumption about the state of intoxication in mice of group III and a slightly enlarged size of red blood cells with a normal indicator of the width of the distribution of red blood cells by volume.

In animals of this group, leukocytosis is observed due to an increase in the fraction of medium blood cells, which is an indicator of the development of an allergic reaction. The relative content of blood granulocytes in the mice of group III is slightly reduced, indicating a decrease in the immune response at the cellular level.

Allergies are often caused by autoimmune diseases, one of the markers of which is thrombocytosis which we noted in group III mice with a slight decrease in the average blood platelet volume. Thrombocytosis can also be a consequence of hemolytic processes.

The results of a comparative analysis of the biochemical parameters of the laboratory mice blood, in the diet of which canned sweet GM maize was introduced, compared to the control groups, are presented in table 2.

Table 2. The comparative analysis of the biochemical parameters of the mice blood.

Indicator	Group of animals		
	Group 1 (universal feed)	Group 2 (universal + non GM feed)	Group 3 (universal + GM feed)
Urea, mmol/l	5.4±0.6	5.9±0.7	8.1±0.8 ^a
Creatinine, mmol/l	54.5±5.6	54.7±5.3	57.3±5.4
Glucose, mmol/l	3.5±0.3	4.1±0.4	6.9±0.7 ^a
ALT, e/l	52.8±5.1	59.8±5.5	75.1±7.2 ^a
AST, e/l	112.9±11.6	127.4±12.9	443.8±41.3 ^a
Total protein, e/l	63.3±6.1	69.1±6.5	99.2±9.7 ^a
Albumin, g/l	31.8±2.9	30.1±2.8	33.7±3.2
Amylase, e/l	913±89.9	903±88.7	954.3±94.5

Lactate, mmol/l	1.7±0.1	1.4±0.1	3.7±0.3 ^a
Triglycerides, mmol/l	0.9±0.1	0.5±0.03	0.5±0.04 ^a
Direct bilirubin, µmol/l	0.0±0.0	0.0±0.0	0.2±0.02 ^a
Total bilirubin, µmol/l	3.7±0.3	3.2±0.3	8.7±0.6 ^a

Note: ^a The difference of the experimental group III from the control groups, $p < 0.05$.

As follows from the data presented in Table 2, in the mice of the experimental group III, blood urea level increases almost 1.5 times as compared to the control groups which may be a sign of incipient renal pathology, since the urea level increases earlier than creatinine in kidney damage.

An increase in blood glucose may occur as a result of a high-calorie diet when sweet corn is introduced into the diet, and a significant increase in it (2 times compared to the control) indicates a slow glucose utilization by the liver, probably as a result of damage and destruction of hepatocytes. Confirms our assumption and an increase in the activity of hepatic transferases, especially a significant increase in the activity of AST, which is often a sign of endogenous intoxication.

The de Ritis coefficient in the experimental group of mice is 3 times higher than the maximum permissible values, which may be a sign of myocardial damage.

The development of hyperproteinemia in mice, in the diet of which GM corn was present, can be explained by the fact that pathological proteins are formed in a number of pathological conditions, in particular, allergies. Our assumption confirms the fact of the predominance of the immunoglobulin fraction in the total serum protein.

According to our data, blood amylase activity in all groups do not have significant differences, which indicates the stability of carbohydrate metabolism and the functioning of the pancreas.

The content of lactic acid (lactate) is greatly exceeded in mice of the third group, which is an indicator of tissue hypoxia and correlates with the data of clinical blood analysis, indicating severe anemia in mice (table 1).

The marker of the hemolytic anemia is a high content of bilirubin in the serum of mice of this group, and a sign of liver damage is the presence of direct bilirubin, which is absent in the serum of the control groups mice.

The blood triglycerides of mice with the GM corn diet is slightly reduced, but are within the physiological norm, indicating a high energy expenditure in animals of these groups, for various reasons.

Thus, a comparative analysis of the hemato-biochemical status of laboratory mice indicates the development of signs of anemia, intoxication and allergy in the group of mice in which sweet preserved GM corn was introduced as compared to intact mice of the control groups.

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