



**POSSIBLE NEGATIVE EFFECTS OF A GENETICALLY MODIFIED PRODUCT
ON THE HEPATOBILIARY SYSTEM OF RATS**

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Abstract:

Introduction: In the experimental group of laboratory animals, visible changes in the liver are noted, characterized by an increase in size, average weight, and changes in the structure and color of the organ under study.

Result:

Macroscopic examination of the liver of laboratory animals of the first generation revealed different parameters between the experimental and control groups was established: a distinct structure of hepatic beams, formations with a pronounced homogeneous structure of the cytoplasm of hepatocytes, a central vein and sinus capillaries without visible changes. Interlobular connective tissue is poorly developed. The artery, vein, and bile duct between the hepatic lobules in both groups of animals were unchanged.

Conclusion:

This means that a genetically modified product-soy flour - negatively affects the condition of the liver.

Keywords: genetically modified product, laboratory animals, liver, morphology.

Introduction

At the moment, much attention is paid to the problems of using genetically modified organisms (GMO) in food, since there is a threat of their negative impact on human health and the environment [5]. Genetically modified (transgenic) organisms are plants, animals, and micro-organisms whose genome has been altered by genetic engineering [6]. Gene technologies are



increasingly being introduced into agriculture and the food industry. Changes in the DNA of plants and animals can affect the body in different ways.

Experts dealing with genetic security issues identify three types of threats that GMO pose: threats to the human body (in the form of allergic diseases, metabolic disorders, etc.), threats to the environment (in the form of vegetating weeds, chemical pollution, etc.), global risks (in the form of activation of critical viruses, threats to economic security) [7].

Scientists have realized that thanks to genetic modification, plants and vegetables become more frost-resistant, are stored longer, and are not eaten by insects.

By definition, GMO are living organisms that have intentionally altered nucleic acid sequences. These changes can be reduced to the introduction or removal of genetic fragments. In this case, both foreign nucleic acid (for example, bacteria containing the human insulin gene) and nucleic acid of this type can be introduced (for example, to increase the starch content in potatoes, the genes associated with starch synthesis can be "duplicated" several times). GMO combine three groups of organisms -genetically modified micro-organisms (GMO), animals (GMO), and plants (GMO). The dominant transgenic crops in the world are soy, corn, cotton, and rapeseed [13].

Creating genetically modified food sources is an inevitable way to solve many nutrition and health problems. The growth of the World's population, which, according to scientists' forecasts, should reach 11 billion people by 2050 (2009 – more than 6 billion), respectively, there is a need to significantly increase world agricultural production, which is impossible without the creation of genetically modified organisms [10].

Genetically modified organisms – an organism or several organisms, any non-cellular, single-celled or multicellular formations capable of reproducing or transmitting inherited genetic material, other than natural organisms, obtained using genetic engineering methods and containing genetic engineering material, including genes, their fragments or a combination of genes [16].

Genetic engineering is a set of techniques, methods, and technologies, including technologies for obtaining recombinant nucleic acids, for isolating genes from an organism, manipulating genes, and injecting them into other organisms.



Genetic engineering is the "heiress" of traditionally conducted breeding works in the field of crop production and animal husbandry. At the same time, with desirable genes, the possibility of transmitting undesirable ones is not excluded, which makes it difficult to separate positive properties from harmful ones. The priority of genetic engineering is the speed and accuracy of obtaining the desired properties, the ability to track and control genetic changes and their consequences [8].

Currently, genetically modified plants are grown in 28 countries around the world, especially in the United States, Brazil, Argentina, India and Canada. The main crops are soy, potatoes, corn, sugar beets, tomatoes, pumpkin, rapeseed [2,9,15].

A genome is a complete set of genes in an organism. DNA (deoxyribonucleic acid) is the "encyclopedia of life", the only type of molecule capable of encoding genetic information [12].

The identification of non-declared genetically modified food sources, as well as GMO combinations, is relevant for ensuring the biological safety of food for the population [1, 3, 4, 14].

Work on genetic modification is carried out in three main areas: agricultural plants, animals and birds, and microorganisms.

Modification of agricultural crops is aimed at searching for properties that provide resistance to herbicides, insecticides, viruses, adverse environmental factors, increasing product yield, improving consumer properties, nutritional value, etc. [11].

Currently, most GM foods are classified as the second class of safety, given the presence in their composition of 1-2 proteins responsible for the manifestation of the desired feature, which distinguishes the transgenic product from the traditional one. The concept of compositional equivalence may become untenable in the near future due to the beginning of mass production of transgenic products with a modified composition. As ways to solve this problem, it is proposed to use such areas of science as genomics-determination of the structure and function of DNA; proteomics-determination of protein profile; metabolomics-determination of secondary metabolites [16].



The biomedical assessment of GM food includes the following areas. Compositional equivalence – protein (amino acid composition), fat (fatty acid composition), carbohydrate composition, mineral composition, vitamin content, specific components, biologically active substances, contaminants (natural, anthropogenic);

Chronic toxicity of GM food-integral indicators, biochemical indicators, hematological indicators, morphological studies, sensitive biomarkers: the activity of enzymes of the I and II phases of biotransformation of xenobiotics, the activity of enzymes of the antioxidant defense system, the content of lipid peroxidation products.

The aim of the work was to study and evaluate the effect of the GM product on the morphological parameters of the liver of laboratory animals in the experiment.

Materials and Methods

Commercial soy flour (soy flour No. 24) was used as a GM product. Experimental studies were conducted on white mongrel rats.

All laboratory animals were divided into 3 groups: the experimental group-animals that included soy flour No. 24 in the General Vivar diet (at a dose of 0.02-0.03 g per 1 rat weighing 160-180 g for 30 days (n=30); the control group - animals that received only a General Vivar diet, without soy flour No. 24 (n=30). Group 3-intact animals (n=30) that were kept in standard vivarium conditions.

As a GM product, the experiments will use soy grown in Kyrgyzstan and imported to our country only for research. The PCR method revealed the presence of the 35S+FMV promoter in the studied GM soy, which proves that the studied soy is a GM product. In ordinary soy, this promoter is not present. All groups were formed at the same time. The laboratory animals involved in the experiment were representative by age, gender, weight, and conditions of keeping and feeding. After 30 days of feeding soy flour No. 24, groups of laboratory animals were killed in a humane way, then autopsies were performed. When killing and dissecting laboratory animals, the rules of biological safety and ethical principles of working with laboratory animals were observed.



To study the morphological parameters of the liver, a macroscopic method (anatomical dissection) was used. Macroscopic studies of animals were carried out on the basis of the meeting of the ethical Committee of the Ministry of health of the Republic of Uzbekistan No. 4/17-1442 dated 21.09.2020. It was based on the provisions of the Helsinki Declaration of the World Medical Association of 1964, supplemented in 1975, 1983, 1989, 1996, 2000, 2002, 2004, 2008, 2013.

To study morphological parameters, research methods widely used in laboratory practice were used. After cutting the material, it was fixed in 10% buffered formalin, then washed in water and dehydrated in alcohols and compacted with benzene. Then they were poured into paraffin and prepared sections 4-6 microns thick, which were stained with hematoxylin and eosin. The sections were examined morphometrically using an eyepiece micrometer DN-107T/ Model CM001 CYAN cope (Belgium).

Mathematical processing was performed directly from the General data matrix "Excel 7.0 "using the capabilities of the program" STTGRAPH 5.1". the standard deviation and representativeness errors were determined. When organizing and conducting research, the principles of evidence-based medicine were observed.

The results of the study and discussion

The parameters of the liver of laboratory animals of the experimental and control groups also significantly differed. Macroscopic examination of the liver of laboratory animals revealed different indicators between the experimental and control groups. Thus, $52.4 \pm 5.6\%$ ($n=25$) of animals in the experimental group showed an increase in the size of the liver, while in experimental animals in the control group, the size of the liver remained at the normal limits. Accordingly, the difference between the compared groups of the first generation was also in the average weight of the liver. If the average liver weight in the experimental group was 7.2 ± 1.3 grams, then in the control group this parameter was equal to 6.1 ± 1.03 grams, which is 1.2 times less than the experimental group. Significant differences were noted in the relative weight of the liver (g / 100 g of body weight) between the main and control groups ($P < 0.05$) - 4.52 ± 0.36 grams versus 3.17 ± 0.37 grams, respectively.



The differences between the compared groups of the first generation concerned such indicators as "change in liver structure" ($P < 0.001$) and "change in liver color" ($P > 0.05$), where the indicators of the experimental group were higher than the parameters of the control group.

If the animals of the control group did not have an increase, change in the structure and color of the liver, then in the experimental groups liver damage is manifested by the development of fatty dystrophy and hepatocytes, these parameters were markedly different compared to the control.

Pathological changes in the liver noted in the experimental group indicate that this GM product negatively affects the state of these organs in experimental animals. The absence of the carcinogenic effect of GM soy flour on the animals of the experimental group, apparently, was due to the short period of exposure to this food product. Thus, comparative differences in the state of the liver, where pathological changes are noted, between the experimental and control groups of the first generation indicate that soy flour No. 24 (GM product) negatively affects the liver condition of experimental animals.

Conclusions

In the experimental group of animals, visible changes in the liver are noted, characterized by an increase in size, average weight, and changes in the structure and color of this organ. Based on a comparative study of the liver in both groups, it was established: a distinct structure of hepatic beams, formations with a pronounced homogeneous structure of the cytoplasm of hepatocytes, a central vein and sinus capillaries without visible changes. Interlobular connective tissue is poorly developed. The artery, vein, and bile duct between the hepatic lobules in both groups of animals were unchanged. Macroscopic examination of the liver of laboratory animals of the first generation revealed different parameters between the experimental and control groups, these differences related to the size of the liver, the average and relative weight of the liver, such indicators as "change in liver structure" and "change in liver color", where the data of the experimental group were significantly higher than the parameters of the control group. Almost identical results were obtained in animals of the second and third generation.



This indicates that GM soy flour No. 24 negatively affects the state of the liver of animals in the dynamics of the experiment.

Histological studies of the liver structure of experimental animals found that there are no visible structural damage or changes in the experimental and control groups of animals.

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