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Description of the level of the effect of gene-modified soy on normal microflora in the experience

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Abstract---The aim of the study was to determine the effect of GM-soy on the microbiocenosis of white colonized rats in the experiment. In the normal microflora of the colon of rats fed with GM-free soybeans, it was found that different quantitative differences were different from those of intact laboratory animals *Bifidobacterium* spp (1.28-fold decrease), *Lactobacillus* spp (1.53-fold decrease), *Enterobacter* spp, and *Proteus* spp (4.1). and an increase of 6.25 times). This did not indicate the development of complete dysbiosis, as no group differences between *Escherichia colilactosanegative* and lactose-positive strains were identified, Symptoms of dysbiosis were poorly developed in GM-free soybeans (DI I), and dysbiosis symptoms were more pronounced in GM-soy-fed soybeans (DI II).

Keywords---various microorganisms, *Enterobacter* spp, *Lactobacillus* spp, *Escherichia colilactosanegative*, normal microflora.

Introduction

In addition to the various microorganisms that enter the body from the external environment, there are also microorganisms in the human body that live in symbiosis with it and form the normal human microflora. They are located in different biotopes and are important for the functioning of the organism. One such biotope is the colon, whose normal microflora of indigenous and facultative microorganisms plays an important role in life.

Disruption of the normal microflora of the colon under the influence of various external and internal factors is characterized by a qualitative and quantitative imbalance of the indigenous and facultative microflora in it and is called intestinal dysbiosis. Many physical, chemical, and biological factors can be examples of factors that lead to intestinal dysbiosis.

Today, a lot of scientific work has been done on the different effects of genetically modified (GM) products on the human body, and experts are divided on this issue, along with the opinion that these products have no adverse effects on the human body [2, 10]. There are many proven works [3 7, 9]. Subsequent scientific studies have shown that GM products have a negative effect on the immune system [1], liver and pancreas [8], thymus and spleen [11], as well as hematological, biochemical changes, mutagenic and reproductive activity [5, 6]. , there are studies showing that it has a negative effect on bone marrow cells [12]. An analysis of many scientific literatures shows that there are few studies to determine the degree of impact of GM products on the microbiocenosis of human biotopes, including the microbiosis of the colon, and they are scattered. In view of the above, the aim of the study was to determine the effect of GM-soy on the microbiocenosis of the colon in white experimental rats.

Materials and Methods

For this purpose, a total of 90 male white rats were involved in the study, which were divided into 3 groups: Group 1 - intact white rats with a standard vivarian diet, not fed with GM or without GM (n = 30). ; Group 2 - GM-free white rats included in the standard vivariate diet (n = 30); Group 3 - white non-GM rats fed with GM-soy in the standard vivariate diet (n = 30). These groups were representative and differed from each other by only one character. Emphasis was placed on whether the studies were randomized and that principles of evidence-based medicine were followed. The study strictly adhered to the ethical principles and biological safety rules of working with laboratory animals [4].

After the colon mass of white rats was delivered to the bacteriological laboratory, bacteriological examinations were performed using Bergy's Manual Systematic Bacteriology (1997) using appropriate nutrient media (Blaurokk, SRM-4 (MRS-4), Endo, Saburo media, egg yolk agar, etc.). Microorganisms were identified and differentiated: Bifidobacterium spp, Lactobacillus spp, Escherichia coli, Enterobacter spp, Proteus spp, Staphylococcus spp, Streptococcus spp, Candida spp. Statistical processing of the results was carried out using traditional variational statistical methods, and the principles of evidence-based medicine were followed in organizing and conducting the research.

Results and their discussion

The results obtained showed that there were convincing differences in the quantitative indicators studied between the groups being compared (Table 1).

Table 1
Quantitative analysis of quantitative indicators of colon microbiocenosis in GM-free soy-fed and intact laboratory animals,
lg KXQB / ml (M ± m)

Microorganisms	1-group, n=30	2- group, n=30
Bifidobacterium spp	5,10±0,2	4,00±0,1*↓
Lactobacillus spp	6,10±0,2	4,00±0,1*↓
Escherichia coli (lactosapostive)	5,15±0,2	5,00±0,2 ↔
Escherichia coli (lactose-negative)	0	0 ↔

Enterobacterspp	1,20±0,1	5,00±0,2*↑
Proteusspp	0,80±0,1	5,00±0,2*↑
Staphylococcusspp	4,10±0,1	5,00±0,2*↑
Streptococcusspp	6,30±0,3	4,00±0,2*↓
Candidaspp	3,60±0,1	7,00±0,1*↑

Note: * -convincing sign of distinction between groups; ↑, ↓ - directions of changes; ↔ - There is no convincing difference.

It can be seen that in 7 of the 9 representatives of the colon microflora studied (77.78%) reliable changes were detected, it should be noted that the quantitative indicators of microorganisms changed in different directions compared to the norm (group 1). Indications for *Escherichia coli* alone did not change convincingly in either group. Formation of metallic glossy fuchsia-red colonies in the Endo environment, acid-gas decomposition of lactose in the Giss series, pathogenic *Escherichia coli* (lactose-positive intestinal bacilli) and in the Endo environment quantitative indicators of *Escherichia coli* (lactozanegative intestinal bacillus), which did not have the characteristic, showed pathogenicity, were close to each other ($R>0.05$).

The analysis showed that a significant decrease in quantitative indicators relative to the control group (intact) in group 2 (consuming soy without GM) was observed among representatives of the normal indigenous microflora of the colon. Quantitative decrease in *bifidobacterium* spp was up to 1.28 times ($R<0.05$), while quantitative decrease in *Lactobacillus* spp was up to 1.53 times ($R<0.05$). This condition has been shown to be the first sign of the onset of processes leading to a dysbiotic state in the colon of group 2 laboratory animals.

A similar situation can be observed with *Streptococcus* spp, another representative of the normal microflora, whose concentration in the colon was reduced by 1.58 times ($R<0.05$). This situation was also interpreted as a prelude to dysbiotic processes. In contrast to the control group, given that group 2 has only one external influencing agent (shadow), the decrease in quantitative parameters of intestinal indigenous microflora was interpreted as a transient condition because these changes were under its influence and were an unfamiliar product for white rats.

When comparing the control group to laboratory animals, it should be noted that the quantitative increase in group parameters was mainly due to enterobacteria and coagulase-positive cocci, which enter the facultative (transitory) microflora of the colon. was observed. Thus, in group 2, a quantitative increase was observed in *Enterobacteria* spp and *Proteus* spp, representatives of the family Enterobacteriaceae - by 4.17 times ($R<0.001$) and 6.25 times ($R<0.001$), respectively. Quantitative increase of these microorganisms was interpreted as the beginning of dysbiotic processes in the colon.

A similar result, but at a lower intensity, was also observed on *Staphylococcus* spp. It should be noted that the intensity of the downward trend of this microorganism was less than that of gram-negative bacteria. The difference between the control and comparison groups was 1.58 times, in favor of the intact animals ($R<0.05$).

Thus, different quantitative differences in the normative microflora of white colonies of white rats with GM-free soy added to the standard vivarian diet were detected compared to intact laboratory animals, quantitative changes in different directions were detected in 7 out of 9 normative microflora (77.78%) ($R < 0.05$).). The main convincing differences were observed for *Bifidobacterium* spp (1.28-fold decrease), *Lactobacillus* spp (1.53-fold decrease), *Enterobacter* spp, and *Proteus* spp (4.16-fold and 6.25-fold increase). Such a disturbance of the balance between indigenous and facultative microflora of the colon is the initial sign of dysbiotic processes and does not indicate the development of complete dysbiosis, as no group differences between pathogenic and non-pathogenic strains of *Escherichia coli*, one of the major microorganisms of intestinal microflora, were identified. The reason for the quantitative changes that occurred was the consumption of soy, which was unfamiliar to the animal organism.

In the next stage of the research, the quantitative indicators of colon microbiocenosis in white-bred rats with GM-soy added to the standard vivariate diet were compared and the obtained data were analyzed. Intact (not consuming GM-soy) laboratory animals were obtained for comparison. All results are presented in Table 2.

Table 2
Quantitative analysis of quantitative indicators of colon microbiocenosis in GM-soy-fed and intact laboratory animals,
lg KXQB / ml ($M \pm m$)

Microorganisms	1-group, n=30	2- group, n=30
<i>Bifidobacterium</i> spp	5,10 $\pm$ 0,2	2,10 $\pm$ 0,1*↓
<i>Lactobacillus</i> spp	6,10 $\pm$ 0,2	2,00 $\pm$ 0,2*↓
<i>Escherichiacoli</i> (lactosapositive)	5,15 $\pm$ 0,2	0 ↓
<i>Escherichiacoli</i> (lactose-negative)	0	5,30 $\pm$ 0,3*↑
<i>Enterobacter</i> spp	1,20 $\pm$ 0,1	5,45 $\pm$ 0,2*↑
<i>Proteus</i> spp	0,80 $\pm$ 0,1	3,00 $\pm$ 0,1*↑
<i>Staphylococcus</i> spp	4,10 $\pm$ 0,1	6,15 $\pm$ 0,2*↑
<i>Streptococcus</i> spp	6,30 $\pm$ 0,3	4,30 $\pm$ 0,2*↓
<i>Candida</i> spp	3,60 $\pm$ 0,1	7,00 $\pm$ 0,4*↑

Note: * -convincing difference sign between groups; ↑, ↓ - directions of changes; ↔ - There is no convincing difference.

When analyzing the quantitative indicators of microorganisms that make up the microflora of the colon presented in Table 2, it was found that all of them have intergroup differences. These differences were observed for all 9 microorganisms studied.

The most profound quantitative changes were interpreted as a significant condition observed on representatives of the normal indigenous microflora of the colon *Bifidobacterium* spp, the decrease was 2.43 times ($R < 0.001$). A similar result was obtained for *Lactobacillus* spp - the quantitative indicators showed a tendency to decrease and the intensity was the same as for bifidobacteria, the quantitative decrease averaged 3.05 times ($R < 0.001$).

A significant decrease in the number of indigenous microflora in the main group (GM-shade-fed) to 2.43-3.05 times relative to the control group (intact) was found to be the beginning of dysbiotic processes in this biotope. These quantitative changes have been confirmed to be the effect of an external factor on indigenous microorganisms, if we consider that only GM-soy is affected as an external factor, the results obtained will be clear that it is an effect.

In the study of the quantitative indicator of *Escherichia coli*, which is another representative of the normal microflora of the colon, we witnessed a different picture. With the ability to break down lactose, the pathogen did not germinate in the control group of these gram-negative bacteria in the amount of 5.15 ± 0.2 lg KXQB / ml, while white groupless rats belonging to group 3 did not germinate from the biological material obtained from the colon. However, when pathogenic *Escherichia coli* strains were infused at a dose of 5.30 ± 0.3 lg KXQB / ml, it was acknowledged that these strains were not detected at all in the control group. This condition is one of the main signs of the developing dysbiosis process in this biotope.

Other members of the Enterobacteriaceae family, *Enterobacter* spp and *Proteus* spp, also underwent changes in lactose-negative *Escherichia coli*, in other words, their quantitative values were above the norm - 5.45 ± 0.2 lg KXQB / ml and 3.00 ± 0 , respectively. 1 lg KXQB / ml. These numbers were characterized by a convincing excess of 4.54 and 3.75 times the norm limits ($R < 0.001$). Such a situation led to an increase in the quantitative decrease of indigenous microorganisms conditionally-pathogenic enterobacteria. This identified appearance is a sign of the formation of dysbiotic processes in the colon.

The above-mentioned abrupt changes in gram-negative bacteria were not observed in gram-positive cocci, although the intensity of the changes was low, although quantitative indicators differed between groups. If *Staphylococcus* spp was significantly increased 1.50 times in group 3 compared to group 1 (4.10 ± 0.1 lg KXQB / ml versus 6.15 ± 0.2 lg KXQB / ml, respectively, $R < 0.05$), we witnessed a reverse picture on *Streptococcus* spp, i.e., group 3 indicators were found to be significantly 1.47 times lower than the control group (group 1) ($R < 0.05$).

Results similar to the parameters of facultative microorganisms consisting of conditionally pathogenic microorganisms were obtained on *Candida* spp. In the colon of GM-soy-fed white rats, the amount of microorganisms belonging to this genus of yeast-like fungi was significantly higher than in GM-soy-fed intact rats (1.94-fold, $R < 0.001$).

Analysis of the results obtained showed that symptoms of colon dysbiosis were observed at the end of the observation period in laboratory animals consuming GM-soy. This condition is manifested in the following:

First, the quantitative indicators of indigenous flora *Bifidobacterium* spp and *Lactobacillus* spp, which are representatives of the normal microflora of the colon, were significantly reduced by 2.43 and 3.05 times, respectively, in GM-soy-fed animals compared to intact rats. A decrease in this amount was an external factor

negatively affecting them, and in this experiment it was interpreted as a GM-soy. This condition was interpreted as the first element of dysbiosis formed in the colon biotope.

Second, in white non-GM-fed rats, unlike intact, lactose-negative *Escherichia coli* flour (intact did not flourish in animals), lactose-positive *Escherichia coli* did not flourish, and vice versa in intact. Lack of lactosanegative strains and the absence of lactose-positive strains have been shown to be a secondary element of colon dysbiosis.

Third, in group 3 laboratory animals, conditionally pathogenic members of the Enterobacteriaceae family were found to be 4.54 and 3.75 times more susceptible to *Enterobacter* spp and *Proteus* spp than the control group, respectively, indigenous and facultative due to GM-soy exposure only as an external effect. this product has been shown to be the main cause of microbial imbalance, which has been proven to be the third element of colonic dysbiosis.

Fourth, in elements 1-3 of colonic dysbiosis, no significant changes in the indicators of gram-positive cocci in this biotope were observed, if the symptoms of this condition were evident, indigenous microflora pathogenogen *Streptococcus* spp in the main group decreased to 1.47 times more than intact laboratory animals, facultative microflora the spp quantitative index increased convincingly to 1.50 times. This intergroup incompatibility was interpreted as the fourth element of colon dysbiosis.

Fifth, *Candida* spp, a representative of the facultative microflora of the colon, was convincingly increased to 1.94 times in GM-soy-fed white rats (group 3) compared to non-GM-soy rats (group 1) as the fifth element of colon dysbiosis.

After the formation and development of dysbiotic processes in the colon of white rats as a result of GM-soy exposure, there was a need to assess the degree of quantitative changes in indigenous and facultative microflora. For this purpose, the ratio of the quantitative indicators of the compared groups to each other was studied. $R < 0.05$ - $R < 0.001$). This condition was interpreted as another indication that they had developed deep dysbiosis under the influence of GM-soy in the colon.

The next phase of the study was a comparative study of quantitative indicators of indigenous and facultative microflora of laboratory animals with GM-free soy (group 2) and GM-soy (group 3) added to the standard vivarian diet. The results obtained are presented in Table 3.

Table 3
Comparative analysis of quantitative indicators of colon microbiocenosis in
laboratory animals fed without GM and with GM,
lg KXQB / ml ($M \pm m$)

Microorganisms	1-group, n=30	2- group, n=30
<i>Bifidobacterium</i> spp	4,00±0,1	2,10±0,1*↓
<i>Lactobacillus</i> spp	4,00±0,1	2,00±0,2*↓

Escherichiacoli (lactosapostive)	5,00±0,2	0 ↓
Escherichiacoli (lactose-negative)	0	5,30±0,3*↑
Enterobacterspp	5,00±0,2	5,45±0,2*↑
Proteusspp	5,00±0,2	3,00±0,1*↑
Staphylococcusspp	5,00±0,2	6,15±0,2*↑
Streptococcusspp	4,00±0,2	4,30±0,2*↓
Candidaspp	7,00±0,1	7,00±0,4*↑

Note: * -convincing difference sign between groups; ↑, ↓ - directions of changes; ↔ - There is no convincing difference.

Although the results of both groups differed from the parameters of the intact laboratory animals, the intensity and depth of the changes were evident in group 3. In this case, it was important to determine the degree of variation of the soywith and without GM.

Representatives of the indigenous microflora of the colon were found to have a difference between the quantitative indicators of Bifidobacterium spp and Lactobacillus spp - a significant decrease of 1.90 times and 2.0 times, respectively ($R < 0.001$).

In 2 of the 9 microorganisms studied (Staphylococcus spp, Candida spp) no group differences were detected ($R > 0.05$), they were quantitatively close to each other. It is noteworthy that 1 of them belongs to the group of facultative microorganisms. No specific pattern was observed in this case. However, indigenous microorganisms (Bifidobacterium spp, Lactobacillus spp) were found to be further reduced in group 3, while facultative microorganisms (Enterobacter spp, Staphylococcus spp) were found to be more abundant. The results obtained for lactose-negative and lactose-positive Escherichia coli showed a sharp difference between these groups. In other words, while GM-shadow-fed laboratory animals had all 5 cited elements of dysbiosis, they did not show up significantly in rats that consumed GM-soy.

In order to summarize all the results obtained, we found it necessary to compare the performance of all three groups (Table 4). In this Table 4, a convincing difference between the groups is clearly seen, the analyzed figures show that there are practically no changes in the normal microflora of the colon of GM-free soy-fed (intact, control) laboratory animals, no signs of dysbiosis were detected; In laboratory animals consuming GM-free soybeans (group 2), the balance between indigenous and facultative microorganisms is partially disturbed, with symptoms of dysbiosis, but it is not formed and developed; In GM-soy-fed animals (group 3), the balance of indigenous and facultative microorganisms was disturbed, signs of dysbiosis were clearly observed, all 5 elements were identified, total dysbiosis of the colon was developed. This condition has been interpreted as a result of GM-soy exposure to white rats. Laboratory animals of GM-soy have been shown to cause total dysbiosis by adversely affecting the normal microflora of the colon.

Table 4
Quantitative status of colonic microflora in white rats with GM and GM-non-GM
rations, lg (M ± m) (KXQB / ml)

Microorganisms	1-group, n=30	2-group, n=30	3-group, n=30
Bifidobacterium spp	5,10±0,2	4,00±0,1	2,10±0,1*^↓
Lactobacillus spp	6,10±0,2	4,00±0,1	2,00±0,2*^↓
Escherichia coli (lactose-positive)	5,15±0,2	5,00±0,2	0 ↓
Escherichia coli (lactose-negative)	0	0	5,30±0,3*↑
Enterobacter spp	1,20±0,1	5,00±0,2	5,45±0,2*^↑
Proteus spp	0,80±0,1	5,00±0,2	3,00±0,1*^↑
Staphylococcus spp	4,10±0,1	5,00±0,2	6,15±0,2*^↑
Streptococcus spp	6,30±0,3	4,00±0,2	4,30±0,2*↓
Candida spp	3,60±0,1	7,00±0,1	7,00±0,4*↑

Note: * - A convincing difference sign between groups 1 and 3; ^ Is a convincing difference sign between groups 2 and 3; ↑, ↓ - directions of changes; ↔ - There is no convincing difference.

To determine the state of the normal microflora of the colon, the degree of development of dysbiosis, the appearance of its depth, criteria for the assessment of dysbiosis have been developed by many studies and presented to practical health care. Among these methods, we selected the one that we considered most appropriate and used it to assess dysbiosis.

This method was developed by Uzbek researchers Garib F.Yu., Adilov Sh.K. and Narbaeva I.E. Recommended by the researchers in 1995, changes in the microflora of the colon are assessed by 2 degrees:

In grade I dysbiosis - changes are observed only among representatives of the indigenous group, Bifidobacterium spp and Lactobacillus spp are reduced relative to lactose-positive Escherichia coli, intestinal dysfunction is not manifested. In grade II dysbiosis - with a decrease in indigenous microorganisms, the number of facultative conditionally pathogenic microorganisms increases, the balance between them is disturbed, the symptoms of intestinal dysfunction are clearly visible. These levels are determined using the dysbacteriosis index (DI):

DII = E.coli KXQB / g / Indigenous microorganisms, KXQB / g < 0,1;

DIII = Optional microorganisms, KXQB / g / Indigenous microorganisms, KXQB / g ≤ 0,5.

Agar DII > 0.1; If DIII ≤ 0.5, it is grade I of dysbiosis, if DI II > 0.5, it is grade II dysbiosis regardless of how much DI I is.

The results of our study were as follows:

In group 1 - 0.31 < 0.1 (DII); 0.37 < 0.5 (DI II);

In group 2 - 0.38 < 0.1 (DII); 0.77 < 0.5 (DI II);

In group 3 - 1.29 < 0.1 (DII); 3.56 < 0.5 (DI II).

The results fully confirmed the above, ie there were no signs of dysbiosis in intact laboratory animals (group 1), in dysfunctional symptoms of GM-free soy (group 2)

poorly developed (grade I), in GM-soy-fed white rats the symptoms of dysbiosis were evident (grade II).

Conclusions

1. GM-free soy-fed white rats in the normal microflora of the colon compared with reliable intact laboratory animals *Bifidobacterium* spp (1.28-fold decrease), *Lactobacillus* spp (1.53-fold decrease), *Enterobacter* spp, and *Proteus* spp (4 , An increase of 16 and 6.25 times, respectively). These are the initial signs of dysbiosis and do not indicate the development of complete dysbiosis, as no group differences between *Escherichia colilactosanegative* and *lactosapostive* strains were identified.
2. Quantitative indicators of *Bifidobacterium* spp and *Lactobacillus* spp in laboratory animals fed with GM-soy were significantly reduced by 2.43 and 3.05 times compared to intact rats. This decrease was an external factor negatively affecting them, and in this experiment it was interpreted as a GM-soy. This condition was interpreted as the first element of dysbiosis formed in the colon biotope.
3. GM-soy-fed white rats, unlike intact ones, produced lactose-negative *Escherichia coli*, while lactose-positive *Escherichia coli* did not, and vice versa. Lactation of *lactosanegative* strains, the absence of *lactose-positive* strains, has been shown to be a second element of colonic dysbiosis.
4. In laboratory animals fed with GM-soy, *Enterobacter* spp and *Proteus* spp were found to be 4.54 and 3.75 times higher, respectively, than in the control group, proving to be the third element of colon dysbiosis.
5. No significant changes in gram-negative cocci were observed in elements 1-3 of elements of colon dysbiosis. *Streptococcus* spp was significantly reduced by 1.47 times in the main group compared to intact laboratory animals, while *coagulazapostive Staphylococcus* spp was found to be 1.50 times more reliable. increased significantly. This intergroup incompatibility was interpreted as the fourth element of colon dysbiosis.
6. The quantitative index of *Candida* spp in white-bred rats fed with GM-soy was significantly increased by 1.94 times compared to those not fed with this product, as the fifth element of colon dysbiosis.
7. While laboratory-fed animals fed GM-soy contained all 5 cited elements of dysbiosis, they did not show up significantly in rats consuming soy without GM.
8. Determination of dysbacteriosis index, indicating the I and II degrees of dysbacteriosis, gave the following results: in group 1 - $0.31 < 0.1$ (DII); $0.37 < 0.5$ (DI II); in group 2 - $0.38 < 0.1$ (DII); $0.77 < 0.5$ (DI II); in group 3 - $1.29 < 0.1$ (DII); $3.56 < 0.5$ (DI II). There were no signs of dysbiosis in intact laboratory animals, the symptoms of dysbiosis were poorly developed in GM-free soyfeeding (grade I), and the symptoms of dysbiosis were pronounced in GM-soy-fed animals (grade II).

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