IMPACT OF A HIGH-FAT AND HIGH-FIBER DIET ON GUT MICROBIOTA IN ICR (CD1) MICE

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Abstract. This study evaluated the effect of different diets on the probiotic (lacto-, bifidobacteria) and opportunistic (yeast, *Escherichia coli*) intestinal microflora of CD1 mice. The high-fat diet contained 40% animal fat (lard) and the high-fiber diet contained 40% freeze-dried fiber. The intestinal microflora was determined by the standard method of seeding the contents of the intestine on selective culture media (MPC, Blaurock, Sabouraud, Endo). The results showed that on the 50th day of the experiment in the group of mice with a high fat content, the population of probiotic cultures of lacto- and bifidobacteria decreased, while the population of yeast and enterobacteria increased, compared with the starting point of the experiment and the control group of mice. The weight of mice in this group by the end of the experiment increased by 16%. In the group of mice with a high content of insoluble fiber, a decrease in the populations of probiotic cultures, yeasts and enterobacteria was observed. At the same time, the weight of mice increased by 13.6%. Thus, high fat intake in the diet entails possible disturbances in the intestinal microbiota, an increase in opportunistic microflora, which can lead to intestinal diseases. When using a large amount of insoluble fiber, on the contrary, it leads to a decrease in microflora in general. This is most likely due to a lack of nutrients and enough nutrients (proteins and fats) in the diet, which are still necessary for the microflora.

Keywords: yeasts, enterobacteria, lactobacilli, bifidobacteria.

List of Abbreviations

ATP – Adenosine triphosphate
CFU – colony-forming units
MPC – Milk Proteins Concentrate
SCFAs – short-chain fatty acids

Introduction

The gut microbiota is a complex dynamic system (Romanchuk, 2020). The versatility of the relationships of the gut microbiota, both with the host organism and within the microbial community itself, gives researchers reason to separate the microbiota into a separate physiological system (Yudina *et al.*, 2019) or consider it as a «new organ» (Mallick, 2017). Numerous studies show a close relationship between the violation of the intestinal microflora and the manifestation of the metabolic syndrome (Croci *et al.*, 2021), the development of type 2 diabetes (Meijnikman *et al.*, 2018), atherosclerosis (Afineevskaya *et al.*, 2020), colon cancer (Kochkina *et al.*, 2019), and neurodegenerative diseases of the brain (Sun *et al.*, 2021). Along with this, the existence of a relationship between the state of the intestinal microbiota, the central nervous system, and complex emotional behavior has been shown (Foster *et al.*, 2016; Sudo, 2016). This relationship has been described as a gut–brain axis in which the microbiome plays a key role (Foster, 2013) (Fig. 1). Thus, studies on the study of possible ways of influencing the intestinal microbiome are becoming relevant and promising. Diet is one of the powerful adaptive mechanisms and promotes the integration of the body into a specific environment (Romanchuk, 2020).

Objective: to conduct a comparative analysis of the effect of different diets (high-fat and high-fiber) on changes in the gut microbiota in ICR (CD1) mice.

Materials and Methods

Ethical Approval

The study was carried out in compliance with the principles of the European Convention for the Protection of Vertebrate Animals used for Experiments and Other Scientific Purposes (Strasbourg, 1986) in accordance with the rules of proper laboratory practice (Moscow, 2016), and was approved by the Ethics Committee of National research Tomsk State University.

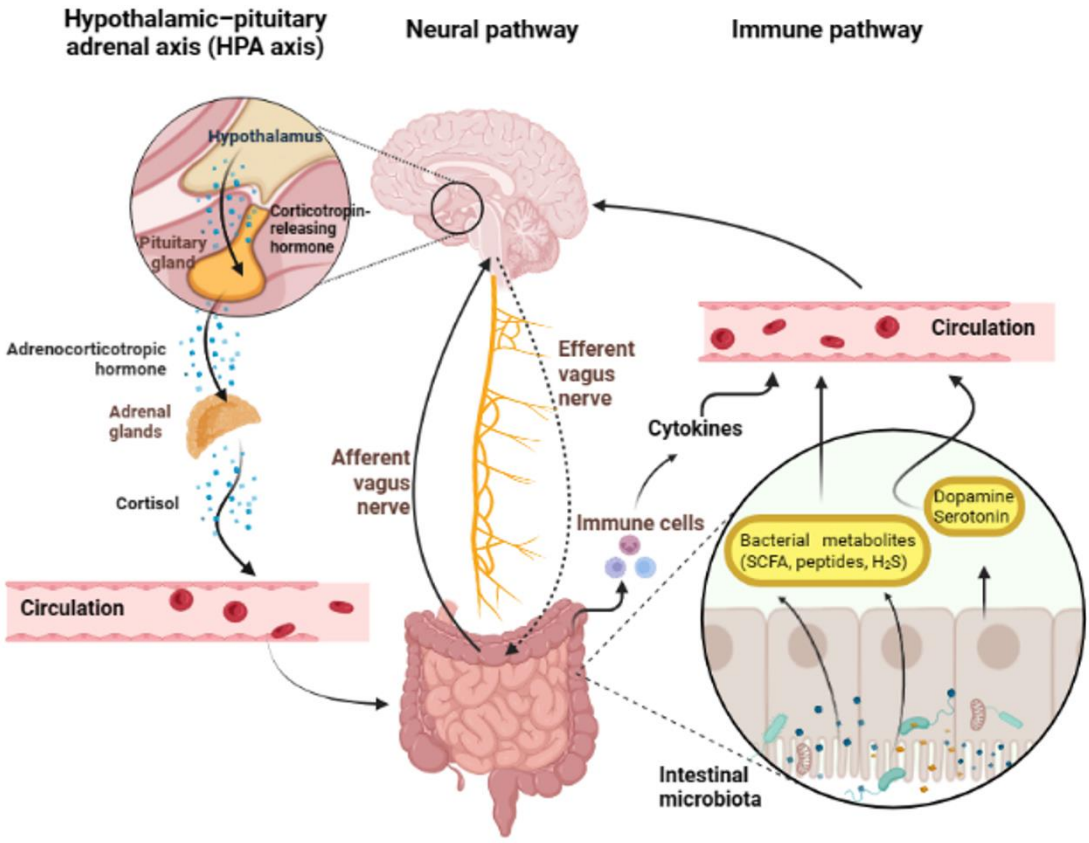

Fig. 1. Gut-brain axis

Animals and experimental design

The studies were carried out on 15 outbred males of the ICR line (CD1) with an initial body weight of 30–35 g. Age at the beginning of the experiment was 12 weeks. The mice were obtained from the vivarium of the E. D. Goldberg Research Institute of Pharmacology and Regenerative Medicine of the Tomsk National Research Medical Center of the Russian Academy of Sciences. During the period of adaptation (14 days) and the experiment, the animals were kept under standard vivarium conditions: air temperature regime 21–24 °C, relative humidity 30–70%, light regime 12:12 h, free access to water.

In the diet of the animals, food was used «Delta Feeds» C-19 (BioPro, Novosibirsk). The animals were divided into 3 groups of 5 animals in each group: 1st group (control group) – animals with a standard diet, received food for keeping laboratory animals, prepared according to GOST 34566-2019 (mass fraction of fat not more than 6%); 2nd group (high-fat group) – a diet with a high-fat content (the feed included 40% saturated fat – lard), 3rd group (high-fiber group) – a diet with a high-fiber content (the feed included 40% wheat and oat fiber (insoluble), fat content no more than 6%). The daily ration was 10 grams per laboratory animal. The duration of the study is 50 days. The amount of food eaten, and liquids drunk by each group, morbidity, mortality, appearance, physical activity, stool condition, changes in behavior were recorded daily. Mice were weighed weekly. The experimental design is shown in Figure 2.

Material selection and cultivation

Feces were taken from each individual mouse, after placing the mouse in a separate cage. The selection and inoculation of the biomaterial was carried out on days 0, 17, 34, and 50 of the experiment. Before sowing, a biomaterial suspension was obtained: 1 g of feces was crushed in 9 ml of distilled sterile water. Next, the corresponding tenfold dilutions (dilution of 10^{-10}) of the biomaterial suspension were inoculated onto nutrient media.

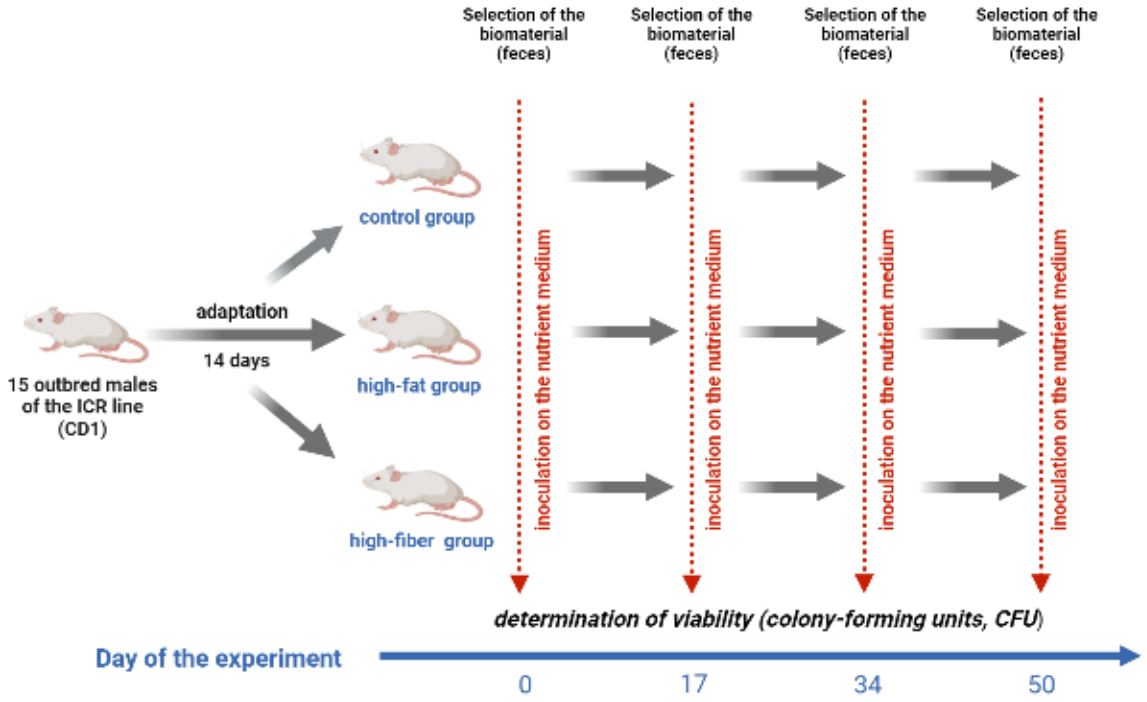

Fig. 2. Experimental design

To determine viable (colony-forming units, CFU) opportunistic pathogens, selective culture media Endo Agar (BioMedia) (for the isolation of *Enterobacteriaceae*) (Abu-Sini *et al.*, 2023) and Sabouraud Medium (Biotechnovation) (for the isolation of yeasts) (Di Paola *et al.*, 2020) were used. The seeding of the biomaterial was carried out on Petri dishes, 100 µl of dilution of the suspension of the biomaterial, dilutions from 10^{-2} to 10^{-10} were used. Determination of CFU of probiotic cultures was carried out on Blaurock Medium (Bifidum-medium, Obolensk) (for the isolation of *Bifidobacterium*) (Khabirov *et al.*, 2022) and Medium MRS agar (Obolensk) (for the isolation of *Lactobacillus*) (Farahmand *et al.*, 2021). Seeding was carried out in test tubes with a volume of 10 ml, 1 ml of biomaterial suspension, dilutions from 10^{-2} to 10^{-10} were used. Cultivation was carried out at 37 °C for 1-7 days. To obtain reliable data, 3 replications of seeding were performed for each experimental point. Colonies were counted on days 1-2, 5, and 7. Determination of the morphology of microorganisms (cell shape, Gram stain, presence of spores and capsules) was carried out by phase-contrast (colony prints) and light microscopy (stained smears). The data was represented as the CFU/g of wet weight fecal sample by applying the dilution factor. The mean and standard deviation were calculated for all the variables in the Microsoft Excel.

Results

Body weights and food intake

By the end of the experiment, mice in all groups gained weight compared to the weight at the starting point of the experiment. The maximum weight gain of mice was noted only in the high-fat group, an increase of 16.0% from the starting point of the experiment (Fig. 3A). In the high-fiber and control groups, the weight of mice also increased, by 13.6% and 12.3%, respectively. At the same time, at the beginning of the experiment, the percentage of food intake (100% was taken as the norm: 10 g of food per 1 mouse per day) in the high-fat group and high-fiber group decreased. But starting from the 15th day of the experiment in these groups, the percentage of food intake began to increase. In the control group, food intake was erratic and remained approximately the same (Fig. 3B). By the end of the experiment, the percentage of food intake increased significantly in the experimental group. The decrease in food intake at

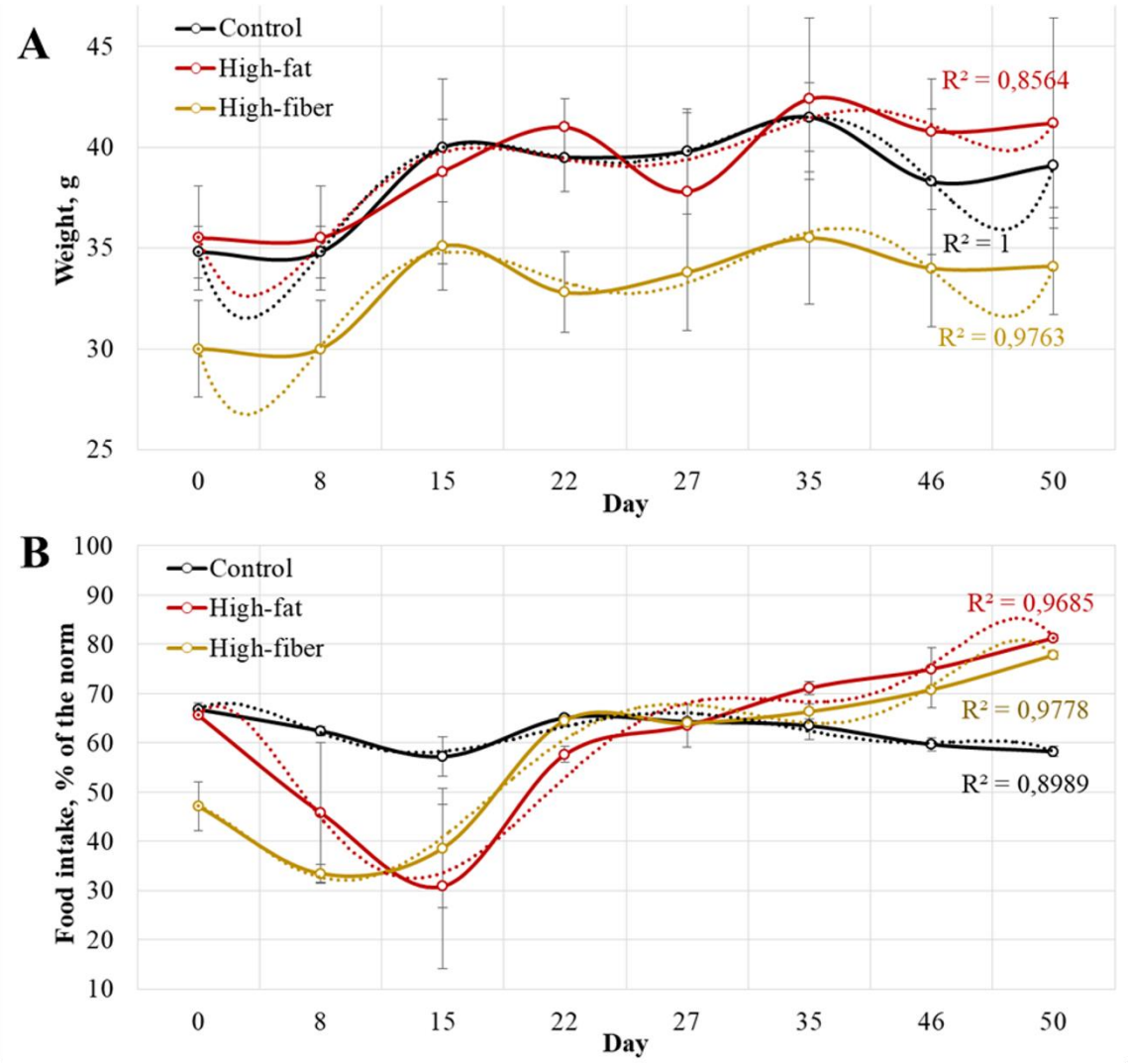

Fig. 3. Body weight of mice and percentage of food intake in groups with different types of diets
Note: A – body weight of mice, B – percentage of food intake, solid line – recorded parameters, dotted line – trend line (polynomial function to the 6th degree), R^2 – approximation confidence factor

the beginning of the experiment can be explained by the adaptation and habituation of mice to a new food, while after adaptation food intake returned to normal.

Colony morphology

Lactobacillus colonies on MRS agar Medium were small (1-2 mm), creamy-white in color and shaped like a «grain» on days 2-3 of cultivation (Fig. 4A). During microscopy, immobile filamentous bacterial rods were observed, sometimes arranged in a chain or pair. The cell size was from 3 to 5 μm; the cells did not form spores or capsules. Gram stain showed Gram-positive bacterial cells (Fig. 4B).

Bifidobacterium colonies on Blaurock Medium on days 2-3 of cultivation were about 0.5-1 mm, disc-shaped colonies, white in color (Fig. 5A). Cells under microscopy were rod-shaped, sometimes slightly curved, 2 to 5 μm long, cells did not form spores or capsules. Gram stain was positive (Fig. 5B).

Colonies of Enterobacteriaceae on Endo agar plates were round with smooth edges, raspberry red with a metallic sheen, glossy, 1-2 mm in size (Fig. 6A). Microscopic examination showed single shortened rods. The cell size was from 1 to 3 μm; the cells did not form spores or capsules. Gram stain confirmed the presence of *Enterobacteriaceae*, which appeared as gram-negative rods (Fig. 6B).

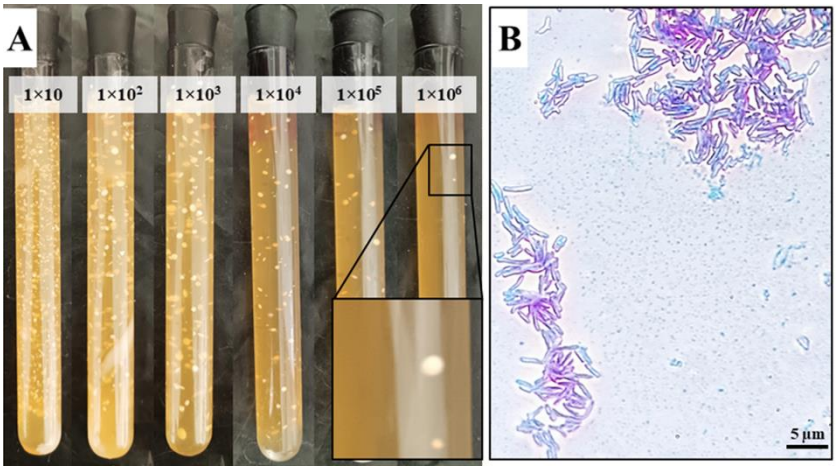

Fig. 4. Colonies of probiotic microorganisms (*Lactobacillus*) on the MPS nutrient medium
Note: A – six-fold dilutions, an enlarged photo of the colony of Lactobacilli, B – *Lactobacillus* cells isolated from colonies, Gram-stained (sample obtained from inoculation of faeces of mice from group high-fat on the 31st day of the experiment)

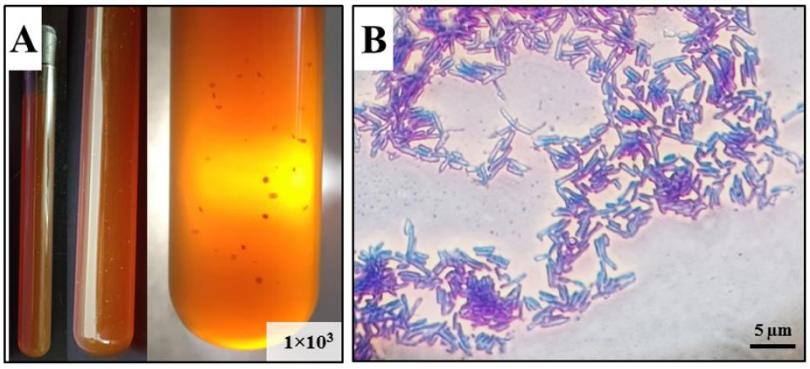

Fig. 5. Colonies of probiotic microorganisms (*Bifidobacterium*) on the Blaurock medium
Note: A – three-fold dilutions, an enlarged photo of the colony of *Bifidobacterium* (in the light), B – *Bifidobacterium* cells isolated from colonies, Gram-stained (sample obtained from inoculation of faeces of mice from group high-fat on the 31st day of the experiment)

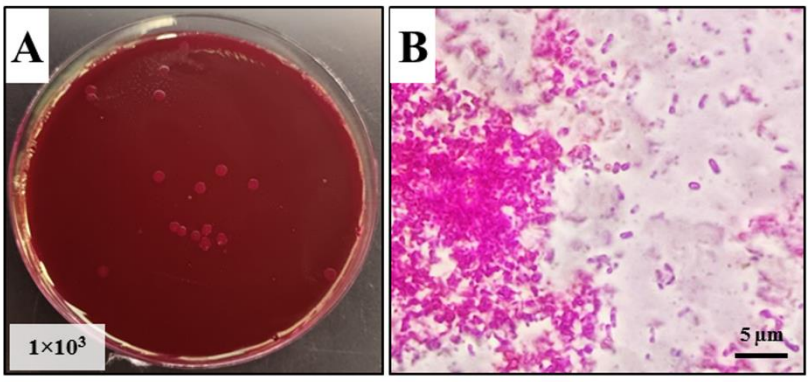

Fig. 6. *Enterobacteria (E. coli*) colonies on Endo medium
Note: A – Triple dilutions, enlarged photo of an *E. coli* colony, B – Gram-stained *E. coli* cells isolated from colonies (sample obtained from fecal inoculation of mice from the control group on the 50th day of the experiment)

Yeast colonies on Sabouraud's medium on days 1-2 of cultivation were larger – 2-4 mm, round, white, glossy, and slightly convex. Microscopic examination revealed large, oval, and oblong cells, ranging in size from 5 to 8 μm (Fig. 7).

Microbial colonies were counted based on the typical colony morphological features on the selective media using the BioRad Chemi-Doc MP universal system colony counter, based on VisionWorks LS software.

Enumeration of fecal Lactobacillus, Bifidobacterium, Enterobacteriaceae (Escherichia coli) and Yeast

The results of the number of microorganisms formed on different media are presented in Table 1. Initial changes in the composition of the microbiota in the high-fat and high-fiber groups were recorded on the 17th day of the experiment and progressed until the end of the study. There was an expected statistically significant increase in *Enterobacteriaceae* in the groups of mice with a high-fat diet – $(8.30 \pm 1.16)\times10^6$, and a decrease in the group with a high-fiber diet – $(10.8 \pm 1.91)\times10^2$ (compared to the control group – $(6.25 \pm 0.58)\times10^4$). A similar pattern was shown for yeast, where an increased value was observed in the high-fat group $(7.28 \pm 0.64)\times10^8$ and decreased values in the high-fiber group $(4.45\pm0.84)\times10^6$. Interestingly, along with opportunistic microflora, the results show a significant reduction in *Lactobacillus* and *Bifidobacterium* in both experimental groups versus the control group. Moreover, for mice of the high-fiber group, a more pronounced decrease in the relative abundance of *Lactobacillus* in fecal samples was shown: from $(6.06 \pm 0.46)\times10^7$ on the first day of the experiment to $(5.45 \pm 0.95)\times10^4$ after 50 days. A statistically significant decrease in the level of *Bifidobacterium* was found for all experimental groups compared with the control group $(6.64 \pm 0.29)\times10^6$, but without significant differences among themselves (high-fat group $(3.64 \pm 0.27)\times10^4$, high-fiber group $(2.84 \pm \pm 0.34)\times10^4$).

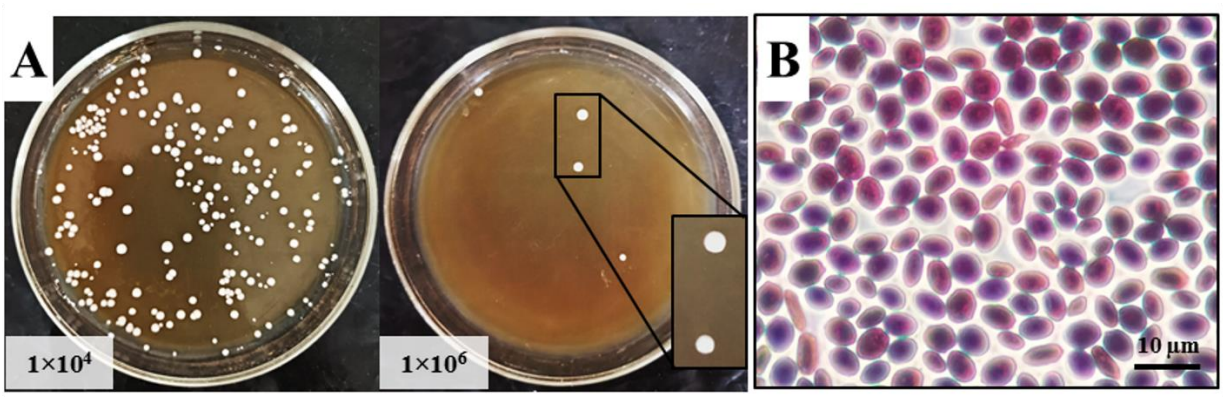

Fig. 7. Colonies of Yeast on the Sabouraud medium
Note: A – six-fold dilutions, an enlarged photo of the colony of *Yeast*, B – *Yeast* cells isolated from colonies, Gram-stained (sample obtained from inoculation of faeces of mice from group high-fiber on the 50st day of the experiment)

Table 1

The content of living microorganisms in 1 g of faeces, CFU×g^{-1}

Group	Day of the experiment			
	0	17	31	50
Yeasts (Sabouraud Medium)				
control	$(7.25 \pm 0.76)\times10^7$	$(6.63 \pm 0.04)\times10^7$	$(6.61 \pm 0.47)\times10^7$	$(7.78 \pm 0.83)\times10^7$
high-fat	$(9.94 \pm 1.70)\times10^7$	$(6.92 \pm 0.36)\times10^7$	$(9.02 \pm 0.71)\times10^7$	**$(7.28 \pm 0.64)\times10^8$**
high-fiber	$(9.25 \pm 0.82)\times10^7$	$(5.31 \pm 1.63)\times10^7$	**$(7.21 \pm 0.55)\times10^6$**	**$(4.45 \pm 0.84)\times10^6$**

End of table 1

Group	Day of the experiment			
	0	17	31	50
Enterobacteria (Endo Agar)				
control	$(7.58 \pm 0.71)\times10^4$	$(7.83 \pm 0.89)\times10^4$	$(5.86 \pm 0.90)\times10^4$	$(6.25 \pm 0.58)\times10^4$
high-fat	$(8.71 \pm 0.96)\times10^4$	$(6.83 \pm 0.75)\times10^4$	**$(8.80 \pm 0.85)\times10^5$**	**$(8.30 \pm 1.16)\times10^6$**
high-fiber	$(5.51 \pm 1.61)\times10^4$	**$(5.94 \pm 0.61)\times10^3$**	**$(8.38 \pm 1.36)\times10^2$**	**$(10.8 \pm 1.91)\times10^2$**
Lactobacilli (MPC Medium)				
control	$(4.42 \pm 0.82)\times10^7$	$(5.81 \pm 0.78)\times10^7$	$(5.52 \pm 0.86)\times10^7$	$(4.72 \pm 0.98)\times10^7$
high-fat	$(5.78 \pm 0.62)\times10^7$	$(7.51 \pm 1.05)\times10^7$	**$(6.84 \pm 0.87)\times10^6$**	**$(4.44 \pm 0.83)\times10^5$**
high-fiber	$(6.06 \pm 0.46)\times10^7$	**$(2.22 \pm 0.95)\times10^6$**	**$(5.12 \pm 1.37)\times10^5$**	**$(5.45 \pm 0.95)\times10^4$**
Bifidobacteria (Blaurock Medium)				
control	$(7.73 \pm 0.66)\times10^6$	$(6.38 \pm 0.41)\times10^6$	$(6.58 \pm 0.45)\times10^6$	$(6.64 \pm 0.29)\times10^6$
high-fat	$(5.98 \pm 0.54)\times10^6$	$(7.31 \pm 0.91)\times10^6$	**$(4.75 \pm 1.40)\times10^5$**	**$(3.64 \pm 0.27)\times10^4$**
high-fiber	$(5.93 \pm 1.87)\times10^6$	**$(5.70 \pm 0.81)\times10^5$**	**$(4.46 \pm 0.75)\times10^5$**	**$(2.84 \pm 0.34)\times10^4$**

Discussion

The notion that the microbiota and its influence is limited only to the host's digestive tract has long given way to a broader view of the association of the microbiota with host development, growth, and host physiology (Sommer & Bäckhed, 2013). Changing the diet or taking antibiotics leads to rapid changes in the microbiota, thereby affecting the state of the host-microbiota relationship (David *et al.*, 2014; Dethlefsen *et al.*, 2008; Walker *et al.*, 2011).

Food consumed by a person, passing through the digestive tract, is broken down into smaller components and provides intestinal bacteria with available nutrients and substrates. In turn, bacteria break down food components, provide the body with the necessary nutrients, stimulate the development of humoral and cellular immune responses, modulate metabolism, and synthesize several metabolites. Among them, the most studied are short-chain fatty acids, gases, vitamins (K2, B12, folic acid, riboflavin, thiamine) and secondary bile acids (Rowland *et al.*, 2018). Interspecific competition of bacteria for life-supporting resources determines the composition of the community (Patnode *et al.*, 2019). It has previously been shown that the microbial composition and function of the gut is highly dependent on diet and is sensitive to specific changes in the host's diet. However, it is very difficult to determine the role of microorganisms in the metabolism of individual nutrients, so the analysis of these relationships in individual diets is in many cases not clear. To date, the greatest interest is the study of the impact on the intestinal microbiota of individual nutritional components, in particular fats, proteins, carbohydrates, as part of various diets, the most famous of which are the Western and Mediterranean diets. For example, in most studies, the term «high-fat diet» (HFD, High-Fat Diet) or the so-called «Western diet» refers to a diet high in fat (usually saturated fatty acids) and simple carbohydrates low in fiber, vitamins, minerals. This diet is often used to induce obesity in experimental animal studies (Malesza *et al.*, 2021). However, the exact ratio of nutrients in this diet has not been determined and varies greatly between experiments, and as a result leads to inconsistent results. In most animal studies, the western diet increases the proportion of gram-negative species in the gut microbiota (including enterobacteria), which is also confirmed by our study (Cani *et al.*, 2007; Kazura *et al.*, 2023; de La Serre*et et al.*, 2010; Kim *et al.*, 2012). The number of *Enterobacteriaceae* bacteria (mainly *E. coli*) in the intestinal contents of mice in the high-fat group began to increase after a month (on the 31st day of the experiment), and by the end of the experiment (50 days) it increased by 2 orders of magnitude. Such a shift towards an increase in gram-negative microorganisms in the intestine leads to increased absorption of bacterial lipopolysaccharides in the intestine and the development of «metabolic endotoxemia», and subsequently to obesity. Metabolic endotoxemia is also promoted by increased intestinal permeability and

bacterial translocation associated with a low degree of intestinal inflammation (Festi *et al.*, 2014).

Also in our study, with a high-fat diet, the amount of yeast and yeast-like fungi in the faeces of mice increased only by the end of the experiment, on day 50. On the one hand, yeasts, predominantly of the *Saccharomyces* genus, play a positive role in health; they are producers of B vitamins, proteins, certain amino acids, trace elements (Foligné *et al.*, 2010), and antioxidants (Badr *et al.*, 2021). Some yeast strains, such as *Saccharomyces cerevisiae* and *Saccharomyces cerevisiae var. boulardii* are used as probiotic cultures for disease prevention (Lazo-Vélez *et al.*, 2018; Badr *et al.*, 2021; Abid *et al.*, 2022), including for the treatment of diarrhea associated with irritable bowel syndrome (Leventogiannis *et al.*, 2019) antibiotic-associated (Ehrhardt *et al.*, 2016), Crohn's disease (Guslandi *et al.*, 2000). Known enzymatic activity of yeast *Saccharomyces* against other microorganisms, namely the production of phosphatase against *E. coli* cells and protein phosphatase, inhibiting toxic surface endotoxins (Buts *et al.*, 2006). Thus, with a diet low in protein and fiber, but with the addition of yeast *Saccharomyces cerevisiae* to the diet, the concentration of *E. coli* was significantly reduced (Bastos *et al.*, 2023). The increase in yeast cells may be a response to the increase in enterobacteria, an attempt to normalize the environment and control the *E. coli* population.

On the other hand, even the common yeast *Saccharomyces cerevisiae* causes fungemia in people with weakened immune systems (Niault *et al.*, 1999; Chertow *et al.*, 1991), and there are also cases of disease in healthy people who used *Saccharomyces cerevisiae* as a probiotic (Smith *et al.*, 2002; Debelian *et al.*, 1997; Herbrecht & Nivoix, 2005). Isolated yeast strains from these patients have pathogenic potential and certain phenotypic characteristics, such as growth at 42°C, some hydrolytic activity, pseudohyphal and invasive growth, switching, and adhesion, which are associated with pathogen virulence (Ghannoum, 2000; Burik & Magee, 2001; Roman *et al.*, 2007; Llanos *et al.*, 2006).

In addition to the yeast *Saccharomyces*, the gut microbiota includes *Pichia* (*P. pastoris*), which are considered saprophytes and are used to some extent in public health (Weinacker *et al.*, 2014). Opportunistic yeast-like fungi that live in the intestines include *Candida* (a prominent representative of *C. albicans)*. Normally, *Candida* overgrowth is suppressed by the gut microbiota through colonization resistance (Fan *et al.*, 2015). But immunosuppressed, increased permeability of the gut mucosal barrier by microbiota, due to malnutrition or broad-spectrum antibiotics, may contribute to the pathogenesis of *C. albicans* (Wang *et al.*, 2023; d'Enfert *et al.*, 2021). Probiotic bacterial cultures, such as *Lactobacillus* (Allonsius *et al.*, 2019; Charlet *et al.*, 2020) and *Bifidobacterium* (Ricci *et al.*, 2022) can enter the fight against this fungus, which are able to inhibit the growth of many fungal cells by affecting their cell wall. In addition, they produce butyrate, which promotes intestinal barrier integrity and prevents bacterial translocation (Wong *et al.*, 2006).

It has long been shown that a lipid-rich diet is associated with a significant reduction in *Lactobacillus* and *Bifidobacterium* (Wall *et al.*, 2009; Cani *et al.*, 2008). At the same time, in mice, a decrease in dietary fiber has a direct effect on microbiota diversity, namely its decrease, and leads to poor production of short-chain fatty acids (SCFAs) generated by the gut microbiota (Fig. 8), which reduce inflammation through various mechanisms (Kashyap *et al.*, 2013; Trompette *et al.*, 2014). In our study, we also observed a decrease in *Bifidobacterium*, by two orders of magnitude, while the number of *Lactobacillus* decreased by only 1 order. Bacteria of the genus *Lactobacillus*, in contrast to *Bifidobacterium*, show a higher ability to adapt to environmental changes, in addition, their numbers are usually higher.

In addition, animal data demonstrate that a Western-style diet promotes weight gain and increases visceral adiposity in animals. However, in our study, there was only 16% weight gain in high-fat group mice from the starting point of the experiment. This may be explained by dietary modification without the additional carbohydrate load in the diet, as is typical of Western style eating.

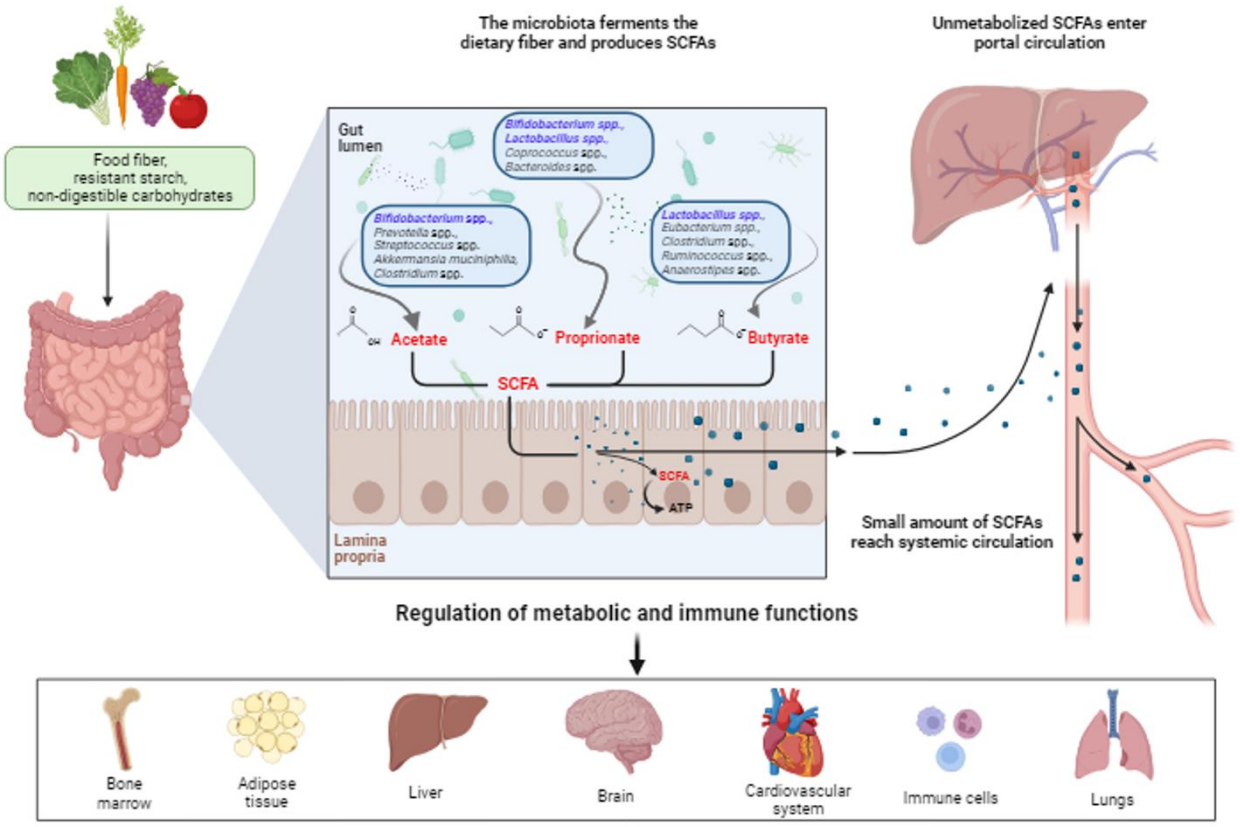

Fig. 8. The role of short-chain fatty acids generated by the gut microbiota
Note: ATP – adenosine triphosphate, SCFA – short-chain fatty acid

On the other hand, a diet rich in dietary fiber have been shown to increase *Lactobacillus* and *Bifdobacterium* in many experiments (Makki *et al.*, 2018). It should be noted that the term «dietary fiber» refers to two types of carbohydrates, fermentable carbohydrates that microorganisms use as a substrate, and non-fermentable (insoluble) carbohydrates that act as a filler (Chawla & Patil, 2010). Soluble fiber not only performs certain important physiological functions, but also contributes to the formation of important microflora, acting as a substrate for beneficial microorganisms, therefore, acts as a prebiotic and improves the health of the host. Insoluble fiber is practically not used as a substrate by microorganisms but serves as a kind of protection against the growth of unwanted microflora. It has the effect of accelerating the transit of food through the gastrointestinal tract, which did not depend on the presence of the microbial community in the intestine but excludes food decay and the development of pathogens. Carefully controlled experiments in mice have shown that the amount and type of carbohydrates fed to the microbiota alter simple and complex microbial communities (Faith *et al.*, 2011; Kashyap *et al.*, 2013; Sonnenburg *et al.*, 2010; Turnbaugh *et al.*, 2009). Our study used a diet with only an increase in non-fermentable fiber, without the addition of protein, lipids, and microbial accessible fiber, and showed a significant reduction in the probiotic microorganisms *Lactobacillus* and *Bifdobacterium* along with *Enterobacteriaceae* and yeast. These results clearly show that the lack of available substrates in food leads to a decrease in the number of microorganisms in the intestine, and as a result, a decrease in metabolites. SCFAs, acetate, propionate, and butyrate are common end products of carbohydrate fermenting microbes in the distal intestine (Wong *et al.*, 2006), and several factors, including dietary substrates, can influence the relative ratios and concentration (Macfarlane & Macfarlane, 2003; Topping &

Clifton, 2001). SCFAs are taken up by the host and serve as reserve calories from otherwise unavailable carbohydrates, but they also play various regulatory roles, including regulation of histone acetylation and signaling through G protein-coupled receptors (Brown *et al*., 2003; Davie, 2003). SCFAs generated by the microbiota are associated with anti-inflammatory effects, namely an increase in the number of regulatory T cells in the intestine (Furusawa *et al*., 2013). The effects of reduced SCFAs production on a diet low in fermentable carbohydrates may be exacerbated by changes in microbiota localization and disruption of the distal intestinal barrier (Wong *et al*., 2006) SCFAs also regulate energy homeostasis (Layden *et al*., 2013). Butyrate has a broad effect on the metabolism and circulating signals of propionate through the afferent nervous system, affecting gluconeogenesis in the intestine, and leads to improved metabolic profiles and reduced weight gain (De Vadder *et al*., 2014; Lin *et al*., 2012). We did not observe significant weight gain in the high-fiber mice, but we noted some passivity in the home cage, and the anxiety level was lower compared to the control group. Perhaps this is due precisely to the lack of SCFAs produced mainly by the probiotic bacteria *Lactobacillus*, *Bifdobacterium* and *Enterobacteriaceae*, and metabolic disorders in general.

A high fiber diet has long been associated with a «healthy» diet and a «healthy» microbiota, such as increased microbial diversity (McBurney *et al*., 2019), but results can be conflicting in some cases (So *et al*., 2018). Thus, several studies have demonstrated the growth of probiotic microorganism (*Lactobacillus, Bifdobacterium*) in response to a high intake of dietary fiber, which included fructans and galactooligosaccharides related to fermentable carbohydrates (So *et al*., 2018). Resistant starch consumption increased *Bifidobacterium, Faecalibacterium, Eubacterium, Enterobacteriaceae* (*E. coli)*, while at the same time decreased some strains of *Ruminococcus* (Martínez *et al*., 2010; Alfa *et al*., 2018). Insoluble non-fermentable fiber such as cellulose can be broken down by cellulose-metabolizing microbes such as *Ruminococcus* and *Fibrobacter* (Flint *et al*., 2008). Thus, the gut microbiota is highly dependent on dietary fiber as a source of energy. Applying the correct ratio of insoluble to soluble fiber can determine the ratio of microbial composition in the gut, the production of SCFAs and other substances.

Conclusion

Obviously, diet is one of the main factors that shapes the appearance and determines the direction of the functioning of the intestinal microbiota. The abundance of certain nutrients leads to the overgrowth of certain types of bacteria, thereby crowding out others. Previously, many studies have shown that both long-term and short-term dietary interventions cause significant changes in the gut microbial ecosystem. However, the exact mechanisms by which certain dietary components exert their influence on the composition of the gut microbiota remain uncertain. Moreover, despite the non-exponential growth of research in this area, dietary impact studies suffer from a lack of specificity, and therefore experimental data vary and cannot be used for medical and therapeutic purposes. The multicomponent nature of the diets used in the experiments, with the partial dominance of a single nutrient, does not allow establishing a clear correlation between changes in the microbiota and the source that causes them. Nevertheless, the results obtained demonstrate the possibility of using dietary manipulation as a therapeutic method for correcting metabolic activity and the concentration of opportunistic microorganisms in the intestine.

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