Entomology and Applied Science Letters
Volume 9, Issue 3, Page No: 32-36

Available Online at: www.easletters.com

ISSN No: 2349-2864

New Biotechnological Forms of Nutritional Supplements Aimed at Improving the Gut Disbiosis and Their Clinical Appraisal

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ABSTRACT

The present study deals with some new biotechnological forms of nutritional supplements and their effectiveness in helping people with gut disbiosis. We have developed four different nutritional supplements to prevent and treat gastrointestinal diseases. The general characteristic of each supplement is given. Nutritional supplement 1 contains modified sorbents to neutralize bacterial endotoxins. Nutritional supplement 2 includes live microencapsulated forms of Bifidobacterium and Lactobacillus aimed at sustaining the immune system. Supplement 3 combines bacterial metabiotics, which absorb endotoxins, thus improving intestinal biocenosis. Nutritional supplement 4 is a plant-based product that enhances the colonization of friendly microbiota and has a protective and anti-inflammatory effect by inhibiting yeast fungi and pathogenic bacteria growth. Ten volunteers aged from 33 to 72 were involved in the clinical trials. They took these four nutritional supplements per os. The supplement intake scheme and treatment duration have been tested, analyzed, and approved. The patients' biochemical, hematological and immunological blood properties, as well as their fecal sugur, feces occult blood, and coprogram were tested before and after the treatment period. The results proved the efficiency of the developed nutritional supplements in improving gut disbiosis.

Keywords: Nutritional supplements biotechnological forms, The gut disbiosis, Preventive measures, Efficiency.

HOW TO CITE THIS ARTICLE: Vekovtsev AA, Zakharenko MA, Gorbushina IS, Pliska OV, Poznyakovsky VM, Tokhiriyon B, et al. New Biotechnological Forms of Nutritional Supplements Aimed at Improving the Gut Disbiosis and Their Clinical Appraisal. Entomol Appl Sci Lett. 2022;9(3):32-6. https://doi.org/10.51847/SqyJlrI16T

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Received: 14/04/2022
Accepted: 19/08/2022

INTRODUCTION

Normal microbiota consists of a number of microbial communities, which can be characterized by a certain composition of microorganisms. These microorganisms colonize people's skin and mucous membranes and serve as the first nonspecific barrier, which protects the body from the adverse factors of both the internal and
external environment. The microbiological film that covers the body's intestinal wall, mucous membranes, and skin consists of 100 milliards of microbial cells. Moreover, the microbiological status of a person is essential for the stable functioning of all organs and systems.

A person's microbiota is mainly concentrated in the intestine. This fact makes the intestine a very vulnerable organ, suffering the most from the unnatural lifestyle, which may involve psychological and emotional stress, eating disorders, uncontrolled intake of medications,

bad habits, etc. The intestine's normal functioning is crucial for the body. At the same time, the gastrointestinal disease is one of the most common reasons for visiting a doctor. Other diseases such as cardiovascular and autoimmune disorders, skin, liver and kidney diseases, allergies, depression, and others are also associated with the gut functioning and flora state [1-11].

Microbiota serves as a reliable and objective indicator of a person's health and diet, so it seems essential to restore the disturbed microbiocenosis, employing the nutrition factor [12-20].

MATERIALS AND METHODS

ArtLife Company was involved in developing biologically active compounds and applying innovative biotechnologies:

- nutritional supplement 1 is designed for metabolic detoxication and gut biocenosis improvement. It contains modified sorbents, which can neutralize bacterial endotoxins;
- nutritional supplement 2 is a biotechnological consortium of probiotics and prebiotics. Probiotics are represented by live microencapsulated forms of Bifidobacterium and Lactobacillus bacteria. This compound helps support the immune system and maintain health;
- nutritional supplement 3 is a biotechnological complex of bacterial metabiotics. It selectively absorbs endotoxins and serves as a metabolic and prebiotic means to improve gut biocenosis;
- nutritional supplement 4 is a plant-based biotechnological product aimed at supporting both the balance of the gut-friendly microflora and the body's defenses. It prevents the growth of yeast fungi and pathogenic bacteria, enhances colonization of the body-friendly bacterial flora, boosts the body's defenses, and has a pronounced anti-inflammatory effect.

The effectiveness of the developed products was evaluated during the clinical trials involving 10 volunteers (1 male and 9 females aged from 33 to 72. All of them were white-collar workers).

They were motivated by the following factors: health promotion, weight loss, and elimination of disagreeable symptoms of digestive system disorders.

The provoking factors affecting the volunteers' health included unfavorable dietary patterns, being overweight, and psychological and emotional stress.

The volunteers had several tests taken before and after the treatment to examine their blood biochemical, hematological, and immunological properties. In addition, they underwent fecal sugur and feces occult blood tests.

After thorough clinical and laboratory studies, the volunteers were diagnosed with fatty liver disease (6 people), obesity (6 people), pancreatitis (4 people), hypothyroidism (4 people), chronic gastritis and duodenal ulcer (8 people), gallstone and acalculous cholecystitis (4 people), irritable bowel syndrome (4 people), and resected stomach (1 person).

RESULTS AND DISCUSSION

All participants demonstrated that gut microbiota disorders ranged from minimal to profound.

All of them completed the questionnaire to evaluate their physical condition on a 10-point scale before and after the program.

All the volunteers took the developed biological compounds following the scheme presented in **Table 1.**

Table 1. Nutritional supplement intake scheme

Nutritional supplements and their form	Dosage and administration
Supplement 1 – hard gelatin capsule with enteric coating	1 capsule twice a day with a meal. Oral administration. Duration – 45 days.
Supplement 2 – colloidal solution	1 teaspoon 3 times a day between meals. Duration – 30 days.
Nutritional supplement 3 – hard gelatin capsule	1 capsule twice a day, 30 minutes before breakfast and 30 minutes before bedtime. Oral administration. Duration – 45 days. It cannot be taken together with supplement 1.
Supplement 4 – hard gelatin capsule with enteric coating	1 capsule 4 times a day, with a meal or immediately after a meal. Administration- oral. Duration – 45 days

Different organs and systems disorders were recorded while evaluating the patients' physical health **(Table 2)**.

Table 2. Subjective evaluation of physical health before and after biologically active compounds intake: questionnaire results

Organs and systems health	Before treatment (points)	After treatment (points)
Skin, hair, nails (hair loss, brittle nails)	9	2
Mouth, nose, pharynx (coated tongue, dry skin)	6	1
Gastrointestinal tract (flatulence, rumbling)	10	1
Nervous system (weakness, fatigue, dizziness)	10	0
Musculoskeletal system (pains, crepitus)	6	4
Stool (consistency, frequency, constipation)	8	1

*Note: 0 – no changes; 10 – pronounced changes

As we can see, the nutritional therapy resulted in 60 % - 100 % improvement in the patient's physical health.

All the volunteers (100 %) showed positive dynamics of cytolysis, cholestasis, and lipid metabolism **(Table 3)**. 5 tests were taken during the program. Each time the blood sample was taken before and after the administration of the supplement.

Table 3. Changes in blood chemistry results before and after supplements intake

Biochemical indicators	1st test		2nd test		3rd test		4th test		5th test	
	Before	After	Before	After	Before	After	Before	After	Before	After
ALAT U/L	N	N	N	N	72	28	N	N	N	N
AST U/L	N	N	N	N	68	32	N	N	N	N
GGTP U/L	N	N	45.5	26.1	92.59	59	N	N	N	N
Total cholesterol mmol/l	5,.3	3,68	7.09	6.5	7.13	6.28	8.23	6.57	6.8	5.4
LDL, mmol/l	3.72	2,12	4.7	3.4	4.72	3.96	5.64	5.08	4.0	3.6
HDL, mmol/l	1.09	1,26	1.3	1.4	1.7	1.6	1.44	1.36	1.1	1.2
Glucose, mmol/l	N	N	7.3	6.2	6.8	5.8	6.8	5.28	5.8	5.2

Stool analyses of 6 volunteers (60 %), taken before the treatment, revealed latent disaccharidase deficiency, which had not been diagnosed previously. None of them (0%) had this disorder after the program.

While studying the gut microbial landscape of all volunteers before the program, we found gut microflora disorders of different extents in 100 % of cases: deficiency of defensive symbionts (Bifidobacterium, Lactobacillus bacteria, Escherichia coli (Lac +) and occurrence of pathogenic microbes (Klebsiella pneumonia, Candida Albicans). Microbiota restoration was recorded in 9 cases (90 %) after the participants finished the 45-day program **(Table 4)**.

Table 4. Changes in the colon microbial landscape

Patient №	Before the program	After the program
1	Escherichia coli (Lac-)- 10^8 CFU/g, Escherichia coli (Lac+) -$5x10^7$ CFU/g	Escherichia coli (Lac-) – not detected Escherichia coli (Lac+) - 10^8 CFU/g
2	Low level of Escherichia coli (Lac+) - 10^5 CFU/g	Escherichia coli (Lac+) - 10^8 CFU/g
3	Pseudomonas aeruginosa - 10^6 CFU/g	not detected
4	Low levels of Bifidobacterium and Lactobacillus bacteria	Up to normal - 10^8 CFU/g - 10^6 CFU/g

5	Klebsiella pneumonia - 10^8 CFU/g	not detected
6	Candida albmans	not detected
7	Low levels of Bifidobacterium and Lactobacillus bacteria	Bifidobacterium level -normal, Lactobacillus -10^5 CFU/g
8	Low levels of Bifidobacterium and Lactobacillus bacteria	normal
9	Low levels of Bifidobacterium and Lactobacillus bacteria	normal
10	Low levels of Bifidobacterium and Lactobacillus bacteria	normal

At the beginning of the program, the participants complained of a change in bowel habits from constipation to diarrhea, bloating and flatulence, rumbling, and abdominal pains of various locations and characters. The presence of mucus in stool was recorded in all the tests. 8 participants (80 %) reported no such complaints after the program, while 2 participants (20 %) reported fewer complaints.

All the patients showed positive changes in their coprogram **(Table 5)**.

Table 5. Changes in stool test results

Patient №	Before the program	After the program
1	Extracellular starch+ intracellular starch+iodoph. flora+	Soaps single units
2	Neutral fat+ soaps + extracellular starch+	Extracellular starch+
3	Extracellular starch + plant cells+ neutral fat+ mucus+	Extracellular starch +
4	Fatty acids+ extracellular starch+ iodophilic flora+	Not detected
5	Iodophilic flora +fatty acids+	Not detected
6	Fatty acids+ soaps+, extracellular starch+	Extracellular starch single units
7	Neutral fat(single units)+, mucus+(specific weight 1.026u), Candida albicans- $5X10^5$ CFU/ml(vaginal) (((vaginal)вагинальная	Neutral fats (single units),sp.w. 1.018 + not detected
8	Soaps++, fatty acids+, mucus+ Candida albkans- $5X10^5$ CFU/ml(vaginal)	Soaps+ not detected
9	Soaps(single units), mucus+	Soaps single units+
10	Soaps ++ starch++ fatty acids+	Soaps + starch +

The volunteers evaluated the tolerability of the 45 days supplements appraisal course as excellent (60 %), good (40 %), and unsatisfactory (0 %).

CONCLUSION

In conclusion, we can state that the presented results prove the efficiency of the developed supplements in improving gut dysbiosis.

ACKNOWLEDGMENTS: The team of authors thanks the administration of the ArtLife company for the opportunity to research its basis.

CONFLICT OF INTEREST: None

FINANCIAL SUPPORT: None

ETHICS STATEMENT: The study was conducted according to the guidelines of the Declaration of Helsinki.

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