

# RESULTS OF THE USE OF ENTEROSGEL PREPARATION FOR THE TREATMENT OF THE GIT ORGANS DISEASES IN RELATION WITH DISORDERED FOOD DIGESTION AND ABSORPTION

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The present problem's urgency is known to stem from a practical lacking of any important advances in treatment modalities for as common diseases as pathological conditions of the small intestine with allergic manifestations as well as those due to the gastric and small intestine resections of different length (malabsorption syndrome), colonic pathology with dysbiosis manifestations (irritable bowel syndrome, constipation syndrome). At the same, it should be mentioned that the disponible modalities of selective enterosorption and nutritional correction of impaired homeostasis are not utilized sufficiently enough.

## RESEARCH OBJECTIVE:

To assess the effectiveness of using Enterosgel in the complex treatment of common diseases such as pathological conditions of small intestine with allergic manifestations and also due to the gastric and intestinal resections of different lengths (malabsorption syndrome), colonic pathologies with dysbiosis manifestations (irritable bowel syndrome, constipation syndrome). The evaluation of followed up therapy included:

- a) verification of clinical efficiency,
- b) monitoring the profile of laboratory parameters,
- c) assessing the effect of Enterosgel on the condition of the gastrointestinal tract.

## GROUP OF PATIENTS, TREATMENT SCHEMES, METHODS:

Enterosgel was clinically investigated by gastroenterology station of the Clinic of Therapeutic Nutrition under the Nutrition Research and Development Institute with the RAMS.

### Experimental group of patients

Under observation were 21 patients with chronic disorders of the digestive system: syndrome of malabsorption - 4 patients (1 patient with non-specific ulcerative colitis, 1 with gluten enteropathy and 2 with chronic enteritis in the acute phase), 7 patients with post-gastric resection syndrome and 2 patients who underwent resection of the small intestine and right-sided hemicolectomy for the mesenteric artery thrombosis, and 8 patients with irritable bowel syndrome. The experimental group included 16 male- and 5 female patients. They were age-ranged from 18 to 70 years.

### Control group of patients

15 patients formed the control group including 8 male- and 7 female patients being age-ranged from 35 to 61 years. 10 patients were with irritable bowel syndrome, 5 patients were with post-gastric resection syndrome.

The experimental and the control groups were age-and-sex comparable and so they were as for the character of the digestive organs affection.

Enterosgel was used perorally in the experimental group in a daily dose of 45 g (15 g 3 times a day, for 1 hour before meals) for 21 days against a background of traditional therapy (diet therapy - 4 and R-table); the enzymic preparations - mezim-forte, pancreatin, vitamin therapy, local treatment - the suppositories with belladonna, microclysters with chamomile and Vinylinum No 20; decoctions of medicinal herbs. Patients of the control group received the standard treatment. Antibacterial agents were not applied.

### Laboratory and instrumental investigations

In the experimental and control groups were conducted: the assessment of actual nutrition and anthropometric indicators, the choice of checking tests for following-up the status of major physiological systems: blood chemistry, clinical blood tests, urine and feces; electron and light microscopy of biopsies of small intestinal mucosa, GIT radiographic and ultrasonic imaging methods, endoscopic methods of investigation of the upper gastrointestinal tract and colon with intestinal segments biopsies; colonic biocenosis examinations.

The severity of dysbiosis was determined against the change of bacterial flora on the feces maps. In patients as examined for dysbacteriosis, various severity dysbacteriosis grades were revealed: 9 subjects in the experimental group showed compensated dysbacteriosis (1<sup>st</sup> grade), 12 patients showed subcompensated dysbiosis (2nd grade). In the control group, 7 patients manifested subcompensated dysbacteriosis and 8 patients showed compensated dysbacteriosis.

Patients underwent the investigation of their organisms for the antioxidant status using indicators of the antioxidant system, including the content of lipid peroxidation (LPO) - diene conjugates and TBA-active products (malone dialdehyde (MDA)) in blood erythrocytes and plasma, as well as the study of enzyme activity of erythrocyte antioxidant - superoxide dismutase (SOD), catalase, glutathione peroxidase (GP) and glutathione reductase (GR), with calculation of antioxidant index (AOI). Antioxidant index (AOI) is an integral indicator of the antioxidant protection status, taking into account, on one hand, the products of LPO and, on the other hand, the activity of erythrocytes antioxidant protection enzymes.

## RESULTS

Results of clinical studies have shown a high efficiency of Enterogel in the complex treatment of digestive diseases. In the first three days of application, the 18 patients of experimental group (85.7%) showed a subjective improvement. After 10-12 days, all patients re-normalized their bowel movements with a tendency to forming the stool masses, with eliminated pain and dyspeptic syndromes. In the experimental group of patients, the normalization of bowel movements was observed during the first week (an average of 7 hours), whereas in the control group only for 18-20 days, and in some cases (6 patients), the conventional therapy was not efficient enough to eliminate the pain syndrome, an unstable stool, and indigestion. It outflows from Table 1 that all patients of the experimental group developed positive shifts in coprogram on the background of Enterogel. These changes consisted mainly in the disappearance or reduction of leukocytes, red blood cells and mucus, iodophilic microflora, intracellular starch, undigested cellulose, steatorrhea and creatorrhea.

**Table 1.**  
*Dynamics of basic clinical manifestations of the disease under the influence of therapy in patients with the digestive system's pathology (in days)*

Indicators	Control group (n=15)	Experimental group (n=21)
Normalization duration of defecations number	20.5 ±1.5	6.0 ±1.4*
Duration of forming of the stool masses	21.4 ±2.5	15.4 ±2.5*
Disappearance time of pain syndrome	19.4 ±1.6	10.6 ±1.9*
Disappearance time of meteorism	18.5 ±1.0	10.5 ±1.8*

Note: \* - the indicators significant difference prior to include Enterogel and after the treatment (p <0,05).

In a majority of patients of experimental group, the positive dynamics of colonic microflora composition was reported (Table 2) (16 patients – 94.1%) pointing on the diminution, and in some cases, the disappearance of microorganisms such as Klebsiella (3 cases), Proteus (2 patients), enterobacteria (4 patients), hemolytic E. coli (8), fungi of the genus Candida (4 patients). It was recorded an increase of total coliform bacteria up to normal numbers (300 - 400 million / g) in 13 patients at the initially decreased level of this indicator. In 5 patients, it was reported the insufficient dynamics in the normalization of eubiosis, which is obviously connected with the necessity of using the Enterogel treatment cycle altogether with the immuno-modulatory and bacterial preparations.

**Table 2.**  
*Dynamics of colonic microflora in on-therapy patients with chronic diarrhea*

Indicators	Control group (n=15)		Experimental group (n=21)	
	Prior to treatment	After treatment	Prior to treatment	After treatment
	Registration frequency			
Increase in the total number of E.coli	15	11	15	5
Reduction or absence of bifidobacteria	17	17	17	17
Identification of Staphylococcus aureus	2	1	1	1

Identification of Klebsiella microbial genus	6	3	9	0
Identification of Proteus microbial genus	4	3	5	0
Identification of Candida fungi genus	10	8	8	0
Identification of hemolyzing E.coli	8	6	12	1

When identifying 16 blood serum biochemical parameters, no significant differences in the experimental and control groups were detected (Table 3). Deviations available in individual patients were not of a regular character.

**Table 3.**  
*Blood serum biochemical parameters in patients with the disordered digestive system.*

Indicators	Normality limits	Control group (n=15)		Experimental group (n=21)	
		Prior to treatment	After treatment	Prior to treatment	After treatment
Total cholesterol, mmol/l	3.9 - 5.2	5.94±0.54	5.45±0.58	5.18±0.7	4.98±0.62
Total protein, g/l	60 – 80	77.4±6.52	78.22±3.65	74.2 ±7.1	79.5±4.2
Total bilirubin, umol/l	8.55 – 20.52	21.15±3.96	19.53±3.42	22.7±1.12	17.11±1.2
Globulin, g/l	23 – 35	25.6±2.8	26.3±4.3	26.6±2.1	29.7±3.7
Albumin, g/l	38 – 50	46.3±1.5	47.1±1.9	46.8±1.2	46.9±1.1
Glucose, mmol/l	3.89 - 6.38	5.62±0.44	5.46±1.2	5.47±0.5	5.46±0.3
AST, IU/L	0 – 40	25±16	29±11	24±12	21±4
ALT, IU/L	0 – 54	47.9±20	48.2±18	48.7±15	45.6±10
Urea, mmol/l	1.70 – 8.30	6.46±0.95	5.6±0.55	5.94±0.98	5.07±0.66
Uric acid, umol/l	125 – 440	270.1±110	250.4±85	264.2±95	223.1±21
Alkaline phosphatase, IU/l	0 – 93	58±7.9	50±5.3	44.4±6.2	42.1±5.0
Amylase, U/l	0 – 90	18.3±4.2	19.1±6.8	21.4±3.4	20.8±2.1
Creatinine, umol/l	62 – 133	68.4±12.3	71.6±14.8	71±8.7	66.1±6.8
Triglycerides, mmol/l	0 – 2.37	1.71±0.48	1.68±0.15	1.28±0.24	1.28±0.12
Calcium, mmol/l	2.12 – 2.52	2.30±0.05	2.30±0.2	2.35±0.01	2.29±0.14
Phosphorus, mmol/l	0.77 – 1.52	0.84±0.12	0.89±0.08	0.92±0.02	0.88±0.07

Patients were evaluated depending on the duration of Enterosgel administration (prior to start on, the administration for 5 days on average, and 15 – 30 days administration). The following changes in biochemical parameters were revealed in the studied patients: total protein tending to increase in the course of treatment (3-4%), probably due to the globulin fraction: globulin increases by 12%, albumin remains within the initial period of therapy, alkaline phosphatase, ALT and AST decreased at the baseline, then raised to the level of baseline; total bilirubin and cholesterol reduced by 25% and 16% respectively as compared with baseline; urea and uric acid had a pronounced reduction dynamics as interconnected with the duration of Enterosgel administration.

Concerning the clinical blood analysis, a marked increase in hemoglobin level is reported after an average of 20 days as well as the increase of color index. At the same time, it was identified in the blood formula an increase in neutrophils PO by 37% and reduced C / I of 5%, the increase in monocytes by 16%, the decrease by 12% of lymphocytes, white blood cells as remaining in the original figures.

Initially, the patients' AOI index was significantly lower than normal (being on average 1.69 against 0 as per the norm), which indicates the presence of oxidative stress in the initial state, i.e., the predominance of free radical oxidation products (LPO) over the activity of protective enzymes (Table 4).

**Table 4.**  
*Activity of antioxidant protective enzymes in patients with a pathology of the digestive system*

Timeline of the study	I	II	III	IV
Indicator				

GR, $\mu\text{mol/ml.min.}$	2.15 $\pm$ 0.121 n=17	2.12 $\pm$ 0.099 n=15	2.15 $\pm$ 0.179 n=15	1.96 $\pm$ 0.05 n=15
GP, $\mu\text{mol /ml.min.}$	39.5 $\pm$ 2.63 n=17	36.6 $\pm$ 2.37 n=15	39.8 $\pm$ 2.74 n=15	43.7 $\pm$ 2.10 n=15
Catalase, $\mu\text{mol /ml.min.}$	155 $\pm$ 10.0 n=17	152 $\pm$ 9.92 n=15	153 $\pm$ 12.1 n=15	175 $\pm$ 11.9 n=15
SOD, cond.U.	1767 $\pm$ 26.5 n=17	1788 $\pm$ 66.7 n=15	1609 $\pm$ 96.8 n=15	1528 $\pm$ 51.0 n=15

When in applying Enterosgel according the dynamics of two terms (7 and 14 days after the preparation administration), the decrease of LPO products level was reported (significantly for the plasma diene conjugates in the second- and for MDA in the first period, respectively). Concerning the total LPO contents, there is also a tendency to decrease, indicating a beneficial effect of the preparation. The level of activity of the erythrocytic antioxidant protection enzymes is somewhat reduced (significantly only in GR), which is also seen as a favorable sign, associated with normalization of the antioxidant function, in contrast to the initial system's inductiveness (Table 5). Due to its positive transition dynamics from significantly negative values to the normality, the AOI normalization is seen as a beneficial effect of Enterosgel associated both with phasing out of the body the free radical oxidation products and supplying the organism by natural antioxidants (vitamins A, E and C).

**Table 5.**  
*LPO and vitamin E levels in patients with pathology of the digestive system*

Timeline of the study	I	II	III	IV
Indicator				
Ery DC nmol/ml	3.18 $\pm$ 0.053 n=17	3.17 $\pm$ 0.043 n=15	3.29 $\pm$ 0.058 n=15	3.18 $\pm$ 0.060 n=15
Ery MDA nmol/ml	1.54 $\pm$ 0.155 n=17	1.34 $\pm$ 0.122 n=15	1.31 $\pm$ 0.131 n=15	1.37 $\pm$ 0.42 n=15
Plasma DC, nmol/ml	6,22 $\pm$ 0,29 n=17	6,16 $\pm$ 0,22 n=15	6,54 $\pm$ 0,19 n=15	6,42 $\pm$ 0,47 n=15
Plasma MDA, nmol/l	2,41 $\pm$ 0,37 n=17	1,68 $\pm$ 0,24 n=15	2,33 $\pm$ 0,49 n=15	1,89 $\pm$ 0,50 n=15
Vitamin E, mg/100 ml	2,16 $\pm$ 1,12 n=8	2,17 $\pm$ 0,93 n=7	1,97 $\pm$ 0,96 n=6	2,01 $\pm$ 0,89 n=7

*Note:* GR - glutathione reductase activity of red blood cells;  
 GP - glutathione peroxidase activity of erythrocytes;  
 SOD - superoxide dismutase activity of erythrocytes;  
 C - the activity of erythrocyte catalase;  
 Plasma DC - Content of diene conjugates in blood plasma;  
 Ery DC - Content of diene conjugates in erythrocytes;  
 Plasma MDA - Content of TBA-reactive products (malondialdehyde) in blood plasma;  
 Ery MDA - Content of TBA-reactive products (malondialdehyde) in erythrocytes;

Morphofunctional study in patients with pathology of the digestive system was carried out in different periods of Enterosgel application. During its application, in the gastric fundus of the stomach has been observed a thickness decrease of mucous membrane, which took place at the expense of mucinous epithelium, while maintaining the depth of glands. Patients showed a decrease in expressiveness of inflammatory changes in the mucosa, which was expressed in decreasing the level of lymphocytic infiltration of the epithelium own plate of mucous membrane. At the same time, it was observed an edematous character of surface epithelium and a number of microhemorrhagies as conditioned by the pathological stage and nature of the upper gastrointestinal tract. In contrast, in the antral gastric region, the mucosa of antral gastric region showed an increase in thickness, namely, due to the increase in thickness of mucin-producing epithelium, whereas the increase in edematous signs of epithelium itself and lymphoplasmic infiltration remained on the previous level. In both parts of the stomach, the infecting of gastric mucosa with *H.pylori* remained as preserved (in patients with gastric and duodenal ulcerous disease). It should be noted that the local changes were associated with the

manifestation of a specific pathology. Since the patients were examined only once, for a more accurate idea about the influence of Enterosgel on the mucosa, it should be conducted one study more in dynamics.

Identified in the proximal small intestine was an increase in mucosa thickness and height of intestinal villi along with a decrease in crypts depth. There was a significant decrease in epithelial swelling, severity of microhemorrhages and level of lymphocytic infiltration of the epithelium. In parallel, there was an increase in number of plasmocytes in the proper mucosal lamina, which reflected a change in immunological reactivity of the small intestine mucosa and may be regarded as a positive result of influence on the local immunity status.

### **CONCLUSIONS:**

1. Enterosgel is a highly efficient medication for treatment of a wide range of chronic diseases of the digestive system as accompanied by irritable bowel syndrome and a disorder of microbiocenosis status.
2. When Enterosgel was included in the complex therapy of pathologies of the digestive system, such an inclusion resulted in normalization of defecation and stool nature, the arrest of pain syndrome and meteorism, decrease of inflammatory process and improvement of the intestinal digestive function according to the coprology data, elimination of the colonization of pathogenic flora and restoration of the colonic normal microflora status.
3. According to the endoscopic and morphologic functional studies, it is identified an increase in thickness of the mucosa and intestinal villi height, with a decrease in crypts depth. Significantly is reduced a swelling of the epithelium, severity microhemorrhages and the level of lymphocytic infiltration of the epithelium, increase in number plasmocytes in the proper lamina of mucous membrane, reflecting the positive effect on the local immunity status.
4. During the Enterosgel investigation for morphological parameters, it was found a large scatter of data and a considerable orientation variability of changes in investigated parameters, which may be due to the difference in effect as conditioned by the pathogenesis of the disease.
5. The leveling down is reported of activity in the erythrocytes antioxidant protection enzymes, which is regarded as a positive sign as conditioned by normalization of antioxidant protective function of a diseased organism.
6. A positive dynamics of the AOI (from significantly negative values to the normality) takes place due both to excretion of the free radical oxidation products from the body and the supply of organism by natural antioxidants.
7. In assessing the complex preparation, it is necessary to proceed by selecting and/or grouping patients homogeneously in terms of clinical and severity factors, age and sex of patients, because these factors influences the morphologic and functional indices.
8. The respective investigation results showed the need for a dynamic and long term examination of patients, allowing us to identify how this preparation influences on various clinical and functional indices and their changing rate in different periods of the disease.
9. Enterosgel in recommended doses and duration of use does not disorder the status of the mineral and vitamin balance of patients.
10. There were not identified any side effects or complications as related to the digestive organs when in use of Enterosgel.
11. Enterosgel is recommended for a widespread use within the complex therapy of patients with chronic diseases of the digestive system, accompanied by inflammatory changes of mucosa and the disorder of the GIT motor-evacuation function.

Performed investigations allowed determining a high clinical efficiency of Enterosgel, its positive effect on both intestinal mucosa and microflora status without disturbing the digestion and absorption processes. Registered is the immunomodulatory effect as conditioned by normalization of the eubiosis status and decrease of inflammatory activity in the intestinal mucosa. When in using the preparation, there were not identified any side events and/or intolerance cases in response to. The investigation pointed on that at the recommendation for use, it is necessary to take into account, altogether with clinical symptoms, particularities of pathogenesis of a disease, because without taking into account the developmental pathology's particularities, the efficiency of Enterosgel can be insufficient or requesting a longer individualized complex therapy.

Enterosgel can be recommended for a wide use in treatment of chronic GIT diseases that are known to be accompanied by disordered defecation and intestinal eubiosis. In order to get a persistent and significant effect, a long term application cycle of Enterosgel is needed altogether with using the immunocorrective therapy.

It is necessary to study in a more detailed way the influence of Enterosgel on the morphologic and functional condition of mucosa doing so in dynamics with using the secretory gastric-and-small intestine function in accordance with significant parameters able to allow us to evaluate objectively the pathogenetic significance at the various pathology of digestive organs and the necessity of any individual nutritional and drug-related therapy. Such a detailed study will allow not only determining the functional effect of Enterosgel, but also proposing the modalities of its efficient application, taking into account the introduction of micronutrients and biologically active food components (vitamins, trace elements, eubiotics, immunomodulators etc.).

*Clinical application of Enterosgel preparation in patients with a pathology of digestion organs. Methodical recommendations. MSMVISU, page 21, 1999*