Using probiotics in acute gastroenterocolitis in children. Results of a clinical study

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The use of probiotics is finding a place in routine practice not only in the field of pediatrics. Probiotics are recommended for recolonization and positive influence on microclimate and settlement of aboral parts of the gastrointestinal tract with modification and support of the physiological metabolism of the large intestine. Recently, a greater emphasis has been placed on immunomodulatory potential of probiotics, prebiotics and paraprobiotics and their use for other types of diseases. However, at the present most indications remain in the therapy of gastroenterocolitis of various etiology. We verified this indication and positive effect in a clinical study in pediatric patients with acute infectious gastroenterocolitis of various etiology by using the probiotics product Biopron®9.

Key words: probiotics, gastroenterocolitis, immunomodulatory potential, Biopron.

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Terminology

Probiotics are live micro-organisms which, when administered in adequate amounts, confer a health benefit on the host.

Prebiotics are indigestible food constituents that support growth or the activity of specific gut microbiota bacteria and thus improve the consumer's health (short-chained: oligofructose, long-chained: inulin, galacto-oligosaccharides).

Synbiotics are products containing probiotics and prebiotics with an expected synergistic effect (yogurt with bifidobacteria and oligofructose).

Paraprobiotics comprise of inactivated microbial cells or cell fractions with an immunomodulatory effect.

Epidemiology

Acute gastroenterocolitis still represents a worldwide problem of high morbidity and mortality. Infectious diarrheal diseases are among the five leading causes of death worldwide, with the highest occurrence in developing countries. Over 50% of deaths in children occur in Africa where the child mortality rate in certain areas reaches up to 270/1000 of live-born children. Diarrheal diseases take the second place within child mortality, after respiratory infections. Third world countries pay a cruel tax for insufficient socio-economic possibilities, health care system and limited therapeutic options in the form of 400,000 thousand deaths per year caused solely by rotavirus infections whose yearly occurrence is comparable to developed countries. To provide a comparison, the yearly death rate of rotavirus infections in Europe is around 230.

According to the Information System of Infectious Diseases (EPIDAT) the most common etiology of gastroenterocolitis in our geographical area is bacterial, viral, parasitic and exceptionally mycotic. There were 21,161 infections by Campylobacter, 8,622 cases of salmonellosis and 450 shigella infections in 2010. Only 8,615 viral intestinal infections were reported. However, the diagnostics and reporting of viral gastroenterocolitis in the field is considerably insufficient, which is indicated by significant discrepancies when compared to developed countries and also differences between the individual regions within our territory.

Treatment

Treatment of acute gastroenterocolitis can be divided into symptomatic, causal and supportive. The symptomatic treatment primarily consists of rehydration (oral or parenteral), ionic and acido-basic correction and realimentation, antiemetics, antipyretics, spasmolytics.

The causal treatment represents an antibiotic intervention in septic infectious diseases caused by enteroinvasive pathogens. The causal treatment also includes intestinal disinfectants (cloroxine, nifuroxazide), possibly adsorbents (Carbo medicinalis). Thanks to defining and understanding not only the colonization but also the immunomodulatory potential at the local as well as system level, probiotics have lately been included in causal treatment.

As for the supportive treatment, prebiotics, vitamin therapy, paraprobiotics, enzyme therapy and other supplements are among its elements. Of course, dietary and regimen measures are essential.

Effects of probiotics

- ***Barrier effect:*** production of antimicrobial substances, blocking pathogen adherence, production of metabolites beneficial for enterocytes (butyrate), defensin synthesis.
- ***Reduction:*** reducing colonization, invasiveness, metabolism and pathogenic bacteria reproduction. It is based on the competition for the binding sites in the epithet and the internal competition for nutrients, the production of hydrogen peroxide, organic acids and other bactericidal substances.
- ***Impact on the gut microbiota*** by means of a decrease in pH, metabolite production, affecting the activity of microbial enzymes and affecting intestinal motility.
- ***Immunomodulating effects:*** supporting non-specific as well as specific immunity both at the local and systematic level, supporting phagocytosis, stimulating growth of plasmatic cells and secretory antidotes IgA, IgM, IgG. Synthesis of anti-inflammatory cytokines and interleukins, stimulating NK cells, T-lymphocytes. Inhibition of anti-inflammatory mediator synthesis – TNF α, interferon γ (1, 2).
- ***Anticancerogenic effect:*** antimutagenic effect on the ability of enterocytes to bind heterogeneous amines from food which are one of the cancerogens. Inhibition of β-glucuronidase.
- ***Cholesterol, LDL and HDL:*** the meta-analysis of 5 studies has confirmed the effect of short-term use of probiotics (2–8 weeks), reducing plasma cholesterol by 4% and LDL cholesterol by 5%. There has not been a significant difference in the LDL concentrations when the use exceeded 6 months but the HDL level increased by 24% (3).
- ***Blood pressure:*** several small-scale studies have confirmed the positive impact on hypertension by the production of the ACE inhibitors like peptid produced in fermentation (4).
- ***Helicobacter pylori eradication:*** part of the ATB treatment and the proton pump blockers.
- ***Irritable bowel syndrome and ulcerative colitis:*** symptom reduction.

Profile and Aim

The study of the clinical effect of using probiotics in acute gastroenterocolitis in a group of 150 pediatric patients that was carried out at our site was a double blinded, randomized, placebo-controlled study. The aim was to evaluate the given parameters: defining the pathogen, the number of stools in every 24 hours, stool consistency, abdominal pain intensity, tenesmus intensity, nausea and vomiting, body temperature, the necessity of parenteral infusion therapy, patient's weight, the transition to peroral intake in patients with the active agent as opposed to placebo.

Methodology

The study was carried out for one year and 150 hospitalized pediatric patients (80 girls, 70 boys) in the ages between 3 and 18, admitted for acute gastroenterocolitis, participated in it. The patients were randomly divided into 2 groups, one of which was administered the Biopron 9 capsules with the effective probiotics agent, containing 9 bacteria strains (*Bifidobacterium bifidum* NCIMB 30179 (PXN 23), *Bifidobacterium breve* NCIMB 30180 (PXN 25), *Bifidobacterium longum* NCIMB 30782 (PXN 30), *Lactobacillus acidophilus* NCIMB 30184 (PXN 35), *Lactobacillus casei* NCIMB 30185 (PXN 37), *Lactobacillus plantarum* NCIMB 30187 (PXN 47), *Lactobacillus rhamnosus* NCIMB 30188 (PXN 54), *Lactococcus lactis ssp. Lactis* NCIMB 30222 (PXN 63), *Streptococcus thermophilus* NCIMB 30189 (PXN 66), 4.5 x 10^9 CFU/capsule). The control group was administered placebo. The group which was administered the active agent consisted of 85 patients and the placebo group consisted of 65 patients. The patients were administered 1–2 capsules a day, reduced according to age and weight. At the same time the patients were receiving standard treatment. The standard administration time was 4 days and in this time the given parameters, physiological functions and the clinical condition of the patients were monitored and evaluated.

Results

The pathogen was microbiologically confirmed in 67 patients out of the total of 150 (**Chart 1**).

In the other patients, according to the course, clinical findings and laboratory results, the disease etiology was evaluated as viral (65%) or bacterial (33%) (**Chart 2**).

Number of stools: When administering Biopron 9 there was a significant decrease in the number of stools, regardless of etiological agent, in comparison with placebo. The stool reduction occurred after 24 hours of administration (**Chart 3**). The most significant effect of Biopron 9 in stool decreasing was achieved in viral infections. In the first 48 hours the frequency decreased by over 50% when administering the active agent in comparison with placebo (**Charts 4 and 5**). In the rotavirus gastroenterocolitis the number of stools on the 4th day decreased by as much as 85% in comparison to placebo (Chart 5). The use of Biopron 9 in bacterial infections did not have such a significant effect on reducing the number of stools as in viral infections. Due to a small number of patients the effect of Biopron 9 could only be evaluated to a limited extent in the Campylobacter and Salmonella entercolitis (**Chart 6**). The infections caused by Campylobacter were the only ones with a negative effect of the active agent on the number of stools when compared to placebo. This number can be distorted by the small group of 19 patients. 15 patients were evaluated in the Salmonella infections group.

The stool consistency demonstrated an earlier transformation from watery to formed in the group that was administered the probiotics. Other parameters (such as abdominal pain intensity, tenesmus intensity, nausea and vomiting, body temperature) were improving correspondingly together with an earlier clinical condition improvement in patients with probiotic treatment in comparison to placebo. The necessary time of administering parenteral rehydration treatment shortened, which was considerably related to the total decrease in hospital time in patients who were administered Biopron 9 at the same time.

Chart 1. Microbe representation

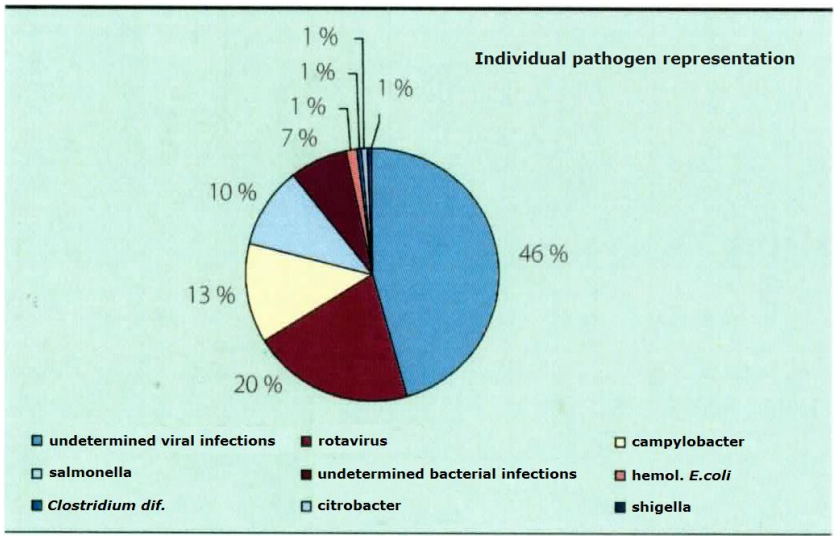


Chart 2. Viral infections 65%, bacterial infection 33%, in the first case it was a mixed infection (campylobacter, rotavirus and adenovirus), once it included decompensation and clinical demonstrations of Crohn's disease and once the demonstrations of ulcerative colitis

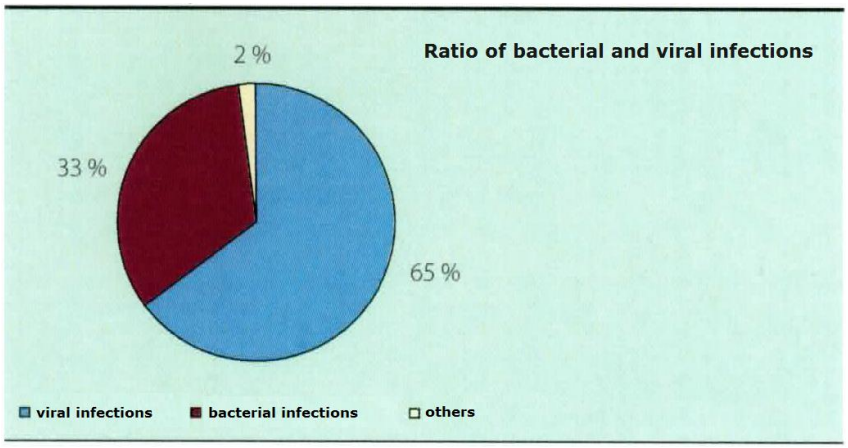


Chart 3. Evaluation of average number of stools in all patients regardless of the infection agent or etiology of ailments for every 24 hours after administration of the preparation

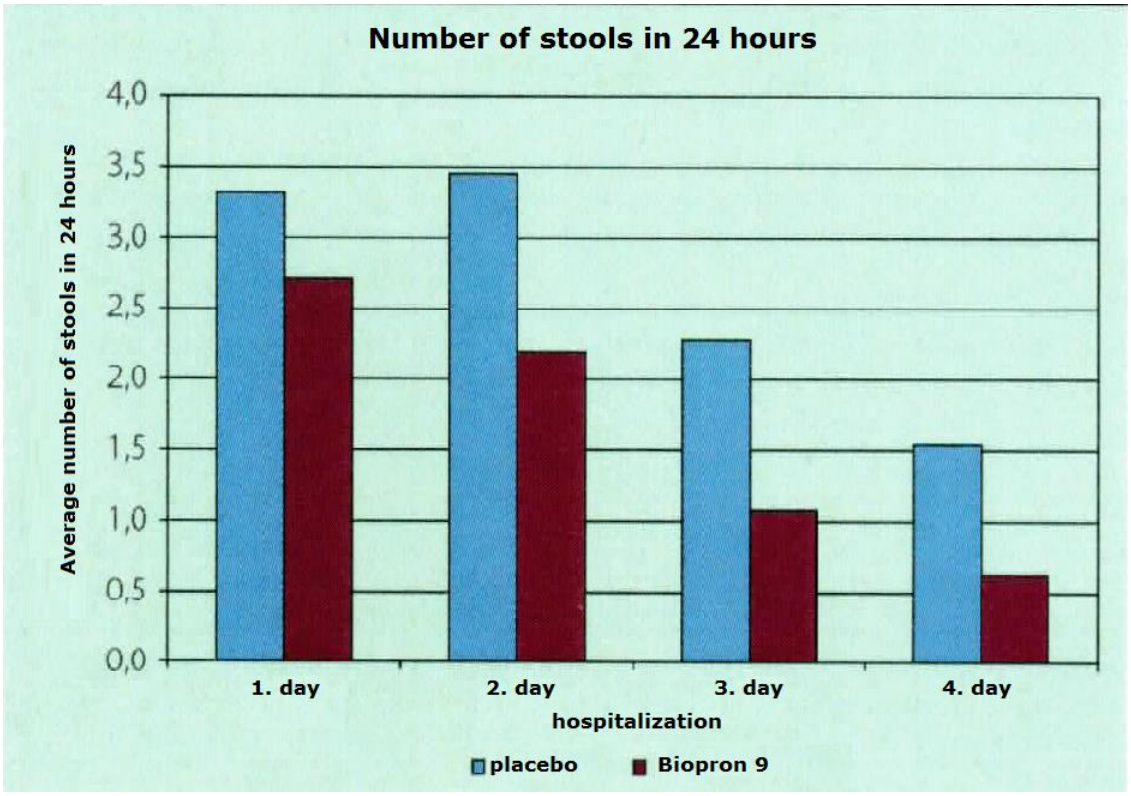


Chart 4. The viral infections demonstrated the most significant decrease in the number of stools. In the first 48 hours the stool frequency decreased by over 50% when administering the active agent in comparison to placebo

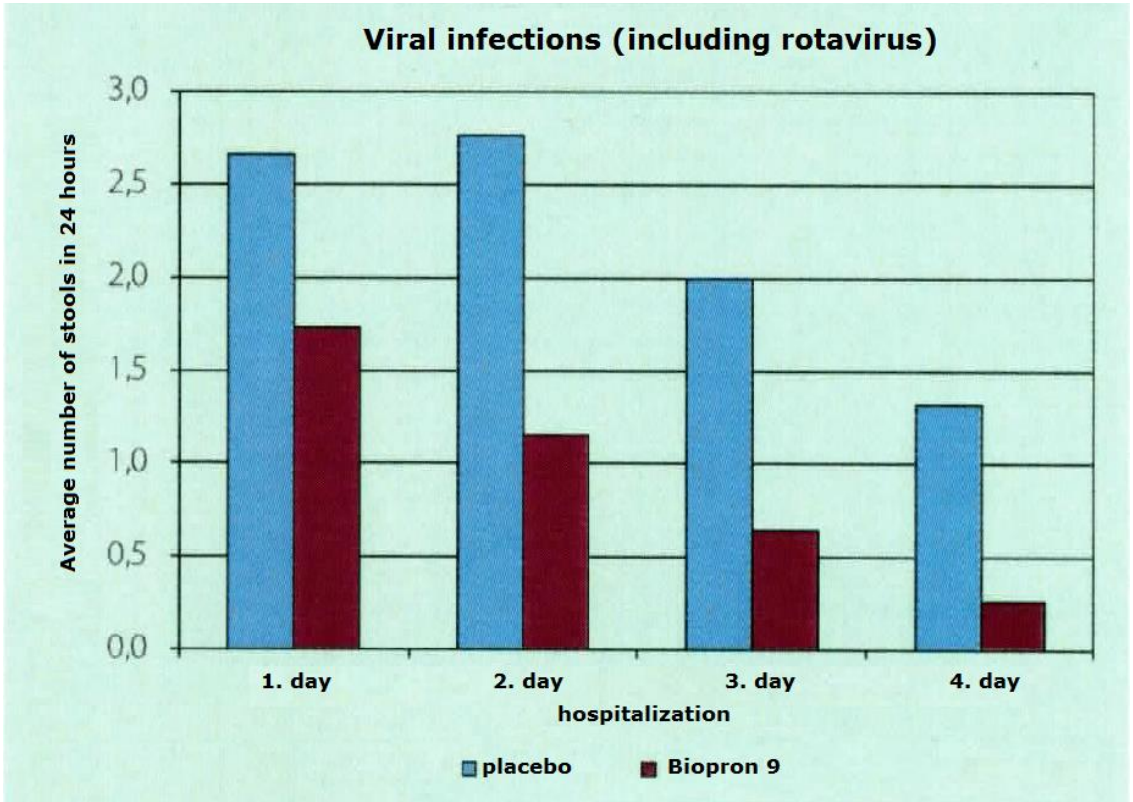


Chart 5. A significant decrease in the number of stools was demonstrated in rotavirus gastroenterocolitis. On the 4th day the number of stools decreased by up to 85% in comparison to placebo

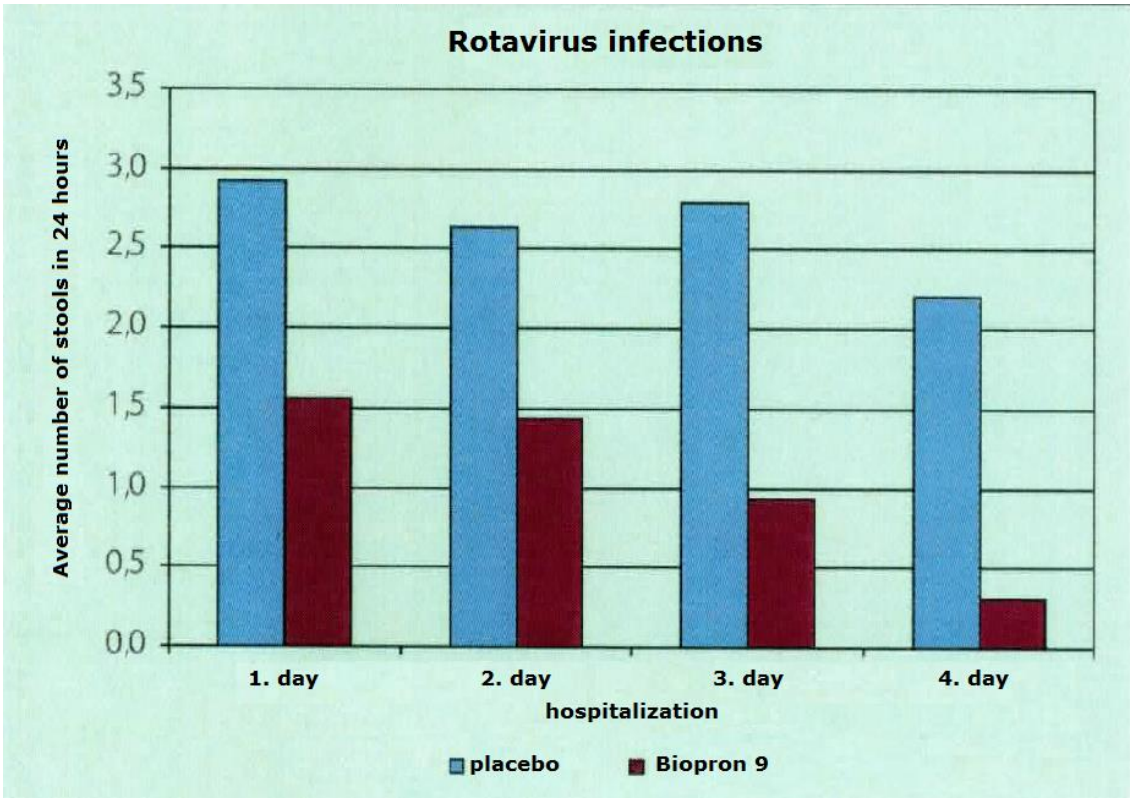
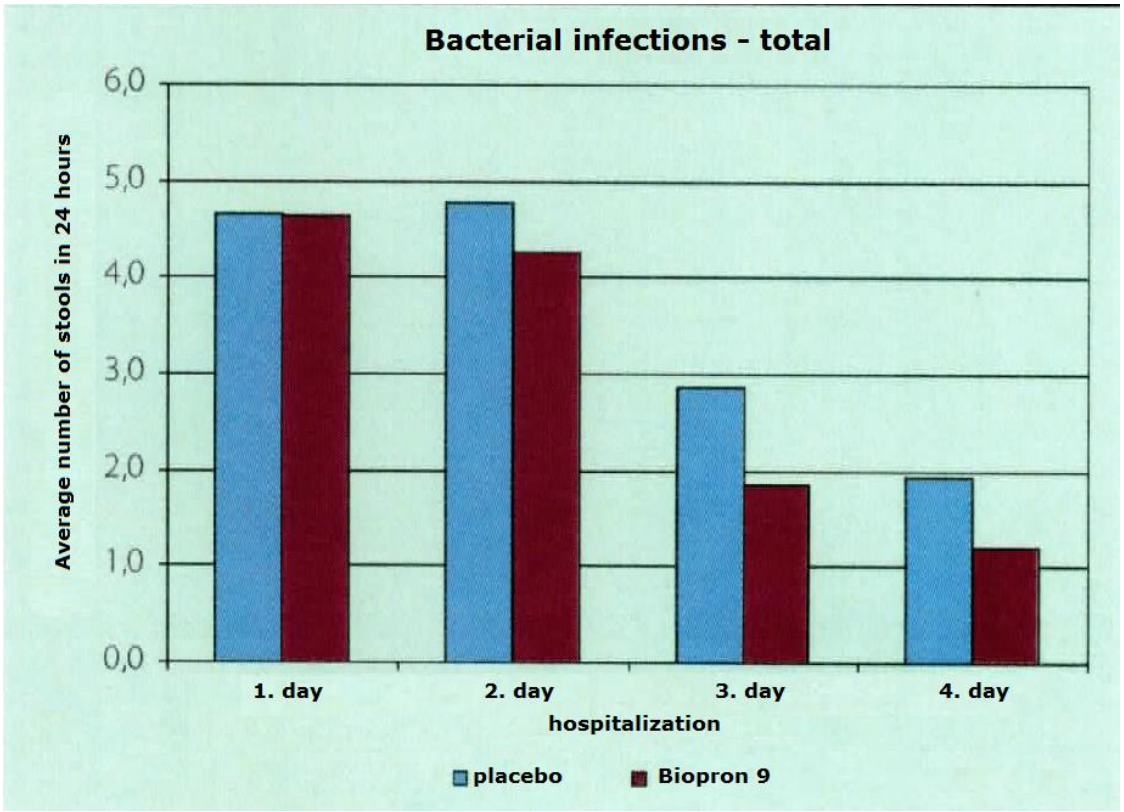


Chart 6. Biopron 9 had only a mild effect on reducing the number of stools in comparison to placebo in bacterial infections



Conclusion

The complex evaluation of the different effects of probiotics is often obstructed by the lack of quality studies with a sufficient number of patients and the awareness that not all probiotic effects can be objectively proved by studies. This is why more studies in the field of microbiology, immunology and clinical studies are essential – for exact verification of the effect and indication specification in clinical practice.

In our study, the effect of using probiotics in the form of Biopron 9 confirmed improvement of all evaluated parameters in accessory treatment of pediatric patients with acute gastroenterocolitis with the exception of using for campylobacteria infections. According to numerous studies, probiotics are a completely indicated treatment group (5, 6) for viral and particularly rotavirus infections. Even the previous studies confirm, among other things, the increase in the serum concentration of the specific IgA antidotes against rotavirus and a shorter time of discharging rotavirus by stool. The lowered prevalence of diarrheal diseases was also noticed when studying children whose milk was enriched by *Bifidobacterium bifidum* and *Streprococcus thermophilus* (7). These study results got confirmed even in the clinical evaluation of our patients with rotavirus infections treated by Biopron 9 who demonstrated a more significant move towards improving health when compared to the placebo group. The total faster modification of clinical condition with reduced number of stools, better consistency but also faster remission of febrilis, reduced observed nausea and number of vomiting are related not only to the intestine colonization and the improved microbial intestine feed but also to the above mentioned immunomodulating potential at the level of the membrane, surpassing into a system effect.

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