

Probiotic Compositions Based on Plant Raw Materials:

Innovative Technology for Support and Nutritional Correction of Dysbiosis and Metabolic Disorders in Comprehensive Therapy

Manufacturer and Developer: ProBioProducts LLC (Russia)

Status: Functional Food Product, Concentrate for Probiotification and Postbiotification of Daily Diet.

Not a drug or dietary supplement.

In Russia these probiotic composition releases by trademarks ZOE and «ЗОО» from Greek “live” Not to be confused with other products from other countries with the same names. We are the developer, manufacturer, and copyright t holder of these fermented probiotic **fermentates**.

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1. Executive Summary for Medical Professionals

ZOE Probiotic Compositions represent a new class of functional food products: **concentrated fermentates** obtained through a patented two-stage deep fermentation technology of plant raw

materials with probiotic strains of lacto- and/or actinobacteria
(patents **RU2790676C1** [1], **EP4403044A1** [2]).

Key Differences:

- **Not a tablet or capsule**, but a liquid concentrate added to prepared food (5 ml per meal). Implements the concept of **probiotification and postbiotification** of the diet.
- **Immediate "from the plate" action:** accumulated bacterial enzymes begin working immediately after addition to food, reducing the glycemic index of the meal and facilitating its digestion throughout the GIT [1, 3].
- **"5 in 1" Composition:** contain actively fermenting probiotic microorganisms (up to 10^{11} CFU/ml), prebiotics, postbiotics (SCFAs, bacteriocins, B vitamins, neurotransmitters), digestive enzymes, and micronutrients in bioavailable form [1, 4, 5].
- **100% plant-based hypoallergenic base:** lactose-free, gluten-free, soy-free, GMO-free. Suitable for patients of all ages (0+), including vegans and individuals with food allergies [6].

Main Proven Effects (confirmed by meta-analyses and studies 2020--2025):

- **Gastroenterology:** normalization of all 14 GIT functions [7, 8], restoration of microbiota [9, 10] and intestinal barrier function (via SCFAs, D-PLA, ILA) [11, 12, 13].
- **Endocrinology:** reduction of postprandial glycemia [14], improvement of insulin resistance (HOMA-IR) [15], and appetite regulation through stimulation of peptide YY synthesis [16].
- **Immunology and Neurology:** reduction of the negative effect of pro-inflammatory cytokines (CRP, IL-6, TNF- α) [15, 17], synthesis of neurotransmitters (GABA, serotonin) [18, 19], metabolic support via the "microbiota-gut-brain axis" [20].

ZOE is a ready-to-use tool for integrative nutritional support for patients with a wide range of disorders, from dysbiosis and IBS to a broad spectrum of metabolic and neurological disorders.

2. Introduction: The Concept of Probiotification/Postbiotification of Daily Diet and the Uniqueness of ZOE Fermentates

ZOE Probiotic Complements implement the concept of **probiotification and postbiotification** of the daily diet by enriching food (adding to a dish) a small amount of concentrated plant-based fermentates that **actively participate in luminal digestion**.

- **Probiotification** --- enrichment of food with live, metabolically active probiotic strains of lactobacteria and/or actinobacteria (bifidobacteria and propionic bacteria).
- **Postbiotification** --- simultaneous saturation of food with a ready-made complex of free biomolecules of microbial and plant origin (enzymes, SCFAs, vitamins, bacteriocins, exopolysaccharides, free phenolic acids, bioactive peptides, and amino acid derivatives).

ZOE concentrates represent a fundamentally new product category, being neither traditional probiotics, nor synbiotics, nor postbiotics in the conventional sense.

According to patents **RU2790676C1** [1] and **EP4403044A1** [2], ZOE is a liquid **concentrated fermentate** obtained from **two-stage deep fermentation** of plant raw materials (5--6 weeks), which combines **five groups of functional components** acting synergistically (details in section 5). We are returning to the diet what was almost lost --- the essential components of traditional fermented foods, but in a modern, high-tech, and safe format.

3. Relevance and Rationale of the Approach

The modern epidemiological picture is characterized by the rise of so-called "diseases of civilization": inflammatory bowel diseases (IBD), type 2 diabetes (accounting for 90--95% of all diabetes cases), obesity, and neuropsychiatric disorders. One of the key pathogenetic factors common to all these diseases is gut microbiota imbalance [21, 22].

Microbiota imbalance is induced and exacerbated by three main factors:

1. Dietary imbalance (predominance of refined food).

2. Exposure to adverse environmental factors (anthropogenic pollution, chronic distress).
3. **The historical reduction in the proportion of traditional fermented foods in the diet** [23, 24].

This leads to a population-wide deficiency of essential microbial fermentation components --- biomolecules produced by beneficial microflora during the fermentation of dietary fibers, which play a critical role in regulating metabolism, immunity, and inflammation. The deficiency of fermented foods in the daily diet is a modifiable risk factor, and their return to the diet is a relevant **therapeutic** and **preventive** direction for public health improvement [24].

4. Disadvantages of Correcting Dysbiosis with Dietary Supplements and Traditional Fermented Foods

Attempts to correct dysbiosis using existing means have systemic limitations:

- **Probiotics:** Need for individual selection of preparations, delayed effect, local zone of action (large intestine). Often act as a passive bacterial mass with sorbent properties [25].
- **Prebiotics:** Selectively stimulate beneficial resident bacteria but can increase gas formation and serve as food for opportunistic flora [26].
- **Synbiotics:** Technical difficulty in properly selecting combinations for different population groups [27].
- **Postbiotics:** Lack active modulating potential; their action is static [28].
- **Traditional Fermented Foods (kimchi, sauerkraut, kefir):** Have unstable microbial composition, contain coarse dietary fibers, and a limited spectrum of bioactive metabolites [29, 30].

ZOE Probiotic Compositions, according to Marco et al., 2025 [24], correspond to "ideal" fermented foods:

- **High and stable bacterial titer:** for ZOE compositions, it is $>5 \times 10^{10}$ CFU/ml after 6 months of storage [6].
- **Accumulated metabolites (postbiotics):** ZOE compositions have a unique diversity of SCFAs, bacteriocins, and peptides, providing polyvalent action [1, 4, 5, 11].

- **Reduced sodium content:** ZOE compositions are made using specialized salt with one-third of NaCl replaced by KCl, additionally enriched with magnesium and iodine [31].
 - **Pronounced antimicrobial activity:** confirmed for ZOE compositions by an independent study [32].
-

5. Scientific Production Base and Patent Protection

ProBioProducts LLC owns its own production facility in the Leningrad Region and has a dedicated Research and Development Department (biologists, microbiologists, doctors, nutritionists).

The technology and product are **protected by an international patent portfolio:**

- RF № **RU2790676C1** [1]
- Eurasian № **EA048767**
- European application **EP4403044A1** [2]
- Chinese application **CN118475256**

The uniqueness of ZOE's technology and composition is confirmed not only by the patent but also by an independent review considering fermented oat hydrolyzate as a new category of functional products, to which ZOE belongs [**Djorgbenoo R. et al., 2023**] [33].

The products have EAEU conformity declarations and have been recognized with professional awards (Green Awards 2024/2025 --- best functional food product for gut health, gold medal "Innovative Product").

6. Unique Technology of Multi-Stage Deep Fermentation

The key difference of ZOE is the patented multi-stage fermentation technology of plant raw materials, allowing the obtainment of a stable high concentration and the widest spectrum of biomolecules of both microbial and plant origin [1].

Production Stages:

1. **Preparation of Plant Medium and Hydrolysis:**

- A plant medium with a rich biochemical composition is used: oat grains and amaranth flour.
 - Enrichment with deficient minerals (pink Himalayan salt, salt with reduced sodium + K, Mg, I) and plant extracts with antioxidants (peppermint, hop cones).
 - Enzymatic hydrolysis to break down complex compounds, followed by wort pasteurization.
 - Removal of coarse bran particles, gluten, anti-nutrients, and potential allergens during hydrolysis, homogenization, and filtration.
2. **Fermentation at 35--45°C using starter cultures of probiotic strains, previously adapted to the plant medium:**
- The process is carried out at an optimal temperature to ensure logarithmic growth of the target probiotic microorganism strains.
3. **Accumulation of Metabolites during Maturation** in closed containers with periodic mixing at a suboptimal temperature for the bacterial strains used (**10--20°C for 4--6 weeks**):
- The temperature is lowered to suboptimal levels. Under these conditions, bacterial growth slows down, but the process of accumulating beneficial metabolites and postbiotics sharply increases: enzymes, short-chain fatty acids (SCFAs), B vitamins, bacteriocins, neurotransmitters. The concentration of live microbial cells remains stably high.
4. **Filtration and Homogenization:**
- Multi-stage filtration combined with homogenization removes coarse fibers and preserves the nutrient base for live active microorganisms.

Result of the Technology: obtaining a stable concentrate with an unparalleled diversity of accumulated metabolites and bioactive components released from the original plant medium. The concentrate possesses maximum functionality. A high concentration of live probiotics is combined with the richest pool of ready-to-act bioactive substances [34].

7. Composition and Release Forms of Probiotic Compositions

ZOE is a concentrated fermentate that combines **five groups of functional components** [1]:

1. **Live and Active Probiotic Microorganisms** --- multi-strain consortia of *Lactobacillus*, *Bifidobacterium*, *Propionibacterium* (including *L. reuteri* DSM 20016, "Narine" strain, etc.) in high concentration (up to 10^{11} CFU/ml), maintained throughout the shelf life [6].
2. **Postbiotics (Biomolecules of Bacterial Origin)** --- short-chain fatty acids (acetic, propionic, butyric), B vitamins, **bacteriocins** (incl. reuterin, pediocin) [4, 5], **exopolysaccharides (including beta-glucans)** [35, 36], enzymes, neurotransmitters (serotonin, GABA) [18], **regulatory peptides, phenyllactate, and indoles** [37].
3. **Digestive and Detoxification Enzymes** --- proteases, amylases, lipases, esterases, accumulated during fermentation and active in environments with different pH [1].
4. **Prebiotics** --- fermented dietary fibers, beta-glucans, oligosaccharides, creating a favorable environment for the growth of normal flora [26].
5. **Nutraceuticals** --- bioactive components of plant raw materials (polyphenols, flavonoids, micronutrients K, Mg, I, Se in bioavailable form), released during fermentation [38, 39].

The product is available in several variants, differing in the composition of probiotic cultures and their targeted effects on the body.

7.1. Composition of ZOE Oat Elixir 03

- Drinking water, oat flakes, amaranth flour, peppermint extract, salt with reduced sodium content (enriched with potassium, magnesium, iodine), pink Himalayan salt, baking soda.
- Probiotic cultures (up to 10^{11} CFU/ml):
 - *Lactobacillus reuteri* DSM 20016, ATCC 23272
 - *Bifidobacterium bifidum* AC-1784, AC-1896, AC-1666
 - *Bifidobacterium longum infantis* B-3487
 - *Bifidobacterium longum longum* 37B AC-1636, Y4 AC-1257
 - *Lactobacillus acidophilus* Er 317/402 ("Narine" strain), B-9020
 - *Lactobacillus plantarum* 12 B-4172, 8PA3 B-11007

- *Lactobacillus rhamnosus* B-3242, 12L B-8238
- *Lactobacillus salivarius* B-2581
- *Lactococcus lactis* ssp. *lactis* B-4591
- *Pediococcus acidolactici* B-1936, B-7534
- *Streptococcus thermophilus* B-3492
- (total 18 species)
- Metabolites, lysates, and enzymes of propionic acid bacteria (*Propionibacterium freudenreichii* subsp. *shermanii* B-1695, 1-63 V-4891).

7.2. Composition of ZOE Oat Propioni 02

- Drinking water, oat flakes, amaranth flour, peppermint extract, salt with reduced sodium content (enriched with potassium, magnesium, iodine), pink Himalayan salt, baking soda.
- Live cultures of propionic acid bacteria (up to 10¹¹ CFU/ml):
 - *Propionibacterium freudenreichii* subsp. *shermanii* (strains B-1695, 1-63 V-4891)
- Metabolites and enzymes of propionic acid bacteria.

7.3. Composition of ZOE Oat Narine 01

- Drinking water, oat flakes, amaranth flour, peppermint extract, salt with reduced sodium content (enriched with potassium, magnesium, iodine), pink Himalayan salt, baking soda.
- Live cultures (up to 10¹¹ CFU/ml):
 - *Lactobacillus acidophilus* hypoallergenic strain "Narine" (Er 317/402)
- Metabolites and enzymes of propionic acid bacteria (*Propionibacterium freudenreichii* strains B-1695, 1-63 V-4891).

8. Unique Mechanisms of Action Throughout the "From Plate to Colon" Journey

Integration into the digestive process throughout the GIT fundamentally distinguishes ZOE Probiotic Complements in concentrated forms from commercial probiotics, which can participate only to a limited extent in parietal digestion in the large intestine. The composition is not simply a bacterial supplement; it integrates into the digestive process [1, 3]. This integration ensures:

- **Activation of Luminal Digestion.** When 5 ml of ZOE concentrate is mixed with food 5--15 minutes before a meal, the bacterial enzymes of the ZOE composition immediately begin hydrolyzing nutrients and are then evenly distributed throughout the food bolus and chyme, participating in luminal digestion throughout the GIT --- from the stomach to the distal intestines.
- **Continuous Synthesis of Biomolecules.** Beneficial metabolites (including SCFAs) and digestive enzymes continue to be synthesized by ZOE bacteria during luminal digestion [24, 40].
- **Increased Adaptability of Beneficial Bacteria.** One of the mandatory characteristics of probiotic bacterial strains is increased resistance to the damaging effects of gastric juice and bile. This is further enhanced when such ZOE bacteria are within the food matrix [41].
- **Innovativeness of ZOE Probiotic Complements.** The process of fermentation and synthesis of beneficial metabolites is transferred from the bioreactor to the plate and then into the GIT, spreading sequentially along the natural food pathway [33].

9. Clinically Significant Effects and Systemic Action

Regular consumption of food enriched with a portion of concentrated probiotic composition provides multi-level effects on the human and animal body [1, 42]:

1. **Increasing Food Functionality:** active enzymatic hydrolysis of nutrients, transformation of a significant part of rapidly digestible starch into resistant starch (dietary fiber), leading to a **reduction in the glycemic index** of consumed food [3, 14].

2. **Comprehensive Normalization of GIT Functions:** improvement of digestive, motor, and, critically, **barrier function** of the intestine [8, 11].
3. **Effective Microbiota Regulation:** selective stimulation of the growth of one's own normal flora and **active suppression of pathogenic and opportunistic microorganisms** due to bacteriocins/fungistatics and competitive exclusion [4, 5, 32].
4. **Systemic Effects via Communication Axes:**
 - **Microbiota-Gut-Brain:** synthesis of neurotransmitters (GABA, serotonin, dopamine), SCFAs, and indoles, positively influencing the status of the blood-brain barrier, emotional state, cognitive functions, and neurodegenerative disorders [18, 19, 20].
 - **Gut-Liver:** modulation of lipid and glucose metabolism, hepatoprotective effects [15, 16].
 - **Gut-Immunity:** regulation of cytokine status towards reducing manifestations of systemic inflammation [17, 24].
5. **Detoxification:** sorption of toxins and their enzymatic breakdown [1, 43, 44].

The product combines the advantages of a probiotic (live cultures), an enzyme preparation (acceleration of digestion), and a postbiotic (complex of free bioactive metabolites).

10. Evidence Base of Efficacy

Below is a detailed evidence base, structured by GIT functions and clinical manifestations of their disorders, indicating specific ZOE components and references to scientific works confirming their effectiveness in improving body systems and self-regulation.

10.1. Влияние на желудочно-кишечный тракт (ЖКТ)

GIT Function	ZOE Components and/or Mechanism of Action	Supporting References
Digestive (nutrient hydrolysis)	Bacterial hydrolytic enzymes (proteases, amylases, lipases) and peptidases , accumulated during fermentation, break down proteins, fats, and carbohydrates directly in the food bolus [1]. Formed bioactive peptides and amino acids are easily absorbed [37].	Zarifyan A.G. et al., 2019 -- fundamental description of digestion physiology (ch. 3-5) [7]; Patent RU2790676C1 -- direct description of enzymatic activity [1]; Mutlu C. et al., 2022 -- modulation of glycemic response by lactic acid bacteria [14]; Fan Y. et al., 2025 -- bacterial polypeptides and their role [45]; Marco M.L. et al., 2025 -- discusses role of fermentation in improving digestibility [24].
Absorptive	Formation of oligopeptides, amino acids, monosaccharides as a result of enzymatic activity facilitates their transport across enterocytes, increasing the bioavailability of nutrients [8].	Mukherjee A. et al., 2024 -- review of the role of fermented foods in improving nutrient absorption [8]; Zheng L. et al., 2025 -- review of absorption mechanisms of bioactive peptides [46]; Zarifyan A.G. et al., 2019 -- physiology of absorption (ch. 6) [7].
Motor (peristalsis)	SCFAs (butyrate, propionate, lactate) stimulate smooth muscle contractions via receptors on enteric	Soret R. et al., 2010 -- direct proof of motility stimulation by butyrate

	neurons [47]. Neurotransmitters (GABA, serotonin) [18] and neuroactive peptides [48] modulate peristalsis through the enteric nervous system.	[47]; Auteri M. et al., 2015 -- review of GABA's role in motility regulation [49]; Briguglio M. et al., 2018 -- neurotransmitters from food [18]; Wei L., Marco M.L. et al., 2025 -- discusses effect of lactate on motility and barrier [11].
Barrier (protection against increased permeability)	SCFAs (lactate, butyrate) stimulate expression of tight junction proteins (occludin, claudin) via GPR81/HCA1 receptors [11, 50]. Exopolysaccharides (including beta-glucans) [35, 36] and bacteriocins [5] strengthen the mucin layer and create a physical barrier. D-phenyllactic acid (D-PLA) and indole-3-lactic acid (ILA) enhance barrier function by activating PPAR- γ and AHR [11, 12, 13].	Peng L. et al., 2009 -- butyrate enhances barrier function via AMPK activation [50]; Wei L., Marco M.L. et al., 2025 -- direct evidence of barrier protection in Caco-2 from cytokine damage by fermented cabbage and its metabolites (lactate, D-PLA, ILA) [11]; Li X. et al., 2024 -- lactate protects barrier via GPR81 [12]; Shelton C.D. et al., 2023 -- role of PLA in lipid metabolism and barrier regulation [13]; Xia Y. et al., 2023 -- ILA attenuates colitis via AHR activation [51]; Volman J.J. et al., 2008 -- immunomodulatory effects of beta-glucans [36].
Metabolic	SCFAs (propionate, acetate) are absorbed and participate in gluconeogenesis, lipid metabolism, and cholesterol synthesis in the liver [52]. Detoxification enzymes and bioactive peptides metabolize xenobiotics and modulate metabolic pathways [45].	den Besten G. et al., 2013 -- review of metabolic effects of SCFAs [52]; Marco M.L. et al., 2025 -- review of metabolic effects of SCFAs and other microbial metabolites [24].
Detoxification	Detoxification enzymes (esterases, hydrolases) break down protein toxins [1]. Fermented plant dietary fibers and the cell walls of lysed	Frankič T. et al., 2020 -- review on binding and destruction of mycotoxins [43]; Zoghi A. et al.,

	probiotic bacteria sorb and eliminate toxins [43, 44].	2021 -- binding of aflatoxins by lactic acid bacteria [44]; Patent RU2790676C1 -- direct description of detoxification mechanism [1].
Immune	Bacteriocins [5], bioactive peptides [37], and SCFAs [53] modulate GALT activity, reduce pro-inflammatory cytokines (IL-6, TNF- α , CRP). ILA activates AHR, promoting an anti-inflammatory response [11, 51].	Setayesh A. et al., 2025 -- meta-analysis of CRP reduction [15]; Wastyk H.C. et al., 2021 -- reduction of inflammation with a diet rich in fermented foods [17]; Wei L., Marco M.L. et al., 2025 -- showed that fermented cabbage and ILA modulate immune response, reducing IL-8 production [11]; Iraporda C. et al., 2015 -- lactate and SCFAs suppress pro-inflammatory responses [53]; Marco M.L. et al., 2025 -- review of immunomodulatory properties [24].
Microbiocenotic	Probiotics [54] and bacteriocins [4, 5] suppress pathogens, prebiotics [26] and regulatory peptides [45] stimulate normal flora.	Maldonado Galdeano C. et al., 2019 -- probiotics and microbiota regulation [54]; Spinler J.K. et al., 2008 -- reuterin against H. pylori [4]; Gu Q. et al., 2024 -- bacteriocins and microbiocenosis [5]; Gibson G.R. et al., 2017 -- consensus on prebiotics [26]; KTU Study, 2021 -- direct antimicrobial activity of ZOE [32]; Marco M.L. et al., 2025 -- discusses role of fermented foods in modulating microbiota [24].
Excretory	Binding of secondary bile acids	Gunness P., Gidley M.J.,

	by dietary fibers and their microbial deconjugation enhance the elimination of sterols and cholesterol with feces.	2010 -- mechanisms of bile acid binding by dietary fibers [55].
Secretory (production of mucus, enzymes, water)	SCFAs (butyrate) stimulate mucin secretion by goblet cells [56]. Neurotransmitters (serotonin) [18] and peptides [48] modulate glandular secretion and gastric acidity.	Barcelo A. et al., 2000 -- effect of SCFAs on mucin secretion [56]; Briguglio M. et al., 2018 -- serotonin and secretion [18]; Martínez-Herrero S., Martínez A., 2022 -- peptides and acid secretion [48].
Incretory (hormone production)	SCFAs (propionate, butyrate, lactate) [57] and bacterial peptides [45] stimulate L-cells to produce GLP-1 and PYY, regulating appetite and metabolism.	Tolhurst G. et al., 2012 -- SCFAs induce GLP-1 secretion [57]; Fan Y. et al., 2025 -- bacterial polypeptides increase PYY and GLP-1 levels [45]; Pedersen M.G.B. et al., 2022 -- oral lactate slows gastric emptying and suppresses appetite [58].

10.2. Regeneration of Atrophic and Damaged Areas of the Gastric Mucosa

ZOE Components	Mechanism of Action	Supporting References
SCFAs (butyrate, propionate) and lactate	Stimulate proliferation and migration of epithelial cells, accelerate healing of erosions and ulcers. Lactate stimulates cell migration via GPR81 [12, 59].	Lee Y.S. et al., 2018 -- lactate accelerates epithelial development mediated by stem cells [59]; Yu Y. et al., 2021 -- L-lactate promotes epithelial cell migration [60]; Park J.W. et al., 2022 -- postbiotics (incl. SCFAs) accelerate gastric mucosa regeneration [61]; Liu J. et al., 2021 -- meta-analysis of probiotic efficacy in gastritis [62].
Peptides of bacterial origin	Activate reparative processes, induce autophagy, promoting tissue restoration.	Li C. et al., 2026 -- peptide-probiotic therapy in models of epithelial restoration [37].

10.3. Support of the Intestinal Mucin Layer

ZOE Components	Mechanism of Action	Supporting References
Bacterial exopolysaccharides (incl. beta-glucans)	Form an additional protective layer on the epithelial surface, interact with immune cells.	Ruas-Madiedo P. et al., 2010 -- review of structure and biological activity of exopolysaccharides [35]; Volman J.J. et al., 2008 -- immunomodulatory effects of beta-glucans [36].
SCFAs (butyrate)	Stimulate MUC2 gene expression in goblet cells, increasing mucin secretion.	Gaudier E. et al., 2009 -- direct proof of MUC2 expression stimulation by butyrate [63].
Prebiotics and polyphenols	Support the growth of <i>A. muciniphila</i> , which regulates the thickness and quality of the mucin layer. Improve conditions for the development of one's own normal flora.	Everard A. et al., 2013 -- <i>A. muciniphila</i> inversely correlates with obesity and improves barrier function [64]; Plovier H. et al., 2017 -- protein from <i>A. muciniphila</i> improves metabolism and barrier [65].

10.4. Normalization of Microbiota (Increased Alpha Biodiversity, Suppression of Pathogens)

ZOE Components	Mechanism of Action	Supporting References
Probiotics (multi-strain consortium)	Competition with pathogens for receptors and nutrients.	Maldonado Galdeano C. et al., 2019 -- review of mechanisms of probiotic influence on immunity and microbiota [54].
Bacteriocins (reuterin, pediocin) and organic acids	Direct suppression of pathogenic bacteria (incl. <i>H. pylori</i> , <i>Candida</i> , <i>E. coli</i> , <i>Salmonella</i> , <i>C. difficile</i>).	Spinler J.K. et al., 2008 -- <i>L. reuteri</i> produces reuterin, active against <i>H. pylori</i> and other enteropathogens [4]; Gu Q. et al., 2024 -- detailed review of antimicrobial mechanisms of bacteriocins [5]; Cotter P.D. et al., 2005 -- general principles of bacteriocin action [66]; KTU Study, 2021 -- direct antimicrobial activity of ZOE against <i>E. coli</i> , <i>S. aureus</i> [32].
Prebiotics (beta-glucans, oligosaccharides, non-starch polysaccharides)	Selective stimulation of normal flora growth (<i>Bifidobacterium</i> , <i>Lactobacillus</i>).	Gibson G.R. et al., 2017 -- ISAPP consensus on definition and properties of prebiotics [26].

10.5. Support for Inflammatory Bowel Diseases (IBD) -- Reduction of Inflammation, Maintenance of Remission

ZOE Components	Mechanism of Action	Supporting References
SCFAs (butyrate, propionate) and lactate	Inhibition of NF-κB, reduction of pro-inflammatory cytokines (IL-6, TNF-α). Lactate reduces inflammation via GPR81 [12, 53].	Iraporda C. et al., 2015 -- lactate and SCFAs suppress pro-inflammatory responses [53]; Wei L., Marco M.L. et al., 2025 -- barrier protection in colitis model [11]; Parada Venegas D. et al., 2019 -- review of anti-inflammatory mechanisms of SCFAs in IBD [28]; Segain J.P. et al., 2000 -- butyrate inhibits NF-κB activation in colon cells of Crohn's patients [67]; Marco M.L. et al., 2025 [24].
ILA and other peptides	Activation of AHR, modulation of immune response, restoration of epithelial barrier [11, 51].	Xia Y. et al., 2023 -- ILA attenuates colitis via AHR [51]; Wei L., Marco M.L. et al., 2025 -- ILA and D-PLA partially protect the barrier [11]; Li C. et al., 2026 -- peptide-probiotic therapy effective in colitis models [37]; Martínez-Herrero S., Martínez A., 2022 -- role of adrenomedullin peptide in IBD protection [48].
Strengthening barrier function	Reduction of bacterial and antigen translocation, reduction of immune load.	Mukherjee A. et al., 2024 -- review of mechanisms linking fermented foods and GIT health [8].

10.6. Support for Functional GIT Disorders in Infants and Children

ZOE is approved for use from 0+ and is applied in pediatrics due to the absence of coarse fibers, hypoallergenicity, and the presence of enzymes and metabolites compensating for the immaturity of the digestive system [6].

Problem	Mechanism of Action (ZOE components)	Supporting References
Infantile colic	Probiotics (<i>L. reuteri</i> DSM 20016 strain) normalize motility and reduce gas formation [68]. Bacteriocins (reuterin) suppress gas-forming pathogens [4]. Enzymes and peptides improve digestion, reducing fermentation [14].	Savino F. et al., 2007 -- pilot RCT showing efficacy of <i>L. reuteri</i> for infantile colic [68]; Spinler J.K. et al., 2008 -- antimicrobial activity of reuterin [4]; Mutlu C. et al., 2022 -- enzymatic action [14].
Constipation in	Fermented dietary fibers (without coarse	Vandenplas Y. et al., 2021 --

children	particles) improve peristalsis and stool passage. Regulatory molecules (SCFAs, peptides) stimulate motility [47, 69].	systematic review and meta-analysis on probiotic use for functional constipation in children [69]; Soret R. et al., 2010 -- SCFAs and motility [47].
Increased gas formation	Enzymes break down undigested carbohydrates [14]. Bacteriocins suppress gas-forming pathogens [5].	Mutlu C. et al., 2022 [14]; Gu Q. et al., 2024 [5].
Immaturity of digestion	Bacterial enzymes (proteases, amylases, lipases) and peptides compensate for the lack of own enzymes in children, facilitating digestion and absorption [70].	Petersen C. et al., 2020 -- review on the role of developing microbiota in the maturation of the immune system and GIT [70].
Protection from pathogenic flora and formation of healthy microbiota	Bacteriocins and antimicrobial peptides create conditions for the colonization of healthy flora, suppressing pathogens [4, 5]. Prebiotics serve as a nutrient medium for normal flora [26].	Gu Q. et al., 2024 [5]; Spinler J.K. et al., 2008 [4]; Gibson G.R. et al., 2017 [26]; Nikonov E.L., Popova E.N., 2019 -- formation of microbiota in early childhood (ch. 9) [9].
Balancing gastric juice acidity	Organic acids, neurotransmitters (serotonin) [18], and regulatory peptides [48] normalize pH in the stomach and intestines, modulating hydrochloric acid secretion.	Briguglio M. et al., 2018 -- neurotransmitters [18]; Martínez-Herrero S., Martínez A., 2022 -- peptides and acid secretion [48]; Zárata G. et al., 2017 -- review of probiotic lactobacilli properties, including influence on environmental pH [71].

10.7. Prevention of Antibiotic-Associated Diarrhea (AAD) and Suppression of *H. pylori*

ZOE Components	Mechanism of Action	Supporting References
Probiotics (high titer)	Rapid restoration of beneficial bacterial populations after antibiotics [72].	Hempel S. et al., 2012 -- meta-analysis confirming probiotic efficacy for AAD prevention [72].
Bacteriocins (reuterin, pediocin) and antimicrobial peptides	Direct suppression of <i>Clostridioides difficile</i> and <i>H. pylori</i> growth [4, 37].	Spinler J.K. et al., 2008 -- reuterin active against <i>H. pylori</i> [4]; Li C. et al., 2026 -- efficacy of peptide-probiotic combination against <i>C. difficile</i> -associated colitis [37].
Prebiotics	Creation of a nutrient medium for normal flora, hindering pathogen proliferation [26].	Gibson G.R. et al., 2017 [26].

10.8. Support for Irritable Bowel Syndrome (IBS)

ZOE Components	Mechanism of Action	Supporting References
SCFAs	Restoration of motility and visceral sensitivity [73].	Balsiger B.M. et al., 2004 -- thesis discussing potential role of SCFAs in IBS [73].
Neurotransmitters (GABA, serotonin) and neuroactive peptides	Reduction of anxiety associated with IBS, modulation of visceral pain and motility [18, 19, 48, 49].	Auteri M. et al., 2015 -- review of GABA's role in GIT [49]; Briguglio M. et al., 2018 -- serotonin [18]; Nikonov E.L., Popova E.N., 2019 -- "microbiota-gut-brain" axis (ch. 8) [19]; Martínez-Herrero S., Martínez A., 2022 - peptides and visceral sensitivity [48].
Enzymes	Reduction of gas formation and bloating [14].	Mutlu C. et al., 2022 [14].

10.9. Metabolic Effects: Support for Prediabetes, Type 2 Diabetes Mellitus, Insulin Resistance

ZOE Components	Mechanism of Action	Supporting References
Bacterial amylases and glucosidases	Immediate action in the food bolus: transformation of rapidly digestible starch into resistant starch, reduction of the glycemic index of food [3, 14].	Mutlu C. et al., 2022 -- review of the ability of lactic acid bacteria metabolites to modulate glycemic response [14]; Demin S.Y. et al., 2025 (anti-diabetic article) -- description of this mechanism for ZOE [3].
SCFAs (propionate, butyrate, acetate)	Systemic action: improvement of tissue insulin sensitivity, modulation of hepatic gluconeogenesis. Acetate reduces postprandial glycemia [24, 74].	Setayesh A. et al., 2025 -- meta-analysis of HbA1c and HOMA-IR reduction [15]; Sanna S. et al., 2019 -- genetic study confirming the protective role of propionate against T2D [74]; Marco M.L. et al., 2025 -- review of acetate's effect on glucose metabolism [24]; Valdes D.S. et al., 2021 -- meta-analysis of acetate's effect on glucose [75].
Bioactive peptides (D-PLA, ILA)	Unblocking glucose transport: activation of GLUT4 [76]. Antidiabetic peptides inhibit DPP-4, increase GLP-1 production. D-PLA activates PPAR-γ, improving glucose and lipid metabolism [13]. ILA	Yamashita H. et al., 2020 -- SCFAs and GLUT4 [76]; Fan Y. et al., 2025 -- bacterial polypeptides and GLP-1 [45]; Zheng L. et al., 2025 -- review of antidiabetic properties of peptides [46]; Shelton C.D. et al.,

	modulates immunity and metabolism via AHR [51].	2023 -- role of PLA in protection against obesity and regulation of lipid metabolism [13].
Overall effect	Improvement of glycemic control, reduction of insulin resistance.	Djorgbenoo R. et al., 2023 -- review confirming antidiabetic potential of fermented oats as a functional product (class to which ZOE belongs) [33]; Setayesh A. et al., 2025 [15].

10.10. Regulation of Appetite and Weight (Stimulation of Peptide YY Synthesis, Effect on Fat Metabolism)

ZOE Components	Mechanism of Action	Supporting References
SCFAs (propionate, butyrate) and lactate	Stimulation of intestinal L-cells to produce peptide YY (PYY) and GLP-1, which suppress appetite [16]. Lactate slows gastric emptying, increasing the feeling of satiety [58].	Chambers E.S. et al., 2015 -- RCT confirming propionate's effect on PYY production and food intake reduction [16]; Pedersen M.G.B. et al., 2022 -- oral lactate slows gastric emptying and suppresses appetite [58]; Marco M.L. et al., 2025 [24].
Bacterial peptides	Direct stimulation of enteroendocrine cells to produce anorexigenic hormones.	Fan Y. et al., 2025 -- bacterial polypeptides RORDEP increase plasma PYY and GLP-1 levels [45].
Modulation of microbiota composition	Increase in the <i>Bacteroidetes/Firmicutes</i> ratio, characteristic of healthy metabolism.	Ley R.E. et al., 2006 -- pioneering work showing the link between microbiota composition and obesity [77].
Effect on brown adipose tissue	SCFAs and some peptides may stimulate thermogenesis and "browning" of white fat.	Kimura I. et al., 2013 -- SCFAs via GPR43 receptor affect metabolism and fat deposits [78].

10.11. Detoxification: Binding, Breakdown, and Elimination of Toxins

ZOE Components	Mechanism of Action	Supporting References
Detoxification enzymes of bacterial origin (esterases, hydrolases)	Breakdown of protein toxins (endotoxins, mycotoxins).	Frankič T. et al., 2020 -- review of the ability of probiotics and their enzymes to bind and destroy mycotoxins [43]; Patent RU2790676C1 -- description of detoxification enzymes [1].

Sorbents (dietary fibers, cell walls of lysed lactobacilli, peptides)	Physical binding of toxins and their elimination with feces.	Zoghi A. et al., 2021 -- review on binding of aflatoxins by lactic acid bacteria [44]; Patent RU2790676C1 -- description of sorption properties [1].
SCFAs	Lowering pH in the large intestine, reducing the activity of some toxins and pathogens.	den Besten G. et al., 2013 [52].

10.12. Antioxidant Protection: Neutralization of ROS, Chelation of Metals

ZOE Components	Mechanism of Action	Supporting References
Bacteria's own antioxidant enzymes (SOD, catalase)	Neutralization of superoxide anion and hydrogen peroxide.	Feng T., Wang J., 2020 -- systematic review of antioxidant mechanisms of probiotic lactobacilli [79].
Chelation of metal ions (Fe²⁺, Cu²⁺)	Prevention of the Fenton reaction and hydroxyl radical formation.	Lin M.Y., Yen C.L., 1999 -- study demonstrating antioxidant activity and chelating ability of lactobacilli [80].
Polyphenols and phenolic acids (from plant raw materials)	Are powerful antioxidants, neutralizing free radicals. Released during fermentation, increasing antioxidant capacity [24, 81].	Kumar N., Goel N., 2019 -- review of antioxidant and other therapeutic properties of phenolic acids [38]; Demin S.Y. et al., 2025 (article on website) -- detailed analysis of mechanisms [81]; Ciniviz M., Yildiz H., 2020 -- phenolic profiles of fermented vegetables [82]; Marco M.L. et al., 2025 -- discusses increased antioxidant activity during fermentation [24].
Bioactive peptides with antioxidant activity	Peptides released during fermentation have the ability to neutralize ROS.	Zheng L. et al., 2025 -- review of antioxidant peptides from fermented plant products [46].
Activation of NRF2 factor	Some metabolites (alkylcatechols, peptides) activate NRF2, enhancing endogenous antioxidant protection.	Mukherjee A. et al., 2024 -- mention of NRF2 role as one of the mechanisms [8].

10.13. Immunomodulatory and Systemic Effects

ZOE Components	Mechanism of Action	Supporting References
Modulation of	SCFAs (butyrate, propionate,	Wei L., Marco M.L. et al., 2025 --

<p>immunity, reduction of systemic inflammation</p>	<p>lactate) -- inhibition of NF-κB, reduction of pro-inflammatory cytokine production (CRP, IL-6, TNF-α). Lactate inhibits LPS-induced inflammation [53]. Bacteriocins and peptides (ILA) -- ILA activates AHR, promoting an anti-inflammatory response [11, 51].</p>	<p>reduction of IL-8 by fermented cabbage [11]; Iraporda C. et al., 2015 [53]; Setayesh A. et al., 2025 -- meta-analysis of CRP reduction [15]; Wastyk H.C. et al., 2021 -- reduction of inflammatory markers with a diet rich in fermented foods [17]; Xia Y. et al., 2023 [51]; Marco M.L. et al., 2025 -- review of immunomodulation [24].</p>
<p>Influence on the "microbiota-gut-brain" axis: synthesis of neurotransmitters, improvement of cognitive functions, mood</p>	<p>Neurotransmitters and precursors (GABA, serotonin, dopamine), produced by bacteria, influence the CNS via the vagus nerve and bloodstream; improve mood, reduce anxiety. GABA has neuroprotective properties [24, 83]. Neuroactive peptides modulate the activity of neurons and glia.</p>	<p>Briguglio M. et al., 2018 -- review of dietary neurotransmitters, including bacterial synthesis [18]; Mayer E.A. et al., 2015 -- fundamental work on the "gut-brain" axis [20]; Nikonov E.L., Popova E.N., 2019 -- detailed description of the "microbiota-gut-brain" axis (ch. 8) [19]; Marco M.L. et al., 2025 -- discusses the presence of GABA in fermented foods [24]; Kang D.W. et al., 2019 -- improvement of ASD symptoms after microbiota transplantation [84].</p>
<p>Support during pregnancy and lactation</p>	<p>Probiotics reduce the risk of gestational diabetes, constipation, vaginal infections. Modulation of maternal immune response [85]. Bioavailable micronutrients and precursors for milk: SCFAs -- precursors for breast milk lipid synthesis; easily digestible peptides and amino acids -- building material; minerals (K, Mg, I, Se) -- replenish their deficiency [86, 87]. Formation of infant microbiota: maternal microflora influences the establishment of infant microbiota; ZOE components can be transmitted through milk [88].</p>	<p>Jarde A. et al., 2018 -- meta-analysis on probiotic use during pregnancy [85]; Article on probioducts.info "Nutrition with ZOE during lactation" -- direct description of mechanisms: precursors for milk synthesis, reduction of energy expenditure [86]; Hofmeyr G.J. et al., 2019 -- role of micronutrients during pregnancy [87]; Baldassarre M.E. et al., 2016 -- study showing influence of probiotics taken by the mother on milk cytokine profile and infant gut colonization [88].</p>
<p>Reduction of food allergenicity and replenishment of bioactive</p>	<p>Enzymes (proteases) break down allergenic proteins in food (e.g., gluten), reducing their immunogenicity [1]. B vitamins are</p>	<p>Patent RU2790676C1 -- description of hydrolysis reducing gluten content [1]; LeBlanc J.G. et al., 2013 -- review of the ability of</p>

substance deficiency	synthesized by bacteria, replenishing their deficiency [89]. SCFAs replenish their deficiency caused by the lack of fermented food in the diet [90]. Polyphenols and flavonoids are released from plant raw materials during fermentation, becoming bioavailable antioxidants [24, 82, 91]. Bioactive peptides -- a source of essential amino acids, possess their own biological activity [46].	lactic acid bacteria to synthesize B vitamins [89]; Duncan S.H. et al., 2007 -- role of pH and SCFAs in determining microbiota composition [90]; Marco M.L. et al., 2025 -- emphasizes the importance of fermented foods as a source of SCFAs and polyphenols [24]; Valentino V. et al., 2024 -- fermentation increases polyphenol bioavailability [91]; Ciniviz M., Yildiz H., 2020 [82]; Zheng L. et al., 2025 -- review of functional properties of peptides [46]; Demin S.Y. et al., 2025 (article on deficiency) -- description of ZOE's role in replenishing deficiency [34].
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11. Stability, Safety, and Practical Characteristics

- **Confirmed Stability:** The concentration of live bacteria remains at a high level $>5 \times 10^{10}$ CFU/ml even after 6 months of storage, confirmed by laboratory tests and an order of magnitude or more higher than the stability of commercial liquid probiotics during long-term storage [6].
- **Shelf Life:** 12 months at a temperature not exceeding $+25^{\circ}\text{C}$ -- microorganisms are in a highly stable nutrient medium.
- **Undemanding nature:** Withstands repeated temperature fluctuations from -20°C to $+45^{\circ}\text{C}$ without loss of consumer properties.
- **Economy:** 1 teaspoon (5 ml) contains $>5 \times 10^{10}$ bacteria (the amount found in 10 liters of quality biokefir). A 500 ml bottle contains up to 100 single servings.

Safety:

- **100% plant base.** Free from dairy components, gluten, lactose, sugar, GMOs, soy.
- **Hypoallergenicity:** Coarse fibers and potential allergens are removed during hydrolysis, homogenization, filtration, and prolonged fermentation.

- **High compatibility with diets and treatment regimens:** Does not cause habituation, compatible with most diets (including vegan) and medication regimens.
 - **Versatility of use:** Intended for the whole family (0+), including infants, children, adults, the elderly, pregnant women, as well as patients with diabetes and allergic diseases [86].
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12. Recommendations for Use

- **Indications:**
 - Intestinal dysbiosis of various origins (incl. after antibiotic therapy).
 - Irritable bowel syndrome (IBS), functional dyspepsia.
 - Metabolic disorders: insulin resistance, prediabetes, type 2 diabetes mellitus, obesity.
 - Food intolerance, some allergic conditions.
 - Support for remission in IBD (as part of comprehensive therapy).
 - Impaired intestinal barrier function.
- **Standard Dosages:**
 - **Adults and children >12 years:** 5 ml (1 tsp) per meal, add to prepared food or drink at room temperature 5--15 minutes before consumption.
 - **Children under 12 years:** 0.1 ml per kg of body weight, add to one of the meals.
 - **Infants (before complementary feeding):** Dilute 5 ml of concentrate in 100 ml of water, give 5 ml of the resulting solution before or after feeding.
- **Important Notes:**
 - Does not cause habituation. No withdrawal syndrome.
 - Regular use is recommended. Courses of 1--3 months are possible.
 - During the adaptation period, minor flatulence may occur, which resolves spontaneously.
 - Contraindications: individual intolerance to components.
- **Topical Application (optional, as indicated):**
 - Intranasally for rhinitis and prevention of acute respiratory viral infections.

- Rectally as microenemas for colitis.
 - Externally as lotions/pastes for dermatitis (due to the content of SCFAs and antioxidants).
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13. Final Summary for the Medical Community

ZOE (ZOE) Probiotic Complements represent an innovative product with scientifically substantiated indications for use, offering the physician a tool for **supportive nutritional correction at the level of pathogenesis cause** --- restoration of the enzymatic potential of food, GIT functions (both digestive and non-digestive), optimization of microbiota balance, normalization of metabolism, and support of the body's self-regulation systems.

The uniqueness of these compositions is ensured by:

1. Protected deep fermentation technology (patents RU2790676C1 [1], EP4403044A1 [2]).
2. A composition combining pro-, pre-, and post-biotics with nutraceuticals.
3. **A unique system for activating luminal digestion throughout the GIT** [1, 3].
4. Confirmed efficacy (independent studies [32], meta-analyses 2024--2025 [15, 24]) and an impeccable safety profile [6].

Due to the unique long-term fermentation technology, ZOE compositions accumulate a wide range of bioactive molecules. The method of their application (a couple of ml of ZOE "into the plate with prepared food") ensures **immediate and prolonged effect on the GIT**, which favorably distinguishes ZOE from existing probiotic and synbiotic dietary supplements and traditional fermented foods.

We are ready to cooperate with clinics and doctors, including:

- trial supplies for clinical evaluation;
 - provision of detailed scientific documentation;
 - development of individual application protocols;
 - development of specialized variations of probiotic compositions.
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Appendix A: List of Publications on ZOE Probiotic Compositions

1. Demin S.Y., Gudkov A.V., Zhukov M.A. Antidiabetic effects of probiotics, synbiotics and fermented foods. In: Optimal nutrition -- the basis for a long and active life. Proceedings of the XIX International Congress of Dietitians and Nutritionists. M.: TORUS PRESS, 2025. pp. 211-214. DOI: [10.30826/94588-332-1](https://doi.org/10.30826/94588-332-1)
2. Demin S.Y., Gudkov A.V., Zhukov M.A. The role of deficiency of essential components of microbial fermentation in the development of "diseases of civilization" and modern food products for compensation. Ibid., pp. 214-219. DOI: [10.30826/94588-332-1](https://doi.org/10.30826/94588-332-1)
3. Djorgbenoo R. et al. Fermented Oats as a Novel Functional Food. *Nutrients*. 2023;15(16):3521. doi:10.3390/nu15163521
4. Demin S.Y., Zhukov M.A. Regulatory and health-improving and nutritional support for persons 45+ and elderly with ZOE food concentrates. [Online] // ProBioProducts : website. 2021. URL: <https://probioducts.info/regulyatorno-ozdorovitel'naya-i-nutritivnaya-podderzhka-licz-pozhilogo-vozrasta-pishhevymi-konzentratami-zoe/>
5. Demin S.Y., Gudkov A.V. Antioxidant potential of fermented plant products. [Online] // ProBioProducts : website. 2025. URL: <https://probioducts.info/antioksidantnyj-potencial-fermentirovannyh-rastitelnyh-produktov/>
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Appendix B: Complete List of References

1. Russian Patent No. RU2790676C1. Probiotic composition based on plant raw materials and method for its production. 2021. <https://patents.google.com/patent/RU2790676C1/en>
2. European Patent No. EP4403044A1 pending. 2024. <https://patents.google.com/patent/EP4403044A1/en> and <https://register.epo.org/application?number=EP22870403&lng=en&tab=doclist>
3. Demin S.Y., Gudkov A.V., Zhukov M.A. Antidiabetic effects of probiotics, synbiotics and fermented foods. In: Proceedings of the XIX International Congress of Dietitians and Nutritionists. M.: TORUS PRESS, 2025. pp. 211-214.
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