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## INNOVATION TECHNOLOGIES FOR HUMAN MICROBIOME IMPROVEMENT



**Introduction.** In recent years, the human microbiome studies have been a relevant direction of biomedical sciences. A progress in the modern science has enabled to consider the microbiome as an additional human organ. It is involved in digestion and many other metabolic processes, as well as in maintaining the integrity of epithelial barrier, organizing the colonization resistance, neutralizing endo- and exogenous toxins, developing and maintaining the immune system and other physiologic functions; also, it optimizes conditions for normal functioning of the human organism as a whole. Therefore, maintaining the physiologic state of microbiome at all stages of the human life, from the early life till the extreme old age, has an enormous importance for promoting good health of population at any age.

**Problems.** There has been observed an increase in the number of children and adults suffering from diseases associated with microbiome dysfunctions. Therefore, developing innovative means for microbiome improvement and creation of new methodologies for their clinical application is an important contribution to maintenance of the public health, treatment and prevention of many diseases.

**Purpose.** Developing innovative technologies for human microbiome improvement.

**Materials and Methods.** Methods for theoretical generalization, microbiological, biochemical and genetic research methods.

**Results.** Modern research in the field of human microbial ecology has been generalized. New generation technologies for producing means of microbiome improvement have been developed. Treatment regimens have been created for patients with different profiles.

**Conclusions.** Innovative biological technologies that provide means of microbiome improvement with high multifunctional biotherapeutic efficiency have been created. In particular, new generation multiprobitics, unique enterosorbent prebitics, and complex means of probiotic and sorption therapy have been designed. The results ensure effective means that facilitate the formation, maintenance, and restoration of healthy microbiome at all stages of human ontogenesis, from the birth to the extreme old age.

**Keywords:** microbiome, symbiosis, microbiota, probiotics, enterosorbents, Symbiter, and Symbiogel.

An important problem of modern medicine is upward dynamics of the number of patients suffering from "diseases of civilization" (cardiovascular and oncological diseases, hepatitis, obesity, diabetes mellitus, gallstones and urolithiasis, allergic manifestations, diseases of joints and con-

nective tissue, etc.). This has led to revising the basic concepts in the field of medical microbiology and switching from methods of total destruction of the microflora to the restoration of natural, harmonious relationships of the human body with natural microbial populations, which underlie its microecosystem (microbiome). Deterioration of reproductive health of fertile age women, perinatal infections, artificial feeding of

infants, inappropriate use of pharmaceuticals, especially antibiotics, environment problems, unbalanced nutrition, neuro-emotional and physical stresses and other factors have a material adverse impact on human microbiome [1–4].

The term "microbiome" was offered in 2001 by the Nobel Prize winner Joshua Lederberg to describe the totality of all microbial groups living in the human body [5]. Today, microbiome is considered as a special microbial and metabolic organ in the human body, which performs a wide range of vital local and system functions that significantly affect the structural and functional state of the visceral organs, the immune system, and the regulation of vital functions [4–8].

In fact, the human body surface open to the environment is inhabited by microorganisms that play an important role in maintaining immunity, metabolism and digestion, functioning of the endocrine and the nervous systems, and in performing other important functions. Oral cavity, hair, nose and auricles, urogenital tract, skin, eyes, gastrointestinal tract, and bronchopulmonary system contain their own unique, specific, microbial complex consisting of special microorganisms with various functions. Recently, specific microbiomes have been detected in placenta, lungs, and blood, i.e. in the organs that previously were considered sterile. All local microbiomes constantly interact with each other and with the macroorganism thereby forming the single supraorganism system [1, 3, 4].

The human microbiome is a specific biochemical reactor in which there occur various reactions catalyzed by numerous enzyme systems of microbiota. The microbial genome (metagenome) called also the "second human genome" provides the macroorganism with additional metabolic capabilities that greatly enrich its enzyme and biosynthetic potential. Thus, the microbiome is an active contributor to the most important physiological functions, in particular, energy homeostasis and metabolism, synthesis of vitamins and other important nutrients, endocrine signaling, prevention of colonization by pathogens, immu-

ne function regulation, metabolism of xenobiotics, toxins, carcinogens, and other harmful compounds. Most of these functions are closely interrelated with human physiology [4, 7, 9].

Modern metagenome studies have discovered the versatility of interdependence of human organism mutualism and symbiotic microbiota. It has become obvious that the microbiome is a crucially important organ for human life support, without which it is impossible to maintain the human organism homeostasis [4, 8, 9].

The formation of microbiome begins long before the birth of child. This process involves numerous mechanisms in the mother health, especially, the state of her microbial system, the conditions of birth, the form of feeding, and the environment impact [4, 10, 11].

Preservation and support of physiological microbial colonization of the basic human body biotopes is one of the most important mechanisms of human organism adaptation to environment conditions, which determines the general state of health and is a powerful factor for reducing morbidity, disability, and mortality, inasmuch as the damaged human microbiome is a source of intoxication and organism sensitization as well as an inducer of local and system pathological processes.

A continuous increase in the number of trigger factors that destabilize the microbiome has led to a significant spread of diseases associated with microbiome and immune disorders among the population of Ukraine. Therefore, an important problem of the present day is to stop the further destruction of the microbiome status of Ukrainian population and to improve the health of children and adults widely using effective probiotics and other means of microbiome recovery.

Recent data suggests that human microbiome disease not only complicates the course of various diseases and accelerates their development into a chronic form, but also reduces the adaptive capacity and impairs the overall health of the population. A wide range of diseases, the etiopathogenesis of which is associated with microbiome

disorders, is caused mainly by the ability of potentially pathogenic microflora to adversely affect the human body [4, 10–15, 25, 29].

An increase in the number of children suffering from severe microbiome disorders starting with the early age is a problem of particular concern. The microflora formation that occurs during the first year of life, lays the foundation for supporting the health, normal growth, and development of the child. At the same time, in the present-day conditions, the nature of primary microbial colonization has undergone critical changes, mainly as a result of deterioration of the reproductive health of young generation, an increase in the contingent of women with perinatal risk factors, inappropriate medical treatment, etc. [4, 6, 7, 10, 11].

Having analyzed the results of studies of the composition, biological properties, and effects of symbiotic microflora on the human health one can be convinced of the fact that any local or system function of the macroorganism is realized with direct or indirect involvement of the microbiome [4, 7, 16–18, 25].

The interrelated disorders in the immune and microbiome homeostasis have been generally recognized to play a significant, and often determinant, role in the etiopathogenesis of a wide range of modern diseases. Therefore, comprehensive treatment schemes for patients with various diseases should ensure the recovery of "friendly" relationships between the macroorganism and the microbiota.

Despite a significant progress in the study of human microbiome, many questions concerning the creation and clinical use of preparations for its recovery remains controversial. Many active discussions have led to the formation of certain opinions on the causal relationships between the microbiome system and the immune disorders and the development of a wide range of diseases associated with dysbiosis, as well as on methods and preparations for the maintenance and recovery of normal microbiome in patients with various diseases. Among the subjects of particularly

sharp controversy there remains the problem of species spectrum and biological peculiarities of microorganisms used in the creation of probiotics, as well as their concentration in preparations. More and more specialists have emphasized risks related to wide and uncontrolled use of probiotics containing potentially pathogenic microorganisms (bacilli, enterococci, *Escherichia*, yeast, etc.) [4, 12, 15, 19, 20, 25].

Therefore, the modernization of probiotic agents, the improvement of production technologies towards creating innovative products, the development of new strategies for their clinical use can play an important role in supporting the health of the population, treating and preventing many diseases.

For a long time, the authors were developing theoretical ideas on the human microbiome, in particular, on its formation in ontogenesis, physiological peculiarities, and mechanisms of the relationship of the most valuable components of symbiotic microbiota with each other and with the macroorganism. Also, they were dealing with practical realization of the results of theoretical studies on the creation of new generation multi-component probiotics and enterosorbents, the organization of their production and introduction into medicine [1–4, 6, 7, 10–16, 19–30].

The long-term theoretical and experimental studies to optimize approaches to the creation of new generation probiotics have resulted in the development of the *Symbiter*® group multi-probiotics. The emergence of these innovative preparations for microbiome recovery was preceded by many years of work on the isolation of apathogenic, saccharolytic bacteria that were dominant in the biotopes of people of all ages, the study of the properties of these isolates, the selection of strains with promising probiotic properties and of improved samples, as well as the creation on their basis of multifunctional multi-probiotic groups using specially designed biotechnology. The breeding strains of the *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, *Streptococcus*, and *Propionibacterium* genera with a wide range of pro-

biotic activity, in particular, with a high antagonistic activity to pathogenic and potentially pathogenic microorganisms, as well as with polysaccharide and vitamin synthesis ability and with natural resistance to antibiotics and digestive tract inhibitors were used as basis.

The results of authors' research have shown that only with the use of mutualistic microbial consortia in which symbiont partners are combined with complex trophic, communicative, metabolic, energy, and genetic bonds into an integrated biological structure, there is an additive effect of microbial components and a maximum functional activity of microbial group in general. Due to these features, the probiotic microflora of the mutualist consortia is capable of dwelling optimal ecological niches of the organism and actively removing foreign microflora therefrom. This process has been convincingly confirmed by clinical studies [4, 6, 10, 16, 24, 29, 32–35].

The microbial ecology dysfunction, as a rule, is accompanied by contamination of the organism inner environment with toxic compounds of both exogenous and endogenous origin. Therefore, it is desirable to include enterosorbents in the regimens for treating patients with microbiome disorders. The most appropriate for treating the microbiome disorders is the use of sorbents based on smectite, a clay mineral with proven antiseptic, anti-inflammatory, and antitoxic properties [4, 16, 31].

Based on the results of long-term research, fundamentally new enterosorbents of *Symbiogel*® series are sterile gels of fine smectite fraction have been developed. Transformation of smectite into gel enables the use of its most active and physiologically valuable fraction. The developed smectite drugs combine the qualities of enterosorbents having high ion exchange and adsorption properties; multi-mineral preparation; cyto- and muco-protector that has a protective effect on the mucous membranes of the digestive tract; indigenous microbiocenoses protector that creates conditions for the optimization of the composition and functions of symbiotic microbiota.

Unlike dry clay preparations, *Symbiogel*® is a "living" mineral, the manufacturing technology of which makes it possible to preserve the most valuable natural properties of smectite. Symbiogel provides a high enveloping ability that allows the preparation to be freely distributed along the digestive tract, which enables an effective interaction of the mineral with glycoproteins of mucus and microbial biofilm. It is important that the smectite gel does not bind bacterial cells, therefore it neither disturbs the microbial balance of the organism nor causes metabolic disorders. The fine smectite gel does not damage the mucous membrane. On the contrary, it has enveloping properties and contributes to the strengthening of the mucous barrier and microbial biofilm. This determines the safety and feasibility of using Symbiogel for treating inflammatory diseases of the oral cavity and gastrointestinal tract [4, 16, 23, 28].

The establishment of the stimulating effect of deeply refined glycemic extract on the viability and probiotic properties of saccharolytic anaerobes of *Bifidobacterium*, *Lactobacillus*, *Lactococcus* and *Propionibacterium* genera has contributed to the creation of *Symbiter*® forte, a new generation of complex preparations for probiotic sorption therapy. Their high efficiency and promising properties has been proved by experimental studies and clinical trials [4, 16, 21].

The history of the use of *Symbiter*® group multi-probiotics in clinical practice dates back to 1993, when the pioneer agent of this group was introduced into the treatment regimens of patients.

The first clinical studies of multicomponent probiotics, which convincingly show their advantages over other probiotic drugs and the feasibility of further detailed study to expand the scope of their application have been conducted at the Institute of Pediatrics, Obstetrics, and Gynecology of the NAMS of Ukraine. As a result of further multilateral studies of the clinical effectiveness of multi-probiotics, a series of optimal patterns of probiotic treatment for patients

with different profiles has been developed. Since then, a considerable experience has been gained in the clinical application of multicomponent probiotics in the complex treatment of various diseases in children and adults [4, 6, 7, 1–16, 19–30, 32–34].

During various clinical trials of multi-probiotics, adjustments to microbial consortia have been made (due to the selection of new bacterial strains), approaches to the selection of valuable probiotic bacteria and the multi-symbiosis design have been modified, and the technology for microbiome recovery has been improved.

The research results have underlain the development of new medical technologies based on the recovery of healthy microbiome in the body and allowed the authors to substantiate and to confirm the experimental and clinical feasibility of the creation of multi-probiotics that contain a broad spectrum of representatives of human physiological microbial symbionts and unique enterosorbents with prebiotic properties.

The series of *Symbiter*® multi-probiotics was created to provide medicine with effective health-improving means that contribute to the formation, maintenance, and recovery of healthy microbiome at all stages of human ontogenesis. This group of preparations contains several options: the gynecological multi-probiotics designed to support and to recover the microbiological health of women; the kid multi-probiotics for optimizing the process of formation of physiological microflora in newborns, for being used in complex treatment of perinatal infections, for preventing and remedying dysbiosis in children under 3 years old; and the multi-probiotics for children of middle and older age and adults. The use of multi-probiotics in combination with *Symbio-gel*® enterosorbents enhances the effectiveness of therapy. Currently, medical industry needs such preparations. At the same time, neither in Ukraine nor abroad there are analogs of probiotics and enterosorbents with the mentioned properties.

As a result of various studies of clinical efficacy of preparations for microbiome recovery, a high

efficacy of therapy with the use of these preparations has been proved, and optimal schemes of probiotic treatment of patients of different profile have been developed.

As long-term experience of the use of *Symbiter*® group multi-probiotics has shown, the preparations effectively remedy dysfunction of the gastrointestinal tract [4, 24]. The use of multi-probiotics as part of complex therapy of patients with infectious pathology of different etiology and localization [4, 24, 32], allergy [27], enzymopathies, chronic diseases of the gastrointestinal tract [24], inflammatory diseases of colon [24], hepatitis [4, 33], and the central nervous system disorders [29]; contributes to raising the effectiveness of treatment and facilitates clinical recovery. The multi-probiotics are successfully used in obstetric and gynecological practice for treating patients with infectious and inflammatory diseases and remedying dysbiotic disorders in women, including pregnant ones [4, 30]. Also, they are used in complex treatment of urogenital infectious diseases in married couples [24, 34].

The developed preparations are especially widely used in pediatrics. In particular, the efficacy of developed multi-probiotics and enterosorbents for the treatment of infectious and somatic diseases of the gastrointestinal tract, respiratory and central nervous systems in children of different age groups has been proved with a high statistical reliability [4, 11, 16, 24, 29, 32].

Thus, the course of *Symbiter*® multi-probiotics has a positive effect on the overall resistance of the organism of children with frequent respiratory diseases, recurrent bronchitis, as well as children with rheumatic diseases. The systematic approach to the use of multi-probiotics from the first days of life, which has been developed and implemented for recovering and supporting the physiological microbiome in children with a risk of developing pathology, significantly reduces the incidence rate. It has been shown that children who administer multi-probiotics according to the prescribed scheme are 2.3 times less likely to suffer from acute infectious diseases of the

The Preparations for Microbiome Recovery and Their Characteristics

Product	Composition	Application	Justification
<i>Symbiter acidophilus</i>	Biomass of mutualistic symbiosis of 14 strains of probiotic bacteria (at least, 10 <sup>9</sup> living cells per a dose)	Prevention and elimination of microbial and immune disorders in children under 3 years old, optimization of the process of primary microbial formation in young children	4, 6, 10, 11, 24, 27, 32
<i>Symbiter acidophilus concentrated</i>	Concentrated biomass of mutualistic symbiosis of 16 strains of probiotic bacteria (at least, 10 <sup>11</sup> living cells per a dose)	Prevention and elimination of microbial and immune disorders in children above 3 years old and adults	4, 12, 19, 22, 24, 27, 29, 33
<i>Symbiter M</i>	Biomass of mutualistic symbiosis of 22 strains of probiotic bacteria (at least, 10 <sup>10</sup> living cells per a dose)	Prevention and elimination of digestive upsets, microbial and immune disorders in children under 3 years old	4, 13, 27
<i>Symbiter M concentrated</i>	Concentrated biomass of mutualistic symbiosis of 22 strains of probiotic bacteria (at least, 10 <sup>12</sup> living cells per a dose)	Prevention and elimination of digestive upsets, microbial and immune disorders in children over 3 years old and adults	4, 13, 27
<i>Symbiter 2</i>	Concentrated biomass of mutualistic symbiosis of 25 strains of probiotic bacteria (at least, 10 <sup>11</sup> living cells per a dose)	Vaginal microbiome disorders (bacterial vaginosis, mycotic vaginitis), urogenital infections, prevention and elimination of microbiome disorders in pregnant women and antibiotic-associated dysbiosis of the urogenital system	4, 12, 14, 24, 30
<i>Apibact with 2.5% propolis</i>	Concentrated biomass of mutualistic symbiosis of 15 strains of probiotic bacteria (at least, 10 <sup>11</sup> living cells per a dose) and propolis extract	Dysbiosis, immunodeficiency, dental diseases, intoxication, inflammatory diseases of the mucous membranes	4, 24, 27, 34, 35
<i>Apibact with 5% propolis</i>	Concentrated biomass of mutualistic symbiosis of 15 strains of probiotic bacteria (at least, 10 <sup>11</sup> living cells per a dose) and propolis extract	Dysbiosis, immunodeficiency, dental diseases, intoxication, inflammatory diseases of the mucous membranes	4, 24, 27, 34, 35
<i>Symbiter® Forte-M</i>	Concentrated biomass of mutualistic symbiosis of 17 strains of probiotic bacteria (at least, 10 <sup>11</sup> living cells per a dose), smectite, wheat germs	Dysbiosis, intoxication, functional disorders of the digestive system, enterovirus infections, immunodeficiency, hypercholesterolemia	4, 16, 21, 26, 27
<i>Symbiter® Forte-M for kids</i>	Biomass of mutualistic symbiosis of 13 strains of probiotic bacteria (at least, 10 <sup>9</sup> living cells per a dose), smectite	Microbiome and immune disorders, enterovirus infections, metabolic disorders in children from 1 to 3 years old	4, 16
<i>Symbiter® Forte gramineous</i>	Concentrated biomass of mutualistic symbiosis of 17 strains of probiotic bacteria (at least, 10 <sup>10</sup> living cells per a dose), smectite, wheat germs	Dysbiosis, intoxication, functional disorders of the digestive system, enterovirus infections, immunodeficiency, hypercholesterolemia, metabolic disorders	4, 16
<i>Symbiter® omega</i>	Concentrated biomass of mutualistic symbiosis of 18 strains of probiotic bacteria (at least, 10 <sup>10</sup> living cells per a dose), smectite, wheat germs, linseed oil, and wheat germ oil	Cardiovascular diseases, inflammatory diseases of the intestine, colitis, gastritis, periodontal disease, metabolic and immune disorders, allergy, hypercholesterolemia, obesity, alcohol intoxication	4, 16, 23, 31

Product	Composition	Application	Justification
<i>Symbiter® forte with propolis</i>	Concentrated biomass of mutualistic symbiosis of 15 strains of probiotic bacteria (at least, 10 <sup>10</sup> living cells per a dose), smectite, and propolis extract	Dysbiosis, intoxication, disorders of mechanisms of antioxidant protection, immunodeficiency, dental diseases, viral infections, intoxication, inflammatory diseases of the mucous membranes	4, 16
<i>Symbiogel</i>	5% sterile gel of smectite	Intoxication, diarrhea, flatulence, functional disorders of the digestive system, enterovirus infections, acid-base balance disorders, hypercholesterolemia, obesity	4, 16, 21, 23, 28, 31
<i>Symbiogel omega</i>	5% sterile gel of smectite, linseed oil, and wheat germs	Cardiovascular diseases, inflammatory diseases of the intestine, colitis, gastritis, periodontal disease, metabolic and immune disorders, allergy, hypercholesterolemia, obesity, alcohol intoxication	4, 16, 23, 28, 29, 31
<i>Symbiogel with propolis</i>	5% sterile gel of smectite, propolis extract	Infections of various etiologies, immune disorders, dental diseases, violation of mechanisms of antioxidant defense, inflammation of mucous membranes	4, 16, 23, 28
<i>Kid's Symbiogel</i>	5% sterile gel of smectite	Intoxication, diarrhea, flatulence, functional disorders of the digestive system, enterovirus infections in children from 6 months old	4, 16, 23, 28
<i>Kid's Symbiogel omega</i>	5% sterile gel of smectite, linseed oil, wheat germs	Inflammatory diseases of the intestine and oral cavity, intoxication, diarrhea, flatulence, functional disorders of the organs of the digestive system, enterovirus infections in children from 6 months old	4, 16, 23

gastrointestinal tract and the respiratory system, 2.1 times rarer have allergic manifestations and 3.6 times less often need treatment at hospital [4, 35].

The introduction of *Symbiter®* preparations to the system of preconceptional preparation of women and to the complex of treatment of urogenital infectious diseases in married couples creates favorable conditions in the physiological microenvironment for smooth gestation course, enhances the resistance of pregnant woman organism to infection, and stimulates adequate immune response [4, 34].

The advantage of multi-probiotics and enterosorbents that have a positive effect on the human body as a whole and on its individual organs and systems, is absolute safety; they have neither side effects nor acquired tolerance in the case of long-term use; improve the human organism condition without the use of potent drugs.

The creation of multi-probiotics and prebiotic enterosorbents has enabled to provide the medical industry with effective health-improving preparations that contribute to the formation, maintenance, and recovery of healthy microbiome system at all stages of human ontogenesis,

from birth to elderly age. A high efficacy of multi-probiotics and enterosorbents has been established by numerical studies [4, 6, 10, 12, 13, 16, 21, 23, 26, 27, 29, 32, 35] and justified their approval as prophylactic and therapeutic agents aiming at normalizing the microbiome and remedying pathological processes.

The *Symbiter*® preparations are successfully used in maternity hospitals to optimize the process of primary microbiome formation in newborns, to prevent the development of primary immunity and microbiome disorders, as well as to prevent and to treat perinatal infectious diseases [4, 10, 11].

The developed health-improving means have been manufactured at *O.D. Prolisok* national research and production company that is specialized in the development and production of new generation multi-probiotics and enterosorbents.

Today, 12 types of multi-probiotics and 5 types of enterosorbents are manufactured (see Table below). A wide range of developed preparations greatly simplifies the choice of scheme for effective microbiome therapy depending on the patient's age, the type and the severity of disease.

Thus, authors' long-term research has resulted in creating innovative biological technologies to manufacture preparations for microbiome recovery with a high multifunctional bio-therapeutic efficacy. Wellness products that have no analogs in Ukraine and abroad have been developed.

Using the phenomenon of biological cross-simulation, it is possible to introduce a broad range of physiologically valuable bacteria in the form of stable multi-component symbiosis that is an active producer of vitamins, antioxidants, bacteriocins, immunomodulatory exopolysaccharides, and antimutagens. The created new generation of multi-probiotics are a living biomass

of physiological microorganisms, the basis of which are biologically active cells of bifidobacteria, lactobacillus, lactococci, and propionic acid bacteria introduced into exopolysaccharide matrix.

The establishment of the stimulating effect of finely cleaned smectite gel on the viability and probiotic properties of saccharolytic anaerobes of the *Bifidobacterium*, *Lactobacillus*, *Lactococcus*, and *Propionibacterium* genera has contributed to the development of a method for rational combination of the properties of probiotic multi-symbiosis and smectite gel and to the creation of unique enterosorbents, prebiotics, and complex preparations for probiotic sorption therapy.

The research implementation has enabled to realize one of the pharmaceutical tasks, i.e. to provide the medical industry with effective means for the formation, maintenance, and recovery of healthy microbiome at all stages of human ontogenesis, from birth to elderly age.

The created multi-probiotics have a wide range of biotherapeutic activity, contain the most physiological microflora that is maximally safe for the human body, promote the effective remedy of microbiome disorders and pathological processes in the human body.

A widespread introduction of new generation multi-probiotics and enterosorbents into practice has a significant medical and social effect due to reducing the cost of existing prophylactic and therapeutic agents and patient treatment as compared with the use of foreign counterparts.

The research results have been protected by 59 patents for inventions and utility models and presented in 160 scholarly research articles, 5 monographs, 3 manuals, and 10 methodological recommendations. On this subject, 17 research works have been carried out, 3 doctoral and 7 candidate theses have been defended.

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#### ІННОВАЦІЙНІ ТЕХНОЛОГІЇ ОЗДОРОВЛЕННЯ МІКРОБІОМУ ЛЮДИНИ

**Вступ.** На сьогодні актуальним та перспективним напрямком біомедичної науки стало вивчення мікробіому людини. Сучасні наукові досягнення дозволяють розглядати мікробіом як додатковий орган людини, який, приймаючи активну участь у травленні, численних метаболічних процесах, підтримці цілісності епітеліального бар'єру, формуванні колонізаційної резистентності, знешкодженні ендо- й екзогенних токсинів, розвитку та підтримці імунної системи й низці інших фізіологічних функцій, оптимізує умови для нормального функціонування організму людини в цілому. Тому підтримка фізіологічного стану мікробіому протягом життя людини, починаючи з раннього дитинства і до глибокої старості, має суттєве значення для поліпшення здоров'я населення усіх вікових категорій.

**Проблематика.** Зважаючи на збільшення чисельності дітей та дорослих, що страждають хворобами, асоційованими з порушеннями мікробіому, значну роль у підтриманні здоров'я населення, лікуванні й профілактиці багатьох захворювань може відіграти створення інноваційних засобів оздоровлення мікробіому та розробка нових стратегій їх клінічного використання.

**Мета.** Розробка інноваційних технологій оздоровлення мікробіому людини.

**Матеріали й методи.** Застосовано методи теоретичного узагальнення, мікробіологічні, біохімічні та генетичні методи дослідження.

**Результати.** Узагальнено сучасний рівень наукових досягнень у галузі мікробіої екології людини. Розроблено нову генерацію технологій виготовлення засобів оздоровлення мікробіому та схеми лікування хворих різного профілю з їх використанням.

**Висновки.** Створено інноваційні біологічні технології, що забезпечують отримання засобів оздоровлення мікробіому з високою багатofункціональною біотерапевтичною ефективністю. Зокрема, розроблені мультипробіотики нового покоління, унікальні ентеросорбенти-пробіотики та комплексні засоби пробіотично-сорбційної терапії. Результати зумовлюють забезпечення медичної галузі ефективними засобами, що сприяють формуванню, підтримці та відновленню здорового мікробіому на всіх стадіях онтогенезу людини: від народження до похилого віку.

**Ключові слова:** мікробіом, симбіоз, мікробіота, пробіотики, ентеросорбенти, «Симбітер», «Симбіогель».

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## ИННОВАЦИОННЫЕ ТЕХНОЛОГИИ ОЗДОРОВЛЕНИЯ МИКРОБИОМА ЧЕЛОВЕКА

**Введение.** Сегодня актуальным и перспективным направлением биомедицинской науки стало изучение микробиома человека. Современные научные достижения позволяют рассматривать микробиом как дополнительный орган человека, который, активно участвуя в пищеварении, многочисленных метаболических процессах, поддержке целостности эпителиального барьера, формировании колонизационной резистентности, обезвреживании эндо- и экзогенных токсинов, развитии и поддержке иммунной системы и ряде других физиологических функций, оптимизирует условия для нормального функционирования организма человека в целом. Поэтому поддержание физиологического состояния микробиома на всех этапах жизни человека, начиная с раннего детства и до глубокой старости, имеет существенное значение для улучшения здоровья населения всех возрастных категорий.

**Проблематика.** В связи с увеличением числа детей и взрослых, которые страдают болезнями, ассоциируемыми с нарушениями микробиома, большую роль для поддержки здоровья населения, лечения и профилактики многих заболеваний может сыграть создание инновационных средств оздоровления микробиома и разработка новых стратегий их клинического использования.

**Цель.** Разработка инновационных технологий оздоровления микробиома человека.

**Материалы и методы.** Использованы методы теоретического обобщения, микробиологические, биохимические и генетические методы исследования.

**Результаты.** Обобщен современный уровень научных достижений в области микробной экологии человека. Разработаны технологии средств оздоровления микробиома новой генерации и схемы лечения с их использованием у больных разного профиля.

**Выводы.** Созданы инновационные биологические технологии, которые обеспечивают получение средств оздоровления микробиома с высокой и многофункциональной биотерапевтической эффективностью. В частности, созданы мультипробиотики нового поколения, уникальные энтеросорбенты-пробиотики и комплексные средства пробиотико-сорбционной терапии. Результаты обуславливают обеспечение медицинской отрасли эффективными средствами, которые способствуют формированию, поддержке и восстановлению здорового микробиома на всех стадиях онтогенеза человека: от рождения до глубокой старости.

*Ключевые слова:* микробиом, симбиоз, микробиота, пробиотики, энтеросорбенты, «Симбитер», «Симбиогель».